THE PAUL G. ALLEN FRONTIERS GROUP

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THE PAUL G. ALLEN FRONTIERS GROUP ANNOUNCES NEW ALLEN DISTINGUISHED INVESTIGATORS

Collaborative projects funded by the awards will address important questions about neurodegenerative disease, nucleus biology, and protein turnover

SEATTLE — **October 8, 2020** — Could scientists detect neurodegenerative diseases like Alzheimer's and ALS years or decades before these disorders manifest outward signs? What could researchers learn by following hundreds of different proteins over their lifetimes inside a single cell? How does the cell's genome-storage center, the nucleus, keep its size and shape?

These are some of the questions posed through five newly awarded projects announced today by The Paul G. Allen Frontiers Group, a division of the Allen Institute. These projects, helmed by eight new Allen Distinguished Investigators, will investigate new areas of biomedical research, technology development, and cell biology. Three of the five projects will focus on discoveries about the nucleus, the largest organelle in our cells and the information center that houses our genome. The other two projects are continuations of 2019 cohorts, one in human stem cell biology and the other in single-cell technology development.

"All eight of these researchers are doing pioneering, outside-the-box research that likely wouldn't be funded by traditional means but could have incredible implications for their fields," said Kathy Richmond, Ph.D., M.B.A., Director of the Frontiers Group. "Our new Allen Distinguished Investigators studying nuclear biology will further our knowledge of the inner workings of the cell, and we're also delighted to expand last year's cohorts to support additional stellar research ideas."

Each award confers $1.5 million in funding over three years for a total of $7.5 million awarded. The Frontiers Group, founded by the late philanthropist Paul G. Allen in 2016, recommends funding to researchers around the world whose work has the potential to accelerate scientific discoveries or launch entirely new avenues of exploration.

This year marks the 10th anniversary of the Allen Distinguished Investigator program, which was launched in 2010 by Allen to back creative, early-stage research projects in biology and medical research that would not otherwise be supported by traditional research funding programs. Including the new awards, a total of 82 Allen Distinguished Investigators have been appointed over the past 10 years.

"As any pathologist will tell you, the nucleus gives us insight into so many types of diseases. This year's Allen Distinguished Investigators have some of the most exciting ideas that will lead to understanding proper cell function and dysfunction in disease," said Kris Dahl, Ph.D., Professor of Biomedical Engineering at Carnegie Mellon University. "Traditional funding sources often play it very safe when they choose projects to back, but the transdisciplinary research supported by the Frontiers Group is the type of science that, if you look through history, has led to the biggest breakthroughs."

The three nucleus biology projects are each led by a collaborative pair of Allen Distinguished Investigators, who bring research expertise from disparate fields to tackle scientific problems in new ways. In recent years, new technologies have made new explorations of nucleus biology possible, enabling large collaborative projects such as the National Institutes of Health-funded 4D Nucleome program. To complement these larger efforts, the Frontiers Group searched for researchers studying the relationships between the nucleus and other structures in the cell.

The two continuing awards provide additional support to researchers using human stem cells to model disease and advance our understanding of human health, and those developing technologies to study molecules at the single-cell level in the context of tissues.

Meet the new Allen Distinguished Investigators

Megan King, Ph.D.
Yale School of Medicine
Simon Mochrie, Ph.D.
Yale University
How does the nucleus keep its size and shape? Megan King and Simon Mochrie are leading a collaborative team to study the physical and molecular forces that maintain the correct size of our cells' largest organelle, the nucleus, which maintains a characteristic volume in healthy cells. This size maintenance is often thrown out of whack in diseases such as cancer, but the mechanisms underlying its maintenance remain unclear.

Nikolai Slavov, Ph.D.
Northeastern University
Nikolai Slavov is leading the development of a new technique, dubbed SCoPE-Dyn, that will allow researchers to follow an individual cell's "protein travelogue": the changes over time in hundreds of different proteins across thousands of human cells. Understanding these details in individual cells could ultimately lead to improvements in the emerging area of targeted protein degradation therapeutics, therapies which harness the cells' protein turnover mechanisms to treat diseases like cancer or Alzheimer's disease.

Daniel Starr, Ph.D.
GW Gant Luxton, Ph.D.
University of California, Davis
Daniel Starr and GW Gant Luxton are studying a protein complex known as LINC, whose role is to physically connect the nucleus to the cell's interior scaffolding system, otherwise known as the cytoskeleton. The LINC complex is involved in translating mechanical forces inside the cell into chemical signals, but how that translation happens and how it is regulated remains unknown. In many diseases, including cancer, heart disease, muscular dystrophy and neurodegenerative disorders, cells lose the ability to correctly translate these cues.

Gene Yeo, Ph.D., M.B.A.
University of California San Diego
Neurodegenerative diseases like Alzheimer's or ALS typically show their devastating effects late in life, but some research hints that the diseases could affect our cells much earlier in life, possibly even before birth. Gene Yeo is leading a team investigating this possibility using human stem cells and brain organoids, tiny clusters of lab-grown brain tissue, that bear genetic mutations linked to certain forms of ALS or muscular dystrophy to study the earliest developmental changes caused by these mutations. Understanding these early effects could point to new pathways for targeted therapies.

Katharine Ullman, Ph.D.
Huntsman Cancer Institute at the University of Utah
Maho Niwa, Ph.D.
University of California San Diego

Katharine Ullman and Maho Niwa are leading a research project to investigate the interactions between the nucleus and one of its neighboring organelles, the endoplasmic reticulum. These two cellular structures are joined at the hip — together, their outer borders form one continuous, folding membrane. Despite their close connections, these structures are often studied independently, and their influences on each other beyond gene expression changes remain poorly understood. Ullman and Niwa plan to study their interactions under several different circumstances; their findings could shed light on basic cell biology and diseases like cancer in which nucleus-endoplasmic reticulum crosstalk may go awry.

About The Paul G. Allen Frontiers Group
The Paul G. Allen Frontiers Group, a division of the Allen Institute, is dedicated to exploring the landscape of bioscience to identify and foster ideas that will change the world. The Frontiers Group recommends funding through award mechanisms to accelerate our understanding of biology, including: Allen Discovery Centers at partner institutions for leadership-driven, compass-guided research; and Allen Distinguished Investigators for frontier explorations with exceptional creativity and potential impact. The Paul G. Allen Frontiers Group was founded in 2016 by the late philanthropist and visionary Paul G. Allen. For more information, visit allenfrontiersgroup.org.

About the Paul G. Allen Family Foundation
For more than four decades the Paul G. Allen Family Foundation has focused on changing the trajectory of some of the world's toughest problems. Founded by philanthropists Jody Allen and the late Paul G. Allen, co-founder of Microsoft, the Foundation initially invested in community needs across the Pacific Northwest with a focus on regional arts, under-served populations, and the environment. Today, the Foundation supports a global portfolio of frontline partners working to preserve ocean health, protect wildlife, combat climate change, and strengthen communities. The Foundation invests in grantees to leverage technology, fill data and science gaps, and drive positive public policy to advance knowledge and enable lasting change.

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