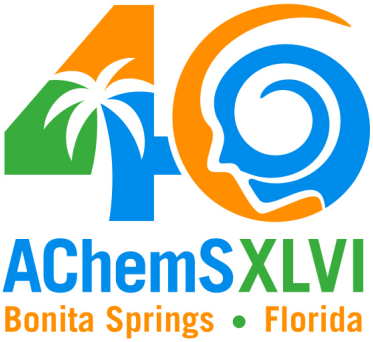

46th Annual Meeting of the Association for Chemoreception Sciences
April 17-20 2024
Bonita Springs, FL

Printable Program & Abstracts

Wednesday, April 17, 2024

10:00 - 11:40 AM	Calusa ABC
Understanding Odor Coding and Odor-Guided Behaviors in the Age of Team Science - PART 1: New Technologies and Data Integration	

Chair(s): Matt Wachowiak

10:00 **Determinism In Odor Receptor Choice**
David Brann
Harvard University

10:25 **How Do Class I Odorant Receptors Recognize Odorants?**
Hiro Matsunami
Duke University

10:50 **Restructuring Of Odor Responses Along Ethologically Important Axes**
Lisa Stowers
The Scripps Research Institute

11:15 **The Tango Toolkit For Circuit Tracing And Manipulation**
Gilad Barnea
Brown University

11:40 - 12:40 PM	Lunch On Own
Lunch On Own	

12:00 - 3:30 PM	Great Egret
AChemS Executive Committee Meeting (Invite Only)	

12:40 - 2:20 PM	Calusa ABC
Understanding Odor Coding and Odor-Guided Behaviors in the Age of Team Science - PART 2: Natural Behaviors and the Olfactory System	

Chair(s): Dima Rinberg

12:40 **Revealing The Neural Encoding Of Odor Intensity**
Beatrice Barra
New York University

1:05 **Olfaction In Drosophila Through The Lens Of Natural Odors**
Elizabeth Hong
Caltech

1:30 **Neural Circuits For Working Memory And Evidence Integration During Olfactory Navigation**
Kathy Nagel
New York University

1:55 **Voluntary Use Of The Vomeronasal System During Freely Moving Behavior**
Lisa Stowers
The Scripps Research Institute

2:20 - 2:35 PM	Calusa Foyer
Coffee Break	

2:35 - 3:50 PM	Calusa ABC
Understanding Odor Coding and Odor-Guided Behaviors in the Age of Team Science - PART 3: Smelling in Time and Space	

Chair(s): Elizabeth Hong

2:35 **The Order Code**
Alex Koulakov
Cold Spring Harbor

3:00 **Untangling The Determinants Of Timing And Tuning In Early Odor Representations**
Matt Wachowiak
University of Utah

3:25 **Olfactory Object Representation In The Brain**
Dima Rinberg
New York University

4:00 - 4:30 PM	Great Egret
AChemS 2024 Codefest	

The goal of the AChemS 2024 Codefest is for you to apply your data analysis skills, learn from others, get feedback, explore others' work, and connect with the larger AChemS community. This year's Codefest will focus on data from a new Olfaction Challenge. We will provide starter code, orient you to the available data, and provide a team of teachers as support for working in both R and Python. We welcome coders of all skill levels and from any chemosensory system!

4:30 - 5:00 PM	Calusa Terrace
Diversity Fellowship Meet and Greet	

5:30 - 6:00 PM	Calusa EFGH
Awards Ceremony	

6:00 - 7:00 PM	Calusa EFGH
Keynote Lecture	

6:00 **Pheromone Communication In Ants**
Daniel Kronauer
The Rockefeller University

7:00 - 9:00 PM	Waterfall Pool Deck
Welcome Banquet (Ticket Required)	

Thursday, April 18, 2024

7:30 - 9:00 AM	Estero Foyer
Breakfast With Industry	

CARGILL
Please join us at our breakfast table to share our excitement about career opportunities at Cargill. Sitting at the heart of the supply chain, we are focused on nourishing the world in a safe, responsible, and sustainable way. Cargill's technical professionals around the world have high impact as we partner with farmers and customers globally to source, make and deliver products that are vital for living.

COCA-COLA COMPANY
Our company purpose is to refresh the world and make a difference. We aim to create beverages with great taste that give consumers more choices. We are investing in R&D to find new approaches to continue delivering great-tasting beverages with zero or reduced levels of sugar. Join us at our table for a conversation on how we can collaborate to meet our shared goals.

KERRY
Please stop by the Kerry Breakfast Table where the science of taste merges with the science of nutrition. Come discuss with passionate people on how we can build impactful sustainable food and beverages for today's consumers. Learn how it's like to be a part of a company strong in food heritage, global insights, marketplace knowledge, and culinary and application expertise. We are currently hiring for a position of Senior Sensory Scientist, we are happy to share with you the career opportunity within Kerry.

W2O FOOD INNOVATION
Please stop by the W2O Food Innovation table. Tell me what you can do and want to do, and I will try to relate you to what the food industry needs. Ask me anything about NeuroFoodScience, that is, the application of Neuroscience in Food Science.

8:00 - 10:00 AM	Estero Ballroom
Poster Session I	

100 **Gaba Release From Palatal Taste Buds After Stimulation With Sweeteners**

Yuryanni A. Rodriguez[1], Gennady Dvoryanchikov [1], Stephen D. Roper[1,2], Nirupa Chaudhari[1,2]
[1]Dept. of Physiology and Biophysics Univ. of Miami Miller School of Medicine, Miami, FL, United States, [2]Dept. of Otolaryngology Univ. of Miami Miller School of Medicine, Miami, FL, United States

Bitter, sweet, and umami tastes stimulate Type II cells to secrete ATP which activates afferent nerve fibers as well as Type I cells (Rodriguez et al 2021). We asked if Type I cells then release GABA, e.g. as a gliotransmitter. Previously, we showed using CHO cells expressing $GABA_B$ receptors and G-protein, Gαqo5(GABA biosensors), that when circumvallate taste buds responded to a bitter tastant, 5μM cycloheximide, GABA biosensors displayed a signal consistent with evoked GABA release from Type I cells. Here, we tested whether *sweet* taste stimulation also could elicit GABA secretion from Type I cells. GABA biosensors, loaded with Ca^{2+} indicator Cal-590AM, reliably responded to GABA above ≈100nM and GABA-evoked responses were reversibly blocked by CGP55845 (300nM, $GABA_B$ antagonist). Further, GABA biosensors on their own did not respond to any of the sweet tastants. We deposited palatal taste buds (from *Gad2*;;GCaMP3 mice) which express GCaMP3 in Type I cells onto a monolayer of GABA biosensors. We perfused the recording chamber with sweeteners: 0.1mM SC45647, 1mM sucralose, 15mM Acesulfame K or 20mM saccharin. In this configuration, Type I cells responded to one or more sweeteners. We also recorded repeated responses from GABA biosensors. These sweet-evoked responses in GABA biosensors were blocked by 300nM CGP, confirming that they likely represent released GABA. Interestingly, saccharin was the most effective of the sweeteners in eliciting biosensor responses. Optimization of the CGP block is ongoing. Our data are consistent with the hypothesis that Type I cells release GABA secondarily to taste-evoked ATP release from Type II cells. Separately, we have observed that GABA modulates taste-evoked responses in gustatory afferent fibers, as expected of a gliotransmitter at a tripartite synapse.

102 **Gustatory Nerve Fiber Innervation Drives Presynaptic Specialization Accumulation In Taste Receptor Cells.**

Shannon M. Landon, Emily R. Holder, Laura Pinto, Saima Humayun, Lindsey J. Macpherson
University of Texas at San Antonio, San Antonio, TX, United States

The taste bud is a robust and highly adaptive sensory organ capable of repair following remarkable trauma, such as burns, nerve injury, and chemotherapy. This is, in large part, thanks to the highly dynamic nature of taste cells that have a finite lifespan and are continually replaced. While this constant turnover is critical for the persistence of taste sensation, it imposes a challenge for the innervating gustatory nerve fibers. When a taste cell reaches senescence and dies, nerve fibers must find and reconnect with a new taste cell. Despite the importance of neuron-taste cell reconnection, how synapses are assembled and how the specificity of synaptic connections is achieved is largely unknown. Here, we employed the use of presynaptic markers, bassoon and calhm1, to probe whether nerve fiber connectivity is an initiating factor for the recruitment of presynaptic machinery. We performed immunohistochemistry to identify whether presynaptic specializations in type II and type III cells were occupied by nerve fibers, and whether or not the presynaptic specializations persisted following nerve fiber transection. We found that the large majority of presynaptic specializations are directly adjacent to nerve fibers, leaving about 5% unoccupied by gustatory neurons. Four days following nerve transection and complete nerve die-off, we found that presynaptic specializations were almost entirely abolished with only ~4% remaining. Given these data, we conclude that presynaptic specializations are only present when nerve fibers are connected to the taste receptor cell, therefore, the innervation of nerve fibers are indeed necessary for the recruitment of presynaptic specializations. These findings aid in understanding the mechanisms driving synaptogenesis within the rapidly changing taste bud environment.

104 **Application Of Expansion Microscopy To Study Taste**

Kang-Hoon Kim, Emma Larsson, Minliang Zhou, Hong Wang
Monell Chemical Senses Center, Philadelphia, PA, United States

The sense of taste can distinguish at least five principal sensory qualities: salt, sweet, sour, bitter, and umami through specialized epithelial cells of taste buds, called taste receptor cells. In general, taste receptor cells express molecular receptors for only one taste quality. However, the responses of taste receptor cells are not always restricted to a single quality. In addition, responses of individual gustatory nerve fibers range from specific, responding to a single taste quality, to multimodal, responding to multiple qualities. However, the origin of this broader responsiveness is still unclear and may reside in the lack of specificity in synapses between taste cells and gustatory nerve fibers. To understand the complex subsynaptic organization of proteins in the pre- and post-synaptic terminals in the surrounding synaptic cleft, we applied hydrogel-based tissue expansion, the so-called expansion microscopy (ExM). Even if the high resolution of transmission electron microscopy (TEM) enables identification of cellular interactions within a taste bud, including taste cell-to-nerve fiber synapses as well as contacts between taste cells themselves, TEM imaging cannot always provide reliable and precise localizations of target synaptic proteins because of technical challenges regarding labeling specificity, probe size, and sample embedding. Here, we optimize antigenicity of several type of taste receptor markers and synapse molecules and improve specificity of immunostaining in hydrogel platform of the tongue tissue. We expect that the hydrogel method can be employed for studying the mechanisms underlying the regulation of synaptic architecture between taste cells and gustatory nerve fibers and providing nanoscale molecular distribution of synaptic proteins *in situ*.

108 **Molecular Identification Of The Remarkable Diversity Of Geniculate Ganglion Sensory Neurons And Glia**

Debarghya Dutta Banik, Tao Tang, Brian A. Pierchala
Indiana University School of Medicine, Indianapolis, IN, United States

Taste qualities in food are initially detected by taste receptor cells that reside in taste buds. While much is known about the taste receptor cells that detect these taste qualities, considerably less is known about the oral sensory neurons located in the geniculate and petrosal ganglia that communicate this information to the CNS. The geniculate ganglion consists of two populations of neurons, half are oral sensory neurons that project to the mouth, and the other half are somatosensory neurons that project to the pinna. These populations are distinguished by expression of their necessary transcription factors, PHOX2B for oral sensory neurons and BRN3A for pinna-projecting neurons. Single cell sequencing techniques were applied to further characterize the oral sensory neuron population, but the modest number of neurons that were able to be sequenced did not permit identification of uncommon cell types. Thus, critical questions remain: how many mature subpopulations of oral sensory neurons exist, how are they distinguished and what are their functions? To this end, we developed a cell nuclei isolation protocol that allowed us to use drop-seq to sequence more than 22,000 geniculate ganglion neurons and 8,500 glia, providing the necessary statistical power to distinguish subclasses. This analysis identified 21 distinct subpopulations of neurons, some of which are rare, accounting for less that 1% of the total number of neurons. Remarkably, this analysis also identified 12 distinct subclasses of glia. We are currently using spatial transcriptomics to validate these findings and provide further information about their morphology and positioning within the ganglion. These data will lay the foundation for a molecular-genetic interrogation of structure-function relationships of oral sensory neurons.

110 **Neuronal Regulation Of Adult Taste Stem Cells**

Jiang Xu[1], Alan Moreira de Araujo[1], Ranhui Xi[1], Xiaoli Lin[1], Chanyi Lu[1], Kurt Hankenson[2], Robert F Margolskee[1], Ichiro Matsumoto[1], Guillaume de Lartigue[1], Myunghwan Choi[3], Peihua Jiang[1]
[1]Monell Chemical Senses Center, Philadelphia, PA, United States, [2]University of Michigan, Ann Arbor, MI, United States, [3]School of Biological Sciences, Seoul National University, Seoul , Korea

Taste bud cells undergo continuous turnover throughout life, relying strictly on innervation for replenishment. This nerve-dependent process was initially described over 150 years ago. Recently, our studies showed that R-spondin alone is sufficient to substitute for neuronal input to induce taste bud regeneration via its interaction with taste stem/progenitor cell-expressed receptor Rnf43/Znrf3. We provided evidence supporting the notion that R-

spondin 2 (Rspo2) might be the elusive factor supplied by gustatory neurons that regulates taste stem cell activity. However, the essentiality of gustatory neuron-supplied Rspo2 in taste tissue maintenance remains unresolved. In this study, we aimed to determine the necessity of gustatory-supplied Rspo2 in taste tissue homeostasis through genetic approaches. We utilized a mouse line with the neomycin-resistance gene (*NeoR*) inserted into one of the intron regions of the *Rspo2* gene, resulting in reduced *Rspo2* expression. This led to a significant reduction in the number of taste buds in both the anterior and posterior tongue when compared to wild-type mice, with a gene dosage-dependent effect. Notably, this phenotypic change could be fully reversed by removing *NeoR* from the *Rspo2* gene. Additionally, we employed Adeno-associated Virus-based delivery of the Cre recombinase in conjunction with a mouse line amenable to Cre-based ablation of Rspo2 exons encoding receptor binding domains. Our results demonstrate that the ablation of Rspo2 in the nodose-petrosal-jugular ganglion complex can lead to a nearly complete loss of taste buds in the circumvallate papilla. Thus, our study unequivocally establishes that Rspo2 is the elusive gustatory neuron-supplied factor that acts on taste stem cells to maintain taste tissue homeostasis.

112 **A Novel Cell Model For Bitter Taste Threshold Prediction Based On Interleukin-6 Release In Human Gingival Fibroblasts**

Johanna Tiroch[1,5], Andreas Dunkel[2], Sonja Sterneder[1,2,5], Sofie Zehentner[1,5], Maik Behrens[2], Antonella DiPizio[2], Jakob Ley[3], Barbara Lieder[1], Veronika Somoza[1,2,4]

[1]University of Vienna, Faculty of Chemistry, Vienna, Austria, [2]Leibniz-Institute for Food Systems Biology at the Technical University of Munich, Freising, Germany, [3]Symrise AG, Holzminden, Germany, [4]Technical University of Munich, School of Life Sciences, Freising, Germany, [5]University of Vienna Doctoral School in Chemistry, Vienna, Austria

Characterization of bitter-tasting and bitter-modulating compounds by psychophysical experiments remains a complex challenge, as sensory panels possess a limited throughput and high variance due to inter-individual differences. The induction of acid secretion in a human parietal cell line (HGT-1) upon application of bitter-tasting compounds can be used as in vitro assay for identification of bitter-masking molecules, although without quantification of the modulating potency. Recently, we demonstrated that the release of the pro-inflammatory cytokine interleukin–6 (IL-6) in human gingival fibroblast cells (HGF-1) upon stimulation with lipopolysaccharides from Porphyromonas gingivalis (Pg-LPS) is repressed by trans-resveratrol via involvement of the bitter taste receptor TAS2R50. Since HGF-1 cells express most of the known 25 TAS2Rs, the quantitation of IL-6 release by HGF-1 cells by means of an enzyme-linked immunosorbent assay (ELISA) was implemented as novel cell model for bitter taste receptor activation. To permit a systematic investigation, 11 compounds were selected from the chemical bitter space and subjected to the HGF-1 cell assay, spanning a concentration range between 0.1 μM and 50 mM. A specific role of TAS2R50 was excluded by analysis of structurally diverse TAS2R agonists and antagonists and by means of a molecular docking approach. For analysis of the quantitative performance of the in vitro model, a linear association ($R^2 = 0.60$, $p < 0.01$) between a compound's effective concentration to repress the Pg-LPS evoked IL-6 release by 25% and the corresponding human bitter taste threshold concentration was established. In conclusion, the poster presents a novel predictive model for bitter tasting compounds utilizing a robust cell model in combination with a high-throughput ELISA detection.

114 **Bitter Peptides Derived From Gastric Digestion Of Sweet-Tasting Thaumatin Ameliorate *H. Pylori* Induced Pro-Inflammatory Il-17A Release Via Bitter Taste Receptor Tas2R16**

Phil Richter[1,2], Karin Sebald[2], Konrad Fischer[3], Angelika Schnieke[3], Malek Jlilati[2], Verena Mittermeier-Kleßinger[4], Veronika Somoza[2,5,6]

[1]TUM School of Life Sciences Weihenstephan, Technical University of Munich, Freising, Germany, [2]Leibniz Institute for Food Systems Biology at the Technical University of Munich, Freising, Germany, [3]Chair of Livestock Biotechnology, TUM School of Life Sciences, Technical University of Munich, Freising, Germany, [4]Chair of Food Chemistry and Molecular Sensory Science, Technical University of Munich, Freising, Germany, [5]Chair of Nutritional Systems Biology, TUM School of Life Sciences, Technical University of Munich, Freising, Germany, [6]Department of Physiological Chemistry, Faculty of Chemistry, University of Vienna, Vienna, Austria

The plant *Thaumatococcus daniellii*, which is mainly native to Africa, contains the protein thaumatin, which tastes about 1600 times sweeter than sucrose and is used as a sugar substitute in foods to reduce their calorie content. Since in one of our previous studies, we demonstrated that bitter-tasting peptides released upon gastric digestion of non-bitter-tasting casein stimulate cellular proton secretion as a key mechanism of gastric acid formation, we hypothesized the sweet-tasting thaumatin to be cleaved into bitter-tasting peptides when subjected to an *in vitro* protocol of gastric digestion. The bitter peptides formed were tested for their ability to stimulate the proton secretion of immortalized human parietal cells (HGT-1) and to reduce pro-inflammatory effects evoked by exposure to *H. pylori* via bitter taste receptors (TAS2Rs). For this purpose, thaumatin was digested using an established *in vitro* digestion approach, and the resulting peptides were identified via LC-ToF-MS. Subsequent quantification by LC-MS/MS was followed by validation of the formation of the peptides in pigs. The *in silico* predicted taste quality of the peptides was validated by sensory tests. Treatment of HGT-1 cells with the bitter peptides stimulated cellular proton secretion and reduced the *H. pylori*-evoked release of IL-17A by up to 89.7 ± 21.9% ($p \leq 0.01$). To investigate a potential involvement of TAS2Rs, the stimulating effects of bitter peptides on proton secretion could be reduced using the TAS2R16 antagonist probenecid. Functional involvement of TAS2R16 in the *H. pylori*-evoked IL-17A release was demonstrated by means of specific siRNA. The results provide the molecular basis for bitter peptides generated upon gastric digestion to help reducing inflammatory processes, e.g. induced by *H. pylori* infection.

116 **The Addition Of Some But Not All Amino Acids To Soil Increases The Feeding Rate Of The Earthworm, *Dendrobaena Veneta*.**

Jonathan G Mebrahtu[1], Folashaye E Araromi[1], Ameena A Mohassib[1], Laura Ortega-Damian[1], Rebeca V Rodriguez[1], Tania C Romero[1], Renalison Farias-Pereira[1], Michael J Rizzo[2], Cecil J Saunders[1]

[1]Kean University, Union, NJ, United States, [2]Wake Forest Unviersity, Winston-Salem, NC, United States

Earthworms derive their nutrients from the organic component of soil and are attracted to soil containing decaying organic material. However, no studies have established individual molecules that modulate the feeding of these animals. Our previous studies have suggested that glutamic acid may trigger increased feeding in the earthworm, *Dendrobaena veneta*. In the present experiments, we test other amino acids to determine if they also modulate feeding rates. To test the rate earthworms consumed soil, we starved earthworms to empty their gastrointestinal (GI) tract, then allowed them to feed on soil for 60 minutes and measured the faction of their GI tract that was filled with soil. In this assay, we have found that earthworms consume significantly more soil when it contains 50 mM alanine or glutamic acid (ANOVA, $p<0.01$) but observed no significant changes in feeding rate with the addition of 50 mM glycine, histidine, and arginine. Since an animal's internal metabolic state (e.g. starvation) can also affect the feeding rate, we also compared the feeding rate after 1 and 2 weeks of starvation and surprisingly found no difference in the rate of feeding. One possible explanation is that these starvation periods are too short to deplete chemical energy stores; thus, we are currently determining tissue trehalose and triglyceride content over these periods. In addition to these behavioral experiments, we have also conducted Pacbio RNA-sequencing on tissues enriched with chemosensory cells to identify possible chemosensory receptor transcripts. Metabotropic glutamate receptor homologs containing a protein domain associated with ligand binding in Tas1Rs (PF00003.21) provide a possible molecular mechanism by which amino acids could be detected and trigger increased feeding behavior in earthworms.

118 **Affective Odors Modulate Neural Processing Of Emotional Visual Stimuli**

Chloe E. Johnson, Colin B. Bowyer, Danielle N. Jones, Austin C. Pauley, James S. Brown, Adam K. Dewan, Christopher J. Patrick
Florida State University, Tallahassee, FL, United States

Emotional processing likely involves the integration of multiple perceptual systems. In prior research, studies have utilized the International Affective Picture System (IAPS) - a set of positive, negative, and neutral pictures – to study how event-related potentials (ERPs) are modulated by emotional state. One of the most consistent findings from these studies is the late positive potential (LPP) – a positive-going ERP that appears approximately 400-600 ms after picture presentation – is enhanced for positive and negative images, suggesting that it may index individual differences in emotional visual processing. Despite extensive research on this topic, virtually no work has examined whether other emotionally evocative stimuli modulate these effects. Therefore, we sought to explore interactions between the olfactory system and the visual processing of emotionally salient IAPS pictures. We measured ERPs from undergraduate and community participants exposed to affective odors (pleasant, unpleasant, and blank) prior to the presentation of IAPS images. Participants provided subjective valence ratings for the odors used. Overall, we found that affective odors (i.e., positive and negative odors) significantly *reduced* expected modulation of the LPP. We also found that, when controlling for individual differences in odor ratings, the LPP varied as a function of odor valence akin to the expected patterns of modulation for visual stimuli. Furthermore, this pattern of modulation was more evident for individuals who reported detecting a larger difference between affective and blank odors. This research indicates that the LPP may encode individual differences in affective salience across sensory modalities.

120 **Predicting Intensity Interactions In Odor Mixtures**

Robert Pellegrino[1], Matt Andres[1], Vijay Singh[2], Josh Nsubuga[1], Khristina Samoilova[3], Cyrille Mascart[3], Alex Koulakov[3], Joel Mainland[1]

[1]Monell Chemical Senses Center, Philadelphia, PA, United States, [2]Department of Physics, NC A&T State University, Greensboro, NC, United States, [3]Cold Spring Harbor Laboratory, Cold Springs Harbor, NY, United States

Most odors encountered in daily life are complex mixtures where molecules interact to overshadow, suppress, inhibit and synergize with each other. Multiple models exist to predict the odor intensity of a mixture from the intensity of its components; however, these interaction models have not been compared systematically and are not based on biophysical interactions. In this study, 15 human panelists rated the intensity of binary (N = 216) and complex (N = 44) mixtures where each component was presented at varying concentrations. Common models, such as euclidean addition and strongest-component, consistently overestimated mixture intensity, as most mixtures were less intense than the strongest component. Based on previous reports showing predictions of neuronal responses to odor mixtures are improved by adding information about each component's concentration-intensity function, we collected intensities at a range of concentrations for several odorants spanning chemical space (N = 62) to successfully train a machine-learning algorithm to estimate the concentration-intensity function for any odorant at any concentration ($r(118) = .88$, $p < 0.001$). A primacy model which weights odor component contributions by their relative affinities rather than their currently perceived intensities accurately estimates the intensity of 2, 3, 5, and 10-component mixtures ($r(258) = 0.84$, $p < 0.001$). Our results demonstrate the ability to predict the full concentration-intensity function for odorants in odor mixtures and use this information to produce better estimates of its odor intensity than previous models. This model ensemble offers a reliable method to predict odor intensity of naturalistic mixtures, essential for understanding and replicating complex scent profiles.

122 **Obsessive-Compulsive Behavioral Traits Do Not Predict Odor Awareness And Olfactory Hyperreactivity In The General Population: Results Of A Representative National Survey In The Czech Republic**

Lenka Martinec Novakova, Dagmar Schwambergova, Jan Havlicek, Iveta Hocko Fajnerova
National Institute of Mental Health, Klecany, Czech Republic

Obsessive-compulsive (OC) behavioral traits and phenomena are common in the general population. They exist on a continuum, and subclinical forms differ from those found in clinical populations in terms of severity rather than content. One prominent OC phenomenon is sensory overresponsivity, which is characterized by challenges in integrating and responding to everyday sensory experiences. In clinical populations, the keen awareness of odors (whether actually present or imagined) and tendency to overreact to them disrupt the individual's everyday activities. The aim of the present study was to examine whether clinical and subclinical OC traits predict greater odor awareness and hyperreactivity in a nationally representative sample of the general population of the Czech Republic (N=1008, 515 F) aged 18-50 years. Respondents were recruited using quota sampling based on gender, age, region, and municipality size. OC traits, odor awareness, and hyperreactivity were assessed with the Yale–Brown Obsessive Compulsive Scale (Y-BOCS, cut-off=12, range 0-40), Individual Significance of Olfaction (ISO), and Chemical Sensitivity Scale (CSS), respectively. Clinically significant OC traits (Y-BOCS > 12) were reported by 124 people (12.3%). Their mean Y-BOCS score was 17.1 ± 3.8, whereas the subclinical subgroup scored 2.7 ± 3.8. Y-BOCS score did not predict ISO or CSS scores in either subgroup or the total sample (all models: $\beta < 0.1$, $R^2 = 0.01$). Visual explorations did not reveal any non-linear patterns of dependence. We conclude that in the general population, self-reported OC traits, regardless of clinical significance, do not predict how individuals interact with odors in everyday situations, and suggest that olfactory processing alterations related to OC phenomena may not be detectable by self-reports.

124 **Zona Pellucida Like Domain Containing 2 Is Involved In The Stimulation-Dependent Neurogenesis Of Specific Olfactory Sensory Neuron Subtypes In Mice**

Karlin E Rufenacht, Kawsar Hossain, Amanda Stenzel, Madeline Smith, Stephen Santoro
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Neurogenesis persists throughout life in the mammalian olfactory epithelium. In mice, each differentiating olfactory sensory neuron precursor selects to express, out of ~1200 possibilities, a single olfactory receptor gene, which determines the mature neuron's subtype. Our lab has found that odor stimulation can accelerate the birthrates of specific neuron subtypes. These findings challenge the established model that neurogenesis within the olfactory epithelium is stochastic with respect to subtype. To explain these findings, we hypothesize that upon stimulation, neurons of some subtypes can signal to progenitors to promote the birth of neurons of the same subtype. To test this, we used scRNA-seq to identify genes enriched in neuron subtypes whose birthrates are accelerated by stimulation. Zona pellucida like domain containing 2 (*Zpld2*), a gene with no known function that is expressed only in the olfactory epithelium and predicted to be a member of the TGF-β receptor type III protein family, was the gene found most enriched. These findings are consistent with the hypothesis that *Zpld2* is a component of a signaling pathway that mediates stimulation-dependent neurogenesis. To test this, we generated and analyzed the phenotypes of a *Zpld2*-null mouse. Using a combination of EdU-birth dating and RNA fluorescent in situ hybridization, we have found evidence that the effect of olfactory deprivation on the birthrates of neuron subtypes that undergo stimulation-dependent neurogenesis is reduced in *Zpld2*-null mice. Additionally, gene ontology analyses of RNA-seq data from *Zpld2*-null epithelia reveal that genes involved in the regulation of neurogenesis and TGF-β signaling are down-regulated in *Zpld2*-nulls. These findings suggest that *Zpld2* mediates stimulation-dependent signaling to promote neurogenesis.

126 **Asymmetric Histone Inheritance Patterns In Mammalian Olfactory Horizontal Stem Cells**

Binbin Ma[1, 2], Guanghui Yang[1, 2], Jonathan Yao[2], Gabriel Manske[3], Sue Hammoud[3], Xin Chen[1, 2], Haiqing Zhao[2]

[1]Howard Hughes Medical Institute, Department of Biology, Johns Hopkins University, Baltimore, MD, United States, [2]Department of Biology, Johns Hopkins University. , Baltimore, MD, United States, [3]Department of Urology, University of Michigan., Ann Arbor, MI, United States

A long-standing question in stem cell field is how distinct cell fates are achieved with one round of division. Histones, a major carrier of epigenetic information, play important roles in regulating differential gene expression and cell fate decisions. Our previous studies have shown asymmetric histone inheritance during asymmetric divisions of *Drosophila* male germline stem cells and intestinal stem cells. However, it is still unclear whether asymmetric histone inheritance is applicable to mammalian adult stem cells. To address this question, we utilized horizontal basal cells (HBCs) in mouse olfactory epithelium to study histone inheritance patterns. First, using polarized distribution of HBC marker p63, we identified ~58% of mitotic HBCs showing asymmetric divisions *in vivo* with asynchronized cell cycle and perpendicular division. Then, we found the asymmetric H4 distribution in asymmetrically dividing HBCs, but not in symmetrically dividing cells, indicating the cellular specificity of the asymmetric histone inheritance. The asymmetric histone density may indicate differential level of chromatin accessibility during cell fate transitions. Moreover, we recapitulated the asymmetric division and histone inheritance with primary cultured HBCs, and further performed paired daughter cell sequencing to uncover the molecular features in the asymmetrically dividing HBCs. Our preliminary data also showed the asymmetric old versus new histone inheritance patterns in HBCs. Moving forward, I will explore the biological significance and regulatory mechanisms of asymmetric histone inheritance during regeneration. Taken together, these results will greatly enhance our understanding of how stem cells retain their epigenetic memory and whether this is a conserved phenomenon across different tissue and species.

128 **The Role Of Evoked Activity In The Survival And Functional Integration Of Newborn Olfactory Sensory Neurons**

Kendall A Curtis, Sarah PR Berg, Claire EJ Cheetham
University of Pittsburgh, Pittburgh, PA, United States

Stem cells are a potential therapeutic intervention for olfactory sensory loss in a range of conditions such as Parkinson's disease and COVID-19-related anosmia, as well as for brain regeneration in other neurological and neurodegenerative diseases. Understanding the mechanisms by which endogenous stem-cell-derived neurons integrate into circuits is integral to effective clinical translation. Olfactory sensory neurons (OSNs) are generated throughout life in humans and mice—unlike most other mammalian neurons—providing a unique opportunity to understand the mechanisms by which these endogenous stem-cell-derived neurons integrate into highly ordered olfactory bulb (OB) circuits. However, we have found that newborn OSNs have a low 14-day survival rate. It is unknown what factors determine immature OSN survival and functional integration into the OB. We have shown previously that immature OSNs provide odor input to the OB. Thus, the immature phase of OSN development may represent a key time window during which survival and functional integration are determined. We hypothesize that evoked activity of immature adult-born OSNs promotes their survival and functional integration into OB circuits. When analyzing activity in the olfactory epithelium, we found that survival of newborn OSNs was significantly higher in odor-exposed mice compared to controls ($p=0.006$), suggesting that evoked activity promotes newborn OSN survival. We are currently determining the effect of altered evoked activity on functional integration of immature OSNs using in vivo optogenetic stimulation of immature OSNs and 2-photon calcium imaging of mitral and tufted cells. Understanding the factors that impact immature OSN survival and functional integration into OB circuits is fundamental to our understanding of olfactory plasticity.

130 **Hedgehog Signaling Regulation Of Embryonic Lingual Muscles Differentiation**

Gabrielle C. Audu[1], Sally Y. Rohan[2], Archana Kumari[1]
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Hedgehog (HH) signaling is vital for embryonic tongue development, including taste cell specification and myoblast migration. Once the taste fungiform papillae are specified, function of HH signaling shifts to its maintenance. However, a shift in HH signaling role in muscle development once they are patterned remains to be studied. HH co-receptor *Gas1* plays crucial role in embryonic craniofacial development, but remains unexplored in the tongue. Our recent studies identified $Gas1^{lacZ}$ in early postnatal muscles but its function is not yet investigated, impeding our understanding of its role in the tongue. To address this knowledge gap, we studied embryonic *Gas1* expression and function. We observed consistent $Gas1^{lacZ}$ gene and GAS1 protein expression in immature taste buds, stroma and muscles throughout. We then used $Gas1^{lacZ/lacZ}$ for loss-of-function studies. We observed that *Gas1* loss altered tongue size as compared to *Gas1* heterozygous or wild-type controls at embryonic day 18.5. Importantly, even though *Gas1* is expressed in apical epithelium or taste bud primordium, its inhibition did not affect embryonic epithelium, taste papillae density or taste bud size, but only affected muscles. Using H&E, we observed muscle enlargement after *Gas1* loss but not with *Gas1* haploinsufficiency, further indicating that *Gas1* functions are not graded. Our initial data indicate upregulation of undifferentiated muscle fibers with downregulation of mature muscle cells, while muscle cell proliferation remains intact. Our data reveal a novel role for *Gas1* in regulating embryonic tongue muscle balance between mature and undifferentiated states. These findings highlight the need for further studies to elucidate the intricate interplay between *Gas1*+ muscle cells and other signaling components in tongue development.

132 **The Endoplasmic Reticulum Protein Canopy1, Plays A Key Role In Vomeronasal Homeostasis And Neuronal Connectivity**

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The molecular identity of neurons is established by differential regulation of unique signaling pathways, which ultimately modulate gene expression/translation. The vomeronasal organ (VNO) comprises two main subtypes of vomeronasal sensory neurons (VSNs), which express either one or two genes from the vomeronasal receptor families V1R or V2R. Recent work on olfactory sensory neurons (OSNs) has suggested that the polymorphism of olfactory receptors (ORs) differentially activates the unfolded protein response (UPR). The UPR is a compensatory mechanism to correct or manage misfolding of proteins in the Endoplasmic Reticulum (ER). The OSNs utilize the UPR to transform the aminoacidic polymorphisms of the ORs into distinct signatures by changing the expression of cell adhesion and axonal guidance molecules. Through the analysis of single-cell RNA sequencing (scRNA Seq) of wild type VSNs, we found that the V2R-expressing VSNs selectively express the ER protein Canopy1 (Cnpy1) from progenitors throughout maturity. Performing scRNA sequencing on the VSNs of Cnpy1 knockout (KO) mice showed altered UPR activation, together with aberrant transcription of cell adhesion proteins, axonal guidance molecules, and altered expression of ribosomal protein subunits. In line with this, histological observations show changes in connectivity of the VSNs to the accessory olfactory bulb (AOB). Though the vomeronasal organ of Cnpy1 KO mice appears indistinguishable from that of controls in peripubertal mice, by 60 days of age, the V2R expressing neurons display degeneration. Our data suggests that Cnpy1 loss of function has effects on protein synthesis, activation of the UPR, connectivity, and homeostasis of the V2R VSNs.

134 **The Psychophysical Analysis Of &Ldquo;Maple&Rdquo; And &Ldquo;Buddy&Rdquo; Aromas In Maple Syrup Products When Exposed To Light And Elevated Temperatures During Storage**

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The aroma chemistry of sugar syrups all contains sotolon (3-Hydroxy-4,5-dimethylfuran-2(5H)-one), with their unique identity determined by trace concentrations of different chemicals, e.g., phenols, thiols, or in the case of maple syrup, pyrazines. The desired aroma of commercial maple syrup is partly defined by manufacturing processes, transportation, and storage conditions. Our research suggests that flavor can also be influenced by exposure of maple syrup to light and elevated temperature during storage. Using Sniff Olfactometry (SO), we investigated the odor perception of various combinations of sotolon and other key odorants in maple syrup. The goal was to determine the probability of perceiving "maple"—the desired aroma— as compared to "buddy"—a common aroma defect linked to climate change—, flavors in maple syrup. To determine the key odorant involved, Gas Chromatography Olfactometry (GCO) was used to identify aroma defects in commercial products, when the classic sensory degree of difference testing revealed "no difference" in test samples. This poster will present computational psychophysical data that explains the configural nature of the "maple" and "buddy" perceptions.

136 **Integration Of A Gustometer And A Sniff Olfactometer Into The Same Psychopy Program To Measure The Effects Of Taste Stimulation On Odor Perception**

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Psychophysical tests are generally more sensitive and reliable in detecting and quantifying stimulus responses than behavioral testing of discrimination and recognition. In our previous work, with a "blast" style olfactometer (referred to as the sniff olfactometer) we are able to embed a 70ms odorant mixtures puff into the middle of deep inhales of greater than a second. Using perceptual data collected from human subjects across varied treatments using the sniff olfactometer (SO), we were able computed stable, reproducible logistic models. Based on the foundational components of the SO, our research group constructed a gustometer that uses the same coding and testing programming to operate peristaltic pumps as well as deliver 600ms pulses of tastants to the tip of the tongue. The data collected from the gustometer produced functional logistic models of taste perception within the same time frame as a deep inhalation during an SO measurement of odor recognition. These two delivery systems could be combined to study multimodal perception to quantitively determine the effects of tastants on odor perception. Preliminary tests have generated stable logistic functions for sucrose and "sweetness", citric acid and "sour", pyrazines and "toast", hexanal and "grass", methanethiol and "rotten cabbage". This poster will present the computational results of odorants and tastants delivered simultaneously and asynchronously to discuss the implications for odor-taste processing such as suppression and enhancement.

138 **Comparing Odor Perception Across Humans And Mice**

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Understanding the relationship between neural activity and perception is a critical question in neuroscience, particularly in the domain of olfaction where we are just beginning to develop methods to robustly quantify perceptual odor quality. Mice and humans have distinct advantages for relating neural activity to perception. Mouse models enable researchers to easily access neural activity, while humans allow researchers to more readily assess detailed perceptual reports. A critical step in establishing this bridge between species involves verifying how well perceptual similarity of odors observed in one species can predict perception in another species. Using a set of common stimuli, we measured the perceptual similarity of 20 odorants in mice using a delayed-match-to-sample (DMTS) task (Nakayama, 2022), and in humans using two separate methods; first the human equivalent to the DMTS, a two-alternative forced-choice paradigm (2AFC), and second, an odor profiling method. We found that, when compared to the 2AFC, perceptual similarity between the species was not significantly correlated ($p = 0.13$). In contrast, perceptual distances generated from the profiling task were weakly correlated with mouse perceptual distances ($r = 0.31$, $p < 0.03$). Both human methods were strongly correlated ($r = 0.49$, $p < 0.001$). Further analysis, using multidimensional scaling, revealed that the first dimension of human perceptual space can be predicted using mouse perceptual embedding. As in previous research, this perceptual dimension is consistent with the perceived pleasantness of the odors. Examining additional odors will allows us to more densely sample perceptual spaces and determine which dimensions can be predicted across species.

140 **Bitter Taste Perception And Its Neuronal Underpinning**

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The bitter taste sensation serves as a defense mechanism against harmful compounds, while also contributing to

the complexity of culinary experiences and potentially signaling medicinal benefits. It is surprising, however, that both the question of whether bitterness is a unified (monoguesic) or a complex sensation, and its system-level underpinning remain unresolved. Behaviorally, rats showed a complete failure to distinguish between briefly sampled bitterant pairs when intensity is removed as a cue. In humans, while bitterants discrimination is still a difficult task, it was shown that some bitterants can be classified differently from others. Interestingly, the overall-accepted bitterness monoguesic perception hypothesis is at odds with results from neuronal activity studies, mainly from early nodes of the taste system, that showed distinct responses to different bitterants. Here we combined rat behavioral bitterant preference tests with electrophysiological recordings from lower and higher brain regions of the taste system to study the logic of the bitter perception and coding. Our results show that given a longer sampling time (10 minutes), rats significantly preferred denatonium over quinine, and quinine over sucrose octaacetate (SOA); a preference relation that was maintained across days. Preliminary electrophysiological recording using Neruopixels probes from the gustatory cortex (GC) showed distinct neuronal responses to iso-intense bitter tastes. Our results suggest that bitterness is not as monoguesic perception as was previously suggested, which is probably supported by distinct activation in different regions of the taste system.

142 **Behaviorally Relevant Features Of The Neural Code In Olfactory Bulb**

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Odor stimuli evoke spatiotemporal patterns of activity at multiple levels in the olfactory bulb, the Glomeruli and subsequent mitral/tufted (MT) cells. How the similarities between patterns of neural activity are related to perceptual similarities between sensory stimuli is still debatable. In this work, we designed an experiment using the 2-alternative-forced-choice paradigm (2AFC) to measure the generalization ability of mice during precise odor discriminations. In this task, we are able to smoothly vary spatiotemporal patterns of activity using three component odor mixtures to identify the relevant features of the neural activity that drive behavioral discriminations. During this task, we trained mice to discriminate a specific mixture of three odors (referred to as the "Target") from a range of different odor stimuli (referred to as "non-Targets"). In subsequent probe trials, we manipulated the composition of the mixture to test the mice's ability to generalize their response. Then, we used two photon Ca2+ imaging and measured the neural activity in mice expressing a fast calcium indicator (GCaMP6f) in pre-synaptic glomeruli. Based on these recordings, we will identify the crucial aspects of neural activity that drive behavior. Our preliminary data showed that this correlation exists within different temporal windows, based on the difficulty of the task. Glomeruli that are activated earlier are more relevant to dicriminate perceptually far odors and glomuruli which are activated in the middle of the neural code are relevant for perceptually near odors. These findings provide valuable insights into how the olfactory system represents and distinguishes between odor mixtures. The importance of the order of neural activity emphasizes the significance of temporal dynamics in encoding odor mixtures.

144 **Loss Of Smell And The Olfactory-Hippocampal Gamma Oscillation Changes In The Acceleration Of Alzheimer'S Disease Progression**

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Alzheimer’s disease (AD) brain pathology includes deposition of β-amyloid (Aβ) plaques, phosphorylated-tau, neurofibrillary tangles, and microglial activation that lead to reduced gamma oscillation power and cognitive impairment (Murty D., 2021). Indeed, multi-sensory stimulation at 40 Hz reduces amyloid burden and increases microglial co-localization with Aβ (Iaccarino, HF., 2016). Loss of smell has emerged as an early feature of AD where decreased smell is linked to faster brain volume loss and cognitive decline (Murphy, C., 2019). Further, sniff-induced gamma oscillations from the olfactory bulb (OB) to the hippocampus suggest that loss of smell decreases hippocampal gamma oscillations. I hypothesize that stimulation of the OB in gamma frequencies will ameliorate AD pathologies by recruiting $CD4^+$ T-cells and shifting microglia to a non-disease like states as well as improve learning and memory in a familial AD mouse model. I present optogenetic studies using OMP-hChR2V mice to stimulate olfactory sensory neurons and entrain the hippocampus in gamma oscillations. LFP recordings in the OB and dorsal CA1 show robust coupling to CA1. In a chemogenetic approach, I express the excitatory DREADD receptor, hM3Dq in CaMKIIa mice granule cells to enhance synchronous gamma firing (Dalal and Haddad, 2022). Oscillatory power changes were dose-dependent of the hM3Dq ligand, clozapine-N-oxide. At a high dose, there was a CA1 gamma power decrease, while at a medium dose, a transient increase followed by a decrease in gamma power in CA1 was observed. These findings contribute to the understanding of the therapeutic effects of gamma frequency stimulation on AD pathology via an intranasal route. Funded by an NIA administrative supplement to R01 DC000566, R01 AG079193 and T32 DC012280

146 **Evolution Of Olfactory Sensitivity In The Mexican Cavefish**

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Astyanax mexicanus, the Mexican tetra, consists of eyed, river dwelling surface populations (surface fish) and multiple eyeless cave populations (cavefish) which have undergone rapid evolution, and therefore provide a unique comparative model by which to understand evolutionary processes. The sensory adaptations of the cavefish include eye loss, an expansion of the sensory organs and associated brain areas governing taste and smell, and enhanced behavioral sensitivity to amino acids relative to their surface counterparts. However, it is unknown where in the olfactory processing pathway altered chemosensory sensitivity is generated. Using 2-photon Ca2+ imaging in transgenic surface and cavefish that express the genetically encoded calcium indicator GCaMP6s, we find enhanced sensitivity to the amino acid L-Serine in the cavefish olfactory bulb. Interestingly, enhanced neuronal sensitivity in cavefish took the form of a broader neuronal response, with nearly the entire imaged cross-section of the olfactory bulb responding at the highest concentration of L-Serine. Since odor identity is thought to be encoded in the olfactory bulb by patterns of neuronal activation, these findings suggest that increased behavioral sensitivity to odors may come at the cost of reduced specificity. Future behavioral and Ca^{2+} imaging studies on an array of odorants will reveal the specific odorants to which the cavefish are more sensitive, and the neural mechanisms mediating enhanced sensitivity.

148 **Altered Odor-Mediated Social Behavior In A Model Of Fragile X Syndrome**

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Fragile X Syndrome (FXS) is a neurodevelopmental disorder characterized by intellectual disability and difficulties in social interaction. In mice, the accessory olfactory bulb (AOB) is implied in the processing of chemical cues that trigger social and sexual behaviors. In addition, the olfactory bulb shows high levels of Fragile X Messenger Ribonucleoprotein (FMRP) during neurodevelopment, the absent protein in the FXS. Here, we show that the *Fmr1* KO mice, a model of FXS, exhibit abnormal odor-mediated social behaviors. Male *Fmr1* KO mice show reduced investigation of conspecifics and social odors (urine and soiled bedding), as well as impaired discrimination between social odors. We have previously shown that the volumetric ratio between anterior and posterior regions of AOB was smaller in *Fmr1* KO compared to WT mice. Together, these findings suggest that disruption in AOB signaling can explain the lesser sociability of these mice. Accordingly, we found that mitral cells (MCs), projection neurons of the AOB, exhibit altered excitability in *Fmr1* KO mice, with faster membrane time constant, and action potential duration. In addition, the firing in MCs, elicited by current stimuli, was lower in *Fmr1* KO mice, suggesting reduced excitability of MCs. In conclusion, the anatomy and physiological differences in the AOB of the *Fmr1* KO mouse could partly explain their deficit in odor-mediated social behavior.

150 **The Superficial Tufted And Mitral Cell Output Neurons Of The Mouse Olfactory Bulb Have A Dual Role In Insulin Sensing.**

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Insulin signaling in the brain may represent one of the many ways in which olfactory and metabolic circuitry are intertwined. The olfactory bulb (OB), like other sensory systems, contains multiple, parallel projection neurons to relay the nature of a stimulus. Triple-colored immunofluorescence and RNAScope^{TM} were used to detect co-localization of the voltage-dependent potassium channel (Kv1.3) and insulin receptor (IR) kinase in mitral cells (MCs) and in the newly-categorized superficial tufted cells (sTCs). In an *ex vivo* slice preparation, we used patch-clamp electrophysiology in a whole-cell configuration to measure biophysical differences between the two projection neurons in terms of intrinsic properties, excitability, action potential (AP) shape, voltage-activated conductances, and neuromodulation by the hormone insulin. We propose that insulin modulation is mediated by a marked difference in voltage-dependent current, representing distinct ion channel populations that affect the kinetics of action potentials, and which evoke a greater increase in sTC firing frequency, albeit both types of projection neurons having similar AP bursting activity. The sTCs were modulated by bath application of insulin – increasing AP firing frequency by 97%, attributable to an 8% decrease in the intraburst interval, and a reduction of the latency to first spike by 37%. Similar to that previously shown for MCs, insulin modulation of sTCs appears to be dependent on Kv1.3 activity. Pharmacological block of the channel vestibule or gene-targeted deletion of Kv1.3 results in loss of insulin modulation of AP firing in sTCs. We conclude that there may be a range of neuromodulators of sTCs that may alter excitability and fine-tune olfactory information processing or metabolic balance.

152 **Effects Of Two Alzheimer&Rsquo;S Disease Risk Factors On Neuronal And Synaptic Properties In The Anterior Olfactory Nucleus Of Mice.**

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Pathological evidence suggests that dysfunction of the anterior olfactory nucleus (AON) contributes to the olfactory deficits in prodromal Alzheimer's disease (AD). However, the impact of AD risk factors including aging and genetic risk factors on the neuronal properties and circuit operation in the AON remains elusive. Here,

we examined the membrane properties of AON neurons in brain slices of aged mice at 60-90 weeks old. In whole cell current clamp, resting membrane potential, action potential (AP) peak amplitude, threshold and frequency were -70.3 ± 1.8 mV, 26.4 ± 4.6 mV, -40.6 ± 1.7 mV, 51 ± 11.5 Hz in AOL (n=6); -70.6 ± 1.3 mV, 30.3 ± 3.4 mV, -45.8 ± 1.8 mV, 42 ± 4.6 Hz in AOD (n=15) and -67.9 ± 1.7 mV, 31 ± 3,4 mV, -42 ± 2.1 mV, 35.8 ± 5.8 Hz in AOV (n=10) respectively. We classified the recorded neurons into pyramidal and nonpyramidal groups based on their fire pattern and will be verified by post hoc reconstruction in subsequent experiments. Specifically, pyramidal cells (n=19), regardless of their location, responded to suprathreshold depolarization with a cluster of double or triple action potentials at the initial phase of current injection, a characteristic separating them from other cell types examined. Compared to pyramidal cells which had small or no AHP, non-pyramidal cells (12) had a significantly large AHP. These studies will be extended to adult (20-30 weeks old) mice and age-matched transgenic mice carrying the human gene allele encoding the apolipoprotein E4, the strongest genetic risk factor for AD. Our work has clearly demonstrated the feasibility of characterizing neuronal and synaptic properties with the whole cell patch clamp technique in brain slices of aging or aged mice and pave the way for future research involving age-dependent neurodegenerative diseases.

154 **The Bitter Side Of Habitual Low-Calorie Sweetener (Lcs) Use: Exploring Associations With Lcs Consumption Patterns And Glucose Metabolism, Sweetness Perception, And Added Sugar Intake**

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Despite their popularity, low-calorie sweeteners (LCS) continue to raise health concerns, including their impact on glucose metabolism. This study investigates whether sweet taste signaling plays a role in postprandial glucose metabolism and whether habitual LCS consumption alters this role in people with obesity. Using a randomized crossover design that included 14 non-habitual (8 males/6 females) and 22 habitual (10 males/12 females) LCS consumers, none with diabetes, we assessed the metabolic responses to three oral glucose tolerance tests (OGTT): 1) a control OGTT, 2) an OGTT where sweetness was inhibited by the addition of lactisole, a human sweet taste receptor antagonist, and 3) an OGTT mixed with lactisole preceded by tasting and expectorating sucralose. We also assessed participants' daily consumption of total and added sugars using the Diet History Questionnaire III and their sweet taste sensitivity and preferences for glucose and sucralose using validated sensory tests. In agreement with previous studies, we found sex-related differences in postprandial glucose responses, with males having higher glycemia than females, but this was observed in the non-habitual LCS group and absent in the habitual LCS group. Compared with the control OGTT, consuming glucose in the absence of its sweetness increased insulin secretion, but only in females. LCS consumption was linked to higher added sugar intake but not to differences in sweet taste sensitivity or preferences. In conclusion, our findings suggest a role of sweet taste in insulin responses to glucose, particularly in females, and a potential influence of habitual LCS consumption on sex-related differences in postprandial glucose responses. These findings also support that LCS augment dietary sweetness rather than serving as sugar substitutes.

156 **Individual Differences In Cephalic Phase Insulin Release**

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Cephalic phase insulin release (CPIR) is a rapid secretion of insulin that occurs following oral sensory stimulation. Previous work in humans and rodents has shown that glucose and glucose-containing carbohydrates in particular are good elicitors of this response. Nevertheless, a high degree of variability in the magnitude of CPIR to these stimuli can be observed across individuals. Here, we report on individual differences in CPIR from two groups of healthy adults following stimulation with either 1 M glucose in solution (liquid form; N=22) or mixed with gelatin (solid form; N=20). In both cases, participants performed a 45-second modified sham feed and blood samples were collected before and after stimulation. Plasma c-peptide (a proxy for insulin secretion) and insulin were then analyzed. Both stimuli elicited CPIR in most but not all individuals; those who showed a positive change in c-peptide or insulin from baseline between 2 and 6 min were categorized as CPIR "responders." We observed a c-peptide responder rate of 91% and 65% for the glucose in liquid and solid form, respectively, and an insulin responder rate of 82% and 57% for the liquid and solid respectively. In addition, a large degree of variability was seen within the responders, with individuals' highest c-peptide measurements ranging from 6 to 138 pmol/L and highest insulin measurements ranging from 0.4 to 32 pmol/L over 2 to 6 min. Individual data over the CPIR period will be presented to highlight this variability and the potential implications will be discussed.

158 **Don Tucker Finalist: Taste And Smell Perception After Metabolic Surgery**

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After undergoing weight loss surgeries, most patients report "taste" changes. However, when we evaluated patients using validated sensory evaluation techniques, we found no changes in perceived taste intensity or sensitivity pre- to post-surgery. Because we assessed participants with pure gustatory stimuli in a fasting state, it is unclear if patients' self-reported "taste" changes are due to retronasal smell/ "flavor" changes or are only

manifested during the fed state. Using a cross-sectional study design, we compared sensory responses in women who underwent metabolic surgery 2-6 years ago (n=15) with a non-operated-BMI equivalent group (n=15) and a normal BMI group (n=15) over two visits: one fed and one fasted. Using a sip-and-spit method, women tasted solutions representative of basic taste qualities containing matching odorants (e.g., sucrose with strawberry extract) with and without nose clips. They used separate general labeled magnitude scales to rate their perceived intensity of taste, smell, flavor, and pleasantness. Results from mixed ANOVAs show that the surgery group rated smell intensity as stronger than the normal BMI group for all stimuli ($p \leq 0.05$); values in the non-operated-BMI equivalent group were intermediate between the other groups. However, all groups rated taste as equally intense and pleasant and displayed similar enhanced taste intensity when tasting samples without vs. with nose clips ($p<0.001$). Feeding conditions failed to affect intensity ratings. Our findings suggest that metabolic surgery is associated with perceiving a stronger intensity of retronasal smell without impact on taste perception and that feeding condition is unimportant for assessing taste or smell intensity perception in women.

160 **Lower Perception Of Odors Intensity In Late Evening May Contribute To Poor Diet Intake In Evening Sleep Phenotypes**

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Evening chronotype (EC), characterized by preference for late bedtime and activity, is linked to unhealthy diet patterns and reduced satiety after 20:00h (biological sleep time), thereby increasing the risk of obesity. Odors guide food choices and exhibit circadian rhythm, yet the relationship between diurnal pattern of smell perception and diet intake in EC remains unclear.Using ecological monetary assessment, healthy-weight participants in Morning chronotype (MC, n=22) and EC (n=21) recorded smell ratings (food and non-food at low and high intensity) and food cravings for 3-days, at 8:00am, 12:00pm, 3:00pm, 6:00pm, 8:00pm, and 10:00pm. The smell identification and threshold scores did not differ between the two chronotypes. Mean intensity ratings for all odors combined were lower for EC vs MC (55.5 vs 42.9, $p=0.03$). Unlike MC, EC reported food odors to be less intense at 6:00 pm, 8:00 pm, and 10:00 pm ($p<0.05$). Odor intensity was a significant predictor of fruit craving ($\beta = 0.290$, $p = 0.033$), % calories from carbohydrate ($\beta = -0.442$, $p = 0.001$) and % calories from total sugar ($\beta = -0.253$, $p = 0.011$). Odor intensity was associated with decreases in fruit craving ($\beta = -0.431$, $p = 0.003$) for the EC. The percent of total calories eaten between timepoints decreased in MC, while it remained relatively stable throughout the day in EC ($\beta = 2.307$, $p = 0.004$). No significant difference in appetite ratings were observed by chronotype and time. Our findings indicate that diurnal variation in smell perception is influenced by sleep phenotype, food odors perceived as less
intense toward the end of the day in EC. This observed pattern in smell perception may contribute to intake of unhealthy diet, potentially increasing the risk of obesity and metabolic disorders in EC.

162 **Defining The Role Of Immature Olfactory Sensory Neurons In Olfaction**

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To better develop strategies to repair damaged brain areas via stem cell-derived neurons, it is imperative to understand how endogenously generated neurons can functionally integrate into existing neural circuitry. The mammalian olfactory bulb (OB) is a valuable model to study the functional integration of adult-born neurons in both the healthy and regenerating brain. Adult-born olfactory sensory neurons (OSNs) go through immature and mature developmental stages as they wire into the OB. We have shown that immature OSNs provide odor input to the mouse OB and exhibit graded responses across a wider odorant concentration range than mature OSNs. Therefore, our hypothesis is that immature and mature OSNs provide distinct, but complementary, odor input to OB neurons. To test this, we employed Gg8-tTA;tetO-hM4Di and OMP-IRES-tTA;tetO-hM4Di transgenic mice to chemogenetically silence either immature or mature OSNs respectively via clozapine N-oxide (CNO) mediated activation of the inhibitory DREADD hM4Di. Following validation, mice completed both olfactory habituation/dishabituation and buried food odor detection tests to determine the effect of silencing immature or mature OSNs on odor-guided behaviors. Silencing mature OSNs reduced odor detection and discrimination ability, whereas silencing immature OSNs affected only odor discrimination. Finally, we imaged odor-evoked responses in GCaMP6s-expressing mitral cells via in-vivo 2 photon microscopy before and after hM4Di-mediated silencing to determine the functional contribution of immature vs. mature OSNs to OB output. Silencing either immature or mature OSNs reduced odor-evoked calcium responses in the OB to varying degrees. Together, these experiments provide new insights into the contribution of immature OSNs to odor processing in the healthy OB.

164 **Irhom2 Regulates The Olfactory Receptor Landscape**

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Olfaction, the sense of smell, relies on the unique ability of olfactory sensory neurons to continuously regenerate and adapt to the environment. Olfactory detection hinges on activation of various combinations of different olfactory receptor types to discern diverse odors. Interestingly, not all receptors are equally represented within the olfactory receptor landscape, depicting the varying ratios or abundance of individual olfactory receptors. The mechanisms underlying these variations, influenced by different genetic and environmental factors, remain poorly understood. To explore how the olfactory receptor landscape is regulated, we investigated the

iRhom2/Adam17 pathway in the olfactory epithelium. iRhom2 is a positive regulator of Adam17 which is an important cell surface metalloprotease known for its involvement in regulating cell survivability via EGFR signaling. We observed that iRhom2 is expressed in a specific subset of mature olfactory sensory neurons. Furthermore, bulk RNAseq on iRhom2 knockout mice reveals that iRhom2 regulates the olfactory receptor landscape, offering a novel perspective on the dynamics of receptor expression in the olfactory system. Additionally, by leveraging publicly available single cell RNAseq datasets we observed that iRhom2 expression is influenced by both odor stimulation and environmental factors. We hypothesize that iRhom2 is important for regulating the olfactory receptor landscape by modulating the odor-dependent survival of the olfactory sensory neurons.

166 **Arl13B Controls Localization Of Pip2 In The Mouse Olfactory Cilia And Neuronal Functional Output.**

Kirill Ukhanov[1], Warren Green[2], Chao Xie[3], Jeffrey Martens[1]

[1]University of Virginia, Charlottesville, VA, United States, [2]University of Florida, Gainesville, FL, United States, [3]Nikon Canada, Toronto, ON, Canada

The small GTPase Arl13b is known to regulate ciliogenesis, protein trafficking, and signaling in primary cilia. Mutations of *ARL13b* have deleterious effects leading to human ciliopathies. Recently, our lab has shown that the loss of Arl13b in early development of olfactory sensory neurons (OSNs) resulted in a delay in neuronal maturation, reduced electro-olfactogram (EOG) and smaller glomeruli in the bulb. However, the role of Arl13b in olfactory cilia in mature OSNs remains largely unknown. Previously published studies revealed the critical role of Arl13b regulating ciliary localization of lipidated cargo proteins including INPP5E. Here, we asked if a similar relationship exists between the two proteins in mammalian chemosensory cilia. First, using an inert lipid probe MyrPalm-GFP ectopically expressed in mature OSNs we found that length and number of cilia in a tissue specific Arl13b-OMP knockout mouse were significantly decreased at 2-month of age. However, cilia length and number were not further affected in 6-month-old KO mice. Notably, the odor-induced EOG did show an age-dependent escalating reduction of the odor sensitivity. Finally, using a PIP2 fluorescent probe (PLC-PH-GFP) expressed in OSNs, we found that the phospholipid was redistributed along the full-length of cilia albeit being short and few. This finding strongly suggested that deletion of Arl13b results in loss of function of INPP5E, which is responsible for proper ciliary localization of PIP2. Further, the kinetics of the EOG evoked by a long 5-sec odor pulse in the Arl13b-OMP knockout phenocopied that of the INPP5E-OMP deficient OSNs as reported previously by our lab. Based on the current findings we hypothesized that in olfactory cilia, Arl13b not only controls phospholipid homeostasis but also may mediate olfactory signaling.

168 **Characterization Of Enhancer Motifs And Transcription Factors That Drive Trace Amine-Associated Receptor Gene Choice**

Maddie Ratkowski[1], Rya Muller[1], Kyungho Seong[1], David Brann[2], Tatsuya Tsukahara[2], Sandeep R. Datta[2], Thomas Bozza[1]

[1]Department of Neurobiology, Northwestern University, Evanston, IL, United States, [2]Department of Neurobiology, Harvard Medical School, Boston, MA, United States

Each olfactory sensory neuron in the mouse nasal cavity chooses to express one allele of one olfactory receptor gene out of >2,000 possible alleles. Olfactory receptor genes comprise two phylogenetically distinct families—a large family of >1,000 odorant receptor (OR) genes, and a smaller family of 14 trace amine-associated receptor (TAAR) genes. Most of what is known about olfactory receptor gene choice has come from studying the ORs and some aspects of TAAR gene regulation appear to differ. We previously characterized two enhancers that are necessary and sufficient for TAAR gene choice. We observe multiple Shared Homologies in the TAAR Enhancers (SHiTE sequences) which contain putative binding sites for the transcription factor Lhx2, which is common to OR enhancers, as well as Nzf, Atf5/Cebpg, and Tbr1, which are unique to the TAAR enhancers. We are currently analyzing the function of these motifs using CRISPR-based mutations in mice. In addition, single-cell sequencing reveals that Tbr1 marks a distinct lineage of OSNs that preferentially express TAARs. We find that knocking out Tbr1 dramatically reduces TAAR gene expression. Our data demonstrate a critical role for Tbr1 in TAAR gene choice and suggest that TAAR enhancer function may be driven by Lhx2, but modulated by a set of other transcriptional regulators including Tbr1.

170 **Flavors And Fragrances Can Modulate Gene Expression Via Epigenetic Changes**

Anandasankar Ray, Rogelio Nunez-Flores, Sachiko Haga-Yamanaka
MCSB, University of California, Riverside, CA, United States

Eukaryotes coevolve with microbiomes and respond to their secreted metabolites. However, little is known about responses to volatile chemicals emitted by microbes. We show that a microbial volatile, diacetyl, and other common related odorants, can alter gene expression in eukaryotes at a distance from their emission source. These structurally-related volatiles inhibit histone-deacetylases (HDACs) differentially. The inhibition occurred with purified human HDACs, increased histone-H3K9 acetylation in human cells, and caused wide changes in gene expression in a range of organisms, including plants, insects, and vertebrates. These epigenetic changes are accompanied by physiological changes in animals and plants. Exposure to vapors slows progression of neurodegeneration in a *Drosophila* model for Huntington's disease, and neurblastoma cancer cell line, like known HDAC-inhibitor drugs. In plants, different HDAC-inhibitory volatiles alter development programs in roots and shoots. Our findings reveal a highly-conserved atypical signaling pathway that modulates gene expression via changes in chromatin from a chemical source at a distance.

172 **Multimodal Olfaction: Neural Mechanisms Underlying Mechanosensation Through Mouse Olfactory System**

Sarang Mahajan, Suhel Tamboli, Susobhan Das, Anindya S Bhattacharjee, Meenakshi Pardasani, Priyadharshini Srikanth, Shruti D Marathe, Nixon M Abraham
Laboratory of Neural Circuits and Behaviour (LNCB), Department of Biology, Indian Institute of Science Education and Research (IISER), Pune, India

The idea of mechanosensation through olfactory system emerged from the seminal works of Adrian and Domino in 1950's (*1, 2*). However, the neural mechanisms underlying such multimodal olfaction remain unknown. While most of the sensory systems encode various features of a single sensory stimulus through multiplexing, the rodent olfactory sensory neurons (OSNs) can process completely distinct stimuli – the mechanical (*3, 4*), and the chemical sensation of odors (*5*). Here, we show that mice can detect and discriminate airflow rates with high accuracy through their nose, independent of whiskers' intactness. The sniffing refinement during the anemo-discrimination and the stimulus- and learning-dependent calcium signals observed in the olfactory bulb (OB) inhibitory circuits confirmed the orthonasal airflow information processing. Genetic perturbation of AMPAR function or the optogenetic modulation of inhibitory circuits bidirectionally shifted anemo-discrimination learning pace, with contrasting phenotypes observed for odor learning. This established the role of OB interneurons in processing anemo-information, and setting the optimal inhibition level for stimulus refinement. Further, the enhanced learning caused by multimodal odor-airflow stimuli at subthreshold levels confirmed the heightened olfactory perception by mechanical stimuli. Our results, thus explain the multimodality of olfaction, and redefine olfactory perception principles. 1. E. D. Adrian, *J Physiol* 114, 4-5p (1951). 2. S. Ueki, E. F. Domino, *J Neurophysiol* 24, 12-25 (1961). 3. T. Connelly *et al*., *P Natl Acad Sci USA* 112, 590-595 (2015). 4. X. Grosmaitre et al., *Nat Neurosci* 10, 348-354 (2007). 5. L. Buck, R. Axel, *Cell* 65, 175-187 (1991).

9:00 - 10:00 AM	Estero Foyer
Coffee Break	

10:00 - 12:00 PM	Calusa EFGH
Chemosensory perception and eating behavior: from inborn variation through gut-brain circuit to COVID-19	

Chair(s): Danielle Reed

10:00 **Chemosensory Perception And Eating Behavior: From Inborn Variation Through Gut-Brain Circuits To Covid-19**

Danielle Reed[1], Joanne Cole[2]

[1]Monell Chemical Senses Center, Philadelphia, PA, United States, [2]University of Colorado School of Medicine , Aurora, CO, United States

This symposium will cover several mechanisms underlying "sensory nutrition" and how chemical sensing in the body, including from the nose, tongue, brain, and gut, affects food intake. Key themes include: i) using the big data approach to explore how genetic variants in taste and olfactory receptor genes affect food preference and food consumption, ii) animal work showing how the gut communicates with the brain to control energy balance, and iii) impacts of COVID-19 on chemosensory perception and eating behavior. The insights presented in this symposium will potentially advance our understanding of personalized nutrition, inform strategies for promoting healthier dietary choices tailored to an individual's genetic makeup, and address the challenges posed by COVID-19.

10:02 **Savor The Flavor: When Covid-19 Silences The Palate**

Sanne Boesveldt[1], Elbrich M. Postma[1,2], Birgit P.M. van Dijk[1]

[1]Division of Human Nutrition and Health, Wageningen University, Wageningen, Netherlands, [2]Smell and Taste Center, ENT department, Hospital Gelderse Vallei, Ede, Netherlands

Taste and smell are fundamental to our food experiences. They drive food preferences, choices, consumptions, and ultimately impact our health. When the Covid-19 pandemic hit the world in 2020, millions of people lost their chemical senses, and while most patients recovered within a few weeks after infection, chemosensory dysfunction turned into a long-term problem for 5-10% of patients. Beyond the immediate realm of chemosensory alteration, the sustained loss of smell and taste is associated with a significant reduction in patients' quality of life, including increased depressive symptoms and nutritional challenges. We set up the COVORTS study to assess the natural progression of smell and taste dysfunction in a prospective cohort over the course of one year, and its impact on eating behavior and quality of life. For this cohort, we recruited 76 patients aged between 18-60 years old with persistent smell dysfunction (> 1 month) after a recent (<3 months) confirmed Covid-19 infection. For a period of one year, patients fill out monthly online questionnaires related to their smell and taste ability, trigeminal sensations, eating behavior (as measured by the Appetite, Hunger and Sensory Perception questionnaire and VAS ratings on food enjoyment and appetite), quality of life (as measured by the Questionnaire of Olfactory Disorders), and perform an at-home smell and taste test. Every three months, psychophysical testing is performed at home, to assess smell and taste function and smell distortions (parosmia). Data collection started in November 2021 and finishes in March 2023. Preliminary results will be presented at the meeting. The insights from this study will help to address one of the challenges posed by (post)Covid and provide patients with appropriate care and nutritional advice.

10:27 **Insulin Modulates Excitatory Drive Of Pyramidal Neurons In The Posterior Piriform Cortex.**

Vaibhav R. Konanur, Celine Sanluecha, Lindsay R. Vivona, Joseph D. Zak
University of Illinois at Chicago, Chicago, IL, United States

Olfactory cues in the environment can signal food availability. Odors associated with nutritive substances initiate anticipatory physiological changes called cephalic phase responses, such as cephalic phase insulin release (CPIR). CPIR is a strong driver of food intake and modulates odor perception. However, little is known about the mechanism through which CPIR modulates odor processing. To address this question, we applied insulin to acute coronal tissue slices of the posterior piriform cortex (PPC; AP: +0.1) while recording from voltage-clamped pyramidal neurons (n = 7). At -70 mV, the average instantaneous frequency (b = -2.30, p <0.01) and the average amplitude of spontaneous excitatory postsynaptic currents (EPSC; b = -1.45, p <0.01) decreased. However, the effects of insulin were heterogeneous. Insulin increased the instantaneous EPSC frequency on a subset of neurons (43%) and it was decreased on a separate subset of neurons (43%). We observed similar results when considering the EPSC amplitudes; 29% of neurons had larger EPSCs following insulin application while another 29% of cells were decreased. The satiety factor, glucagon-like peptide 1 (GLP-1) has been shown to modulate insulin signaling in the olfactory system. Therefore, we hypothesized that hindbrain GLP-1 neurons in the nucleus of the solitary tract (NTS) project to the PPC where they can modulate pyramidal cell excitability. To address this, we injected a retrograde fluorescent tracer, cholera toxin subunit b (CTb), into the PPC. We indeed observed neurons containing CTb in the NTS. Future studies will identify the peptidergic contents and functionality of these neurons. Our data suggest the possibility of NTS GLP-1 neurons projecting to the PPC to modulate olfactory processing.

10:45 **Influence Of Common Missense Variants In Chemosensory Receptor Genes On Food Preferences**

Danielle Reed[1], Liang-Dar Hwang[2], Cailu Lin[1], Paule Joseph[3]

[1]Monell Chemical Senses Center, Philadelphia, PA, United States, [2]The University of Queensland, Brisbane, Australia, [3]Section of Sensory Science and Metabolism (SenSMet), National Institute on Alcohol Abuse and Alcoholism & National Institute of Nursing Research, Bethesda, MD, United States

We investigated the influence of genetic variants within taste and olfactory receptor genes on human food preferences. We analyzed 5,338 common missense variants (minor allele frequency >= 0.05) within 425 non-pseudo taste and olfactory receptor genes and 140 food-liking traits in the UK Biobank (N = 162,006 unrelated individuals of European ancestry; mean age = 57) and identified 830 associations (FDR-corrected p-value <0.05), of which 88 are also associated with their corresponding food intake traits in the UK Biobank. These variants account for more than 0.1% of the variance in 99 individual food preferences, with the highest being 0.22% for grapefruit liking. One variant can affect up to 22 preferences (i.e., *TAS2R1* rs7135018), and 99 variants affect only one specific trait. We replicate 62 associations in the younger Avalon Longitudinal Study of Parents and Children (ALSPAC; N = 2,802 unrelated individuals of European ancestry; mean age = 25), including the *OR2T6* rs6587467 for onion liking (p-value = 5.4×10^{-41} in the UK Biobank and 2.9×10^{-4} in the ALSPAC). In conclusion, we show direct genetic influences on food preferences, which helps understand individual differences in eating behavior and has implications for improving dietary intake through personalized strategies.

11:10 **Gut Influences On Central Feeding Circuits**

Amber L Alhadeff
Monell Chemical Senses Center, Philadelphia, PA, United States

Food intake is regulated by complex biological processes involving sensory food properties (i.e. tastes, smells), gut nutrient sensing, and the brain. Our understanding of how these processes interact to control feeding behavior is incomplete. Deep within the hypothalamus, agouti-related protein (AgRP)-expressing neurons are critical regulators of feeding behaviors that are activated during hunger and inhibited by food. This talk will explore how sensory and nutritive signals influence the endogenous activity patterns of AgRP neurons, and how this information guides food preference and intake.

11:35 **Phenome-Wide Association Analysis Of Supertaster Gene *Tas2R38* Reveals Novel Relationship With Bipolar Disorder And Kidney Function**

Liang-Dar Hwang[1,2], Amanda WY Lim[2], Quimbe Dy[1], Jue-Sheng Ong[2], Caroline Brito Nunes[1]

[1]Institute for Molecular Bioscience, The University of Queensland, Brisbane, Australia, [2]QIMR Berghofer Medical Research Institute, Brisbane, Australia

Background: Hundreds of studies have investigated how taste perception of phenylthiocarbamide and/or propylthiouracil, primarily determined by genetic variation in the bitter taste receptor gene *TAS2R38*, affects human dietary and related health outcomes. Objectives: We utilize publicly available summary results statistics from large-scale genome-wide associations studies (GWAS) to validate previous findings observed in small studies and explore novel associations. Methods: We examine the associations between three *TAS2R38* variants (rs713598, rs1726866, and rs10246939) and 139 food liking traits and 29 food intake traits using GWAS data from the UK Biobank. We further search for their associations in published GWASs using three online platforms (OpenGWAS, Open Targets, and GWAS Atlas) to explore their relationships with health conditions. Results: Our results show that the *TAS2R38* taster alleles are associated with decreased preferences and/or consumption of horseradish, salty food, grapefruit, and alcohol (but only for whiskey, red wine and spirits), increased preferences for cucumber and melon, and increased consumption of tea (p <Bonferroni-corrected threshold of 0.00128). We identify a trend of novel associations between taster alleles and impaired renal function ($p = 9.80 \times 10^{-5}$) and an elevated risk of bipolar disorder ($p = 4.01 \times 10^{-5}$). We found no evidence for an association with obesity or body mass index. Conclusion: This study provides further evidence for/against the impact of *TAS2R38* genotype on preference and consumption and reveals novel associations with kidney function and bipolar disorder that warrant further investigations into the role of TAS2R38 in human health.

10:00 - 12:00 PM	Calusa ABC
Chemosensory mechanisms that drive innate behavior	

Chair(s): Lisa Stowers

10:00 **How Does Vomeronasal Sensing Differ From Taste Or Olfaction?**

Lisa Stowers
Scripps Research, La Jolla, CA, United States

In addition to taste and smell, most terrestrial vertebrates also sense chemosignals through the vomeronasal system. Humans are outliers and do not have the functional capability to experience this modality. The main olfactory system has the capability to detect most volatile chemicals, the taste system additionally detects a subset of non-volatile ligands, while the vomeronasal system detects both volatiles and non-volatile small molecules, peptides, and proteins that partially overlap with taste and smell detection. However, the vomeronasal system is thought to serve an entirely different function than taste or smell becuase its neurons and projection to the brain are separated from, engage different circuits, and express unrelated sensory receptors and signal transduction machinary. The field does not know what function the vomeronasal system provides to complement taste and smell. Here we are using head-mounted mini-endoscopes to study the activity of the vomeronasal sensory neurons during freely moving natural sensation. This approach now enables us to begin to determine the functional 'blind spots' of taste and smell that the vomeronasal system fills. Understanding the relationship between the three chemosensory systems will enable us to know if humans are missing an animal superpower, or if we evolved beyond its tether; perhpas losing this system parially accounts for our remarkable behavioral flexibility.

10:02 **Chemosensory Mechanisms That Drive Innate Behavior**

Lisa Stowers
Scripps Research, La Jolla, CA, United States

Innate behavior is essential for the fitness and social cohesion of a species. Chemosensation powerfully drives the display of many innate behaviors, however, the identity of relevant ligands, mechanisms of sensaiton, neurodevelopment of the system, and circuit mechanisms that link sensation to behavior are still largely unexplored. This symposium will showcase latest progress to understand how chemosensation promotes innate behaivor. The work highlights a variety of model organisms (worms, fly, mouse) with diverse experimental methods (transcriptomics, moledular genetics, biochemistry, neuroscience, and behavior). The diverse studies are expected to complement each other to promote identification and new understanding of common strategies that enable the chemical senses to drive behavior. All speakers will present their work in a context that will be broadly relevena to the ACHemS community.

10:20 **A Modular Circuit Architecture Coordinates The Diversification Of Courtship Strategies In *Drosophila***

Rory T. Coleman[1], Ianessa Morantte[1], Gabriel T. Koreman[1], Megan L. Cheng[1], Yun Ding[2], Vanessa Ruta[1]
[1]Rockefeller University and Howard Hughes Medical Institute , New York, NY, United States, [2]University of Pennsylvania, Philadelphia, PA, United States

Mate recognition systems evolve rapidly to reinforce the reproductive boundaries between species, but the underlying neural mechanisms remain enigmatic. Leveraging the rapid coevolution of female pheromones and male pheromone circuits in *Drosophila,* we provide insight into how the architecture of mate-recognition circuits facilitates their diversification. While in some *Drosophila* species, females produce unique pheromones that act to arouse their conspecific males, the pheromones of most species are sexually monomorphic such that females possess no distinguishing chemosensory cues that males can use for mate recognition. We show that *D. yakuba* males evolved the ability to use a sexually-monomorphic pheromone, 7-tricosene, as an excitatory cue to become aroused and guide courtship. By comparing key nodes in the pheromone circuits across multiple *Drosophila* species, we reveal that this sensory innovation arises from coordinated peripheral and central circuit adaptations: a distinct subpopulation of sensory neurons has acquired sensitivity to 7-tricosene and, in turn, selectively signals to a distinct subset of P1 neurons in the central brain to trigger courtship. Such a modular circuit organization, in which different sensory inputs can independently couple to parallel courtship control nodes, may facilitate the evolution of mate recognition systems by allowing novel sensory modalities to become linked to male sexual arousal. Together, our findings suggest how peripheral and central circuit adaptations can be flexibly linked to underlie the rapid evolution of mate recognition strategies across species.

10:45 **Instinctive Behavior Circuit Development Is Shaped By Chemosensory Input, Sex, And Function**

Harris Kaplan[1], Brandon Logeman[1], Kai Zhang[2,3], Celine Santiago[4], David Ginty[4], Bing Ren[2], Catherine Dulac[1]
[1]Department of Molecular and Cellular Biology, Howard Hughes Medical Institute, Center for Brain Science, Harvard University, Cambridge, MA, United States, [2]Department of Cellular and Molecular Medicine, Center for Epigenomics, University of California, San Diego School of Medicine, La Jolla, CA, United States, [3]Current address: Westlake Laboratory of Life Sciences and Biomedicine, School of Life Sciences, Westlake University, Hangzhou, China, [4]Department of Neurobiology, Harvard Medical School, Howard Hughes Medical Institute, Boston, MA, United States

How does animal behavior emerge developmentally? This question, and particularly the underlying contributions of genetic versus environmental information, has been fiercely debated by generations of scientists, leading Nikolaas Tinbergen to codify developmental issues as one of his Four Questions in the study of animal behavior. Despite this historical spotlight, modern studies of neuronal circuit development have largely focused on sensory systems or prenatal stages. To gain insight into behavior development, we focused on the preoptic area (POA) of the hypothalamus. Recent work has identified molecularly defined neuronal types in the POA that appear dedicated to specific social behaviors (e.g. mating or parenting) or homeostatic functions (e.g. sleep or thirst). However, this work has been carried out exclusively in adults; how these cell types emerge developmentally remains unknown. We molecularly profiled POA cell types in mice using single-nucleus RNA-sequencing and paired ATAC-sequencing at eight ages from late embryo to adult. We identified key stages of POA development, including the perinatal emergence of sex differences, postnatal maturation of signaling networks, and nonlinear transcriptional changes accelerating at the time of weaning and puberty. We next asked how POA development is affected by environmental inputs by examining five mutant lines, each impaired in a specific sensory modality crucial for POA function. This uncovered a major role for vomeronasal input in POA cell type maturation, while other sensory inputs have little to no effect. Altogether, our work paints a picture of POA development as surprisingly sensitive to extrinsic factors, and lays the foundation for future work addressing the origin of instinctive behaviors and their control at various life stages.

11:10 **Recognition Of Predator Threat Through The Vomeronasal Organ In Mice**

Sachiko Haga-Yamanaka
University of California, Riverside, CA, United States

Animals have the innate ability to select optimal defensive behaviors with an appropriate intensity in response to predator threats in specific contexts. Decisions regarding innate defensive behaviors are thought to be computed through the neural circuit including the medial hypothalamic nuclei that contain neural populations controlling defensive behaviors. The vomeronasal organ (VNO) is one of the major sensory input channels through which predator cues are detected and sends ascending inputs to the medial hypothalamic nuclei, especially to the ventromedial hypothalamus (VMH), via the medial amygdala and bed nucleus of the stria terminalis. It is therefore reasonable to hypothesize that predator signals detected by the VNO are processed in the VMH, triggering appropriate defensive behaviors. Our research aims to elucidate the VNO-derived sensory circuitries that regulate defensive behaviors induced by predator cues in different contexts. I will discuss our recent findings regarding the sensation of imminence of predator threat through the VNO in mice. Our results provide a framework for understanding molecular and neural mechanisms underlying the decision making process of innate defensive behaviors in mice.

11:35 **Brain-Wide Networks That Control Olfactory Navigation In *C. Elegans***

Talya S Kramer[1,2], Flossie K Wan[1], Adam A Atanas[1], Sarah M Pugliese[1], Jinyue Luo[1], Steven W Flavell[1]
[1]Picower Institute for Learning and Memory, Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, MA, United States, [2]MIT Biology Graduate Program, Massachusetts Institute of Technology, Cambridg, MA, United States

To survive in their natural environments, animals must select behaviors that are informed by their sensory surroundings. *C. elegans* navigates its environment using olfactory cues, moving towards food or away from harm. The brain-wide networks that coordinate this adaptive behavior are not well characterized. We determined wild type animals' olfactory navigation strategy using high-resolution behavioral tracking during chemotaxis. In contrast to the prevailing 'biased random walk' model, this revealed that reorientations during chemotaxis occur in a directed manner to improve animals' heading in the odor gradient. This suggests that animals can compute and correct their error in olfactory gradients. We next used brain-wide calcium imaging to identify neurons whose activities underlie directed turning. This identified a large group of neuron classes that display asymmetric activities correlated with turning direction. Activity in this network occurs as a stereotyped sequence during directed turns. Optogenetic experiments revealed many of these neurons directly control reorientation frequency and angle during chemotaxis. We further show that the tyraminergic neuron RIM, which provides a synaptic link between the reorientation and steering circuits, is critical for animals to correct their bearing during reorientations. Brain-wide calcium imaging in tyramine-deficient animals revealed broad activity deficits in the turning network. These studies identify a network with stereotyped, sequential activity that underlies error-correcting turns in sensory gradients and show how the neuromodulator tyramine coordinates activity in the network.

12:00 - 1:00 PM	Lunch On Own
Lunch on Own	

1:00 - 3:00 PM	Calusa EFGH
Structural Biology of Chemosensory Receptors	

Chair(s): Hiro Matsunami

1:00 **Introduction**

1:02 **Molecular Recognition Of An Aversive Odorant By The Murine Trace Amine-Associated Receptor Taar7F**

Christopher Tate[1], Anastasiia Gusach[1], Yang Lee[1], Armin Nikpour Khoshgrudi[2], Elizaveta Mukhaleva[3], Ning Ma[3], Eline Koers[2], Qingchao Chen[1], Patricia Edwards[1], Fanglu Huang[4], Jonathan Kim[5], Filippo Mancia[5], Dmitry Verprintsev[2], Nagarajan Vaidehi[3], Simone Weyand[4]

[1]MRC Laboratory of Molecular Biology, Cambridge, United Kingdom, [2]University of Nottingham, Nottingham, United Kingdom, [3]Beckman Research Institute of the City of Hope, Duarte, CA, United States, [4]University of Cambridge, Cambridge, United Kingdom, [5]Columbia University, New York, NY, United States

There are two main families of G protein-coupled receptors that detect odours in humans, the odorant receptors (ORs) and the trace amine-associated receptors (TAARs). Their amino acid sequences are distinct, with the TAARs being most similar to the aminergic receptors such as those activated by adrenaline, serotonin and histamine. To elucidate the structural determinants of ligand recognition by TAARs, we have determined the cryo-EM structure of a murine receptor, mTAAR7f, coupled to the heterotrimeric G protein G_s and bound to the odorant N,N-dimethylcyclohexylamine (DMCH) to an overall resolution of 2.9 Å. DMCH is bound in a hydrophobic orthosteric binding site primarily through van der Waals interactions and a strong charge-charge interaction between the tertiary amine of the ligand and an aspartic acid residue. This site is distinct and non-overlapping with the binding site for the odorant propionate in the odorant receptor OR51E2. The structure, in combination with mutagenesis data and molecular dynamics simulations suggests that the activation of the receptor follows a similar pathway to that of the b-adrenoceptors, with the significant difference that DMCH interacts directly with one of the main activation microswitch residues.

1:27 **Structural And Functional Studies On Bitter Taste Receptors**

Weixiu Xu[1,2], Tian Hua[1,2], Zhijie Liu[1,2]

[1]iHuman Institute, ShanghaiTech University, Shanghai, China, [2]School of Life Science and Technology, ShanghaiTech University, Shanghai, China

The taste sensory system helps us to avoid ingestion of harmful substances. Taste perception is initiated by the physical interaction of tastants with the receptors located on the surface of taste receptor cells (TRCs) on the tongue and palate. In humans, tastants evoke five taste sensations: sweet, bitter, salty, sour and umami. Among the five taste modalities, ion channels transduce sour and salty signals, while bitter, sweet and umami tastes are mediated by G protein-coupled receptors (GPCRs). A distinct group of type 2 taste receptors (TAS2Rs) is responsible for bitter taste perception. TAS2Rs display low sequence identity (<20%) with other GPCRs and are classified as a separate class T GPCR subfamily. TAS2Rs recognize thousands of different bitter molecules. In humans, there are only ~25 TAS2Rs to cover this broad chemosensory space. Furthermore, the TAS2Rs are distributed, not only in the oral cavity, but also in extraoral tissues, including the upper and lower airways, gut, adipose tissue, brain, heart and immune cells. These ectopic bitter taste receptors are involved in a variety of physiological processes and are associated with different diseases. However, there are no bitter receptor structures solved so far. Here we report the cryo–electron microscopy structures of human TAS2R46 complexed with chimeric mini–G protein gustducin, in both strychnine-bound and apo forms. Several features of TAS2R46 are disclosed, including distinct receptor structures that compare with known GPCRs. This study provides a basis for further exploration of other bitter taste receptors and their therapeutic applications.

1:52 **Making Sense Of Scents: Structural Insights Into Odor Detection**

Navid Paknejad, Xiao Fan, Dragana Nesic, Beth Graczyk, Vanessa Ruta
Rockefeller University/HHMI

Olfactory systems must detect and discriminate an enormous diversity of chemicals in the environment. To contend with this challenge, diverse species from humans to insects, have converged on a common strategy in which odor identity is encoded through the combinatorial activation of large families of olfactory receptors, thus allowing a finite number of receptors to detect an almost infinite chemical world. Our lab has been using the insect olfactory system as a window into the structural logic of odor detection. Insects rely on an enormous and highly divergent family of odorant-gated ion channels which have we have been using as an inroad to gain insight into the structural logic of odorant detection. I will discuss recent work that shed light on the architecture, function, and evolution of this receptor family and how they confer insects with the ability to navigate a complex chemical world.

2:17 **Molecular Mechanisms Of Sensory Adaptation**

Corey AH Allard, Nicholas W Bellono
Harvard University , Cambridge, MA, United States

The molecular mechanisms by which major novel traits originate and diversify is a critical and unresolved question in biology. Answering this question requires exploration of how molecular evolution generates changes in gene expression and protein function that translate to novel organismic physiology and behavior. Here, I will discuss the molecular basis underlying the emergence of new sensory systems and how they adapt to facilitate sophisticated behaviors using octopuses and fish with “legs” as models. Collectively, these comparative studies exploit animals with unique or exaggerated traits to reveal novel physiological mechanisms and conserved biological principles.

2:35 **How Do Mammalian Odorant Receptors Recognize Odorants?**

Hiro Matsunami
Duke University, Durham, NC, United States

A key challenge in olfaction research is determining how the system detects and distinguishes odorants with diverse physicochemical properties and molecular configurations. This process involves the combinatorial activation of about 400 olfactory G protein-coupled receptors (GPCRs) in the human genome. The odorant receptor (OR) family consists of two main classes: Class I ORs, sensitive to carboxylic acids, and Class II ORs, which respond to various odorants and constitute the majority of the human repertoire. The process of ORs recognizing chemically diverse odorants is not well understood, mainly due to difficulties in visualizing odorant binding to ORs. Our research aims to offer mechanistic insights into how odorants bind to ORs. Utilizing cryogenic electron microscopy (cryo-EM), we first determined the structure of the activated human OR51E2 bound to propionate, a short-chain carboxylic acid. In OR51E2, the carboxylic acid group specifically interacts with Class I-specific residues in the binding pocket. Altering variable residues within the binding pocket changes the recognition spectrum for carboxylic acids of varying chain lengths. We also explored Class II OR interactions with diverse odorants using a consensus protein design strategy, enabling high-level expression in heterologous cells for protein production and purification. The tractability of consensus ORs facilitated three cryo-EM structures of distinct Class II ORs, each showing unique ligand recognition properties. These structures reveal different odorant-binding and activation mechanisms between Class I and II ORs. Our findings shed light on the molecular basis of odorant recognition, laying a foundation for future research in this field.

1:00 - 3:00 PM	Calusa ABC
Action olfaction across species	

Chair(s): Matt Smear

1:00 **Introduction**
Matt Smear
University of Oregon

1:02 **Perceptual And Non-Perceptual Components Of Sniff Responses To Odors**
Vivek Sagar[1], Guangyu Zhao[1], Gregory Lane[1], Thorsten Kahnt[2], Christina Zelano[1]
[1]Northwestern University, Chicago, IL, United States, [2]NIDA Intramural Research Program, Baltimore, MD, United States

Olfactory perception is intimately associated with sniffing. Sniffing is traditionally considered to be an important aspect of the odor percept, modulating the activity of the olfactory cortex. However, precisely how the olfactory regions process the perceptual and non-perceptual aspects of odorant sniffing remains unclear. In this study, we analyzed an fMRI dataset from 3 human subjects sniffing 160 different odorants over 4320 trials. Our findings show that sniffing patterns vary among odors with distinct percepts; and sniffing could be used to decode the identity of the odorants. We employed representational similarity analysis, revealing that similarities in sniffing patterns correspond to the perceptual qualities of odors. Additionally, canonical correlation analysis helped in identifying sniffing features strongly associated with odor perception. Notably, in primary olfactory and orbital areas, we observed distinct voxel groups favoring either sniffing features or their canonical correlates with perception. Our research also highlights temporal disparities between odor perception and sniffing patterns, suggesting that there is an optimal time window during a sniff that can be used to decode information about odor identity.

1:27 **Don Tucker Finalist: Respiration Coordinates The Olfactory Cortical Code**
Robin M Blazing, Kevin M Franks
Duke University School of Medicine, Durham, NC, United States

Respiration profoundly influences patterns of spontaneous activity across the olfactory system, ranging from the olfactory bulb (OB) to piriform cortex (PCx). A variety of studies have shown that OB mitral and tufted cells, as well as PCx neurons, exhibit phase locking to the respiratory cycle, with a broad distribution of preferred phases across cells. Theoretical and experimental work has suggested that respiratory-phase modulation of neurons in the olfactory system gates sensory responses. There is, however, little experimental evidence to support this hypothesis. To address this question, we used patterned optogenetic stimulation of the OB glomeruli to assess how respiration phase influences the encoding of sensory inputs to the olfactory system. We recorded spiking activity in both the OB and PCx while stimulating one out of ten different glomerulus-sized spots in the OB every 300ms. Post-hoc, we binned each trial by its respiration phase and found that PCx neurons exhibited strong tuning to the phase of stimulation that was invariant to the identity of the stimulated spot. Moreover, across the sniff cycle, the distribution of preferred phases uniformly tiled the sniff cycle. In contrast, OB mitral and tufted cells exhibited much weaker stimulation phase tuning, and cells that were tuned exhibited a preference for inputs arriving during early inhalation. Finally, naris occlusion strongly attenuates stimulation-phase-tuning within PCx, indicating that respiratory modulation of cortical coding has a peripheral origin. Together, these results suggest that PCx implements a filtering operation to selectively and uniformly represent the timing of glomerular responses relative to the respiration phase, a function that may be required to encode temporally fluctuating odorants.

1:45 **The Impact Of Olfactory Cues On Mouse Social Vocalizations**
Joshua P. Neunuebel
University of Delaware, Newark, DE, United States

Communication plays an integral role in human social interactions, and a myriad of neurodevelopmental disorders are characterized by abnormal social communication. Because of their genetic tractability, mice are emerging as an important model system for studying the neurobiology of social behavior. While recent work has started decoding the meaning of mouse ultrasonic communication during social behavior, olfaction's role in modulating social and vocal dynamics is unclear. In today's talk, I will describe the innovative computational tools we use to decipher the complex, active social and vocal behavior of mice. I will then highlight some of our fundamental discoveries that detail how vocal communication shapes social behavior. Next, I will share preliminary data addressing the interplay between olfactory and auditory cues and how these signals regulate mouse social behavior. Finally, I will discuss the importance of multi-modal sensory information in active behavior and potential future steps towards understanding this sophisticated process.

2:10 **Bilateral Sensory Signals For Odor Source Localization In Freely-Moving Mice**
Kevin Bolding[1], Jiayue Tai[2], Dan Leman[3], Ian Davison[4]
[1]Monell Chemical Senses Center, Philadelphia, PA, United States, [2]Tufts University, Department of Biology, Medford, MA, United States, [3]Brandeis University, Department of Biology, Waltham, MA, United States, [4]Boston University, Department of Biology, Boston, MA, United States

During sensory-guided navigation, animals refine their ongoing movement through dynamic, iterative sensorimotor algorithms. In natural contexts, odors signal the location of resources and hazards, offering an ethologically relevant window on motivated sensory search. While odor responses have been studied intensively in head-fixed animals, little is known about the dynamic sensory signals that guide active sensory exploration and strategies that enable motivated search. Animals may navigate by comparing signals across successive samples, using instantaneous comparison across hemispheres, or employ both under different conditions. To measure bilateral odor responses in unrestrained mice, we developed miniaturized microscopy tools for large-scale visualization of neural activity, and imaged both hemispheres of the main olfactory bulb in mice exploring odor sources in an open arena. Sensory-evoked activity occurred in discrete bursts in a restricted area of ~10 cm surrounding the odor source. Increasing proximity to the source activated additional glomeruli, revealing that spatial information is encoded by progressive recruitment of receptors of varying affinity. At close proximity, left and right hemisphere glomeruli exhibited a directional bias in activity for stimuli near the corresponding naris. Our imaging approach enabled identification of bilateral, homologous pairs of glomeruli by their temporally-correlated signals. Differences in pair signals predicted turning in a motivated foraging task. These data suggest that animals may employ multiple strategies to localize odor sources during free exploration, initially comparing the degree of glomerular recruitment across time during early approach phases, and ultimately reading out a bilateral direction code at close proximity.

2:35 **Genetic Dissection Of Active Antennal Sensing Circuits And Mechanisms In *Drosophila***

Marie P Suver[1, 2], Ashley M Medina[2], Katherine I Nagel[2]

[1]Vanderbilt University, Nashville, TN, United States, [2]NYU Langone Health, New York, NY, United States

Animals use a variety of sensors to extract information to navigate the world and survive. Many of these sensors move during behavior, with some actively controlled by muscles for behaviors known as ‘active sensing’. Active sensor movements tune sensation for particular behaviors, extending their function beyond an unactuated sensor. However, the behavioral function of active sensor movements, and the cellular and circuit bases for these behaviors, are not fully understood. In this talk, I will describe our recent work developing a new model for active sensing in the antennal mechanosensory and motor center in the fruit fly *Drosophila melanogaster*. First, I will describe our anatomical work mapping the antennal motor system from muscles towards higher sensory circuits. Next, I will show how fruit flies actively move their antennae to alter tuning of a mechanosensory feature and surprising evidence suggesting that these mechanisms remain unchanged in the presence of attractive odor. Lastly, I will present neural connectomics evidence for direct synaptic input between the antennal olfactory and motor systems, suggesting novel interactions between these systems. Together, this work sheds new light on mechanisms enabling animals to modify how they acquire sensory information for stability during behavior.

3:00 - 3:30 PM	Calusa Foyer
Coffee Break	

3:30 - 4:30 PM	Calusa ABC
The Barry Davis Funding Workshop for New Investigators	

This workshop will include an overview of research, training, and funding opportunities for graduate students, postdoctoral fellows, and early stage investigators. The discussion will provide practical information on how grant applications are processed within NIH/NIDCD, including Institute and study section assignments, the peer review process, Advisory Council activities, pay lines, and the roles of program and review staff.

Chair(s): Merav Sabri, Ph.D

3:30 - 5:00 PM	Great Egret
HISTORY JOURNAL CLUB – 2024: APPETITION	

This year's journal club will highlight the classic work of Anthony Sclafani in uncovering key principles of a phenomenon that he coined "appetition". In contrast to satiation, where post-ingestive signals suppress gustatory pleasantness (that third piece of cake doesn't taste nearly as good!), appetition refers to the processes that promote ingestive behaviors. Tony's work emphasized a paradigm-shifting concept- that there are also post-ingestive reward signals. This has a number of important implications-- not only do such signals amplify hedonic value of tastes but they can also differentially condition liking. The interaction between taste and post-ingestive reward signals has a major impact on driving eating behavior and food choice. During the journal club, we will also discuss recent work that has begun to uncover the peripheral and central mechanistic bases for these phenomena.

Introduction: Dr. Ann-Marie Torregrossa

CLASSIC PAPER

Dr. Anthony Sclafani
• Zukerman S., Ackroff, K. and Sclafani, A Rapid post-oral stimulation of intake and flavor conditioning by glucose and fat in the mouse. Am J Physiol Regul Integr Comp Physiol 301: R1635-R1647, 2011

TO THE PRESENT: Dr. Molly McDougle
• Separate gut-brain circuits for fat and sugar reinforcement combine to promote overeating Molly McDougle 1, Alan de Araujo 2, Arashdeep Singh 3, Mingxin Yang 3, Isadora Braga 4, Vincent Paille 5, Rebeca Mendez-Hernandez 6, Macarena Vergara 2, Lauren N Woodie 7, Abhishek Gour 8, Abhisheak Sharma 8, Nikhil Urs 9, Brandon Warren 10, Guillaume de Lartigue 1Cell Metab 2024 Feb 6;36(2):393-407.

Wrap-up: other relevant data & synthesis (Dr. Lindsey Schier)

4:30 - 4:45 PM	Calusa ABC
The BRAIN Initiative® Program: Understanding Circuits Program Funding Opportunities	

The National Institute on Deafness and Other Communication Disorders (NIDCD), one of the participating institutes in the NIH BRAIN Initiative, is hosting an informative workshop on the BRAIN initiative program. The workshop will include an overview of various funding opportunities and guidance for prospective and current NIDCD applicants.

Chair(s): Merav Sabri, Ph.D.

4:45 - 5:00 PM	Calusa ABC
NIDCD Extramural Clinical Trials	

This workshop will provide investigators an overview of how NIDCD approaches extramural clinical trials. The goal of this session is to help investigators determine clinical trials risks, select the most appropriate funding opportunity as well as highlight important points to consider when planning an NIDCD clinical trial. Investigators will also gain an understanding of how NIDCD manages clinical trials.

Chair(s): Trinh Ly, MD

5:00 - 5:45 PM	Calusa ABC
AChemS 2024 Codefest Presentations	

Participants from the AChemS 2024 Codefest will present their findings from the new Olfaction Challenge dataset.

5:00 - 6:00 PM	Great Egret
Meet the Editors	

Chemical Senses is the premier journal focused on the science of smell, taste and chemesthesis in humans and other animals. It is also the official journal of five scientific societies devoted to chemosensory science, including the Association for Chemoreception Sciences. This session will discuss the many advantages of publishing in your society journal, the journal's review and publication processes, and journal policies and new initiatives. After a short presentation by Editor-in-Chief Steven Munger, the session will include a Q&A session with a panel of the journal's executive editors to address questions from the audience and add their own perspectives.

5:00 - 6:00 PM	Calusa Foyer
Career/Networking Social	

6:00 - 7:00 PM	Dinner On Own
Dinner On Own	

7:00 - 9:00 PM	Calusa EFGH
Award Lectures	

Chair(s): Alfredo Fontanini

7:00 **Achems Young Investigator Awardee**

7:30 **Award For Research Excellence In The Psychophysics Of Human Taste And Smell**

8:00 **Ajinomoto Awardee**

Max Mozell Awardee: Sequential Activity Of Ca1 Hippocampal Cells Constitutes A Temporal Memory Map For Associative Learning In Mice

Ming Ma[1], Fabio Simoes de Souza[1,2], Gregory L. Futia[3], Sean R. Anderson[4], Jose Riguero[4,5], Daniel Tollin[4,5], Arianna Gentile-Polese[1], Jonathan P. Platt[6], Kira Steinke[7], Naoki Hiratani[8], Emily A. Gibson[3,5], Diego Restrepo[1,5]

[1]Department of Cell and Developmental Biology, University of Colorado Anschutz Medical Campus, Aurora, CO, United States, [2]Center for Mathematics, Computation and Cognition, Federal University of ABC, Sao Bernardo do Campo, Brazil, [3]Department of Bioengineering, University of Colorado Anschutz Medical Campus, Aurora, CO, United States, [4]Department of Physiology and Biophysics, University of Colorado Anschutz Medical Campus, Aurora, CO, United States, [5]Neuroscience Graduate Program, University of Colorado Anschutz Medical Campus, Aurora, CO, United States, [6]Department of Neurosurgery, University of Colorado Anschutz Medical Campus, Aurora, CO, United States, [7]Integrated Physiology Graduate Program, University of Colorado Anschutz Medical Campus, Aurora, CO, United States, [8]Department of Neuroscience, Washington University, St. Louis, MO, United States

Sequential neural dynamics encoded by “time cells” play a crucial role in hippocampal function. However, the role of hippocampal sequential neural dynamics in associative learning is an open question. We used two-photon Ca^{2+} imaging of dorsal CA1 (dCA1) neurons in the stratum pyramidale (SP) in head-fixed mice performing a go-no-go associative learning task to investigate how odor valence is temporally encoded in this area of the brain. We found that SP cells responded differentially to the rewarded or unrewarded odor. The stimuli were decoded accurately from the activity of the neuronal ensemble, and accuracy increased substantially as the

animal learned to differentiate the stimuli. Decoding the odorant valence from individual SP cells responding differentially revealed that decision-making took place at discrete times after stimulus presentation. Prediction of odorant valence did not correlate linearly with lick behavior and prediction of odorant valence for error trials was associated with prediction in correct trials. In contrast, lick prediction decoded from the ensemble activity of cells in dCA1 correlated linearly with lick behavior. Our data indicates that sequential activity of SP cells in dCA1 constitutes a temporal memory map used for decision-making in go-no go odorant discrimination associative learning.

101 **Genetic Deletion Of *Ace2* In Taste Buds Alters Peripheral Taste Function And Lingual Macrophage Density In Male Mice**

Emma Heisey[1], Jaeshia Lindsay[1], Guangkuo Dong[3], William Garcia[1], Yang Shi[2], Lin Gan[1], Lynnette McCluskey[1]

[1]Department of Neuroscience and Regenerative Medicine, Medical College of Georgia, Augusta University, Augusta, GA, United States, [2]Division of Biostatistics and Data Science, Department of Population Health Sciences, Medical College of Georgia, Augusta University, Augusta, GA, United States, [3]Department of Cell Biology and Physiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, United States

Angiotensin-converting enzyme 2 (Ace2) is the primary receptor utilized for viral entry of severe acute respiratory syndrome coronavirus 2 (Sars-CoV-2), which is characterized by the loss of taste, smell, and chemesthesis. Endogenous Ace2 acts as a negative regulator of the renin-angiotensin-aldosterone system (RAAS) which mediates fluid balance, blood pressure, and inflammation in tissues such as the heart, lungs, and kidneys. Ace2 is downregulated following viral entry, releasing the break on RAAS inducing a proinflammatory environment. Currently little is known about the biological role of Ace2 in the taste system. To address this gap, we developed a novel *Ace2*$^{fl/fl}$*: K14-Cre* mouse strain ("*Ace2* cKO") to conditionally delete *Ace2* from taste buds and surrounding lingual keratinocytes. We tested peripheral taste function by recording from the chorda tympani (CT) nerve which transmits activity from the anterior taste buds to the brain. Neurophysiological changes in CT responses to sweet and sour stimuli were sex specific. Responses to the sweet stimuli, sucrose, and acesulfame-K, were enhanced, while citric acid responses were diminished in male *Ace2* cKO mice. Responses to salt, bitter, tactile, warm, and cool stimuli were similar among strains. These results suggest that under normal conditions Ace2 regulates taste input to the brain in males. We also quantified CD68+ macrophages as an indication of lingual inflammation and found that male *Ace2* cKO mice had significantly elevated macrophage densities compared to male *Ace2*$^{fl/wt}$ controls. Thus, Ace2 in taste buds modulates local inflammation as well as sweet/sour responsiveness in males. Ongoing studies focus on the regulation of additional lingual inflammatory markers and morphological changes in taste cells as a basis for altered taste function.

103 **The Relationship Between Chronic High Fat Diet Consumption And Taste Bud Number In Male And Female Rats.**

Daniel /M Gaines, Lisa/ A Eckel
Florida State University, Tallahassee, FL, United States

Inflammation arising from diet-induced obesity has been associated with a decline in taste bud number in male rodents. Specifically, 8-10 weeks of HFD consumption decreased the number of fungiform papillae (FP) in a region of interest on the anterior tongue as well as the number of taste buds within the circumvallate papillae (CVP). In contrast, a study in female rats found no reduction in the number of FP across the entire anterior tongue or taste buds in the CVP following similar exposure to HFD. Because estrogens have anti-inflammatory effects, these discrepant findings may be related to sex differences in the response to chronic high fat diet consumption. To test this hypothesis, the current study exposed age-matched male and female rats to chow or a 45% HFD for 10 weeks, during which time body weight and food intake were monitored daily. At the end of the experiment, body composition was assessed via EchoMRI and tongue tissue was collected for subsequent quantification of the number of FP and taste buds within the CVP. Availability of the HFD promoted a transient (1-2 week) increase in caloric intake in both sexes. This overconsumption was associated with an increase in percent weight gain and body fat that was more pronounced in males, compared to females. There was no effect of HFD exposure on the total number of FP across the anterior tongue in either sex. Quantification of FP within a region of interest (similar to prior work in males) and the number of taste buds in the CVP is ongoing. Current findings suggest that diet-induced reductions in FP may be restricted to a small portion of the anterior tongue. Ongoing work should reveal greater insight into the relationship between chronic HFD exposure and taste bud number and whether this may be sexually dimorphic.

105 **Endogenous Tagging Of The Proton Channel And Sour Receptor Otop1 Reveals Its Apical Localization In Taste Receptor Cells**

Joshua P. Kaplan[1], Ziyu Liang[1], Paul Cohen[2], Emily R. Liman[1]

[1]University of Southern California, Department of Neurobiology, Los Angeles, CA, United States, [2]Rockefeller University, Department of Molecular Metabolism of , New York, NY, United States

Sour taste allows animals to identify acids in potential foods and generally drives avoidance behavior. The gustatory response to acids has been shown to require OTOP1, a proton-selective ion channel found in Type III taste receptors cells that mediate sour taste. More recently OTOP1 was shown to also function as a sensor for the taste of ammonium chloride, which alkalinizes the cell cytosol, creating a driving force for proton entry. However, how OTOP1 is able to transduce a change in extracellular pH or ammonium within the oral cavity to an electrical impulse is still poorly understood. Here we addressed the most basic question: where in taste cells is OTOP1 localized? To localize the OTOP1 channel, we generated a mouse strain in which an HA tag is inserted into the 5-prime region of the Otop1 gene, generating a functional N-terminally tagged OTOP1 channel. Using this mouse and high-resolution imaging, we are able obtain cellular and subcellular localization of the channel

protein. We find that OTOP1 is highly localized to the actin-rich apical tips of taste receptor cells as well as to a compartment immediately below the tight junctions defined by expression of Zonula Occludens-1 (ZO-1). A similar distribution is found in taste cells throughout the oral cavity and larynx. The apical localization of OTOP1 supports its function as a taste receptor, constrains models for sour taste signaling, and suggests that OTOP1 may be accessible to orally available compounds that could act as sour taste modifiers.

107 **Title: Immune Surveillance Pathways In Taste Papillae**

Abdul Hamid Siddiqui, Salin Raj Palayyan, Sunil K Sukumaran
University of Nebraska- Lincoln, Lincoln, NE, United States

The taste tissue is continually exposed to a diverse array of microbes; most of these are commensal, but some are pathogenic. Animals have a remarkable mucosal immune system consisting of Microfold (M) cells that trancytose microbes and present them to intraepithelial lymphoid cells. We recently found that type II taste cells have gene expression patterns like those of M cells. RANKL, a growth factor required for M cell differentiation upon administration highly upregulated the M cell marker genes in type 2 taste cells. At the same time, knock out of *Spib*, a transcription factor that is essential M cell development completely abrogated this upregulation seen upon RANKL administration. This finding highlights possible role of these structures in immune surveillance. To identify the immune cells associated with the taste tissue, we conducted scRNASeq of CD45+ cells isolated from lingual lamina propria. Multiple subtypes of immune cells were identified, including T and B cells, all three subtypes of innate lymphoid cells, monocytes, macrophages, Langerhans cells, neutrophils, and mast cells. The distribution of these cells in the circumvallate papillae and associated von Ebner's glands was determined using RNAScope. Additionally, we investigated the impact of RANKL and LPS treatment on the abundance and distribution of immune cells in these tissues. Finally, we conducted bioinformatic analyses to identify potential immune cell- taste cell signalling pathways. Our study provides a detailed description of taste papillae associated immune cells and lays the groundwork for future hypothesis driven- studies of their role in taste cell homeostasis and its perturbation in injury and infection.

109 **More Than Fat And Protein: Product Characteristics That Contribute To Reduction Of Capsaicin-Induced Oral Burn**

Justin M Gaiser[1, 2], John E Hayes[1, 2]

[1]Sensory Evaluation Center, The Pennsylvania State University, University Park, PA, United States, [2]Department of Food Science, The Pennsylvania State University, University Park, PA, United States

It is widely accepted that milk provides the greatest relief from oral burn caused by capsaicin, an effect typically attributed to its fat content and temperature. Previously, Lawless reported partitioning lipophilic capsaicin in fat reduces burn while Green showed lower temperature reduces burn. Recent research shows dairy and non-dairy proteins also reduce capsaicin burn, suggesting multiple factors can reduce oral burn from chilies. Here, we investigated the effectiveness of different rinses with varied textures, temperatures, and sugar, fat, and protein content. Specifically, we tested ice cream, Italian ice, yogurt, lassi, cold water, and warm water. Participants rinsed with a 5ppm capsaicin solution, then with a test rinse, before rating the intensity of oral burn continuously for 2 minutes on a general Labeled Magnitude Scale (gLMS). Visual inspection of the time-intensity (TI) curves revealed that all samples performed better than warm water. Italian Ice performed on par with cold water, which did better than yogurt. Pairwise comparisons of curves showed ice cream and lassi had significantly lower burn ratings at some points throughout the rating period than either water sample. We extracted various scaffolding parameters for each TI curve, finding that ice cream and lassi had the lowest areas-under-the-curve and the greatest percent decrease from their maxima, with ice cream performing slightly better in both. These data support the view that it is a combination of product factors that reduce oral burn, including fat content, protein content and temperature. More research is required to determine the relative weight of these factors in combination, given the multiple mechanisms underlying burn reduction.

111 **Improved In Silico Models Of The Bitter Taste Receptors Facilitate Drug Discovery Using A Combination Of Traditional High Throughput Screening And Machine Learning Approaches**

Muhammad Mirza[1], Purshotam Sharma[1], Daniel Meister[1], Aziz Abu-Saleh[1], Michael French[2], Richard Ho[2], Pat Charmley[2], John Trant[1]

[1]Trant Lab, University of Windsor, Windsor, Canada, [2]Amaro Therapeutics, Inc., New York, NY, United States

The bitter taste receptors (TAS2R) are a family of G-protein coupled receptors with 25identified members and recognize a series of “bitter” compounds. Curiously, these receptors are ubiquitously expressed outside the oral cavity and likely play additional roles in cellular regulation beyond taste. Drug discovery, especially hit identification, has been significantly accelerated through the application of in silico methods, but the simple-to-use tools have limited applicability to highly dynamic membrane-bound GPCRs, and this has slowed progress. In this presentation we discuss the methods used to generate new models of all 25 members of this family, the validation of these tools, the application of both traditional and machine learning methods to accelerate initial discovery, and the absolute need to conduct thorough all-atomic computational investigations (molecular dynamics and free energy perturbation calculations) to generate useful data. We consequently highlight the suite of approaches employed in this collaboration between Amaro Therapeutics and the Trant Team at the University of Windsor to tackle challenging problems with low structural information in the GPCR drug discovery space. Consequently, we strongly emphasize the need for building accurate models that consider the composition of the lipid membrane, and the need to be cautious when over-relying on hyped tools such as Alpha Fold 2, machine learning, and neural networks when they may not be the proper tools for the job.

113 **Human Parietal Cells In Culture Release Satiating Serotonin In Response To Bitter Peptides Formed During Digestion Of Pea Protein Hydrolysates, And Demonstrate Enhanced Mechanisms Of Gastric Acid Secretion Via Bitter Taste Receptors Tas2R4 And Tas2R43**

Katrin Gradl[1,3], Veronika Somoza[2,3,4]

[1]TUM School of Life Sciences, Technical University of Munich, Freising, Germany, [2]Chair of Nutritional Systems Biology, Technical University of Munich, Freising, Germany, [3]Leibniz Institute for Food Systems Biology at the Technical University of Munich, Freising, Germany, [4]Department of Physiological Chemistry, Faculty of Chemistry, University of Vienna,, Vienna, Austria

Shifting from meat-based diets toward plant-based diets could help to substantially reduce greenhouse gas emissions from the agri-food sector. From a technological perspective, plant-based diets require different processing technologies as compared to meat-based diets. For dietary proteins, e.g., plant-derived proteins require hydrolyzation steps due to their limited solubility in water. These hydrolyzation steps result in protein hydrolysates which often demonstrate a bitter off-taste. Although this bitter off-taste limits the sensory attractiveness of protein hydrolysates, the bitter taste quality has been hypothesized to be associated with stimulating effects on mechanisms regulating digestion and satiation via activation of gastro-intestinal bitter taste receptors (TAS2Rs). Here, we demonstrate a less bitter tasting pea protein hydrolysates (PPH, sensory analysis) to be cleaved into the three bitter tasting peptides (BTPs) EELEK, VPE and EWR (UHPLC-Time-of-Flight Mass Spectrometry, qNMR), whereas the *in vitro* stimulated gastric digestion of a stronger bitter tasting PHH revealed the three BTPs YPYPR, YNDQDTPVI, ALEPDN. All six BTPs similarly stimulated cellular proton secretion (pH-sensitive fluorescence) as key mechanism of gastric acid secretion via functional involvement of TAS2R4 and TAS2R43 (CRISPR-Cas9 ko approach and qPCR). In contrast, the release of the satiating hormone serotonin (ELISA) in human gastric parietal cells in culture (HGT-1 cells) when tested in equal concentrations was significantly higher after HGT-1 exposure to EELEK, VPE, and EWR vs. YPYPR, YNDQDTPVI, ALEPDN. Taking into consideration that YNDQDTPVI was formed in 50-fold higher amounts than the BTPs, this peptide is hypothesized to be most effective in *in-vivo* conditions, which needs to be verified in future studies.

115 **Taste Signaling Proteins Play A Protective Role In Response To Pathobiont Microbes In The Colon**

Defu Yu[1], Hao Lei[1], Yan-Bo Xue[1], Yi-Hong Li[1], Shi-Meng Gong[1], Yuan-Yuan Peng[1], Kai-Fang Liu[1], Damiano Buratto[1,2], Yisen Yang[1], Sai-Sai Zhang[1], Ruhong Zhou[1,2], Liquan Huang[1]

[1]Zhejiang University, Hangzhou, China, [2]Zhejiang University Shanghai Institute for Advanced Study, Shanghai, China

Taste signaling proteins have been found not only in taste buds in the oral cavity but also in many extraoral tissues. They are known to play various roles in different tissues. In particular, a rare type of epithelial cells, tuft cells, also expresses these signaling proteins and has been found to contribute to the detection of and responses to allergens, bacteria, protists, helminths and other pathogenic microbes. It is, however, not fully understood how many different types of irritants and pathogens they can help sense and what exact roles they play in different pathophysiological conditions. In this study, we utilized genetically engineered mouse lines with the taste signaling proteins Trpm5 and Gγ13 ablated along with wild-type control mice, and established mouse models with the abundant anaerobic pathobiont microbes of *Ruminococcus gnavus* in the colons to mimic some medical disorders that are associated with diarrhea, inflammatory bowel disease, pouchitis and other conditions. We found that oral administration of the pathobiont microbes can increase the number of tuft cells in the proximal colon whereas the lysate of the microbes can activate the Gγ13-PLCβ2-Trpm5 taste signaling pathway and release the cytokine interleukin-25 from these tuft cells. Abolishment of Gγ13 or Trpm5 reduces the expression of gasdermins C2, C3 and C4, and increases apoptosis in the proximal colon. Our data indicate that these taste signaling proteins are not only involved in the detection of the pathobiont bacteria but also help prevent apoptotic cell death and protect the integrity of the colonic epithelium.

117 **Molecular Basis Of Bitter Taste Receptor Tas2R1 Activated By Anti-Hiv Drugs Lopinavir And Ritonavir**

Jiao Wen[1], Xinyi Zhou[1], Yongcheng Lu[1], Shurui Chen[1], Keman Xu[1], Meng Cui[1, 2]

[1]Department of Pharmaceutical Sciences, School of Pharmacy, Bouvé College of Health Sciences, Northeastern University, Boston, MA, United States, [2]Center for Drug Discovery, Boston, MA, United States

The World Health Organization (WHO) recommends the use of protease inhibitors (PIs), specifically lopinavir/ritonavir (LVP/r), as the primary treatment for children aged three and older infected with the human immunodeficiency virus (HIV). LVP/r is typically available in liquid formulations, facilitating administration in children who cannot swallow tablets. However, the strong bitter taste associated with LVP/r poses a significant challenge for patient adherence, particularly in young children. This bitterness has been shown to impact adherence and, consequently, the survival rates of children with HIV. Addressing the need for more child-friendly formulations is crucial to eliminate the unpleasant bitter taste associated with pediatric HIV/AIDS drugs, ensuring better adherence and improved outcomes for children living with HIV. Bitter taste blockers function by either binding to bitter taste receptors or disrupting signal transduction pathways, reducing or masking the bitter taste. A critical aspect of designing these blockers is identifying the drug's receptor binding sites. In our previous work, we identified the human bitter taste receptors activated by lopinavir and ritonavir: TAS2R1 and TAS2R13 responded to lopinavir, while ritonavir activated TAS2R1, TAS2R8, TAS2R13, and TAS2R14. Our current study goes further by revealing specific binding sites for LPV/r on the TAS2R1 binding pocket, and identifying the critical residues for drug-receptor interactions using molecular modeling and mutagenesis. This discovery serves

as a valuable guide for developing targeted inhibitors, given the significance and specificity of TAS2R1 for the bitterness of LVP/r drugs.

119 **Olfactory Stimulation Induces Fragrance-Specific Modulation Of Physiological Biomarkers Associated With Arousal, Vigilance, And Sustained Attention**

Robert Assini, Lalit Damodaran, Anshul Jain
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Among sensory modalities, olfaction is uniquely positioned with preferential access to centers of emotional and cognitive processing. This neuroanatomical organization allows the olfactory system to directly influence cognitive performance via a direct path through the limbic system as well as indirect neocortical pathways. Advances in physiological sensor technology, such as electroencephalography (EEG) and electrocardiography (ECG), have engendered the ability to quantify the effect of olfactory stimulation on physiological biomarkers associated with arousal and attentional vigilance. Here we report fragrance-specific, covarying modulation of arousal and attentional vigilance using EEG and ECG. To measure the impact of this physiological modulation, we employed the Continuous Temporal Expectancy Task, a behavioral test designed to assess distractibility and one's ability to sustain attention. Participants performed the task remotely in their own home office setting, while utilizing a custom designed WiFi-enabled and remotely controllable scent dispersion device. Devices were pre-loaded with either a putatively energizing or relaxing fragrance, as measured in our in-lab EEG/ECG experiments, and an unscented cartridge which served as a control. While not statistically significant, we observed fragrance-specific modulation in the hypothesized directions. The putatively energizing fragrance enhanced performance ($n = 18$, $p = 0.08$) on the task, and the putatively relaxing fragrance diminished performance ($n = 21$, $p = 0.05$). We propose that olfactory stimulation has the potential to influence general physiological arousal and to facilitate associated cognitive performance. Future research is needed to further elucidate factors underlying the influence of scent on specific cognitive functions.

121 **Rational Design Of Antagonists For Cigarette Smoke Odors**

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The field of malodor blocking currently relies on the experience of highly trained perfumers as well as trial and error to develop new molecules that alter the perception of unpleasant odors. Here, we used rational methods to identify and validate antagonists that alter human perception of two key components (1-pentanethiol and guaiacol) in cigarette smoke odor, which has negative health consequences due to its ability to increase the urge to smoke. After preliminary screening via odorant interaction effects on heterologously expressed odorant receptors and human odor perception we did split-nostril experiments to evaluate central versus peripheral effects. Using isointense concentrations of the most effective blocking odorants, we compared suppression by dichorhinic stimulation (one component to each nostril) versus physical mixture stimulation (both components to the same nostril). We identified two effective blocking odors: Citronellal reduced the perceived intensity of 1-pentanethiol and methyl-2-methylbutyrate reduced the perceived intensity of guaiacol. The intensity reduction occurred when the masking and target odorants were given as physical mixtures to the same nostril, but not when delivered as dichorhinic mixtures. In addition, we found no correlation between blocking effectiveness and odor pleasantness. We conclude that these blocking odors are acting at the periphery, most likely as antagonists of the odorant receptors most responsible for perception of the malodors. These results offer proof of principle that blockers for specific malodors can be identified through rational approaches.

123 **Effects Of Physical Exercise And Olfactory Training With Pleasant And Unpleasant Odors On Verbal Fluency And Depression**

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Mechanisms of olfactory training (OT) in older adults require a more profound understanding, considering its potential beneficial effects in age-related olfactory, cognitive, and affective decline. To address this question, we examined the role of OT odor hedonics in 128 participants aged between 50 to 85 years ($M_{age} = 68.3 \pm 7.2$; 25 men). Additionally, we explored the role of physical activity in possible changes in olfactory function, depression score, and cognitive outcome. Participants were randomly assigned to one of four groups, of which two performed OT with either a) pleasant or b) unpleasant odors, one c) performed physical exercises and no OT, or d) a control group without OT or physical exercises. Results indicate a beneficial effect of OT, both with pleasant and unpleasant odors, on cognitive function, as measured with verbal fluency. Such an influence was particularly noted in the OT group exposed daily to unpleasant odors which may be caused by the activating effects of unpleasant stimuli on cognitive processes. Furthermore, physical exercise alone also caused an increase in verbal fluency, even though the effect was weaker compared to both OT groups. Finally, a significant beneficial effect of OT on depression score was noted, but only in the group that, in the pre-training appointment, displayed relatively robust depression symptoms. OT may be of particular use for older people due to their risk of age-related cognitive decline and depression.

125 **Greater Olfactory Awareness Promotes Increased Connectedness To Nature And Wellbeing**

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As the world urbanizes, human beings are experiencing increasingly less contact with and connection to nature. This includes a substantial decrease in chemosensory experiences from the natural environment for our species. Contrary to popular belief, human well-being is dependent upon exposure to a range of olfactory environments, including natural ones. To assess how natural environments affect well-being through olfactory experiences, we have collected survey data from 693 participants (age range 18-77 years old, 50.4% women) residing for at least 3 years in 8 countries (Australia, Canada, Ireland, Israel, New Zealand, South Africa, UK, and USA, N =80-95 per country). The tools used are: a shortened version of the Olfactory Awareness Scale[1], similarly constructed questionnaires on visual and auditory awareness, the Connectedness to Nature Scale[2], the OECD well-being index, and the shortened Perceived Stress Scale (PSS-4). Results reveal that the frequency of contact with nature significantly correlates with connectedness to nature ($\varrho = 0.29$, $p < 0.001$) and well-being ($\varrho = 0.17$, $p < 0.001$). Participants with greater olfactory and visual awareness report greater well-being (olfactory: $\varrho = 0.08$, $p < 0.05$, visual: $\varrho = 0.12$, $p < 0.01$) and reduced perceived stress (olfactory: $\varrho = 0.17$, $p < 0.001$, visual: $\varrho = 0.19$, $p < 0.001$; auditory: $\varrho = 0.20$, $p < 0.001$). Individuals exposed to parks and the wilderness, rather than neighborhood trees, show greater olfactory awareness and stress reduction (parks: $\varrho = -0.28$, $p < 0.001$, wilderness: $\varrho = -0.2$; $p < 0.05$; neighborhood trees: $\varrho = -0.1$, ns). These preliminary data suggest that wellbeing benefits from nature contact which may be promoted by olfactory awareness.

127 **Don Tucker Finalist: Developmental Changes In Retronasal Smell Perception In Early Childhood**

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Flavor perception is a critical determinant of food choice, which directly relates to risk for disease. Previous work has shown that early childhood marks a critical time for establishing flavor preferences. An understanding of flavor perception in young children could thus inform early-life interventions aimed at modifying eating behavior and reduce health risks later in life. Often referred to simply as “taste”, flavor is in fact a multisensory experience that combines taste and retronasal olfaction. Although taste preferences are innate, the development of retronasal odor preferences remains unknown, partly due to the difficulty in assessing flavor perception in young children. The primary goal of this study is to validate a novel protocol for assessing flavor preferences in children and provide new insight into the development of retronasal odor perception. Children ages 3 to 6 years old (n=82) and one of their parents (n=82) were asked to sample solutions containing either a taste or odor. A three step protocol was implemented to assess detection, hedonic evaluation, and perceived intensity using a pictorial rating scale. Detectability and hedonic ratings for sweet and bitter tastes followed predictable patterns, and were stable with age, demonstrating validity of the rating scale. With respect to odor perception, several differences were observed between children and adults: detectability of odors was lower among children, and hedonic ratings of retronasal odors showed higher variability in children. This suggests that retronasal odor preferences are not innate and can potentially be modified by experience. Ongoing work focuses on the relationships between retronasal odor perception and individual differences in exposure.

129 **Fezf1 Is Required For The Proper Development Of The Terminal Nerve Of Rodents.**

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The nasal placode (NP) gives rise to diverse neurons, including olfactory, vomeronasal, Gonadotropin-releasing hormone-1 (GnRH-1), and terminal nerve (TN)/pioneer neurons. The GnRH-1 neurons are essential for regulating the hypothalamic-gonadal (HPG) axis, influencing puberty and fertility. During embryonic development in mammals, the GnRH-1 neurons migrate from the developing vomeronasal organ (VNO) anlage to the hypothalamus along the axonal projections of the TN. In mice, TN neurons express Prokineticin receptor 2 (Prokr2). Genetic tracing experiments indicate that the TN neurons are distinct from olfactory, vomeronasal, and GnRH neurons. Pioneer/TN neurons have been previously implicated in inducing olfactory bulb morphogenesis. Incorrect development and migration of GnRH-1 neurons can lead to hypogonadotropic hypogonadism (HH). HH is clinically defined as Kallman syndrome (KS) when associated with impaired olfactory system development. The transcription factor Fezf1 is crucial for proper olfactory system development. Fezf1 loss-of-function has been linked to KS in human and mouse models. Using Fezf1GFP Knock-in/out reporter mice, we observed that GnRH-1 neurons do not express Fezf1. However, by crossbreeding Fezf1GFP mice with Prokr2cre/R26R we observed that Fezf1 is expressed by the TN neurons. Analyses of ProKr2Cre traced Fezf1 KO suggest cell-autonomous effects of Fezf1 on TN development. Our data provide a new paradigm to comprehend the cellular/molecular etiology of KS in humans.

131 **Tracing The Multipotent P63/Keratin5 Basal Progenitor Cells Of The Non-Sensory Epithelium Of The Vomeronasal Organ Of Rodents.**

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The Vomeronasal organ (VNO) is a part of the accessory olfactory system, which detects pheromones, which are chemical signals that trigger a large spectrum of sexual and social behaviors. The vomeronasal epithelium (VNE) shares several features with the epithelium of the central olfactory epithelium (MOE). However, it is a distinct neuroepithelium populated by chemosensory neurons that differ from the olfactory sensory neurons (OSNs) in cellular structure, receptor expression, and connectivity. The VNO of rodents comprises a sensory epithelium and a thin non-sensory epithelium that morphologically resembles the respiratory epithelium. Sox2-positive cells have been previously identified as the stem cell population that gives rise to neuronal progenitors in MOE and VNE. In addition, the MOE also comprises p63 positive horizontal basal cells (HBCs), a second pool of quiescent stem cells that become active in response to injury. The HBCs can give rise to neurons and support cells. Immunolabeling against the transcription factor p63, Keratin-5 (Krt5), Krt14, and Krt5Cre lineage tracing experiments highlighted that the NSE of rodents is, like the respiratory epithelium, a stratified epithelium where the p63/Krt5+ basal progenitors self-replicate and give rise to the apical columnar cells facing the lumen of the VNO. In addition, we found that the basal progenitors of the NSE proximal to the marginal zones give rise to the horizontal basal cells of the VNO. Our data suggest that the p63/Krt5 basal progenitors in the olfactory are multipotent cells able to give rise to multiple cell types in a context-dependent fashion.

133 **Inhibition Of Fak Promotes Olfactory Neurogenesis And Function Recovery Following Acute Inflammation Through Cntf**

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Adult neurogenesis in the olfactory epithelium (OE) maintains the sense of smell. Failure to regenerate olfactory sensory neurons (OSNs) causes olfactory dysfunction. Defining signaling pathways that regulate OE neurogenesis would reveal new therapeutic targets to improve olfactory deficits. Our previous study showed that ciliary neurotrophic factor (CNTF) is expressed in horizontal basal cells (HBCs) and FAK inhibition promotes OE neurogenesis via CNTF. Acute OE inflammation destroys OSNs and leads to anosmia/hyposmia. Here, we investigate whether CNTF and FAK affect olfactory neurogenesis and function recovery following methimazole-induced acute OE inflammation in mice. Methimazole increased CNTF and did not affect the levels of phospho-FAK in the OE, suggesting that it increases CNTF not via FAK. Intranasal instillation of a FAK inhibitor following methimazole further enhanced CNTF. FAK inhibitor did not affect TNF expression, suggesting that it does not interfere with methimazole-induced acute OE inflammation. Methimazole-induced CNTF and the effect of FAK inhibition in HBCs were confirmed using primary HBC culture. Methimazole increased basal cell proliferation and regeneration of new OSNs in wildtype mice, but not CNTF-/- littermates. The recovery of olfactory function following methimazole-induced anosmia/hyposmia was impaired in CNTF-/- mice. These data indicate that CNTF is required for OE neurogenesis and olfactory function recovery following acute inflammation. Importantly, intranasal instillation of FAK inhibitor boosted methimazole-induced basal cell proliferation in C57BL/6 mice, suggesting a therapeutic potential of FAK inhibitors to improve olfactory neurogenesis and function after injury.

135 **Dream Olfactory Mixtures Prediction Challenge**

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Recent advances in predictive methods and availability of perceptual data have paved the way for a growing interest in olfactory perception predictions from chemical representations of molecules. This has led to a growing consensus that it is possible to build models using the chemical structure of a molecule to predict the perceptual values of natural language attributes of its smell. However, predictions have mainly focused on single molecules and not the real-world situation of complex mixtures of diverse molecules. Using publicly available data from 3 different studies (Bushdid et al. 2014, Snitz et al. 2013, Ravia et al. 2020) for a total of 703 unique mixtures and 447 measurements of mixture pairs discriminability, participants will be tasked to predict the discriminability of 44 unpublished mixture pairs. We will here present the details of the datasets and the challenge timeline/scoring approach.

137 **Exploring The Impact Of &Ldquo;Kokumi Compounds&Rdquo; On The Psychophysics Of Tastes Perception**

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“Kokumi” is a word used to describe the modulating effect of reduced glutathione on umami tastants, e.g. glutamate, 5’-nucleotides, … In this study, we presented subjects with combinations of glutathione and 5’-nucleotides to the tip of the tongue using a sip gustometer as 600ms pulses during a 6 second water wash. Using PsychoPy© to control stimulant presentations and data collection, we could produce logistic functions and computational values that represented the effects of the stimulants on each other. When presented with single compound, taste thresholds could be determined for each kokumi and umami substants. Preliminary results with

sucrose and citric acid produced logistic models that were well formed, stable and reproducible within a single subject. Critical values e.g. thresholds, equal odds ratios (EOR), and mixture effect parameters were variable across subjects. The goal is to create a model that is reproducible within subjects and variable across treatments. These experiments contributed to our understanding of how kokumi compounds influence the perception of umami and provides valuable insights into the nuanced interplay between kokumi compounds and other taste perceptions.

139 **Autoclaving Polymer-Based Canine Detection Training Aids Prior To Odor Capture Alters Absorptive Properties And Headspace Composition**

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Previous use of polymer-based odor capture and release (POCR™) training aids to safely present odor composites of hazardous targets demonstrated canine generalization from training to operational phase. Sterilization using a rigorous 2-step autoclave method resulted in training aid with a higher suggested configuration-dependent odor learning than non-sterilized. These results suggested incorporation of this configuration in earlier task training phases could improve generalization upon final testing. In this project, the initial POCR™ task learning begins with non-relevant odors such as calibrant compounds 1-bromoperfluorooctane and tris perfluorobutylamine. A sterilization configuration step was evaluated to determine if odor charged post-autoclaving could be an effective means for odor-based task training. The canine screening of the post-autoclaved charge process resulted in diminished odor recognition. Performance results were supported by comparative headspace analysis of autoclaved and non-autoclaved POCRs™ using Proton Transfer Reaction Mass Spectrometry (PTR-MS) demonstrating altered mass spectra. A significant increase in masses associated with depolymerization products were identified in the headspace of autoclaved POCRs™ along with elevated water cluster presence, which may alter both the polymer affinity for certain odors as well as physically prevent absorption due to surface hydrate. When a thermally safe alternate compound, amyl acetate, was used to charge POCRs™ before or after autoclave, canine performance and gravimetric analysis of post-charge mass gain indicated altered vapor capture and dissipation. These results further characterize the POCRs™ composition, interactive properties and the retention of odor profiles under varied conditions following sterilization.

141 **Discrimination Between Food Odours In Pinnipeds: Do They Show Some Preferences ?**

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Pinnipeds use olfaction in different situation such as mother-young recognition, mate selection or foraging and feeding. They have been experimentally shown to discriminate between different airborne natural odors. Here, different species of pinnipeds from different institutions were tested behaviorally in France: California sea lions (Zoo de La Fleche), South American sea lions and South American fur seals (Parc Zoologique de Paris). The animals lived in different conditions with different fish species as food. To date, 13 individuals (4 adult females, 6 adult males and 3 juveniles) have been tested (experiments are still in progress). We used four food odors: oily fish, lean fish, squid and trout. Reactions to these odors were compared with a control odor, i.e., that of water from the animals' pool. Oily and lean fish were commonly distributed during the daily meals of animals, while squid and trout were either uncommon to the tested pinnipeds or used as a treat for some of them. Odor stimuli were presented following two complementary procedures, i.e., sequentially and simultaneously, two methods that gave similar results. Several behavioral parameters were assessed: approach near the odor source, nostrils' opening, vibrissae movements, mouth openings, vocalizations. We found that pinnipeds can discriminate between different food odors, even if some of them never had access to this kind of food. Results seemed to indicate that some food preferences occur but that lean fish induced weak reactions similar to the control. In our conditions, pinnipeds showed stronger discrimination response when exposed to a food odor that they do not encounter on a daily basis (squid or trout) as too expensive, but can be used as a treat or to give them some novelty in their diet routine (e.g., food enrichment).

143 **The Behavioral Sensitivity Of Mice To Acyclic, Monocyclic, And Bicyclic Monoterpenes**

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Monoterpenes, a large class of naturally occurring fragrant molecules, are commonly used in olfactory studies to survey neural activity and probe the behavioral limits of odor discrimination. For centuries, monoterpenes (typically in the form of essential oils) have been used for therapeutic purposes and have pivotal roles in various biological and medical applications. Despite their importance for multiple lines of research using rodent models and the role of the olfactory system in detecting these volatile chemicals, the murine sensitivity to monoterpenes remains mostly unexplored. We assayed the ability of C57BL/6J mice to detect nine different monoterpenes (the acyclic monoterpenes: geraniol, citral, and linalool; the monocyclic monoterpenes: r-limonene, s-limonene, and γ-terpinene; and the bicyclic monoterpenes: eucalyptol, α-pinene, and β-pinene) using a head-fixed Go / No-Go operant conditioning assay. We found that mice can reliably detect monoterpenes in the low parts per billion

range. Specifically, mice were most sensitive to geraniol (0.7 ppb) and least sensitive to γ-terpinene (18.1 ppb). These estimations of sensitivity serve to set the lower limit of relevant concentrations for functional experiments in mice. To define an upper limit, we estimated the maximum concentrations that a mouse may experience in nature by collating published analyses of monoterpene concentrations emitted from natural sources. We found that for most natural sources, monoterpenes were in the ppb range. It is our hope that this dataset will help researchers use appropriate concentrations for functional studies using monoterpenes and provide context for the vapor-phase delivery of these chemicals in studies investigating their biological activity in mice.

145 **Achems Undergrad Finalist: Olfactory Bulb Local Field Potentials Track Breathing Rhythms At Multiple Timescales**

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The external chemical world cannot be accessed without actively sampling the environment. To optimally orient by olfactory information, the brain must unify odor-driven activity with representations of self-movement and context. Studies in other sensory modalities demonstrate that contextual signals are common in primary sensory areas, and it has long been known that olfactory bulb (OB) local field potential (LFP) is coupled with behavior. Our lab has recently found that individual olfactory bulb neurons track the long-timescale rhythmic structure of breathing, in the absence of experimenter applied stimuli or tasks. To better understand the coupled rhythms of breath and OB population activity dynamics, we analyzed local field potentials. Breathing and LFP differ between head-fixed and freely-moving states. During free movement, respiration is rhythmically organized into discrete states lasting minutes, whereas these states are not apparent during head fixation on a stationary platform. This discrete organization is likewise apparent in the ongoing dynamics of the OB. LFP amplitudes in various frequency bands are associated with distinguishable rhythmic behavioral states, some of which are absent in head fixation. In addition to these state-selective signals, we also found that low frequency LFP oscillations correlate with sniff frequency, and that LFP waveforms in multiple frequency bands are aligned to inhalation. Thus, OB LFP tracks relevant information about timing and frequency of the respiratory cycle, and the amplitude may encode behavioral state and/or represent a sensory feedback gain. We propose that these contextual signals, particularly those dependent on active sampling, facilitate the incorporation of olfactory information into cognitive maps of self and environment.

147 **The Influence Of Respiration And Nasal Airflow On Olfactory And Non-Olfactory Signaling Differs Across Neuronal Populations In The Olfactory Bulb**

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Even the earliest olfactory neurophysiology observed oscillatory rhythms in the neural activity in the olfactory bulb (Adrian 1950). Here we synthesize data from diverse experiments showing the influence of nasal airflow on signaling in different parts of the olfactory bulb circuit (olfactory nerve terminals, short axon cells, periglomerular cells, and mitral cells) at rest, during olfactory stimulation, and during non-olfactory somatosensory stimulation. Activity from each cell type was assessed using optical neurophysiological methods to observe population-level calcium dynamics using GCaMP6f expressed in different mouse lines. Key experiments include effects of tracheotomy and naris occlusion on spontaneous oscillations, demonstrating that some oscillations in some parts of the circuit are primarily driven by peripheral airflow but some respiration-coherent activity does not require peripheral airflow. Odor-evoked activity was strongly coupled to respiration in all cell types (though with disparate phase lags), which may reflect phasic exposure to the physical odorant. However, non-olfactory stimuli like tail shock and trigeminal nerve stimulation *also* evoked respiration-locked activity in periglomerular, short axon, and mitral cells that was *also* dependent on nasal airflow. We conclude that phasic nasal airflow plays a critical role in shaping olfactory bulb activity beyond mere imposition of temporal structure on odor stimulus delivery. The contributions of peripheral and centrifugal respiratory inputs across early olfactory circuitry suggest a differential role in olfactory information processing. Limitations of these studies include the use of anesthesia (to permit tracheotomy and trigeminal stimulation) and the inability of the imaging method to follow oscillations faster than12 Hz.

149 **Cell Type- And Layer-Specific Plasticity Of Olfactory Bulb Interneurons Following Olfactory Sensory Neuron Ablation**

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The loss of neurons is often irreversible, as most are generated before or shortly after birth. Understanding how new neurons integrate into established systems will be essential in developing treatments for brain injury and neurodegenerative diseases. The olfactory system presents a rare region of postnatal neurogenesis, in which neuroblasts born in the subventricular zone migrate to the olfactory bulb (OB) and differentiate into multiple interneuron subtypes. We selected three of these subtypes: those expressing tyrosine hydroxylase (TH), parvalbumin (PV), or calretinin (CR). We compared their density 7, 14 and 35 days after methimazole (MMZ)-mediated ablation of olfactory sensory neurons (OSNs), corresponding to timepoints during and after OSN repopulation, to saline-injected control mice. TH+ neuron density was reduced at 7 and 14 days post-MMZ but recovered to baseline by 35 days, reflecting the activity-dependence of both TH expression and TH+ neuron survival in the OB. In contrast, there was no change in the density of PV+ neurons, a subtype known to be generated before birth and only briefly postnatally in the healthy olfactory system, at any timepoint. However, PV+ soma size was reduced in MMZ-treated mice. We also found an increase in CR+ neuron density in the

glomerular and external plexiform but not the granule cell layer at 7 days post-MMZ that returned to baseline by 14 days. Using EdU to label newborn neurons, we found increased CR+EdU+ neuron density 7 days post-MMZ that was not sufficient to account for the transient increase in the CR+ neuron density, as well as an increase in CR fluorescence intensity. Our study reveals novel changes in two OB interneuron subtypes in response to OSN ablation, providing new insight into the range of plasticity mechanisms employed by OB circuits.

151 **The Mouse Olfactory Bulb Is Innervated By A Genetically Heterogeneous Population Of Orexin-Expressing Neurons**

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Centrifugal projections from higher-order brain regions impact sensory processing in the olfactory bulb (OB). One of these pathways includes a monosynaptic input from orexin-expressing neurons to the OB. However, the anatomical and neurochemical nature of the orexin inputs to the OB remains unclear. To determine whether orexin inputs are distributed throughout the entire OB, and whether they include non-orexinergic neurotransmitters, immunohistochemistry for orexin, vesicular glutamate transporter type 1 (VGLUT1) and 2 (VGLUT2) was performed in a series of OB sections. Orexin expression was uniformly distributed through the entire OB which indicates that orexin inputs in the OB are spatially homogeneous. A morphological analysis of the orexin expression revealed two distinct groups of labels: fine processes smaller than 0.8 μm^2 in area, and larger varicosities ranging between 0.8 – 3 μm^2 in diameter. Nearly 50% of the larger varicosities co-expressed either VGLUT1 or VGLUT2, and co-expression was found in every OB layer. Moreover, the VGLUT expression was restricted to the larger varicosities, supporting the morphological analysis. The results indicate that the OB is innervated in part by a neurochemically heterogeneous population of orexin neurons that co-release glutamate, and that orexin can be released on different layers within the OB circuit.

153 **Sensory-Induced Gamma Oscillations In The Olfactory Bulb Reflect Cognitive Load**

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Gamma (35–110 Hz) and beta (15–30 Hz) band Local Field Potential (LFP) oscillations in the rat Olfactory Bulb (OB) mark specific behavioral states. Previous studies have linked gamma elevation during odor sampling to better fine (similar) odor discrimination. Moreover, blocking gamma oscillations in the OB disrupts fine odor discrimination for rats, mice, and honeybees. However, we still don't know the cognitive elements driving increased gamma during an odor discrimination task. Based on previous results, we hypothesize that cognitive load influences gamma elevation in the OB. We designed a variation of a Two-Alternative Choice (TAC) protocol, which manipulates the cognitive load of rats when performing the task. Higher cognitive load is achieved through an increased number of stimuli, some of which are very similar, and a harder task with a low level of predictability (high load) compared to an easier task with a higher level of predictability (low load). We decrease the cognitive load by associative training of context cues that convey information about the previously learned perceptual grouping of the upcoming stimulus on each trial. The control group receives an uninformative similar cue. Male and female rats were implanted with bipolar electrodes in the left OB, anterior piriform cortex, and dorsal hippocampus. We recorded LFPs from all of these areas while the rats performed the TAC task with informative or non-informative cues. We show that rats can successfully learn and perform this difficult variation of the TAC task, showing faster reaction times and lower gamma power during odor sampling when provided with an informative context cue in the low load condition.

155 **Salivary Amylase Regulates Blood Glucose**

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α- Amylase breaks down complex starches into simple sugars and is primarily expressed by two genes: *AMY1* in the salivary glands and *AMY2* in the pancreas. We have developed a CRISPR knock-out (KO) mouse with a deletion of *AMY1*. This mouse does not express salivary α-amylase (sAA) but maintains normal pancreatic amylase expression and function. Salivary AA has been implicated in the cephalic phase insulin response (CPIR), as it releases “sweet” molecules from starch. CPIR is an increase in circulating insulin that precedes spikes in circulating glucose and has been linked to “sweet” and glucose sensing in the oral cavity (Glendenning et al., 2018). To determine the role of sAA in blood glucose levels, AMY1 KO mice were given either 10% maltodextrin or 8% glucose via gavage or oral intake test. Blood glucose levels were collected at 5-, 15-, and 60-minutes post-intake. Circulating glucose levels were significantly higher at all time points in the KO after oral consumption of the maltodextrin compared to the wild-type (WT) animal ($p<0.05$); heterozygous (HET) animals also showed significantly higher blood glucose levels than WT at 15 and 60 minutes ($p<0.05$). There was no difference between groups when the oral cavity was bypassed and maltodextrin was delivered directly to the

stomach by gavage or when glucose was offered. Our results are consistent with the hypothesis that absence of sAA leads to a lack of sweet/glucose receptor signaling during a starch meal, which could result in decreased insulin release and prolonged increases in blood glucose. Thus, sAA activity may be linked to an array of metabolic diseases including type II diabetes mellitus.

157 **"The Relative Effectiveness Of Intraoral Vs. Intragastric Infusions Of Glucose To Elicit Release Of Insulin And Glucose-Dependent Insulinotropic Polypeptide In The Rat."**

Valentina Nisi[1], Myrtha Arnold[2], Ginger D. Blonde[1], Brenna Row[1], Graciela Sanchez-Watts[3], Alan G. Watts[3], Wolfgang Langhans[2], Alan C. Spector[1]

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We used our unique preparation with surgically implanted intraoral (IO) and intragastric (IG) cannulas for stimulus delivery, as well as jugular vein (JV) catheters for blood sampling to test the effects of 10-min and 1-min IO vs. IG infusions (1 ml/min) of 1.0 M glucose (Glu) on plasma insulin, glucose-dependent insulinotropic polypeptide (GIP), and blood glucose sampled (140 μL) from the JV (min: -4, -2, 1, 2, 3, 5, 10) in fasted male rats (n=10-15). Confirming and extending previous findings, IO Glu caused a greater ($p \leq .05$) early rise (3-min AUC) in insulin levels than IG Glu despite no significant difference in blood glucose levels between the two delivery routes; this was true for both the 10-min and 1-min infusion and was first evident at 1 min. Although more modest, we also found that GIP levels were higher ($p \leq .05$) after IO vs. IG Glu delivery by 3 min (3-min AUC) but only for the 10-min Glu infusion. While GIP levels were higher after 1-min IO than after 1-min IG Glu infusion, this difference was statistically equivocal. To examine sugar specificity, we also tested the effects of 10-min IO vs. IG infusions of 1.0 M fructose (Fru) on insulin and GIP levels. IO Fru produced marginally higher insulin and GIP levels than IG Fru, reaching statistical significance only at 1 min for insulin and at 3 min (AUC) for GIP. As we presented Fru as the last stimulus, conditioning by the prior Glu exposure may have contributed to the observed differences. In sum, the results obtained with our rigorous approach confirm that there is an oral stimulation of insulin release; they also suggest a somewhat less robust oral stimulation for GIP release under some conditions. Finally, these endocrine responses display some degree of chemospecificity.

159 **Achems Undergrad Finalist: Olfactory Nudging Promotes Short-Term Weight Loss**

Victoria Esparza[1], Angela Pfammatter[2], Valentina Parma[3], Surabhi Bhutani[1]

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Odors guide food choices, yet olfactory strategies are not included in current interventions for weight loss. We posit that short and often unconscious exposure to “healthy” food odors can serve as an "olfactory nudge" (ON) to increase healthy food intake, while prolonged unconscious exposure to “unhealthy” odors elicits olfactory-specific satiety via “olfactory habituation” (OH). To explore the effectiveness of these strategies, we conducted a two-week pilot intervention with normosmic adults with overweight/obesity (N= 6F; 83% white; age:21-55 years old, BMI:28.8±3.3). The results showed a significant effect of olfactory strategies on weight loss [$F(1,12)=6.591$, $p=0.02$]. Individuals in the ON group (exposed to banana/strawberry fruit smells before lunch and dinner), experienced an average weight reduction of -1.6±1.1 lb. Similarly, the OH group(10-minute habituation to banana pudding/strawberry cake smells), achieved a weight reduction of -1.2±0.4 lb. There were no significant differences between the two olfactory conditions ($p=0.89$). The control group exhibited a smaller overall weight reduction of -0.3±1.8 lb, which was significantly lower than that of the ON group ($p=0.05$), but not significantly different from the OH group ($p=0.16$). All groups demonstrated a significant increase in Olfactory Awareness post-intervention ($V = 26.5$, $p=0.04$). The Self-Report Behavioral Automaticity Index (SBAI) showed a nominal increase only in the olfactory groups. No significant changes emerged in the diet intake measured through a 3-day food diary, Short Self-Regulation Questionnaire (SSRQ), and Food Craving Questionnaire (FCQ), post-intervention. These preliminary findings support the use of olfactory behavioral strategies to influence weight loss.

161 **A Graph Neural Network Self Supervised Learning Approach To Generate A Meaningful Chemical Latent Space For Olfactory Tasks**

Grant D McConachie, Meg A Younger, Brian DePasquale
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Identifying ligands that bind to receptors on olfactory sensory neurons (OSNs) and elicit maximal excitation is known as deorphanization. Deorphanization is crucial for a fundamental understanding of odor encoding in the brain; however, experiments are both challenging and time-intensive. Recently, graph neural networks (GNNs) have demonstrated proficiency in performing intricate olfactory tasks, such as predicting human odor perception based on chemical structures. Although powerful, these networks demand substantial data, making it challenging to predict the neural response of different ligands in deorphanization experiments. In this study, we use self-supervised learning methods with GNNs to generate a representation of odors (e.g., a chemical latent space) for improved performance on these small datasets. We utilize Zinc15, a large public dataset of commercially-available compounds (~750 million compounds cut down to ~12 million compounds that are potential odors), to pre-train a GNN which is then fine-tuned on smaller deorphanization datasets. We explore how different self-supervised learning methods impact performance compared to a baseline GNN trained solely on the deorphanization dataset. Simple self-supervised learning tasks, such as node and edge masking, diminish the GNN's performance on deorphanization experiments, necessitating more complicated tasks for improvement.

These experiments provide an avenue for applying powerful machine learning techniques to answer crucial questions about odor encoding using small datasets, potentially leading to models that can adequately capture the intricate nuances of odor-receptor interactions.

163 **Don Tucker Finalist: Human-Associated Odorants Drive Host Invasion In The Human-Infective Nematode Strongyloides Stercoralis**

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Over 610 million individuals globally are infected with the skin-penetrating gastrointestinal parasitic nematode *Strongyloides stercoralis*. *S. stercoralis* infects hosts as developmentally arrested infective third-stage larvae (iL3). iL3s navigate through the soil searching for hosts in a process that involves attraction to host-associated odorants. They then invade hosts by burrowing through the skin. We have identified human-associated odorants that stimulate the skin-penetration behaviors of *S. stercoralis* iL3s. The responses to these odorants are species-specific – they do not stimulate skin penetration in the closely related rat-parasitic nematode *Strongyloides ratti*. We are now investigating the neural and molecular mechanisms that underlie these responses. Large families of G protein-coupled receptors encode odorant receptors (ORs) in nematodes and have been thoroughly identified in the model nematode *Caenorhabditis elegans*. We verified and manually curated putative OR genes in *S. stercoralis*. Through transcriptional analysis of differential gene expression between iL3s and free-living life stages of *S. stercoralis*, we identified several OR genes that are highly expressed and upregulated in iL3. Fluorescent reporter constructs using the promoters for these OR genes revealed expression in specific subsets of head sensory neurons, enabling us to genetically target putative olfactory neurons for the first time. We are now testing the requirement for these neurons during skin penetration using chemogenetic silencing and examining their activity using calcium imaging. We are also investigating the requirement for individual OR genes using CRISPR. Together, these experiments are providing insight into how skin-penetrating nematodes invade human hosts, with broad implications for nematode control.

165 **Receptors That Detect Human Skin-Derived Carboxylic Acids In Malaria Mosquito**

Joshua Raji, Christopher Potter
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Mosquitoes are vectors of many deadly diseases. The *Anopheles* mosquito transmits malaria parasites, which cause the death of hundreds of thousands every year. The vectorial success of mosquitoes is highly reliant on their powerful sense of smell. Human skin emanations comprise a plethora of different odor volatiles. Elevated skin carboxylic acids on human skin have been linked to increased mosquito attraction. Ionotropic receptor 8a (IR8a) is crucial for detecting carboxylic acids in mosquitoes. We analyzed the odor-tuning IRs that interact with IR8a to adjust sensitivity to acidic volatiles. We combined transcriptomic profiling with whole-mount fluorescent in situ hybridization to identify a total of 19 IRs in the female *Anopheles coluzzii* antennae. Double colocalization of IR8a-IRx complexes reveals 8 candidate IRs that interact with IR8a. In silico analysis and molecular docking of carboxylic acid ligands to the target IRs revealed a strong binding affinity between the ligands and the receptor binding sites. This result suggests that the target IRs may be responsive to carboxylic acids. Further validations will involve loss-of-functions mutation of select candidate IRs, and an *Ex-vivo* functional screen of exogenous *Anopheles* IRs expressed in the *Drosophila* antennae. Uncovering the molecular targets mediating carboxylic acid sensing in mosquitoes could offer insights into new ways of controlling their vectorial capacity.

167 **Response To Mixtures Of Odorants In A Given Olfactory Receptor/Response Cell Depends On The "Efficacy Ratio" Of The Individual Odorants.**

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We developed a dynamic model of olfactory reception of mixtures of odorants using linear differential equations. The basic model has four components – unbound (no odorant bound), spontaneously active (no odorant bound, active anyway), bound to an odorant, and bound activation. We present two primary findings. First, we can effectively model the response of individual olfactory response neurons to mixtures of odorants, and we demonstrate using calcium imaging data of multiple neurons responding to a pair of odors in varying combinations. These data include inhibitory and excitatory contributions of individual odorants. Second, the nature of the olfactory response to a mixture (inhibitory or excitatory) depends on the “efficacy ratios” of the specific receptor odorant pair and the spontaneous activation properties of the cell. We establish conditions, in terms of the model parameters, that classify the odorant as an excitatory addition to a preexisting mixture (increases the level of activation), or an inhibitory one (reduces the level of activation). It is a feature of the model that an odorant that reduces activity when added to one mixture might increase activity if added to another. The label inhibition/ excitation is not fixed for a given odorant but depends on what it is mixed with. We define the efficacy ratio as the ratio of activated bound locations to un-activated bound locations, and we propose that this ratio determines how a given odorant will change the response when added to a mixture.

169 **The Role Of Tex15 In Shaping Stochastic Olfactory Receptor Gene Choice**

Nusrath Yusuf[1], Jerome Kahiapo[1], David Brann[3], Alina Irvine[2], Pavithra Veera[1], Irina Ruzina[1], Mallika Ravi[1],

Bob Datta[3], Kevin Monahan[1]

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The main olfactory epithelium (MOE) can detect a vast diversity of smells with incredible specificity through the function of olfactory sensory neurons (OSN). Each OSN expresses olfactory receptor (OR) genes, which encode the proteins that bind chemical odorants. A mature OSN stochastically transcribes only one allele of an OR gene. It can choose to express any one of the approximately 1400 OR genes or 2800 alleles. This diversity of ORs expressed is important to the MOE's ability to detect a vast range of smells with precise specificity. The choice of an OR gene occurs as OSN progenitors mature into an OSN. Recent work has revealed remarkable remodeling of the local chromatin and co-expression of multiple OR genes during this period, but the molecular mechanisms governing these processes and their connection to a singular OR allele expression in a mature OSN remain unknown. Tex15 is transiently expressed during the critical gene regulation window in OSN progenitors. Tex15 protein has only been studied in the testes where it regulates methylation and silencing of transposons. We show that Tex15 is crucial for stochastic OR gene choice, where when knocked out there is a dramatic reduction in the diversity of expressed OR genes with a few class II OR genes dominating stochastic choice. These class II OR genes are the first to be transcriptionally activated in wild-type OSN progenitors. We hypothesize that Tex15 is regulating monoallelic olfactory receptor gene choice through either methylation patterns or through its effect on chromatin state of developing olfactory sensory neurons. We elucidate a novel aspect of how OSNs come to stochastically choose a single OR and how Tex15 gene and protein guides this specific yet diverse choice.

171 **Is Mouse Nose A Miniature Version Of A Rat Nose? - A Further Examination Of The Coiled Parallel Olfactory Gas Chromatograph Theory**

Zhenxing Wu[1], Jianbo Jiang[2], Fritz W. Lischka[2], Kai Zhao[1]

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Despite mouse being a widely used animal model in biomedical research, including those focused on the olfactory and respiratory system, limited studies exist on its nasal aerodynamics, potentially due to its small size. Here, we created an anatomically accurate 3D computational nasal model based on postmortem high-resolution micro-CT scans (isotropic pixel resolution 10.5 um) of an adult B6 mouse, and showed similar separation of respiratory and olfactory flow regimes to that of a rat, featuring a high-speed dorsal medial (DM) stream that increases odor delivery speed and efficiency to the ethmoid (olfactory) recess (ER), while the respiratory airflow flows ventrally, joined at the nasopharyngeal meatus before exiting the nasal cavity. The DM stream in the mouse split into axial and secondary paths in the ER as found in the rat, although the secondary flow in the mouse is less extensive, which may have functional implications related to the olfactory odorant transport. We compared the gas chromatograph efficiency of the rat and mouse olfactory regions based on our previously published parallel coiled chromatograph theory and found moderate differences due to their structural differences. As validation, the deposition rate of airborne particles was also simulated and matched well with experimental data. In conclusion, this study quantitatively reveals the characteristics of mouse nasal airflow and mass transport that haven't been detailed before and finds key differences to that of rat nose, which will deepen our understanding of its physiological functions. Further research on this topic will likely shed additional light on the complex interplay between nasal structure and function and on the multifaceted adaptations of mammalian species to diverse ecological settings.

Friday, April 19, 2024

7:30 - 9:00 AM	Estero Foyer
Continental Breakfast	

8:00 - 10:00 AM	Estero Ballroom
Poster Session III	

200 **Determinants Of Sweet Taste Liking In Individuals Of African And East Asian Ancestry Groups Living In The United States**

Lauren Zami[1], Fabien Ca[1], Faye Guarneri[1], Liz Cortes[1], Janel Clovis[1], Caren Ghali[1,2], May M Cheung[1]
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Some people like sweet taste more than others. Individual differences in sweet taste liking may be influenced by environmental exposure to sweet taste (i.e., habitual added sugars intake during early childhood), and these factors may differ across ancestry groups. Theoretically, migrants born in countries with a lower overall added sugars intake than the U.S. may be exposed to less sweet-tasting foods during early life. To identify the determinants of sweet liking, we collected data on sweet taste liking, anthropometric measurements, demographics data, and dietary intake from 121 young adults (age 22.2 ± 5.9 years) from two underrepresented groups in research in the U.S., the African and East Asian ancestry groups, with 51 (19 African and 32 East Asian) migrants. Sweet taste liking data was collected at home using the *Simple Sweet Test*, a psychophysical method. Participants were further categorized into sweet Dislikers, Moderate Likers, and Extreme Likers. Added sugars intake was assessed using the *Short Healthy Eating Index Survey*, a validated food frequency questionnaire. We found that a higher percentage of U.S.-born individuals are Moderate Likers and Extreme Likers in both ancestry groups. Sweet taste liking was positively associated with added sugars intake only among migrants but not U.S.-born individuals. This suggests that the high-sweet food environment in the U.S. may favor the development of sweet-liking tendencies. Furthermore, the discordance between sweet liking and added sugars intake in U.S.-born individuals may indicate aberrant taste and food relationships. Future studies should aim to understand how individual genetics and cultural background contribute to a person's unique taste preferences.

202 **The Scent Of Organo Leaves Regulates Sodium Chloride Consumption In Mice.**

Kazumi Osada[1], Motoko Ohata[1], Nana Aoyagi[1], Akira Hosono[1], Issei Yokoyama[1], michio komai[2]
[1]Nihon University, Fujisawa, Japan, [2]Tohoku University, Sendai, Japan

Although several food odors might modulate salt appetite in rodents and humans, nothing is known about the direct evidence of odors modulating sodium consumption of mice in the experimental setting. The present study aims to investigate the effect of the scent of oregano to control the preference for sodium chloride in mice, and then explore the active component of odorants to control the salt appetite. Carvacrol, the candidate of the active component, was identified from dried oregano leaf with GC-MS in conjunction with HS-SPME. Sixty-six C57BL/6j mice (Male 72, Female 54; 2-5 months old) were employed in the olfactory behavioral study. Before experiments, all experimental mice were generalized with the scent of oregano, then conducted the two-bottle choice test (water vs 0.15M NaCl aqueous solution) presence or absence of an odor generator with 1g oregano. As a result, in females, the oregano and carvacrol odor significantly decreased the rate and amount of saline intake. The oregano odor achieved similar results in males as in females. Although carvacrol significantly reduced the rate of saline intake for males, the inhibition effect was weaker than in females. This exposure of oregano to the male mice induced Fos-immunoreactivity of the ventral parts of the bed nucleus of the stria terminalis (BST) to control salt intake without activating the proximal area, including other parts of the BST. In addition, the sensitivity of female mice to the oregano odor was more sensitive for most of the detected areas than males however, the ventral parts of the BST were the most sensitively respond to the oregano odor. The scent of oregano decreases salt liking, and this effect is at least partly due to carvacrol as the active component of salt reduction in the oregano odor.

204 **Comparing Sensory And Emotional Responses To Chemosensory Stimuli Between Autistic And Neurotypical Children**

Asmita Singh[1], Khoa Luu[2], Se-Woong Park[3], Leslie Neely[4], Han-Seok Seo[1]
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Children with autism spectrum disorder (ASD) are known to demonstrate atypical responses to sensory stimuli. They also often encounter challenges in expressing and understanding emotions. There is still limited research regarding how ASD affects sensory and emotional responses to food-related stimuli associated with individual acceptance and preference for foods. To address this topic, this study aimed to compare the sensory and emotional responses to odorous and tasting cues of ASD and neurotypical (NT) groups. This study included 42 autistic children (mean age = 10 years old) and a group of sex- and age-matched neurotypical children (n = 42, mean age = 10 years old) recruited from the Northwest Arkansas and San Antonio communities. The participants in both groups were asked to rate five tasting solutions and nine odorants, respectively, based on liking, intensity, familiarity, edibility, and willingness to try again. They were also asked to report their emotional responses using self-reported emojis and facial expressions. Our findings showed that both groups differed in their ratings of tasting solutions and odors. Moreover, the ASD and NT groups displayed significant differences in their use of emojis to respond to chemosensory stimuli. We also found that the severity level of autism was linked to food neophobia. In conclusion, our findings provide empirical evidence that autistic children exhibit unique sensory and emotional responses to chemosensory stimuli compared to neurotypical children. Furthermore, these results highlight the importance of using explicit and implicit measures to capture the emotions evoked by chemosensory stimuli.

206 **The Geometry And Role Of Sequential Activity In Olfactory Processing And Perceptual Generalization**

Jonathan V Gill[1], Mursel Karadas[1], Shy Shoham[1,3,5], Dmitry Rinberg[1,2,4]

[1]NYU Langone Health, Neuroscience Institute, New York, NY, United States, [2]New York University, Center for Neural Science, New York, NY, United States, [3]NYU Langone Health, Tech4Health Institute, New York, NY, United States, [4]New York University, Dept. of Physics, New York, NY, United States, [5]NYU Langone Health, Dept. of Ophthalmology, New York, NY, United States

Animals encode sensory stimuli with precisely timed activity across modalities. For example, mice can rapidly recognize odors, independent of their concentration, based on complex spatiotemporal patterns of mitral and tufted cell (MTC) activity in the olfactory bulb. Yet, it remains unknown how sequential MTC activity is organized, and what role sequential activity plays in guiding perception. We performed fast 2-photon calcium imaging of hundreds of MTCs with sub-sniff temporal resolution to a battery of odors. We constructed a space of MTC tuning using the pairwise correlations between MTC odor responses averaged over a single sniff. We then analyzed the propagation of sequences in this space and discovered that sequences originated in a set of similarly tuned neurons and propagated to more distantly tuned neurons, so that the latency of MTC activation was linearly related to distance in tuning space. Further, we found that the early but not the later part of sequences carried concentration invariant information about odor identity. Finally, inspired by the discovery that similarly tuned MTCs are activated sequentially across odors, we propose a role of activity sequences in training the piriform cortex to learn perceptually generalizable odor representations. Like the role of retinal waves in establishing the retinotopic organization of visual processing, MTCs sequentially activated together across odor responses may be responsible for establishing odor cortical maps, even for odors that have never been experienced. These ideas were tested in a proof-of-principle computational model for sequence-based unsupervised training of synapses from MTCs to the piriform cortex, which revealed that sequential activity across the entire sniff permits perceptual generalization for novel odors.

208 **Frequency-Dependent Phase Locking Of Tubular Striatum Neurons To The Respiratory Cycle In Behaving Mice**

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The timing of action potentials to the respiratory rhythm is important for odor perception. Here we investigate the synchronization of single-unit activities in the tubular striatum (TuS) with the respiratory cycle as mice engage in an odor discrimination task. We used eight-channel tungsten electrode arrays in the TuS to record signal-unit activity, with an intranasal cannula to record respiration simultaneously as mice learned to discriminate odors. We found that odor-responsive neurons exhibited significant phase locking to the respiratory cycle and that this phase-locking was highly dependent upon the respiration rate. For respiration rates below 6 Hz, neuronal spiking predominantly aligned with the late phase of inhalation. For the respiration cycles greater than 6 Hz, phase locking significantly shifted towards exhalation phases. Moreover, in preliminary analyses we found that the phase-locking of spikes to the respiratory cycle became forward-shifted as mice became proficient in an odor discrimination. These findings are in accord with the dynamic modulation of olfactory processing by the respiratory rhythm and suggest an important influence of experience on this effect.

210 **Understanding The Odorant Receptor-Based Configurational Coding Of Walnut Odor**

Franziska Haag, Dietmar Krautwurst
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Walnut kernels are a popular snack and a common ingredient of baked goods and confections. The distinct aroma of fresh walnut kernels sets them apart from other tree nuts, such as hazelnuts, cashew nuts, and almonds. The molecular basis of walnut aroma was recently clarified: The 1:1 mixture of fenugreek-like smelling 3-hydroxy-4,5-dimethylfuran-2(5*H*)-one (sotolon) and oatmeal-like smelling (2*E*,4*E*,6*Z*)-nona-2,4,6-trienal (nonatrienal) is responsible for the characteristic aroma of walnuts, but clearly differs from the odor qualities of the single components. So far, OR8D1 has been identified as selective receptor for sotolon. A receptor for nonatrienal has been elusive. Here, we report on the functional identification and characterization of cognate odorant-receptor

combinations (‘hits’) for both components of walnut aroma and their binary mixture, by transient expression of >750 recombinant human OR variants together with cAMP signaling components in a test cell system, utilizing GloSensor® technology. Beyond, our results may explain the configurational odorant-receptor coding underlying the chemosensory percept of walnut aroma.

212 **Evolution And Functional Characterization Of Olfactory Receptors In Birds**

Robert Driver[1], Christopher Balakrishnan[2], Hiroaki Matsunami[1,3,4,5]

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Vertebrates detect odor molecules with olfactory receptors (ORs), a gene family expressed in the olfactory epithelium. Among species, OR diversity is associated with reliance on smell, with some mammals exceeding 1000 OR genes. Birds are the most speciose class of terrestrial vertebrates, inhabiting nearly all land environments and with diverse social structures and foraging strategies, yet were long thought to make limited use of olfactory signals. Recent behavioral work in birds has shown important roles for olfaction in foraging and species recognition, among other behaviors. Contributing to this surge of interest in avian olfaction, our recent work has shown that birds have hundreds more OR genes in their genomes than previously realized. We have examined the genomic OR repertoire of over 120 bird genomes spanning the avian phylogeny, revealing between 50 and 1,100 intact ORs in all species surveyed. To discern the functional roles of ORs, we measured OR mRNA expression levels in the olfactory epithelium of four bird species and found that the majority of the bird OR genomic repertoire is expressed in tissue relevant to smell. To confirm the ability of bird ORs to detect odors, we expressed chicken ORs in mammalian cell culture, bombarded ORs with multiple odors, and measured OR activation in response to each odor. We found that chicken ORs respond to several types of pyrazines, a group of chemicals found in green peppers. Additionally, we show the preservation of OR and ligand relationships between mammals and birds, showing that receptor function is conserved across hundreds of millions of years of vertebrate evolution. Together, these results show that bird ORs are diverse, evolve dynamically, are expressed in the olfactory epithelium, and are capable of functionally detecting odors.

214 **Don Tucker Finalist: Investigating The Mechanisms Of Enantiomer Discrimination By An Odorant Receptor**

Ichie Ojiro[1,2], Keisuke Ito[1], Claire A. de March[3], Hiroaki Matsunami[2]

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Enantiomers are chiral molecules with identical chemical formulas and atom connectivities but differ in spatial arrangement. These enantiomers, perceived distinctly as odorants by humans and animals, likely elicit different responses from the roughly 400 odorant receptors (ORs) we possess. Yet, the mechanism by which ORs differentiate enantiomers remains elusive. Leveraging recent advances in mammalian OR structures at the atomic level, we adopted a structure-function strategy to explore enantiomer discrimination using consensus OR1 (consOR1), representing family 1 ORs. ConsOR1 exhibits varied responses to enantiomers such as carvone, menthol, and citronellal in heterologous expression assays. We employed site-directed mutagenesis within the canonical binding pocket, based on its structure, to examine enantiomer discrimination in mutants. Our results show that some mutations altered overall responsiveness without affecting selectivity, while others modified consOR1's selectivity compared to the wild type. Notably, mutations that altered selectivity for one enantiomer pair did not necessarily affect another, suggesting that key residues for enantiomer distinction are odorant-specific. These findings offer insights into the mechanisms of enantiomer discrimination by the mammalian olfactory system.

216 **Conspecific Odor Representation In Piriform Cortex**

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Conspecific odors are important for dictating the social behavior of rodents. Processing of these odors is done through the two olfactory systems, main and accessory, with the focus being the accessory olfactory system. While the accessory olfactory system appears essential for detecting conspecific odors and influencing social behavior, the main olfactory system may also play an important role. A small subset of neurons in the main olfactory bulb shows strong responses to conspecific urine. With main olfactory projections to the piriform cortex, this implicates that a population of neurons within the piriform cortex may be responsible for responding to conspecific odors. These responding neurons may represent principal connectors of the anterior piriform cortex to other regions of the brain relevant to social behavior such as the amygdaloid complex. Therefore, we utilized head-mounted miniature microscopes to record neurons in the anterior piriform cortex of freely moving male mice investigating conspecific urines. To do this, we placed males in a rectangular apparatus and then presented them with a series of social and non-social odorants, in random order, placed on circular filter paper in a small Petri dish. Overall, we found that a larger subset of neurons responded to female urine compared to male urine. Additionally, we found that the neurons responding to female urine showed a stronger response than neurons responding to male urine. Current work is focused on determining whether neurons within piriform

cortex that respond to social odors are specific to social odors compared to non-social odors. Overall, our work suggests that circuits within the main system that respond to conspecific odors may act in parallel with those in the accessory system to shape social behaviors of individuals.

218 **The Role Of The Higher-Order Brain Regions In Olfactory Identification**

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Introduction: The neurobiological basis of odor-identification remains unknown. We hypothesized that match and mismatch olfactory fMRI tasks could be used to isolate areas of odor-identification and that these areas would include primary/secondary olfactory areas in the brain. *Method*: Twenty-five healthy controls and eighteen MCI subjects took part in an olfactory fMRI oddball detection task. Subjects completed one pseudorandomized and counterbalanced run of the fMRI task. Subjects had to press a button with their right index finger to identify an oddball during scanning. *Results*: A contrast of HC>MCI, for all odor conditions, yielded activation in the left TPJ, left inferior frontal gyrus, left supramarginal gyrus, and left superior temporal gyrus. These areas were significantly active during the olfactory identification task in both groups and were used as the basis for subsequent correlation analyses. Greater activation in these areas correlated with lower ID scores in HC. Although not significant, this correlation was positive in MCI. *Conclusion*: The differences between HC and MCI may be due to differences in sample size and in MCI severity. The left TPJ's activity may be indicative of ventral attention network activation, a primary function of which is to attend to behaviorally relevant, salient, or unexpected stimuli.

220 **The Role Of Trigeminal Activation In Perceived Odor Intensity**

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Most volatile compounds entering the nasal cavity activate both olfactory sensory neurons and chemosensory trigeminal fibers, leading to olfactory and somatosensory (e.g., irritation) sensations. These systems interact at the peripheral and central levels, leading to a change in perceived intensity. To understand this interaction, we compared physiological and perceptual responses in mice and humans, respectively. We delivered varying concentrations of 2-phenethylalcohol (olfactory agonist) and CO_2 (trigeminal agonist) and their mixtures in different ratios and recorded electro-olfactogram (EOG) responses in mice, and intensity ratings were recorded for humans. In mouse olfactory epithelia, CO_2/PEA mixtures induced EOG responses greater than the olfactory stimulus alone. In TRPA1/V1-knockout mice, which lack TRPA1, the trigeminal receptor for CO_2, responses evoked by the PEA/CO_2 mixture were not significantly different from those evoked by PEA alone. In humans, lower concentrations (10-20%) of CO_2 increased the perceived intensity of the mixture, whereas higher CO_2 concentrations overshadowed the contribution of PEA. Established odor intensity models do not predict this interaction. In summary, a trigeminal agonist modifies both neural and perceptual responses, and models of odor intensity need to account for this interaction.

222 **The Social Vocalizations And Behavior Of Olfaction-Impaired Mice**

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Animal social behaviors are affected by the environment and the actions of conspecifics through multiple sensory modalities, including olfaction and audition (Chen & Hong, 2018). During socialization, mice emit ultrasonic vocalizations (USVs), which influence the behaviors of social partners (Sangiamo et al., 2020). However, olfactory signals can also play a pronounced role in modulating the social behaviors of mice (Barabas et al., 2021). To understand the interplay between olfactory and auditory cues in modulating mouse social behavior, we sought to record USVs and social behaviors of freely interacting mice with impaired olfactory function. Our results showed that adult (PD49) C57BL/6J mice irrigated with 0.7% Triton X-100 (n = 14, median = 300 seconds) took significantly longer to find buried food compared to saline irrigated mice (n = 13, median = 15 seconds; Wilcoxon, W = 182, p <0.0001), suggesting Triton X-100 nasal irrigation effectively impaired mouse olfactory function. Using a sound source localization system (Warren et al., 2018), we continuously recorded and analyzed 5 hours of audio and trajectory data with mixed-sex groups (2 males and 2 females per group). We found that Triton X-100 irrigated mice (n = 7 groups, median = 6 vocalizations) produced significantly fewer USVs compared to saline irrigated mice (n = 7 groups, median = 7092 vocalizations; Wilcoxon, W = 49, p <0.01). Moreover, Triton X-100 irrigated mice (n = 28, mean = 211.9 meters) moved far less than saline irrigated mice (n = 28, mean = 395.3 meters; t-test, t = 11.04, p <0.0001). Our data suggests mice with impaired olfactory function showed a drastic decrease in vocal production and movement, and requires further investigation into how olfaction modulates vocal and social behaviors.

224 ***Single Cell Transcriptomics Of Vomeronasal Neuroepithelium Reveals A Differential Endoplasmic Reticulum Environment Amongst Neuronal Subtypes***

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Specialized chemosensory signals elicit innate social behaviors in individuals of several vertebrate species, a process that is thought to be mediated via the accessory olfactory system (AOS). The AOS comprising the peripheral sensory vomeronasal organ (VNO) has evolved elaborate molecular and cellular mechanisms to detect chemo signals. To gain insight into the cell types, developmental gene expression patterns and functional differences amongst neurons, we performed single cell transcriptomics of the mouse vomeronasal sensory epithelium. Our analysis reveals diverse cell types with gene expression patterns specific to each, which we made available as a searchable web resource accessed from www.scvnoexplorer.com. Pseudo-time developmental analysis indicates that neurons originating from common progenitors diverge in their gene expression during maturation with transient and persistent transcription factor expression at critical branch points. Comparative analysis across two of the major neuronal subtypes that express divergent GPCR families and the G-protein subunits Gnai2 or Gnao1, reveals significantly higher expression of endoplasmic reticulum (ER) associated genes within Gnao1 neurons. These gene expression patterns, along with differential localization of ER chaperones and structural proteins indicate fundamental differences in ER function associated with neuronal differentiation.

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Impaired Iron Gluconate Identification In Sars-Cov-2 Igg^{+} Subjects And Associated Lower Transcript Levels Of The Human Foliate Papillae Tongue Transcriptome

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Chemosensory impairment reduces the quality of life during and often long after SARS-CoV-2 infections. This study investigated the link between sensory impairments due to a former SARS-CoV-2 infection, based on correlating changes of the tongue transcriptome. 158 hospital employees were divided into four groups of participants based on previously assessed SARS-CoV-2 immunoglobulin G status ($IgG^{\pm}$) and self-reported sensory impairment ($SSI^{\pm}$). Forced choice taste tests were performed by a subgroup of 141 participants. A whole transcriptome analysis of the foliate papillae area on the tongue was agreed upon by 43 subjects. IgG^{+} participants choosing the iron gluconate solution correctly had a lower IgG titer than IgG^{+} subjects who did not identify metallic taste ($p = 0.03$). Transcriptome analysis of the foliate papillae area isolated from IgG^{+}/SSI^{+} subjects revealed lower RNA expression levels of 5356 genes in contrast to the other three comparator groups. Investigation of these genes using gene ontology enrichment provided evidence for smell perception as the most impaired biological process. Overall, 166 olfactory receptors (OR) and 9 taste-associated receptors (TAS) had lower transcript levels in IgG^{+}/SSI^{+} participants. TAS2R7, OR5K1, OR1A2, OR2J2, OR1A1, and OR1G1 are known for an agonist profile, which can be associated with metal perception. In conclusion, odorant receptors on the tongue can be hypothesized to play a role in virus-induced sensory disturbances and metal perception.

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Taste And Smell Disorders In The United States: Risk Factors And Healthy People 2030

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Healthy People (HP) 2030 is an initiative to promote improvements so all people can achieve their full potential for health and well-being. Taste and smell disorders are common, increase with age, and can have major negative effects on health and quality of life. They can signal serious health problems important to identify early. When diagnosed, some taste and smell disorders can be managed with lifestyle changes, medication, oral health care, or surgery. The National Health Interview Survey (NHIS), a nationally representative US sample, is used to assess the HP2030 objective HOSCD-12: increase the proportion of adults with smell or taste disorders who discuss the problem with a health care provider. We report findings from the 2021 NHIS Taste and Smell Supplement (adults 18+ years old; n=29,482). Logistic regression was used to estimate risk factors after adjusting for socio-demographic factors. Prevalence of COVID-19 history was 14.2%. Prevalence of disorders for taste was 13.3% (COVID-19: 41.3%) and for smell was 19.7% (COVID-19: 50.7%). Prevalence of either taste or smell disorders was 23.3% (COVID-19: 55.9%) and of both was 9.7% (COVID-19: 36.0%). In addition to COVID-19, other

risk factors were poor general health, heart disease, anxiety or depression, asthma, dry mouth, cold/flu past year, prescription medications, allergy, hearing loss, and smoking; vaccination for COVID-19 reduced risk. Among adults 40+ years, 15.5% (COVID-19: 27.1%) had discussed smell/taste problems with a healthcare professional. The COVID-19 pandemic has amplified the need for evidence-based guidance for assessment, treatment, and management of smell/taste disorders. The HP2030 Taste and Smell objective baseline has been established using 2021 NHIS data and tracking measures will be obtained with NHIS 2024 and 2027.

230 **Identification And Confirmation Of Neurocircuit For Petrification And Micturition**

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When animals are greatly terrified, petrification and micturition (P&M) can occur simultaneously across the phyla. However, the underlying neurocircuit is essentially unknown. Here, we first established a stable P&M model based on Pavlovian conditioned reflex in mice. Combination of viral labelling, fosTRAP2 and cre-line identified the Barrington's nucleus neurons (Bar^{vGlut2}) involved in micturition. AAV-RV tracing results showed the strongest input to Bar^{vGlut2} being from the periaqueductal gray (PAG). Optogenetic activation and patch clamp confirmed the direct $lPAG^{vGlut2} \rightarrow Bar^{vGlut2}$ connection. Fiber optic recording of $lPAG^{vGlut2}$ terminals in Bar revealed the coupling of Ca^{2+} signal and P&M. Behaviorally, weak optic activation of the $lPAG^{vGlut2}$-Bar terminals in Bar led to micturition only, while strong activation, P&M, probably due to backpropagation of action potential. Otherwise, inhibition of $lPAG^{vGlut2}$ eliminated P&M. Therefore, other than Bar, another pathway should be involved in freezing. Analyzing the c-fos patterns in brain induced by different optic intensities at $lPAG^{vGlut2}$ terminals in Bar discovered the most significant difference being in the Magnocellular reticular nucleus (McRN). Tracing with locked-AAVs and in situ hybridization disclosed that $lPAG^{vGlut2}$ projects to both Bar and McRN, forming $McRN \leftarrow lPAG^{vGlut2} \rightarrow Bar^{vGlut2}$ bifork network. Activating these $lPAG^{vGlut2}$ somas triggered P&M. Inhibiting Bar^{vGlut2} and activating these $lPAG^{vGlut2}$ somas simultaneously resulted in freezing without micturition. In summary, we identified the network $McRN \leftarrow lPAG^{vGlut2} \rightarrow Bar^{vGlut2}$ mediating P&M, with Bar branch for micturition and McRN branch for freezing. The results provide a possible general mechanism for coordinating different actions in the same event using different neuro-collaterals.

232 **Central Terminals Of Penk+ (T3) Gustatory Neurons Show A Regionally Restricted Distribution**

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Taste buds of anterior tongue and palate are innervated by gustatory geniculate ganglion neurons. Based on transcriptional profiling, a major subset termed T3 is marked by proenkephalin (Penk) expression. We asked whether Penk+ neurons innervate a defined taste bud cell type and how their central projections are distributed in the rostral NST (rNST). Our earlier studies quantifying fluorescence intensity of 32 taste buds from 5 *Penk*;;tdTomato transgenic mice showed Penk+ fibers preferentially associated with sour-sensing type III versus type II taste bud cells. However, tdTom was seen in cells adjacent to taste buds and in many neurons in the hindbrain. Thus, to selectively target Penk-expressing sensory neurons, we injected *Penk*-Cre mice with AAV-PHP.S-*flex*-tdTom. We observed a similar preferential association of T3 fibers with type III taste bud cells in both transgenic and AAV models. In 7 *Penk*-Cre mice, 13%-42% of geniculate ganglion T3 neurons expressed tdTom following AAV-PHP.S-*flex*-tdTom injection. In hindbrain cryosections of these mice, we observed tdTom+ fine fibers and terminals within the gustatory rNST, as defined by P2X3 staining. Fluorescence intensity was quantified for tdTom and P2X3. tdTom+ terminals were dispersed throughout the P2X3+ field rostrally (Bregma -6.18 to -6.6). In more caudal sections (beyond Bregma -6.6), tdTom+ terminals progressively become concentrated ventro-laterally compared to the P2X3+ field. The maximum intensity for tdTom was detected in sections at ≈ Bregma -6.45, dropping off caudally. In summary, Penk-expressing T3 neurons involved in sour-sensing have central terminals which exhibit broad or discrete distributions along the rostro-caudal axis of the rNST. The neuroanatomical significance of this pattern regarding circuitry remains to be determined.

234 **Exploring The Underlying Circuit Mediating Grp-Grpr Signaling Between Gustatory Cortex And Basolateral Amygdala**

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Sensory satiety, a habituation behavior independent of homeostatic needs, occurs due to a recurring orosensory exposure to a certain food (stimulus) and leads to the subsequent decline in the perceived pleasantness of that food and change in dynamic regulation of palatability. Little is known about the underlying neural circuits mediating sensory satiety. In the gustatory portion of insular cortex (GC), which is involved in dynamic processing of taste and taste related decision making, a subtype of neurons express the anorexigenic neuropeptide gastrin releasing peptide (GRP). Preliminary data from our lab show a dense projection from these neurons to the basolateral amygdala (BLA), a region which is extensively involved in taste palatability and feeding behaviors. Here, we test the hypothesis that BLA neurons expressing the GRP receptor (GRPR neurons)

regulate satiety through projections from GC-GRP+ neurons. To examine this, first we characterize the identity and anatomical distribution of GRPR neurons in BLA using immunohistochemistry and RNAscope in situ hybridization and reveal the heterogeneity of GRPR neurons. To explore the effect of GRP on BLA-GRPR+ neurons, we perform patch clamp recordings from GRPR neurons in acute slices containing BLA and bath-apply GRP. We observe a change in parameters associated with synaptic functions and no change in intrinsic properties of BLA-GRPR+ neurons. Results from this work will help us understand how GRP signaling at the GC-BLA input regulate feeding behaviors. Furthermore, this study has important implications for public health as it will advance our understanding of the neural mechanisms underlying eating disorders and it may provide a novel target for therapeutic interventions.

236 **Differential Effects Of Amiloride And Benzamil On Salt Taste Physiology And Behavior: The Case For Phasic Responses In The Generation Of Na^+ Appetite**

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Amiloride is the most widely used drug to study salt taste driven behaviors in rodents, but benzamil, a more potent and selective analog of amiloride, is becoming more prevalent in electrophysiological studies of sodium (Na^+) taste. Electrophysiological experiments have shown that amiloride and benzamil block NaCl responses in NaCl selective N neurons. In contrast, NaCl responses in A neurons—which respond best to ammonium chloride (NH_4Cl) but also respond well to NaCl—are unaffected by amiloride or benzamil. A seminal paper by Roitman and Berstein (1999) showed that amiloride abolishes Na^+ appetite when rats are in a Na^+ deplete state. Here, we aimed to determine whether benzamil is as effective as amiloride in blocking Na^+ appetite. Conditioned taste aversion (CTA) experiments were used to determine whether benzamil, like amiloride, is tasteless to mice (Eylam et al., 2003). Mice were unable to develop an aversion to benzamil or amiloride. Na^+ appetite experiments revealed that, unlike amiloride, benzamil is ineffective at blocking lick rates to NaCl taste in Na^+ depleted mice. Chorda Tympani (CT) nerve recordings in rats showed that compared to benzamil, amiloride was more effective in blocking the phasic response to NaCl, whereas amiloride and benzamil blocked tonic responses to the same degree. Amiloride and benzamil had virtually no effect on NH_4Cl responses. Consistent with CT nerve results, microstructural licking patterns suggested that while benzamil may not block early components of Na^+ recognition, it does block later tonic activity. We conclude that while benzamil appears to be tasteless in rodents, it does not block NaCl taste responses in a manner that recapitulates amiloride, suggesting that early phasic responses to NaCl through N neurons are necessary for driving Na^+ appetite.

238 **Parabrachial Cgrp Neurons Affect Taste-Guided Behaviors**

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The parabrachial (PB) nucleus mediates taste processing and integration with other senses. Diverse PB areas, including the lateral and medial PB, express neurons positive for calcitonin gene-related peptide (CGRP), albeit only limited data have described their influence on taste. Here, the role of PB-CGRP neurons in taste-guided behaviors was studied with chemogenetics in mice (n = 56). Using bilateral microinjections under anesthesia, a Cre-dependent virus encoding either an inhibitory designer receptor exclusively activated by designer drugs (hM4Di) or a control element (mCherry) was delivered to the PB of heterozygous *Calca*-Cre mice. *Calca* marks CGRP-positive PB cells. Following recovery, hM4Di and mCherry mice entered brief-access tests where they all received the hM4Di ligand clozapine-N-oxide (5 mg/kg, i.p.) prior to daily tests. Mice were proffered multiple 10 sec licking access trials with quinine solutions (0 [water], 0.1, 0.3, and 1 mM) during test sessions over 4 days. Some mice participated in other brief-access tests with sucrose (0, 0.1, 0.3, 0.5, and 1 M). Data were collected blind to mouse condition. Preliminary analyses found a reduced avoidance of quinine in thirst-motivated hM4Di mice with silenced PB-CGRP cells (reduction (i.e., flattening) of the slope of the quinine licking avoidance function compared to control; mixed model analysis of log-transformed licks to accommodate data skew, $t(46) = 2.7$, $p = 0.011$). Furthermore, some trend was noted for a reduced preference for sucrose in male hM4Di mice (reduced slope of the sucrose preference function compared to male controls, $t(74) = -2.0$, $p = 0.047$), suggesting PB-CGRP cells affect diverse tastes. This study is still ongoing, with an emphasis on identifying covariates (e.g., sex) that may also account for observed effects.

240 **Sniffing Behaviors Of Freely Behaving Mice**

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Mammals use strong, fast, nasal inhalations, or sniffs, to actively smell odors. Short bouts of sniffs can be evoked by a wide range of stimuli, from new odors to startling auditory or visual cues. However, animals also sniff continuously, even in the absence of clear cues, to seek out olfactory information. Despite the prominence of this behavior in rodents, little is known about the continuous dynamics of their spontaneous sniffing. Further, although it is clear that sniffs are coordinated with head movements, little is understood about how they are coordinated with the rest of the body. To address these gaps, we developed tools to simultaneously record respiratory signals and fast, high-resolution videos of freely behaving mice. We find that sniffing can be described as a sequence of stereotyped motifs, which are re-used in predictable patterns. Some motifs show clear correspondence with full-body movements, as well as spatial biases in the open field arena, reflecting their different behavioral usages. We also find phase-locking between sniffing and body movements. Overall, these data reveal the presence of highly stereotyped olfactory sensing motifs that are strung together to create

meaningful patterns of behavior. These data will provide a foundation for studying the neural circuitry underlying olfactory-guided behaviors in the mouse.

242 **Modulation Of Pharmaceutical Taste Aversiveness In Drosophila Melanogaster**

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Many pharmaceuticals are bitter tasting when presented in non-capsule or pill formulations (e.g. liquid formulations, rapid dissolves, chewables). We hypothesized that Drosophila are an effective model system for testing the aversive nature of pharmaceuticals that humans find bitter-tasting and for suppressing this aversiveness. Method: Food deprived wildtype Canton-S (CS) flies were tested for their proboscis extension response to bitter compounds mixed in sucrose. Individual flies were tested a minimum of three times each. A response was considered positive when the fly extended its proboscis at least 3 times; if proboscis extension occurred once or twice the fly was tested 5 times. Water was offered to satiation before testing and in between each stimulus test. Bitter stimuli included: quinine-HCl, caffeine, denatonium, MgSO4, diphenhydramine-HCl, dextromethorphan, and caffeine. Results: Flies rejected exemplar taste stimuli that humans find bitter: quinine, denatonium, and MgSO4. Flies were also sensitive to the three aversive pharmaceutical agents tested in this study: diphenhydramine-HCl (Diph), dextromethorphan (Dex), caffeine (Caff). As with humans, the addition of sugar rendered the pharmaceuticals less aversive for flies. We titrated aversiveness precisely by controlling the level of sugar with the pharmaceutical. We further demonstrated that salt additives, monosodium glutamate, NaCl, adenosine monophosphate sodium salt, and KCl, ameliorated the aversiveness of Diph, Dex, and Caff for the flies. The three sodium salts were highly effective as aversiveness ameliorating agents. Conclusion: We believe this model system is relatively simple way to predict the orosensory aversiveness of pharmaceuticals and to test bitterness ameliorating additives that will be proven effective in humans.

244 **Mice Learn To Identify And Discriminate Sugar Solutions Based On Olfactory Cues**

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The odor of sugar solutions can alter ingestive responses of mammals. We asked whether mice use these odors to help identify sugar solutions and faciliate discrimination of different sugar solutions. Experiment 1 measured ingestive responses of C57BL/6 (B6) mice to 1M glucose, fructose and sucrose solutions. We subjected mice to a 30-min acceptability test (water vs. sugar) before and after rendering them anosmic with $ZnSO_4$ treatment. We used latency to initiate licking as a measure of odor-mediated response, and licks per trial as a measure of solution acceptability. Before $ZnSO_4$ treatment, mice learned to initiate licking for the glucose and fructose (but not the sucrose) solutions more quickly than for water. $ZnSO_4$ treatment nullified this learned behavior. In contrast, the mice immediately licked more quickly for all sugar solutions than for water, both before and after $ZnSO_4$ treatment. Thus, sugar solution acceptability was not impacted by learning or olfactory loss. Experiment 2 asked whether olfaction was necessary for T1R3 knockout mice to discriminate 0.44M glucose and 0.44M fructose. All mice were subjected to 1-hr two-bottle preference tests with the glucose and fructose solutions, before and after exposure to the same solutions. During the exposure period, some mice were rendered anosmic and others were left normosmic. Before exposure, neither type of mouse preferred the glucose solution. After exposure, the normosmic mice preferred the glucose solution, but the anosmic mice did not. Our results reveal that mice can learn to use their sense of smell to identify and discriminate some sugar solutions.

246 **Palatability Modulation Of Amino Acid-Based Oral Rehydration Therapy In Children**

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Increasing acceptance of bitter stimuli is important for the health of pediatric patients who must consume bitter medicines or nutritional interventions. The aim of this study was to determine if children age six months to five years accept an amino acid (AA)-supplemented oral rehydration formula of our design that contains multiple bitter tasting AAs. These AAs can be clinically advantageous to the gastrointestinal tract, which could benefit children during acute diarrhea. Methods: Sodium chloride, sodium gluconate, zinc sulfate and sucralose were used to decrease bitterness and increase palatability. Participants were trained to give the solutions they liked to a plush toy of Big Bird$_{TM}$ and those they did not like to a plush toy of Oscar the Grouch$_{TM}$. Participants were offered the solutions to drink and the volume consumed was also measured. Results: The addition of sodium chloride and zinc sulfate did not significantly increase acceptance of the solution. Participants rejected this solution equally to a negative control solution of quinine hydrochloride. Sodium gluconate and sucralose were added to the formulation and acceptance significantly increased ($p<0.05$). There was no significant difference in acceptance of the amino acid-based formula containing sodium chloride, sodium gluconate, zinc sulfate, and

sucralose compared to the standard oral rehydration therapy or a comparably sweetened sucrose control solution. Participants drank and tolerated up to 80 mL of the bitter-reduced amino acid-based formulation in one 15 min sitting. Conclusion: This study demonstrates that pediatric participants will accept a bitter-reduced AA-based formulation of oral rehydration therapy, providing evidence that children are likely to accept this solution, which will be used in a clinical trial this year.

248 **Aging Decreases Behavioral Preferences For Salts, But Not For Sucrose, And Alters The Ultrastructural Morphology Of Fungiform Taste Pores In Mice**

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Previously, we showed that rat chorda tympani nerve responses and ultrastructural characteristics of fungiform taste pores changed with age. The effects of aging on the taste system in mice, the preferred model for chemosensory research, has been largely unstudied. The aim of this study was to examine whether aged mice had differences in taste preferences to sucrose, NaCl, and NH_4Cl, and whether they had differences in ultrastructural characteristics of fungiform taste pores using scanning electron microscopy (SEM). Thirty-minute two-bottle preference tests indicated that preferences for NaCl and NH_4Cl, but not sucrose, were significantly different in aged mice (16-17 months old) relative to young mice (5 months old). In the same animals, we found that the aged group had a significantly lower percentage of fungiform papilla with taste pores present. Microvilli of taste bud cells extend into the taste pores of fungiform papillae. The absence of a taste pore on fungiform papillae strongly suggests that taste stimuli cannot interact with taste bud cells beneath the epithelial surface and consequently decrease taste nerve activity. These findings are consistent with our recent findings in rats, where advanced aging had a significant impact on the magnitude of chorda tympani responses to salt and ultrastructural characteristics of fungiform taste pores. Collectively, these data suggest that aging significantly affects fungiform taste pore morphology and has a significant impact on taste processing. While the morphological changes at the level of the fungiform taste pore in aged mice are might have played a role in differences in behavioral taste preferences to salt stimuli, it is possible that changes in central taste processing occur as well.

250 **Don Tucker Finalist: Dietary Habits Can Affect Fat Intake Independent Of Obesity**

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Human obesity is typically associated with decreased taste sensitivity and increased fatty food intake. These changes can perpetuate a cycle of weight gain and overeating fatty foods. Whether rodents display the same changes in preference and intake after obesogenic dieting has not been fully elucidated. Methods: We tested the hypothesis that after 12 weeks on a 60% kcal fat diet (HFD), mice would eat more cake frosting in a brief access test compared to mice on a 10% kcal fat diet (LFD). 12 mice (C57BL/J) were given 5 frostings (Crisco, sucrose syrup, vanilla extract) of varying fat:sugar ratios (1:3, 2:3, 1:1, 4:3, 5:3) before and after 12 weeks of a HFD or LFD. Each group had 5 minutes to eat the frostings, presenting 1 frosting a day. Results: Mice fed the LFD for 12 weeks ate more frosting at every fat:sugar ratio than did mice fed the HFD. This is counter to our hypothesis. We tested a second hypothesis that the very high-fat and very low-fat diets used in our test were too extreme and not representative of typical human diet. The second test used a 45% kcal high fat diet to induce obesity in 6 mice and kept another 6 mice on low fat standard chow (16% kcal fat). We simplified the experiment using only the 1:1 frosting ratio for the brief access test. Our results showed that mice receiving 12 weeks of 45% kcal fat feeding ate more 1:1 fat:sugar frosting than mice on 16% chow. Conclusions: These results suggest that 1) the physiology of obesity influences fat intake and 2) diet plays an important role in food preference and intake, independently of obesity. Future work will analyze plasma endocannabinoid content to understand if there is a correlation with dietary patterns and adiposity.

252 **Emergence Of Adaptive Taste Choices In A Closed-Loop Task**

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A crucial aspect of behavior is the ability to actively gather information and use that information to guide subsequent choices. However, traditional approaches reduce behavior to independent stimulus-response contingencies where the experimenter controls the stimulus, and the animal responds reactively. Such approaches ignore the influence of response outcomes on future actions. I designed a paradigm where animals are allowed to sample information in their environment freely in order to examine how choice outcomes influence subsequent choices. Rats perform a 2-alternative free choice task with two taste options available through two nose pokes. Triggering either nose poke leads to delivery of a drop of sucrose solution or water into the animal's oral cavity through an intra-oral cannula. Poke A offers 70mM sucrose with a probability ranging from 10-40%; poke B offers 30mM sucrose with a probability of 50-90%. Probabilities are fixed for the duration of a single daily session (1 hour in duration) but vary between sessions. Analysis of choice behavior reveals that animals preferentially choose the option with the highest expected sucrose concentration, which is the product of absolute concentration and probability. This preference emerges over the course of each individual session and is most pronounced at the end of a session. The observed pattern of results suggests that animals spontaneously integrate information from multiple reward dimensions to maximize caloric intake. Our paradigm establishes a way to study how adaptive behavior emerges from closed-loop interactions within the environment, where animals dynamically update the value of choice options based on the outcome of previous choices. Ongoing work is aimed at modeling choice behavior using reinforcement learning theory.

254 **The Role Of Saliva In Astringency Perception Of Cocoa Polyphenols**

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Polyphenols are linked to multiple health benefits, but they elicit astringency through one or more mechanisms. Prior work has typically used extractable polyphenols in wine, tea, or model solutions. However, cocoa includes both extractable and non-extractable polyphenols. Here, we report on salivary proteins and astringency from a cocoa beverage. After providing stimulated saliva, 72 adults rated astringency, bitterness, sourness, sweetness, and chocolate flavor of a cocoa beverage over 90 seconds. Salivary flow and intensity ratings were analyzed by hierarchical clustering on principal components, resulting in four clusters of participants. Clusters separated based on maximal astringency (Imax), area-under-the-curve (AUC), decay to half-Imax, and salivary flow. Pooled saliva from each cluster was then combined with cocoa polyphenols and analyzed alongside untreated saliva using SDS–PAGE; band intensities for each cluster were calculated. Multi-Factor Analysis of pooled salivary proteins and sensory ratings revealed 82.1% of the variance can be described by 2 dimensions (Dim1: 48.8%, Dim2: 33.3%). The maximal intensity (Imax) and cystatins contribute most to Dim 1, showing a direct relationship to imply that greater astringency intensity associates with a greater loss of cystatins when exposed to polyphenols. In Dim2, salivary flow rate shows an inverse relationship to the time to Imax and decay rate, suggesting salivary flow is mainly responsible for how fast astringency is perceived and decays rather than the maximal intensity. Greater loss of acidic proline-rich proteins (aPRPs) was related to decreased rate of decay. These data add to a growing body of evidence that the specific type of salivary protein, not merely the amount, is predictive of individuals' differences in astringent sensations.

256 **Assessing Recruitment Strategies And Challenges In Studying Racial And Ethnic Variations In Bitter Taste Perception**

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Background—Racial and ethnic differences in taste perception may influence food preferences, diet, and medication adherence, impacting disease prevention, treatment, and health disparity. Difficulties recruiting from racial and ethnic minority populations may limit the understanding and application of these differences. Purpose—This study evaluates the recruitment approaches used by researchers to enroll participants of Sub-Saharan African (n=127) and Asian (n=154) into a bitter taste perception and medicine study. Methods—Recruitment occurred from January 2021 – December 2022 using five main recruitment strategies: 1) Paper Flyers 2) Paid Advertisements 3) Internet-based and social media outreach 4) Professional Networking 5) Personal Networking. Eligible participants were over 18 and identified as a 1st, 2nd, or 3rd generation immigrant. Results—The recruitment process extended beyond the anticipated timeline, and the effectiveness of strategies varied among the ancestry groups. Recruitment goals for individuals of Asian and European ancestry were met within the first year, with flyers and online advertisements being more successful in recruiting 52% of those participants. Recruiting participants of African ancestry required more intentionality and was not achieved until the second year, with 66% of participants recruited through professional and personal networking. Discussion—Sensory-based research may be key to understanding nutrition behaviors and disease risk; thus, adequate representation of diverse populations is necessary. Results suggest that researchers may have misunderstood fundamental differences when recruiting multi-ancestral groups. Limitations exist in understanding unique barriers and facilitators to research participation among different ethnic groups.

258 **Adiponectin Signaling Modulates Fat Taste Responsiveness And Sensitivity In Mice**

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Adiponectin is a fat tissue-derived hormone with insulin-sensitizing and anti-inflammatory functions. Adiponectin receptors are highly expressed in taste buds, suggesting a potential role of adiponectin signaling in the modulation of taste function. Previously, we showed that the adiponectin receptor agonist, AdipoRon, acts to enhance calcium responses to fatty acids in human taste cells by increasing the translocation of CD36 to the cell surface (Lin et al. Int J Mol Sci 24:5801, 2023). Using calcium imaging, we found that adiponectin and AdipoRon enhances cellular responses to fatty acids in isolated taste bud cells from male and female wild-type (WT) mice, but not AdipoR1 knockout (KO) mice. Two-bottle preference and conditioned taste aversion behavioral assays in AdipoR1 KO mice indicated a critical, sex-dependent role for adiponectin signaling in the modulation of taste responsiveness. Female AdipoR1 KO mice showed a diminished preference and reduced taste sensitivity for linoleic acid compared to WT controls, while no such differences were found in male AdipoR1 KO and WT mice. No significant differences were seen in their preference for sweet, bitter, umami, and sour stimuli in either sex. Moreover, loss of AdipoR1 did not appear to significantly inhibit the strong preference for or intake of either Intralipid or a high fat diet. Together, these data indicate that adiponectin acts via AdipoR1 in mouse taste bud cells to enhance their responses to fatty acids and adiponectin signaling may play a key role in the recognition of fatty acids, however, such taste modulation by AdipoR1 signaling alone does not appear to effect significantly dietary fat intake. Supported by NIH DC013318 (tag).

260 **Selective Increases In Taste Sensitivity To Glucose As A Function Of Hunger Status**

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Investigators have identified glucose transporters (SGLT1 and GLUTs) in taste cells, and have suggested that they contribute to a distinct glucose-specific signaling pathway. However, the functions of this glucose-specific pathway in the oral cavity are not well understood. We hypothesize that the glucose-specific taste pathway may be involved in the detection of glucose in times of hunger. If true, glucose would be perceived as more intense compared to other non-glucose containing sweeteners when subjects were hungry. We tested this hypothesis by comparing the relative taste sensitivities between glucose and fructose when subjects were hungry vs. full. Overnight fasted subjects (N=29) completed a series of 3-AFC tests comparing one target (one glucose from a range of concentrations) and two constants (200 mM fructose) before and after consuming mild-tasting breakfast sandwiches until full (600-1500 calories). The concentrations of glucose considered iso-intense with 200mM fructose were 436 vs. 464mM on average, when subjects were hungry vs. full; the relative taste sensitivity to glucose compared to fructose was significantly higher when individuals were hungry vs. full (paired t-test, $p < 0.05$). We replicated this finding, comparing fixed sucralose (0.04mM) to the same range of glucose concentrations ($p < 0.001$). Importantly, we found that, when comparing fixed sucralose (0.4mM) to a range of fructose concentrations, there was no difference in iso-intense concentration before and after eating ($p > 0.05$). These findings support the hypothesis that glucose-specific taste pathway may be involved in the sweetness detection of glucose in times of hunger.

262 **Otop1 Mediates Chorda Tympani And Behavioral Responses To Ammonium Chloride (Nh4Cl)**

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Ammonium Chloride (NH_4Cl) has been commonly used as a taste stimulus in gustatory vertebrate animal research for decades. Despite its prevalence, the mechanism by which it activates the gustatory system has been relatively unexamined. Here we present data indicating the involvement of sour receptor OTOP1 in the gustatory response to NH_4Cl in mice. OTOP1 is a proton-selective channel expressed in Type III taste cells in mice. Chorda Tympani nerve responses to NH_4Cl are greatly reduced or eliminated in mice lacking functional OTOP1 channels (*Otop1*$^{-/-}$ mice) as compared to wild-type littermates. Behaviorally, NH_4Cl is an aversive stimulus to wild-type mice, eliciting increased avoidance as the concentration rises. In *Otop1*$^{-/-}$ mice, this avoidance is attenuated. When both OTOP1 and Type II taste receptor cells (those that respond to bitter, sweet, or umami stimuli) are eliminated in a double knockout *Otop1*$^{-/-}$, *Skn-1a*$^{-/-}$ mouse line, behavioral avoidance of NH_4Cl is abolished entirely. These data demonstrate that the sour receptor OTOP1, in addition to responding to acidic compounds, also mediates a large portion of the taste response to NH_4Cl. How Type III cells and OTOP1 might differentially mediate responses to such disparate sensory stimuli as acids, water (Zocchi et al., 2017), and now ammonium remains a mystery.

264 **Mechanism Of Long Term-Lasting Virus-Induced Olfactory Loss**

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Respiratory virus infection is a major cause of olfactory loss. As the olfactory epithelium (OE) is exposed to the external environment, it can be directly accessed and infected by viruses. Antiviral defense mechanisms are activated so that the OE damaged by the virus can recover within, typically, a short time. However, severe long-term olfactory loss is observed in a subset of patients and its mechanism remains unclear. Recent studies showed that genetic errors in innate immune pathways can weaken antiviral responses in some patients. We hypothesized that the innate immune response errors result in impaired clearance of viruses, which may lead to chronic inflammation and incomplete regeneration of the OE. In this study, we used a knockout (KO) mouse model of interferon regulatory factor 3 (Irf3), a viral defense gene. We examined the role of Irf3 in tissue damage, viral clearance, and regeneration in the virus-infected OE by immunohistochemistry and qRT-PCR. Intranasally applied influenza virus mainly infected olfactory sensory neurons (OSNs) and microvilli of supporting cells in the OE of both control and Irf3 KO mice, while Irf3 KO mice produced much less antiviral IFN-β but more inflammatory TNF in the OE at 7 day post-infection (dpi). In addition, the RNA levels of influenza virus were significantly higher in Irf3 KO mice compared to control mice at 14 dpi. At 30 dpi, the numbers of dying OSNs, proliferating basal stem cells, and immature OSNs in the OE were significantly higher in Irf3 KO mice compared to control mice. At 60 dpi, the basal stem cells in the OE of Irf3 KO mice lost proliferating ability. These results suggest that Irf3 plays important roles in viral clearance and inhibition of chronic inflammation, and deficiency in Irf3 leads to severe, long-term post-viral olfactory loss.

266 **Olfaction Evaluation In Dogs With Sudden Acquired Retinal Degeneration Syndrome (Sards)**

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PURPOSE: To evaluate olfaction in dogs with sudden acquired retinal degeneration syndrome (SARDS) compared to sighted dogs and blind dogs without SARDS as control groups. METHODS: Olfactory testing was performed on three groups: SARDS, sighted, and blind/non-SARDS using eugenol as test odorant. The olfactory threshold was determined when subjects indicated detection of a specific eugenol concentration with behavioral responses. Olfactory threshold, age, body weight, and environmental room factors were compared among groups. RESULTS: Sixteen SARDS dogs, 12 sighted dogs, and 12 blind/non-SARDS dogs demonstrated mean olfactory threshold pen numbers of 2.8 (SD=1.4), 13.8 (SD=1.4), and 13.4 (SD=1.1), respectively, which correspond to actual mean concentrations of 0.017 g/mL, $1.7*10^{-13}$g/mL and $4.26*10^{-13}$ g/mL in the SARDS dogs, sighted dogs, and blind/non-SARDS dogs, respectively. Dogs with SARDS had significantly poorer olfactory threshold scores compared to the two control groups ($p<0.001$). Age, weight, and room environment did not differ among the three groups. CONCLUSIONS: Dogs with SARDS have severely decreased olfaction capabilities compared to healthy, sighted dogs and blind/non-SARDS dogs. This finding supports the general principle that SARDS is a systemic disease causing blindness, endocrinopathy, and hyposmia. Since the molecular pathways are similar in photoreceptors, olfactory receptors, and hormone synthesis with all using G-protein coupled receptors in the cell membrane, the cause of SARDS may exist at the G-protein associated interactions with intracellular cyclic nucleotides. Further investigations into G-protein coupled receptors pathway and canine olfactory receptor genes in SARDS patients may be valuable in revealing the cause of SARDS.

268 **Study Of Chemosensory Enhancement Through Neuromodulation Training (Scent): Design And Methodology Of A Randomized Clinical Trial For Covid-Related Persistent Smell Loss**

Bernadette M. Cortese[1], Mary Clare Koebel[1], Nicole Cash[1], Aicko Y. Schumann[1,2], Lisa M. McTeague[1,3], Thomas W. Uhde[1], Rodney J. Schlosser[4], Bashar W. Badran[1]

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Along with its status as a hallmark feature of COVID-19, smell loss has earned the additional distinction as one of the more common symptoms of long COVID. In turn, the dearth of evidence-based treatments for chemosensory dysfunction exposed a large gap in healthcare. While smell training (ST) shows great promise, its efficacy in COVID-related smell loss requires additional study. Outcome latency of ST may limit its overall acceptance and utility as well. Thus, adjunctive methods that improve ST efficacy by accelerating recovery are needed. Early evidence suggests trigeminal nerve stimulation (TNS) as a monotherapy may facilitate olfaction. Here we describe the study design and methodology of our novel home-based clinical trial to investigate the combination of TNS and ST in the treatment of persistent smell loss and associated long COVID-related neuropsychiatric deficits. 180 adults with COVID-related, subjective, persistent smell loss will be recruited into this randomized, double-blind, sham-controlled clinical trial. After baseline assessment of smell, mood, sleep, and cognitive function, participants will be randomly assigned to one of three arms: 1) active ST, 2) placebo ST, or 3) combined TNS+ST. Participants will self-administer their assigned treatment at home, twice daily, at least 5 days per week, for 12 weeks. Participants will return to the clinic after 4 and 12 weeks of training for follow-up assessments. The primary outcome is the effect of active versus placebo ST on psychophysical and subjective olfactory-specific deficits and associated neuropsychiatric impairments. The TNS-enhanced effects of ST will also be assessed. Special considerations addressed during the design and execution of this at-home clinical trial including remote monitoring and safety will be discussed.

270 **Investigating The Behavioral Effects Of Anosmia And Repetitive Mild Traumatic Brain Injury In A Murine Model**

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Anosmia (loss of smell) has many negative effects on quality of life and has increased in prevalence due to the SARS-CoV2 (COVID-19) pandemic. Regardless of its origin, anosmia remains understudied relative to other sensory disorders. Anosmia is one of the most common, yet least understood, sensory deficits following traumatic brain injury (TBI), including repetitive mild TBI (rmTBI). Here, we report the development of a model of anosmia in the context of rmTBI, which we implemented via a novel closed-skull impact device. We enrolled 75 adult male and female C57Bl6/J mice in a longitudinal study with rmTBI only, anosmia only, rmTBI+anosmia, and control (double-sham treatments) groups. rmTBI was induced via nine impacts to the dorsal skull over the course of three weeks. Anosmia was induced chemically via intranasal instillation of a combination of $ZnSO_4$ (a mild toxin for the olfactory epithelium) and Triton-X100 (detergent). On each animal, we performed a battery of 6 behavioral assays at baseline (pre-treatment), 1-2 weeks post-treatment, ~3 months post-treatment (~6 months postnatal), and ~9 months post-treatment (~12 months postnatal). Here, we present preliminary results from 2 of the 6 behavioral tests performed (buried food task and sucrose preference test). The buried food task showed little evidence of total anosmia in most animals, but many injured mice showed altered behavioral patterns that simple metrics (latency to find the cookie) did not capture. Animals in the rmTBI+anosmia group showed a 5.6% and 5.2% decrease in sucrose preference at Follow-Up #1 and #2 respectively, an indication of anhedonia. These preliminary results illustrate the utility of this experimental approach, which will serve as the basis for further studies into behavioral impacts of anosmia in the context of rmTBI.

272 **Effects Of Congenital Blindness On The Development And Plasticity Of The Olfactory System : Input From Odor-Evoked Sniffing And Optical Imaging Recordings**

Nouhaila Bouguiyoud[1], Syrina Al Aïn[1], Johannes Frasnelli[1], Belkacem Messaoudi[2], Samuel Garcia2[2], Anne-Marie Mouly[2], Philippe Litaudon[2], Emmanuelle Courtiol[2]

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2.2 billion people are visually impaired worldwide. The absence of a sensory modality induces brain plasticity and a reorganization of the remaining sensory functions. While this phenomenon has been widely described in the auditory and tactile domains, the impact of blindness on olfactory functions, an invisible but critical sense in our daily life, and their neurobiological correlates remain poorly studied. In addition, the evolution of this plasticity in blindness individuals across development and its underlying neural mechanisms are still poorly known. The objective of this study is to test the development and plasticity of the olfactory system induced by the absence of the visual system. We chose to address this question in rodents, an animal model that mainly relies on its olfactory sense to perceive and adapt to its environment (food search, social interactions, detection of predators, etc.). Specifically, we used a mouse model of congenital blindness (ZRBDA) where in a same litter half of the conspecifics are born blind (homozygous) and the other half are born sighted (heterozygous). To test the development and plasticity of the olfactory system, we first investigated the mouse olfactory perceptual function using physiological and behavioral measures using a paradigm suitable throughout ontogeny. To do so, we measured the odor-evoked sniffing and behavior at three different ages: (1) in infants (Postnatal day PN10-13, before their eyes opened), (2) in juveniles (PN 30-34, after weaning) and (3) in adults (PN60-62) in both male and female in a whole-body plethysmograph. Second, to assess the underlying neural mechanisms, all of the above adults were used to map the activity of their olfactory bulb using optical imaging. Preliminary results will be presented in this poster.

274 **Digital Accessible Remote Olfactory Mediated Health Assessments For Preclinical Ad**

Andreas Runde[1], Colin Magdamo[1], Alysa Alejandro Soto[1], Benoit Jobin[1,2], Alefiya Albers[1], Mark Albers[1]

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Early detection of Alzheimer's Disease (AD) is critical to investigate the efficacy of therapies prior to the onset of symptoms. Many studies have demonstrated that olfactory dysfunction is a biomarker that predicts cognitive decline in presymptomatic stages of AD. We developed the remote AROMHA Brain Health Smell Test (consisting of odor percept identification (OPID), percepts of odor episodic memory (POEM), and odor discrimination (OD)) to assess olfactory function and validated self-administration in at-home settings. Participants determined to be cognitively normal (CN) via self-report or cognitive assessment from the Massachusetts Alzheimer's Disease Research Center (MADRC) were given the option to self-administer the smell test. 66 CN participants (mean age: 41.8) were observed during self-administration (in-person or via Zoom), while 29 (mean age: 63.0) opted for self-administration without observation. These two groups performed similarly across OPID ($p=0.59$), identification confidence ($p=0.22$), OD ($p=0.68$), POEM ($p=0.436$), and odor intensity ($p=0.77$). Through the MADRC, we recruited 28 subjects who expressed Subjective Cognitive Complaints (SCC) or received a Mild Cognitive Impairment (MCI) diagnosis. They performed significantly worse than CN participants in unadjusted analyses on OPID ($p<0.001$), OD ($p=0.0013$), and POEM ($p=0.0041$), while having lower odor intensity ($p=0.016$), and identification confidence ($p<0.001$). The AROMHA Brain Health Test's accessibility through self-administration makes it suitable for widespread use. As a non-invasive, time-efficient screening tool, the test holds promise for early AD detection. Incorporation in clinical trials and epidemiological studies with key biomarkers for detection of AD and other related dementias is ongoing to provide further validation.

276 **G Protein Coupled Receptors In Sea Lamprey Pharyngeal Tissue Containing Taste Buds**

Zeenat Aurangzeb[1], Sirinart Ananvoranich[1], Gianfranco Grande[1], Gheylen Daghfous[2], Rejean Dubuc[2], Barbara Zielinski[1]

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Chemical stimuli in food are detected by chemosensory neuro-epithelial cells in taste buds, transmitting signals to the central nervous system. Gustatory mechanisms in fish and mammals involve dedicated G protein-coupled receptors (GPCRs) for bitter, sweet, sour and umami. Taste cells express type 2 or type 1 receptors activating a phospholipase signal transduction pathway with G-proteins. In the sea lamprey, a basal vertebrate, taste buds are located along the lateral pharyngeal surface. These respond to sweet, sour, bitter, amino acid and bile acid stimuli. The analysis of sea lamprey mRNA transcripts using the basic local alignment research tool (BLAST) revealed no amino acid sequences for vertebrate taste type 2 receptors. Interestingly, the amino acid sequence of the sea lamprey vomeronasal receptor showed similarities to sweet and bitter taste type 1 and 2 receptors found in zebrafish, mammals and medaka fish. Moreover, vomeronasal receptors belong to the same GPCR families as taste receptors. RT-PCR analysis revealed V1R324, V1R4, V1R342, V2R1 in lamprey pharyngeal tissue containing taste buds. Further studies are needed to determine whether these receptors are expressed in taste buds or in non-taste cells surrounding the taste buds through methods such as immunolabelling or in-situ hybridization. This research offers valuable insights into the molecular mechanisms of taste transduction in this basal vertebrate, which may improve our understanding of the evolutionary history of taste perception

9:00 - 10:00 AM	Estero Foyer
Coffee Break	

10:00 - 12:00 PM	Calusa EFGH
Exploring Cellular and Molecular Dynamics in the Developing Olfactory System	

Chair(s): Paolo Forni

10:00 **Exploring Cellular And Molecular Dynamics In The Developing Olfactory System**

Paolo Forni[1], Ron Yu[2]

[1]University at Albany, SUNY, [2]Stowers Institute for Medical Research

The main and accessory olfactory systems play pivotal roles in diverse aspects of vertebrate biology, from foraging behaviors to social interactions and reproduction. Advances in single-cell transcriptomics and genetic approaches are reshaping our understanding of the cells and the molecular mechanisms that underlie the development and connectivity of olfactory systems in vertebrates. This symposium aims to provide a platform for researchers to share their cutting-edge findings, fostering interdisciplinary discussions and inspiring new collaborations.

10:02 **Investigating The Molecular Mechanisms Governing Axonal Projections Of Vomeronasal Sensory Neurons**

Thelma T Chiremba[1], Limei Ma[1], Max Hill Jr.[1], Hannah Wilson[1], Cathy McKinney[1], C. Ron Yu[1,2]

[1]Stowers Institute for Medical Research, Kansas City, MO, United States, [2]University of Kansas Medical Center, Kansas City, KS, United States

The mouse apical vomeronasal sensory neurons (VSNs) express >230 V1r receptors. These VSNs project their axons to the anterior accessory olfactory bulb (aAOB). Despite decades of study, the precise molecular mechanisms governing this stereotypic projection pattern remain elusive. We previously identified V1re9 and V1re12 as receptors for mouse female urine-specific cues, and V1rj2 and V1rj3 as receptors for female estrus cues. Combining these cues robustly triggered innate male mating behaviors. In this study, we use transgenic methods to trace VSNs expressing the V1re and V1rj receptors to elucidate the neural circuitry processing female pheromone information. Each receptor was tagged with a fluorescent marker or Cre recombinase. Confocal imaging on tissue-cleared adult mouse AOBs revealed clade-specific projection patterns of VSNs. Notably, most of the Vr1j-expressing VSNs project to glomeruli concentrated in a distinct spatial location of the aAOB, whereas glomeruli targeted by V1re-expressing VSNs are evenly distributed within the aAOB. Using V1re9 and V1re12 double-reporter mice, we observed both homotypic and heterotypic convergent projection patterns of the VSNs. Most glomeruli were exclusively targeted by VSNs expressing either of the receptors. Surprisingly, other glomeruli were targeted by both V1re9- and V1re12-expressing VSNs. We analyzed scRNA-seq data of VNO epithelia to identify potential mechanisms underlying these projection patterns. We identified combinations of axon guidance molecules (AGs) and transcription factors (TFs) that are distinctively expressed by the V1re9 and V1re12 VSNs. Interestingly, we also found AGs and TFs that are shared between the receptor types. These exclusive and shared expressions of AGs and TFs may influence the homotypic and heterotypic VSN projections.

10:22 **Elucidation Of Mouse Olfactory Glomerular Network**

Pavan Rao[1], I-Hao Wang[1], Hao-Ching Jiang[1], Sung Jin Park[1], Zhiping Weng[1], Fei Chen[2], Evan Z. Macosko[2], Paul L. Greer[1]

[1]University of Massachusetts Chan Medical School, Worcester, MA, United States, [2]Broad Institute of Harvard and MIT, Cambridge, MA, United States

The ability of the mammalian olfactory system to detect and discriminate a vast array of odors is essential for survival. However, how this is accomplished remains incompletely understood. We have recently found that each type of olfactory sensory neuron (OSN) within the mouse olfactory system expresses a unique transcriptional program that is distinct from all other OSNs in the olfactory epithelium. We have taken advantage of this observation and a combination of single-cell RNA sequencing, spatial transcriptomics, and machine learning, to generate a map of the majority of glomerular positions in the mouse OB. We find that there appears to be a relationship between the Cartesian coordinates of the glomerulus within the olfactory bulb and the chemoreceptive properties of the corresponding odorant receptor, suggesting that the anatomic location of glomeruli may assist the brain in decoding the identity of the odor that it has sensed. We have begun to investigate this possibility by beginning to characterize the properties of the Mitral and Tufted (M/T) cell projection neurons, which innervate these glomeruli before relaying the information they receive to the higher brain regions responsible for generating odor percepts. Here, we present our progress on characterizing M/T cell populations integrating single nuclear RNA sequencing, neuronal viral tracing, and viral barcoding techniques.

10:42 **Mechanisms Controlling Specification Of Olfactory Receptor Neuron Subtypes**

Kevin Monahan

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There are hundreds of subtypes of olfactory receptor neurons (ORNs) in mice, each of which expresses a different odorant receptor (OR). These subtypes are specified in a hierarchical fashion, with ORN progenitors first committing to express a specific class of OR genes. For the large family of Class II ORs, the set of ORs available for selection is further restricted depending on anatomical position within the olfactory epithelium. This restriction is followed by stochastic selection of one allele of a single OR gene from the available set. The process of OR choice coincides with a dramatic remodeling of the spatial positioning and chromatin state of OR genes within the nucleus. Strikingly, changes in the chromatin structure of OR genes closely correlate with the class and spatial restriction of OR gene choice. We are investigating the mechanisms that remodel OR gene chromatin in OSN progenitors and their relationship to OR choice. Here, we show that Testis expressed 15 (Tex15) is required for the spatial restriction of class II OR choice and for the normal pattern of stochastic choice across all OSN classes. Intriguingly, germline deletion of Tex15 results in biased OR selection choice in favor of OR genes that are expressed early in OSN differentiation. Moreover, Tex15 null mice exhibit altered patterns of heterochromatin deposition on OR genes, which suggests that Tex15 may repress OR genes in OSN progenitors, analogous to its known role in the silencing transposons in spermatocytes.

11:07 **Glomerular Map Formation In The Control Of Social Behaviors**

Sydney Fearnley[1,2], Neelima Vaddadi[1,3], Emilie Dumontier[1], Jean-Francois Cloutier[1,2,3]
[1]Montreal Neurological Institute and Hospital, Montreal, QC, Canada, [2]Anatomy and Cell Biology, McGill University, Montreal, QC, Canada, [3]Neurology and Neurosurgery, McGill University, Montreal, QC, Canada

The flow of information and its processing in the nervous system relies on the formation of selective connections between neurons. More specifically, the establishment of accurate neural maps in sensory systems permits the detection and interpretation of cues from the environment. The formation of this circuitry depends on multiple processes, including the guidance of axons to their target fields and the formation of synapses with their synaptic partners. In the accessory olfactory system, which regulates social and sexual interactions in mice, vomeronasal sensory neurons (VSNs) project their axons to the accessory olfactory bulb (AOB), where they form synapses with second-order mitral cells inside glomeruli. Axons of VSNs expressing the same type of vomeronasal receptor coalesce together to form homogenously innervated glomeruli that are spatially conserved in the AOB. The establishment of this glomerular map is proposed to contribute to the representation of the phenotypic qualities of chemosignals detected by VSNs and to the expression of specific social behaviours. Members of the Kirrel family of receptors play a critical role in the accurate coalescence of VSNs axons into glomeruli and in the formation of the AOB glomerular map. Using cell-type specific Kirrel3 loss-of-function approaches to disrupt glomerular map formation, we establish a link between the accurate formation of the AOB glomerular map and vomeronasal acuity in the modulation of VNO-dependent behaviours.

11:32 **Terminal Nerve Cells In Rodents As A Bridge Between Olfactory Development And Fertility**

Rico Amato, Ed Zandro M Taroc, Paolo E. Forni
Biology Department -The RNA Institute, University at Albany

During embryonic development, the olfactory placode (OP) gives rise to migratory neurons, including olfactory pioneer neurons, cells of the terminal nerve (TN), and Gonadotropin-releasing hormone-1 (GnRH-1) neurons. Pioneer migratory neurons originating from the olfactory trigger the olfactory bulb morphogenesis. In mice, the GnRH-1 neurons are first detectable in the developing olfactory system around mid-gestation. From the nose, the GnRH-1 neurons migrate along the TN axons to various brain regions. The GnRH-1 neurons are essential for regulating the hypothalamic-pituitary-gonadal (HPG) axis. Kallmann syndrome is characterized by impaired olfactory system development, defective olfactory bulb formation, compromised secretion of GnRH-1, and infertility. The mechanistic connection between the aberrant olfactory system and defective GnRH-1 migration in Kallmann syndrome remains elusive. Human and mouse studies underscore the significance of the Prokineticin-2/Prokineticin-Receptor-2 (Prokr2) signaling pathway in both olfactory bulb morphogenesis and GnRH-1 neuronal migration. Loss-of-function mutations in Prokr2 can lead to Kallmann syndrome, making the Prokr2 signaling pathway an attractive model for unraveling the olfactory/GnRH-1 connection. Our investigation revealed that the TN neurons transiently express Prokr2 during the critical period of GnRH-1 neuron formation, migration, and induction of olfactory bulb morphogenesis. Prokr2Cre genetic lineage tracing and Single-cell RNA sequencing identified that TN comprises neurons distinct from olfactory and GnRH-1 neurons. Notably, the TN neurons express multiple genes linked to Kallmann syndrome (KS). Our study posits that the aberrant development of pioneer/TN neurons may contribute to the spectrum of Kallmann syndrome.

10:00 - 12:00 PM	Calusa ABC
Coding Principles in the Olfactory and Gustatory Cortex	

Chair(s): Kevin Franks

10:00 **Introduction**

10:02 **Synaptic Plasticity And Ensemble Representation In Piriform Cortex**
Anne-Marie M. Oswald
Neurobiology, Neuroscience Institute, University of Chicago, Chicago, IL, United States

Olfactory stimuli are typically mixtures of different odor molecules. Odor mixtures can be identified elementally, whereby individual components drive perception, or configurally as an odor object. The odor components are parsed by the olfactory bulb, which relays this information to the anterior piriform cortex (APC) where component information may be recombined. Within the APC, pyramidal neurons (PNs) receive afferent odor information on their distal dendrites and recurrent excitation proximally. Coactivation of afferent and recurrent pathways results in associative plasticity at recurrent synapses. This plasticity is thought to underlie to the formation of long-term ensemble representations of olfactory stimuli. To assess synaptic strength within neural ensembles following odor learning, we used transgenic Fos^{ERT} mice that allow targeted recombination in active populations (TRAP). We trained Fos^{ERT} mice to discriminate two overlapping mixtures in a digging task. Once the mice reached criterion, we used TRAP to express tdTomato and ChR2 in ensembles that were specifically active during presentation of the rewarded or unrewarded odor mixture. We then reactivated the ensemble PNs *in vitro* to compare synaptic strength between PNs within ensemble (tdtom+) versus PNs outside the ensemble (tdtom-). We found that synapses are specifically strengthened within ensembles that respond to the rewarded odor. Surprisingly we found that synapses remain weak within ensembles responsive to the unrewarded odor. Further experiments revealed that mice use component (elemental) information to solve the task, rather than the mixtures as a whole (configural). Our findings suggest this task-specific information is represented by changes in synaptic strength between PNs within ensembles in APC.

10:25 **Learning Embeds Mixed-Selectivity And Associative Encoding In Piriform Cortex**
Antonia Marin-Burgin
IBioBA-CONICET-Max Planck partner Institute, Buenos Aires, Argentina

Olfaction is influenced by contextual factors, past experiences, and the animal's internal state. Whether this information is integrated at the initial stages of cortical odor processing is not known, nor how these signals may influence odor encoding. Here we revealed multiple and diverse non-olfactory responses in the primary olfactory (piriform) cortex (PCx), which dynamically enhance PCx odor discrimination according to behavioral demands. We performed recordings of PCx neurons from mice trained in a virtual reality to associate odors with visual contexts to obtain a reward. We found that learning shifts PCx activity from encoding solely odors to a regime in which positional, contextual, and associative responses emerge on odor-responsive neurons that become mixed-selective. The modulation of PCx activity by these non-olfactory signals was dynamic, improving odor decoding during task engagement and in rewarded contexts. This improvement relied on the acquired mixed-selectivity, demonstrating how integrating extra-sensory inputs in sensory cortices can enhance sensory processing while encoding the behavioral relevance of stimuli.

10:50 **Exploring Drift In Gustatory Cortex Taste Identity And Valence Representations**
Max Fletcher, Martin A Raymond, John D Boughter
University of Tennessee Health Science Center

Recent studies have revealed that cortical ensemble activity evoked by stimuli does not remain constant over time; instead, it undergoes significant fluctuations spanning days and weeks, a phenomenon referred to as representational drift. Drift has been described in several sensory systems, including olfaction, where odor representations of given odor in piriform cortex become less similar over time. In this study, we explored the extent of drift in gustatory cortex taste representations using miniscope recordings in freely moving mice. Water-restricted mice were presented with a panel of palatable and unpalatable tastes once a week for five weeks. We followed activity from over 700 cells from five mice throughout the entire study. To explore drift in taste coding, we compared pooled, averaged taste responses both within and across sessions for all tastes using a variety of approaches, including vector correlations, principal component analysis, and classification analysis. Like other sensory systems, we find that representations drift with time. However, while this drift appeared at a similar rate for each taste, the directionality of the drift was not random but appeared in such a way as to further separate tastes based on their palatability. Current work focuses on whether these effects are more driven by time or experience.

11:13 **Coding In The Gustatory Cortex: Tasting The Past, The Present And The Future**
Alfredo Fontanini
Department of Neurobiology and Behavior, Stony Brook University, Stony Brook, NY, United States

Over the years, the gustatory cortex (GC) has established itself as an excellent model for studying how sensory cortices integrate coding of sensory and cognitive variables. In addition to encoding chemical stimuli that are present on the tongue and ascribing them to one of the five taste qualities, neurons in GC can also be activated in the absence of taste, either prospectively or retrospectively. Prospective activation of GC neurons occurs when

crossmodal cues associated with taste predict the identity of upcoming tastants. Retrospective activation is observed when the memory of a gustatory stimulus is required to guide a specific action. Encoding of what precedes the tasting experience, what is present on the tongue, and what follows can occur within the same trial, facilitated by GC's ability to represent signals through extended temporal dynamics. In this presentation, I will discuss findings demonstrating the involvement of GC in representing past, present and future events. Upon reviewing work on how anticipatory cues can engage GC and how this prospective activation can impact behavior, I will present results showing how GC transitions from encoding gustatory stimuli to using this information for generating preparatory activity. I will present electrophysiological and calcium imaging data from mice performing taste-based, two-alternative choice (2AC) tasks and show how time-varying patterns of population activity can account for multiplexing of sequential signals. Altogether, the presentation will provide an account of the integration of gustatory, anticipatory, and preparatory signals in GC, and point at open questions and future areas of investigation.

11:36 **Smell The Lizard: Ancestral Molecular Signatures Of Olfactory Cortex Neurons**

Sara Zeppilli[1], Alonso Ortega Gurrola[2], Pinar Demetci[3], David H. Brann[4], Noga Zilkha[5], Tali Kimchi[5], Sandeep R. Datta[4], Ritambhara Singh[3], Maria A. Tosches[2], Anton Crombach[6], Alexander Fleischmann[1]

[1]Department of Neuroscience and Carney Institute for Brain Science, Brown University, Providence, RI, United States, [2]Department of Biological Sciences, Columbia University, New York, NY, United States, [3]Department of Computer Science, Center for Computational Molecular Biology, Brown University, Providence, RI, United States, [4]Department of Neurobiology, Harvard Medical School, Boston, MA, United States, [5]Department of Brain Sciences, Weizmann Institute of Science, Rehovot, Israel, [6]Inria Centre de Lyon, Villeurbanne, France

The remarkable repertoire of mammalian behaviors and cognitive abilities is thought to arise from the vast diversity of neuronal cell types and circuits of the cerebral cortex. Intriguingly, the 3-layered mammalian olfactory cortex resembles the cortical cytoarchitecture of non-mammals, despite over 200 million years of coevolution alongside the mammalian neocortex. To determine the molecular mechanisms driving cell type and circuit diversification across distinct cortical traits, we performed single-nucleus transcriptome and chromatin accessibility analyses across cortical areas in mice, reptiles, and amphibians. We found that, in contrast to the 6-layered mouse neocortex, principal neurons of the 3-layered olfactory cortex displayed a continuous rather than discrete variation in transcriptomic profiles. Surprisingly, subsets of pyramidal cells with conserved transcriptomic profiles were distinguished by distinct, area-specific epigenetic states. Furthermore, we determined the transcriptomics profiles of a prominent population of piriform immature neurons and observed a high degree of divergence between piriform pyramidal cells in lab versus wild-derived mice. These results suggest a critical role for adult immature neurons in enhancing the adaptability of olfactory circuits. Finally, we show olfactory cortex neurons displayed marked transcriptomic similarities to cortical neurons in turtles, lizards, and salamanders. Together, these data suggest that the mammalian olfactory cortex retains molecular signatures representative of ancestral cortical traits.

12:00 - 1:00 PM	Calusa EFGH
Membership Business Meeting	

Get involved! Join us for reports from the society leadership on the state and future of the association. All members are welcome and encouraged to attend.

1:00 - 4:30 PM	Lunch On Own
Free Time	

4:30 - 6:00 PM	Calusa ABC
The Great Debate: The role of artificial intelligence in olfaction	

Recent advances in statistical learning, machine intelligence, chemoinformatics and psychophysics appear to be bringing us closer to a holy grail of chemical biology: to be able to predict what a molecule will smell like based upon its structure alone. But, given the limits of the technologies and data, how close are we to actually reaching this elusive goal? Are these new computational approaches the key to new insights into the biology of smell, or a shiny distraction from the hard experiments necessary to understand how the brain transforms chemistry into perception? What are the right and wrong questions to ask using these methods? And given the deep role played by personal experience in smell, will it ever be possible to make accurate predictions in individuals? Here we assemble a diverse panel of experts to offer their differing perspectives on the promise and perils of AI in the study of smell. Join us as these experts engage in a vigorous open debate to render clear where these approaches stand now, and what progress we can reasonably expect in the future.

Participants:
Bob Datta (Harvard University)
Alex Wiltschko (Osmo)
Noam Sobel (Weitzmann Institute)
Stuart Firestein (Columbia University)
Ann-Sophie Barwich (Indiana University)
Pablo Meyer (IBM)
Barry Smith (University of London)
Joel Mainland (Monell Chemical Senses Center)

Chair(s): Bob Datta

4:30 - 6:00 PM	Great Egret
Demonstrations of test procedures for evaluating human smell and taste function	

This workshop will provide participants with first-hand experience in employing a wide range of procedures for assessing human smell and taste function. A brief discussion of the strengths and limitations of each approach to testing will be provided.

Chair(s): Thomas Hummel and Richard Doty

6:00 - 7:00 PM	Dinner On Own
Dinner on Own	

7:00 - 9:00 PM	Calusa EFGH
Polak Awards Lectures	

The Polak Foundation Awards are in honor of the Elsje Werner-Polak Memorial Fund in memory of our niece gassed by the Nazis in 1944 at age 7: Ghislaine Polak and the late Ernest Polak.

Chair(s): Dan Wesson

The Role Of Trigeminal Activation In Perceived Odor Intensity
Aiden Streleckis, Robert Pellegrino, Matthew Andres, Johannes Reisert, Joel Mainland, Federica Genovese
Monell Chemical Senses Center, Philadelphia, PA, United States

Most volatile compounds entering the nasal cavity activate both olfactory sensory neurons and chemosensory trigeminal fibers, leading to olfactory and somatosensory (e.g., irritation) sensations. These systems interact at the peripheral and central levels, leading to a change in perceived intensity. To understand this interaction, we compared physiological and perceptual responses in mice and humans, respectively. We delivered varying concentrations of 2-phenethylalcohol (olfactory agonist) and CO_2 (trigeminal agonist) and their mixtures in different ratios and recorded electro-olfactogram (EOG) responses in mice, and intensity ratings were recorded for humans. In mouse olfactory epithelia, CO_2/PEA mixtures induced EOG responses greater than the olfactory stimulus alone. In TRPA1/V1-knockout mice, which lack TRPA1, the trigeminal receptor for CO_2, responses evoked by the PEA/CO_2 mixture were not significantly different from those evoked by PEA alone. In humans, lower concentrations (10-20%) of CO_2 increased the perceived intensity of the mixture, whereas higher CO_2 concentrations overshadowed the contribution of PEA. Established odor intensity models do not predict this interaction. In summary, a trigeminal agonist modifies both neural and perceptual responses, and models of odor intensity need to account for this interaction.

7:20 **A Glomerular Hierarchy For Olfactory Discriminations**
Walter G. Bast[1], Cina Aghamohammadi[1,2], Priyanka Gupta[1], Tatiana Engel[1,2], Florin Albeanu[1]
[1]Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, United States, [2]Princeton University, Princeton, NJ, United States

Can we predict the perceptual similarity of two odorants from knowing which odorant receptors (ORs) they activate? This seemingly simple question remains unsolved as difficulties in controlling stimuli at the level of receptor types preclude disentangling their individual contribution in shaping olfactory perception. To overcome this limitation, we exploited the anatomical clustering of ORs to individual glomeruli. Using two-photon and widefield imaging in transgenic mice, we identified numerous glomeruli and determined their responses to 123 odorants. We created synthetic olfactory stimuli by optogenetically activating combinations of glomeruli with sub-glomerular resolution. To determine perceptual distances between glomerular sets, we asked mice to report differences in stimulus identity and quantified the contribution of each glomerulus in shaping the perception of these stimuli. Our psychophysical model revealed a striking perceptual glomerular hierarchy: some glomeruli were up to six times more potent than others in creating a reference percept. We further investigated whether this hierarchy is rooted in the glomerular (ORs) odor response spectra. Indeed, we found a significant correlation between the perceptual weight of each glomerulus and the average similarity of its odor response spectrum to the spectra of other glomeruli in the pattern. Alternatively stated, the more similar the odor responses of a given glomerulus are to other glomeruli in the pattern, the lower its perceptual weight. Our work contributes to elucidating how the brain maps differences in odorant receptor activation patterns to distinct olfactory percepts. The unifying framework we propose bridges the gap between the biophysical features of sensory input units and the structure of the perceptual space.

7:40 **Utilizing Olfactory Receptor Defined Glomeruli To Understand The Transformation Of Odor Representations In The Mammalian Olfactory Bulb**
Madison A. Herrboldt[1], Mona A. Marie[2], Hiroaki Matsunami[2,3], Matt Wachowiak[1]
[1]Department of Neurobiology, University of Utah School of Medicine, Salt Lake City, UT, United States, [2]Molecular Genetics and Microbiology Department, Duke University School of Medicine, Durham, NC, United States, [3]Neurobiology Department, Duke University School of Medicine, Durham, NC, United States

An essential component of olfactory encoding in the olfactory bulb (OB) is the transformation of signals from input (olfactory sensory neurons: OSNs) to output (mitral/tufted cells: MT cells). However, signal transformation from OSNs to MT cells has only been delineated in a single class II receptor, expressed in its non-native zone. Functional characterization of additional olfactory receptors (ORs) is needed at both the pre- and post-synaptic levels of processing to delineate general principles of signal transformation in the OB. To address this, we generated four mouse lines expressing mKate2 in the OSNs of a given OR, including two class I and two class II receptors. We then used two-photon imaging in awake, head fixed mice expressing genetically encoded calcium or glutamate reporters in MT cells to characterize the sensitivity and selectivity of OR-tagged glomeruli, as well as map the transformation of odor information along the OSN-MT neuronal circuit. Each OR-tagged glomerulus was probed with a large panel of 30-50 odorants, chosen based on in vitro response data and in vivo activity dependent changes in pS6 expression, to delineate pre- and post-synaptic tuning. Presynaptic glutamatergic input as well as MT cell calcium responses were far more narrowly tuned than OR responses in vitro. We also found that MT cell tuning closely mimics that of presynaptic, glutamatergic, input onto the MT cells, with the important exception that MT cells of certain ORs exhibit stereotyped suppression that is not present in the input. This suggests the presence of lateral inhibition that is odorant-specific and stereotyped across individuals for a given OR. This ongoing work will shed light on whether the logic of signal transformations in the OB can be generalized across ORs or is specific to receptor class.

8:00 **Basolateral Amygdala And Gustatory Cortex Interact Bidirectionally During Taste Processing In Rodents**
Abuzar Mahmood, Jessica Steindler, Donald Katz
Brandeis University, Waltham, MA, United States

Taste responses in Gustatory Cortex (GC) and Basolateral Amygdala (BLA) evolve as sequences of 3 states during the ~1.5 seconds following tastant delivery onto the tongue of the rat. GC activity reflects first somatosensation, next identity (taste quality), and then palatability across these 3 states; BLA activity, meanwhile, reflects both identity and palatability during the 2nd state. Previous work using symmetric connectivity (i.e., cross-coherence) measures has shown that GC and BLA remain strongly interacting throughout all 3 states, while the "pattern" of interaction changes with each state. However, the assumption of symmetric back and forth flow of information inherent in the above analyses is likely simplistic. To test this assumption and thereby gain a better understanding of systemic taste processing, we used multi-region electrophysiology and characterized the dynamics of the directional influence between BLA and GC using lags in the population state transitions, spectral Granger Causality, and Poisson Generalized Linear Modelling (GLM). Our analyses reveal that: 1) GC and BLA begin recurrently interacting after 300ms following stimulus delivery—at the onset of identity coding; 2) this recurrence is likely initiated by the onset of BLA->GC influence, while the GC->BLA influence is uniformly strong; 3) GC and BLA influence one another in different frequency bands, a fact that suggests non-overlapping projection populations; and 4) this suggestion of non-overlapping projection populations is confirmed using Poisson GLMs. These results further characterize GC->BLA modulation during the evoked taste response and show that BLA and GC are bidirectionally interacting only during the period from 300ms post-stimulus delivery till generation of the taste-evoked behavioral response.

8:20 **Activation Mechanisms And Competitive Antagonism In Class I Odorant Receptors**

Mona A. Marie[1], Hiroaki Matsunami[1,2,3,4,5]

[1]Molecular Genetics and Microbiology Department, Duke School of Medicine, Durham, NC, United States, [2]Neurobiology Department, Duke Schoole of Medicine, Durham, NC, United States, [3]Duke Institute for Brain Sciences, Durham, NC, United States, [4]Duke Cancer Institute, Durham, NC, United States, [5]Duke Initiative for Science & Society, Durham, NC, United States

Olfaction allows organisms to discern a wide variety of chemical compounds. In humans and vertebrates, this sense is predominantly facilitated by activating a broad family of odorant receptors (ORs). Ranging from hundreds to over a thousand, these ORs are part of the G-protein-coupled receptors (GPCRs) class. Interestingly, some ORs are also expressed in non-olfactory tissues. Recent advancements revealed the three-dimensional structure of OR51E2, a notable Class I human OR with established extra-olfactory roles, as it is present in the gut, the carotid body, and prostate cancer. OR51E2 recognizes short-chain fatty acids (SCFA), key bacterial metabolites. The Cryo-EM structure of OR51E2 serves as a model for other Class I ORs attuned to carboxylic acids, as it exhibits Class I-specific conserved residues essential for coordinating the functional group. However, variable residues in the binding pocket allow for accommodating different sizes of carboxylic acids, crucial for tuning specificity. This raises the possibility that carboxylic acids not fitting the binding pockets might act as competitive antagonists. We used cell-based assays to test the hypothesis. Our data suggests that longer-chain carboxylic acids can antagonize OR51E2 activation by propionic acid, consistent with this model. This competitive interaction aids in understanding the activation mechanisms common to Class I ORs. Additionally, the study hints at identifying small molecules that modulate Class I ORs, potentially offering insights into the varied biological functions of OR51E2 beyond olfaction.

8:40 **An Essential Role For Depolarization Block In Odor Discrimination**

David Tadres[1,2,*], Philip Wong[1,3,*], Naomi Khosalim[1], Mariana Lopez[4], Matthieu Louis[1]

[1]University of California, Santa Barbara, Santa Barbara, CA, United States, [2]current address: Stanford University, Palo Alto, CA, United States, [3]current address: University of California, Los Angeles, Los Angeles, CA, United States, [4]Centre for Genomic Regulation, Barcelona, Spain

With a limited repertoire of odorant receptors, olfactory sensory systems identify and differentiate between a large number of odors over concentrations varying across several orders of magnitude. According to the combinatorial receptor code theory each odor is represented by the activation of a unique combination of olfactory sensory neurons (OSNs). We recently discovered that OSNs enter a silent state due to depolarization block at ~3 orders of magnitude above their detection threshold. We speculated that this silent activity state ensures the sparseness of the combinatorial code even at high odor concentrations, which facilitates discrimination between odors eliciting similar patterns of OSN activity. Using larvae with a minimal olfactory sensory system genetically reduced to two functional OSNs, we investigated this prediction in an odor discrimination assay using classical (Pavlovian) conditioning as a behavioral readout. By combining electrophysiological recordings and a biophysical model of the OSN response properties, we characterized the neuronal activity of each OSN during the olfactory choice behavior of freely-moving larvae. We find that larvae can discriminate between odors if the concentration of one odor leads to silencing due to depolarization block in one OSN. In larvae with a fully functional olfactory system, we show that a single neuron undergoing depolarization block can be necessary to enable discrimination between two odors. Our results shed light on the basic mechanisms underlying the representation of odors in the peripheral olfactory system. They highlight that depolarization block is not a 'bug' but a feature of the olfactory code, which may explain why humans perceive odors differently at high versus low concentrations.

201 **The Effect Of Furaneol Through Olfactory Stimulation On Spontaneous Locomotor Activity**

Motoko Ohata, Momoka Kinowaki, Issei Yokoyama, Masato Tsuda, Akira Hosono, Kazumi Osada
Nihon University, Fujisawa, Japan

Furaneol, emitting a sweet caramel odor generated by the Maillard reaction, has been known as an inducer of food intake in rats without altering their body weight (Yokoyama et al., J. Food Sci., 85, 1338-1343, 2020). We investigated the effects of furaneol olfactory stimulation on feeding and energy expenditure by measuring dietary intake, body weight gain, and spontaneous locomotor activity (SLA) in mice. Olfactory stimulation of furaneol induced a significant increase of SLA over time, but the body weight was not affected by the exposure of furaneol odor. Thereafter, some gene expression patterns in the brain (olfactory bulb, hypothalamus, and amygdala) and stomach of mice were investigated to clarify the mechanism by which olfactory stimulation of furaneol increases SLA in mice. In the hypothalamus, mRNA expression levels of orexin and its receptors, oxytocin receptor, and growth hormone secretagogue receptor were decreased, but of corticotropin-releasing hormone were increased by the spontaneous locomotor exercise absence of the olfactory stimulation of furaneol. However, furaneol odor exposure not only restored the changes of neural signals caused by SLA, but also increased mRNA expression levels of and thyrotropin-releasing hormone in the hypothalamus. Moreover, furaneol odor exposure increases the transcriptional activity of ghrelin in the stomach. Together, the transcriptional pattern change of these neuropeptides and hormones in the brain and the stomach with furaneol odor exposure may indicate the neurophysiological molecular basis related to increased SLA.

203 **Lack Of Salivary A-Amylase Results In Increased Taste Responding To Medium But Not Long-Chain Maltodextrin**

Verenice Ascencio Gutierrez[1], Rachel D. Fan[1], Kamila D. Nixon[1], Emily Demieri[1], Kimberly F. James[1], Petar Pajic[2], Charles Lee[3], Omer Gokcumen[2], Ann-Marie Torregrossa[1,4]
[1]Department of Psychology, University at Buffalo, Buffalo, NY, United States, [2]Department of Biological Sciences, University at Buffalo, Buffalo, NY, United States, [3]The Jackson Laboratory for Genomic Medicine, Farmington, CT, United States, [4]Center for Ingestive Behavior Research, University at Buffalo, Buffalo, NY, United States

Salivary α-amylase (sAA) begins starch digestion in the oral cavity by cleaving complex sugars into simple sugars. Simple sugars are then perceived by the sweet taste heterodimer T1R2+T1R3. Starches are cleaved into maltose polymers by sAA and reduced further to glucose by oral glucosides. “Starches” and maltodextrins are not perceived as sweet stimuli and instead are thought to produce a “starch” taste via an unidentified receptor independent of the sweet taste receptor. Salivary AA is thought to modify the oral perception of starches by breaking them down from the stimulus for “starch” receptors into the stimulus for the “sweet” receptor. Here, we asked what the relative contribution of sAA is to taste-driven behaviors of multiple taste qualities. We successfully created a knock-out (KO) mouse model that encompasses normal (wild-type, WT), low (heterozygous, HET) and no (KO) sAA while pancreatic amylase is maintained. We examined taste-driven behaviors to several taste qualities in a brief-access taste test using the Davis Rig. All animals were tested water deprived for hedonically negative stimuli (NaCl, Tannin, Ethanol, and MSG+amiloride) and water replete for hedonically positive stimuli (sucralose, long and medium chain maltodextrin, glucose, and sucrose). While no differences in licking for the long-chain maltodextrin were observed, sAA HET and KO mice showed an increased response to the high concentrations of med-chain maltodextrin compared to WT (geno x conc: p’s <0.01). These data suggest that animals with low or no sAA are more responsive to the hedonic aspect of starch over sweet. We found no differences between genotypes for NaCl, ethanol, tannin, MSG+amiloride, sucralose, glucose and sucrose directed licking, suggesting changes are specific to amylase substrates.

205 **Glomerular Sequence Represents Odor Quality In The Mouse Olfactory Bulb**

Joshua S Harvey[1], Khristina Samoilova[2], Hiro Nakayama[1], Farhad Pashakhanloo[2], Alexei Koulakov[2], Dmitry Rinberg[1]
[1]Neuroscience Institute, New York University Langone Health, New York, NY, United States, [2]Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, United States

Understanding how odor space is constructed by the olfactory system will allow us to decode olfactory information from neural recordings, and align representations across multiple animals. Here, we compare odor identity (quality) spaces constructed from both neural recordings and perceptual judgments obtained in mice. Using wide-field calcium imaging to monitor olfactory sensory neurons in the mouse olfactory bulb, we obtain spatio-temporal patterns of glomerular activity in response to 24 odors. We find glomerular sequence rank correlation provides a distance metric by which a concentration-invariant odor identity space can be constructed, allowing cross-concentration odor decoding with low-dimensional embeddings. In addition to rank correlation, we explore odor spaces constructed by overlaps in primacy sets of glomeruli, i.e. those activated early in the sniff cycle. We find rank correlation and primacy sets construct similar spaces, indicating the information richness of the early part of glomerular sequences. We show the rank correlation metric enables the alignment of odor representations across animals, and explore cross-animal alignment using a subset of anchor odors. We develop a heuristic that reliably predicts which subsets of odors are optimal anchors, providing the best alignment performance. Finally, we explored the relationship between neural and perceptual spaces, measuring

perceptual distances in 10 mice with a delayed match-to-sample behavioral paradigm. We find perceptual space can be aligned to neural space, allowing for accurate odor decoding. Overall, we show that odor identity is represented by a common low-dimensional manifold, for both neural responses and odor percepts, suggesting that odor similarity relationships are preserved from sensory transduction through perception.

207 **Human Piriform Cortical Representations Of Perceived Odor Intensity**

Andrew Sheriff[1], Guangyu Zhou[1], Robert Pellegrino[3], Matthew Andres[3], Julia Jamka[1], Mahmoud Omidbeigi[1], Joshua M. Rosenow[2], Stephan Schuele[1], Chima Oluigbo[5], Mohamad Koubeissi[6], Gregory Lane[1], Joel Mainland[3,4], Christina Zelano[1]

[1]Department of Neurology, Northwestern University Feinberg School of Medicine, Chicago, IL, United States, [2]Department of Neurosurgery, Northwestern University Feinberg School of Medicine, Chicago, IL, United States, [3]Monell Chemical Senses Center, Philadelphia, PA, United States, [4]Department of Neuroscience, University of Pennsylvania, Philadelphia, PA, United States, [5]Division of Neurosurgery, Children's National Medical Center, Washington, DC, United States, [6]Department of Neurology, George Washington University, Washington, DC, United States

Perceived intensity of odors is an important component of olfactory processing. However, most studies use odor concentration as a proxy for perceived intensity. While odor concentration is related to perceived intensity, perceptual ratings, which are only available in human participants, are required to dissociate the two. Neural correlates of odor concentration in rodents—including spike rates and latencies, and ensemble synchrony—have been shown in the olfactory bulb and piriform cortex. In order to characterize representations of perceived odor intensity in humans, we collected perceived intensity ratings on each presentation of different odors of different concentrations during direct recordings of local field potentials (LFPs) of human piriform cortex. In a 3x3 experimental design, participants (n = 5) smelled 3 odorants (benzaldehyde, 2-heptanone, and diethylprazine) at 3 concentrations (low, medium, and high). To ensure the concentration of each stimulus was consistent across trials, odors were delivered through a controlled system involving a sealed nalophan bag filled with 10L of medical grade air containing vaporized liquid odorants at concentrations previously matched for odor intensity. For analysis of human piriform LFPs, trials were sorted by perceived odor intensity ratings collapsed across odor identities. Preliminary data suggest differences between neural correlates of perceived intensity and those of odor concentration, including amplitude and latency effects in distinct oscillatory bands of piriform LFPs. Findings here will help connect findings of neural correlates of odor concentration and perceptual intensity in rodents with those in humans.

209 **Chemosensory Encoding In Tangential Inputs To The *Drosophila* Navigation Center**

Kavin M. Nunez, Jacob D. Freed, Katherine Nagel
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Like most animals, *Drosophila melanogaster* use chemosensory information to guide navigation and foraging. Tangential inputs to the fan-shaped body are anatomically poised to provide chemosensory input to the fly navigation center; a few of these have been shown to respond to select odorants and tastants. However, how chemosensory information is encoded across the diverse tangential input population of ~150 connectomically-defined neuron types is unknown. Here we aim to characterize chemosensory encoding across this population. First, we used wide-field calcium imaging to survey responses of developmental classes of tangential neurons to odors of varying valences. We found that most populations showed broad responses to odor with substantial variation across flies. These data suggest that chemosensory information is represented by a population code across the array of tangential inputs and strongly modulated by behavioral state or experience. From our survey, we identified three populations with strong odor responses: ventral DL1 inputs showed onset/offset excitation with occasional inhibition during the stimulus, dorsal DM4 inputs showed transient excitation to select odors, while dorsal LAL1v1 inputs showed inhibition to most odors. Currently, we are using whole-cell electrophysiology to characterize the responses of neurons in each cluster to odorants and tastants. Preliminarily, we find diverse neuron types in DL1 that exhibit distinct electrophysiology properties and odor/tastant tuning. Ongoing work aims to link recordings to connectome identities and determine how tangential neurons are modulated by experience on different timescales. These data will illuminate how chemosensory stimuli are represented in the central brain to guide navigation and foraging decisions.

211 **Engineering Insect Odorant Receptors As A Detection Mechanism For Disease Associated Volatiles**

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Odorant receptors (ORs) are highly sensitive chemical receptors that respond to a diverse range of volatile compounds. While organisms relying on olfaction for survival possess remarkable abilities to detect trace chemicals, our current chemical sensing technology is inadequate in comparison. Recent studies have shown significant differences in the chemical profile of human breath between healthy individuals and those infected with pathogens such as malaria, tuberculosis, or COVID-19. Leveraging the unique chemical profiles associated with diseases could provide a robust method for disease detection. In this study, our objective is to engineer insect ORs to selectively activate in the presence of volatiles associated with diseases. Specifically, we focused on MhOR5, an odorant receptor from the Jumping Bristletail (*Machilis hrabei*), a basal insect that lacks the OR co-receptor (Orco) found in modern insects. MhOR5 is a well-characterized receptor with broad selectivity and an experimentally determined structure, making it an ideal candidate for targeted engineering. We expressed

MhOR5 in a heterologous cell system using HEK293T cells and tested its response to disease-associated volatiles (DAVs). Through structural analysis, we identified key residues that potentially contribute to ligand selectivity, and tested mutations made at these residues for altered ligand selectivity. Our findings revealed distinct ligand selectivity among most mutants in response to individual DAVs. Additionally, we are developing a platform for high-throughput, non-biased screening of combinatorial mutants. This methodology will establish a solid foundation for engineering ORs with specificity towards particular chemicals and for developing engineered OR arrays for disease diagnosis.

213 **Chemosensory Responses To Carbon Dioxide Shape Parasite-Host Interactions In A Skin-Penetrating Human-Infective Nematode.**

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Skin-penetrating nematodes are intestinal parasites that infect nearly one billion people worldwide. The developmentally arrested infective larvae (iL3s) of these nematodes actively seek out hosts, invade hosts via skin penetration, resume development inside hosts (activation), and navigate inside hosts, ultimately ending up as parasitic adults in the small intestine. How chemosensation contributes to host seeking, intra-host development, and intra-host navigation –three crucial steps of the parasite-host interaction – remains poorly understood. Carbon dioxide (CO_2) is a host-associated cue that these nematodes encounter throughout their life cycle. We are studying the role of CO_2 in promoting parasite-host interactions in the human-infective threadworm *Strongyloides stercoralis*. We find that *S. stercoralis* shows life-stage-specific preferences for CO_2. While iL3s are repelled by CO_2, activated iL3s are attracted and free-living adults are neutral to CO_2. CO_2 repulsion by iL3s may facilitate dispersal, driving them off host feces to host seek. CO_2 attraction by activated iL3s may facilitate intra-host navigation. Using *in vivo* calcium imaging and neuronal silencing, we have identified the CO_2-detecting neurons that drive CO_2-evoked behavioral responses in *S. stercoralis*. These neurons show enhanced CO_2-evoked calcium responses in activated iL3s, suggesting an increased CO_2 sensitivity upon host entry. Using CRISPR, we have identified the receptor guanylate cyclase GCY-9 as a molecular CO_2 sensor that promotes CO_2-evoked behavioral responses and facilitates intra-host development of *S. stercoralis*. Our study provides the first insights into the neural basis of chemosensation in any human-parasitic nematode and may aid in the identification of new molecular targets for novel anthelmintic drugs.

215 **The Role Of Surface Adhesion Molecules In Cellular Connections**

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The rodent accessory olfactory system (AOS) consists of two main components: the vomeronasal organ (VNO) and the accessory olfactory bulb (AOB). The vomeronasal epithelium (VNE) comprises two primary types of vomeronasal sensory neurons (VSNs) that express vomeronasal receptors (VR) from the V1R or V2R gene families. Basal VSNs, which express V2R receptors, project to the posterior AOB (pAOB), while apical VSNs, expressing V1R receptors, project to the anterior AOB (aAOB). The axon terminals of these VSNs establish synapses with the dendrites of second-order neurons in the AOB, forming neuropil-rich structures known as glomeruli. Cell adhesion, axon growth, pathfinding, fasciculation, synapse formation, and stabilization rely on the crucial roles played by adhesion molecules. A family of such molecules, Protocadherins (Pcdhs), has been previously identified within the main olfactory system. Yet, their influence on the wiring of the AOS has not been explored. By analyzing single-cell RNA sequencing data from VSNs, we found that VSNs expressing different VRs also differ in their combinatorial profiles of adhesion molecules. Notably, seven non-clustered Pcdh genes were found to have highly variable expression levels among neurons expressing different V1R receptors. Pcdh7 was specifically found in V1R VNs, while V2R-expressing VNs exhibited higher levels of Pcdh9. Investigation of Pcdh7 knockout mice unveiled ectopic projections and glomeruli formation of apical VSNs into the pAOB. Moreover, our data also suggests that several unclustered Pcdhs undergo local translation in the axon terminals of VSNs during glomeruli formation. We propose that the localized and combinatorial expression of Pcdhs is crucial for specifying the spatial and specificity of the targeting of VSNs to the AOB.

217 **Leveraging Fluid Dynamic Cues For Olfactory Navigation In Turbulent Environments**

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The fluid dynamic cues present in odor plumes provide information that may be leveraged by organisms in olfactory navigation. In a turbulent odor plume, a sensing organism receives a complex time series of olfactory cues as it encounters odor signals that have been stretched, folded, diffused, and separated in the flow. The importance of these spatiotemporally complex odor fields for olfactory navigation has long been recognized. However, the odor information does not arrive in isolation; a rich set of mechanosensory cues from the fluid flow itself arrives simultaneously, including the fluid acceleration, rotation (vorticity), and strain (deformation) fields. Many organisms use finely tuned architecture to sense both flow and odor cues, such as the long antenna seen on arthropods that include both mechanosensory hairs and odorant chemoreceptors. Can the fluid dynamic signals received by the organism provide exploitable information about odor signal behavior, and in some cases even herald the arrival of odor packets? To explore this question, we leverage the fluid dynamic concept of Lagrangian

Coherent Structures (LCS) as an intuitive framework for relating the odor signal dynamics to the underlying fluid flow structure. Described as the 'hidden skeleton' of fluid flow, LCS are evolving structures that organize the fluid flow into characteristic patterns and are closely tied to the chaotic dynamics of flow cues and odor transport. Grounded in the LCS framework, we analyze data from turbulent odor plume simulations to develop a statistical framework to quantify the spatiotemporal relationships between flow and odor signals. Finally, we suggest ways in which the statistical relationships may provide organisms with actionable cues for plume navigation.

219 **Tauro-Deoxycholic Acid Modulates Chemosensory Behavior Via The Accessory Olfactory System In Mice**

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The accessory olfactory system (AOS) in mammals detects social chemosignals and provides information about gender, social status and identity. Previous studies showed that fecal bile acids are natural ligands for the mouse AOS. However, there is still limited understanding of the full repertoire of natural AOS bile acid ligands, including their specific receptors and the neural pathways involved in mediating behavioral responses. To explore the mechanisms by which the AOS encodes and processes bile acid information, we screened the bile acid sensitivity of peripheral vomeronasal sensory neurons (VSNs) using volumetric GCaMP6s Ca^{2+} imaging. In this screening, VSNs were exposed to primary bile acids (CA, CDCA), secondary bile acids (DCA, LCA, UDCA, IsoDCA, DHCA), muricholic acids (β-, λ-, δ-), tauro-conjugates (TCA, TDCA, TLCA, TCDCA), glyco-conjugates (GCA, GDCA, GLCA, GCDCA) and keto-conjugates (7-keto DCA, 12-keto DCA, 7-keto LCA). We discovered that taurine-conjugated bile acids are highly active AOS ligands, and that they activated VSNs that are insensitive to previously-identified bile acids. We found that tauro-deoxycholic acid (TDCA) was a particularly strong ligand, activating many VSNs at sub-micromolar concentrations. *In vivo* exposure to rodent fecal extracts infused with TDCA induced several stress-associated behaviors, supporting our hypothesis that TDCA is a "kairomone" for mice. These studies reveal new molecular underpinnings of mammalian behavioral responses to bile acid chemosensation.

221 **The Effect Of Social Experience On Gene Regulation, Neural Activity And Behavior In *Drosophila Melanogaster***

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Social behaviors of animals are modulated by signals from the environment. The molecular and neural circuit-based mechanisms underlying experience-dependent behavioral regulation remains poorly understood. Emerging evidence from both mammals and insects indicates the intimate connection between behavioral modulation, neural transcription, and neuronal activities. The *Drosophila melanogaster* is an excellent model where links among stereotyped courtship behaviors, genes and circuits have been elucidated. Transcription factors Fruitless and Doublesex control innate and learned male courtship behaviors of Drosophila, respectively. At the neural circuit level, a single cluster of P1 command neurons in the brain, which is both *fruitless* (*fru*) and *doublesex* (*dsx*) positive, drive male courtship behaviors. However, how social experience regulates master genes controlling courtship at the level of transcription in different courtship circuits remains unclear. Single-pair courtship assays showed that socially isolated male flies displayed more vigorous courtship behaviors compared to group housed males. The increase in courtship vigor in isolated males was accompanied by an increase in the response of P1 command neurons in the central brain. Single cell RNAseq of cells in courtship circuits of male flies raised under different social contexts showed that the transcriptome profiling of individual cells performs differently in different clusters. In addition, disrupting pheromone receptor function in the olfactory system altered the expression level of neuromodulatory in both peripheral and central nervous system. These results suggest that social context alters gene expression in the courtship circuits partially through the olfaction system, and ultimately modifies neuronal activity and courtship behaviors.

223 **Transgenic Tools For Investigating Bile Acid Detection And Information Processing In The Mouse Accessory Olfactory System.**

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In most mammals, the vomeronasal organ (VNO) detects social chemosignals and influences social, territorial, and mating behaviors. Recent work has demonstrated that bile acids excreted in feces are detected by multiple populations of vomeronasal sensory neurons (VSNs). To investigate the role of bile acid-sensitive VSNs, we generated a transgenic knock-in mouse in which Cre recombinase and eCFP are expressed in cells expressing *Vmn1r16*, a bile acid-sensitive vomeronasal receptor (VR). These mice were crossed to the "Ai9" reporter line, which allows for cell type-specific tdTomato expression in *Vmn1r16*-expressing cells. We confirmed that mating Vmn1r16-Cre-eCFP mice to Ai9 mice resulted in offspring with tdTomato in VSNs, with minimal expression in other tissues. In adult mice, the number of VSNs expressing tdTomato was larger than expected based on monoallelic expression estimates, and only a small subset of tdTomato-expressing cells also expressed eCFP. To

further understand the tdTomato-expressing VSN population, we evaluated (1) tdTomato+ axon terminals in the accessory olfactory bulb (AOB), and (2) single-cell mRNA expression in tdTomato+ VSNs. tdTomato was only observed in the anterior AOB, indicating selective labeling in VSNs expressing members of the "V1R" family of receptors. Single-cell RNA sequencing results indicated enriched expression of V1Rs located proximally to *Vmn1r16* on chromosome 6. In separate experiments, GCaMP6s Ca^{2+} imaging in labeled VSNs identified multiple bile acid-sensing subpopulations. Combined, these results suggest that *Vmn1r16* is expressed in many VSNs during maturation, and then downregulated in favor of other bile acid-sensitive V1Rs during specification. We expect these mice to be valuable tools for assessing mammalian chemosensation and social behavior.

225 **Homoeriodictyol Counteracts The Bitterness Response Elicited By Pt-Based Chemotherapeutics In A Cellular Model System And Reduces Bitter Phantogeusia In Cancer Patients**

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Chemotherapy often causes taste dysfunctions, affecting patients' food intake and quality of life. A multifactorial etiology of taste dysfunctions has been hypothesized, but the role of bitter taste receptors (TAS2Rs) is relatively unclear, and effective treatments for increased bitter taste sensitivity and bitter phantogeusia are missing. We investigated the underlying mechanisms of Pt-based chemotherapeutics in human parietal cells (HGT-1), a cellular surrogate model of TAS2R-linked bitter response. The bitter-masking flavor compound homoeriodictyol (HED), an antagonist for several TAS2Rs, was used to counteract these effects. Our results show that cisplatin (5 – 50 μM) and carboplatin (50 – 750 μM) elicit a dose-dependent bitterness response in HGT-1 cells, albeit to different extents, while 200 μM HED counteracts the bitterness response caused by 50 μM cisplatin by -75 ± 15% and the effect of 200 μM carboplatin by -76 ± 11%. The functional role of specific TAS2Rs in the bitter response induced by Pt-based drugs was confirmed by using corresponding HGT-1 kd or ko cells. In addition, a clinical pilot trial was conducted on ovarian cancer patients receiving a carboplatin-based chemotherapy. Hereby, an increased bitter taste sensitivity indicated by a lower recognition threshold of caffeine was reported in a sensory study. These results support our hypothesis that intravenously administered Pt-based chemotherapeutics are excreted into saliva and contribute to bitter taste dysfunctions *via* activation of oral TAS2Rs, and that HED shows a promising bitter-masking potential. To what extent the use of HED in cancer patients with bitter taste dysfunction may help to improve consecutive side effects such as loss of appetite, body weight and quality of life needs to be clarified in a clinical trial.

227 **Neurocircuit Identification And Functional Revelation Of Sniffing**

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Sniffing is the active sampling of odors through the nasal cavity. It is a critical part of olfaction and linked with motivated behaviors, thus playing important roles in surviving and reproduction. However, the neuronal networks underlying this basic behavior is largely unknown. here, we employed an array of technologies to reveal and verify the neurocircuit and some of its functions. Trans-multi-synaptic pseudorabies viral tracers revealed a very complex network controlling the diaphragm, with the strongest signals in the amygdalopiriform transition area (APir), the central amygdala (CeA) and the parabrachial nuclei (PB). Gringer causality analysis of local field potential data from the most likely regions involved in sniffing disclosed a coherent information flowing inward network, composed of the olfactory bulb, the piriform cortex, Apir, CeA and PB. Combining the antero-trans-multi-synaptic herpes simplex and retro-trans-monosynaptic adeno-associated/rabies viral tracers, a pathway made up of APir-CeA-PB was identified, from up- to down-stream. With opto- and chemo-genetic manipulations of cell bodies and axonal terminals, electrical and behavioral recordings confirmed the pathway functionally. More detailly, each of the three regions is necessary for sniffing and disruption of the region and the down-stream point eliminated sniffing behavior. The cell-types involved were identified as Vglut1 in APir, Gad in CeA, and Vglut2 in PB, and further confirmed by transgenic cre-lines along with optogenetic manipulation. Interruption of sniffing had significant effects on behaviors including forage and habituation. In summary, our study has identified the neurocircuit and revealed some functions of sniffing.

229 **Gustatory Processing Within And Beyond The Subesophageal Zone In Drosophila**

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Gustation is essential for distinguishing healthy foods from toxins and for positive quality of life. Yet, the mechanisms underlying gustation are poorly understood. There are two main ideas about how gustatory signals

are encoded: 1) labeled lines, which posits that relatively few taste categories exist and are encoded by parallel, independent paths through the brain, and 2) combinatorial codes, which suggests that tastes are encoded by combinations of simultaneously active neurons. Drosophila melanogaster is a powerful model system that allows comprehensive and reproducible experiments to address this controversy at the level of single neurons. Because the labeled line idea argues that pathways for different tastes will not converge, we used anatomical and physiological approaches to test for the convergence of multiple types of first- order gustatory receptor neurons (GRNs) onto a single second-order suboesophageal zone (SEZ) interneuron named G2N-1 (Miyazaki et al, 2015). First, with GFP Reconstitution Across Synaptic Partners (GRASP), we found that GRNs expressing the receptors PPK23 (responds to salty or bitter tastants), PPK28 (responds to water or low salt) and GR64f (responds to sugars) all converge onto G2N-1. Next, using calcium imaging, we found that G2N-1 is activated by optogenetic stimulation of neurons expressing GR64f or PPK28. And finally, we showed that G2N-1 is activated when 500mM sucrose or 500mM NaCl is delivered to the fly's proboscis. We are now exploring how information is formatted after the SEZ. Using the EM connectome and TransTango, we have identified cells in the superior lateral protocerebrum and the superior medial protocerebrum that likely encode gustation. By recording from these cells, we will elucidate gustatory encoding beyond the converged signal in the SEZ.

231 **Elicitation Of Fos Immunoreactivity And Orofacial Behaviors By Intraoral Infusion Of Sodium Carbonate In Rats**

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Sodium carbonate (Na_2CO_3), a divalent salt, tastes 6-10 times stronger than NaCl to freely-licking thirsty and sodium-depleted rats (Morrison, 1969, Morrison & Young, 1972, St. John, McBrayer, & Krauskopf, 2017). Electrophysiological studies of the chorda tympani nerve confirmed that low concentrations of Na_2CO_3 produce a potentiated tonic response, and revealed a novel finding that Na_2CO_3, but not NaCl, produces a water response during the poststimulus rinse period (Breza & St. John, 2023). We investigated the hedonic properties of Na_2CO_3 in this study by examining orofacial responses (i.e., taste reactivity) of rats (N=10) to intraorally-infused Na_2CO_3 and rinse water trials, and by assessing the relative stimulation of central gustatory regions using the c-fos method. Rats were tested either sodium-replete or sodium-deplete. Sodium depletion was accomplished by furosemide injection (8 mg/kg, s.c.) and access to sodium-free diet (Inotiv Teklad 90228). Regardless of physiological state, 0.5 M NaCl elicited more ingestive behaviors than either 0.05 M NaCl or 0.05 M Na_2CO_3, whereas 0.05 M Na_2CO_3 and 0.5 M NaCl elicited more aversive gapes than 0.05 M NaCl (N=10). Behavior did not differ during water rinse trials. For the c-fos experiments, rats received 30-min intraoral infusion of either 0.05 M Na_2CO_3 (N=8) or 0.05 M NaCl (N=4) equally divided into sodium-replete or deplete subgroups. While physiological state did not have a noticeable influence, there was a robust effect of higher levels of c-fos expression to 0.05 M Na_2CO_3 in nearly every brain area examined (nucleus of the solitary tract, reticular formation, parabrachial nucleus, and gustatory thalamus, but not the inferior colliculus). The potency of 0.05 M Na_2CO_3 in eliciting gapes and Fos immunoreactivity is consistent with previous studies.

233 **Cortical And Subcortical Connectivity Changes With Taste Neophobia And Attenuation**

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The fear of unfamiliar tastes and its subsequent attenuation following benign exposure, known as Taste Neophobia (TN) and Attenuation of Neophobia (AN), are innate survival behaviors. While much research has identified brain regions involved in TN and AN, little work has delved into the connectivity changes between these regions during the course of the behavior. To explore this, we made simultaneous electrophysiological recordings from tetrode bundles placed in several regions known to be involved in taste-mediated behaviors including the prefrontal cortex, gustatory cortex, nucleus accumbens shell, and vertical limb of the diagonal band of Broca in head-fixed mice during TN and AN. For the neophobia paradigm, animals underwent 2-3 days of water (H2O) training in which head-fixed, water-restricted mice were trained to lick a small amount of water from a tube following the presentation of a brief tone. This was followed by 3 days of randomized saccharin and H2O trials presented in the same manner. Animals were able to freely lick the tube throughout the session and tastants were rinsed out after each trial. Simultaneous video recordings of the ventral portion of the animal's face were taken throughout each session. Off-line analysis of the video using Deep Lab Cut allowed us to quantify licking for each trial. Time-resolved analysis of local field potentials showed power and coherence changes relative to the taste window between the several regions and gustatory cortex during both TN and AN. Current work is focused on exploring these connectivity changes relative to changes in tastant consumption that occur during TN and AN.

235 **Trigeminal Co-Stimulation Alters The Eeg Signature Of Olfactory Stimuli**

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As other sensory stimuli, chemosensory stimuli generate neural representations that are spatially distributed and can be observed with electroencephalography (EEG). Most odorants activate to sensory system, namely the olfactory system and the trigeminal system. The objective of this study was to compare the EEG patterns and power spectrum density (PSD) of different frequency bands in response to (1) a pure olfactory stimulus (phenyl ethanol, PEA, rose odor), (2) a mixed olfactory-trigeminal stimulus (eucalyptol, EUC, eucalyptus odor), as well as (3) ipsilateral (IEP) and (4) contralateral (CEP) combinations thereof. We hypothesized that (a) chemosensory processing is associated with activation that is spatially distributed in different frequency bands; (b) mixing an olfactory component with a trigeminal component alters the neural representation; (c) neural representation and frequency band activities are different between contralateral and ipsilateral combinations. We used an olfactometer to deliver stimuli (200ms; 40s of inter-stimulus interval; 40 stimulations per condition) to 31 healthy individuals (18 females; mean age of 24.6 (2.5) years). We recorded participants' EEG continuously throughout the process. We identified three distinct ERP peaks with significantly different amplitudes between conditions. Further, topographic PSD maps showed theta and alpha bands activity in the prefrontal lobe, and delta band activity in the parietal lobe in all conditions. These results suggest that adding a trigeminal component modulates and enhances the neural representation of an olfactory stimulus.

237 **Neural Circuitry Underlying Negative Valuation Of Sweetness In *Drosophila***

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Sugar is a well-known appetitive tastant for feeding in flies. However, recent evidence suggests that it can also decrease option value in a non-feeding decision-making task. Specifically, flies accept a sugary agarose for egg-laying when it is the sole option but reject it when a sugar-free agarose is available. The neural mechanism by which sugars devalue option for egg-laying is not well understood, but input from the leg sweet neurons has been shown to be critical. Here we identified a circuit that converts input from the leg sweet neurons into a negative value signal for decision-making. First, we found a group of SEZ-targeting projection neurons in the VNC that are post-synaptic to the leg sweet neurons; these neurons respond to sugars and are required to devalue sweet options for egg-laying. Next, we found that these SEZ-targeting VNC neurons synapse onto specific SLP-targeting projection neurons in the brain, and, like their presynaptic partners, these SLP-targeting neurons also respond to sugars and are required to devalue sweet options for egg-laying. Notably, these neurons are GABAergic and can inhibit the egg-laying command neurons (oviDNs). This devaluing circuit (from legs -> VNC -> SEZ -> SLP -> oviDNs) is task specific and does not regulate feeding. Lastly, analysis of an African natural variant that prefers sugary agarose for egg-laying identified a single gene whose expression change in this circuit drives this variant's altered sugar preference. In conclusion, we have uncovered a circuit that uniquely confers a negative value to sugars and showed how its genetic modification can diversify flies' sugar valuation for egg-laying in nature. This discovery lays the groundwork for determining the circuit and genetic basis for sensory-value transformation.

239 **Multimodal Integration Of Olfactory And Gustatory Stimuli In Locust Superior Lateral Protocerebrum And Accessory Calyx Neurons**

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The experience of flavor requires both olfactory and gustatory input. Many studies have explored how olfactory and gustatory information are processed separately in the brain, yet the specific mechanisms by which individual neurons process and integrate multimodal input remain unclear. We addressed this question in a simple model system, the locust Schistocerca americana. We first mass-stained 1st and 2nd order olfactory and gustatory neurons and traced their projections, seeking to idenitfy sites where the two pathways converge. We stained peripheral neurons in the antenna (olfactory) or palp (gustatory) with a neurobiotin solution and conjugated the dye with fluorophores. To stain 2nd order neurons, we inserted blunt glass microelectrodes loaded with dye into the antennal lobe (olfactory) and the glomerular lobe (gustatory). Confocal microscopy was then used to image the stained tissue, revealing potential convergence sites in the superior lateral protocerebrum (SLP) and accessory calyx (AC). Next, we made in vivo intracellular recordings from SLP and AC neurons. With a novel delivery system that controls stimuli with high temporal precision (~50 ms) we presented odors to the antenna and tastants to the palp. Preliminary results indicate that certain AC neurons respond to both olfactory and gustatory stimuli, exhibiting distinct firing patterns for odors and tastes. Our preliminary results from simultaneous odor and taste delivery suggest integration is best described as the average of the separate inputs, as predicted by theoretical studies (Xu et al 2017). Our findings contribute to a better understanding of the dynamic integration of odor and taste and shed light on how the brain integrates complex multimodal information.

241 **A Split-Sample Approach To Examining Sweet Preferences And Alcoholic Beverages**

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Previous research suggests that sweetness is an important quality in both the decision to consume alcohol and

alcohol abuse. The taste of alcohol, however, is characterized by a number of sensory properties in addition to sweetness, such as astringency and bitterness, that may also affect preference and consumption. To examine a wider variety of taste sensations, consumers can be classified into three sweet-sensory liking clusters (High Sweet-Liking, Moderate Sweet-Liking, and Inverted-U) that differ in their sweetness optima and sensory-liking patterns (relationship between liking and sweetness, bitterness and astringency perception in a food model); those clusters have been previously used to predict acceptability for phenol-rich vegetables (Spinelli et al.,2021). The present work evaluated and replicated the sweet sensory-liking clusters previously observed in the literature in a new set of participants, and extended the predicted value of these clusters by examining their relationship to gender and specific types of alcoholic beverages. The sweet sensory-liking clusters were able to predict the liking and familiarity of some alcoholic beverages characterized by stronger tastes; alcohol intake, as measured by weekly intake levels, were not predicted by the clusters. Thus, although sweet sensory-liking clusters may be associated with the kind of alcoholic beverages that a person will drink and enjoy, as well as the frequency with which a particular type of alcoholic beverage is consumed, these clusters are poor predictors of the quantity of alcohol that a person ingests over the course of a week.

243 **Encoding Of Odours With Taste Qualities In The Human Primary Gustatory Cortex**

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Odours have a unique role in food consumption, both as anticipatory cues and during the consummatory stage, where they combine with taste. This results in an association so strong that odours are able to enhance taste perception, such that they take on taste qualities in the absence of a tastant. While this link between odour and taste is well-established, the exact mechanism of how this occurs remains unknown. Here, we build on previous research showing distributed pattern encoding of tastants in the insula and the frontal operculum, in addition to activations in these structures in response to odours, to investigate how odours amplify flavour processing. Specifically, we test the hypothesis that odours evoke the same distributed patterns of encoding in the taste cortex by combining behavioural psychophysics and functional neuroimaging. Healthy volunteers (N = 28) attended one behavioural session, where they are familiarised with a sweet flavour (a sweet taste with a sweet odour) and a savoury flavour (a savoury taste with a savoury odour), followed by two fMRI sessions where they received the tastants and the odourants separately. Replicating previous work in the field, univariate analyses showed activation in the insula and the piriform cortex in response to tastants, and the piriform cortex in response to odourants. We subsequently use multivariate pattern analysis to differentiate neural encoding of taste-associated odours in the primary taste cortex, in addition to cross-modal decoding to determine the overlap between odour and taste identity encoding in the primary taste cortex. Taken together, these findings highlight the strong link between chemosensory modalities that emerge through lifelong associative learning. Leveraging such learning may facilitate healthier and more sustainable diets.

245 **Discovery Of Bb99: A Potent T2R54 (Tas2R39) Antagonist That Blocks The Bitterness Of Select Active Pharmaceutical Ingredients (Apis)**

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Bitterness of active pharmaceutical ingredients (APIs) is a significant barrier to compliance, especially in the pediatric and geriatric populations. It is estimated that more than 66% of all drugs exhibit some level of bitterness and that 25% of these have a very bitter off-taste. In foods and beverages, bitterness often reduces palatability. Unfortunately, current solutions (e.g., coating and added sugar) still present limitations while the demand for new and/or alternative solutions continuous to increase with new products entering the pipeline. Using our bitter taste receptor screening platform, we identified T2R54 (TAS2R39) as a key receptor mediating the bitterness imparted by certain APIs, nutraceuticals, foods and beverages. Subsequently, we initiated a TAS2R39 antagonist discovery and optimization campaign that led to the identification of BB99 as a development candidate. In sensory evaluation, BB99 significantly attenuates the bitterness of APIs such as Acetaminophen (the active ingredient in Tylenol®, used to alleviate fever and pain) and Guaifenesin (the active ingredient in Mucinex®, used to help clear mucus). BB99 may also provide the opportunity to block the bitter taste of other APIs, nutraceuticals as well as foods and beverages ingredients that activate TAS2R39.

247 **The Power Of Senses - Savoury Taste Phenotypes Modulate Food Acceptance, Consumption And Body Mass Index: Insights From A Large Population Sample**

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The aim of the study is to explore the relationship between taste system functionality, eating habits, attitudes towards food and nutritional status in a large population cohort from the Italian Taste project (https://www.it-taste.it/). A total of 2878 volunteers (54.5% F; age: 18–30y, 33.8%; 31–45y, 29.8%; 46–60y, 34.4%) rated overall liking and perceived intensity of 3 sensations (salty, umami and overall flavor) for a model food (bean purée)

spiked with 4 increasing levels of a prototypical tastant (i.e., sodium chloride). Individuals self-reported anthropometric information (weight and height), psycho-attitudinal traits (Sensitivity to Punishment, SP and Sensitivity to Reward, SR) as well as consumption data of 19 food categories were also considered. K-means clustering performed on Pearson's coefficients calculated individually to estimate the relationship between liking and responsiveness to the target sensations revealed two clusters characterized by distinct sensory-liking patterns: Savoury taste 'Likers' (n=1845) and 'Dislikers' (n=1033) phenotypes for which liking, respectively, increased or decreased along with NaCl concentration in the model food. The 'Likers' phenotype was characterized by a lower sensitivity to salty ($p<0.05$), umami ($p<0.05$) and overall flavor ($p<0.05$), consumed more frequently caloric food ($p<0.001$), presented higher SR scores ($p=0.06$) and showed a higher BMI ($p<0.01$) than the 'Dislikers' phenotype. The present data suggest that taste is an important explanatory variable in the development of unhealthy eating patterns which might be associated with weight gain and stress the importance of considering chemosensory factors for the implementation of personalized dietary interventions.

249 **Sourness Of Citric Acid And Citrate Salts In Humans**

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With the recent identification of the sour taste receptor OTOP1 in mice, interest in perception of sourness has increased. However, little is known about the human response to different organic acids and their salts; additionally, the effect of counterions on sourness perception remains underexplored. Here we report on several dose-response experiments of citric acid and citrate salt mixtures that are commonly used as antioxidants, acidulants, acidity modifiers, and emulsifiers in food. Pre-screened participants (total n = 241) rated attribute intensities on a gLMS scale for equimolar mixtures of citric acid with monosodium citrate (n = 60), disodium citrate (n = 62), trisodium citrate (n = 60), and tripotassium citrate (n = 59), each at three different concentrations. Resultant dose-response curves for sourness were reflective of molar concentration and citric acid present in each mixture; as molar concentration and citric acid content in the mixture increased, sourness increased. Additionally, the counterion also affected perceived intensity, with tripotassium citrate consistently being perceived as less sour than the three sodium salts, suggesting a role of the counterion on sourness perception. Additional research is needed to study the role of other organic acids and counterions.

251 **How Bitter Is It? Odor-Induced Bitter Taste Modulation Of Bitter Ligands**

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Recent computational methods and machine learning models predict that 14% of the known bitter compounds might also have a smell. The aim of this study is to better understand the impact of retronasal olfaction in the perception of bitter taste and chemesthetic irritation of known bitter compounds. To achieve this, we evaluate individuals' perceptions of bitterness and irritation in response to multiple suprathreshold concentrations of various pharmaceutical and food-grade ligands, both with and without the use of nose clips. Employing a panel of well-trained healthy adults, we gathered taste, smell and irritation intensity ratings from 35 participants, all adept in utilizing the general labeled magnitude scale (gLMS). Participants followed a sip-and-spit protocol to sample nine different bitterants, randomly presented at three concentrations (including Naringin 10/50/100mM, Ibuprofen 10/44/100mM, Theobromine 1/10/30mM, Acesulfame K 1/12/100mM, Sodium Benzoate 50/100/300mM, Acetaminophen 1/10/100mM, Propylthiouracil 0.056/0.18/0.56 mM, Dextromethorphan 0.01/0.1/1mM, and Diphenhydramine 0.5/1/10 mM). Our findings align with the predictions of computational models, indicating that the majority of the bitterants in our study lacked any discernible smell. Therefore, for most of the compounds, bitterness (and irritation) ratings remained consistent whether tasted with or without nose clips. However, the nose clip condition had a significant effect on the perception of ibuprofen and naringin. Particularly noteworthy is that the retronasal influence enhanced the bitterness (and irritation) of ibuprofen while inhibiting the bitterness of naringin. These findings contribute to our understanding of the complex dynamics involved in the integration of taste and odor perception of bitter stimulants.

253 **The Bitter Taste Of Medicines And Their Modifiers In People Of Diverse Ancestries**

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The bitter taste of medicines is often a barrier to adhering to drug prescriptions. Medicines are more bitter for some people than others, and adding ingredients to reduce their bitterness is only partly effective. Moreover, people worldwide differ in their sense of taste, which may be partly due to genotype. To better understand how people from diverse ancestries differ in their perception of medicines and taste modifiers, 338 adult participants

of diverse ancestries (European and recent immigrants to the US and Canada from Asia, South Asia, and Africa) rated the bitterness intensity of taste solutions on a 100-point generalized visual analog scale. The solutions were four medicines used to treat common infectious diseases - tenofovir alafenamide (TAF), moxifloxacin, praziquantel, and amodiaquine - and propylthiouracil (PROP), a medicine with a well-known relationship for its bitterness and a single genotype. Participants also rated four other solutions for bitterness: TAF mixed with sucralose (sweet, reduces bitterness) or 6-methylflavone (tasteless, reduces bitterness), sucralose alone, and sodium chloride alone. Participants provided a saliva sample for genotyping. Individual differences in drug bitterness were striking. Bitterness ratings differed by ancestry for two of the five drugs (amodiaquine and PROP) and for TAF mixed with sucralose (but not with the other bitter reducer). Genetic analysis showed that people with variants in one bitter receptor variant gene (*TAS2R*38) reported PROP was more bitter than did those with a different variant (p= 7.6e-19) and that people with either an *RIMS2* or a *THSD4* genotype found sucralose more bitter than did others (p=2.6e-8, p=7.9e-11, resp.). Our findings may help guide formulation of bitter medicines to meet the needs of those most sensitive to them.

255 **Test-Retest Reliability Of Unipolar And Bipolar Electrogustometric Thresholds And Their Association With Waterless Empirical Taste Test (Wett&Reg;) Scores.**

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Electrogustometry (EGM) is a practical way to evaluate human taste function. In this study, 55 healthy subjects underwent electrogustometer threshold assessments on the anterior tongue. A counterbalanced design and a single staircase procedure were employed, utilizing both unipolar and bipolar electrodes. A subset of 30 participants underwent a retest within a period ranging from 22 to 544 days [mean (SD) = 308 (145.8)]. Additionally, 41 participants were administered the Waterless Empirical Taste Test (WETT®) after their first EGM test. The test-retest reliability coefficients (n=30) for the bipolar central and bipolar annular disks were 0.70 and 0.59, respectively. For the unipolar electrodes, these values were 0.54 for the anode and 0.33 for the cathode. All coefficients were significant at $p < 0.001$. The test-retest difference scores were unrelated to sex, age, side of tongue tested and test-retest time. Significant correlations were evident between all the EMG thresholds and the WETT® sour subtest scores (r's ranging from -0.33 to -0.48; all ps <0.001). No meaningful correlations were observed for the sweet, bitter, salty, and umami WETT® subtest scores. Among the subtests within the WETT®, NaCl and umami subtest scores were significantly correlated ($r = 0.56$, $p < 0.001$). The major conclusions of this study are that (a) anodal EMG thresholds based on the central disk of the bipolar electrode are most reliable and (b) EGM threshold scores are most strongly related to suprathreshold WETT® sour taste values regardless of the electrode employed.

257 **Unique Roles Of Type Ii & Type Iii Taste Cells In Fatty Acid Signaling**

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Unlike the case for most classes of tastants, we have shown that polyunsaturated fatty acids (PUFAs) are capable of activating both Type II and Type III taste cells. While both cell types respond to fatty acids over a similar concentration range, electrophysiological and functional imaging data support the notion that different transduction pathways underlie responses in Type II and Type III cells, with the former mediated by eventual activation of TrpM4/5 channels and the latter involving the activation of store-operated Ca^{2+} channels. In addition to exploring the specific elements of the transduction pathway in Type II and Type III cells, our data raise questions about functional roles of these cell types in fatty acid signaling. We hypothesize that Type II cells may serve to directly detect nutrients like PUFAs, while Type III cells may play a long-term regulatory role in terms of dietary experience, disease, or hormone fluctuations. To address this question, we have begun using a multidisciplinary approach to unravel the receptors and signaling elements involved in fatty acid signaling in Type II and Type III taste cells. Utilizing GFP-tagged transgenic strains, we have developed effective cell sorting techniques for the isolation of these primary taste cells. Subsequently, we conducted genetic, molecular, and functional assays, critically comparing the distinct fatty acid signaling pathways in both cell types. Data show that Type III cells are uniquely responsive to fatty acids and do not share the same characteristics noted in broadly responsive Type III cells. Our work in progress is providing new mechanistic information underlying fat signaling in Type II and Type III taste cells, and the role these cells may have in peripheral taste signaling. Supported by NIH DC021103 (tag).

259 **Don Tucker Finalist: Activation Of The Sour Receptor Otop1 By Ammonium Chloride, A Key Component Of Salty Licorice**

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States

Humans and most other vertebrates detect and discriminate among five basic tastes sweet, bitter, sour, salty, and umami, for which receptors are now known. In addition, high concentrations of salts, such as ammonium or potassium chloride, evoke an aversive taste that is distinct from the ENaC–mediated attractive sodium taste. Ammonium and other non-sodium salts are detected by both Type II taste receptor cells (TRCs), which mediate bitter, sweet, and umami tastes, and Type III TRCs, which mediate sour taste. Type III TRCs express the proton channel OTOP1 which functions as a sour receptor. Because NH_4Cl alkalinizes the cell cytosol, we hypothesized that OTOP1 might function as a sensor for the taste of NH_4Cl. Indeed, millimolar concentrations of NH_4Cl evoked large inward currents in OTOP1-transfected HEK-293 cells. The magnitude of the currents correlated with the degree of intracellular alkalization as measured with a fluorescent pH sensor, pHlourin. Similar responses were observed for human OTOP1, whereas relative NH_4^+ sensitivity was diminished in zebrafish OTOP1 and enhanced in chicken OTOP1. The large magnitude of the currents and species variation led us to hypothesize that the OTOP1 channels were gated by the change in intracellular pH, rather than passively responding to the pH gradient. Indeed, a charge-neutralizing mutation (R292A) of a conserved arginine located in the tm 6-tm 7 linker selectively reduced NH_4^+ sensitivity without affecting acid responses. Finally, using an *Otop1*$^{-/-}$ mouse strain, we showed that OTOP1 is required for sensory responses of isolated Type III TRCs to NH_4^+. These data together reveal an unexpected role for the proton channel OTOP1 in mediating a major component of the taste of NH_4Cl and a novel channel regulation mechanism conserved across species.

261 **The K_{Atp} Channel Component Of The Oral Metabolic Signaling Pathway Affects Glucose Taste *In Vivo* And Glucose Signaling *In Vitro***

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Glucose signals orally via both the sweet taste receptor T1R2-T1R3 and an oral metabolic signaling (OMS) pathway that includes glucose transporters, glucokinase, and the ATP-gated potassium channel (K_{ATP}). We determined if the K_{ATP} component influences glucose taste in: oral detection in humans, calcium responses in cultured human fungiform taste papillae cells (HBO), and gustatory nerve responses in mice. Methods: 15 humans were tested for oral thresholds with glucose, fructose, methyl-D-glucopyranose (MDG) (non-metabolizable glucose) and sucralose with 5 mM tolbutamide (K_{ATP} closer) or 5 mM pinacidil (K_{ATP} opener). Chorda tympani (CT) recordings were made in WT, T1r3 KO, Sur1KO and T1r3KO+Sur1KO mice stimulated with glucose, fructose and sucralose with 500 μM tolbutamide and 300 μM diazoxide (K_{ATP} opener). Fura-2AM calcium imaging was performed on cultured HBO when glucose was applied with either 100 μM glibenclamide (K_{ATP} closer) or 100 μM diazoxide. Immunohistochemistry was performed on human taste bud biopsies to identify the K_{ATP} channel components, SUR1 and Kir6.2. Results: In humans, tolbutamide increased and pinacidil decreased sensitivity to glucose and fructose, but not to MDG or sucralose ($p<0.05$). In T1r3 KO mice, tolbutamide increased and diazoxide reduced CT nerve responses to glucose, whereas there was no effect on sucralose. Compared to WT, Sur1KO mice had reduced responses to glucose but not to sucralose ($p<0.05$). In cultured HBO, glibenclamide increased the calcium response to glucose while diazoxide reduced it ($p<0.05$). Immunohistochemistry determined that K_{ATP} components SUR1 and Kir6.2 overlapped significantly with T1R3 in human taste bud cells. Conclusions: The K_{ATP} channel component of the OMS participates in taste transduction and taste perception in humans and mice.

263 **"Longitudinal Assessment Of Subjective And Objective Changes In Olfactory Function Following Sars-Cov-2 Infection: A Focus On Odor Identification, Intensity, And General Smell Function"**

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Infection by variants of the Sars CoV-2 virus has consistently been associated with self-reported changes to taste and smell function. We are interested in the relationship between subjective assessments of general smell function, subjective evaluations of odor intensity, and objective performance on a test of odor identification in a longitudinal setting. Participants sampled three odors (grape, smoke, and soap) one at a time, using peel-and-sniff odor labels on a card. They used a self-administered app to report on the intensity of odors. They then identified each odor and indicated their confidence level in their choice. Participants in this analysis, grouped as having had no prior history of Covid (Covid-, n=89), having had COVID within the past 6 months (CovidP, n=47), having had COVID between 6 months and a year ago (CovidD1, n=82), and having had COVID over a year ago (CovidD2, n=138), completed the odor card twice, six weeks apart. While the accuracy of odor identification remained stable in all Covid subgroups in this 6-week repeated testing paradigm, the two measures with subjective components (evaluations of odor intensity and the general assessment of smell function) were

significantly different via paired t-tests. Participants without a Covid history reported lower average ratings of general subjective smell function ($p<0.001$) and a higher perceived evaluation of odor intensity ($p<0.002$) over the six-week window. Participants in all the COVID history subgroups showed similar trends over the 6 weeks, with significant decreases in self-reported smell function and increases in ratings of odor intensity. Together, these natural history results have important implications for design of clinical trials to test therapies to accelerate recovery of smell function following SARS-CoV-2 infection.

265 **A Life Without Smell: Olfactory Function In People Working In Odorless Rooms**

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Objectives: Odorous stimulation helps to maintain or to improve olfactory function. In contrast, odor deprivation has been suggested to facilitate olfactory impairment. The aim of this study was to investigate the effects of odor deprivation in people working in an odorless environment. Methods: Fifty people working in an odorless environment for extended periods of time and 50 people not working in such environments were recruited. Participants were examined for olfactory function (using Sniffin' Sticks), nasal airflow (using Peak Nasal Inspiratory Flowmetry), self-rated olfactory function, self-rated nasal airflow, and well-being. Correlation analyses were used to explore the associations between the duration of working in odorless environment and olfaction, nasal airflow, and well-being. Results: The cleanroom workers exhibited slightly, but significantly reduced olfactory scores (sensitivity 7.0±2.5, discrimination 11.4±1.8) compared with controls (sensitivity 8.9±2.5, $F=4.33$, $p=0.03$; discrimination 12.7±1.6. $F=5.50$, $p=0.001$), even when controlling for age and rated nasal patency, with their self-rated olfactory function being not affected. The years of working in cleanrooms were negatively associated with olfactory function ($r= 0.35$, $P=0.013$). No significant correlations were observed between scores of olfactory function, nasal patency, and well-being. Conclusion: Compared to controls cleanroom workers exhibited slightly, but significantly lower olfactory scores, nasal peak flow, and well-being. Their decreased odor sensitivity was found to be associated with the number of years they had worked in the cleanroom. Overall, these results may suggest that odorous stimulation supports olfactory functioning.

267 **Comparison Of Patient Characteristics And Olfactory Sensitivity For Trigger Odorants In Parosmia And Phantosmia**

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Objectives: This study aimed to determine the characteristics of patients with qualitative olfactory dysfunction (qualOD) and whether individuals with parosmia exhibit increased sensitivity to previously reported odorous triggers of parosmia. Methods: This study included individuals aged ≥ 18 years, divided into quantitative OD only, parosmia, and phantosmia groups. Data collected included: clinical-demographic data, “Sniffin’ Sticks” scores, questionnaires (depression scale, importance of olfaction) and information about parosmia and phantosmia. A proportion of patients underwent trigger odor threshold testing for 2-Furfurylthiol [FFT] found in coffee and 2,6-nonadienal [Nonadienal] found in cucumber. Results: Those with parosmia were typically younger women, with shorter OD duration due to post-viral OD (PVOD), hyposmic / normosmic, and experienced parosmia more severely. Parosmia was 3.5 times more likely in PVOD. Those with phantosmia were older, with longer OD duration due to idiopathic OD, hyposmic / anosmic, and experienced phantosmia less severely. There were no significant differences between FFT and Nonadienal threshold scores in patients with parosmia, phantosmia, or only quantitative OD; but all groups had significantly increased olfactory sensitivity for trigger odors compared to phenyl ethyl alcohol (PEA). Conclusion: Parosmia and phantosmia patients have distinct characteristics. This may provide clinicians with a better understanding of possible olfactory outcomes in these patients. The higher olfactory sensitivity of all groups to trigger odors compared to PEA raises interesting points about parosmia triggers and odors in the context of warning for danger, in relation to the pathophysiology of parosmia that may be worth exploring in future studies.

269 ***Investigating Inflammatory Modulation Of Olfactory Sensory Neurons And Immune Cell Populations In The Main Olfactory Epithelium***

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The nasal epithelium, a frontline defense against inhaled exposures, also contains the main olfactory epithelium (MOE), the site of olfaction. MOE dysfunction, resulting in hyposmia or anosmia, significantly impacts quality of life. The MOE’s diverse cell types include olfactory sensory neurons (OSNs), supporting, epithelial, and immune cells. Neuronal-immune communication in the MOE is relevant in diseases with olfactory dysfunction

(e.g., allergic rhinitis or respiratory infections). OSNs must maintain olfactory function during inflammation, then subsequently repair during recovery. However, inhaled substances and odors may activate both OSNs and local immune cells. We hypothesized that resident immune cells and olfactory neurons are activated by olfactory stimuli and inflammatory mediators. Using single-cell RNA sequencing and flow cytometry, multiple subsets of OSNs, support, and immune cells were identified in the MOE. Using confocal microscopy, we found that in areas where OSNs and CD45+ resident immune cells were in close proximity, immune cells localized to both apical and basolateral regions. *Ex vivo*, we functionally assessed immunogenic and non-immunogenic stimuli on OSN and resident immune cell activation in mice expressing a genetically encoded Ca^{2+} indicator, GCaMP6s, in either OSNs (Omp-Cre x Ai96) or immune cells (Cx3cr1-Cre x Ai96) isolating MOEs *en bloc* and exposing to stimuli. Using volumetric objective-coupled planar illumination (OCPI) microscopy we identify and measure Ca^{2+} activity during stimulation resulting in mixed sensitivities across cells. These findings provide preliminary evidence of interactions between resident immune cells and olfactory neurons, with future studies using this experimental system to further evaluate the influence of mucosal inflammation.

271 **Subjective Impairment Decreases Significantly Over Time In Patients With Olfactory Disorders: A Cohort Study**

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Objective: Subjective self-assessment of olfactory ability is unreliable. Nevertheless, it can be assumed that the self-assessment is related to the subjective impairment caused by the olfactory disorder. We aimed to investigate how subjective impairment changes over time. Methods: Five hundred twenty-four patients (median age, 54 years; range, 15-88 years, 265 females and 259 males) seeking advice in our smell and taste clinic were examined two or more times. Subjective impairment was evaluated in consecutive patients using a visual analogue scale (VAS) ranging from 0 (no impairment) to 10 (very intense impairment). Subjective olfactory function (both identification and discrimination) was evaluated with a VAS (0-10) as well. Endonasal endoscopy and olfactory testing (lateralized Sniffin´ Sticks) was performed in all patients. We analyzed subjective impairments over time with generalized linear models—accounting for patient-level confounders and within-patient clustering. Results: 1,201 examinations were performed in 524 patients (382 [73%] were examined twice, 123 [23%] three times; overall range 2-6 exams). The median time interval between the event and first examination and first and last examination was 9 (interquartile range [IQR], 5-14) and 11 months (IQR, 8-21), respectively. Subjective impairment decreased significantly (adjusted p<.001) over time from a median of 9 (IQR, 6-10) to 7 (IQR, 4.5-9.5), subjective assessment of olfactory function increased from a median of 0.5 (IQR, 0-2.5) on VAS to 1.2 (IQR, 0-4; adjusted p=.001). Conclusion: Subjective impairment caused by olfactory disorders decreases significantly over time even if subjective olfactory ability improves only slightly—but significantly as well. Coping mechanism seem to be effective to reduce subjective impairment.

273 **Title: Structure And Functional Impact Of Neural Circuits Mediating Crosstalk Among Gustatory Receptor Neurons (Grns) In *D. Melanogaster***

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How taste signals are processed after the initial transduction of taste chemicals remains unclear. However, recent findings are beginning to clarify the unexpected complexity of gustatory coding in the sensory periphery, which appears to involve more than the activation of individual taste-sensitive cells. Understanding gustatory coding requires knowing whether and how taste sensitive cells functionally interact and whether these interactions ultimately shape gustatory behaviors. Here, with a comprehensive anatomical screen combined with molecular genetic and histological approaches in *Drosophila*, we found that at least five gustatory receptor neurons (GRNs) broadly-tuned to bitter taste chemicals are synaptically connected. With paired electrophysiological recordings we established that at least four pairs of synaptically connected GRNs functionally interact in what appears to be an activity-promoting feedforward circuit. We identified the neurotransmitter receptor subtype mediating the synaptic interactions and generated a null mutant lacking the receptor subtype. In flies bearing this mutation, interactions between the neurons responsive to bitter tastes were abolished, and taste avoidance behaviors were substantially and significantly different from behaviors of wild type flies. Our findings establish the existence and functional significance of synaptic interactions among taste sensitive cells in gustatory coding by showing that: (1) spiking in even a single GRN can influence the spiking of another synaptically connected GRN; (2) multiple synaptically connected GRNs appear to form a functionally active circuit; and (3) this circuitry shapes gustatory behavior.

Saturday, April 20, 2024

7:30 - 9:00 AM	Estero Foyer
Continental Breakfast	

8:00 - 10:00 AM	Estero Ballroom
Poster Session V	

300 **Don Tucker Finalist: Poor Olfaction And Risk Of Stroke In Older Adults: The Atherosclerosis Risk In Communities (Aric) Neurocognitive Study**

Keran W. Chamberlin[1], Chenxi Li[1], Anna Kucharska-Newton[2], Zhehui Luo[1], Mathew Reeves[1], Jayant M. Pinto[3], Srishti Shrestha[4], Jennifer Deal[5], Vidya Kamath[6], Priya Palta[7], David Couper[8], Thomas Mosley[4], Honglei Chen[1]

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Background: Poor olfaction in older adults may have health implications beyond neurodegenerative diseases. Recent data showed a cross-sectional relationship between poor olfaction and stroke, but evidence from prospective studies is sparse. Methods: We included 5,799 older adults with no prior history of stroke in 2011-2013 from the ARIC Neurocognitive Study (75.5±5.1 years). Olfaction was assessed by the 12-item Sniffin' Sticks odor identification test and defined as poor (number correct≤8), moderate (9-10), or good (11-12). Participants were followed from baseline to the date of the first stroke, death, last contact, or December 31, 2020, whichever occurred first. We used discrete-time sub-distribution hazard models to estimate cumulative incidence of stroke across olfaction groups and adjusted risk ratio (aRR), accounting for covariates, attrition and the competing risk of death. Results: After 9.6 years of follow-up, we identified 332 (5.7%) incident stroke events (256 ischemic). The adjusted cumulative incidence of stroke at the end of follow-up was 5.3% (95% confidence interval [CI]: 4.2-6.2%), 6.0% (95%CI: 4.8-7.0%), and 7.8% (95%CI: 6.5-9.1%) for the good, moderate, and poor olfaction group, respectively. Comparing poor with good olfaction, poor olfaction was associated with higher stroke risk throughout the follow-up. The aRR however gradually attenuated from 2.16 (95%CI: 1.23-3.91) at 2-year follow-up to 1.46 (95%CI: 1.16-1.96) at the end of the follow-up. Results were robust to additional adjustment for the Fried's frailty phenotype, exclusion of participants with dementia at baseline, or restriction to ischemic stroke as the analytic outcome. Conclusion: In older adults, a single olfaction test result was associated with incident stroke risk over a 10-year period.

302 **Myeloid Cell Dysregulation And Eicosanoid Overproduction Define Distinct Endotypes Of Chronic Covid19 Chemosensory Dysfunction**

Dante Minichetti[1], Amelia Boyd[1], Jonathan Hacker[1], Caitlin Wong[1], Evan Lemire[2], Wenjiang Deng[2], Kathleen M. Buchheit[1], Stella E. Lee[3], Rachel E. Roditi[3], Reagan w. Bergmark[3], Adam L. Haber[2], Tanya M. Laidlaw[1], Lora Bankova[1]

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Chemosensory dysfunction (CSD) persists beyond 6 months in 2-4% of patients recovered from COVID19, accounting for over 4 million people in the US. We aimed to define the mechanistic correlates and characteristics of chronic COVID19 CSD. Study subjects (n=73) with COVID19 CSD and controls with no history of

COVID19 CSD (n=21) at the time of enrollment were recruited and underwent objective evaluations of smell (UPSIT) and taste (B-WETT) acuity. Nasal cells and fluid were collected with self-applied Floqswabs and nasosorption strips, respectively. Among study subjects with chronic COVID19 CSD (24±5 months), UPSIT(23±7) and BWETT(16±4) were significantly reduced compared with controls (UPSIT33±4, $p<0.001$; BWETT19±3, $p<0.01$). Three endotypes of COVID19 CSD emerged: dysosmia (UPSIT≤25, B-WETT≥17), dysgeusia (UPSIT ≥26, BWETT ≤16), and combined dysosmia and dysgeusia (≤25, ≤16). All COVID19 CSD subjects had significantly increased nasal swab immune cells (53%) compared with normosmic controls (28%, $p=0.02$). Flow cytometric analysis indicated that the infiltrating immune cells were predominantly macrophages and neutrophils. Transcriptionally, subjects with dysosmia without dysgeusia had a differentially increased signature of myeloid derived suppressor cells. In subjects with dysgeusia or dysgeusia and dysosmia, several linoleic acid metabolites were significantly elevated and negatively correlated with BWETT scores: 9- and 13-HODE, $r(64)= -0.4$ $p<0.01$, 12,13di-HOME, $r(64)= -0.5$, $p=0.001$. An imprint of dysregulated myeloid immune signature emerges for COVID19 dysosmia, while eicosanoid dysregulation marks and differentiates the dysgeusia endotype. Chronic COVID19 CSD is a multifactorial syndrome with distinct endotypes.

304 **Factors Determining Olfactory Function Within The Adult General Population: Findings From The Chris Study**

Johannes Frasnelli[1,2], Martin Gögele[3], David Emmert[3], Christian Fuchsberger[3]

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The sense of smell enables us to evaluate the composition of our chemical environment. Reduced olfactory function is linked to various factors, including age, gender, health, and lifestyle conditions. However, many studies identifying variables influencing olfactory function have methodological weaknesses, such as differences in study design, participant selection, and recruitment biases, often including convenience samples or specific age groups. To address these issues, we conducted a study on the Cooperative Health Research in South Tyrol (CHRIS) cohort, a population-based cohort, using a validated odor identification test and by excluding individuals with impaired nasal patency. We included 6944 participants without acute nasal obstruction and assessed various biological, social, and medical parameters. A basic model revealed that age, gender, years of education, and smoking status collectively explained approximately 13% of the total variance in the data. Additionally, we found that variables related to medical conditions (positive screening for cognitive impairment and Parkinson's disease, history of skull fracture, stage 2 hypertension) and lifestyle factors (alcohol abstinence) negatively impacted odor identification scores. In conclusion, the ability to identify odors is influenced by medical, demographic, and lifestyle variables.

306 **Comparing The Number Of Cribriform Plate Foramina In Patients With Acquired And Congenital Anosmia**

Jerry Hadi Juratli[1], Brigit High[1,2], Akshita Joshi[1], Eren Yilmaz[3], Duzgun Yildirim[4], Aytug Altundag[5], Thomas Hummel[1]

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Purpose: Cribriform foramina allow for the passage of olfactory nerve fibers from the nasal cavity to the olfactory bulb. Disruption of the olfactory nerve fibers is known to affect olfactory function, but little is known about the role of the number of cribriform foramina in congenital anosmia. Furthermore, we aimed to investigate whether there was a reduction in foramina in patients with acquired anosmia. Methods: Paranasal CT image stacks were analyzed from 20 patients with congenital anosmia (n = 6), acquired anosmia (n = 6), or normal olfactory function (n = 8). Cribriform foramina were counted by three observers from the slice revealing the base of the crista galli and the ethmoidal slits. The two closest values from each subject were analyzed in comparison across the three groups using one-way ANOVA. Results: Patients with congenital, but not acquired, anosmia had significantly fewer cribriform foramina compared to healthy, normosmic controls. There was no significant difference in foramina count between congenital and acquired anosmics. Conclusion: A reduced number of cribriform foramina is found in individuals with congenital anosmia. Examination of cribriform foramina could be helpful in counseling patients with olfactory loss.

308 **Using Novel &Ldquo;Smell-Aids&Rdquo; To Improve Olfactory Function In Patients With Broad Etiologies Including Long Covid: A Clinical Trial**

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The Ohio State University: Department of Otolaryngology - Head & Neck Surgery, Columbus, OH, United States

Eye glasses, hearing aids, and etc. serve to enhance the sensory stimuli to enable patients to see or hear things that they wouldn't otherwise be able to, but we have no equivalent technology for olfaction. We attempt to invent "Smell-Aids" by enhancing intranasal odorant delivery to the olfactory epithelium, using two prototypes: (a) a nasal foam plug with a diagonal channel embedded to direct air/odor flow upwards to the olfactory region; (b) a clip (similar to what synchronized swimmers use) pinching a critical nasal valve region that may intensify the airflow vortex to the olfactory region; and tested them on 54 patients with confirmed olfactory losses (age 21-

80y, median 54.5). Majority (37/54=69%) were post-COVID long haulers (infected 12/15/2019 to 10/4/23; persisted 30 to 1260 days, median 22 months), while non-COVID smell losses (n=17) span from 5m-27 years (median 8.5 y). The 9-item NIH toolbox odor ID score significantly improved after application of both smell aids (in counter-balanced order, baseline: 4.30+-2.27, pinch 4.82+-2.06, plug 5.11+-2.32, mixed model $p<0.05$), especially among the non-COVID cohort. For COVID long haulers, only the nasal plug showed significance improvement ($p<0.05$). Rated confidence score among both cohorts significantly improved with the nasal plug but not the pinch prototype. Further subgroup analysis on patients who reported diminished (hyposmia/anosmia 38/54) vs distorted smell (parosmia/phantosmia 27/54, n=11 reported both) showed that the nasal plug remains effective for both cohorts, while the pinch is only effective for the hypo/anosmia cohort. These results preliminarily demonstrated the potential to improve olfactory function through different peripheral mechanisms for different patient cohorts and may one day lead to an effective OTC smell aid.

310 **Enhancing Preclinical Alzheimer Cognitive Composite (Pacc) Via Olfactory Testing**

Qing X Yang, Prasanna Karunanayaka, , Biyar Ahmed, Rommy Elyan, Ren Pang
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The ultimate goal of Alzheimer disease (AD) research is to develop methods for prevention and treatment AD from “presymptomatic” phases of the disease. It is important to first develop outcome measures sensitive to the earliest disease-related changes. Recent years, a cognitive composite outcome measure of Preclinical Alzheimer Cognitive Composite (PACC) has been developed, for clinical trial in preclinical AD. The PACC combines tests that assess episodic memory, timed executive function, and global cognition. It has long been established that olfactory deficits are prevalent in early MCI and AD which can precede symptoms of memory and cognitive decline. Longitudinal studies of patients have indicated that olfactory deficits are related to the severity of dementia and are significantly different from normal aging effects. Thus, the objective of this report is to examine if odor identification and threshold can be used for assessing AD severity above and beyond cognitive impartments included in the PACC. In this study, MCI (n=20, 11 F, age 70.10 ± 7.48) and healthy controls (HC) (n=27, 18 F, age 65.15 ± 5.44) underwent neuropsychological testing and olfactory identification and threshold testing. Principal component analysis was performed with the neuropsychological test scores followed by a linear model regression correlating the category the participant was placed in, i.e., HC or MCI, versus the principal components and age with and without olfactory measures. A two-way ANOVA test resulted in a Chi-squared value of 0.0277. These findings demonstrated that olfactory testing scores improves the ability to distinguish MCI from HC.

312 **Impact Of Aging And Apolipoprotein E4 On Mitral Cells In The Mouse Olfactory Bulb**

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Mice with the knockin (KI) human gene encoding the apolipoprotein E4 (APOE4), the strongest genetic risk factor for the late onset Alzheimer’s disease (AD), exhibit age-dependent network dysfunction in the olfactory bulb (OB) and its downstream structure the piriform cortex, indicating that the OB output is subject to influence of two AD risk factors - aging and APOE4 gene. However, the mechanisms at the cellular level remains unclear. In this study, the in vivo multi-channel extracellular recording approach was utilized to compare the OB network oscillatory activities and spontaneous spiking of mitral cells (MC), the principal OB output neurons, between control and APOE4 KI mice at the age of 120 weeks in anesthetized conditions whereas whole cell patch clamp recordings were carried out to assess the neuronal excitability and synaptic activities in MCs in OB slices. We found much fewer actively spiking units and altered oscillation power in recordings from APOE4 KI mice compared to their age- and sex-matched control animals. Consistently, MCs in OB slices prepared from APOE4 KI mice showed a significantly lower level of spontaneous firing activities and altered action potential parameters compared to control animals, indicating detrimental effects of APOE4 on MC excitability. Interestingly, MCs in OB slices from APOE4 KI mice also exhibited a reduced level of spontaneous inhibitory postsynaptic currents, suggesting an altered interaction between excitatory and inhibitory local neurons as well as the related networks. To determine whether these APOE4 effects are age-dependent, we will extend these studies to adult (~25 weeks) mice. Taken together, our findings demonstrate the detrimental actions of APOE4 on the principal OB output neurons and related network operation in aged mice.

314 **Cross-Cultural Evaluation Of Olfactory Dysfunction: Insights From A Bilingual Longitudinal At-Home Smell Test**

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Olfaction showcases a unique complexity compared to sensory systems like vision or audition, as it is intricately intertwined with cultural influences due to odor-specific exposure, familiarity, and association variations. To address these gaps, we have developed a bilingual longitudinal at-home smell test to study olfactory dysfunction and evaluate its cross-cultural validity by examining odor responses in a subgroup of Spanish-speaking participants recruited from Puerto Rico and comparing these results with English-speaking participants recruited across the United States. Study participants completed a 5-minute assessment of olfactory function once a week for 12 weeks, completing the sequence of 6 unique odor cards twice. Initial findings reveal no significant differences in average intensity ratings and accurate odor discrimination between groups for any of the 12 testing events. However, given our interest in the cultural generalizability or the cultural sensitivity to specific odors among language groups, we examined and compared odor-specific results on these measures of intensity and discrimination. Patterns of intensity ratings by card (odor 1, 2, and 3) show a remarkably characteristic shape whether the rater is an English or a Spanish speaker, suggesting that the groups are sensing and evaluating our panel of odors similarly. The impact of familiarity introduced by the second completion of the card produces a shift in the perception of intensity that is also surprisingly consistent within a card. With regards to the odor

discrimination task, Spanish speakers demonstrate better discrimination of the dirt odor (84% accuracy) than English speakers (71% accuracy). Our results emphasize the importance of examining odor-specific data in this manner to build a culturally sensitive test.

316 **Unveiling The Olfactory Function Spectrum: Linking University Of Pennsylvania Smell Identification Test (Upsit) Scores To Subjective Evaluations**

Shima T. Moein[1,2], Rafa Khan[1], Richard L. Doty[1,2]

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Understanding the crucial link between patients' subjective evaluations of olfactory dysfunction and objective clinical measurements is paramount for informed healthcare decisions. In this cross-sectional study, subjects were meticulously selected from a dataset of 4,009 data records at the University of Pennsylvania Smell & Taste Center. The focus was on 1,948 patients with olfactory function complaints, compared to 502 patients without such complaints. The standardized protocol included a detailed questionnaire and psychophysical objective assessments using the University of Pennsylvania Smell Identification Test (UPSIT). Participants were categorized into six groups based on subjective evaluations: anosmia (n = 1,202, females = 669), phantosmia (n = 74, females = 42), parosmia (n = 163, females = 101), hyposmia (n = 460, females = 263), hyperosmia (n = 49, females = 28), and normosmia (n = 502, females = 270). UPSIT scores revealed a distinct spectrum pattern, with average [95% CI] scores as follows: anosmia (15.74 [15.29, 16.19]), phantosmia (25.85 [23.92, 27.78]), parosmia (25.40 [24.04, 26.76]), hyposmia (24.98 [24.14, 25.81]), hyperosmia (31.57 [29.75, 33.39]), and normosmia (32.05 [31.52, 32.58]). Anosmia patients exhibited significantly lower UPSIT scores compared to all other groups (ANOVA, $p < 0.0001$). Patients with parosmia and phantosmia had UPSIT scores not significantly different from those with hyposmia ($p = 0.95$, $p = 0.99$ respectively). Intriguingly, objectively assessed hypersensitive patients showed lower UPSIT scores than those with a normal sense of smell, challenging assumptions about odor sensitivity in clinical settings. This study unveils the relationship between subjective odor perception and objective measurements, shedding light on the complexities of olfactory dysfunction.

318 **Evaluating The Burden Of Smell Loss On General Health And Well-Being**

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The sense of smell has gained recent interest as a tool for assessing the overall health of the population (1). Previous studies have shown that the ability to smell is closely linked to quality of life and general health, particularly among older individuals (2). To investigate the impact of a decline in the sense of smell on health, we analyzed the data from the 2011-2012 National Health and Nutrition Examination Survey (NHANES) (3). Our preliminary analysis focused on self-reported health status variables taken from the HSQ 470-490 module, exploring health in the past 30 days and the self-reported ability to smell in the past 12 months (CSQ010), in order to determine the burden of smell loss on general health. The sample included 3067 individuals (age: 59.8± 12 years; 50.9% F; 39% non-hispanic white, 19.1% hispanic, 28.1% non-hispanic black, 11.5% asian, and 2.3% other ethnicities). Preliminary findings indicate a significant association between the ability to smell and health-related quality of life in individuals aged 40 and above. We assigned health status as poor, fair, or healthy based on the number of days over the last 30 days that respondents self-reported they were in poor physical and mental health, and how many days they were inactive due to their poor health. Preliminary analysis found that physical health status (X^2=11.7, df=2, p=0.003), mental health status (X^2=24.1 , df=2, p<0.0001), and inactivity due to poor physical and mental health (X^2=26.3 , df=2, p<0.0001) are all linked to a self-reported reduction in the ability to smell. These results will provide an estimate of the overall impact of smell loss in the general population and inform on how lacking to measure and address smell dysfunction creates harm to those suffering from this condition.

320 **Long-Term Impacts Of Covid-19 On Multiple Sensory Systems: A Preliminary Report**

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COVID-19 may have significant neurotropic impacts on sensory functions. This ongoing study aims to capture the long-term impact of post-acute sequelae of SARS-CoV-2 infection (PASC) on broad sensory systems. We tested, for 1) olfaction: 9-Item NIH Toolbox odor identification, detection threshold to phenyl-ethyl alcohol (PEA), and retro nasal flavor identification (candy); 2) Taste: modified NIH toolbox; 3) chemesthesis: menthol lateralization thresholds; 4) hearing: standard pure tone audiometry, otoacoustic emissions testing (OAE) and speech-in-noise (SiN) recognition; 5) vestibular: video head impulse testing (vHIT), Subjective Visual Vertical (SVV), and modified Romberg balance test on force plate. Preliminary analysis included 19 patients (age 29-74 years old, median 51), who contracted COVID-19 from 3/15/2020-1/12/2023, with symptoms persisting from 3 to 45 months (median=23.5 months). Overall, subjects self-reported a high and overlapping incidents of multisensory losses: smell (79%), taste (58%), and vestibular (50%) that differ from objective testing. Only 10.5% of subjects had olfactory losses per NIH toolbox, 36.8% showed losses on retro nasal candy tests and 5.3% showed losses on NIH taste test. Across all subjects, none showed abnormalities on SVV or vHIT, and 2/16

failed balance tests. These discrepancies varied across sensory modalities. Particularly for hearing, fewer patients (3/19) reported losses, yet all losses were confirmed with objective hearing tests with one additional patient having a SiN deficit. While preliminary, our findings suggested potential different mechanisms of dysfunctions (peripheral vs central) across different sensory modalities or a lack of sensitivity of some tests for this population, which awaits further investigations with a larger sample.

322 **Importance Of Olfaction Throughout Lifespan In Scotland And Pakistan**

Agnieszka Sorokowska[1], Michal Misiak[1,2], S. Craig Roberts[2,3], Piotr Sorokowski[1]

[1]1Institute of Psychology, University of Wrocław, Wroclaw, Poland, [2]Being Human Lab, University of Wrocław, Wroclaw, Poland, [3]Department of Psychology, University of Stirling, Stirling, United Kingdom

While developmental changes in so-called objective olfactory abilities are relatively well-documented, subjective importance of odors has received less scientific interest, particularly from a developmental perspective. It also remains unknown if importance of different odor categories is entirely independent. Likewise, there are very few odor importance studies conducted outside Western communities, even though existing research points to significant cultural differences in olfactory awareness or importance. To address these research gaps, we tested the perceived importance of various aspects of odor perception across different developmental stages and in two countries that are very different in terms of cultural and environmental conditions: Scotland and Pakistan. Seven hundred and four respondents in Scotland and Pakistan (48.9% females) aged between 5 and 75 years completed a novel questionnaire on importance of olfaction. The scale comprised 18 items targeting six main functions of odor perception: appetite and regulation of food intake, pathogen and hazard avoidance, mating, social relations, bonding, and sensual pleasure. We found that the importance of olfaction was well-developed in children: odors related to pathogens and food were rated as even more important by children than adults. Overall, age affected the importance of olfaction in the areas of food, bonding, pathogen avoidance, and mating, while culture – in the areas of food, pleasure and bonding. Our research shows that odor importance is a complex construct, and its various elements develop differently throughout the lifespan. Age- and culture-related differences we observed indicate the need for further developmental and cross-cultural research on subjective smell perception.

324 **The Birthrates Of Olfactory Sensory Neurons That Express Specific Odorant Receptors Are Accelerated By Discrete Odors.**

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In mammals, the birth of olfactory sensory neurons (OSNs) occurs throughout life, presumably solely to replace damaged neurons. Each OSN precursor is thought to stochastically choose, out of hundreds of possibilities, a single odorant receptor gene, which defines the subtype identity of the mature OSN. Thus, neurogenesis in the olfactory epithelium (OE) is considered stochastic regarding subtype. Recently, however, we have found that the birthrates of specific OSN subtypes are accelerated by olfactory stimulation. These findings raise questions about the nature of the neurogenic stimuli and their relationship to the subtypes whose birthrates are altered that are critical for understanding the mechanism and function of this process. Using RNA-seq and scRNA-seq, we found evidence that OSNs of subtypes that detect male and/or musk odors are more abundant in mice exposed to male odors and can undergo stimulation-dependent neurogenesis. Based on these findings, we hypothesized that the stimuli that promote the birthrates of specific OSN subtypes are discrete odors that selectively activate the subtypes whose birthrates are accelerated. To test this, we exposed female mice to male-specific odors or muscone and then quantified the neurogenesis rates of the OSN subtypes that detect these odors using combined RNA Fluorescent in situ hybridization and EdU-birthdating. Our findings indicate that male-specific and musk odors selectively promote the birthrates of OSN subtypes that are activated by these odors. These results reveal that some discrete odors can selectively increase the neurogenesis rates, and therefore, representations of cognate OSN subtypes in the OE, and suggest that persistent neurogenesis may play an unknown adaptive function.

326 **A Cross-Species Comparison Of The Nasal Microenvironment**

Pia LaPorte[1], Ludmila Globa[1], Oleg Pustovyy[1], Melissa Singletary[1,2]

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It is unknown how differences in the respiratory and olfactory nasal cavity microenvironments influence function within and across species. The microenvironment of other mucosal sites demonstrate an integral relationship regarding the function of epithelial development, immunological regulation, and overall homeostasis. This limited understanding of the olfactory and respiratory nasal cavity microenvironments is being addressed through anatomical, histological, immunohistochemical (IHC), and microbiotal comparisons between the nasal cavities of dogs, rats, and cats. Nasal cavities of each species were dissected for Respiratory Epithelium (RE) and Olfactory Epithelium (OE) from the nasal septum and ethmoidal turbinates. Tissues were preserved and stained with H&E, PAS, OMP (IHC), and GAP43 (IHC). Initial microbiotal characterization was performed by PCR-amplified DNA with the 16S universal Eubacterial primers. Amplicons were sequenced by the PacBio Sequel platform for identification of the microbiota. These mammalian models all have distinct anatomical differences, histological discrepancies, and IHC reactivities. Histology and IHC of the OE and RE of these animals has revealed differences in gland structure, neuronal presence, and relative epithelial thickness. Pilot microbiota characterization of the rat revealed distinctions between the OE and RE. Although many features of the evolutionarily ancient sense of olfaction are similar across taxa, discrepancies exist between species likely affecting epithelial development, olfactory sensory neuron turnover, olfactory ability, and the general health of the organism. Further studies will include comparative analyses of the nasal cavity microbiome across species and determine how differences in microbial community in the OE influence olfaction.

328 **The Role Of Trpa1 And Trpv1 On Astringency Perception In Humans**

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One mechanism of astringency posits the sensation is evoked following the binding of astringent compounds to TRPA1 and/or V1 channels. Although interactions between astringent compounds and TRP channels have been observed *in vitro*, no corroborating evidence has been shown in humans. Presently, we investigated the role of TRP channels by assessing astringency following TRP channel desensitization. To induce desensitization of either TRPA1 or V1, mustard oil (MO:0.5%) or capsaicin (CAP:100ppm) respectively, was painted onto one half of the dorsal anterior tongue surface of each subject (n=34). Deionized water was painted on the other side as a control. After the onset of desensitization (ca. 5-10 min), subjects were asked to swish 10mL of an astringent solution [epicatechin (EC:1mM), epigallocatechin gallate (EGCG:1.1mM), potassium alum (alum:0.4mM), and tannic acid (TA:0.25mM)] in their oral cavity and assess perceived astringency intensity on both sides of the tongue by rubbing the dorsal anterior surface against the palatine rugae 3-5 times. Subjects first performed a 2AFC and selected the side of the tongue with the stronger astringent sensation, and then rated astringency bilaterally using a 10-pt line scale. For all astringent compounds, following MO desensitization of TRPA1, a significant majority of subjects did not choose any side as stronger, and no significant intensity rating differences were noted between the MO and control treated sides. Following CAP desensitization of TRPV1, a significant majority of panelists selected the desensitized side as being more astringent when assessing EC, alum, and TA, however no significant bilateral intensity differences were noted for any solution. Results suggest TRPA1 and V1 are not involved in the mechanism underpinning human astringency perception.

330 **Relationship Between 6-N-Propylthiouracil (Prop) Bitterness, Prop Taster Status, Bitter Taste Receptor Gene Tas2R38 (Rs713598), And Taste Qualities Of Ferrous Sulfate And Copper Sulfate.**

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Individual differences in bitterness perception have been extensively studied. However, individual differences in metallic sensation remain relatively unexplored. In this study, we examined the perception of two metallic compounds, ferrous sulfate (FeSO4) and copper sulfate (CuSO4) and assessed the relationship with propylthiouracil (PROP) and genetic variability in a bitter taste receptor gene (*TAS2R38,* SNP rs713598, A49P). A total of 121 participants sampled PROP (0.32mM), FeSO4 (0.3mM, 1.0mM, 3.0mM), and CuSO4 (0.3mM, 1.0mM, 3.0mM) and rated intensity on a Generalized Labeled Magnitude Scale for sweetness, bitterness, saltiness, sourness, and metallic. PROP taster status was determined based on bitterness ratings: non-tasters (n=40), medium tasters (n=33), and supertasters (n=37). Mixed model Analysis of variance (ANOVA) revealed that PROP taster status was not associated with metallic sensation for either compound. Similarly, the bitterness of FeSO4 was not significantly associated with PROP taster status; however, there was a significant association with CuSO4 ($p=0.001$). Pearson's correlation revealed a significant correlation between the bitterness of PROP and CuSO4 (0.3mM: $r=0.26$; 1.0mM: $r=0.28$; 3.0mM: $r=0.33$; p's<0.05). In terms of genetic variability, an ANOVA revealed that there was no association between *TAS2R38* A49P and any reported intensities for either compound. These findings indicate that PROP bitterness, but not genetic variability in *TAS2R38*, is related to the individual differences in the bitterness perception of CuSO4. While this provides important insights into the differences in perception of two metallic ions, more research is needed to identify whether genetic variability in taste or chemesthetic receptor genes explains the individual differences in metallic perception.

332 **How Sweet Is It? Sex-Related Differences In Sweetness Perception Of Habitual And Non-Habitual Consumers Of Low-Calorie Sweeteners.**

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Roughly 50% of US adults turn to low-calorie sweeteners (LCS) to reduce sugar and calorie intake. Surprisingly, instead of replacing sugars, many end up adding LCS into their diets, leading to increased overall sweetness consumption. This study examines whether regular consumption of low-calorie sweeteners (LCS) dulls the perception of sweetness, potentially driving individuals to seek more sugar to attain the same desired level of sweetness. We hypothesized that habitual low-calorie sweetener consumers (HC) would exhibit increased adaptation to repetitive sweet taste stimulation compared to non-habitual consumers (NHC). Additionally, we investigated whether sweet adaptation patterns varied by sex. We conducted sensory tests on 40 HC (22 females/18 males) and 44 NHC (27 females/17 males), involving the tasting of sugar (glucose or fructose) and a LCS (sucralose) at different concentrations. HC consumed >5 and NHC <1 diet soda or LCS equivalent product per week. Sucralose solutions were presented alone or mixed with a small amount of sugar (111M glucose or 45M fructose) over 8 consecutive trials. We found that, consistent with previous findings, adaptation was more pronounced with sucralose alone compared to sucralose mixed with a small amount of sugar. However, there were no overall differences in the patterns of sweetness adaptation between HC and NHC, whether with sucralose alone or blended with sugars. Interestingly, a sex by LCS group interaction emerged, with female HC displaying greater adaptation and male HC showing less adaptation than their respective NHC counterparts. These sex-related differences in sweetness adaptation depending on LCS consumption are intriguing and warrant further investigation to confirm their validity and explore potential underlying mechanisms.

334 **Functional Localization Of The Primary Taste Cortex In The Anesthetized Macaque Monkey**

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The insular cortex is a recipient of direct thalamocortical inputs relaying sensory information from various bodily regions, including the oral cavity and gastrointestinal tract. This cortical region plays a pivotal role in regulating homeostasis related to feeding, digestion, and bodily functions. In this study, we utilized novel taste delivery systems to help pinpoint the primary taste area in both humans and macaques. Beginning with human psychophysical testing, followed by ultra-high field 7T fMRI in anesthetized macaques (n = 8), we evaluated tastant stimuli at varying concentrations. Our findings consistently revealed activation in specific regions of the macaque insula, particularly highlighting the mid-insula dorsal fundus (Idfm) and dorsal anterior insular cortex (dAIC), alongside an additional activation cluster in the ventral anterior insular cortex (vAIC). Through comparisons with human functional homologs and neuroimaging meta-analyses, we aimed to discern the existence of a common gustatory area. Our translational investigation suggests a degree of homology between primate species, underscoring a notable resemblance, between the macaque and human insula and surrounding opercula, in the localization of fMRI voxel-wise activity correlated with gustatory processing.

336 **Don Tucker Finalist: Dopaminergic Modulation Of Cortical Motor Circuits During Gustatory Sensorimotor Transformation**

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The anterior-lateral motor cortex (ALM) is implicated in the genesis of sensory-guided licking. It remains unknown what neuromodulatory mechanisms mediate ALM function in sensorimotor transformations. One potential mechanism is dopaminergic signaling through D1 receptors (D1Rs) in ALM. We examined dopamine (DA) release and the role of neurons expressing the D1Rs in mice performing a taste-guided, 2-alternative choice task. We chose a taste-guided behavior because tasting and licking are inherently linked, and it is unknown how ALM is involved in the use of gustatory information to guide licking. Mice were trained to discriminate tastants (sucrose or NaCl) sampled from a central spout, plan their response during a delay period and report the identity of the tastant with directional licks towards two reward spouts (lick left vs. lick right). Fiber photometry recording with the DA sensor, GRAB-DA2h, in ALM revealed phasic DA signals related to licking for a taste cue, followed by an enhanced ramping signal for preparation of contralateral licks during the delay period. Calcium imaging in ALM revealed that activity of ALM D1R+ neurons tracked these DA signals, and their responses are distinct from those of non-D1R expressing neurons (D1R-). Weak tuning to specific taste stimuli was found in neurons, regardless of receptor expression. However, D1R+ responses encoded a bias for contralateral lick trials when compared to D1R- responses, with D1R+ population coding also exhibiting stronger direction selectivity during the delay epoch. Finally, optogenetic inhibition of D1R+ neurons during the delay reduced contralateral lick performance. Our findings suggest that cortical DA signaling is a key neuromodulatory mechanism in ALM during taste-guided sensorimotor transformations involving directional licking.

338 **The Role Of Component Reliability In Behavioral And Neural Response To Bimodal Flavor Mixtures**

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Flavor perception results from integration of multiple sensory inputs, including taste and odor. One site where this integration occurs is the gustatory cortex (GC), but the computations are still unknown. In line with findings from other multisensory systems, we hypothesized that reliability of the components of a taste-odor mixture are crucial in determining integration. We measured behavioral and neural responses to taste-smell mixtures and components. Reliability was varied by changing concentration of the taste component (10 or 40 mM sucrose); the odor component was constant (0.025% amyl acetate). Behavioral responses were measured as consumption in a series of two-bottle preference tests (mixture or component versus water). Neural responses to the same solutions delivered via intra-oral cannulae were measured as spiking activity of single GC neurons in awake behaving rats. Behavioral results show that preferences for mixtures are a weighted average of component preferences. Low taste concentrations yielded more variable preferences and carried less weight in determining mixture preferences compared to high taste concentrations. At the neural level, single-unit responses (n=143 excitatory responses) to mixtures were intermediate to their component responses. Responses to mixtures with high taste concentration were closer to taste responses while responses to mixtures with low taste concentration were closer to odor responses. Similarity between mixture and component responses could not be explained by the strength of the component responses, suggesting that the integrative operation does not result from input strength, but circuit- or network-level interactions. In conclusion, component reliability affects integration of multisensory flavor mixtures at the behavioral and neural levels.

340 **Olfactory Biomarkers Associated With Brain Volumes And Cognition In Former Professional American Football Players: Results From The Harvard Football Players Health Study**

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Traumatic brain injuries (TBI) are a common cause of olfactory impairments. However, it is unclear if olfaction is altered in populations who experience repetitive head impacts such as professional American football players and how olfactory functioning could reflect brain health in this population. We aimed to determine the clinical and neuroimaging correlates of olfactory functioning in a sample of former professional football players. Grey matter volumes and cortical thickness of olfactory-related structures were extracted (Freesurfer) in a group of 97 participants (mean age=48.58, SD=7.73). We used the AROMHA Brain Health Smell Test to measure odor discrimination (OD10), odor memory (POEM), and odor percept identification (OP18). NIH Toolbox Cognition Battery subtests were used to assess cognitive speed, language, memory, and executive functioning. Concussion-related symptoms and losses of consciousness during the career were self-reported. Multivariable regression models included professional years played, age, race, and body mass index (BMI) during playing years. Pearson correlation analyses were performed between OD10, POEM, OP18, grey matter volumes, and cognition. Multivariable regression analysis showed that the concussion-related symptoms rated retrospectively for their playing years was a significant predictor of the olfactory composite score (β=-0.003, p=.005) and OD10 (β=-0.002, p<.001) while other factors were not (p>.05). OD10 was significantly related to hippocampus (r=.26, p=.01) and thalamus (r=.29, p=.006) volumes, and the Picture Sequence Memory Test (r=.21, p=.03). In former professional football players, current olfactory functioning was associated with retrospective ratings of symptoms of concussions during their playing years, and their hippocampal and thalamic volumes.

342 **Neural Processing Of Oral Thermal Stimuli In The Somatosensory Cortex**

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Eating is a multimodal experience, combining gustatory, olfactory, and somatosensory cues leading to a percept known as flavor. Oral thermal signals have been shown to influence food preferences and are relevant to nutrition. While our previous research has started investigating the neural correlates of oral temperature in the gustatory cortex (GC), less information is available on the thermal response properties of the oral somatosensory cortex (SC). This study aims to bridge this knowledge gap by conducting electrophysiological recordings from SC neurons in active licking mice to evaluate the cortical processing of temperature variations in deionized water. In brief, we utilized movable tetrode bundles to record single-unit ensembles in the SC. These recordings were made as the mice licked seven times to a dry spout to obtain 4μl of water at three distinct, non-harmful temperatures: 14 °C, 25 °C, and 36 °C. To discern potential thermal effects caused by thermal differences in the dry spout or fluid, neuron responses were analyzed with respect to the first lick to the dry spout and to fluid delivery. Overall, we found a substantial fraction of SC neurons being modulated by fluid and tactile thermal stimuli. Surprisingly, we found a majority of the SC thermal-responsive neurons responding to 25°C (close to room temperature) and less to cool and warm (14°C and 36°C) stimuli. Altogether, we will present a set of data that begins to unveil how the SC represents oral thermal cues in awake and behaving mice and provides additional information on how the mammalian cortex is representing oral sensory information relevant to flavor and food choice.

344 **Metastable Dynamics In Gustatory Cortex During Taste Mixture-Based Perceptual Decision-Making**

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Neural activity in gustatory cortex (GC) is characterized by abrupt transitions between ensemble-coordinated firing rates called metastable states. Previous work has shown metastable dynamics underlie GC's role in mediating taste-based decision-making. However, it is unclear what properties of metastable states allow for encoding of decision-making task-relevant variables, and how this framework applies when taste stimuli are mixtures that vary along a continuum. Here we investigate metastability in the GC of mice performing a sucrose/NaCl binary taste mixture-based decision-making task. The task requires animals to (1) sample a sucrose/NaCl mixture (ranging from 0/100 to 100/0) from a central spout, (2) wait for a delay period, then (3) lick a lateral spout for a water reward based on the dominant mixture component (i.e., sucrose>NaCl --> lick left; else --> lick right). Hidden Markov Models extracted metastable states from GC ensembles recorded using Neuropixels probes. Linear classifiers revealed that state duration contains information about the stimulus and the animal's directional choice. We classified each state based on whether its mean duration vs. stimulus profile was best fit by a line or step function. We focused on these functions because of their natural interpretations as reflections of continuous sensory and binarized decision information, respectively. State onset time distributions indicated linear-coding states tend to precede step-coding states, consistent with sensory coding preceding decision coding in this task. Altogether, our results implicate metastable state duration as a key property for representing taste-based decision-making task-relevant variables. Ongoing work is directed at explaining these dynamics in terms of circuit-level mechanisms via computational modeling.

346 **Insulin Modulates Excitatory Drive Of Pyramidal Neurons In The Posterior Piriform Cortex.**

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Olfactory cues in the environment can signal food availability. Odors associated with nutritive substances initiate anticipatory physiological changes called cephalic phase responses, such as cephalic phase insulin release (CPIR). CPIR is a strong driver of food intake and modulates odor perception. However, little is known about the mechanism through which CPIR modulates odor processing. To address this question, we applied insulin to acute coronal tissue slices of the posterior piriform cortex (PPC; AP: +0.1) while recording from voltage-clamped pyramidal neurons (n = 7). At -70 mV, the average instantaneous frequency (b = -2.30, p <0.01) and the average amplitude of spontaneous excitatory postsynaptic currents (EPSC; b = -1.45, p <0.01) decreased. However, the effects of insulin were heterogeneous. Insulin increased the instantaneous EPSC frequency on a subset of neurons (43%) and it was decreased on a separate subset of neurons (43%). We observed similar results when considering the EPSC amplitudes; 29% of neurons had larger EPSCs following insulin application while another 29% of cells were decreased. The satiety factor, glucagon-like peptide 1 (GLP-1) has been shown to modulate insulin signaling in the olfactory system. Therefore, we hypothesized that hindbrain GLP-1 neurons in the nucleus of the solitary tract (NTS) project to the PPC where they can modulate pyramidal cell excitability. To address this, we injected a retrograde fluorescent tracer, cholera toxin subunit b (CTb), into the PPC. We indeed observed neurons containing CTb in the NTS. Future studies will identify the peptidergic contents and functionality of these neurons. Our data suggest the possibility of NTS GLP-1 neurons projecting to the PPC to modulate olfactory processing.

348 **Fast Updating Feedback From The Piriform Cortex To The Olfactory Bulb Relays Multimodal Identity And Reward Contingency Signals During Rule-Reversal**

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Animals adjust their behavior to adapt to relevant environmental changes, but the neural pathways enabling these changes remain unclear. Mice excel in discriminating odorants in complex sensory conditions. However, little is known about (1) how changes in stimulus contingency modify odor representations and (2) how updating odor representations is causally related to behavioral adjustments. The anterior piriform cortex (aPCx) sends dense feedback to the olfactory bulb (OB) and shapes, specifically the activity of mitral cells (MCs), one of the OB output channels. However, the role of aPCx feedback in shaping bulb output according to behavioral needs remains unclear. To investigate the role of aPCx feedback in supporting flexible behaviors, we designed a novel Go/No-Go task with rule reversal guided by olfactory and auditory cues. Within the same session, stimulus-reward contingencies were reversed across blocks of trials. In parallel, we monitored the aPCx-to-OB feedback (GCaMP) using multiphoton microscopy. The aPCx feedback activity triggered by the task cues preceded the behavioral reporting (licking) and mirrored the reversals in stimulus-reward contingency throughout each session. Within seconds of each rule reversal, we observed the re-shaping of individual bouton responses to the same sensory cue in tight correlation with the behavioral output switch. Optogenetic perturbation of the aPCx feedback within the OB (Jaws) disrupted the behavioral performance. Our results indicate that the aPCx-to-OB feedback multiplexes stimulus identity and reward contingency signals and is rapidly re-formatted according to changes in the behavioral output. In ongoing experiments, we analyze the interplay between OB feedforward and aPCx feedback signals supporting behavioral flexibility.

350 **Longitudinal Analysis Of Taste Representational Drift In The Gustatory Cortex**

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Recent studies have revealed that cortical ensemble activity evoked by a given stimulus changes over time. This phenomenon, termed representational drift, has been observed in various sensory systems, including olfaction and vision. It is unknown if drift occurs in gustatory cortex taste ensembles and how this impacts taste and valence coding over time. In this study, we explored the extent of drift in gustatory cortex taste representations using miniscope recordings in freely moving mice exposed to a panel of appetitive and aversive tastes (sucrose, NaCl, citric acid, quinine, and water) once a week for five weeks. We monitored the activity of over 700 cells (present in all recording sessions) from five mice. To quantify drift in taste coding, we compared pooled and averaged taste responses within and across sessions for all tastes using vector correlations, principal component analysis, and within and across-day classification analysis. Similar to other sensory systems, our findings indicate that cortical taste representations drift over time, with across-day correlations of individual tastes decreasing linearly with increasing time intervals. Similarly, classifiers trained on early sessions perform progressively worse at taste identification when tested on data from later sessions. While this drift appears to occur at a consistent rate for each taste, the directionality of the drift is non-random as representations of appetitive tastes further diverge from representations of aversive tastes with time. Together, these findings suggest that drift in taste representations may be influenced by both time and experience. Ongoing work is focused on further delineating the influence of each on representational drift.

352 **Quiescent Horizontal Basal Stem Cells Act As A Niche For Olfactory Neurogenesis In A 3D Organoid Model**

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The olfactory epithelium contains two basal stem cell populations that facilitate the normally life-long ability for neuronal regeneration that is required for maintaining our sense of smell over the long term. Horizontal basal cells (HBCs) are generally quiescent and only become active after major direct injury to the epithelium. Globose basal cells (GBCs) lie apical to HBCs and are responsible for the normal, homeostatic generation of olfactory neurons. Studying the stem cell dynamics of how these two neurogenic stem cell populations replenish olfactory sensory neurons is hampered by a lack of robust culture models. Here, we report the development of a 3-dimensional organoid model that recapitulates the neurogenic cascade while maintaining both HBCs and GBCs in culture. We use this model to demonstrate that while HBCs remain relatively quiescent in culture, they form a critical niche for the rest of the organoid.

354 **Exploring Odor-Evoked Activity In Diagonal Band Cholinergic Neurons In Awake Mice.**

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Cholinergic neurons, located in the horizontal limb of the diagonal band of Broca, project to several areas along the olfactory pathway, including the olfactory bulb and piriform cortex. While several studies have demonstrated the impact of cholinergic modulation on olfactory bulb odor responses, olfactory learning, and odor discrimination, the circumstances that drive cholinergic activity in awake animals are unknown, especially in regard to olfactory processing. For example, little is known about how olfactory system projecting cholinergic neurons respond under baseline conditions, following olfactory and non-olfactory stimuli, or during olfactory-guided exploration. To address this question, we expressed the calcium indicator GCaMP8 in cholinergic neurons of the horizontal limb of the diagonal band of Broca via viral injection in ChAT-cre mice. Using this approach, we explored the characteristics of cholinergic cell activity in awake, head-fixed, and freely behaving mice using head-mounted microendoscope recordings. Overall, we find that these neurons display little activity, while mice are anesthetized and display transient activity when awake. Additionally, we find that these cells are reliably activated by brief odor presentations when animals are head fixed. However, in freely moving mice, we find cholinergic cell activity more complex, with increased activity observed during odor exploration as well as during exploratory bouts in the absence of odors. Current work is focused on correlating cholinergic cell activity with behavioral events in awake mice and further exploring the specificity of these responses in terms of novel versus familiar stimuli.

356 **Incidental And Reinforced Olfactory Learning In The Newborn Rabbit: Differential Involvement Of Endocannabinoid And Noradrenergic Systems**

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Memorizing social/environmental odors is crucial for mammalian newborns, who must learn to interact optimally with the mother and prepare for autonomy. In newborn rabbits, the mammary pheromone (MP) emitted by lactating females elicits a typical orocephalic response allowing rapid localization and oral seizing of the nipples. MP also functions as reinforcer by promoting the same response to an initially neutral odorant A after its reinforcement by direct pairing with MP (A-MP conditioning). A-MP conditioning can also mediate a specific response to another neutral odorant B never explicitly paired with MP but previously paired with A during a preconditioning stage. These A-B preconditioning and A-MP conditioning allow to evaluate the role of different neuromodulatory systems in non-reinforced (incidental) and reinforced olfactory learning, respectively. Interestingly, recent data in adult rodents propose that the brain endocannabinoid system plays a crucial role in incidental learning during preconditioning and data in human/rodent neonates indicate that the noradrenergic system is involved in reinforced neonatal odor conditioning. Here we evaluated the role of the endocannabinoid and noradrenergic systems in these two forms of learning in newborn rabbits. Intraperitoneal injection of rimonabant, a cannabinoid type-1 receptor antagonist, blocked A-B preconditioning but had no effect on A-MP conditioning. Conversely, intraperitoneal injection of propranolol, a beta-adrenergic receptor antagonist, had no effect on A-B preconditioning but abolished A-MP conditioning. This double dissociation allows to extend the specific role of the endocannabinoid system in incidental learning from adults to neonates and to generalize the selective role of noradrenergic system in reinforced learning in newborn mammals.

358 **Neophobia Attenuation Is Linearly Correlated To The Magnitude And Fidelity Of Neuronal Signaling In Gustatory Cortex**

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Neophobia, the innate fear of an unfamiliar food, is an evolutionary necessity in animals. New foods will not be consumed in large quantities until they have been deemed safe through experience. While lesion and inhibition approaches have begun to identify the brain regions involved in food or taste neophobia, there have been few attempts to explore how neophobia and its subsequent attenuation shape neural responses in key areas of the central taste pathway, such as the gustatory cortex (GC). Here, we used microendoscopes to image calcium

responses from GC neurons in freely moving mice (n=8) exposed to a four-day taste neophobia paradigm. We identified and recorded from over 450 individual neurons across all four days. Using a brief access paradigm, mice were presented with randomized trials of water or saccharin each day. On the first day of taste exposure mice showed reduced licking to saccharin trials. Licking increased on subsequent days, demonstrating attenuation of neophobia (AN). Statistical analysis of excitation/inhibition failed to identify significant changes in the number of saccharin-responsive GC neurons over time. The average change in response (Δ F) for the entire population of cells also showed no discernable difference between novel (saccharin) and familiar taste(water). However, the strength of those responses (response magnitude) continued to increase each day when compared to controls. Additionally, Day 1 trial to trial response correlations to saccharin were significantly lower than correlations taken from trials on subsequent days, suggesting that AN is represented by increased response fidelity of the novel stimulus. Taken together, the response data demonstrates a linear correlation between changes in GC activity and an increase in saccharin consumption brought about by AN.

360 **Latent Enhancement Of Aversion Learning Following Benign Taste Experience Requires Basolateral Amygdala Activity**

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Conditioned taste aversion (CTA) trains an animal to dislike a particular taste that has been paired with malaise. Benign experience with a taste stimulus that will later be conditioned has long been known to reduce the strength of CTA learning. Our work has continuously replicated a related phenomenon wherein experience to “benign” taste stimuli conversely strengthens a later learned aversion to novel sucrose (latent enhancement [LE] of CTA) in Long Evans Rats. *Our in-vivo* electrophysiology studies have provided insight into this phenomenon suggesting that taste experience may increase discriminability/salience of the later portion of Gustatory Cortical (GC) responses that code for palatability of a novel taste – a result that could boost the associability of that taste and enhance learning. Given that palatability information has been shown to be relayed by the basolateral amygdala (BLA), we test the role of the BLA in LE of CTA using inhibitory designer receptors exclusively activated by designer drugs (iDREADDs) in 24 female Long Evans rats. iDREADDs were activated so to inhibit the BLA during taste experience sessions prior to CTA training toward novel sucrose. We collected *in-vivo* electrophysiological activity from GC during BLA-inhibited taste experience sessions and BLA-intact CTA learning. We predict that the previously noted enhancement GC response discriminability will be disrupted in the later portion of the taste response that reflects palatability when BLA is inhibited during taste experience. Our preliminary results support this prediction suggesting that the BLA is a vital part of the circuit responsible for integrating benign taste experience into later associative learning.

362 **The Impact Of Innocuous Taste Experience On Long-Term Taste Learning And Memory Persistence**

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The five senses allow for the interpretation of experiences that are crucial for survival. One wrong food choice can lead to detrimental repercussions-including death. Taste experiences pave the way for robust learning. Rats can learn to associate a negative consequence, like malaise with a taste, after only one negative experience. This type of learning is called conditioned taste aversion (CTA), and the strength of association between the taste and the consequence is known to be modulated by experience. For example, familiarity with a taste protects that taste from future negative associations. The fact that benign familiarity can impact learning toward a known taste raises the question of how our everyday inconsequential taste experiences can impact learning. Our lab has shown that animals who have had prior inconsequential experience with an array of tastes learn stronger aversions towards novel tastes. Here, we hypothesize that aversions formed after inconsequential taste experiences are more adeptly stored in long term memory as compared to taste naïve rats. Female Long Evans rats experienced inconsequential tastes (water, salty, and sour) followed by a conditioned taste aversion (CTA) to novel sucrose. Aversion memories were tested 24 hours, 72 hours, 1 week, or 2 weeks later. Thus far, our results show that experienced rats retain aversion memories longer than taste naïve rats. We measured synaptic plasticity through the immediate early gene Npas4 which is specific to long-term potentiaion. We hypothesize that incidental taste experience will also enhance the expression of Npas4 within primary taste cortex; a region known for taste processing. These results are the first to demonstrate the impact of inconsequential taste experience on synaptic plasticity and long-term memory retention.

364 **Parallel Genetically-Distinct Basal Amygdala Pathways Route Affective Information To Ventral Striatum Subregions**

Sarah E Sniffen[1], Sang Eun Ryu[1], Milayna M Kokoska[1], Janardhan Bhattarai[2], Yingqi Wang[2], Ellyse R Thomas[1], Graylin M Skates[1], Natalie L Johnson[1], Andy Chavez[1], Sophia Iaconis[1], Daisy Valle[1], Minghong Ma[2], Daniel W Wesson[1]

[1]Department of Neuroscience and Department of Pharmacology and Therapeutics, Center for Smell and Taste, University of Florida, Gainesville, FL, United States, [2]Department of Neuroscience, University of Pennsylvania, Philadelphia, PA, United States

The basolateral amygdala (BLA) is a critical mediator of emotion and its diverging projections into higher-order and other limbic structures have emerged as key factors for modulating affective states. Previous work established the differential roles of distinct BLA cell populations in affective responses and have demonstrated how these single cell populations can bidirectionally control behaviors through their diverging projection targets. Two of the known genetically-distinct populations of BLA projection neurons express either the *drd1* or *drd2*

genes, encoding for the dopamine D1 or D2 receptors, respectively. Here, using a combination of viral tracing, *ex vivo* brain slice recordings, chemo- and opto-genetics, and behavior, we identified that the D1+ and D2+ BLA neuron populations form a parallel pathway for the bidirectional modulation of affective states depending upon their ventral striatum projection target. These neurons arise from the basal nucleus (BA) of the BLA with D1+ BA neurons monosynaptically exciting predominately D1+ ventral striatum neurons, and D2+ BA neurons non-preferentially exciting a small population of D1 and D2+ ventral striatum neurons. These two distinct pathways differentially influence affective states, and do so depending upon where they synapse – with divergent contributions of D1+ and D2+ BA to NAc vs BA to TuS neurons. Overall, these results contribute to a model whereby parallel, genetically-distinct, BA to ventral striatum circuits inform emotional states in a projection-specific manner and altogether expand our appreciation for how the BLA regulates olfactory emotions.

366 **Using External And Self-Generated Olfactory Cues As Landmarks To Learn A Spatial Goal By *Drosophila Melanogaster***

Yang Chen[1,2], Robert Alfredson[2], Ulrich Stern[2], Dorsa Motevalli[2], Sydney Fogleman[2], Chung-Hui Yang[2]
[1]Dept. Biology, Duke University, Durham, NC, United States, [2]Dept. Neurobiology, Duke University Medical School, Durham, NC, United States

Olfaction is well known to be important for associative learning and navigation. In associative learning, animals learn to approach or avoid a neutral olfactory cue depending on the valence of the reinforcers it was previously associated with whereas in odor beaconing, animals follow an appetitive olfactory cue to find its source. However, the ability of animals to learn olfactory cues as landmarks – cues that signal the location of a goal from a distance – for navigation purposes remains under-explored. Here, using a high-throughput optogenetics-assisted spatial learning paradigm we developed where flies must rely on non-visual cues to locate a rewarded spatial goal, we demonstrate that flies can use olfactory cues as landmarks for spatial learning. Our finding reveals that flies are capable of using external odors positioned away from a rewarded goal to successfully locate the goal. More notably, we found that in addition to social communicational purposes, flies can learn to use self-deposited pheromones near the rewarded goal location to navigate towards it, especially when the environment lacks external odor landmarks. Further, we discovered that whereas the olfactory learning circuit alone is competent to support spatial learning when the goal location can be deduced from prominent external odor landmarks, a circuit sensitive to self-movement is engaged to enhance spatial learning in scenarios where self-generated scents are the sole olfactory landmarks. Together, we show that *Drosophila* can accomplish a spatial learning task by exploiting both external and self-generated olfactory landmarks along with adaptive reliance on egocentric movement-sensing circuit depending on the nature of the olfactory landmarks.

368 **Employing Two-Photon Imaging And Holographic Stimulation To Probe The Cellular Basis Of Odor Engrams In The Hippocampus.**

Kira A. Steinke, Gregory Futia, Connor McCullough, Emily A. Gibson, Diego Restrepo
University of Colorado Anschutz Medical Campus, Aurora, CO, United States

Memory-related diseases, such as Alzheimer's and dementia, are a growing concern in the United States, affecting approximately 6.5 million people in 2023 and ranking as the second most significant neurological burden in the country, with trends suggesting these numbers will increase. A hallmark symptom of Alzheimer's is the lost sense of smell, highlighting important connections between memory and olfaction. Thus, it is increasingly relevant to study the biological processes underlying memory formation and recall in olfactory settings. An emerging model for memory encoding and retrieval is cellular priming and pattern completion for the recall of episodic memories, where memory engrams represent encoded experiences. However, there has been a lack of studies focusing on targeted, holographic replay of olfactory engram cells encoding learned behavioral responses. This research focuses on memory engrams formed in the hippocampus, particularly in dorsal CA1 (dCA1), as critical players in temporal learning and memory, as dCA1 has been shown to track changes in cue-outcome associations over time. We have developed a method for simultaneous calcium imaging and holographic optogenetic stimulation in neurons co-expressing GCaMP and ChRmine in stratum pyramidale neurons of dCA1. Our research focuses on both excitatory neurons and inhibitory interneurons, as they both play crucial, but differential roles in olfactory-based learning and decision making. This research will provide valuable insights into the fundamental processes underlying memory formation and recall, shedding light on the neural mechanisms that may be compromised in memory-related diseases and opening new avenues for potential interventions.

370 **Trpm8 Participates In Conditioned Preferences For Oral And Ingesta Temperatures In Mice**

Kyle T. Zumpano, Christian H. Lemon
University of Oklahoma, Norman, OK, United States

Here we studied if innate preferences for oral temperatures in mice can change when paired with calories and the role of TRPM8 in recognition of conditioned temperatures. Water-restricted C57BL/6J mice (B6, $n = 6$) were trained on a 10-day conditioning procedure with 15°C 8% glucose (CS+) and 30°C water (CS-) in a custom contact thermo-lickometer. On interleaved days, mice were offered the CS+ or CS- thermal fluid over 30, 5-sec trials. B6 mice are innately indifferent to 15° and 30°C water in orosensory tests (our prior data). After training, water-replete mice entered testing with 15° and 30°C water in a brief-access fluid licking test. During testing, mice showed a preference for 15° over 30°C water (e.g., test day 2, sign rank test, $p = 0.03$), changing their innate indifference, that extinguished with further testing (test day 3, $p = 1$). A second squad of mice (B6, $n = 8$; TRPM8 knockout (-/-), $n = 8$) was trained with 30°C as the CS+ (8% glucose) and 15°C as the CS- (water). For testing, a third "catch" stimulus of 33°C water was added to determine if mice generalized a conditioned preference to 30°C (mild oral cooling) to warmer temperatures. Water-replete B6 and TRPM8-/- mice showed greater licking for 30° and 33° than 15°C water on the first two test days (Friedman's ANOVAs; $p < 0.05$).

During test days 3 and 4, B6 mice were indifferent across temperatures ($p > 0.5$), and trended to show extinction and reduced licks to 33°C. In contrast, TRPM8-/- mice continued to lick more to 30° and 33° over 15°C ($p < 0.5$), implying these mice are unable to discern the CS+ and catch temperatures. These data begin to show that innate oral thermal preference in mice can change with ingestive experiences and that TRPM8 is needed to discern fine differences between cool and warmer temperatures.

372 **Charaterization Of Gastrin Releasing Peptide Receptor Neurons In The Gustatory Cortex And Their Role In Modulating Eating Behavior**

Maria Isaac[1,2], Carlo Fontanini[1], Arianna Maffei[1,2]

[1]Department of Neurobiology and Behavior, Stony Brook University, Stony Brook, NY, United States,

[2]Graduate Program in Neuroscience, Stony Brook University, Stony Brook, NY, United States

Eating is a multiphasic process that is directed by physiological and hedonic drivers responsible for the initiation, continuation, and termination of eating. The Gustatory Cortex (GC), the primary cortical taste region, is a key player in mediating eating behavior. However, its role in meal termination remains elusive. Gastrin releasing peptide (GRP) signaling has been extensively linked to the termination of eating [1-2]. Furthermore, recent studies demonstrated the functional relevance of GRP signaling in associative learning; particularly in the context of aversive learning [4]. GRP expression is concentrated in the GC making it a promising signaling mechanism for modulating meal termination in the primary taste cortex. This suggests that GRP might modulate meal termination by shaping palatability in an experience dependent manner. Using Conditioned Taste Aversion (CTA) we demonstrate that GRP terminates eating by modulating shifts in hedonic value ascribed to a tastant. Utilizing a transgenic mouse line labeling GRPR expressing cells, we probe for inhibitory makers and show that the GRPR neurons are comprised of a neurochemically heterogenous population of excitatory and inhibitory neurons. This heterogeneity was further validated using in situ and analysis of membrane properties using patch clamp. Bath application of GRP in slice whole cell recording showed that GRP considerably increases inhibitory drive onto GRPR cells. The findings from our study show that GRP signaling is a powerful recruiter of inhibitory circuits, engaging a diverse population of cells. We further demonstrate that GRP serves to modulate palatability-based termination of eating.

374 **Sequential Activity Of Ca1 Hippocampal Cells Constitutes A Temporal Memory Map For Associative Learning In Mice**

Ming Ma[1], Fabio Simoes de Souza[1,2], Gregory Futia[3], Sean Anderson[4], Jose Riguero[4,5], Daniel Tollin[4,5], Arianna Gentile-Polese[1], Jonathan Platt[6], Kira Steinke[7], Naoki Hiratani[8], Emily Gibson[3,5], Diego Restrepo[1,5]

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Sequential neural dynamics encoded by “time cells” play a crucial role in hippocampal function. However, the role of hippocampal sequential neural dynamics in associative learning is an open question. We used two-photon Ca2+ imaging of dorsal CA1 (dCA1) neurons in the stratum pyramidale (SP) in head-fixed mice performing a go-no-go associative learning task to investigate how odor valence is temporally encoded in this area of the brain. We found that SP cells responded differentially to the rewarded or unrewarded odor. The stimuli were decoded accurately from the activity of the neuronal ensemble, and accuracy increased substantially as the animal learned to differentiate the stimuli. Decoding the odorant valence from individual SP cells responding differentially revealed that decision-making took place at discrete times after stimulus presentation. Prediction of odorant valence did not correlate linearly with lick behavior and prediction of odorant valence for error trials was associated with prediction in correct trials. In contrast, lick prediction decoded from the ensemble activity of cells in dCA1 correlated linearly with lick behavior. Our data indicates that sequential activity of SP cells in dCA1 constitutes a temporal memory map used for decision-making in go-no go odorant discrimination associative learning.

9:00 - 10:00 AM	Estero Foyer
Coffee Break	

10:00 - 12:00 PM	Calusa EFGH
Olfaction and Taste: Biomarkers for Health	

Chair(s): Valentina Parma

10:00 **Olfaction And Taste: Biomarkers For Health**

Valentina Parma[1], Katie Boateng[2], Nancy Rawson[1]

[1]Monell Chemical Senses Center, Philadelphia, PA, United States, [2]Smell and Taste Association of North America, Philadelphia, PA, United States

Based on a recent survey of more than 6,000 patients and caregivers led by the Smell and Taste Association of North America, the Monell Center, and Thomas Jefferson University, most respondents reported significant difficulties in having their disorder recognized, receiving a diagnosis, or receiving adequate support. This is particularly true for groups that are already disenfranchised by healthcare. Chemosensory loss is associated with marked reduction in quality of life, poor mental, nutritional and brain health, and with increased 5- and 10-year mortality in older adults. The availability of routine administration of direct smell screening as part of normal health care would significantly improve health care experiences, health outcomes, and quality of life for current and prospective patients, as well as reduce the economic burden of chemosensory dysfunction and its consequences. In this symposium, we will explore how chemosensory testing can be utilized in various aspects of health and functioning to identify specific patient subpopulations, provide early diagnosis, and monitor treatment outcomes.

10:02 **Taste And Smell Dysfunction In Wolfram Syndrome, A Genetic Model For Diabetes And Neurodegenerative Diseases**

M. Yanina Pepino[1,2], Raul Alfaro[1], Tamara Hershey[3,4], Jessica Nicanor-Carreón[2]

[1]Department of Food Science and Human Nutrition, University of Illinois at Urbana-Champaign, Urbana, IL, United States, [2]Division of Nutritional Sciences, University of Illinois at Urbana-Champaign, Urbana, IL, United States, [3]Department of Psychiatry, School of Medicine, Washington University, St Louis, MO, United States, [4]Department of Radiology, School of Medicine, Washington University, St Louis, MO, United States

Wolfram syndrome (WFS) is a rare autosomal recessive disorder characterized by insulin-dependent diabetes, vision loss, hearing loss, and neurodegeneration leading to higher risk for midlife fatality. The most common form of the disease stems from mutations in the *WFS1* gene, leading to increased endoplasmic reticulum stress-induced cell death, particularly impacting the brainstem at an early age. This presentation will focus on the discussion of data from several recent studies from our research group investigating the impact of WFS on smell and taste perception as well as on the intricate interplay between these chemosensory systems, specifically through odor-induced taste enhancement and taste-induced odor enhancement. To evaluate olfactory and gustatory capabilities, we conducted tests such as n-butanol detection thresholds, the University of Pennsylvania Smell Identification Test, and the NIH toolbox for gustation. Stimuli used for gustation included taste stimuli alone or mixed with odorants, with intensity perception assessed with vs. without nose clips. We found that, aside from reduced sensitivity in the anterior tongue, the sense of taste remained largely unaffected in WFS. Conversely, WFS exhibited profound qualitative olfactory dysfunction unrelated to olfactory insensitivity or diabetes. Intriguingly, despite impaired smell identification and hyposmia, the phenomena of odor-induced taste enhancement and taste-induced odor enhancement were preserved in WFS. These findings underscore the necessity of comprehensive sensory assessments in clinical settings. They also demonstrate the remarkable resilience of the human sensory system and suggest that incorporating odors into meals or beverages could potentially enhance flavor enjoyment for individuals coping with olfactory dysfunction.

10:27 **Smell And Taste Changes In Children With Cancer: No &Ldquo;One-Size-Fits-All&Rdquo; Solution**

Mirjam van den Brink[1,2], Wim J.E. Tissing[1,3], Marta Fiocco[1,4,5], Remco C Havermans[2]

[1]Princess Máxima Center for Pediatric Oncology, Utrecht, Netherlands, [2]Laboratory of Behavioural Gastronomy, Centre for Healthy Eating and Food Innovation, Maastricht University Campus Venlo, Venlo, Netherlands, [3]Department of Pediatric Oncology and Hematology, University of Groningen, Beatrix Children's Hospital, University Medical Center Groningen, Groningen, Netherlands, [4]Mathematical Institute, Leiden University, Leiden, Netherlands, [5]5Medical Statistics, Department of Biomedical Data Science, Leiden University Medical Center, Leiden, Netherlands

Childhood cancer survival rates have markedly improved in recent decades. Increased survival can be attributed to providing new therapies and more intensive treatment regimens. However, as a result, almost all children suffer from severe treatment-related side effects such as pain, nausea, and changes in appetite. Although frequently overlooked in clinical practice, taste changes occur in up to 60% of children with cancer and have been reported to be the third most common bothersome symptom. All these symptoms together can contribute to

impaired nutritional status, which have been associated with more infections, worse survival, and poor quality of life. As previous studies relied on self-report, small samples, and did not include smell function, it remained unclear how, when, and among which types of childhood cancer chemosensory changes are experienced during treatment. Therefore, we conducted several studies in children with any type of childhood cancer including psychophysically measured smell and taste function (Sniffin' Sticks and Taste Strips) and self-report (questionnaires and semi-structured interviews). We found that changes in smell and taste are very common but rather heterogeneous in its presentation. That is, smell and taste sensitivity can be either decreased or increased or perceived as completely different than before. In general, we conclude that smell sensitivity seems higher during treatment, specifically in children with acute lymphoblastic leukemia. In contrast, taste sensitivity seems lower during active treatment with chemotherapy. Moreover, most cases of taste loss were found among children with lymphomas and solid tumors specifically. During this talk, we will further share how children with cancer cope with these different types of chemosensory distortions.

10:45 **Taste And Smell Dysfunction In Individuals At Risk For Alcohol Use Disorder: A Study Of The 2013-2014 Us National Health And Nutrition Examination Survey (Nhanes)**

Khushbu Agarwal[1,2], Tanique Schaffe-Odeleye[1,2], Marinza Marzouk[1,2], Paule V Joseph[1,2]

[1]Section of Sensory Science and Metabolism, National Institute on Alcohol and Alcoholism, Bethesda, MD, United States, [2]National Institute of Nursing Research, BETHESDA, MD, United States

Alcohol intake affects taste and smell function, but a comprehensive study on its relationship with chemosensory function is missing. Using NHANES 2013-2014 dataset, we aim to investigate this link by analyzing clinical, demographic, taste/smell measures, and alcohol-related data. Participants were categorized as no-intake (n=888); light intake (up to 3 drinks per occasion; n=2061); risky-intake (heavy, n=1340; binge drinkers, n=3). We hypothesized increased odor identification and reduced bitter and salt taste perception in risky- vs. light or no intake behaviors. Chi-square analysis revealed an overall lower percentage of participants with risky intake who self-reported an improved ability to taste bitterness in the past 12 months (χ^2=11.08; df=4; p=0.02). Further on adjusted general linear models (age, gender, smoking status), risky and light intake individuals rated 1mM Quinine in the whole-mouth test as less intense compared to with no-intake behavior (*Risky vs. no-intake:*b=-5.6, df=872, p=0.01; *Light vs. no-intake:*b=-4.0, df=872, p=0.02). Risky-intake was associated with elevated identification ability for hazardous and appetitive odors; smoke (*vs. no-intake:* b=0.91, df=935, p=0.01), grape scents (*vs. no-intake*: b=0.57, df=935, p=0.01; *vs. light-intake:*b=0.42, df=935, p=0.01). Light vs. no-intake behavior related to better identification of leather scent (b=0.64, df=935, p=0.001). The overall olfactory identification score was significantly higher in risky- and light-intake groups (*Risky vs. no-intake*: b=0.26, df=935, p=s0.01; *Light vs. no-intake*: b=0.18, df=935, p=0.04). These findings, consistent with prior studies, emphasize the importance of chemosensory markers in understanding and managing alcohol-related behaviors.

11:10 **Chemosensory Dysfunction In Anxiety: Usable Clinical Information?**

Wen Li
University of Texas Health Science Center-Houston, Houston, TX, United States

Anomalies in chemosensory perception are identified in multiple major neurological and psychiatric disorders, strongly implicating the chemosensory system in neuropathophysiological processes. While abnormal chemosensory perception in anxiety has been recognized for a long time, its direct linkage to the neuropathophysiology of anxiety is still poorly understood, obscuring its clinical implications and applications. In this talk, I will present human functional magnetic resonance imaging (fMRI) and electroencephalogram (EEG) data from our lab, mechanistically associating aberrant olfactory processing with trait anxiety, state anxiety, and clinical anxiety. Dysfunctions in two fundamental sensory processes—sensory cortical inhibition and multimodal sensory integration—will be featured as putative olfactory mechanisms underlying the neuropathophysiology of anxiety. The talk will conclude with a discussion of the clinical implications and therapeutic interventions related to these olfactory dysfunctions.

11:35 **Smell In Aging: When To Start Testing For Neurodegeneration?**

Claire Murphy[1,2], Paul Wheeler[1]

[1]San Diego State University, San Diego, CA, United States, [2]University of California, San Diego, La Jolla, CA, United States

Olfactory impairment is significantly impaired in Alzheimer's disease (AD), in those with significant risk for AD due to mild cognitive impairment (MCI) or the Apolipoprotein ε4 allele (ApoE ε4), and thus is a promising biomarker for AD. Because AD pathological processes begin years before clinical symptoms can be diagnosed, biomarkers are critical for identifying candidates for early pharmaceutical interventions or clinical trials. The ApoE ε4 allele is the most robust genetic risk factor for AD, thus carriers of the ε4 allele are a special population for studying preclinical biomarkers for AD. We examined olfactory function using the San Diego Odor Identification Test and measures of odor threshold and remote odor memory (familiarity) in cognitively normal individuals who did or did not convert to AD and MCI patients who did or did not convert to AD, recruited from the UCSD Alzheimer's Disease Research Center (ADRC). We had previously assessed olfactory impairment in a large population study using the San Diego Odor Identification Test. In the ADRC population, different tests predicted transitions from cognitively normal to AD and from MCI to AD in those who were at genetic risk for AD. Combining different olfactory tasks that reflect pathology in different areas increases sensitivity and specificity. In the population study, impaired odor identification increased with age and predicted cognitive decline at 5 yrs. and at 10 yrs. Combining biomarkers may best describe AD development in preclinical populations; therefore, tests of olfactory dysfunction may be particularly useful when combined with other

markers. The question of how and when to test olfactory function as a biomarker for AD will be discussed within the context of the underlying pathology, cognitive screening and drug development.

10:00 - 12:00 PM	Calusa ABC
The Brainstem: Transforming chemosensation to behavior	

Chair(s): Hojoon Lee

10:00 **The Brainstem: Transforming Chemosensation To Behavior**
Hojoon Lee
Northwestern University, Evanston, IL, United States

The mammalian brainstem serves as a crucial center where sensory signals combine with other external (exteroceptive) and internal (interoceptive) input, such as those related to hunger, thirst, and well-being. The integrated information is subsequently relayed to various regions of the brain to exert appropriate behavioral responses. Over a century ago, Ramón y Cajal meticulously mapped the intricate connections within the medulla, yet our understanding of the brainstem remained largely limited to a macroscopic "nucleus" level. This limitation was primarily due to the formidable challenges posed by traditional experimental approaches, given the brainstem's deep location within the mouse skull, positioned beneath the cerebellum, and the risk of disrupting numerous delicate but essential bodily functions. Recent technological advancements have enabled us to directly monitor and manipulate neuronal activity within deep brain regions. In this symposium, we propose to assemble a panel of experts who employ cutting-edge techniques to unravel the mysteries of brainstem function.

10:02 **Central Circuit For Taste-Dependent Salivation**
Gyujin Park, Jiahao Ye, Hojoon Lee
Department of Neurobiology, Northwestern university, Evanston, IL, United States

Taste input is a strong trigger for salivation. When we feast on a meal with tangy tomato sauce, flavorful drinks, and sweet desserts, the food stimulates our eyes, nose, and mouth, leading to salivation. This physiological response involves the activation of salivary glands situated in the cervical and mandibular regions, which produce saliva to facilitate the digestive process. The parotid glands are activated by preganglionic fibers of the glossopharyngeal nerve from the inferior salivatory nucleus. For the submandibular and sublingual glands, parasympathetic innervation starts in the superior salivatory nucleus. However, there is limited evidence showing how the sensory aspects of taste integrate with the salivary circuit. The detection of tastants initiates a complex neural cascade, contributing to our taste experience. This process begins with ganglion neurons transmitting signals from the tongue, entering the brain through connections with the rostral nucleus of the solitary tract (rNST) in the brainstem; the information ultimately reaching the taste cortex. Here, we delineate how the neural circuit for taste sensation converges onto the preganglionic salivary neurons to regulate salivation.

10:27 **Parabrachial Cgrp Neurons Affect Taste-Guided Behaviors**
Neville Ngum, Jinrong H Li, Kyle T Zumpano, Catori J Roberts, Traci L Redwine, Damilola V Adesina, Christian H. Lemon
University of Oklahoma, Norman, OK, United States

The parabrachial (PB) nucleus mediates taste processing and integration with other senses. Diverse PB areas, including the lateral and medial PB, express neurons positive for calcitonin gene-related peptide (CGRP), albeit only limited data have described their influence on taste. Here, the role of PB-CGRP neurons in taste-guided behaviors was studied with chemogenetics in mice (n = 56). Using bilateral microinjections under anesthesia, a Cre-dependent virus encoding either an inhibitory designer receptor exclusively activated by designer drugs (hM4Di) or a control element (mCherry) was delivered to the PB of heterozygous *Calca*-Cre mice. *Calca* marks CGRP-positive PB cells. Following recovery, hM4Di and mCherry mice entered brief-access tests where they all received the hM4Di ligand clozapine-N-oxide (5 mg/kg, i.p.) prior to daily tests. Mice were proffered multiple 10 sec licking access trials with quinine solutions (0 [water], 0.1, 0.3, and 1 mM) during test sessions over 4 days. Some mice participated in other brief-access tests with sucrose (0, 0.1, 0.3, 0.5, and 1 M). Data were collected blind to mouse condition. Preliminary analyses found a reduced avoidance of quinine in thirst-motivated hM4Di mice with silenced PB-CGRP cells (reduction (i.e., flattening) of the slope of the quinine licking avoidance function compared to control; mixed model analysis of log-transformed licks to accommodate data skew, $t(46) = 2.7$, $p = 0.011$). Furthermore, some trend was noted for a reduced preference for sucrose in male hM4Di mice (reduced slope of the sucrose preference function compared to male controls, $t(74) = -2.0$, $p = 0.047$), suggesting PB-CGRP cells affect diverse tastes. This study is still ongoing, with an emphasis on identifying covariates (e.g., sex) that may also account for observed effects.

10:45 **Functional Architecture In The Interoceptive Brainstem**
Chen Ran[1,2], Jack C. Boettcher[2], Judith A. Kaye[2], Catherine E. Gallori[1,2], Yandan Wang[2], Stephen D. Liberles[2]
[1]Department of Neuroscience, Dorris Neuroscience Center, The Scripps Research Institute, La Jolla, CA, United States, [2]Department of Cell Biology and Howard Hughes Medical Institute, Harvard Medical School, Boston, MA, United States

Our external senses of sight, smell, sound, touch, and taste enable us to perceive the external world. In addition, our interoceptive system monitors the physiological state of peripheral organs. This bodily sensory system orchestrates multi-organ physiological responses, regulating feeding, drinking, sickness behaviors, and generating the internal senses such as satiety, hunger, nausea, malaise, and visceral pain. However, despite the scientific and clinical importance, the principles that define visceral sensory processing remain poorly defined. Previously, we developed an in vivo two-photon mouse brainstem calcium imaging preparation to understand

internal organ representations in the nucleus of the solitary tract (NTS), the interoceptive gateway in the brain. Combining the imaging platform with stimulation of multiple visceral organs, we uncover diverse neuronal responses to internal stimuli, while functionally defined cell types are highly organized within the NTS. Using state-of-the-art spatially patterned in vivo brainstem optogenetics, we precisely stimulate different neuronal ensembles and show that spatial domains of the NTS differentially modulate autonomic functions. Using mouse genetics and functional manipulations of specific brainstem circuits, we reveal viscerosensory information streams that have distinct functions. Our study defines the functional architecture of brainstem viscerosensory pathways, laying the foundation for future research to understand interoceptive processing throughout the brain.

11:10 **Area Postrema Neurons Mediate Interleukin-6 Function In Cancer-Associated Cachexia**

Bo Li[1,2]

[1]Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, United States, [2]Westlake University, Hangzhou, China

11:35 **A Role For The Locus Coeruleus In The Modulation Of Feeding And Taste**

Will Fan[1], Natale Sciolino[1-4]

[1]Department of Physiology and Neurobiology, [2]Department of Biomedical Engineering, [3]Department of Psychological Sciences, [4]4Institute for the Brain and Cognitive Sciences, University of Connecticut, Storrs, CT, 06269, USA

Taste plays a fundamental role in our consummatory decisions. The primary gustatory cortex (GC) constructs holistic food perceptions by integrating taste with multisensory information, bodily states, and experience. The GC receives a prominent neuromodulatory input from norepinephrine-containing neurons in the locus coeruleus (LC), yet the impact of this input on taste processing remains unexplored. Using pathway-specific optogenetics, we found that stimulation of the LC-GC pathway significantly heightens the preference for a novel, palatable tastant (saccharine) and facilitates appetitive taste learning. To determine the impact of LC input on GC encoding, we used a miniature microscope system to activate LC axons while monitoring either the spontaneous or taste-evoked calcium activity in individual GC neurons. Our results demonstrate that activation of the LC-GC pathway exerts divergent effects on the spontaneous activity of GC taste responsive neurons. Given that LC neurons are transiently activated during anticipation of gustatory rewards, we next sought to determine if brief activation of the LC-GC pathway would influence GC taste-evoked responses. We found that brief activation of LC axons during sucrose approach predominantly enhanced GC excitatory response to sucrose consumption. Further, we found that activating LC projection broadens the tuning of GC neurons to four basic tastes (sweet, salty, sour, bitter), highlighting LC's capacity to restructure cortical taste representation. In conclusion, our findings uncover a novel role for LC neurons in modulating cortical taste encoding, as well as taste perception and learning.

Funding Sources: National Institutes of Health, NIDDK Grant R00DK119586 (NRS); Brain Research Foundation Seed Grant BRFSG-2023-09 (NRS).

12:00 - 1:00 PM	Lunch On Own
Lunch on Own	

1:00 - 3:00 PM	Calusa EFGH
Nutrient Sensing, Learning and Reward	

Chair(s): Kathryn Deibler and Linda Flammer

1:00 **Introduction**
Kathryn Deibler

Foods that are energy-dense, delectable, and delicious are ubiquitous and have long been thought to be a leading factor for the obesity epidemic. For decades, the prevailing theory has been that the sensorial pleasure derived from the eating experience was key in driving our food choices. However, new evidence is challenging this viewpoint. Nutrient-sensing receptors have been discovered in the mouth, intestine, vagus nerve, and hepatic portal vein and belong to a separate neural pathway from the sensory pathway. Additionally, these two discrete neural pathways each engage a different part of the brain's reward system. Further, the nutrient-sensing pathway activates areas of the brain involved in metabolism and learning suggesting that this neural pathway plays a more primary role in guiding feeding behavior and the development of food preferences.

1:02 **Re-Thinking Food Reward: Is "Deliciousness" A Cause Of The Obesity Epidemic Or A Solution To It?**
Mark Schatzker
Modern Diet and Physiology Research Center, McGill University

It is widely believed that the obesity epidemic is driven in large part by an overabundance of energy-dense, hyperpalatable foods that overwhelm appetitive brain systems that evolved in a calorie-scare environment. But what do words such as "hyperpalatable," "delicious" or "reward" mean? Dopamine, once thought to be the "pleasure neurotransmitter," is now understood to mediate motivation or "wanting," while a separate group of neurotransmitters mediate "liking." In this survey of empirical research and food technology, I will argue that the primitive and powerful dopaminergic system has dominated not only the development of "rewarding" processed foods but our scientific understanding of those foods. Meanwhile, the example of Italy—a food culture that prizes food quality and the experience of eating and yet has surprisingly low rates of obesity— shows that a better understanding of "liking" may offer insights into understanding and solving our epidemic of overconsumption.

1:27 **Evidence That Human Oral Glucose Detection Involves A Sweet Taste Pathway And A Glucose Transporter Pathway**
Paul Breslin
Monell Chemical Senses Center

The taste stimulus glucose comprises approximately half of the commercial sugar sweeteners used today, whether in the form of the di-saccharide sucrose (glucose-fructose) or half of high-fructose corn syrup (HFCS). Therefore, oral glucose has been presumed to contribute to the sweet taste of foods when combined with fructose. In light of recent rodent data on the role of oral metabolic glucose signaling, we examined psychopharmacologically whether oral glucose detection may also involve an additional pathway in humans to the traditional sweet taste transduction via the class 1 taste receptors T1R2/T1R3. In a series of experiments, we first compared oral glucose detection thresholds to sucralose thresholds without and with addition of the T1R receptor inhibitor Na-lactisole. Next, we compared oral detection thresholds of glucose to sucralose and to the non-metabolizable glucose analog, αmethyl-D-glucopyranoside (MDG) without and with the addition of the glucose co-transport component sodium (NaCl). Finally, we compared oral detection thresholds for glucose, MDG, fructose, and sucralose without and with the sodium-glucose co-transporter (SGLT) inhibitor phlorizin. In each experiment, psychopharmacological data were consistent with glucose engaging an additional signaling pathway to the sweet taste receptor T1R2/T1R3 pathway. Na-lactisole addition impaired detection of the non-caloric sweetener sucralose much more than it did glucose, consistent with glucose using an additional signaling pathway. The addition of NaCl had a beneficial impact on the detection of glucose and its analog MDG and impaired sucralose detection, consistent with glucose utilizing a sodium-glucose co-transporter. The addition of the SGLT inhibitor phlorizin impaired detection of glucose and MDG more than it did sucralose, and had no effect on fructose, further evidence consistent with glucose utilizing a sodium-glucose co-transporter. Together, these results support the idea that oral detection of glucose engages two signaling pathways: one that is comprised of the T1R2/T1R3 sweet taste receptor and the other that utilizes an SGLT glucose transporter.

1:45 **Brain Networks Underlying Hunger And Reinforcement**
Sam Bacharach
Monell Chemical Senses Center

The act of eating is driven by distinct networks in the brain which signal to an animal both its need for calories and nutrients to maintain homeostasis, and its desire for food that provides sensory pleasure. The goal of the present research is to understand the neural mechanisms by which hunger-sensing networks communicate with reward and reinforcement networks in the brain to guide feeding behavior. Agouti-related peptide (AgRP)-expressing neurons in the Arcuate nucleus of the hypothalamus (Arc) are tuned to the hunger state of the animal

and are a critical node that controls feeding. Previous work from our lab demonstrated that activity in these "hunger neurons" influences signaling in food reinforcement centers. Specifically, when AgRP neurons are active, the dopamine response to food presentation in the nucleus accumbens (NAc) is greater. However, AgRP neurons do not project directly to dopaminergic centers, and little is known about how AgRP circuits regulate the dopamine system to influence the reinforcing value of food. Here, we simultaneously record dopamine signaling in the NAc while optogenetically stimulating seven distinct AgRP pathways. We find that stimulation of certain pathways increases food consumption concurrent with increases in dopamine release in response to the detection of food. Dopamine release to these cues predicted the subsequent amount of food that was consumed. Furthermore, stimulation of these pathways even in the absence of food stimulates dopamine release, which may increase the motivation to eat in the future. Current studies are examining the ability of food cues vs. intragastric signals to influence dopamine release and food consumption. Overall, this research has identified candidate networks in the brain that link hunger-sensing AgRP neurons with reward and reinforcement systems in the brain.

2:10 **Non-Canonical Roles For Endogenous Opioids In Affect, Motivation, And Metabolism**

Daniel C. Castro
Washington University in St. Louis

Since their discovery, opioids have been shown to play a profound role in shaping motivation, affect, and reward. This is perhaps best captured by the current opioid epidemic in the United States, which claims more than 100,000 lives from overdose every year. While decades of research have primarily focused on classical reward circuits in the brain, comparatively little effort has been made to understand how opioids shape behaviors outside of these canonical systems, and indeed, outside of the brain. Using some of the most advanced technologies available, we have discovered that opioids act in unanticipated ways, and even the most basic "mechanisms of action" may in fact differ from prescribed ideas. In this panel, we will discuss how opioids shape ingestive and other motivated behaviors via non-canonical reward circuits in the brain. Specifically, we will examine how opioids act in the dorsal raphe nucleus, a brain area most commonly associated with the mood regulating serotonergic systems, to powerfully modulate behaviors. Additionally, we will explore how opioids act in non-neuronal organs in the periphery, such as the endocrine pancreas. Here, opioids can directly influence metabolic signaling to retune glucose homeostasis and insulin/glucagon secretion. Together, these non-canonical central and peripheral opioid effects have major implications for how we think about food consumption, nutrient sensing, and associated pathologies such as obesity, addiction, and diabetes.

2:35 **The Inherent And Learned Factors For Consumer Selection Of Macronutrient-Rich Foods**

Jing Zhou
Ingredion

There are many factors that contribute to why consumer chose certain foods to eat. It was suggested that there are intrinsic factors that signify the homeostatic regulation of essential nutrients intake. On top of that, social and environmental factors also play a role. Historically, the preferred taste of sweetness and umami had been associated with the metabolic drive to seek for carbohydrate and protein. More recently, fat taste, termed oleogustus, was also discovered. Although sweet is a universally accepted pleasant taste, umami or oleogustus were only perceived as pleasant in certain food contexts. It is debated whether the evidence is sufficient to support the notion that the ability to detect sweet, umami, or fat are the evolutionary cause of seeking for macronutrients when in need. In this presentation, we will review the oral (inherent) and post-ingestive consequences (learned) that may contribute to the drives to select foods abundant in the three macronutrients, carbohydrate, protein, and fat, and explore how food formulators may leverage the mechanisms to design healthier foods and beverages that are also preferred by consumers.

1:00 - 3:00 PM	Calusa ABC
Clinical impact on damage to chemosensory pathways.	

Chair(s): Robert Pellegrino

1:00 **Taste Loss And Flavor Perception**

Linda M. Bartoshuk[1], Derek J. Snyder[1,2]

[1]University of Florida, Gainesville, FL, United States, [2]Amerian Psychological Association, Washington, DC, United States

Flavor and smell are essentially two different sensations that are both conveyed by the olfactory nerve. Flavor sensations (retronasal olfaction) are evoked by volatiles that have reached the olfactory receptors from the mouth by way of the retronasal space. Smell sensations (orthonasal olfaction) are evoked by volatiles that have reached the olfactory receptors from the outside world by way of the nostrils. Retronasal and orthonasal olfaction are not processed in the same brain areas. For the brain to distinguish flavor and smell it needs to know which sense is using the nerve. We suggest that taste is a sense distinct from flavor and smell that plays an important role in telling the brain that incoming olfactory information should be processed as flavor. To demonstrate this, we have sought ways to remove taste sensations leaving olfactory sensations intact. We have used *Gymnema sylvestre* to abolish sweetness and tested foods with predominantly sweet tastes. Maple syrup provides a good example. When the sweetness of maple syrup was nearly abolished with Gymnema sylvestre, the maple flavor was nearly abolished as well; the maple smell was unchanged. In addition, during recovery as the ability to taste sweetness returned, the maple flavor returned. Links between taste and flavor are also demonstrated with clinical data showing that partial taste loss produces partial flavor loss. Most recently, we evaluated a patient with total taste loss (possibly due to covid) who had normal olfactory ability. She was unable to perceive any flavors. We conclude that without taste, the brain cannot determine that incoming olfactory information should be processed as flavor.

1:30 **Taste Loss And Burning Mouth Syndrome**

Derek J. Snyder[1,2], Miriam Grushka[3], Linda M. Bartoshuk[1]

[1]University of Florida, Gainesville, FL, United States, [2]Amerian Psychological Association, Washington, DC, United States, [3]William Osler Health Centre, Toronto, Canada

Clinical damage to the chorda tympani taste nerve (CN VII) produces a number of unexpected effects because chorda tympani input inhibits other sensory input centrally such that damage to the chorda tympani releases that inhibition. We have shown that chorda tympani damage can: 1) intensify sensations from fats, intensify fat palatability, and cause weight gain; 2) intensify taste on the posterior tongue and produce taste phantoms. In addition, 3) topical anesthesia of the mouth can intensify taste phantoms in some patients; we interpret that as evidence that the phantoms are central. The observation that many patients who suffer from burning mouth syndrome (BMS) also experience taste phantoms led us to suspect that BMS patients might have damage to the chorda tympani and that BMS might be a sensory pain phantom in at least some patients. To test this, we did spatial taste testing on 55 BMS patients and found losses to bitter, particularly on the anterior tongue. Topical anesthesia of the whole mouth intensified the burn in most patients (suggesting a central locus for BMS). In addition, density of fungiform papillae (which house taste buds on the anterior tongue) correlated with the most intense burn experienced during BMS $r = 0.8$, $p < 0.0001$. Viral infections appear to be a common source of damage to the chorda tympani. Viruses can move from the nose/mouth to the middle ear through the Eustachian tube. The chorda tympani nerve passes through the middle ear on its way to the brain. Recently, BMS was found to be significantly more common in covid-19 patients. This raises the possibility that the covid-19 virus might damage the chorda tympani in the middle ear. Such taste damage might be responsible for the association between covid-19 and BMS.

2:00 **Trigeminal Function After Damage Of The Olfactory System Or Other Neuronal Structures**

Thomas Hummel

Smell & Taste Clinic, Department of Otorhinolaryngology, TU Dresden, Dresden, --, Germany

2:30 **Scents And Circuits: Can Odorants Modulate The Extended Amygdala And Combat Sudden Unexpected Death In Epilepsy (Sudep)?**

William Nobis

Vanderbilt University Medical Center, Nashville, TN, United States

Odors have been used as therapy for illness for millennia, including as treatment of epilepsy. There remains a lack of investigation into the mechanisms by which olfactory and activation of olfactory pathways could alter epilepsy and seizure severity. Our group was inspired by the relationship between nasal breathing, olfaction and the amygdala and recent work showing that odorants can block stress-induced activation of extended amygdala (ExtA) neurons. Our goal was to determine the effect of odorants on mortality and seizures in an epilepsy model that has known seizure-related respiratory dysfunction and high rate of sudden unexpected death in epilepsy (SUDEP).

We used a Dravet Syndrome (DS) mouse model (scn1a+/-) to accomplish these goals. We hypothesized that odorants that have actions on olfactory to ExtA pathways will decrease SUDEP, potentially through the ability to attenuate neuronal activation in the ExtA. 2-phenylethanol (2PE) is of interest for its ability to block stress-induced activation of ExtA nuclei. The amygdala has been implicated as a site important for forebrain control of

respiration. Thus, exposure to odorants that diminish activation in ExtA regions may be a therapeutic option to prevent SUDEP in this mouse model.
DS mice were exposed for 8 hrs/day to 2PE or vehicle odorant in group housed cages. This was repeated daily for 15 days starting at postnatal day 20/21. Mortality in each group was recorded. Our preliminary results show a strong trend for decreased mortality in the 2PE exposed group (16% mortality 2PE (n=31) vs 39% mortality in vehicle control (n=26), p=0.06).
Our preliminary data support that odorant exposure can decrease mortality in a DS mouse model, suggesting that the circuitry involved may illuminate new targets and therapies for preventing SUDEP

3:00 - 3:30 PM	Calusa Foyer
Coffee Break	

3:30 - 5:00 PM	Calusa EFGH
DEIB Lecture	

3:30 **Building Your Scientific Clan By Nurturing Diversity And Mentorship - Sharing Insights From My Journey**
M. Yanina Pepino
University of Illinois at Urbana-Champaign

5:00 - 6:00 PM	Estero Foyer
Diversity Networking Reception (Invite Only)	

5:00 - 7:00 PM	Dinner On Own
Dinner on Own	

7:00 - 9:00 PM	Calusa EFGH
President's Symposium: Regenerative Medicine and the Senses	

Chair(s): Paul Breslin

7:00 **Regenerative Medicine And The Senses**
Paul Breslin[1,2]
[1]Rutgers University, New Brunswick, NJ, USA, [2]Monell Chemical Senses Center, Philadelphia, PA, USA

Humans have very few regenerative tissues and organs. These are tissues that when removed or severely damaged can regenerate completely with full function and without scarring. For example, various non-human animals are known to regenerate complete limbs and fins, certain brain tissues, severed spinal cords, pieces of heart, the kidney, the pancreas, the retina, and the cochlea. None of these tissues are spontaneously regenerative in humans. Rather, we possess five main regenerative tissues, which are all chemosensory: gustatory epithelium, olfactory epithelium, endothelial lining of the intestine, the liver, and our finger and toe tips. In this symposium we explore human tissue and organ regenerative capabilities by focusing on gustatory and olfactory epithelia and highlight a non-regenerative organ that has been manipulated to regenerate in children, the cochlea. Linda Barlow will discuss how taste tissue regeneration is perturbed by chemotherapy treatment that disrupts taste function in cancer patients. Hong Wang will discuss when the regenerative capacity of taste tissue is gated by inflammatory molecules that allow or prevent regeneration. Jim Schwob will discuss repair and regeneration of the olfactory epithelium and how the regenerative basal stem cells are affected by aging. And Zheng-Yi Chen, who just completed the first successful gene therapy trial for human genetic hearing loss, will discuss work on regeneration of inner ear hair cells as a potential therapy for hearing loss. Although the human cochlea is not spontaneously regenerative, the cochlea of chickens and fish are regenerative, which inspired the treatment of the human cochlea. We hope that the spontaneously regenerative chemosensory tissues in humans will inspire work on non-regenerative human tissues.

7:05 **The Sense Of Taste Is Reliable Until It'S Not: The Myriad Impacts Of Cancer Therapies On Taste Bud Homeostasis**
Linda Barlow
Department of Cell and Developmental Biology and the Rocky Mountain Taste and Smell Center, University of Colorado Anschutz Medical Campus, Aurora CO USA

Taste distortion or dysgeusia is a common side effect of many anti-cancer drugs used to treat a variety of malignancies; 50-90% of cancer patients experience distorted taste during treatment. Crucially, dysgeusia is extremely disruptive, dramatically affecting patient quality of life. Among the main side effects, taste impairment is associated with depression, malnutrition, and morbid weight loss, and can require interruption of treatment. Despite its prevalence, we understand little of the cellular and molecular mechanisms of cancer therapy-induced dysgeusia. Intriguingly, patient experiences suggest different types of therapies result in different taste "pathobiologies", implying that different drugs affect the taste system differently. Cells within taste buds are short-lived and continually and rapidly renewed; this constant cell turnover is thought to make taste particularly prone to disruption by cancer therapies. However, the underlying and likely multiple mechanisms perturbed that result in dysgeusia are not known, partly because mechanisms governing normal taste bud homeostasis are also only partially understood. Here I discuss how targeted cancer therapies that inhibit known and newly identified molecular regulators of taste homeostasis affect distinct cellular mechanisms underlying taste bud cell renewal.

These findings shed light both on how taste is maintained in health, and the diverse ways cancer therapies affect this process.
Supported by DC018489, DC012383 and CA236480 to LAB

7:30 **Inflammatory Cytokines In Taste Loss And Regeneration**
Hong Wang
Monell Chemical Senses Center, Philadelphia, PA, USA

The peripheral taste tissue is robust in its ability to renew throughout the lifespan, and yet persistent taste loss can still occur under some conditions, such as post-viral infection and certain recurring autoimmune diseases. Evidence suggests that excessive and chronic inflammation contributes to taste loss, and the role of inflammation in chemosensory dysfunction has begun to emerge. Our studies have shown that some inflammatory cytokines, such as interferon-γ and tumor necrosis factor, are particularly destructive to the taste tissue by either inducing cell death or inhibiting taste receptor cell regeneration. Persistent induction of these inflammatory cytokines causes loss of taste buds and taste function. However, taste buds can regenerate to a large extent when the levels of the inflammatory cytokines return to baseline. Although inflammation often causes collateral tissue damage, it at the same time promotes tissue regeneration through a number of mechanisms, such as induction of a complex network of growth factors and cytokines that stimulate cell proliferation and differentiation. However, the specific roles of these regulatory factors in taste tissue regeneration are mostly unknown. Our data from an in vitro organoid model showed that certain cytokines associated with immune responses could promote taste receptor cell regeneration or differentiation, suggesting that such cytokines may have therapeutic potential for treating taste loss.

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FCOI DECLARATIONS: none

7:55 **How To Fix A Broken Nose**
James E Schwob
Tufts University School of Medicine, Boston, MA, United States

The well-known, life-long capacity of the peripheral olfactory system to maintain or regenerate the population of olfactory sensory neurons has its limits. In humans, smell function deteriorates with age and as a consequence of multiple antecedent disease processes, including viral or bacterial infection, toxin exposure, and head trauma. Common to all forms of olfactory dysfunction is a degradation of the composition/structure of the olfactory epithelium (OE) accompanied by abnormalities in connectivity with the olfactory bulb target. Thus, potential strategies for repair of the olfactory periphery and restoration of smell function begin with an understanding of the nature of the pathological and pathophysiological causes of the disordered function. That knowledge informs attempts to halt and then reverse the consequences of the disease processes by regenerating the sensory periphery and its connectivity with the bulb. Of necessity, the attempt to repair begins with the characterization of the two populations of neurocompetent stem cells of the OE – Globose Basal Cells (GBCs) and Horizontal Basal Cells (HBCs) – and the processes regulating their self-renewal and progenitor function. Efforts are underway, with an eye to 1) maintaining adequate GBC stem cell capacity and 2) activating unhelpfully dormant HBCs by artificial means; both approaches aim to restore the full population of GBCs and their neuronal descendants when both have been depleted as a consequence of disease. Progress toward that end gives us reason to hope that one or more candidate approaches will bear fruit in the not-too-distant future.

8:20 **Reprogramming By Drug-Like Molecules In Hair Cell Regeneration In The Mature Inner Ear**
Zheng-Yi Chen
Department of Otolaryngology-Head and Neck Surgery, Harvard Medical School and Mass Eye & Ear, Boston MA, USA

Hearing loss is one of the most common sensory deficits affecting 1.5 billion people without an FDA-approved drug. One major cause of permanent hearing loss is the irreversible damage to and the loss of hair cells, the inner ear sensory cells that detect sound and sense balance. In human newborns, the inner ear is fully mature. Any strategies to regenerate hair cells as a potential therapy for hearing loss have to overcome obstacles due to the lack of regeneration capacity in the fully mature mammalian inner ear. We have previously demonstrated that co-activation of c-Myc and Notch1 reprograms supporting cells and promotes hair cell regeneration in the mature inner ear. To develop a strategy of hair cell regeneration relevant to the clinic, we performed single-cell RNAseq of adult mouse cochlea under MYC/NOTCH activation. We showed that MYC/NICD “rejuvenates” the adult mouse cochlea by activating multiple pathways, including Wnt and cAMP, whose blockade suppresses hair cell regeneration potential despite Myc/Notch activation. We screened and identified a cocktail consisting of drug-like molecules of small molecules and siRNAs, which activate the pathways of Myc, Notch, Wnt, and cAMP. We showed that the cocktail effectively replaces Myc and Notch1 transgenes and reprograms fully mature mouse supporting cells for hair cell-like cells regeneration in vitro. We further demonstrated that the cocktail is capable of reprogramming adult cochlea for hair cell regeneration in wildtype mice with hair cell loss in vivo. We identify a strategy using a clinically relevant approach to reprogramming a mature inner ear for hair cell regeneration, laying the foundation for hearing restoration by hair cell regeneration.

9:00 - 12:00 AM	Mangroves & Belvedere
AChemS Closing Dance Party	