



# Monell Chemical Senses Center 2021 Virtual Spring Colloquium



**March 24, 2021**

*Gut Health and Gut-Brain Communication:  
A Chemosensory Perspective*

**March 25, 2021**

*Smell, Emotion, Motivated Behavior, and Cognition:  
Sense or Sensationalism?*

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Note as part of our meeting green goals this book is completely virtual and links to other resources typically available at the Spring Colloquium.

We are pleased to announce that our [Publications List](#) and [Monell in the News](#) list are now available on our new website and available for viewing at your leisure.

If you have any questions about these materials email our Director of Communications, Karen Kreeger, at [kkreeger@monell.org](mailto:kkreeger@monell.org)

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# SCHEDULE OF EVENTS

Wednesday, March 24<sup>th</sup>

<b><i>Gut Health and Gut-Brain Communication: A Chemosensory Perspective</i></b>		
Chair: Hong Wang		
<b>8:30 am</b>	Coffee Welcome Session	
<b>9:00 am</b>	Taste Signaling Proteins in Regulation of Gut Inflammation	H. Wang
<b>9:30 am</b>	Immune Cells, Microbiota, and Inflammatory Bowel Diseases	S. Kim*
<b>10:00 am</b>	<b>Coffee Break</b>	
<b>10:30 am</b>	Making Sense of Type 2 Mucosal Immunity	P. Jiang
<b>11:00 am</b>	Gut-Brain Signaling Pathways Underlying Feeding Behavior	A. Alhadeff
<b>11:30 am</b>	Discussion	

Thursday, March 25<sup>th</sup>

<b><i>Smell, Emotion, Motivated Behavior, and Cognition: Sense or Sensationalism?</i></b>		
Chair: Pamela Dalton		
<b>8:30 am</b>	Coffee Welcome Session	
<b>9:00 am</b>	Sleeping and Smelling to Remember (or Forget)	J. Gottfried*
<b>9:30 am</b>	How Do We, and the Brain, Approach Odor Valence?	J. Lundström
<b>10:00 am</b>	<b>Coffee Break</b>	
<b>10:30 am</b>	Odor Effects on Behavior and Physiology: New Insight into Underlying Mechanisms	L. Saraiva
<b>11:00 am</b>	The Nose Knows: Olfactory Influences on Eating Behavior and Food Navigation	S. Boesveldt*
<b>11:30 am</b>	Discussion	

**\*Guest Speakers**

**Sanne Boesveldt, PhD**  
Associate Professor  
Wageningen University

**Sangwon Kim, PhD**  
Assistant Professor  
Jefferson University

**Jay Gottfried, MD, PhD**  
Professor of Neurology  
University of Pennsylvania

# Presentation Abstracts

## Taste Signaling Proteins in Regulation of Gut Inflammation

Hong Wang

Taste-receptor-mediated signaling can shape gut inflammatory status through a number of mechanisms, such as by influencing dietary choice, changing gut microbiome, and/or direct regulation of immune responses. Diet has a strong impact on gut health – high-fat and high-sugar diets contribute to gut inflammation, whereas vegetables contain various biologically active compounds that have anti-inflammatory activities. Studies have shown that genetic polymorphisms in taste receptor genes are associated with preference and consumption of vegetables, fruits, and carbohydrates. Diet also affects gut microbiota composition. Furthermore, recent research indicates that taste signaling proteins are directly involved in regulating immune responses in various tissues. In gut, tuft cells, a rare type of gut epithelial cells, express taste signaling proteins and play important roles in immune responses to parasites. Our recent studies showed that genetic deletion of the taste signaling proteins Gnat3 (also known as  $\alpha$ -gustducin) and TrpM5, both involved in sweet, umami, and bitter taste signaling, led to aggravated gut inflammation in a mouse model of inflammatory bowel disease. Gnat3- or TrpM5-knockout mice exhibited more tissue damage and immune cell infiltration in the colon than did wild-type control mice, supporting that these taste signaling proteins are important regulators of gut inflammation. Further work is needed to explore the potential implications of genetic variations in these receptors on susceptibility to various GI disorders and to evaluate the potential therapeutic benefit of targeting these cells with pharmacological or dietary modulators of the taste pathway.

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# Immune cells, Microbiota, and Inflammatory Bowel Diseases

Sangwon Kim

Inflammatory bowel disease (IBD) is chronic inflammatory disease of the gut, affecting 300 per 100,000 people in the Western world with increasing prevalence in Asia and the Middle East. The major clinically defined forms of IBD are Crohn's disease (CD) and Ulcerative colitis that differ in the affected area. It has been thought that IBD is a form of autoimmune diseases in which the immune system excessively attacks its own tissues, indicating dysregulation of immune responses. While it is believed that IBD has some genetic bases with increased occurrence with family history of IBD, studies on monozygotic twins indicates that genetic causes can explain only a portion of IBD occurrence. Current studies suggested that environmental factors may play a critical role in the IBD development, such as microbiota, diet, and smoking. The brief history of IBD, the role of immune cells, and the influence of microbiota and diet will be presented at the talk.

## References

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- Cleynen I. Vermeire S. (2015) "The genetic architecture of inflammatory bowel disease: past, present and future." *Curr. Opin. Gastroenterol.* 31: 456-463.

# Making Sense of Type 2 Mucosal Immunity

Peihua Jiang

“Type 2 immunity is the arm of the immune system typically associated with both allergy and effective defense against helminth worm infections. Type 2 cells release a range of soluble multifaceted effector cytokines that accelerate intestinal nematode expulsion and wound repair, but also exacerbate disease in allergic patients when dysregulated.” Excerpt from LÖser & Maizels, 2018.

Helminth (worm) infection is prevalent, affecting more than 1 billion people worldwide. It can cause malnutrition and impairment in physical, intellectual and cognitive development in children. Host-resistance and disease-tolerance toward worms are largely dependent on type 2 immunity. Recently, it has been shown that intestinal tuft cells, which express taste transduction elements, initiate type 2 immune responses. Tuft cells release interleukin-25 (IL-25) and other bioactive mediators (e.g., leukotrienes) upon worm detection, which is mediated by tuft cell-expressed receptors (e.g., *Sucnr1*) and taste transduction elements (e.g., *gustducin*, *Trpm5*). Following that, IL-25 will activate IL-13-expressing group 2 innate lymphoid cells (ILC2) to trigger IL-13 secretion. As a prototypical type 2 cytokine, IL-13 will exert its bioactivity on multiple target cells, including intestinal epithelial cells via interacting with its receptor IL-13RA1/IL-4RA. Consequently, profound remodeling occurs in the intestinal epithelium, resulting in tuft and goblet cell hyperplasia and goblet cell enlargement. These cellular changes, along with molecular changes, facilitate worm expulsion. In this presentation, I'll provide our current understanding of worm-induced type 2 mucosal immunity and highlight gaps in our knowledge which warrant further investigation in the future.

## References

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# Gut-Brain Signaling Pathways Underlying Feeding Behavior

Amber Alhadeff

Food intake is tightly regulated by complex and coordinated gut-brain interactions. My lab is interested in understanding how these gut signals, especially different macronutrients, influence neural activity in key feeding centers in the brains of awake, behaving mice. In our recent work, we demonstrated the ability of nutrients in the gut to rapidly modulate neural activity in a small population of hunger-sensitive, hypothalamic neurons expressing agouti-related protein (AgRP). Because individual macronutrients engage specific receptors in the gut to communicate with the brain, we reasoned that macronutrients may use different pathways to reduce activity in AgRP neurons. Indeed, we found site-specific differences in intestinal detection of distinct macronutrients by AgRP neurons. We explored the relative roles of vagal, spinal, and hepatic portal signaling in the regulation of AgRP neuron activity, and demonstrated that different gut-brain pathways can mediate effects of fat vs. sugar on hypothalamic neuron activity: fat signals are transmitted by vagal afferents, and sugar signals are transmitted by spinal afferents. Taken together, our findings demonstrate that macronutrients engage distinct gut-brain pathways that ultimately converge in the hypothalamus to inhibit feeding behavior via reduction of AgRP neuron activity. Ongoing studies seek to understand the neural subtypes mediating gut-brain signaling of different macronutrients. Unraveling the specific neural pathways and signals that account for our metabolic and behavioral responses to fat vs. sugar is an important step toward the development of personalized nutrition and therapeutic interventions to shift food intake toward healthier patterns and reduce obesity and metabolic disease.

## References

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Alhadeff, A.L., Goldstein, N., Park, O., Klima, M.L., Vargas, A., Betley, J.N. (2019) "Natural and drug rewards engage distinct pathways that converge on coordinated hypothalamic and reward circuits." *Neuron*. 103(5), 891-908.

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# Sleeping and Smelling to Remember (or Forget)

Jay Gottfried

Sleep is pervasive throughout most of the animal kingdom -- even jellyfish and honeybees do it. Although the precise function of sleep remains elusive, research increasingly suggests that sleep plays a key role in memory consolidation. Newly formed memories are highly labile and susceptible to interference, and the sleep period offers an optimal window in which memories can be strengthened or modified. Interestingly, a small but growing research area has begun to explore the ability of odors to modulate memories during sleep. The unique anatomical organization of the olfactory system, including its intimate overlap with limbic systems mediating emotion and memory, and the lack of a requisite thalamic intermediary between the nasal periphery and olfactory cortex, suggests that odors may have privileged access to the brain during sleep. Indeed, it has become clear that the long-held assumption that odors have no impact on the sleeping brain is no longer tenable. Here, I summarize recent studies from our lab showing that odor stimuli experienced in the waking state modulate olfactory cortical responses during slow-wave sleep, with selective impact on enhancing declarative memories and weakening fear memories. Data reviewed here spotlight the emergence of a new research area that holds far-reaching implications for future neuroscientific investigations of sleep, learning and memory, and olfactory system function.

## References

- Shanahan, L.K. and Gottfried, J.A. (2014) "Olfactory insights into sleep-dependent learning and memory." *Progress in Brain Research*. 208, 309-343.
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# How Do We, and the Brain, Approach Odor Valence?

Johan Lundström

In 1878 Margaret Wolfe Hungerford wrote that “Beauty is in the eye of the beholder”, suggesting that what one person finds beautiful, others may not. Just as visual beauty, some argue that odor preference (valence) is likewise subjective. Indeed, by simply naming an odor ‘vomit’ or ‘parmesan cheese’, the valence is rated at either extreme in a name-dependent manner. But, at the same time, valence has been suggested to be the primary perceptual axis for odors and valence ratings can be predicted from physicochemical properties; two views that are difficult to reconcile.

I will in this talk argue, and present data supporting, the notion that these two opposing views can coexist and jointly contribute to the final valence odor percept if a temporal dimension is included. In an ongoing project, we have in multiple experiments attempted to answer what is the primary role of the initial neural processing stage of the human olfactory system, the olfactory bulb. I will present data supporting the view that the human olfactory bulb is initially focused on extracting and amplifying information that might indicate a potential threat and that this information is then conveyed to the motor system to facilitate a potential rapid behavioral avoidance response. Pleasant odors do not seem to activate this pathway. Information processing in the olfactory bulb is, however, continuously updated by reciprocal connections from the piriform cortex; an area that we recently demonstrated process information from multiple sensory systems. Human odor valence perception can therefore be argued as a two-stage process, driven and regulated by the inherent need for approach/avoidance decisions. Negative odors are processed rapidly by the olfactory bulb, partly determined by their threat-associations, and automatically acted upon whereas positive odors are mainly processed in areas down-stream from the olfactory bulb and more influenced by multisensory inputs and past experiences. Taken together, our results suggest that the olfactory system initially promotes fast processing of potential avoidance responses, partly driven by the odors’ physicochemical properties and by the individual’s past experiences. Only later, are these responses attuned to the processing of potential approach behavior of positive odors, partly driven by contextual information and learned associations. Jointly, they form our final odor valence percept.

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- Arshamian, A., Laska, M., Gordon, A. R., Norberg, M., Lahger, C., Porada, D. K., Jelvez Serra, N., Johansson, E., Schaefer, M., Amundin, M., Melin, H., Olsson, A., Olsson, M. J., Stensmyr, M., & Lundström, J. N. (2017). “A mammalian blood odor component serves as an approach-avoidance cue across phylum border - from flies to humans”. *Scientific reports*, 7, 13635.

# Odor Effects on Behavior and Physiology: New Insight into Underlying Mechanisms

Luis R. Saraiva

Scents have been employed for millennia to mask repugnant odors and modulate human emotion (e.g., fear) or basic drives (e.g., appetite), but whether they do so is poorly understood. The mechanisms by which odors stimulate pleasant/aversive sensations or modulate physiology are largely a mystery, as are those by which spices and perfumes can mask repugnant odors.

In mice, these sensations are easily reflected in innate attractive/aversive responses or other behavioral and physiological changes to different odor cues. Odor detection in the mouse nose is mediated by ~1000 different odorant receptors and 14 trace amine-associated receptors (TAARs). The importance of smell is reflected in the fact that the genes encoding olfactory receptors (ORs) constitute the largest mammalian gene family. The OR gene repertoire is largely species-specific, suggesting that it is shaped by the nature and necessity of chemosensory information (e.g. food sources) for survival in each species' niche. Moreover, gender, health (e.g. obese vs lean) and internal homeostatic states (e.g. hungry vs fed) can modulate olfactory performance and sensitivity, which can in turn affect odor-guided behaviors.

We employ a multidisciplinary strategy to better understand how evolution shaped the gene expression in the mammalian olfactory system, and how odor exposure can ultimately result in complex changes in behavior or physiology. In this context, we are particularly interested on the modulatory effects of odors in fear, stress and appetite.

Here, I will present novel and important findings here that are very relevant to human perception as they provide the first insight into mechanisms underlying the age-old practice of odor masking and aromatherapy.

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# The Nose Knows: Olfactory Influences on Eating Behavior and Food Navigation

Sanne Boesveldt

The chemical senses, in particular smell and taste, are important determinants of (human) eating behavior, for creating flavor and driving our food preferences, but also as a more functional feature of food. E.g. smell is thought to play a role during the anticipation phase of eating: it detects and attracts us to food, and triggers our (specific) appetite. However, how odors actually affect our eating behavior, and to what extent and under which circumstance they determine appetite, food choices and potentially intake, remains unclear.

Although the human sense of smell is mostly underappreciated, I will discuss recent insights from my behavioral and physiological studies suggesting that humans, like other species, use their olfactory sense in their foraging (eating behavior) strategies; i.e. to navigate for food in different environments, to trigger salivary responses and appetite, and that this may happen outside of our awareness. Such knowledge has great potential to steer people towards healthier eating behavior, and thereby reduce nutrition-related diseases.

## References

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# RESEARCH INTERESTS OF SCIENTIFIC STAFF

The following lists the current research interests of the staff of the Monell Center. Click their name to go to the scientist research page on our website. These pages include information on their education, research summary, and relevant publications.

## **Director & President**

### **[Robert F. Margolskee](#)**

MD; Ph.D., Molecular Biology & Genetics; Johns Hopkins School of Medicine (USA)

Dr. Margolskee's long-standing research focus is on the molecular mechanisms of taste transduction, utilizing molecular biology, biochemistry, structural biology, electrophysiology and transgenesis to study the mechanisms of signal transduction in mammalian taste cells. More recently he has been studying the chemosensory functions of taste signaling proteins in gut and pancreatic endocrine cells. Other projects in the Margolskee lab focus on taste stem cells and endocrine properties of taste cells.

## **Distinguished Member**

### **[Gary K. Beauchamp](#)**

Ph.D., Biopsychology; The University of Chicago (USA)

My research interests include: 1) genetics of taste perception; 2) development of human chemosensory perception and preference; 3) genetics and behavior of individual olfactory identity; 4) odors as diagnostic tools; and 5) adult human flavor perception.

## **Members**

### **[Paul A. S. Breslin](#)**

Ph.D., Experimental Psychology; University of Pennsylvania (USA)

I am interested in human oral perception and its genetic basis. The primary focus of my work is on taste perception with an emphasis on taste discrimination, taste enhancement and suppression, and taste localization. I also study oral irritation/chemesthesis, mouthfeel, and astringency. The interactions among gustation, chemesthesis, and olfaction that comprise flavor are the topic of an ongoing research program that includes fMRI as a tool to understand regional brain involvement. In addition to human research, I conduct parallel genetic studies of the chemical senses in my Fly Lab, which uses *Drosophila melanogaster* as a model.

### **Pamela Dalton**

Ph.D., Experimental Psychology; New York University; M.P.H., Drexel University (USA)

My research attempts to broadly understand how cognitive and emotional processes modify the way we perceive odor and sensory irritation from volatile chemicals. One approach involves examining the associations and disassociations between subjective (self-report) and objective markers of irritation (e.g., ocular inflammation, nasal blood flow, respiratory patterns) resulting from chemical exposure. Another line of investigation examines the relationship between exposure frequency, adaptation and clinical sequelae from exposure to airborne chemicals, both in the laboratory and in occupational and community settings. In a related effort, modeling how odorant transport factors (e.g., physico-chemical characteristics of the odorant, nasal airflow, inflammatory changes) affect these processes can provide additional insight into variation in olfactory perception among the population.

### **Bruce A. Kimball**

Ph.D., Ecology; Colorado State University (USA)

I am a chemical ecologist with the USDA National Wildlife Research Center (NWRC). My research at Monell focuses on wildlife behavior and the chemical signals that identify friend, foe, and food. The goals of my research are increased understanding of wildlife behavior and development of practical tools to minimize wildlife damage to agricultural resources. Current research topics include: 1) phytochemical basis of herbivore foraging behavior; 2) olfactory signals associated with animal disease states; 3) cues associated with novelty or conditioned aversions; 4) mechanisms of herbivore repellents; 5) attractants for wildlife baiting systems.

### **Julie A. Mennella**

Ph.D., Biopsychology; The University of Chicago (USA)

Dr. Mennella's research program focuses on the role of early experiences on food and flavor preferences and growth and the effects of alcohol and tobacco on women's health and infant development. Current research studies focus on the following areas: 1) how maternal diet alters the aromatic profiles of amniotic fluid and mother's milk and how such early flavor experiences affect food preferences during weaning and childhood; 2) elucidation of sensitive periods in flavor learning and developing evidence-based strategies to promote acceptance of fruits and vegetables among children; 3) determine the behavioral and physiologic mechanisms by which diet composition affects energy balance and growth in infants studying the pharmacokinetics and pharmacodynamics of alcohol in women; 4) determine effects of age and genotype on taste sensitivity and preference across the lifespan; 5) determine efficacy of strategies of reducing bitter taste in children and impact taste has on medication compliance and acceptance; and 6) effects of alcohol and tobacco

use during lactation on various aspects of women's health, lactational performance and mother-child interaction. In addition to her research, she founded and then directed a program at Monell Center from 1991-2007 that encouraged under-represented minority high school and undergraduate students to pursue careers in science and medicine. Dr. Mennella has held a number of leadership positions in professional scientific societies and working groups at the National Institutes of Health and other international scientific and health organizations. She is the recipient of several grants from the National Institute of Deafness and Other Communication Disorders and the Eunice Kennedy Shriver National Institute of Child Health and Human Development; the author or co-author of numerous peer-reviewed research papers and an internationally recognized speaker on the ontogeny of flavor preferences and its implications for health and nutritional programming.

### **Danielle R. Reed**

Associate Director, Monell Chemical Senses Center  
Ph.D., Psychology; Yale University (USA)

We do studies to understand the exact relationship between genotype and phenotype in both animal models and in human subjects including twins. Phenotypes of interest include taste perception, food preferences and obesity.

### **Michael G. Tordoff**

Ph.D., Physiological Psychology; University of California, Los Angeles (USA)

My research interests are broadly focused on taste and nutrition. One area involves topics related to mineral appetite, including calcium taste and appetite, the physiology of salt intake, appetite specificity, and how the postingestive consequences of minerals influence taste preferences. Another area involves the genetics of taste perception, including the preferences for alcohol, sweetness, saltiness and calcium. A third area involves characterizing the environmental contribution to individual differences, particularly the influences of early environment, husbandry procedures, and food choice on taste preferences and dietary obesity.

## **Associate Members**

### **Peihua Jiang**

Ph.D., Neurobiology; University of Pittsburgh (USA)

Until recently, it was thought that all mammals can detect the five basic tastes that humans can. Our work and others have showed that there are many exceptions to this general belief. Many mammalian species show specific taste loss due to the pseudogenization of taste receptor genes and loss of taste receptor function appears directly related to a change in diet. Understanding the precise relationship among taste receptor structure, dietary choice and the associated metabolic pathways constitutes one of my two main research interests.

The other line of my research aims to study adult taste stem cells. Taste cells regenerate constantly during an animal's life, yet the identity of adult taste stem cells for replenishing taste epithelium remains elusive. I am interested in identifying reliable markers for adult taste stem cells and characterizing such cells subsequently. Current research projects include: 1) structure-function analysis of the mammalian sweet taste receptor T1R2/T1R3; 2) comparative genetics of sweet taste and carbohydrate metabolism in Carnivora; and 3) identification and characterization of adult taste stem cells. We utilize a broad range of approaches in these studies, including molecular, genetic, cellular, computational and imaging techniques.

### **Johan Lundström**

Ph.D., Psychology; Uppsala University (Sweden)

My research is aimed toward a better understanding of the cerebral basis for chemosensory and multimodal processing. Several different lines of ongoing research explore how the human brain allows us to perceive, process, and understand chemosensory and multimodal information. In particular, our lab is concerned with the complex processing of social chemosignals, signals that act along the border between perception and cognition. Lately, we are also investigating the neuronal basis of multimodal processing using our chemical senses, a natural multimodal sensation, as a stepping board.

### **Joel D. Mainland**

Ph.D., Neuroscience; University of California, Berkeley (USA)

A fundamental problem in neuroscience is mapping the physical properties of a stimulus to perceptual characteristics. In vision, wavelength translates into color; in audition, frequency translates into pitch. By contrast, the mapping from chemical structure to olfactory percept is unknown. In other words, there is not a scientist or perfumer in the world who can view a novel molecular structure and predict how it will smell. My research goal is to develop a

predictive model relating molecular structure and olfactory perception using a combined psychophysical and molecular approach.

### [Ichiro Matsumoto](#)

Ph.D., Molecular Biology; University of Tokyo (Japan)

My primary research interest is the coding mechanism of taste modality, specifically whether gustatory neurons are heterogeneous or homogeneous. Also, I am interested in the turnover of taste receptor cells and establishment and maintenance of peripheral gustatory wiring between taste receptor cells and gustatory neurons.

### [Nancy Rawson](#)

Associate Director and Vice President, Monell Chemical Senses Center  
Ph.D., Biology; University of Pennsylvania (USA)

The health of the biological systems we use for detecting tastes and odors is paramount to insure optimal health and well-being, and these systems are now known to be used not only for sensing the external environment but the internal chemical milieu as well. Their importance for survival is underscored by their remarkable regenerative ability, which helps to insure function in the face of exposure to harsh environments, whether externally facing in the nose or mouth, or internally facing, such as in the GI tract or lung. Cell-based tools are used to understand the development and function of chemosensory receptor cells and to leverage this understanding through multidisciplinary collaborations to address health challenges in the prevention and management of health conditions related to weight management and metabolic status, aging and neurological disorders.

### [Johannes Reisert](#)

Ph.D., Physiology; University of Cambridge (UK)

My laboratory investigates one of the first steps in olfactory perception: the conversion of an odorous stimulus into a nerve signal. Olfactory receptor neurons located in the nose detect odorants and generate the electrical response, which is then conveyed to the brain for further processing. The focus of my research is to understand 1) how olfactory receptor neurons code odor signals of different odorants and, 2) the cellular mechanisms that lead to the generation and termination of those responses. We also are interested in investigating the contribution of olfactory receptor neurons to olfactory adaptation, which is the waning of our perception of odorants over time. My approach uses both electrophysiological and cell imaging techniques to address these question.

## **Hong Wang**

Ph.D., Molecular Biology; Yale University (USA)

Chemosensory disorders substantially impact the quality of life. Impairment of taste and smell contributes to malnutrition, cachexia, and depression in a large percentage of cancer and AIDS patients. In spite of the rapid progress in identifying chemosensory receptors and signaling molecules, the mechanisms of chemosensory disorders remain largely unknown and there is a lack of specific and effective treatment for these disorders. Thus, the primary focus of our laboratory is to identify the molecular and cellular mechanisms underlying chemosensory disorders.

Our current research projects include: 1) taste abnormalities in animal models of inflammatory diseases; 2) expression and signaling of inflammatory cytokines and innate immune receptors in the chemosensory systems; 3) regulation of taste bud degeneration and regeneration; 4) mechanisms of taste loss during cancer chemotherapy; 5) interactions between inflammatory and taste receptor-mediated signaling pathways in the gut.

## **Paul M. Wise**

Ph.D., Psychology; University of California, San Diego (USA)

Chemical irritation constitutes a continuing focus. In particular, I am interested in how nasal irritation changes over time in the face of steady stimulation, and how one may trade time and concentration to maintain a constant level of detectability to understand how the sensory system integrates over time. Other interests include perception of carbonation, and chemical stimuli as triggers of cough. Within the area of olfaction, my primary interest is mixture interactions in odor detection. An additional interest that cuts across sensory modalities is in methods to measure sensory thresholds.

## **Assistant Members**

### **Amber Alhadeff**

Ph.D., Psychology, University of Pennsylvania (USA)

What controls hunger? How do we know when we are full? And how does what we eat influence our brain activity? Maintaining balance between nutrient need and consumption requires exquisite coordination between the gut and the brain.

The Alhadeff Lab is interested in understanding how gut-brain connections, and activity across circuits in the brain, influence motivated behavior. Our research employs a combination of modern neuroscience tools and surgical approaches to understand how external stimuli (e.g. food and drugs) affect in vivo neural activity, and how this brain activity drives behavior.

### Marco Tizzano

Ph.D., Congenital Metabolic Physiopathology; University of Verona (Italy)

Chemical irritation of the airways and other mucosae is my main focus. I study solitary chemosensory cells (SCCs), a specialized chemosensitive nasal epithelial sentinel cell type innervated by the trigeminal nerve, which responds to bitter compounds, irritants, and bacterial metabolites. When activated, SCCs trigger protective reflexes and inflammatory/immune responses. At the behavioral level I'm interested in motivated avoidance responses to inhaled irritants which activate the SCCs. I'm also particularly interested in long-range inflammation of the meninges as a consequence of nasal irritation and the mechanisms underlying neurovascular pathophysiology, such as headaches and migraines, which are triggered by exposure to airborne irritants, odorants, and bacterial molecules. My lab's current research projects include: (1) testing whether activation of the SCCs by irritants/odorants triggers long-range meningeal inflammation, (2) studying the mechanisms underlying migraine pathophysiology, and (3) better understanding the avoidance behavior responses to inhaled irritants.

### Yali V. Zhang

Ph.D., Biochemistry, Cellular and Molecular Biology; The Johns Hopkins University School of Medicine (USA)

The research goal of my laboratory is to address how animals sense the complex food environment to control feeding behaviors. To tackle this big questions, we use the model organism such as the fruit fly to identify the receptors or channels in the peripheral taste organ that enable animals to sense different features of food such as the chemical composition, food texture and food temperature. Furthermore, we investigate the physiological functions of sensory cells or neurons that allow animals to detect the chemical and physical stimuli from the food landscape. Moreover, using the functional Ca<sup>2+</sup> imaging, optogenetics and electrophysiology, we map the neural circuit in the brain that decodes the external food environment. In summary, we aim to unravel how the brain integrates different types of sensory modalities such as the chemosensory and mechanosensory stimulation, in order to make appropriate feeding decisions.

## **Adjunct Faculty**

### **Noam Cohen, Adjunct Member**

MD, Johns Hopkins University; Ph.D. Neuroscience; Johns Hopkins University Associate Professor, Otorhinolaryngology, University of PA School of Medicine Staff Surgeon, Philadelphia Veterans Administration Medical Center

The main interest of my lab is the pathophysiology of chronic rhinosinusitis, a syndrome that affects nearly 15% of the population manifesting in poor mucus clearance from the upper airways. To better understand the root cause of this syndrome, the focus of my laboratory has been on sinonasal epithelial function in the context of innate defense mechanisms, specifically mucociliary clearance and alterations in respiratory cilia function in response to microbial interactions and mucosal biofilm formation. To this end we have well-established and published techniques for growing both upper and lower respiratory epithelium from humans, visualizing and quantifying respiratory cilia function, live cell imaging to ascertain real time alterations in signaling cascades such as intracellular calcium and nitric oxide as well as other cellular properties (e.g. intra- and extra-cellular pH and cellular redox states), mucus clearance and hydration and techniques for growing and studying several respiratory pathogens. Most recently we have focused on the role that taste receptors, which are expressed in respiratory epithelium, play in upper airway innate immunity. The overall goal of my work, both in the clinical and research realms, focuses on understanding and treating disorders of the nose and paranasal sinuses. It is through this balance of clinical expertise and biological investigation that I hope to advance the care of rhinologic patients.

### **Yuzo Ninomiya, Adjunct Member**

Ph.D., MD.Sci; Nagoya University (Japan)  
Distinguished Professor at Kyushu University

Using electrophysiology and molecular biology we are seeking to understand the coding mechanisms underlying salty, umami (savory) and sweet taste qualities. We are also studying how hormones regulate taste responses. My group has found that hormones including leptin and endocannabinoids modulate peripheral sweet taste responses. Our studies show that modulation of peripheral sweet taste signaling by hormones likely contributes to the regulation of ingestive behavior.

### **Valentina Parma, Adjunct Assistant Member**

PhD, University of Padova, Italy  
Research Assistant Professor, Temple University (USA)

Both my basic and translational work aim at understanding how to capitalize on the clinical potential of human olfaction. By using behavioral and physiological methods, I have been studying the ways in which odors influence typical and atypical social and motor

behavior across development. Recently the COVID-19 pandemic has added a new dimension to my research in clinical olfaction. It has been an honor to lead hundreds of scientists, clinicians, and patient advocates in Global Consortium for Chemosensory Research (GCCR) to understand how smell, taste and chemesthesis are affected by COVID-19 and explore diagnostic solutions as well as strategies to inform recovery.

### **Luis Saraiva, Adjunct Associate Member**

Ph.D., Genetics; University of Cologne (Germany)

Investigator – Associate Level, Sidra Medical and Research Center, Qatar

Humans, like most animals, display complex behaviors and social structures. Complex behaviors are highly variable between individuals, resulting from the interplay between an individual's innate qualities, internal homeostatic state, and experiences with the surrounding environment. Despite being a very active field of study, the neurobiological basis of complex behaviors (and how it can lead to changes that ultimately may result in disease or mortality) still remains one of the greatest unanswered questions in modern neuroscience. Understanding how environmental and homeostatic cues interact with sensory systems is crucial to unravel the neural mechanisms underlying the behavioral and physiological responses these cues can elicit.

Broadly, we are interested in the molecular and neural mechanisms underlying the transformation of environmental and homeostatic cues in complex behaviors and physiological changes. In this context, a major line of research in our lab involves how the olfactory, metabolic and appetite systems interact, and how these interactions change with diet and disease. We also aim to understand how individual genetic variation, gender, age, and social experience impact these mechanisms. Another major line of research focuses on the molecular and functional logic underlying the rigid spatial organization of the main olfactory system. To achieve these goals, we employ a multidisciplinary experimental approach combining conventional techniques and novel technologies.

Furthermore, we are using “omics” technologies to find biomarkers and link specific variants to complex traits and/or diseases involving olfactory phenotypes (e.g. obesity, anosmia/hyposmia, Kallman Syndrome, Alzheimer's disease and others). To this end, we are analyzing human samples and data from countries around the world.

Our ultimate goal is to use these results to learn more about the molecular and functional mechanisms underlying olfaction, and to identify biomarkers that can help us predict the onset and progression of certain illnesses.

## **Senior Research Associates**

### **Linda J. Flammer**

Ph.D., Psychology; Temple University (USA)

My primary research interest is in creating a better understanding of the interrelationship among the sensorial, cognitive, metabolic and genetic influences on human ingestive behavior. I am particularly interested in sweetness and bitterness perception and discovering ways to modulate them. Further, having started my career at Monell investigating chemesthesis, the topic is still near and dear, especially mouthfeel. The goal of this research is to help stem the global obesity epidemic by enabling the creation of healthier foods and beverages without compromising on their palatability. Finally this work also identifies solutions to make bitter medicines more palatable, with the hope of increasing patient compliance, especially among children suffering from life-threatening illnesses.

### **M. Hakan Ozdener**

M.D., Ondokuz Mayıs University, Samsun (Turkey); Ph.D., Biochemistry; Ondokuz Mayıs University (Turkey); MPH (Public Health); Temple University (USA)

My primary research focuses on the development of in vitro chemosensory cell culture systems for the study of chemosensory biology and disorders. I utilize chemosensory cells obtained from human and from rodent to examine the factors involved in differentiation and maturation and to better understand how chemosensory receptor cells interact in their responses to stimuli. This work will enable us to develop and characterize novel tastent and new therapeutic targets to promote regeneration following injury from surgery, radiation, toxic exposures or deterioration due to aging or neurodegenerative disease.

### **Catherine Peyrot Des Gachons**

Ph.D., Medical and Food Sciences; Université de Bordeaux (France)

My research interests are human oral perception, its genetic basis and its implications in nutrition and health. Somatosensation, such as irritation and mouthfeel, is my main current focus through the study of natural products like wine, olive oil and spices. I am using several techniques to investigate the field of somatosensation, including molecular biology, cellular calcium imaging and psychophysics.

### **Karen K. Yee**

Ph.D., Physiology; Virginia Commonwealth University (USA)

My research interest is in taste mechanisms, utilizing various methods (i.e., immunohistochemistry) to identify novel pathways in mammalian and human taste cells.

Findings will provide additional knowledge about which components help modify taste sensitivity and function and their roles in gustatory function, appetite, satiety, diabetes and obesity. Another research interest is in the plasticity of mammalian olfactory system.

## **Research Associates**

### **Cristina Jaén**

Ph.D., Medical Sciences, Physiology; University of South Florida (USA)

My research interests focus on how odorant perception affects human psychological and physiological responses. Many organic volatile compounds can elicit an odorant and irritant response. Olfactory cues such as smoke or rotten food alert us from perils and may produce an anxious reaction. I am interested in understanding how odorant perception affects different subpopulations, e.g. asthmatic subjects (who have respiratory problems) versus non-asthmatic subjects. This research may lead to a better understanding and management of asthma after being exposed to perceived dangerous odorant stimuli.

### **Brian Lewandowski**

Ph.D., Neuroscience; University of Pennsylvania (USA)

My research is focused on understanding the cellular and molecular basis of salty taste. There are at least two pathways underlying salty taste in mammals, distinguished by their sensitivity to the cation channel inhibitor amiloride. While much has been learned about these pathways, some important questions remain unanswered. What types of taste cells express salt taste receptors? What is the identity of the receptor/channel responsible for amiloride-insensitive salt taste? How does cell-to-cell communication within the taste bud influence salt signal transduction? My goal is to help answer these and other questions related to salt taste transduction. My experiments combine physiological analyses of taste cells using calcium imaging and electrophysiology with single cell molecular techniques to assay gene transcription.

Prior to coming to the taste field, I used in vivo electrophysiology in awake, behaving animals to study the systems and neural networks underlying vocal communication. This background in neural networks fuels my broader interest in understanding how cell-to-cell communication in the taste bud shapes taste signal transduction and mediates the perceptual interactions between different taste qualities. My focus on salty taste is motivated by evidence from perceptual and physiological studies that suggest cell-to-cell signaling plays a particularly important role in salt taste transduction.

### [Cailu Lin](#)

Ph.D., Animal Genetics; Rheinische Friedrich-Wilhelms University of Bonn (Germany)

My research focuses on the genetic analysis of complex traits, such as taste perception and obesity in mice and humans. I participate in collaborative studies in the laboratories of Drs. Bachmanov and Reed. The objective of these studies is to identify the chromosomal locations of the genes associated with these quantitative trait phenotypes. The ultimate goal of my studies is to identify genes that are involved in taste perception, alcohol consumption, and obesity. To achieve this goal, I study genotype-phenotype associations in humans, breed and analyze various consomic and congenic mouse strains, and use a combination of physiological, molecular, and quantitative genetic approaches.

### [Jiang Xu](#)

M.D., Medicine; Beijing Medical Staff College (China)

My current project mainly focuses on studying cellular responses to volatile chemical stimuli. I use fluorescence imaging of intracellular calcium and pharmacological agents to characterize the transduction processes in live olfactory and trigeminal neurons.

## **Postdoctoral Fellows**

### [Dolly Ai Koborssy](#)

Ph.D., Neuroscience; Florida State University (USA)

I am interested in studying olfaction at the level of the olfactory epithelium. Binding of an odorant molecule to its receptor triggers a signaling cascade in the olfactory epithelium involving different secondary messenger molecules and ion channels. We don't know, however, the exact contribution of each component of the olfactory signaling transduction to olfactory perception. To answer this question, I'm using single-cell electrophysiology on olfactory receptor neurons to understand how the olfactory nerve signal is generated in response to specific odorants, how the olfactory response is terminated, and the details of the mechanism underlying olfactory adaptation.

### [May Cheung](#)

Ph.D., Nutrition Sciences, Drexel University (USA)

My research interest is to understand the interplay between taste preferences, energy metabolism and obesity in humans. Overconsumption of high-caloric, low-micronutrient foods can lead to dysregulation of energy-regulating hormones, contributing to obesity and related chronic diseases. Food choices are strongly influenced by hedonic responses to preferred foods. Therefore, taste preferences play an important role in forming a healthy

dietary pattern. Furthermore, emerging evidence suggests that increase in carbon dioxide in the atmosphere can lead to lower concentrations of protein and minerals in crops, further contributing to the obesity/malnutrition paradox. My goal is to explore the feasibility of taste adaptation to sustainable, nutrient-dense novel foods and subsequent health effects in humans.

### **Federica Genovese**

Ph.D., Neuroscience; University of Heidelberg (Germany)

In the mammalian nose, the trigeminal system detects irritants and the olfactory system detects odorants. Traditionally, these systems have been considered separate sensory modalities, but a more complex picture has recently emerged. Psychophysical and electrophysiological studies show evidence of interaction between these two chemosensory systems, suggesting that olfactory perception is the result of olfactory-trigeminal integration, rather than an isolated system. Although most odorants can also activate the trigeminal system, and most irritants can also be detected by olfactory sensory neurons, the nature of olfactory-trigeminal interaction is still unclear.

I am interested in investigating the mechanisms underlying the interaction of the trigeminal and olfactory chemosensory systems during the detection of volatile irritants, with a special focus on the role of solitary chemosensory cells (SCCs), specialized chemosensitive nasal epithelial sentinel cells.

### **Mackenzie Hannum**

Ph.D., Food Science & Technology, The Ohio State University (USA)

My research interest involves understanding how and why people perceive taste and smell the way they do. There is a physiological component to perception, driven by different mechanisms and structures, but there is also a psychological component that can be heavily influenced by past and current experiences. In trying to better understand the interplay between the two on an individualized level, I am interested in employing novel methodologies and data analysis techniques to capture this information.

Therefore, my main research aim is to employ the Monell Flavor Quiz to collect information on taste and smell on a global scale – distributing the quiz to individuals across the world. And there is nothing more individualized than knowing someone's DNA. By collecting saliva samples along with their answers to the Monell Flavor Quiz, we are able to investigate the relationship between someone's DNA and their perception and preference of different tastants and odorants. This information allows us to assess global food preferences underscored by the interplay between someone's genetic makeup and any psychological influences on their perception such as liking or engagement with the task.

### [Kuei-Pin Huang](#)

Ph.D., Physiology, University of California, Davis (USA)

Food consumption induces the release of gut signals that are locally sensed by the gastrointestinal tract-innervated peripheral nerves. These signals are rapidly conducted to the different brain regions, which modulate the eating behaviors.

My research interest is in understanding how different nutrients (sugars, fat, and proteins) are sensed by the peripheral nervous system and how these different signals modulate food intake in physiological and disease stages. We use different mouse models and the latest neuroscience tools to record in vivo neuronal activity and manipulate the specific population of neurons to reveal the potential target for eating disorders.

### [Stephanie Hunter](#)

Ph.D., Nutrition, Purdue University (USA)

It is clear that people choose diets because of their sensory properties. Further, an enjoyable sensory experience is essential for adherence to any dietary regimen. My research interests lie in understanding how the chemical senses contribute to food choice and eating patterns, with the aim of developing strategies to alter the sensory properties of the diet to better align with dietary recommendations. I am specifically interested in understanding how to practically alter food preferences through sensory manipulation and sensory influences on appetite, ingestive behavior, metabolic outcomes, and risk for chronic disease. Alternatively, I am interested in understanding the impact of COVID-19 on taste and smell, and how lack of taste or smell influence food choice and eating patterns.

### [Akihito Kuboki](#)

M.D.; St. Marianna University School of Medicine (Japan)

My research interests are to understand the mechanisms of adaptation in olfactory sensory neurons to an odorous stimulus and the factors involved in homeostatic regeneration of the olfactory epithelium. By investigating the first step of olfactory perception, I want to investigate the pathophysiology of olfactory dysfunctions in the periphery. I will use electrophysiological as well as cell biological approaches to address these questions.

### [Young Eun Lee](#)

Ph.D., Organic Chemistry; University of Pennsylvania (USA)

My research is focused on identifying the volatile biomarker signature of ovarian cancer in human plasma. Controlled studies demonstrate that dogs can detect ovarian cancer sample from normal ovarian sample with above 95% success rate by using their highly developed

sense of olfaction. We will determine the most prominent volatile organic compounds (VOCs) of the unique order signature of early stage ovarian cancer using analytical organic chemistry. Gas chromatography-mass spectrometry (GC/MS) techniques are ideal for identification and quantification of mixtures of VOCs found in the cancer sample. Our ultimate goal is development of a practical diagnostic system for early stage ovarian cancer to save people from the deadliest gynecologic oncology.

### [Chanyi Lu](#)

Ph.D., Microbiology, Fudan University (Shanghai, China)

Tuft cells are chemosensory cells in the intestinal epithelium which express a number of taste-signaling elements. Despite being discovered decades ago, the function of tuft cells in the small intestine was only recently discovered. Tuft cells mediate host defense against parasitic infection or other pathogens by regulating type 2 immunity. My research interest is clarifying the parasites' ligands and sensing receptors in tuft cells.

### [Emily Mayhew](#)

Ph.D., Food Science; The University of Illinois (USA)

My research interest lies in using the chemical and physical properties of stimuli to explain and predict human sensory perception. At Monell, the focus of my work will be the prediction of odor characteristics of molecules based on structural characteristics of the molecules. Our first aim is to collect rich sensory data from human evaluations of the presence/absence of an odor and the sensory characteristics of the odor for a diverse set of molecules. Combining this information with a wide array of physicochemical and structural variables, we will build and train models using machine learning to predict both whether a compound is odorous or odorless and what type of odor perception a molecule elicits. These models can enable more accurate prediction of the total number of possible odorous molecules and identify key molecular features that influence odor perception.

### [Ting-Wei Mi](#)

Ph.D., Plant Science; China Agricultural University (China)

Taste is a fundamental sense required to perceive food flavor including food taste, texture, temperature, etc. To unravel how animals detect the physical and chemical information from the food environment, we use model organisms such as the fruit fly and mouse to explore the peripheral and central gustatory mechanisms that regulate food preference and feeding behavior.

### **Robert Pellegrino**

Ph.D, Food Science; University of Tennessee (USA)

My interests are to understand and predict behavioral responses to odors. In naturalistic settings, odors are composed of numerous odorants that are carried in plumes. At Monell, the focus of my work is to predict odor mixture perception and behavioral outcomes based on structural characteristics of the constituent odorants. Our first aim is to collect reliable and valid human sensory data for a large set of odor mixtures at different concentration ratios. This information, combined with physicochemical and structural variables, will help us build predictive models that can be used with behavioral measurement tools to understand outcomes to naturalistic odors.

### **Alyssa Smethers**

Ph.D., Nutritional Sciences, Pennsylvania State University (USA)

R.D., Nutrition, Marywood University

Prior to coming to Monell, I conducted a series of controlled feeding studies testing how environmental factors, particularly portion size and energy density, and individual differences influence preschool children's energy intake over time. At Monell, the goals of my research are to build upon this knowledge and develop a broader understanding of how individual differences contribute to preferences and appetite. I'm particularly interested in the relationship between a person's genes and their taste preferences (e.g. sweet and bitter) and how this influences ingestive behavior.