THE PAUL G. ALLEN FRONTIERS GROUP

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 helmed 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.

The Allen Discovery Center at Stanford University

Systems Modeling of Infection

The Allen Discovery Center at Tufts University

Reading and Writing the Morphogenetic Code

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 Discovery Center team's multiscale modeling will focus on 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 modeling approach the team employs will lead to the identification of better, more sophisticated antimicrobial strategies by integrating multiple biological pathways and networks, allowing for heterogeneous cellular phenotypes, including host-pathogen interactions during infection and accounting for the in vivo environment. Combined, these inputs will yield powerful, predictive and highly relevant models.

The goals of the Allen Discovery Center at Stanford include major advances in several fields. In addition to improving whole-cell modeling of both host cells and infectious bacteria, the team will advance the modeling of interacting cells, improve computational power to boost simulation run time, create new visualization tools and employ deep learning for data analysis, and describe computational measurements of observations of cellular processes and dynamics.

Ultimately, the team's models will suggest experiments with the highest likelihood of generating new knowledge, shortening the path to breakthroughs, and be able to predict or diagnose complex, multi-network phenotypes, both within individual cells and as a result of cell-to-cell interactions and heterogeneity.

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 Discovery Center 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.

Bioelectricity is one layer of a complex morphogenic field that harnesses individual cell behavior toward the anatomical needs of the body. However, it is not simply yet another mechanism of single-cell control. Briefly altering the bioelectric connectivity of a cellular network enables permanent rewriting of an organism's target morphology, making it a convenient and tractable entry point for understanding and rationally controlling information processing that maintains larger-scale order in vivo.

The team seeks to understand where bioelectric patterns originate, how they map the organization of cells, and how their code is interpreted by cells. This will enable the team to create the first quantitative theory of top-down pattern control, and ultimately harness new modalities for reading and writing the bioelectric code with applications in embryogenesis, regeneration, cancer and bioengineering.