Expedition Monell: IMPROVING GLOBAL HEALTH

ANNUAL REPORT 2018-2019
We Are the Explorers

Our Values

**COMMITMENT:**
We view basic science as the foundation of discovery.

**COLLABORATION:**
We practice interdisciplinary science with diverse partners to inspire new perspectives and discoveries.

**OPEN COMMUNICATION:**
We share our knowledge widely to impact global health and well-being.

**MENTORSHIP:**
We train the next generation of chemosensory scientists to assure a bright future.

**BROAD IMPACT:**
We work across sectors to advance science that solves problems.

Our Mission

*Improve health and well-being by advancing the scientific understanding of taste, smell and related senses.*
This was a momentous year for Monell, as we celebrated our 50th year as a world-renowned leader in groundbreaking chemosensory research.

Looking back, we recognized the impact of Monell’s discoveries in improving human health. Techniques pioneered by Monell to biopsy and culture living human taste cells are being used today to discover new ways to reduce the bitterness of pediatric pharmacologic formulations so more children will take their life-saving medicines. We identified “taste” receptors in the nose and gut with therapeutic potential for treating such diseases as diabetes, obesity, and intestinal parasites. And research showing that most of the salt we eat comes from commercially-prepared foods led to new Federal Drug Administration guidelines lowering the amount of salt in manufactured and restaurant foods -- a major step in addressing our nation’s high rate of heart disease. Those are just a few exciting examples.

Inspired and energized by that look back, we now look ahead to our next 50 years.

Our vision from the vanguard:
A future where Monell’s discoveries in taste, smell, and related senses lead to early detection, prevention, and treatment of disease.
One in which we assure the healthy function of these essential senses throughout a person’s lifetime.
A future where this vital work improves health and well-being for every one of us, everywhere.

This year, Monell embarked on a strategic planning process that prioritizes four research aims. Our roadmap for the future aligns Monell’s chemosensory science with the allied fields of disease prevention and diagnosis, health promotion, and regeneration of the senses through innovative collaborations and partnerships in academia and industry. You’ll learn more in the following pages.

For example, through our new collaborative grant program with Thomas Jefferson University, we are making progress in four translational research areas, combining Monell’s research on taste and smell with Jefferson’s complementary strengths in clinical neurosciences to address intractable health problems in novel ways. Our shared goal is to accelerate the translation of basic science on taste and smell into real improvements in human health.

Roadmap in hand, we are on an expedition to explore new frontiers to improve public health.

Thank you for joining us on our remarkable journey. Together, we are creating a healthier world.
Exploring Taste and Smell in Sickness and in Health

STRATEGIC AIM: DIAGNOSE AND TREAT DISEASES

Monell is advancing new technologies to monitor volatile chemicals that signal disease and harness solitary chemosensory cells to target innate immunity.

One way people and animals stay healthy is by avoiding those who are sick. Two studies this year extend the scope and significance of personal odors as a source of information about an individual’s health and advance Monell’s work in detecting illness.

• Chemical ecologists Bruce Kimball, PhD, and Stephanie Gervasi, PhD, partnered with behavioral biologist Gary Beauchamp, PhD, to show that not only do bodily odors signal disease, but odors of healthy animals change when they share an environment with sick ones.

The researchers injected mice with a non-infectious bacterial toxin that causes inflammation and activates the immune system, then housed them in cages with healthy animals. In a behavioral test, “sniffer” mice trained to differentiate between healthy and sick animals demonstrated that mice housed with the toxin-injected mice smelled more like sick ones than otherwise healthy animals. These findings were also supported by chemical and statistical analyses.

Odors that indicate health status could be important biomarkers for detection and diagnosis of disease and may lead researchers to develop new disease detection techniques, such as electronic sensory devices.

• Animals, including humans, communicate via smell. Monell research has shown that the urine of sick animals contains chemical cues that healthy animals can detect. Bruce Kimball, PhD, sensory neuroscientist Johan Lundstrom, PhD, and collaborators at the Karolinska Institute in Sweden reported that acute inflammation can cause changes in human urine odor that healthy people are able to detect in behavioral smell tests. These findings were supported by chemical analysis.

Johan Lundstrom, PhD
Monell scientists have in recent years identified taste receptors beyond our mouths – in the nose and intestine – that protect the body from infection by detecting invaders and triggering immune responses. Building on this work, two new studies shed further light on the molecular mechanisms that underlie this immune response.

- Inflammatory bowel disease (IBD) is a debilitating immune-related condition affecting more than 1.4 million Americans. Molecular biologists Hong Wang, PhD, and Robert Margolskee, MD, PhD, and colleagues at Shanxi University and Zhejiang University in China explored the role of the taste-signaling protein gustducin in IBD. In a mouse model of severe colitis, the team found that animals lacking functional gustducin mounted an excessive inflammatory response with severe tissue damage, showing just how critical the protein is for protecting a healthy gut. Understanding the taste-signaling pathways in IBD at the molecular level could point to new treatment strategies.

- Molecular biologist Liquan Huang, PhD, partnered with colleagues at Zhejiang and Jilin University in China on a gene expression study describing how cells in the lining of the gut detect the parasite *Trichinella spiralis* and initiate signaling an immune system response. Modulating the signaling components may lead to new ways to combat infection by these ubiquitous parasites that pose a serious health risk to humans and animals worldwide. This project is among Monell’s broadening research on immune health sentinels in the intestinal tract, which also includes investigations by associate member Peihua Jiang, PhD, on the succinate receptor expressed in gut tuft cells that detects other infectious microbes.
The Big Data Approach –
Matching Taste Preferences to Make Healthier Food Choices

Sensory nutrition is an emerging field that examines how sensation affects what we choose to eat or drink and how these choices affect our health. Do personal differences in the experience of taste drive overconsumption of certain foods? Can we predict who will like a particular food and who truly can’t resist it?

Monell researchers are mining “big data” through machine learning and genome-wide association studies (GWAS) to integrate knowledge from sensory science with nutrition and dietetics to promote good health.

- Monell behavioral geneticist Danielle Reed, PhD, and olfactory neurobiologist Joel Mainland, PhD, partnered in a text-mining analysis of customer reviews on Amazon to gain real-world insight on the food choices we make. In this first large-scale study of food choice beyond the artificial constraints of laboratory taste-testing, they analyzed nearly 400,000 reviews of 67,000 commercially available food products posted by 256,000 Amazon customers over 10 years. Using a statistical modeling program, the team identified words related to taste, smell, healthfulness, among other categories and computed the number of reviews that mentioned each.

The findings revealed that many people find the foods in today’s marketplace to be too sweet. Nearly one percent of reviews, regardless of food type, used the phrase “too sweet.” Sweet taste was mentioned in 11 percent of reviews (three times more often than bitter taste), and over-sweetness was mentioned 25 times more often than under-sweetness.

In addition to advancing the field of sensory nutrition, such insights on preferences can help the food and beverage industry deliver products that make it easier for consumers to reach their dietary goals without sacrificing flavor.
• In seeking to understand the biological factors that drive us to consume sugar and create strategies to reduce it, scientists often look to the known taste receptor genes. New findings from Monell suggest broadening the search.

Danielle Reed, PhD, and sensory scientist Paul Breslin, PhD, collaborated with colleagues in Australia and the UK to perform GWAS of perceived intensity and sweetness of sugars, liking of sugars, and total intake of sugars on more than 176,000 individuals. While they found genetic evidence for the involvement of the brain in sweet taste perception and sugar intake, the researchers saw the strongest association for the intake of sugars with the \textit{FTO} gene, which is linked to body mass index, obesity, and diabetes, rather than being directly involved in sugar detection.

• Breslin, Reed, and their Australian colleagues also explored the genetic underpinnings of bitter taste, which arises when certain chemicals come into contact with bitter receptors on the tongue. Due in part to genetic variations in bitter receptors, people perceive bitterness differently, which can affect their food preferences and intake. Bitter receptors are also found in tissues beyond the tongue, including the airways and gut. Previous Monell research has shown that the ability to taste the bitter compound phenylthiocarbamide influences susceptibility to respiratory infections.

Given the importance of the genetics of bitter taste, the team extended the scope of one of its previous GWAS that found associations for perceived bitterness of quinine, one of the first anti-malarial drugs. The latest study is the first evidence linking a bitter taste receptor to perception of caffeine and confirms associations for quinine and other bitter compounds. Researchers now have a more solid foundation for determining the biological pathways linking perception of bitter substances with the cellular processes underlying it, which may assist with personalized nutritional strategies and precision medicine.
The Road to Regeneration

STRATEGIC AIM:
TACKLE LOSS OF SMELL AND TASTE

Monell researchers seek to restore or prevent loss of smell and taste throughout a lifetime using regenerative medicine and behavioral strategies.

Stem cells – the powerhouse precursors to every type of cell in the human body – hold great promise for halting or restoring sensory loss from genetic or degenerative causes. Historically, Monell has been a leader in identifying, developing, and using cultured smell and taste stem cells for basic science. The end goal is to shape the process by which stem cells differentiate into mature taste and smell receptor cells in order to restore sensory loss.

Monell researchers have significantly advanced this work in taste cells, with their breakthrough discovery of taste stem cells and their later development of a method to grow organoids containing taste cells.
This year brought important discoveries about the molecular mechanics of smell cells. Understanding olfaction at the molecular level provides a foundation for future studies on restoring smell loss and strategies to keep a healthy sense of smell at all stages of life.

- Olfaction is, in essence, a complex conversation of molecular signaling between the nose and the brain. It begins in the nasal mucus, when an airborne chemical molecule binds with an olfactory receptor embedded on a nerve cell within the nose. The receptors are located on cilia — extremely thin, threadlike structures less than 0.000004 inches in diameter, about a thousand-fold narrower than a human hair. Cell physiologist Johannes Reisert, PhD, and computational neuroscientist Jurgen Reingruber, PhD, of the École Normale Supérieure in Paris, used mathematical modeling, electrophysiology, and computer simulation to explain how cells convey the molecular signals resulting when an odor has bound to its receptor in such extremely constricted spaces as the olfactory cilia.

The odorant-receptor binding starts a complex cascade of molecular signals inside the olfactory cell. Pores in nerve cell walls, called ion channels, allow positively and negatively charged molecules (ions) to flow in and out of the cell, changing its overall electrical charge and ultimately stimulating the cell to send a signal to the brain. Analyzing these ion dynamics, the researchers showed how olfactory cells produce the correct ion currents to elicit an electrical signal while also maintaining the healthy structure and function of the cilia. In addition to shedding light on cellular signaling in olfaction, the findings will inform future studies in other strictly confined spaces of the nervous system, such as small nerve endings, where damage is associated with neurodegenerative diseases like Alzheimer’s.

- Despite the critical role of olfactory mucus in our sense of smell, little is known about its molecular make-up and how it changes throughout life. Cognitive psychologist Pam Dalton, PhD, and Monell adjunct member Noam Cohen, MD, PhD, of the University of Pennsylvania, analyzed the proteome — all expressed proteins — of nasal mucus from a group of young (21 to 40 years old) and elderly (65 to 80 years old) people and correlated the levels of mucus proteins with an individual’s olfactory sensitivity. Among their key findings: 20 of the almost 3,000 identified mucus proteins show age-related changes, and mucus from elderly participants contained high levels of inflammation-related proteins, including those known to drive the accumulation of amyloid plaques, which can cause a decline in cognition associated with Alzheimer’s disease.

With this comprehensive catalogue of nasal mucus proteins, researchers are in a stronger position to understand age-related decreases in olfaction and how it affects quality of life. The catalogue may also help identify biomarkers for diagnosing Alzheimer’s and other neurodegenerative disorders.
From Bench to Bedside – Monell and Jefferson

In 2018, with a shared vision of improving human health, Monell and Thomas Jefferson University signed an Agreement of Cooperation with the intent of building translational research opportunities. At the end of that year, the institutions announced an innovative funding mechanism – five collaborative pilot grants for research projects that combine Monell’s expertise in the senses of taste and smell with Jefferson’s strengths in the basic and clinical neurosciences. The projects are:

• People with neurodegenerative disease often lose their sense of smell long before other symptoms appear. One team is asking if testing for smell loss can lead to early-stage diagnosis of amyotrophic lateral sclerosis, also known as “Lou Gehrig’s disease.”

• Children often spit out their bitter-tasting oral medicines. One team is exploring how to block many different bitter receptors at the same time by targeting universal molecular mechanisms inside all bitter taste cells.

• Patients with sinonasal inverted papilloma—a rare, cancer-like disease of the nose—require frequent, invasive treatments and follow-up screenings. One team is examining whether measuring certain compounds released by the papilloma tissue could serve as a less-invasive diagnostic to monitor recurrence of the disease.

• Cancer chemotherapy can negatively alter taste perception, which in turn can affect a patient’s diet, nutrition, and overall health. By looking at immune system pathways that have a similar effect on taste, one team is seeking ways to improve the nutritional health and recovery of patients with cancer.

• Little is known about how sour taste is perceived. One team is testing an idea to verify a new sour receptor. The findings could help identify ways to change the off-putting sour taste of certain healthy foods and medicines.
Accelerating Translational Research

An entrepreneurial environment that supports collaboration with industry partners is fundamental to Monell’s ability to translate its discoveries into real-world health solutions in real time. Our unique corporate partnership program has become a model for academic-industry collaborations within an atmosphere of unbiased scientific excellence and transparency, resulting in tools and knowledge that have helped to solve problems and create value within many of the world’s most innovative global companies in the food, flavor, fragrance, ingredient, and pharmaceutical industries.

Pairing Monell’s basic research expertise, intellectual property, and the nimble flexibility of an independent research institution through partnerships with innovative start-ups and small companies with specialized technologies leads to combined entities greater than the sum of their parts.

This year, two commercial-academic partnerships funded by grants from a federal small business technology grant program stimulated technological innovations to improve human health:

- **Scientists at Monell** – pioneers in human taste cell culture technology – and Discovery BioMed, Inc. – experts in validating and screening with cell-based assays – are collaborating to develop next-generation screening technologies to identify bitter taste blockers. Ultimately, the work may help improve the taste of nutritious plant-based foods and palatability of lifesaving oral medicines.

- **Health Via Modern Nutrition (HVMN)** – a nutrition product producer – is partnering with Monell to better understand the sensory impact of the key ingredient in its nutritional beverage designed to improve muscle recovery after injury. The sensory properties of the ketone ester compounds in the drink, and their biological basis, have not been previously studied. This collaboration holds potential for advancing basic sensory research, as well as identifying targets for modulating bitter taste and developing a better product for healing muscle injuries.

### Université Côte d’Azur, Nice, France

Monell’s newest academic affiliate is a premier institution for the chemical analysis and synthesis of fragrance chemicals. The partnership originated in research collaborations to explore the molecular underpinnings of sweet taste, with the goal of designing new sweet-taste modulators which ultimately could help address the global health challenges of diabetes- and obesity-related illnesses. The relationship expanded this year with a joint international tele-symposium to share expertise and spark new research collaborations. The affiliation will blossom next spring into a combined sensory research, public outreach, and scientific training project at the 2020 Pennsylvania Horticultural Society Flower Show. In keeping with the show’s theme of “Riviera Holiday”, teams of Université Côte d’Azur students will compete to design Monell’s educational booth based on lavender, the floral hallmark of Provence and the French Riviera. Exploring such sensory related questions as why the scent of lavender can be so calming, the winning student team will travel to Philadelphia and join Monell researchers at the flower show and in the laboratory to learn sensory research techniques and how Monell communicates science to the public.
The work of the Monell Chemical Senses Center is supported from three principal sources. One is government funding, consisting chiefly of competitive federal grants with the National Institutes of Health (NIH) the primary funder. Additional funds come from corporate sponsorship fees and industry-sponsored basic or translational research. Finally, the Center receives significant support from generous gifts and grants from private individuals and philanthropic foundations. In 2018-2019, total revenue increased by nearly $1 million, including increases of 23 percent in government funding from an expanded portfolio of NIH grants, and 10 percent in philanthropic income, largely associated with the 50th Anniversary campaign. With a modest expense increase of four percent driven by the additional grant revenue, the Center posted a surplus of $760,000, a substantial increase over last year. In 2019-2020 we expect the increase in federal funding to continue, along with a corresponding increase in our research activities. The Center is most grateful for the continued generosity of the Monell Foundation, the Center’s founding funder and largest private donor.
AS WE CONCLUDE OUR 50TH ANNIVERSARY YEAR, WE ARE PLEASED TO ANNOUNCE Sensing the Future: The Campaign for Monell @ 50.

This fundraising initiative propels the Center into our next half-century of discovery. Through this campaign, we will raise $12 million to improve health and well-being by advancing the scientific understanding of taste, smell, and related senses.

Monell has been quietly laying the groundwork for this campaign and we are delighted to share that at the close of the 2018-2019 year, we are 77 percent of the way to our fundraising goal. Because of this strong support in the early stages of the campaign, we are well on our way to reaching our goals.

The campaign will be successful through many gifts of all sizes. You can play a vital role.

To discuss a gift to the Sensing the Future campaign, please contact Jenifer Trachtman, Director of Development, at 267-519-4715 or jtrachtman@monell.org. Visit www.monell.org/giving to make a secure online contribution today.
MONELL CENTER DONORS

One of our greatest pleasures is to THANK YOU – the friends, alumni, employees, foundations, and businesses – who support Monell’s research mission through philanthropic gifts and grants. Below, we gratefully recognize donors of $1,000 or more during the academic year (July 1, 2018 to June 30, 2019).

MONELL IS MY SECOND SCIENTIFIC HOME

“I spent a year at Monell but the greatest impact Monell has had on me, and the reason I am a firm supporter, is because of the opportunity I’ve been afforded to collaborate with Monell scientists over the last 30 years.”

ANDREW SPIELMAN, DMD, PhD

Monell Circle ($1,000+)

Todd Abraham
James J. Albrecht
Altria Group
Amiga Fund
Anonymous
Gary and Fay Beauchamp
Robert Bedoukian, Bedoukian Research
Raymond and Barbara Bendure
Doug L. Bayley
Richard L. Berkman
Mary Bertino
Paul Breslin
Lyn M. Buchheit
Robert H. Cagan
Susan W. Catherwood
The Charina Endowment Fund
Carol Christensen
Darlene Clark
Jennifer Douglas
Robert Eilerman
The Charles E. Ellis Trust
Gallagher
Bill & Melinda Gates Foundation
Neil Hammerstrom
Robert W. Harkins
Haverford Trust Company
Herman Goldner Co, Inc.
John and Teresa Hickey
Howson & Howson
Jade Yoga
Janssen Global Services, LLC
Philip S. Johnson
Thomas Jefferson University
Kaleidoscope of Hope Foundation

IDENTIFYING TREATMENTS FOR SMELL AND TASTE DISORDERS

“After attending Monell’s conference on smell and taste disorders, it became clear that there is not yet widespread appreciation of and funding for this area of research, and I decided I wanted to step forward and make a contribution.”
Our long-standing commitment to Monell began with my family’s essential oils and vanilla company and has grown over the years, primarily because I firmly believe in Monell’s research and its impact on healthy aging.”

KUMIKO NINOMIYA, PhD

Christine Kelly
Kerry
Robert J. Kleberg Jr. and Helen C. Kleberg Foundation
Kreischer Miller
John N. Labows
Alan I. Leshner
Harry Levine
Dale Lowry
William J. Ludlum
The Christopher Ludwick Foundation
David and Kathy Macnair
Stephen R. Manheimer
Robert F. Margolskee
The Ambrose Monell Foundation
Ambrose K. Monell
Maurizio J. Morello
Grace Nejman
Kumiko Ninomiya
Yuzo Ninomiya
Lee O’Neill
PWP Video
Sam Rao
Nancy E. Rawson
Dwight R. Riskey
Marjorie Rosner
Joseph Salkowitz
Gail E. Seygal
John Shapiro, Shapiro-Silverberg Foundation
Louise Slade
Lewis S. Somers, 4th
Andrew Spelman
Vernekoff Foundation
Zelda R. Wasserman
The Wawa Foundation
Judith Wellington
Hiroko Yamazaki
Tomoko Yamazaki
William N. Zeiger

Every effort has been made to ensure the accuracy of these lists. If we have inadvertently misspelled or omitted your name, please accept our apologies and notify Jenifer Trachtman. To view a full list of donors and matching gift companies, and to see consistent, long-term support of the Monell Center, consecutive year donors, and donors by affinity group, please visit www.monell.org/thankyou.
BOARD OF DIRECTORS

David Macnair, PhD (Chair)
Vice President (retired), Global Petcare Research & Development, Mars Incorporated

Robert F. Margolskee, MD, PhD
Director and President, Monell Chemical Senses Center

Richard L. Berkman, Esq
Of Counsel, Dechert LLP

Kevin Foskett, PhD
Isaac Ott Professor and Chair, Department of Physiology, Perelman School of Medicine, University of Pennsylvania

Deborah L. Hayes
Senior Vice President, Corporate Affairs, Federal Reserve Bank of Philadelphia

Philip Johnson, Esq
Senior Vice President (retired), Intellectual Property Policy & Strategy, Johnson & Johnson

Stephen R. Manheimer
Vice President, Enzymology

Ambrose K. Monell
President and Director, The Ambrose Monell Foundation & The G. Unger Vetlesen Foundation

Maurizio Morello, Esq
Director, The Ambrose Monell Foundation & The G. Unger Vetlesen Foundation

Dwight R. Riskey, PhD
Principal, Riskey Business Solutions, LLC

Louise Slade, PhD
Principal, Food Polymer Science Consultancy

BOARD OF DIRECTORS EMERITUS

Arthur K. Asbury, MD
Van Meter Professor of Neurology Emeritus, University of Pennsylvania

Susan W. Catherwood
Board Member, The Glenmede Trust, N.A.

Alan I. Leshner, PhD
Chief Executive Officer Emeritus, American Association for the Advancement of Science

INTERNATIONAL ADVISORY COUNCIL 2018

Todd Abraham, PhD (Chair)
Senior Vice President (retired), Research, Development & Quality, Mondelez International

James J. Albrecht, PhD
Consultant to Food Industry and Agribusiness

Carlos Barroso
President, CJ Band Associates

Margaret Bath, PhD
Principal, Strong Harbor, LLC

Ahmet Baydar, PhD
Executive Vice President (retired), Flavor & Fragrance Research & Development, International Flavors & Fragrances

Larry Clark, PhD
Director, National Wildlife Research Center, USDA-APHIS-WS

Robert Eilerman, PhD
Senior Vice President (retired), Global Flavor Science & Technology, Givaudan Corporation

John D. Fernstrom, PhD
Professor of Psychiatry, Pharmacology & Behavioral Neuroscience University of Pittsburgh School of Medicine

Takeshi Kimura, PhD
Member of the Board & Corporate Vice President for Research & Development, Ajinomoto Co., Inc.

Shawn M. Marcell
Chairman & CEO, ReadCoor, Inc.

Charles M. Peterson, MD, PhD
Senior Advisor, Geneva Foundation in support of Congressionally Directed Medical Research Programs (CDMRP), U.S. Army Medical Research and Materiel Command

Edmund Pribitkin, MD, MBA
President, Jefferson Medical Group Chief Medical Officer, Thomas Jefferson University Hospital Thomas Jefferson University and Jefferson Health

Arthur H. Rubenstein, MBBCh
Professor of Medicine, Division of Endocrinology, Diabetes and Metabolism, Perelman School of Medicine, University of Pennsylvania

Gary J. Schwartz, PhD
Professor of Medicine, Neuroscience, and Psychiatry & Behavioral Sciences, Albert Einstein College of Medicine

Judith Wellington, PhD
President and CEO (retired), Clay Center for the Arts and Sciences
Over the course of the 2018-2019 year, Monell celebrated its 50-year legacy of excellence with initiatives highlighting our important contribution to science and health. Many thanks to all whose presence at our events and charitable contributions helped to honor our first half-century.

Monell 50 years 1968-2018

Special thanks for logo design to Susan Kare, a colleague of renowned artist Paul Rand who designed our original, iconic “M” logo.

The anniversary year kicked off with a proclamation from the City of Philadelphia naming December 15th – the day that the Monell Foundation approved its very first grant to establish the center – Taste and Smell Day. Pictured is State Representative James Roebuck with Robert Margolskee.

A snowstorm could not keep guests away from Dinner and a Show, Monell’s capstone 50th anniversary event featuring a special sensory menu prepared by local celebrity chef Daniel Stern and a live performance by the hosts of the award winning food podcast, Gastropod.

Hundreds turned out for the Identifying Treatments for Taste and Smell Disorders conference that Monell hosted with the University of Florida and the University of Colorado.

The 50th celebration concluded with an alumni reunion. Bob Cagan, one of Monell’s first faculty members, speaks to alumni, friends, and current staff.

Susan Kare, daughter of Monell Founder Morley Kare and noted graphic designer, helps Robert Margolskee and Gary Beauchamp blow out the candles on Monell’s 50th birthday cake.