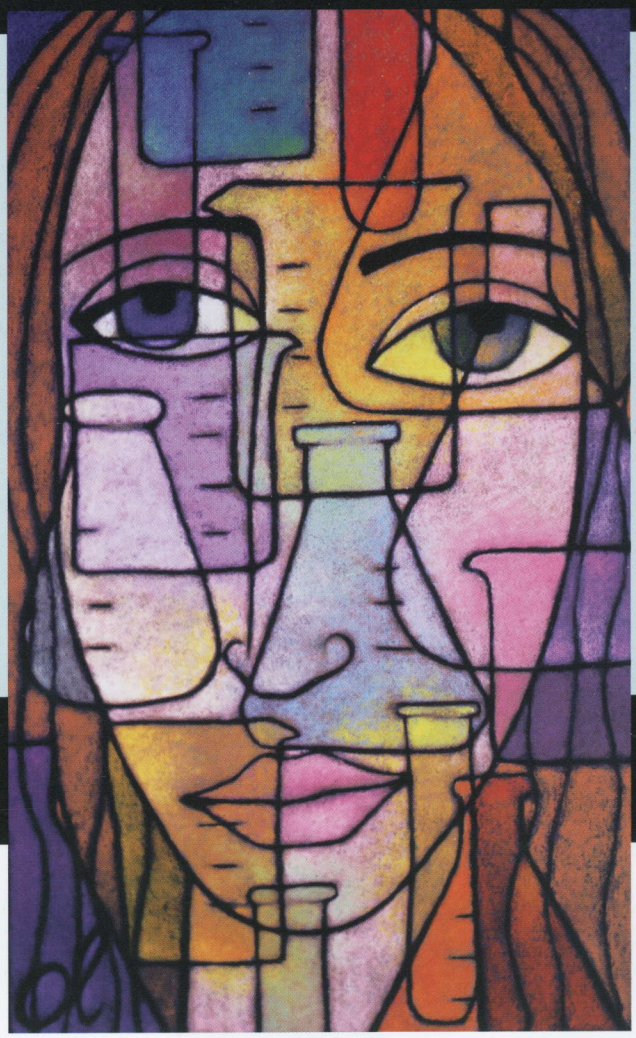
THE MONELL CONNECTION

THE NEWSLETTER OF THE MONELL CENTER

The Flavor of Health



Phillip Dvorak/Images.com

For those who think our ability to smell or taste just helps us enjoy good chocolate and perfume, a recent Monell symposium was a real eye-opener. The well-attended symposium revealed in detail how highly sensitive chemical sensors in our tongue, nose and even our gut can significantly influence human health across the lifetime.

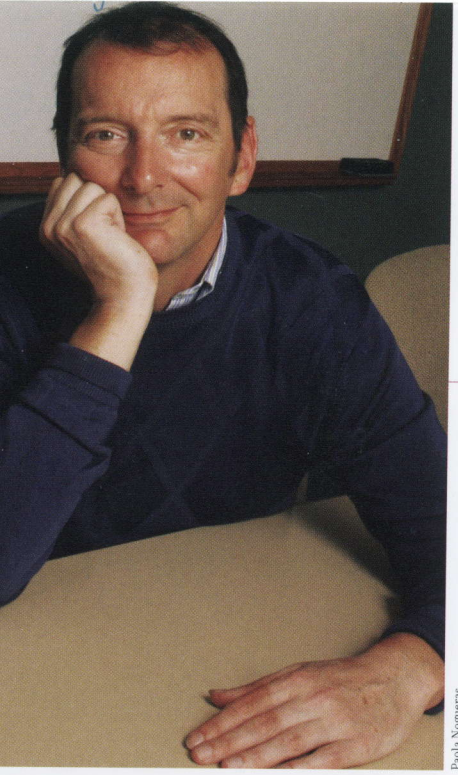
The symposium, entitled "The Chemical Senses and Health," brought together leading academic, industry, and government scientists from around the world. Representing diverse fields of study, they gathered to present the most recent scientific findings on the impact of taste and smell on human health and nutrition.

Jointly sponsored by Monell and the Agricultural and Food Chemistry Division of the American Chemical Society (ACS), "The Chemical Senses and Health" symposium was held at the ACS's national meeting in Philadelphia this past August.

Thirty talks and two days later, it was clear that we are beginning to understand the true importance of the chemical senses. Also, that basic research on taste and smell is increasingly providing a foundation for developments that enhance our health and well-being. The influence of these senses extends across myriad realms, from nutritional and metabolic diseases, such as obesity and diabetes, to diseases of aging, including Alzheimer's disease and osteoporosis.

EXPANDING OUR TASTE PALETTE

Many talks by scientists from or associated with Monell focused on a recent explosion of findings on the sense of taste. Gone are the days when reciting the taste qualities



Paola Nogueras

Michael Tordoff

Spearheading the effort to have calcium recognized as a specific taste quality is Monell behavioral geneticist Michael Tordoff, PhD. By pinpointing genetic differences across various strains of mice that differ in their liking for calcium, he identified calcium-detecting taste receptors on the tongue. Similar receptors had previously been found by others in the gut, bone, brain and other organs, but Tordoff was the first to discover them on the tongues of mice.

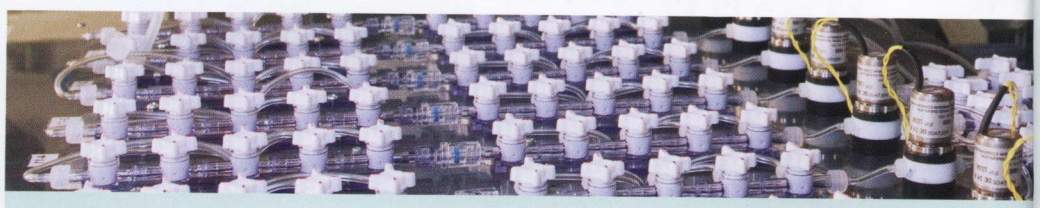
According to Tordoff, humans have genes that code for the same calcium-sensing receptors he found on mouse tongues, making it likely that we too can taste calcium. Taste tests reveal that people can't describe calcium as being particularly like the other known tastes. At high enough concentrations, most people find "it tastes nasty," notes Tordoff and its nastiness is not easily masked. "Many people find calcium-enriched orange juice or vegetables high in calcium unpalatable," Tordoff pointed out.

Continued from cover page

could be boiled down to something easy enough for a second-grader to grasp. We now may have to extend the basic tastes beyond salty, sour, sweet, bitter, and umami/savory compounds to add tastes for fats and even the mineral calcium. And forget about the tongue and mouth being the only place to taste, because it turns out there are also taste sensors throughout our gut.

Calcium Counts Too

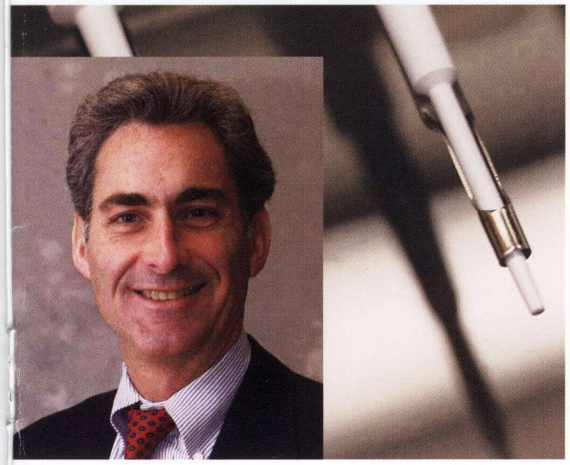
Taste evolved to help us recognize chemicals needed for survival; salty taste, for example, detects the essential dietary element sodium, necessary for many functions throughout the body. Another essential mineral is calcium, required for muscle, heart, and bone health. If we can taste salt, why not calcium?



Sniffing Out Disease

Several Monell-related presentations at the conference discussed how scent detection can be used to sniff out various forms of disease. Kunio Yamazaki, PhD, Koichi Matsumura, PhD and their colleagues were able to train mice to use odors from urine to detect other mice with a form of lung cancer. Working with George Preti, PhD, Michelle Gallagher, PhD, found that the chemical odor signatures emanating from skin of patients with basal cell carcinoma differ from those from healthy skin. Preti used a similar approach to search for a chemical signature in the odors emitted by the bacteria that commonly cause sinus infections.

Identification of disease-associated odors leads to the possibility of eventually developing electronic sensors for early detection and rapid diagnosis of certain disorders. Although electronic olfaction may sound fanciful, A.T. Charlie Johnson Jr., PhD, of the University of Pennsylvania, working with Monell's Alan Gelperin, PhD, and Preti, has already created a prototype "e-nose" that can sense minute amounts of biologically-based odor chemicals. The electronic nose is comprised of microscopic carbon tubes coated with different segments of DNA. Gelperin said, "We expect that our new generation of electronic olfactory devices will help physicians use odorant sensing for disease diagnosis, particularly for skin and lung cancers."



Richard Mattes

The unpleasant taste of calcium-rich foods could help explain why most people do not consume enough calcium to meet their recommended dietary allowances (RDA). Tordoff's findings may ultimately lead to the development of ways to make calcium-laden foods more tasty, perhaps by directly affecting the tongue's calcium-sensing receptors.

A Fat Tooth?

Next on the list is fat. A better understanding of how we detect fat may provide insight into why some people are more or less likely to eat high-fat foods. Monell alumnus Richard Mattes, PhD, now Professor of Foods and Nutrition at Purdue University, reported that humans can detect and make fine distinctions between different types of fats. People are able to distinguish fats comprised of short, medium or long chains as well as those that are saturated, mono-unsaturated and polyunsaturated, for example.

Once fat enters our body, how the body uses that fat has consequences for many of today's pressing health concerns, including obesity, diabetes and cardiovascular disease. Mattes reported that fatty acids detected in the mouth act as signals that trigger changes in the body's fat metabolism. When he gave people fatty foods to chew and spit out (so there would be no gut-related effects), there was an increase of their blood concentration of triglycerides, a risk factor for cardiovascular disease. Clearly, there's more to fat taste than just creaminess.

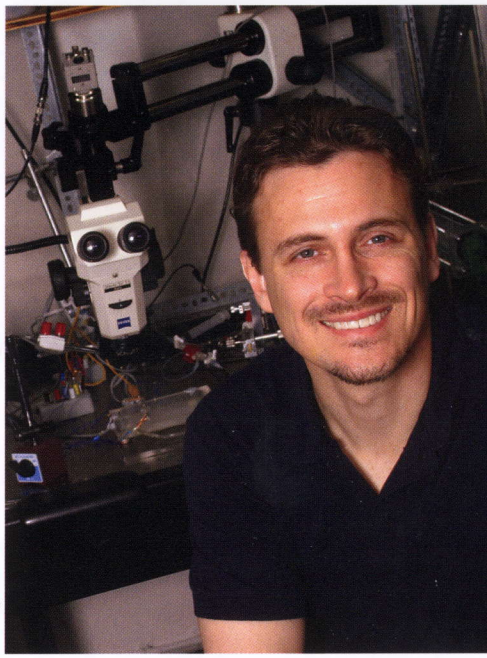
GUT REACTIONS

Good health also depends on having enough protein in the diet, and once again taste is making sure we get what we need. Umami taste may help to ensure that we recognize and eat protein, via specialized receptors that detect protein components such as glutamate or other amino acids. It turns out that these receptors are found not only on the tongue, but also in the gastrointestinal tract. The function and potential clinical significance of "taste receptors beyond the mouth" were discussed in several presentations.

Just as the mouth's taste receptors provide signals about what the body is about to ingest, taste receptors in the gut give the brain information that helps it regulate metabolic and digestive processing. Charles Horn, PhD, a behavioral neuroscientist at Monell, found that amino acids put in the gut of rats triggered nearby nerves to send electrical signals to the brain. He noted that this research might "provide insight into how ingested amino acids act on the gut-brain signaling pathway to help control nutrition, gut function, and feeding behavior."

Monell alumnus and collaborator Kunio Torii, DVM, PhD, of the Japanese-based Ajinomoto Company, Inc., added that the "gut-brain axis is a two-way street." Recent research from his laboratory reveals that once glutamate receptor signals are sent from the gut to the brain, the brain then boosts production of saliva, gastric digestive juices and intestinal mucin to aid digestion of the dietary protein. Torii commented on the significance of this system, pointing out the potential for new approaches to aid in the treatment of digestive and gastrointestinal tract disorders.

Charles Horn



Paola Nogueras

Kunio Torii

Paola Nogueras

Robert Margolskee

The important role that gut taste receptors play in the control of body weight and diabetes was underlined by the 2008 recipient of Monell's Mastertaste-Manheimer Award, Robert Margolskee, MD, PhD, of the Mount Sinai School of Medicine in New York. He found that mice genetically manipulated to lack either a component of the sweet taste receptor, or a compound that is part of the receptor's signaling pathway, had faulty regulation of their blood sugar and insulin levels. "There are whole taste signaling pathways present in the gut that could be manipulated to provide novel treatments for obesity, diabetes, and malabsorption," Margolskee said.

TASTE: GATEWAY TO GOOD HEALTH

Salt intake is linked to high blood pressure and cardiovascular disease in susceptible individuals, adding a sense of urgency to the quest to understand the still-elusive receptor mechanism for this taste quality. Monell biophysicist Joseph Brand, PhD, and many others have spent the past two decades trying to definitively identify the salty taste receptor, a challenging task indeed.

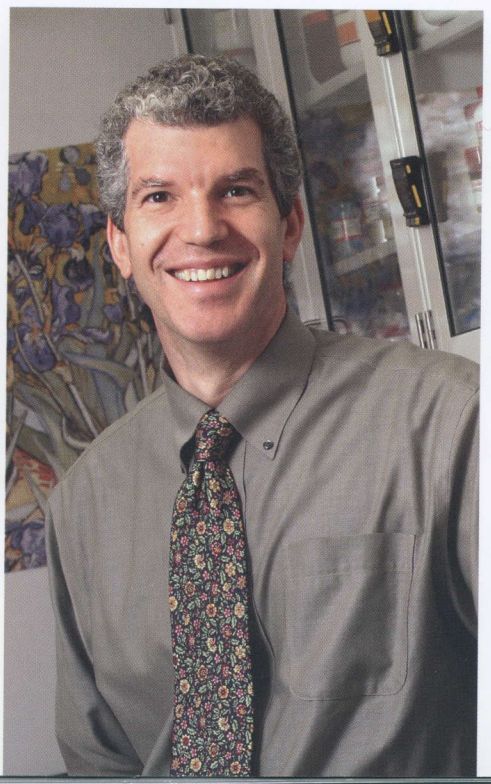
Salty taste is so highly specific for sodium that attempts to find salt substitutes have, for the most part, not proven fruitful. Instead, Brand and his Monell collaborators have focused on enhancing the taste of sodium chloride (table salt) so people can ingest less of the compound without losing the pleasurable aspects of salty taste. By studying the structure of the amino acid arginine, reported in the patent literature to enhance the saltiness of sodium chloride, they identified the part of the arginine molecule responsible for salty taste enhancement. Brand reported that this critical piece is the guanidinium group. He went on to report on other similar molecules that can also enhance the taste of sodium.

Surprisingly, most of the effective enhancers taste bitter on their own, but, when mixed with a sodium salt, their bitterness subsides and the salty taste is amplified. "By enhancing salty taste, these compounds may help at-risk individuals use less sodium without sacrificing the flavor of food," Brand said. "And, because they likely act at the receptor level, these salt-active compounds will be very useful tools for our studies to identify and characterize the salty taste receptor."

We have approximately 25 different bitter taste receptors in our mouth that, unlike the salt taste receptor, are broadly tuned so they can detect thousands of different bitter chemicals in foods. Genetic variations in those taste receptors affect how we experience the taste of food and explain why broccoli can taste bitter to one person while sweet to another, for example. Sensory geneticist Paul Breslin, PhD, found a "very nice relationship" between people's genotype for a bitter taste receptor known as T2R38 and how they rated the bitterness of cruciferous vegetables, such as broccoli and cauliflower. Those people who had two copies of the gene for this variant of the receptor rated some vegetables as significantly more bitter compared to those with only one copy.

Joseph Brand

Paul Breslin



Julia Mennella

Paola Nogueras

Gary Beauchamp

"The sensitivity of the receptor determines the sensitivity of the person," Breslin said, noting that more research is needed to determine whether individual differences in sensitivity influence food choice and subsequent nutrition and health.

That sensitivity to bitterness changes with age. Some children are more sensitive than adults to bitter compounds, studies by Monell developmental psychobiologist Julia Mennella, PhD, reveal. "Children live in a different sensory world than adults—they have a heightened taste preference for salt and sweet and some may have a stronger distaste for bitterness," she said. Small children's keen sensitivity for bitterness can be problematic, as most medicines are bitter; yet, most young children can't swallow capsule forms of drugs that prevent the bitter taste from permeating the mouth. "The unpalatable flavor of many medicines can thwart the benefits of even the most powerful of drugs," Mennella said. Referring to young children who need to take highly unpleasant-tasting anti-retroviral drugs for HIV, she said, "It is such an important issue – if these children miss just one med, it can be life threatening." Mennella urged continued basic research in the science of distaste that could lead to the development of better tasting medications and increased compliance for the smallest consumers.

Another health priority is to find new ways to relieve the inflammation that is linked to many disorders, and a serendipitous sipping of olive oil is helping in that regard. Several years ago, when Monell Director Gary Beauchamp, PhD, was at a food conference in Italy, he sampled an extra virgin olive oil and found it produced the same sting at the back of the throat as

Marking Monell's Birthday

The ACS symposium commemorated the 40th birthday of Monell and scientists from around the world gathered to help the Center celebrate. Many speakers included words of praise about the occasion, including Linda Bartoshuk, PhD, of the University of Florida who noted that she was "excited about Monell's 40th anniversary because Monell symbolizes the import of the chemical senses." Monell has served as a catalyst for hundreds of research scientists in the chemical senses. One alumnus, Richard Mattes, PhD, of Purdue University, began his presentation by recognizing this, saying, "It's a pleasure to help Monell celebrate its 40th anniversary because much of my talk had origins at Monell." Other speakers commented on Monell's unique ability to collaborate with academic, government, and industry scientists. As noted by Mark Zoller, PhD, Chief Scientific Officer of Senomyx, Inc., "Monell is the best example of an academic facility that can bring together industrial researchers, who are in many cases competitors with one another, to talk about science."

When all was done, Monell Director Gary Beauchamp, PhD, looked to the promise of the future, saying, "From the beginning, Monell has been about collegiality, discovery and progress. Our understanding of taste and smell has come a long way since 1968, and we can only imagine where we'll be 40 years from now. But, one thing is certain: Monell will continue to be a major contributor of far-reaching advancements in the science of taste and smell."

Paola Nogueras

Amos Smith, III

does the inflammation-relieving compound ibuprofen. This led him and a number of collaborators, including Monell colleagues Breslin and chemist Amos Smith, III, PhD, to isolate and synthesize the compound in the olive oil that was causing its bite. The researchers found that the olive oil compound, which they named oleocanthal, inhibits the same inflammation-causing molecular pathway as does ibuprofen.

The two compounds have other common pharmacological properties. Smith presented new findings that indicate that, like ibuprofen, oleocanthal stems the formation of key components of the brain plaques and neurofibrillary tangles linked to Alzheimer's disease. As such, "Oleocanthal holds promise as a lead for the treatment for Alzheimer's and other neurodegenerative diseases," said Smith. He pointed out that a Mediterranean diet high in olive oil is linked to low incidence of such diseases, as well as a lower incidence of other disorders, including heart disease, stroke, and certain cancers, thought to be caused, in part, by inflammation.

Taste may even play a role in alcoholism. Monell behavioral geneticist Alexander Bachmanov, DVM, PhD, reported that mice that prefer and consume sweet drinks also prefer and drink more alcohol. This trait has a genetic basis, and genetic mapping reveals that alcohol appears to activate a sweet taste receptor. According to Bachmanov, mice genetically manipulated to lack this receptor no longer prefer alcohol. He suspects that sweet taste receptors influence the preference for alcohol in people as well, mentioning data presented by Mennella in her talk that suggest the liking for sweets is linked to a genetic vulnerability to alcoholism. Bachmanov recognizes that it's not just the effects of alcohol on sweet taste receptors that leads one down the road to drink, and that effects of alcohol on the brain also are a big factor. But he noted that for some people, how they respond to the taste of alcohol "might help tip the balance towards a predilection to over-drink."

Alexander Bachmanov

Overall, the Monell symposium substantiated how extensively smell and taste contribute to human health. "This is an exciting field in an exciting time," notes Beauchamp, who was one of the symposium's organizers. "Basic research on taste and smell is opening up new avenues for the prevention and treatment of many common disorders. There is tremendous potential, because as we continue to study these senses, we find that there is so much more to learn." ▮▮

— Margie Patlak