



THE  
PAUL G. ALLEN  
FRONTIERS GROUP

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## ALLEN DISCOVERY CENTERS

The Allen Discovery Centers are a new type of center for leadership-driven, compass-guided research in partnership with major research organizations and universities. The Allen Discovery Centers respond to worldwide community enthusiasm for a right-sized, risk-tolerant mechanism to support exploration. The Centers embody our commitment to support the freedom needed to navigate uncertain territory—on a compass direction to the unknown.

We will make patient, long-term investments in these Centers, typically providing \$10 million for the first four years, with the intention to expand in a second four year phase with an additional \$10 million, matched by partner support, for a potential total scope of activity of \$30 million.

We will fund research efforts led by visionary leaders and coherent teams, pioneering expeditions that will pursue new discoveries, principles and insights.

Over time, the Allen Discovery Centers will also interact—with each other, with our Allen Distinguished Investigators, and with the larger community—through a rich network of events and associations. These interactions reflect our belief that making lateral connections visible across the intellectual landscape can produce unexpected and radically productive new insights and ideas.

### 2017

#### The Allen Discovery Center at UW Medicine

Cell Lineage Tracing  
Leader: Jay Shendure, M.D., Ph.D.

#### The Allen Discovery Center at Boston Children's Hospital and Harvard Medical School

Human Brain Evolution  
Leader: Christopher A. Walsh, M.D., Ph.D.

### 2016

#### The Allen Discovery Center at Tufts University

Reading and Writing the Morphogenetic Code  
Leader: Michael Levin, Ph.D.

#### The Allen Discovery Center at Stanford University

Systems Modeling of Infection  
Leader: Markus Covert, Ph.D.

# ALLEN DISCOVERY CENTERS

## The Allen Discovery Center at Stanford University

Systems Modeling of Infection  
Leader: Markus Covert, Ph.D.

Multiscale models that can integrate data from the levels of genes and proteins to a full cell, to collections of cells within a tissue, and ultimately to tissues and organs, is a grand challenge for systems biology. These kinds of models will be capable of predicting how perturbations at one level of scale, such as gene expression, affect important outcomes at other levels of scale, like phenotype and function.

In order to understand the molecular basis for disease—an essential to developing effective, next generation cures—we need these kinds of multiscale models that comprehensively represent whole cells, as well as their dynamic environments and interactions.

The team at the Allen Discovery Center at Stanford University will focus on modeling the interaction between the pathogen *Salmonella* and macrophages, part of the first line of the innate immune defense. Studying and modeling this particular system will have specific, immediate impact on a global biomedical challenge of antibiotic-resistant pathogens, as well as generally enhance our understanding of complex diseases.

## The Allen Discovery Center at UW Medicine

Cell Lineage Tracing  
Leader: Jay Shendure, M.D., Ph.D.

Scientists have been asking questions about the ancestry and lineage of cells for over a century, but tracing the relationships between generations of cells has faced significant technical challenges. In the past several years, teams led by Jay Shendure, M.D., Ph.D., at the University of Washington, Michael Elowitz, Ph.D., co-leader, and Long Cai, Ph.D., at Caltech and Alex Schier, Ph.D., at Harvard have created new technologies that take advantage of modern gene editing methods to effectively trace cells as they divide, move and differentiate throughout an organism's development.

The Allen Discovery Center for Cell Lineage Tracing will use these new technologies and paradigms to develop lineage maps for the zebrafish and mouse - the first global maps of development in any vertebrate. They will also develop genomic systems to record the molecular events that regulate development.

## The Allen Discovery Center at Tufts University

Reading and Writing the Morphogenetic Code  
Leader: Michael Levin, Ph.D.

Living systems are able not just to grow tissues, but to maintain them over time and, in some cases, regenerate them when they are altered by injury or disease. Underlying this ability is the morphogenetic code, which consists of the mechanisms and information structures by which networks of cells represent and dynamically regulate the target morphology of the system.

With the ultimate goal being the top-down control of complex biological shape, we need to understand how biological systems control anatomy, from the level of tissues to the entire body plan. Control over these processes would have transformative implications for not only biology and medicine but many other disciplines.

Current technology and conceptual schemes target the level of proteins, genes and cells, but are unable to link these to large-scale anatomy. The Allen Discovery Center at Tufts University team will fill this major gap by building new tools that exploit endogenous bioelectric and regulatory pathways, resulting in impactful new capabilities in regenerative medicine.

## The Allen Discovery Center at Boston Children's Hospital and Harvard Medical School

Human Brain Evolution  
Leader: Christopher A. Walsh, M.D., Ph.D.

The human brain is the product of remarkable evolutionary changes that have resulted in our ability to use language, create complex societies, pursue science and create art. While we have some understanding of the genes that separate all modern humans from other primates, none of those genes can explain changes in behavior that took place in the last 50,000 years, meaning there is no simple genetic "switch" that can explain key aspects of brain evolution.

The Allen Discovery Center for Human Brain Evolution will take a multidisciplinary approach to this question, with the goals of identifying key genes that have driven human brain evolution, analyzing their roles in human behavior and cognition, and studying their functions to discover evolutionary mechanisms.