



# THE MONELL ANOSMIA PROJECT IMPACT REPORT 2019

## Introduction

Individuals with anosmia cannot smell their own children, smoke from a fire, natural gas, spoiled milk or their grandmother's apple pie. Those suffering with anosmia report fear of being exposed to danger, and feelings of anxiety, anger and isolation.

While the two primary causes of anosmia are head injury and some of the same viruses responsible for the common cold, another common cause is aging. Indeed, the number of older Americans with full or partial smell loss and related disorders exceeds 10 million. Some 36% of anosmics report a loss of motivation to eat and 64% report a decrease in enjoyment of food. In an aging population, anosmia poses very serious nutritional and health risks. Currently no established and validated treatments are available for olfactory deficits – patients must adapt, or fail to thrive.

But, restoring the sense of smell – and its power and potential – is within our grasp.

Monell is bringing its 50 years of scientific leadership to create a multidisciplinary research program to discover why smell loss occurs – and to prevent or cure it. When fully funded, Monell's anosmia research will have the potential to impact millions of individuals worldwide who so desperately are seeking answers for an underappreciated affliction. Our discoveries will inform consumer goods companies in their effort to improve the aroma and taste experience of products, supporting healthy aging, and improving the quality of life for all.

The Monell Anosmia Project was founded in 2014 and has grown to become a vital part of the Monell Center's mission to advance discovery in taste and smell. Below, we have summarized the overall impact of the Project through December 31, 2019:

# Anosmia Studies Undertaken	9
# Media Placements	20
Dollars Raised	\$1,749,144
Total # of Donors	301
# of Donors, \$1,000+	22
# Individuals Added to Anosmia Mail List	2469

The Monell Center extends its thanks to you for making a contribution to support the Monell Anosmia Project. Following is a report on our 2019 impact.

## Smell Loss with Aging

It is well documented that aging is associated with higher levels of systemic inflammation. This association led Drs. Hong Wang and Pamela Dalton of Monell to explore whether inflammation in the nasal cavity is related to age-related smell loss. The answer is YES and their results suggest that reducing inflammation in the nasal cavity could help preserve a normal sense of smell.



Dr. Hong Wang is a molecular biologist who investigates how inflammatory processes alter or damage the tissues and cells involved in smell and taste. Dr. Pamela Dalton is a public health psychologist who studies how humans perceive and respond to environmental odors and irritant chemicals.

Many humans experience a decline in their ability to detect and identify odors as they age and the decline becomes especially evident in the fifth decade of life and beyond. There are many contributing factors to age-related smell loss including decades-long exposure to air-borne compounds, some of which may be harmful. There are also physiological changes, including changes to the mucus layer that bathes and protects the olfactory receptors and respiratory tissue in the nose.

Drs. Wang and Dalton are the first scientists to report the effects of aging on the composition of the mucus layer in the region of the nose where the odor receptors are located – the olfactory cleft. This is a difficult area to access because it is deep within the nasal cavity. Twenty-four healthy adult men and women including 12 young subjects (ages 21-40) and 12 elderly subjects (ages 65-80) participated in the study. In addition to collecting and analyzing their mucus, subjects were assessed for their sensitivity to odors (odor thresholds) and their ability to identify odors.

The investigators found that inflammation was higher in the nasal mucosa of elderly subjects with significant elevations in the levels of certain inflammatory compounds. As expected, elderly subjects were less sensitive to odors than younger subjects and had greater difficulty identifying individual odors. Importantly, individuals that had higher levels of several of the inflammatory compounds also exhibited greater smell loss. This is the first study to link smell loss to specific inflammatory compounds. The study will soon be published in a scientific journal.

## Brain and Behavior Changes with Anosmia

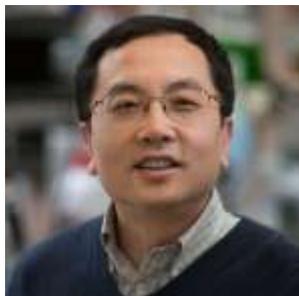
Dr. Johan Lundström is an Associate Member of Monell and a faculty member in Clinical Neuroscience at the Karolinska Institutet in Stockholm, Sweden. He investigates how the human brain is altered by deficits in the ability to smell and the consequences of these neural changes on perception and behavior.



Lundström recently completed and published several large studies with congenital anosmics in Sweden; i.e. those with a lifelong loss of smell. He investigated how cortical areas of the brain that receive large inputs from smell pathways are altered by congenital anosmia. We become consciously aware of our sensory world when the cortex is stimulated. Using magnetic resonance imaging (MRI), he and his team measured the size, shape and functional connections of olfactory cortical areas. They were surprised to discover that the primary cortical area for smell (piriform cortex) did not differ appreciably between congenital anosmics and controls. He speculates that this may be due, in part, to stimulation from sniffing, even if odors cannot be detected. In contrast, a higher level cortical area that processes both olfactory and other sensory input, was significantly altered in congenital anosmics. The preservation of certain smell-related cortical areas in congenital anosmics could mean that someday the sense of smell might be restored if an odor-detecting device could stimulate the brain directly.

At Monell, Dr. Lundström is currently conducting two studies with individuals that have developed smell loss in adulthood. He is examining behavioral and neural approaches to enhance their ability to smell odors. In one study, he is examining several different smell training protocols in people with polyps to determine which approach is best and most efficient at improving smell. In the other study, Dr. Lundström is examining whether non-invasive electrical stimulation of olfactory-related brain areas enhances the sense of smell and how it contrasts with behavioral approaches. He expects to complete these studies by the end of the year.

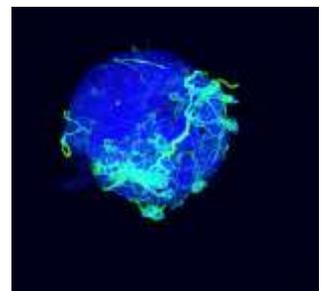
### Restoring the Sense of Smell with Adult Stem Cells



During the past year, Monell Associate Member Dr. Peihua Jiang and his team have continued to optimize approaches for culturing both mouse and human nasal stem cells to determine the culture conditions that allow these cells to grow, expand and differentiate into mature olfactory neurons. The ultimate goal is to develop technology for use in regenerative medicine to restore olfactory function in anosmic individuals who have non-functional nasal olfactory neurons.

Dr. Jiang's team is now able to routinely culture mouse olfactory stem cells that can live for more than 45 days and proliferate into many cells and cell types, including, they believe, olfactory receptor neurons. They will soon be conducting confirmatory fluorescent imaging using olfactory marker protein (OMP). Based on the shape of the cells and other imaging results, they expect positive results. They will then need to demonstrate that the olfactory neurons present in the culture are also functional. One way to do this is to flow odors over the cell culture and record whether the olfactory cells are electrically stimulated by the odors just as they are in the nose. Dr. Jiang expects to accomplish this in 2020.

The team has not yet had success in reliably growing human olfactory tissues from nasal stem cells. The biopsy tissue he receives



**Fig 1. A mouse olfactory organoid.** An organoid (day 45) generated from mouse olfactory tissues was stained with anti-tubulin (neuronal marker, green) antibody, showing multiple well-differentiated olfactory-like neuron (green).

is coming from patients with a long history of nasal respiratory disease. The tissue is scarred and difficult to culture. He is exploring options to obtain biopsy tissue from healthier patients. In the interim, the mouse model holds great promise to be instructive for future human uses in regeneration.

Dr. Jiang begins a new study that is funded by donor contributions to Monell's Anosmia Research Program. He will directly inject into the nasal cavity of mice some of the very same growth factors that he now uses to grow olfactory cells in a culture dish. He hopes that this treatment will stimulate the stem cells in the nose to grow and differentiate into olfactory receptor neurons just as these factors stimulate growth in the culture dish. This is high risk/high return research. It may not work, but it will be very exciting if the method is successful. If so, then the same type of approach can be explored in humans.

### Identifying Genes that Cause Smell Loss

Monell Associate Member Dr. Joel Mainland is completing the second year of his two-year National Institutes of Health (NIH) grant to identify genes that cause smell loss in individuals from birth (congenital anosmia). Identifying genetic alterations that lead to anosmia can lead to the development of gene therapies that restore the sense of smell.



Over 100 altered genes have been discovered in patients born without hearing and over 200 genes are implicated in patients born without sight.

These numbers are in stark contrast to the number of genes implicated in congenital anosmia. So far, researchers have identified only two genes (CNGA2 and TENM1) associated with congenital smell loss. Our lack of understanding of congenital anosmia prevents many anosmics from knowing if their condition is acquired or genetic, temporary or permanent, and provides them little hope for diagnosis and treatment.

The first year of the grant focused on recruitment and data collection. The Mainland team recruited 18 families from around the world who reported that at least two members of the family had been anosmic since birth. Using families allows researchers to more readily discern patterns of gene changes that may be causal for congenital anosmia. The second year is focusing on data analysis. The Mainland group uses whole exome sequencing, which captures all of the genes involved in protein synthesis. Even with narrowing genetic analyses to this portion of the genome, more than 20,000 genes are analyzed for each individual in the study.

Thus far, three gene families have emerged that are associated with congenital anosmia: cytochrome P450, solute carrier and ZHX protein gene families. These genes serve many functions in the body. The cytochrome P450 enzymes are known to have important functions in the nasal mucus. Certain enzymes metabolize odorants and thus affect how odors are perceived. Other enzymes serve to metabolize and detoxify compounds that are inhaled. Solute carrier proteins are involved in transporting compounds into and out of cells such as ions, glucose and hormones. Their specific role in olfaction is not well understood. The same can be said for the ZHX family of genes.

This research project expands the list of genes that are potentially involved in smell loss. However much research remains to be done to determine whether these genes are directly involved in the development of congenital anosmia.



**GCCR**

Global Consortium for  
Chemosensory Research

### COVID-19 and Smell Loss

Coronavirus (COVID-19) is a virus that causes respiratory illness in people and is extremely contagious. Cases of COVID-19 began to emerge in late 2019, becoming a world-wide pandemic by March 2020. Several Monell scientists are part of a Global Consortium for Chemosensory Research (GCCR) that mobilized in March 2020 to coordinate world-wide crowdsourced research to understand the reports of the COVID-19 chemosensory issues. As a community concerned with smell loss, we are interested in the work of the GCCR because it has the potential to inform knowledge about all types of post-viral anosmias, and potentially other anosmias. The GCCR

includes medical professionals, scientists, researchers, and health advocates from around the globe. Monell's Dr. Danielle Reed sits on the leadership team.

### ITTSD Conference

Monell hosted the conference, Identifying Treatments for Taste and Smell Disorders (ITTSD) in November 2018. The conference was chiefly funded by the National Institutes of Health-National Institute on Deafness and other Communication Disorders (NIH-NIDCD) – the leading source of federal funds for basic and translational research on taste and smell function and dysfunction. This was a first-of-its kind event that included multiple internationally recognized research groups and engaged patients and clinicians as active participants. The goal of the conference was to identify gaps and opportunities in the research and to create a roadmap for the future.



At the closing of 2019, the conference organizers were completing a White Paper to summarize the recommendations that came out of the conference, slated for publication in 2020.

Building on one of the recommendations of the White Paper to encourage anosmia patient advocacy groups to form, Monell hosted a dinner in Washington DC in November of a group of interested patient advocates. This group has since coalesced more formally and is in early stages of forming a US-based advocacy organization.



### Website

The anosmia section of Monell's website continues to be a heavily used source of information for the anosmic community. In 2019, 3,570 people visited the Monell website's anosmia landing page.

## Anosmia Awareness Day

On Anosmia Awareness Day 2019, we encouraged our community to set up Facebook campaigns to raise awareness of and raise funds for anosmia research. Through this campaign, we saw:

- 27,000+ people reached through Facebook fundraisers
- 101 donations received for anosmia research
- \$4,500+ raised for anosmia research

## Social Media

We continue to use Monell's social media (primarily Facebook and Twitter) to promote anosmia-related activities. These efforts help to grow our mail list and keep Monell and anosmia research front and center.

## Anosmia Newsletter

2019 saw the continuation of the anosmia newsletter we debuted in 2018. Our audience remains interested in the content: the newsletter consistently shows higher open and click-through rates than newsletters from non-profits typically see.

## Many Thanks

Thank you for being part of the solution for the millions living life without smell. We are proud of our growing anosmia research program. It is developing steadily and thoughtfully, building on Monell's 50-year history and the scientific expertise of our researchers. Because of the strong support we have received, Anosmia research is now a key pillar of Monell's *Sensing the Future* campaign and of the Monell Strategic Plan.

