# 46th Annual Meeting of the Association for Chemoreception Sciences (AChemS)

**Monell AChemS abstracts**

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Link to Conference Program: https://achems.org/2024/printable-program-abstracts.php

## Thursday, April 18

Poster Session I - 8:00am - 10:00am

Poster #104, Poster Session I - 8:00am - 10:00am

**Application Of Expansion Microscopy To Study Taste**

Kang-Hoon Kim, Emma Larsson, Minliang Zhou, Hong Wang
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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 types 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*.

Poster #110, Poster Session I - 8:00am - 10:00am

**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]
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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.

Poster #120, Poster Session I - 8:00am - 10:00am

**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]
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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.

Poster #138, Poster Session I - 8:00am - 10:00am

**Comparing Odor Perception Across Humans And Mice**

Elizabeth Hamel[1], Robert Pellegrino[1], Mebelyn Urena[1], Sebastian Ceballo[2], Saeed Karimimehr[2], Khristina Samoilova[3], Matt Andres[1], Jenny Margolis[1], Alexei Koulakov[3], Dima Rinberg[2], Joel Mainland[1]

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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 allow us to more densely sample perceptual spaces and determine which dimensions can be predicted across species.

10:00 am - 12:00 pm: Symposium

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

Organizers: 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.

10:45am, Chemosensory Perception And Eating Behavior

**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 = $5.4 \times 10^{-41}$ in the UK Biobank and $2.9 \times 10^{-4}$ 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 am, Chemosensory Perception And Eating Behavior

**Gut Influences On Central Feeding Circuits**

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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.

1:00 pm - 3:00pm, Oral session: Action olfaction across species

2:10 pm, Action olfaction across species session

**Bilateral Sensory Signals For Odor Source Localization In Freely-Moving Mice**

Kevin Bolding[1], Jiayue Tai[2], Dan Leman[3], Ian Davison[4]
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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.

Poster Session II, 9:00 pm - 11:00 pm

Poster #121, Poster Session II, 9:00 pm - 11:00 pm

**Rational Design Of Antagonists for Cigarette Smoke Odors**

Timothy S. McClintock[1], Evan Meredith[1], Abby Frazier[1], Samantha L. Schnabel[1], Matthew Andres[2], Marissa L. Kamarck[2,3], Paul M. Wise[2,4], Pamela H. Dalton[2], Joel D. Mainland[2,3]
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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.

Poster #125, Poster Session II, 9:00 pm - 11:00 pm

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

Jonas Yde Junge[1,2], Chaja Levy[3], Connor Lashus[3], Gregory Bratman[3], Valentina Parma[1]
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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 ($\rho = 0.29$, $p < 0.001$) and well-being ($\rho = 0.17$, $p < 0.001$). Participants with greater olfactory and visual awareness report greater well-being (olfactory: $\rho = 0.08$, $p < 0.05$, visual: $\rho = 0.12$, $p < 0.01$) and reduced perceived stress (olfactory: $\rho = 0.17$, $p < 0.001$, visual: $\rho = 0.19$, $p < 0.001$; auditory: $\rho = 0.20$, $p < 0.001$). Individuals exposed to parks and the wilderness, rather than neighborhood trees, show greater olfactory awareness and stress reduction (parks: $\rho = -0.28$, $p < 0.001$, wilderness: $\rho = -0.2$; $p < 0.05$; neighborhood trees: $\rho = -0.1$, ns). These preliminary data suggest that wellbeing benefits from nature contact which may be promoted by olfactory awareness.

Poster #135, Poster Session II, 9:00 pm - 11:00 pm

**Dream Olfactory Mixtures Prediction Challenge**

Joe Mainland[1], Andreas Keller[2], Leslie Vosshall[2,3,4], Jake Albrecht[5], Pablo Meyer[6]
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Kavli Neural Systems Institute, NY, NY, United States, [5]Sage Bionetoworks, Seattle, WA, United States, [6]IBM Research, NY, NY, United States

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 present the details of the datasets and the challenge timeline/scoring approach.

Poster #159, Poster Session II, 9:00 pm - 11:00 pm

**Olfactory Nudging Promotes Short-Term Weight Loss**

Victoria Esparza[1], Angela Pfammatter[2], Valentina Parma[3], Surabhi Bhutani[1]
[1]San Diego State University , San Diego, CA, United States, [2]University of Tennessee, Knoxville, TN, United States, [3]Monell Chemical Senses Center, Philadelphia, PA, United States

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.

Poster #171, Poster Session II, 9:00 pm - 11:00 pm

**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]
[1]Department of Otolaryngology - Head & Neck Surgery, The Ohio State University, Columbus, OH, United States, [2]Monell Chemical Senses Center, Philadelphia, PA, United States

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

Poster Session III, 8:00 am - 10:00 am

Poster #220, Poster Session III, 8:00 am - 10:00 am

**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.

Poster #242, Poster Session III, 8:00 am - 10:00 am

**Modulation of  Pharmaceutical Taste Aversiveness In Drosophila Melanogaster**

Paul Breslin[1,2], Natasha Rivers[2], Carter Green[3]
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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 a relatively simple way to predict the orosensory aversiveness of pharmaceuticals and to test bitterness ameliorating additives that will be proven effective in humans.

Poster #246, Poster Session III, 8:00 am - 10:00 am

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

Caroline Payton Harmon[1], Jennifer M. Manuola[1], Amani Hill[1], Paul A.S. Breslin[1,2]
[1]Rutgers University, New Brunswick, NJ, United States, [2]Monell Chemical Senses Center, Philadelphia, PA, United States

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.

Poster #250, Poster Session III, 8:00 am - 10:00 am

**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.

Poster #256, Poster Session III, 8:00 am - 10:00 am

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

Patrice A Hubert[1], Ha Nguyen[1], Amy Huang[1], Paule V Joseph[2], Caliu Lin[1], May Cheung[3], Danielle R Reed[1]

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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.

Poster #264, Poster Session III, 8:00 am - 10:00 am

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

Akihito Kuboki, Jidong Tan, Katelyn Tu, Cailu Lin, Peihua Jiang, Johannes Reisert, Hong Wang
Monell Chemical Senses Center, Philadelphia, PA, United States

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.

4:30 pm - 6:00 pm

The Great Debate: The role of article 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**)**

7:00 pm - 9:00 pm: Polak Awards Lectures

7:00 pm: Polak Awards Lecture

**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.

Poster Session IV, 9:00 pm - 11:00 pm

Poster #207, Poster Session IV, 9:00 pm - 11:00 pm

**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.

Poster #253, Poster Session IV, 9:00 pm - 11:00 pm

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

Ha Nguyen[1], Cailu Lin[1], Katherine Bell[1], Amy Huang[1], Mackenzie Hannum[1], Vicente Ramirez[1], Carol Christensen[1], Nancy E. Rawson[1], Lauren Colquitt[1], Paul Domanico[2], Ivona Sasimovich[1], Riley Herriman[1], Paule Joseph[3], Oghogho Braimah[4], Danielle R. Reed[1]

[1 Monell] Chemical Senses Center, Philadelphia, PA, United States, [2 Clinton] Health Access Initiative, New York, NY, United States, [3 National] Institute of Alcohol Abuse and Alcoholism & National Institute of Nursing Research, Bethesda , MD, United States, [4 Countess] of Chester Hospital, Chester, United Kingdom

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.

Poster #261, Poster Session IV, 9:00 pm - 11:00 pm

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

Emily C. Hanselman[1], Anilet Tharpe[2], Linda J. Flammer[2], Mehmet H. Ozdener[2], Masafumi Jyotaki[2], Karen K. Yee[2], Robert F. Margolskee[2], Paul A.S. Breslin[1,2]

[1 Rutgers] University, New Brunswick, NJ, United States, [2 Monell] Chemical Senses Center, Philadelphia, PA, United States

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-2 AM 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.

## Saturday, April 20

Poster Session V, 8:00 am - 10:00 am

Poster #318, Poster Session V, 8:00 am - 10:00 am

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

Vicente Ramirez, Valentina Parma
Monell Chemical Senses Center, Philadelphia, PA, United States

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.

10:00 am - 12:00 pm: Olfaction And Taste: Biomarkers For Health, Oral Session

10:00 am, 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**.**

1:00 pm - 3:00pm: Nutrient Sensing, Learning, and Reward
Chairs: Kathryn Deibler and Linda Flammer

1:27 pm: Nutrient Sensing, Learning, and Reward

**Evidence That Human Oral Glucose Detection Involves A Sweet Taste Pathway And A Glucose Transporter Pathway**

Linda Flammer
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 psychopharmacological 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 composed of the T1R2/T1R3 sweet taste receptor and the other that utilizes an SGLT glucose transporter.

1:45 pm: Nutrient Sensing, Learning, and Reward

**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.

1:00 pm - 3:00 pm: Clinical impact on damage to chemosensory pathways

Robert Pellegrino, chair

7:00 pm - 9:00 pm, President’s Symposium: Regenerative Medicine and the Senses

7:00 pm, Regenerative Medicine And The Senses

Paul Breslin, Rutgers University, Monell Chemical Senses Center

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.

### 7:30 pm, Inflammatory Cytokines In Taste Loss And Regeneration

Hong Wang, Monell Chemical Senses Center

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.