COLUMBIA | Zuckerman Institute

MORTIMER B. ZUCKERMAN MIND BRAIN BEHAVIOR INSTITUTE

# Three Zuckerman Institute Investigators Receive Inaugural Herbert and Florence Irving Professorships

~ Their work promises to advance cancer research, by building bridges with neuroscience and cellular development. ~

**Date**: March 3, 2021
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NEW YORK — Columbia University has established three Herbert and Florence Irving Professorships at the Mortimer B. Zuckerman Mind Brain Behavior Institute. These prestigious professorships form the bedrock of the Herbert and Florence Irving Cell Research Program at the Zuckerman Institute, which was established as part of the transformative, nearly $1 billion bequest Columbia University and NewYork-Presbyterian received in 2017 from the late Herbert and Florence Irving. Leveraging the Zuckerman Institute's strength in the molecular and cell biology of neurons, the Irving Cell Research Program will catalyze the investigation of a fundamental scientific question with strong implications for cancer: What are the biological mechanisms governing the life and death of different cell types?

"My co-directors and I are incredibly honored to be a part of this pioneering gift from the Irvings, which affords us the rare opportunity to pursue one of the most mysterious aspects in cellular biology," said Rui Costa, DVM, PhD, director and CEO of the Zuckerman Institute. "Why do some cells last a few days and others like neurons last a lifetime? Understanding the unique aspects of neurons that allow them to last a lifetime, while other cells are born and die on a regular basis, could dramatically transform our understanding of the most aggressive forms of cancers, such as neuroblastomas, moving us toward treatments and eventual cures."

Zuckerman Institute Principal Investigators Elizabeth Hillman, PhD, Stavros Lomvardas, PhD, and Gary Struhl, PhD, are the inaugural recipients of the Herbert and Florence Irving Professorships. The significant strides they have made in their respective fields of biomedical engineering, molecular biology and genetics, coupled with their highly collaborative and cross-disciplinary approaches to research, hold great promise for advancements in cancer research.

"It is a privilege to award the inaugural Irving Professorships to this highly accomplished trio of scientists," said Dr. Costa. "At the Institute, we focus great attention not only in attracting talent but also in supporting and developing that talent. These Professorships permit scientists to perform transformative science."

Dr. Hillman, a professor of biomedical engineering at Columbia's Fu Foundation School of Engineering and Applied Science, specializes in developing imaging systems that reveal the behavior of living tissues.

“Seeing is believing,” said Dr. Hillman, who is also a professor of radiology at Columbia’s Vagelos College of Physicians and Surgeons. “There is just so much left to learn about biology and medicine, and we love to make new methods that let us see things that we just couldn’t see before.”

One of the techniques she has pioneered, wide-field optical mapping (WFOM), enables imaging of neural activity and blood flow in the living mouse brain. In a recent collaboration with Peter Canoll, MD, PhD, a professor of pathology and cell biology at Columbia’s Vagelos College of Physicians and Surgeons, she applied this method to provide unprecedented views of spontaneous seizures originating from the tumor’s borders and showed that seizures drove vasoconstriction within the tumor. The study demonstrated how WFOM can provide a platform for the rapid evaluation of new therapies for seizure suppression and tumor treatment.

Another of Dr. Hillman’s inventions is Swept Confocally Aligned Planar Excitation (SCAPE) microscopy. Licensed to Leica Microsystems, SCAPE creates high-resolution, three-dimensional images of living organisms.

Dr. Hillman has helped researchers all over the world start using SCAPE. For instance, she worked with Columbia’s Center for Radiological Research to incorporate SCAPE into its heavy ion beamline to be able to study the effects of radiation therapy on tumor pathophysiology.

She has also developed the handheld Medi-SCAPE. Capable of taking clinical histological images of intact, living tissues, this technology could guide surgical removal of tumors in the brain and spine.

“If you can judge what the tissue is without cutting it out, surgery can be more precise, effective and efficient,” said Dr. Hillman.

Dr. Lomvardas, a professor of biochemistry and molecular biophysics and neuroscience at Columbia’s Vagelos College of Physicians and Surgeons, studies the olfactory system. Hundreds of human genes are dedicated to the expression of olfactory receptors, and each receptor is responsible for detecting a different odiferous chemical. Somehow, each olfactory neuron expresses one and only one type of receptor, chosen randomly.

“Over the years, we’ve discovered a unique and amazing mechanism responsible for this process,” said Dr. Lomvardas. Strands of DNA form loops, creating compartments that silence the genes. One random gene escapes and is expressed, while also preventing any others from escaping.

But this looping can cause damage to the DNA, and proteins must come along to repair it.

“So there is this unexpected but close relationship between protecting DNA from mutagenesis and our sense of smell,” said Dr. Lomvardas. “This is very, very exciting for us.”

Understanding this process of genetic damage and repair could lead to new treatments for a type of cancer called an olfactory neuroblastoma, or other types of cancer that are more deadly and less treatable. He hopes to test the idea that forcing distant pieces of DNA to come into close proximity increases hotspots of genetic recombination and mutation.

Dr. Lomvardas said he appreciated the appointment for two reasons.

“First of all, it’s a tremendous honor to carry the Irving name as a professor,” he said. “They were remarkable people.”

“Secondly, when you have stable funding of this nature, you can pursue novel and risky research not typically funded by traditional sources like the National Institutes of Health,” he said. “Failing often points you to the right path. So, having this luxury to take risks is extremely important for basic research.”

Dr. Struhl, professor of genetics and development at Columbia’s Vagelos College of Physicians and Surgeons, said his work touches on cancer in many ways.

“My primary interest is in pattern formation, which reduces to how cells know where they are in a tissue, and how they use that information to decide what to do,” he said. “Without the processes of pattern formation, you couldn’t get things like a hand or a butterfly wing.”

He studies a set of molecular signaling systems — Wnt, BMP, Delta-Notch, and Hedgehog — predominantly in fruit flies. These systems are conserved across many animal species, so whatever he learns about the development of fruit fly wings, which is relatively easy to manipulate and study in the lab, can teach us about humans.

Dr. Struhl delineates the feedback loops that help cells coordinate in order to decide what kinds of cells they will be, and when to stop replicating.

“One of the phenomena that remains extremely mysterious in all animal systems is the phenomenon of organized growth,” he said.

Wings from one fly to the next usually end up almost identical. But sometimes things go wrong in an organism, and a cell replicates out of control, creating a tumor.
“Cancer is a lack of appropriate regulation of growth and of the relationship of cells to each other within growing tissue,” Struhl said. “So, by studying normal development, we are effectively studying the regulations which go awry when you have cancer.”

The Irving Cell Research Program will also support the recruitment of two junior professors whose work is contributing in new ways towards understanding cell death and survival. The Irving bequest is also funding a biennial symposium on neuro-ocology at the Zuckerman Institute, as well as a cryo-electron microscope (Cryo-EM), which can image proteins within

cells at molecular resolution and is essential to advances being made in understanding cancer, neurodegeneration, and even novel viruses, such as COVID-19.

“At the Zuckerman Institute, the search is on for a diverse, twenty-first century scientific community in passionate pursuit of ideas that transcend the boundaries of any one laboratory,” said Dr. Costa. “The Herbert and Florence Irving Professorships are a fundamental aspect of that endeavor, allowing people the intellectual freedom to transform their science, to really move the needle. We’re very excited.”

**About the Irving Cell Research Program at the Zuckerman Institute**
***Transforming the study and treatment of Cancer at Columbia***

The Herbert and Florence Irving Cell Research Program was endowed through an extraordinary bequest to support investigation into the fascinating topic of cell death and survival using a comparative approach that has strong implications for both cancer and neurodegeneration. While many human cells are constantly being generated and live just a few days, such as epithelial cells in the gut, others, especially neurons, can survive a lifetime--up to a century in certain instances. Current knowledge of the mechanisms by which cell types perish at different rates is limited and yet absolutely essential for understanding, treating and eventually curing diseases that dramatically increase in prevalence with age.

Central to the Irving Program’s pursuit of an answer to this basic yet perplexing biological question are the three Herbert and Florence Irving Professorships, which were awarded to Dr. Elizabeth Hillman, Dr. Stavros Lomvardas and Dr. Gary Struhl. Each scientist is engaged in a highly collaborative research program with strong implications for cancer biology, in particular for tumors of the brain and the nervous system.

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**The Irving Legacy**

Both born and raised in Brooklyn, Herbert and Florence Irving played a leading role in philanthropy and service in their generous support for Columbia University Medical Center. Herbert Irving was a co-founder and former vice chairman of Sysco Corporation, the nation’s largest food distributor. Florence Irving served in leadership positions on the boards of several nonprofit institutions, including The Metropolitan Museum of Art, where she was a trustee. Herbert Irving passed away on October 3, 2016, and Florence Irving passed away on July 25, 2018.

Across Columbia, the Irvings' generosity has transformed the study and treatment of cancer. The Irvings' donations to Columbia University and NewYork-Presbyterian total nearly $1 billion. They left a bequest of $700 million, including $600 million in new funds in addition to previously announced pledges, to these two institutions to advance research and clinical programs for the treatment of cancer.

In September 2016, Columbia University named the Medical Center in honor of the Irvings. The Herbert and Florence Irving Medical Center is home to the Herbert Irving Pavilion, the Irving Cancer Research Center, the Irving Institute for Clinical and Translational Research, the Irving Radiation Oncology Center, the Irving Bone Marrow Transplant Unit, and the Herbert Irving Comprehensive Cancer Center, the Irving Pediatric Oncology Program, and the Irving Comprehensive Skin Cancer Center, as well as a long list of named professorships, faculty chairs, and clinical and research facilities. The Irving Medical Center is also home to the Herbert and Florence Irving Basic Science Scholars in Pediatric Cancer. The Irvings' focus on fighting cancer extends across the University to the Morningside and Manhattanville campuses as well, where the following programs reside: the Herbert and Florence Irving Institute for Cancer Dynamics, the Herbert and Florence Irving Cancer Data Fellows, the Herbert and Florence Irving Cancer Research Data Scientists, and the Herbert and Florence Irving Cell Research Program.