



***THE FUTURE OF
TASTE & FLAVOR***

**2019 Monell
Spring Colloquium**

Monell Chemical Senses Center 2019 Spring Colloquium



A LOOK TO THE FUTURE

April 11-12, 2019

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SCHEDULE OF EVENTS

Event Summary

Our understanding of flavor and fragrance perception has advanced both with respect to their biological underpinnings and their function in our health and behavior. Remarkable advances in virtual reality, machine learning, exomics, metabolomics, gene editing, and sensor technology are driving discoveries that could not have been imagined 10 years ago. What will the science look like 5 – 10 years from now? What problems will have been solved? Will odors be detected and delivered via cell phone? Will “taste” compounds be used to prevent or treat disease? Presenters will take participants on a journey from the current state of scientific knowledge into the future, imagining what questions we will have answered and what new ones will be at the forefront.

Thursday April 11th

The Future of Taste and Flavor

Location: Quorum

- | | | |
|-----------------------|---|----------------|
| 1:00 pm | Global Taste: An Around-the-World Taste Adventure | D. Reed |
| 1:40 pm | Multisensory Processing of Food Flavor: Behavioral Markers and Neural Correlates | J. Lundström |
| 2:20 pm | Getting to More Predictive Bioassays for Human Taste | E. Schwiebert* |
| 3:00 pm | Extraoral Taste Receptors: Function in Health and Well-Being | M. Tizzano |
| 3:40 pm | Commercial Perspective & Discussion
Discussant: Dr. Harish Radhakrishna is a cell biologist with expertise in receptor signaling, taste modulation, and sensory science. He has worked in academia, at the NIH and Georgia Tech, as well as in the food industry, at the Coca-Cola Company and Chromocell Corporation. He has focused on taste biology and taste modulation over the past thirteen years. | |
| 4:30 – 6:30 pm | Reception and Tours at Monell | |

Friday April 12th

The Future of Fragrance and Aroma

Location: Quorum

7:30 – 8:30 am Continental Breakfast

8:30 am Global Smell: An Around-the-World Olfactory Adventure J. Mainland

9:10 am From the “What” to the “Where” in the Human Olfactory System J. Gottfried*

9:50 am Metabolic Regulation of Olfaction D. Al-Koborssy

10:30 am Biosensors for Volatiles: Capabilities, Limitations, and Future Opportunities C. Johnson*

11:10 am Commercial Perspective Discussion

Discussant: Dr. Michelle Murphy Niedziela is a behavioral neuroscience expert in neuropsychology, psychology and consumer science. She has experience from academia (Purdue University, Monell Chemical Senses Center) and industry (Johnson & Johnson, Mars Chocolate) in R&D of innovation technologies and methodologies for consumer research. As VP of Research and Innovation at HCD Research, Michelle focuses on integrating applied consumer neuroscience tools with traditional methods used to measure consumer response.

***Guest Speakers**

Jay Gottfried, MD, PhD

Arthur H. Rubenstein University Professor
University of Pennsylvania

A. T. Charlie Johnson, PhD

Director
Penn Nano/Bio Interface Center
Professor Physics & Astronomy
University of Pennsylvania

Michelle Murphy Niedziela, PhD

Scientific Director
HCD Research

H. Radhakrishna, PhD

Consultant
Taste Science Consulting

Erik Schwiebert, PhD

CEO, and Chief Scientific Officer
Discovery BioMed

PRESENTATION ABSTRACTS

Global Taste: An Around-the-World Taste Adventure

Danielle Reed, PhD

The human sense of taste fuels our love of sugar and salt and avoidance of bitterness (e.g., in vegetables and medicines) which in turns creates global health problems in the form of obesity, hypertension and other diseases. But taste is usually studied only locally. By locally we mean that scientists study people that live in only one part of the world who are often of similar or identical ancestry. Thus, we have no data to help us understand whether all the people in the world perceive taste stimuli in the same way, although we can draw on work by physical anthropologists, studying a single bitter compound, which suggests that there can be profound differences in human taste among populations. Further indirect evidence of human perceptual differences in taste comes from the different types of cuisine and the diversity of food and preparation methods which hint at profound geographic differences in taste perception. Here we explore a big idea which is to study the taste of people world-wide and our dream of the collection of data from a million people across the globe. We introduce the *Monell Flavor Quiz* and discuss the power and promise but also the perils of measuring the full range of the human taste experience.

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Reed DR, Knaapila A. Genetics of taste and smell: poisons and pleasures. *Prog Mol Biol Transl Sci.* 2010;94:213-40. doi: 10.1016/S1877-1173(10)94008-8. Review. PubMed PMID: 21036327; PubMed Central PMCID: PMC3342754.

Multisensory Processing of Food Flavor: Behavioral Markers and Neural Correlates

Johan Lundström, PhD

Odors form part of the complex sensory experiences during food consumption and during recognition of food in the environment, creating a learned link between a food's nutritional value and its outward appearance. Associative learning about configural contingencies, i.e. the natural transition between flavor objects that exists outside the laboratory setting, within these complex sensory stimuli is thus thought to be crucial for adaptive choices about food intake; indeed, familiar stimulus combinations tend to evoke appetite, while unfamiliar combinations elicit avoidance behavior. The more ecologically relevant assessment of subtle deviations between learned associations and novel complex sensory stimuli is, however, to date poorly understood, both in terms of its associated perceptual experiences and its cortical processing. To address this, we studied perceptual acuity to variations in olfactory-gustatory and olfactory-visual sensory overlap, its behavioral relevance, and potential underlying perceptual and functional-anatomical mechanisms. Our data show that humans are highly sensitive to variations in crossmodal perceptual overlap, and that this sensitivity is directly behaviorally relevant for the emotional appraisal of complex chemosensory stimuli. We further delineate a top-down controlled cortical pathway that supports the formation of such assessments during conditions of perceptual difficulty. The talk will at the end outline future directions and unanswered important questions.

References

Seubert, J., Ohla, K., Yokomukai, Y., Kellermann, T., & Lundström, J. N. (2015). Superadditive opercular activation to food flavor is mediated by enhanced temporal and limbic coupling. *Human brain mapping*, 36(5), 1662-1676.

Fondberg, R., Lundström, J. N., Blöchl, M., Olsson, M. J., & Seubert, J. (2018). Multisensory flavor perception: The relationship between congruency, pleasantness, and odor referral to the mouth. *Appetite*, 125, 244-252.

Lundström, J. N., Regenbogen, C., Ohla, K., & Seubert, J. (In press). Prefrontal Control Over Occipital Responses to Crossmodal Overlap Varies Across the Congruency Spectrum. *Cerebral Cortex*.

Getting to More Predictive Bioassays for Human Taste

Erik Schwiebert, PhD

Bitter taste in foods and medicines presents a barrier to overcoming global public health challenges: food insecurity, poor nutritional health, and poor compliance with medication use, particularly among children and the elderly. Sugar and salt, the mainstays to address these challenges, further erode nutritional health, and current alternatives have adverse taste attributes of their own. Several approaches for identifying compounds that impair, suppress or block bitter taste have been pursued with varying degrees of success. These include: (a) electronic tongue technologies, (b) molecular modeling of T2Rs, (c) functional expression of bitter receptors in heterologous systems, (d) rodent brief access taste testing, and (e) human sensory evaluation. Each of these methods has strengths and weaknesses. There is, however, widespread acknowledgement of continued need for solutions that are both broadly effective and practical and that demonstrate the need for improved approaches. An alternative approach is based upon earlier work at the Monell Center by Dr. Hakan Ozdener and Nancy Rawson, demonstrating the potential for human taste cells obtained via biopsy to be propagated in culture. Our hypothesis is that these cells, by virtue of expressing the full spectrum of taste detection and transduction machinery, may be more predictive of human taste sensation than other *in vitro* or *in silico* approaches. To test this hypothesis and advance this research tool for commercial applications, a partnership was formed with Discovery Biomed, a company with specialized expertise in the use of physiologically-relevant human cell platform technology in ligand discovery. With funding from the Bill & Melinda Gates Foundation, work proceeded to begin to use cell lines derived from Monell's primary cultures and selected for responsiveness to bitter stimuli, for identification of candidate bitter blockers. This work provided the foundation for a successful Phase I Small Business Technology Transfer Grant from the NIH under the direction of Erik Schwiebert from DBM and Danielle Reed and Nancy Rawson from Monell. The focus of this work is to establish primary and immortal human taste bud epithelial cell (hTBEC) cultures from at least 20 different donor tissues that vary by sex and ethnicity. This effort begins to address the heterogeneity of bitter taste responses. Functional assays include both real-time cell calcium imaging and real-time detection of ATP transmitter secretion in response to a panel of different bitter tastants in conjunction with cytotoxicity testing. Proof-of-concept that this approach works has recently been achieved using bitter stimuli, such as bitter-tasting medicines given to humans in the developing world to fight malaria, parasitism, HIV/AIDS and other ailments. Ongoing work is examining the 'bitterome' or the full complement of bitter taste receptors and key signal transduction effectors in the best candidate immortal and primary bitter-

responsive hTBEC cultures. Quantitative RT-PCR is confirming expression of specific TAS2R bitter receptors in these hTBEC platforms. This approach might also be used to pre-screen therapeutic candidates or alternative ingredients for those less likely to elicit unpleasant taste profiles to streamline the development process. While no *in vitro* approach is likely to be perfectly predictive of human perception, we feel this technology will fill an important gap in the current arsenal of tools for the development of bitter taste modulators.

Monell and DBM gratefully acknowledge the support of the National Institute of Deafness and Other Communication Disorders (NIDCD) from grant 1R41DC017693-01 and from the Bill & Melinda Gates Foundation.

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Extraoral Taste Receptors: Function in Health and Well-Being

Marco Tizzano, PhD

Taste perceptions provide sensory guidance for humans and animals in the intake of nutrients and ions; toxicant avoidance during food consumption; and contribute to the hedonic enjoyment of food intake. There are five basic taste modalities: salty, sour, bitter, sweet and umami. Signal transduction of salty and sour taste involves ionotropic receptor channels while signal transduction of sweet, bitter and umami taste relies on metabotropic receptors T1Rs and T2Rs called G-protein coupled receptors (GPCRs). In the last 20 years, it has been shown that T1Rs and T2Rs are located outside the gustatory system in most of the body mucosae and organs, including airways, oral cavity, gut, urethra, kidney, testis, thymus, uterus, vagina, gingiva, thyroid gland smooth muscle, etc. Solitary chemosensory cells¹ (SCCs), are present in most of the mucosal epithelium and express several elements of the taste signaling transduction cascade including T1Rs and T2Rs. Activation of extraoral taste receptors produces a diverse range of biological responses under normal and pathological conditions allowing detection of pathogens and initiation of innate immune responses. For example, SCCs in the nose detect pathogenic bacterial quorum-sensing compounds [e.g., acyl-homoserine lactones (AHLs)]; tuft cells in the gut respond to helminthic parasites, evoking innate immune responses to clear the parasites; and brush cells in the urethra are implicated in controlling urinary tract infections. Although the pathophysiological roles of T2Rs have traditionally focused on the respiratory tract, their roles in other systems have begun to emerge. For example, starvation increases the expression of T2Rs in the heart with strong association with cardiovascular disease; depletion of T2R105 leads to male infertility and problems in renal tubule function; T2R expression is dysregulated in Parkinson's and schizophrenia; T2Rs have also been detected in colon and breast cancer cells; and have been implicated in longevity, and in regulation of blood glucose, body weight, and the microbiome. Benign triggers such as the flavors present in foods can activate extraoral taste receptors and may have therapeutic value to initiate innate immune responses against pathogens and to trigger other physiological functions important in disorders and diseases. As we seek to reduce bitter compounds in foods and use flavors in more product contexts, we may be having an impact beyond the sensory experience. The implications of these emerging discoveries for the development of functional foods and flavors is an important new area of research that may lead to an entirely new paradigm for health preservation and promotion.

1 Solitary chemosensory cells (SCCs) are also known as brush, tuft, microvillous, caveolated, multivesicular or fibrillovesicular cells in different parts of the body.

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Global Smell: An Around-the-World Olfactory Adventure

Joel D. Mainland, PhD

Each of us lives in a unique sensory world; odors that are disgusting to some are pleasant to others. In this talk, we will explore your responses to the *Monell Flavor Quiz*, a tool for measuring the smell and taste preferences in large groups of people. We will outline the different sources of variability across individuals, with a focus on emerging research that relates perceptual variation to genetic differences. Recent advances in sequencing technology allow us to measure genetic variability and public databases exploring the genetic differences across the globe allows us to predict perception for novel populations or individuals. This research can be used by product developers to understand the variable perception of products and tailor development to specific markets, by consumers to understand the basis of their food preferences and identify novel foods that they may prefer, and by researchers to understand how receptors encode stimuli and have evolved in response to changing diets.

References

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From the “What” to the “Where” in the Human Olfactory System

Jay Gottfried, MD, PhD

The ability to detect, recognize, and identify smells is a fundamental feature of the olfactory system. As such, a major emphasis of olfactory neuroscience research has been to elucidate how the brain encodes and interprets information about smells, and how odor representations inform perception, learning, and behavior. Our work has brought insights to the functional organization of the human olfactory system and its impact on perceptual processing. Conceptually this domain of research falls under the “what” questions of odor coding, that is, what receptors, circuits, and systems, underlie the perception of smells.

A unique aspect of odors is their ability to travel through the air over long distances. In this manner, the sense of smell can gather valuable predictive information about an odorous object, enabling animals to navigate either toward or away from an odor source as needed. Notably, in contrast to the “what” questions of olfaction, the role of the olfactory system in spatial navigation is less well studied, though no less important. This research domain falls under the “where” questions of odor coding.

In this presentation I will discuss our recent investigations of the “what” and “where” questions of human olfaction, with focus on two themes. The first theme explores the role of smell in infiltrating the sleeping brain to induce replay of visual content previously learned while awake, with associated gains in memory performance. These findings shed light on new approaches for enhancing what people remember and minimizing what people forget. The second theme explores the role of smell in human olfactory navigation, with data demonstrating the ability to orient and path-find within abstract and physical (virtual reality) spaces defined purely by odors. These new data promise a new experimental framework for investigating how the olfactory system guides animals, including humans, towards things they need and away from things they ought to avoid.

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Metabolic Regulation of Olfaction

Dolly Al-Koborssy, PhD

Food intake is regulated by internal mechanisms such as the motor functions of the stomach and the rich repertoire of hormones, peptides, and nutrients released in the bloodstream. The central nervous system also senses and responds to inputs from the same hormones, peptides, and nutrients. More recently, the focus has shifted towards studying the influence of environmental factors and sensory stimuli on feeding behavior. Olfaction, in particular, is modulated by the nutritional status.

Satiation decreases, and fasting increases odor detection abilities. In addition, a battery of *orexigenic* and *anorexigenic* molecules can cross the blood-brain barrier, and modulate the electrical activity of principal cells in key olfactory areas. Here I will focus on the key neural elements underlying our sense of smell: from the periphery (olfactory epithelium), to the first relay point (olfactory bulb), to the brain region which receives odor information (piriform cortex). Within this context, we will explore the following questions: Which metabolic-related molecules are expressed in these olfactory areas? What is their effect on the electrical activity of olfactory neurons? And how is the olfactory system modulated by hunger, satiety, and different diets? During the discussion, we will consider the implications of this for developing more effective ways to insure adherence to healthy diets.

Orexigenic: appetite-stimulating

Anorexigenic: appetite suppressing

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Biosensors for Volatiles: Capabilities, Limitations, and Future Opportunities

A.T. Charlie Johnson, PhD

Single-atom thick materials such as graphene and carbon nanotubes have emerged as a scientific playground for the exploration of new phenomena, with numerous potential applications already demonstrated and proposed. Along with the basic science of the materials, my group has explored all-electronic chemical detectors based on bio-nano hybrids, where a biomolecule provides chemical recognition and a graphene or carbon nanotube field effect transistor enables electronic readout. Capitalizing on rapid advances in 2D materials research and biomolecular engineering, this sensor class represents a promising approach towards sensitive and selective detection of liquid- and vapor-phase analytes. Such bio-nano hybrids enable detection of protein cancer biomarkers, antigen from various pathogens, small molecule targets, and nucleic acid oligomers at femtomolar concentrations and below. Related methods can be used to create all-electronic vapor sensors that are able to discriminate between highly similar compounds such as enantiomers and very similar complex vapor mixtures characteristic of humans. Recently we have shown the promise of this system for diagnosis of disease based on volatile biomarkers.

RESEARCH INTERESTS OF SCIENTIFIC STAFF

The following lists the current research interests of the staff of the Monell Center. For a complete listing of publications, please visit our website at www.monell.org.

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.

Beverly J. Cowart

Ph.D., Psychology; The George Washington University (USA)

For most of my scientific career, the overall goal of my research program was to understand chemosensory dysfunction as a disease entity, develop appropriate clinical measures of chemosensory function, identify etiologies of dysfunction, and investigate such issues as the impact of chemosensory dysfunctions on patients, the demographic characteristics of individuals with chemosensory dysfunctions, and the prognoses for chemosensory dysfunctions. This work has naturally fed into and helps to support Monell's current Anosmia Research and Awareness Initiative. Most recently, I have also become involved in studies of the protective role of extra-oral taste receptors in nasal-sinus disease.

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.

George Preti

Ph.D., Organic Chemistry; Massachusetts Institute of Technology (USA)

Research in my laboratory focuses upon the nature and origin of human odors, particularly those from the underarm (axillae) and the oral cavity. We have identified the structures of many human axillary odorants, demonstrated the presence of human primer and modulator pheromones in the axillary secretions and have used our

knowledge of body chemistry to diagnose disease and the time of optimum fertility in females. We are pursuing the structures of the active pheromone constituents via a bioassay-guided isolation procedure as well as employing gas chromatography-mass spectrometry (GC/MS) to generate metabolic profiles (“metabolomics”) of human urine, skin and axillary secretions to identify biomarkers of disease, individual identity and stress. In addition we study the amelioration of malodors from humans with the odor producing metabolic disease, Trimethylaminuria, as well as from agricultural and environmental activities via cross-adaptation, odor absorption and anti-microbial agents.

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

Liquan Huang

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

My research is directed at the molecular mechanisms underlying taste and smell signal transduction and receptor cell regeneration. The focus is on identifying and characterizing molecules that are involved in the recognition and transmission of taste and olfactory stimuli in the oral and nasal cavities, respectively, and on the progenitor cells’ differentiation and maturation in the olfactory epithelium. This work has implications for understanding the cellular and molecular basis of chemosensation

under various circumstances, which may lead to effective treatments of such taste and olfactory disorders as dysgeusia and anosmia.

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, 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

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 Ca²⁺ 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 (Japan)

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.

Luis Saraiva, Adjunct Assistant Member

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

Investigator – Assistant 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

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.

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.

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.

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.

Sunil K. Sukumaran

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

My work at Monell aims at understanding taste sensation with a focus on sweet taste. We believe there are alternate mechanisms for sweet taste sensation in addition to the one involving T1R2/T1R3 genes. We are studying these genes to see if they are present in the sweet taste cells and further to find out what role(s) they play in these cells. In addition, we are also doing experiments to identify all the genes expressed in taste cells using microarrays and deep sequencing using RNA amplified from single taste cells. Interesting genes identified by the above experiments will be studied further using molecular, knockout and/or transgenic approaches. We hope that these

studies will help us design improved non-caloric sweeteners, provide a better understanding of nutrient sensing in the tongue and beyond and ultimately, treat metabolic disorders like diabetes and obesity.

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.

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.

Affiliated Scientists

Debra Zellner

Ph.D., Experimental Psychology; American University (USA)

My research interest is discovering environmental and cognitive factors that influence how much we like and how we perceive stimuli, mostly food. This includes, but is not limited to, multimodal interactions and hedonic contrast. Recently I have been studying how these factors increase vegetable consumption in school lunchrooms.

Director's Fellow

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.

Postdoctoral Fellows

Dolly AI Koborssy

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

I'm 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.

Genevieve Bell

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

My research interest involves understanding the underlying mechanisms in which diet-induced changes in the gut influence taste preference and overall appetite. More specifically, my research will examine how specialty diets (high-salt, high-fat, etc.) alter gut physiology and microbiota to impact taste bud physiology. To answer these questions, I will be taking advantage of the behavioral techniques of my laboratory, while also expanding my knowledge of cellular and molecular techniques, using an

ex-vivo model system, organoid cell culture, in conjunction with the laboratory of Dr. Peihua Jiang.

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.

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 a development of a practical diagnostic system for early stage of ovarian cancer to save people from the deadliest gynecologic oncology.

Chanyi Lu

Ph.D., Microbiology, Fudan University (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, University of Illinois at Urbana-Champaign (USA)

The collection of all organic molecules comprises millions of known molecules in public databases as well as a much larger number of theoretically possible molecules. How many of these molecules have an odor? What features of the molecule most strongly influence what the molecule will smell like?

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.

Patrick Millet

Ph.D., Molecular Genetics and Genomics; Wake Forest University (USA)

Many species can communicate their health status through odor. These disease-related odors can carry vital information to other members of that species, such as which individuals should be avoided to prevent the spread of disease. Recent research demonstrates that different immune stimuli can produce distinct disease-related odortypes. My work at the Monell Center will explore the molecular mechanisms behind these odortypes. I will be using both Y-maze trained mice and molecular biology techniques to determine the immune and metabolic pathways responsible for these odortypes, with the goal of tying specific immune stimuli to profiles of volatile metabolites. My hope is that this research will lead to new ways of diagnosing disease using volatile metabolites found in body odor.

Carolyn Novaleski

Ph.D., Hearing and Speech Sciences; Vanderbilt University (USA)

My research focuses on the health effects of chemicals using controlled exposure studies. Specifically, I am measuring the effects of different exposure durations and concentrations of indoor fragrance devices and propylene glycol on respiratory function and subjective rating of sensory irritation. The long term goal of my research is to study the role of chemosensation in the larynx and to understand the chemosensory origin of voice and airway diseases characterized by hypersensitivity to chemical irritations and abnormal laryngeal constriction.

Alissa Smethers

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

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.

Molly Spencer

Ph.D., Food Science (Sensory Science Emphasis); University of California Davis (USA)

In my research at Monell and beyond, there are a few topics that I'd like to address: 1) psychophysics of taste, smell, and chemesthesis, 2) consumer food preferences and eating behavior, and 3) sensory and culinary strategies to improve nutrition and sustainability in the diet. At Monell, I will be focusing on the psychophysics of flavor interactions, masking, and enhancement amongst taste, smell, and chemesthetic stimuli, by drawing on a variety of methods and measures used in psychophysics, psychology, sensory and consumer science, physiology, and neurology. A more thorough understanding of the cognition and perception of taste, smell, and the chemical sense and how they interact, as well as the cognitive and emotional processes by which food preferences and eating behavior are developed and formed, will provide insight into sensory and culinary strategies that can successfully and permanently improve the nutrition and sustainability in the diet without sacrificing the fundamental enjoyment of eating.

Junpei Yamashita

Ph.D., Bioengineering; Tokyo Institute of Technology (Japan)

My research interests are mammalian chemosensory systems, especially taste. My goal is to understand how chemosensory systems recognize chemical substances in the external environment molecular and cellular levels. To identify an important gene involved in the chemical senses, I use mouse genetics and in situ hybridization, immunohistochemical analysis. I am also interested in the function of intestinal tuft cells.

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