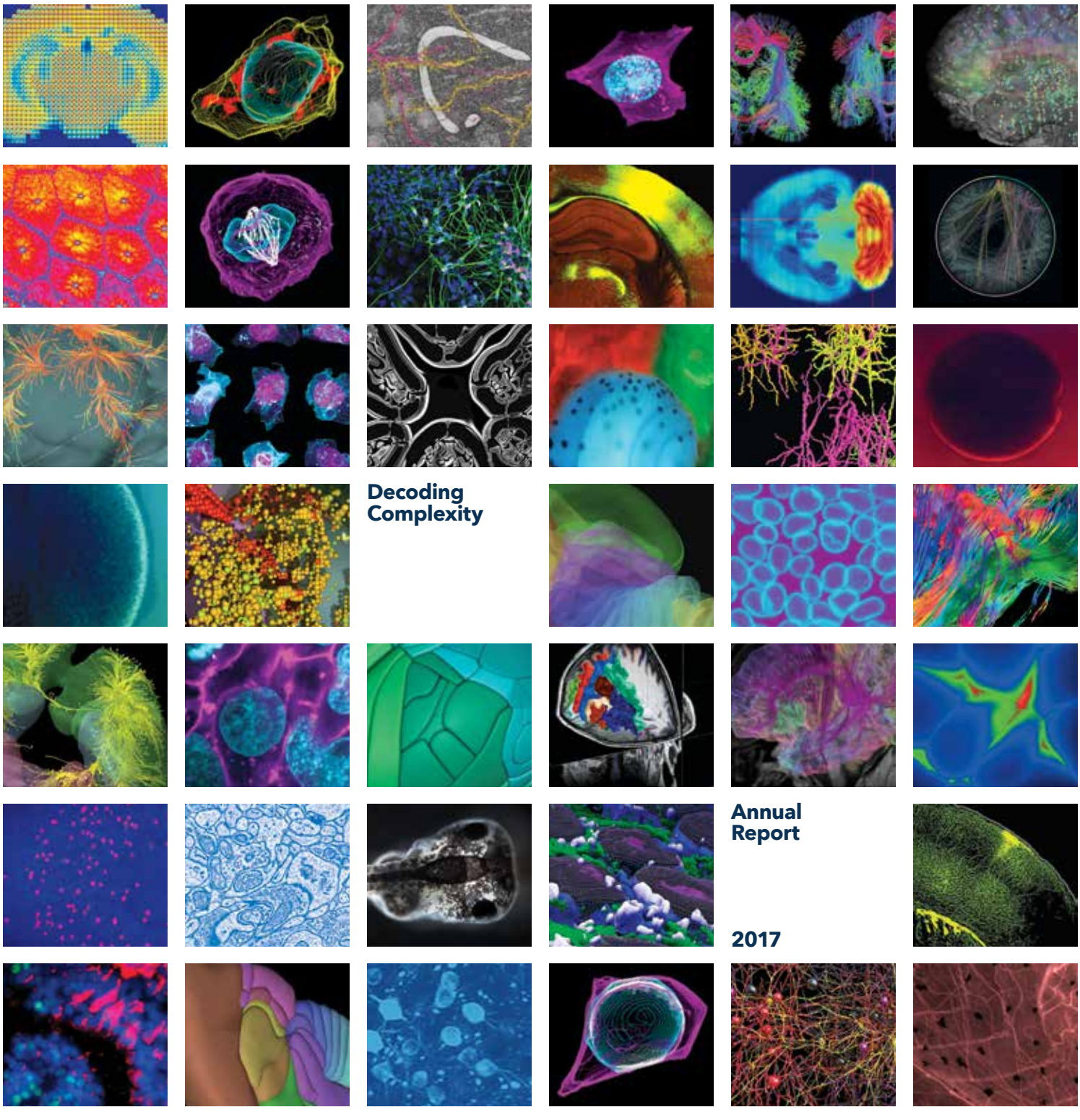
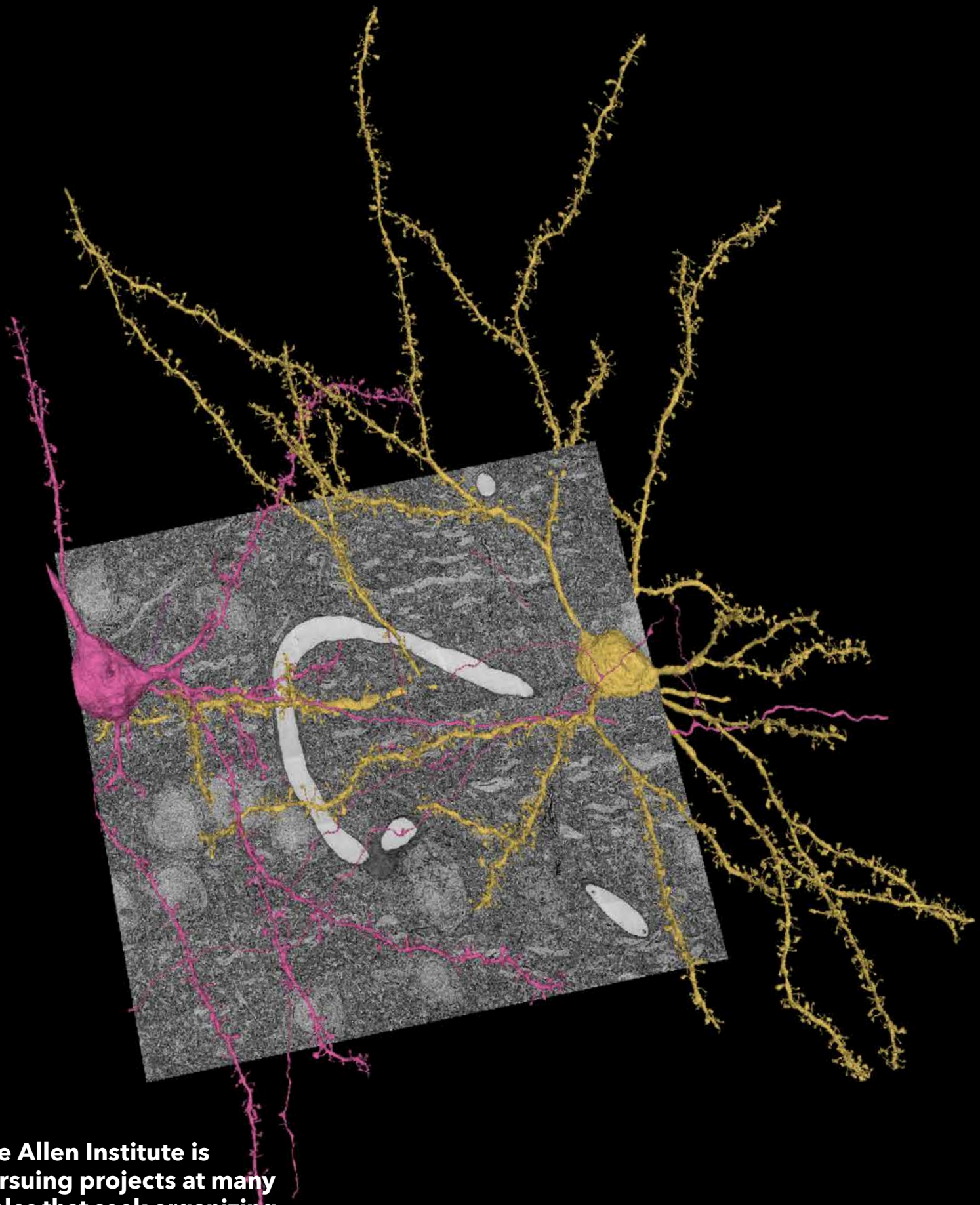
ALLEN INSTITUTE



Decoding Complexity

Annual Report

2017



The Allen Institute is pursuing projects at many scales that seek organizing principles, models and codes to make sense of bioscience's incredible complexity.

Decoding Complexity

Consider one of the cell's most basic functions: replication and division. Without this fundamental process, none of us multicellular organisms would exist. But then consider the sheer number of parts involved. Three billion proteins, 30 billion lipids, 50 million RNAs, two meters of mission-critical DNA—all being duplicated in less than a day. Biological systems, even small-scale ones, are stunningly complex.

The only way we will ever make sense of this complexity is to reveal its organizing principles. At the Allen Institute, we are creating models that can understand how brain circuits will behave, predict where parts of a cell will be during its various stages, and untangle how our cells communicate to build entire organisms. We are also setting foundational standards in the form of scientific tools and resources—including gene edited stem cell and mouse lines—and working toward a periodic table of cell types in the brain.

Our big, team and open science approach has given us a unique ability to pursue these projects at a large and exciting scale. We hope that our efforts to decode biology's complexity, and to freely share what we discover and create, will drive scientific progress in labs and institutions around the globe.

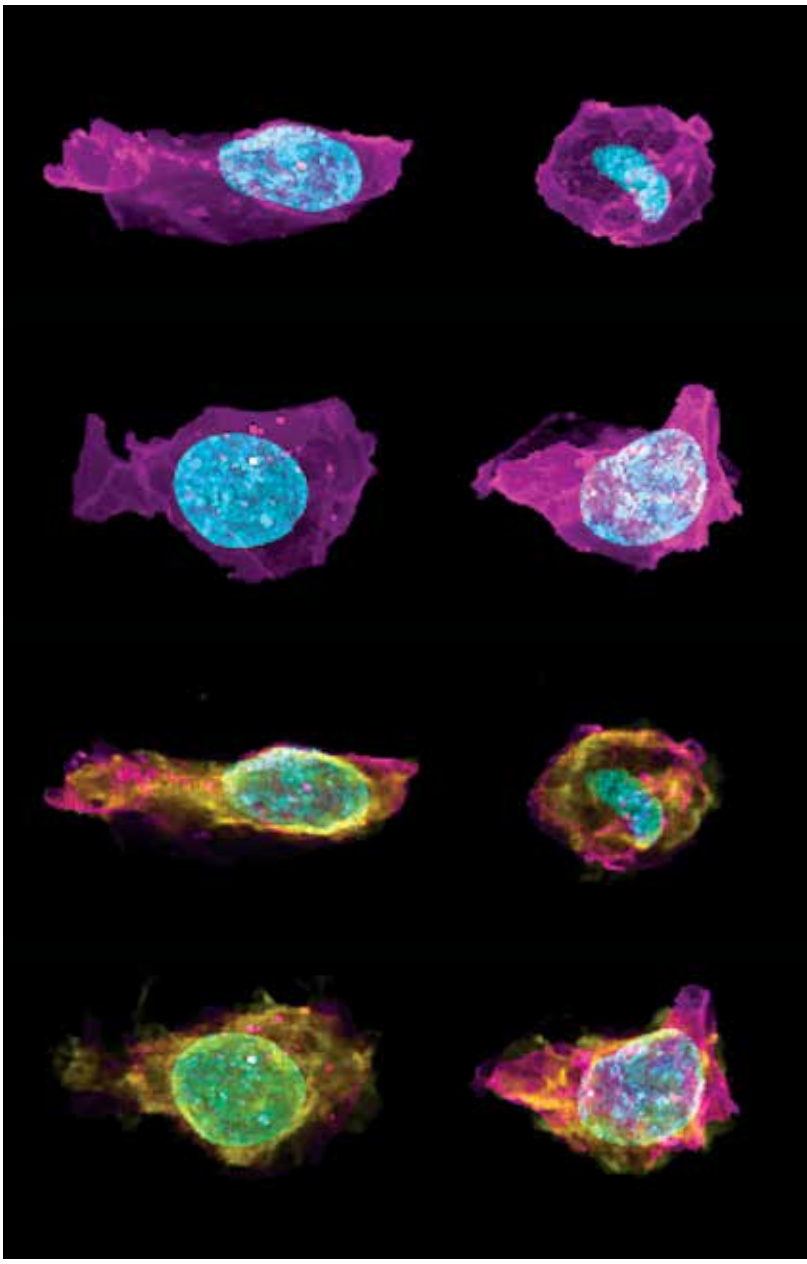
Allan Jones, Ph.D.
President & Chief Executive Officer

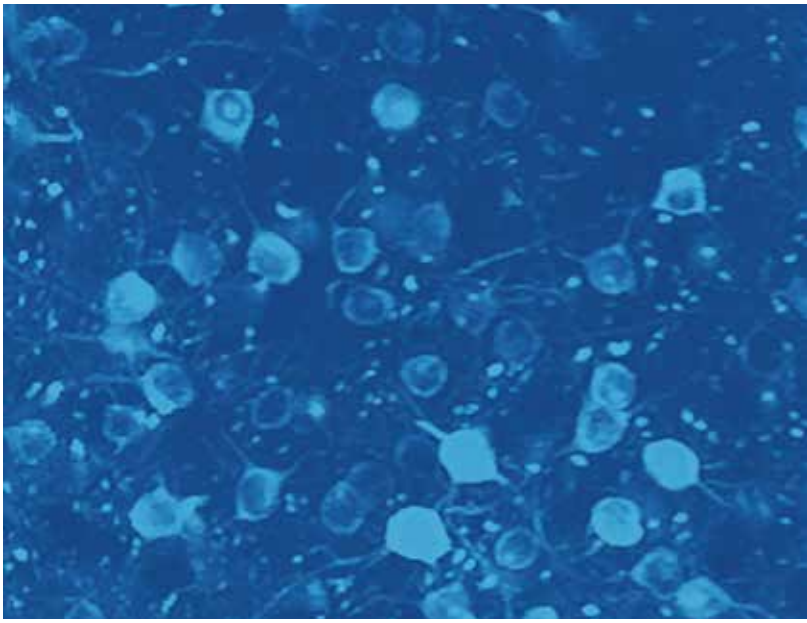
The Allen Institute team

Left Layer 2/3 neurons that were recorded *in vivo* and then reconstructed *ex vivo* from serial section electron microscopy.

Finding Order

Biology is complex at every level. The Allen Institute is generating models and uncovering codes that get to the heart of that complexity and help us make sense of our world.

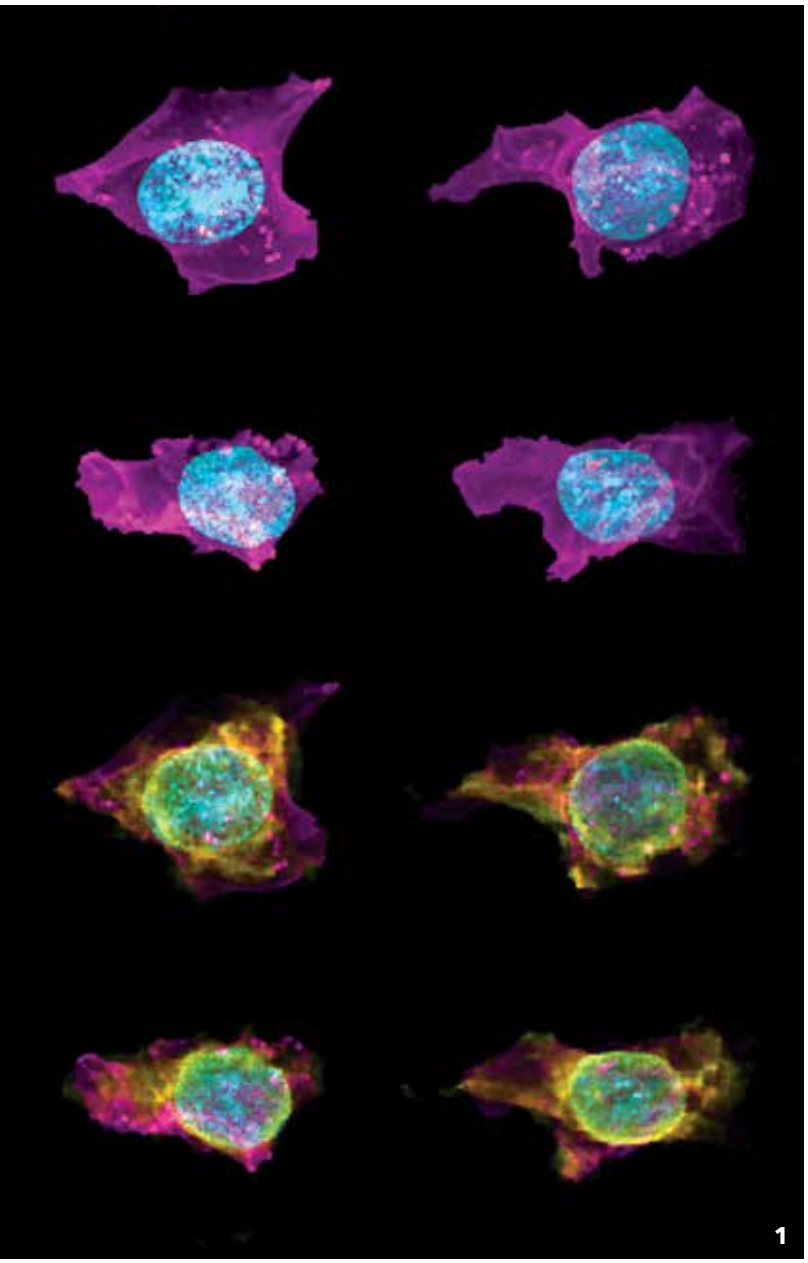




Integrated Cell Models
The Allen Institute for Cell Science is combining gene editing methods with deep learning machine algorithms to make predictive 3D models of human stem cells—with a startling accuracy that lets us see the cell as an integrated whole for the first time. **1**

Allen Brain Observatory
A first-of-its-kind cellular-level window into the brain's behavior, the Allen Brain Observatory from the Allen Institute for Brain Science encompasses not only robust data from a survey of nearly 40,000 cells in the visual cortex, but also visualizations and algorithms that help researchers around the world explore and understand how information is processed. **2**

Cracking the bioelectric code
Researchers at the Allen Discovery Center at Tufts University are revealing the electric code that cells use to control how our bodies are shaped. This pioneering work will help us answer basic questions about body plans, like how your thumb ended up opposite your pinky, and uncover how we can manipulate those cellular decisions to make meaningful strides in regenerative medicine. **3**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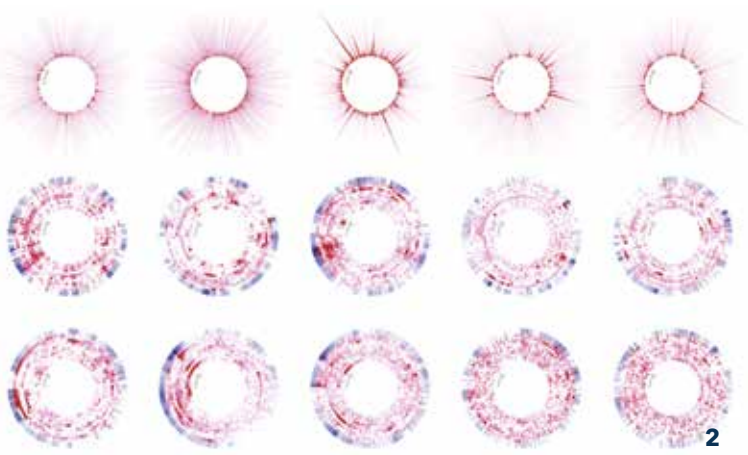
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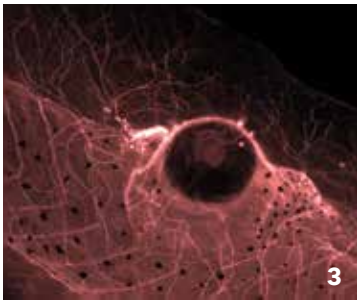
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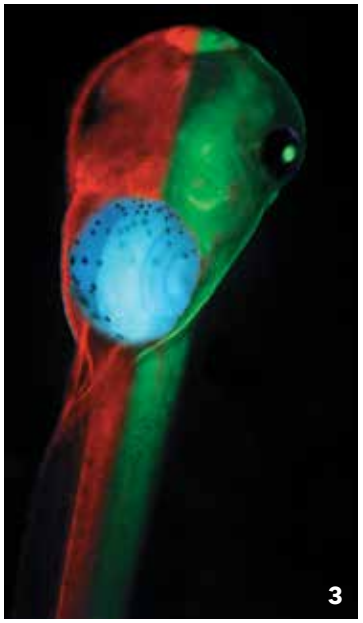
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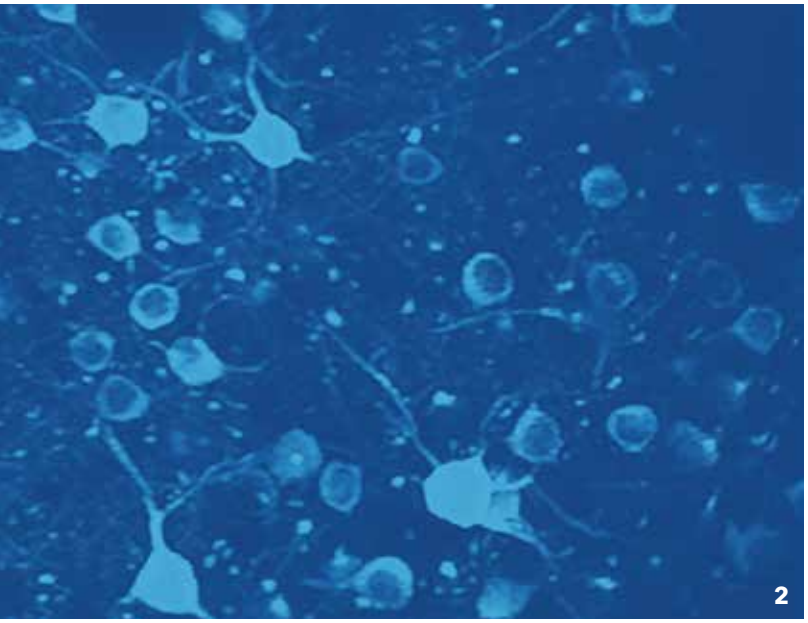
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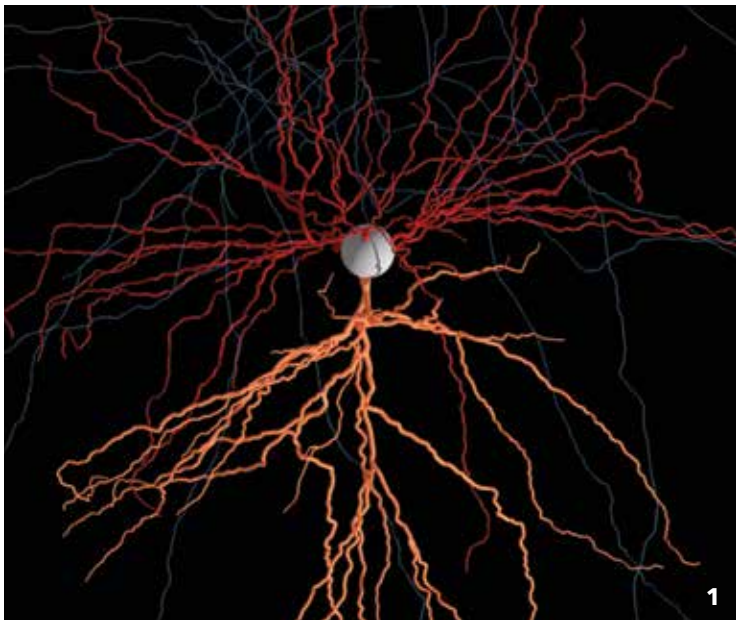
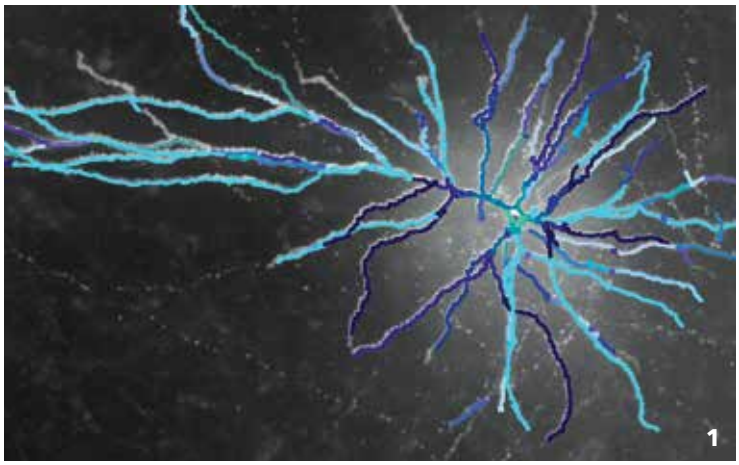
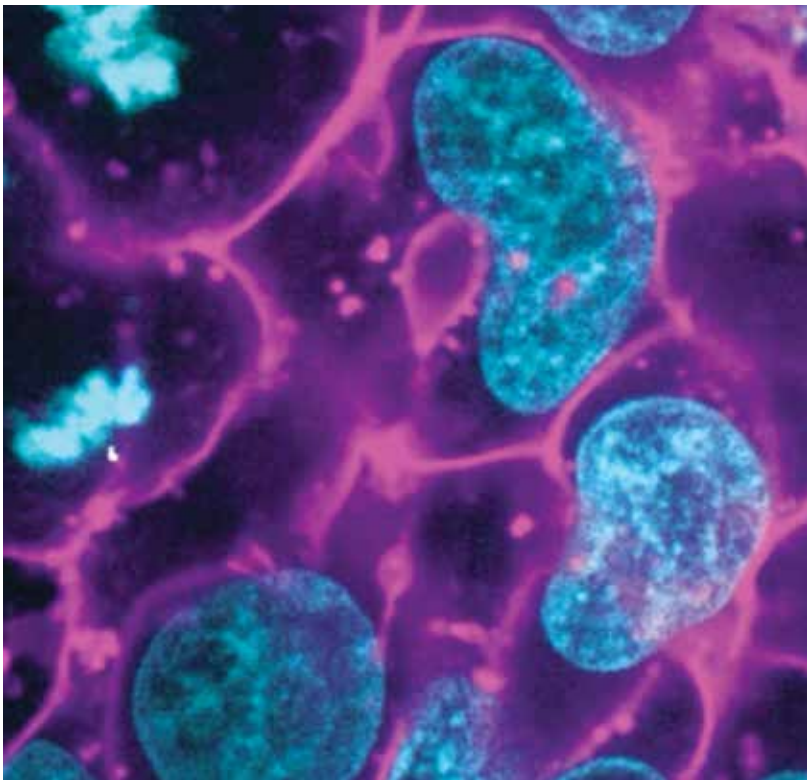
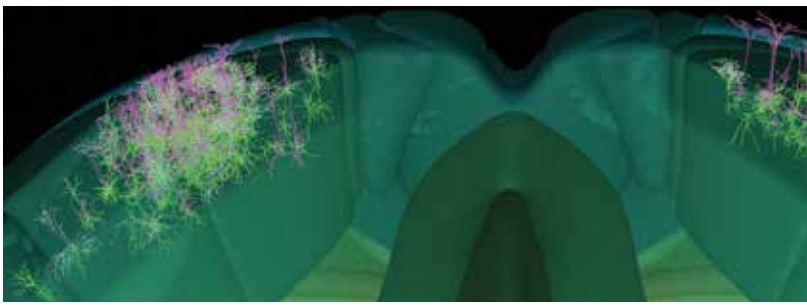
Setting the Standard

The Allen Institute has been instrumental in establishing foundational standards for life science fields. These tools are critical for the scientific community at large to share data and ideas and create a common working language to guide investigation.





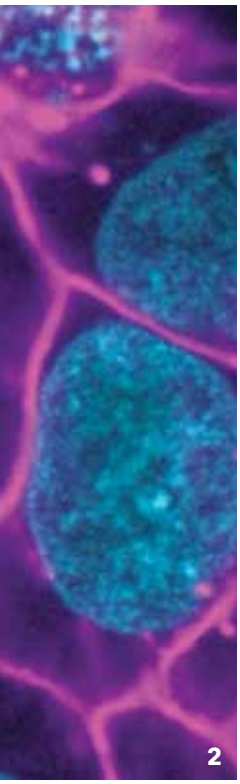


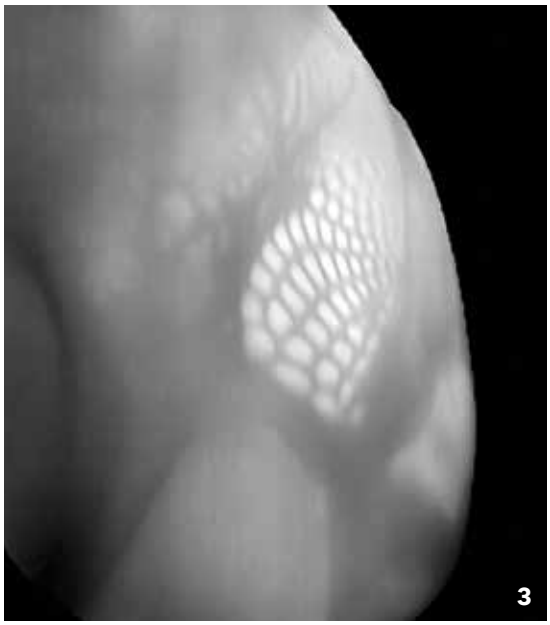


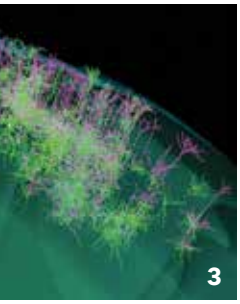
Allen Cell Types Database
Our effort to create a "periodic table" of cell types, the Allen Cell Types Database provides shape, electrical and genetic information about individual nerve cells in the mouse—and now human—cortex, to guide our understanding of the building blocks of the brain. **1**

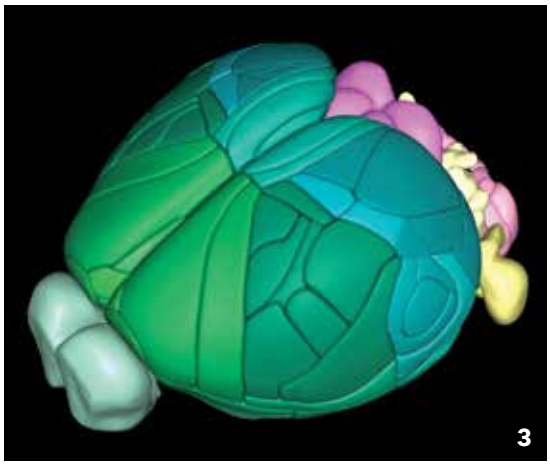
Allen Cell Collection
These powerful lines of human induced pluripotent stem cells are gene edited for precise tagging of individual parts of the cell. The cell lines are putting the power to peer into the human cell in the hands of researchers in labs around the world. **2**

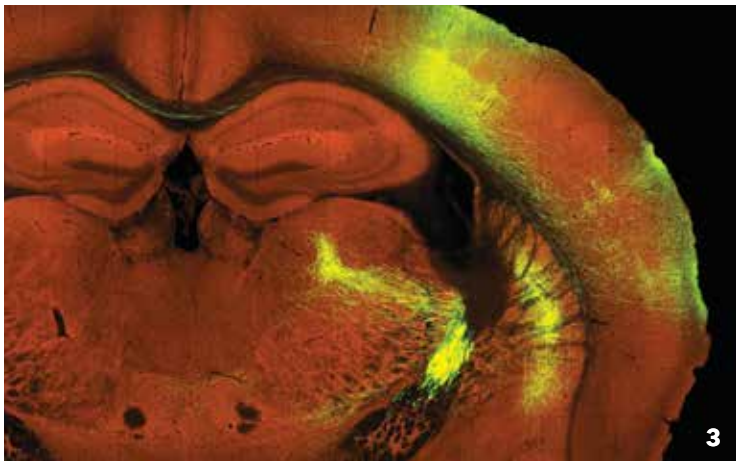
Allen Mouse Common Coordinate Framework
The Allen Institute is taking brain mapping into three dimensions, creating and sharing the first 3D atlas of the mouse brain. **3**









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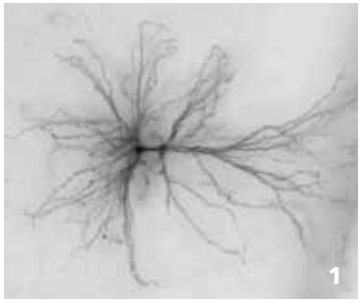
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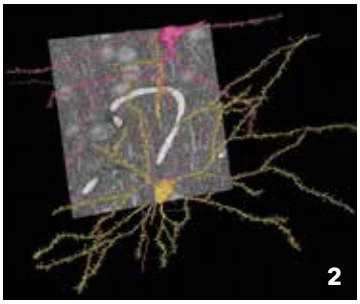
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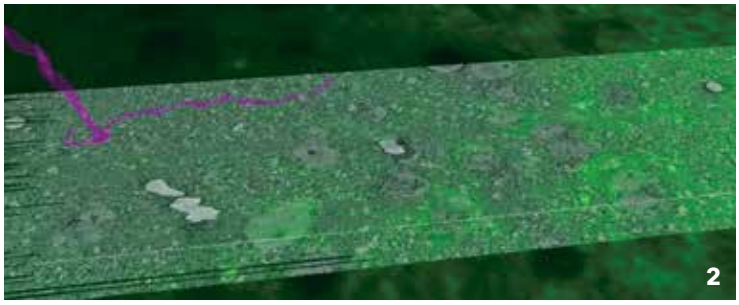
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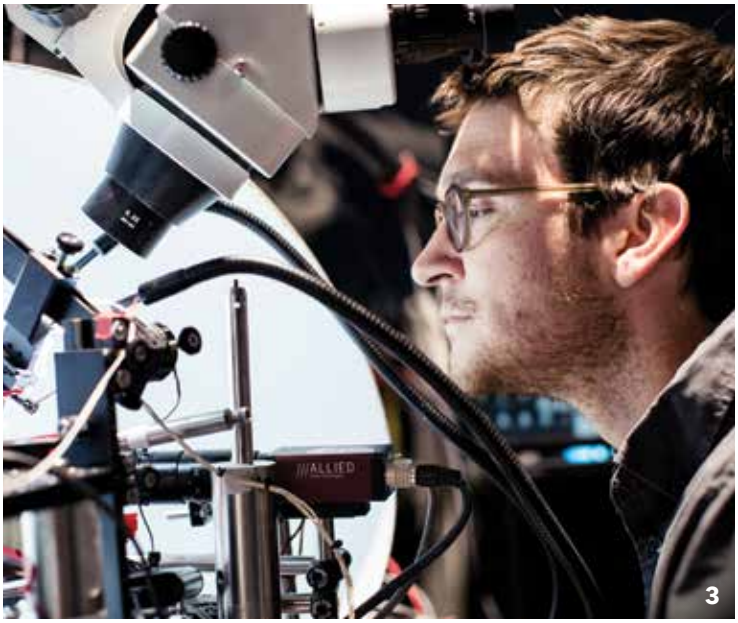

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Parsing the Brain

The Allen Institute for Brain Science is pursuing its ultimate goal of understanding the components and computations that underlie cognition in the brain, embracing the power of scientific inquiry at a large scale.

Human data in the Allen Cell Types Database

This year, the Allen Institute for Brain Science made an exciting addition to the Allen Cell Types Database with data from live human neurons. In partnership with neurosurgeons in the Seattle area, researchers studied small pieces of neurosurgically excised tissue from the cortex that would typically be discarded as medical waste, analyzing the structure and function of neurons in those tissues through the same experimental pipeline used for the mouse brain tissue. The extensive, standardized data on the shape, electrical patterns and gene expression of individual human cells allow researchers around the world to sort and categorize the building blocks of the human brain and shed light on what makes the human brain unique. **1**

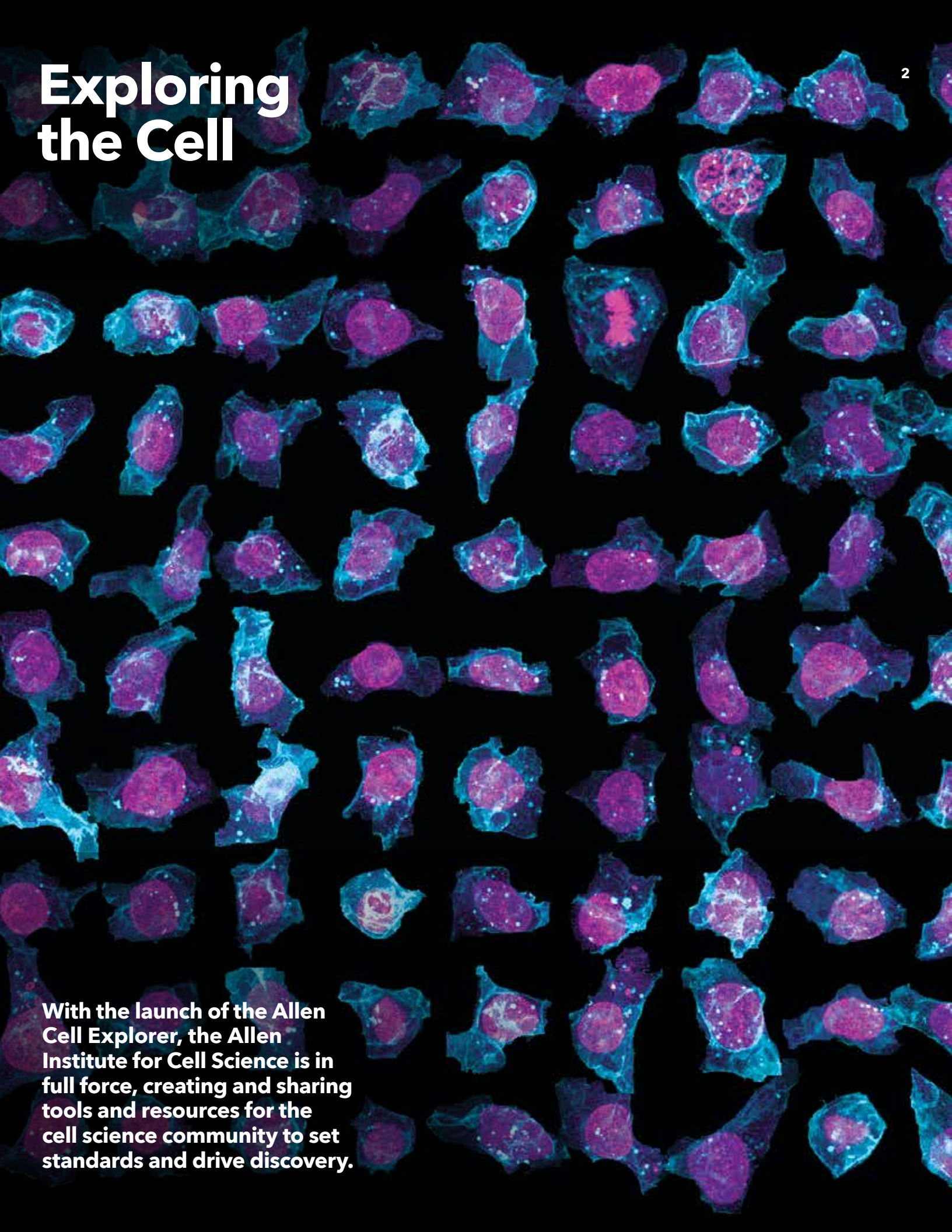
Reconstructing a cubic millimeter of the mouse brain

It takes a massive pipeline to reconstruct a piece of brain the size of a grain of sand. This year, Allen Institute researchers have made strides toward reconstructing the largest piece of mouse brain tissue to date, setting up a successful pipeline as part of a collaborative project to slice and image more than 25,000 sections of brain, each a hundredth the width of a human hair. Taken together, these data will give a singular view into the complexity and connectivity of the cortex. **2**

Probing the brain

Announced in a paper in *Nature* late this year, Neuropixels probes represent a major advance in instrumentation, allowing researchers to record dynamic brain activity from hundreds of neurons at fractions of a millisecond—far finer than any existing technology. Created in collaboration with scientists and engineers at imec, HHMI Janelia Research Campus and the University College London, the whisper-thin silicon probes will allow for the most precise understanding yet of how cells in the brain coordinate to give rise to behavior and cognition. **3**

Exploring the Cell



With the launch of the Allen Cell Explorer, the Allen Institute for Cell Science is in full force, creating and sharing tools and resources for the cell science community to set standards and drive discovery.

Allen Cell Explorer launched

The Allen Cell Explorer is a one-of-a-kind portal and dynamic digital window into the human cell, combining large-scale 3D image data, image analyses, predictive models based on deep learning, gene edited human stem cell lines and a growing suite of powerful tools. The website is the platform for these and future publicly available resources created and shared by the Allen Institute for Cell Science.

A growing Allen Cell Collection

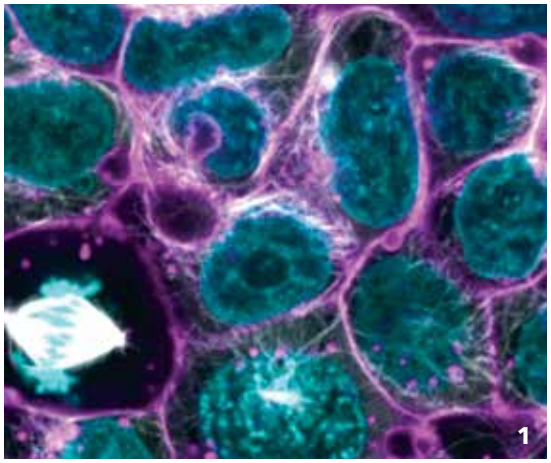
The Allen Cell Collection contains numerous gene edited human stem cell lines, each precisely tagging a single part of the cell. Researchers around the world can obtain these valuable cell lines, and the plasmids used to create them, to drive progress toward understanding how healthy human cells look and behave in their own labs. **1**

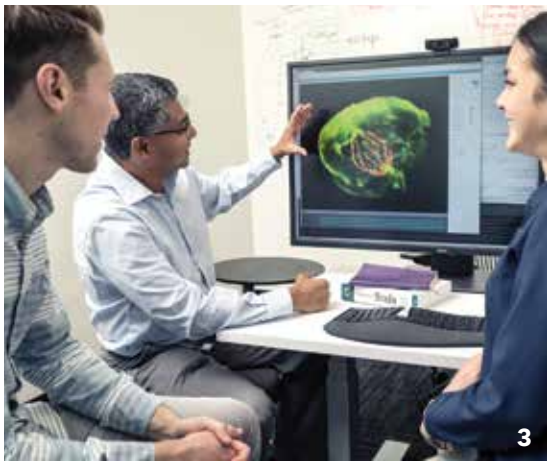
A deeper analysis

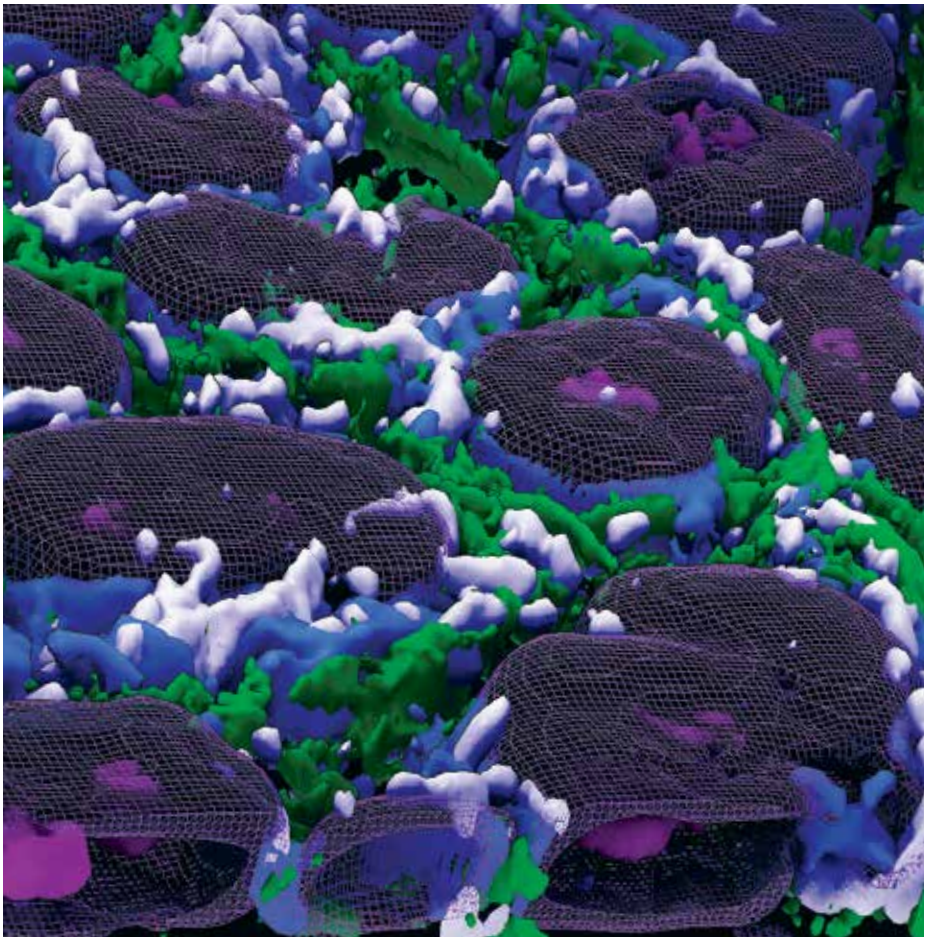
Collecting images from over 16,000 cells has led to many interesting observations about the cell, including the surprising diversity of shape and organization. Allen Institute researchers have created tools and models to analyze this variance, and are sharing their knowledge as part of the Allen Cell Explorer. **2**

Creating a pipeline

Generating enormous amounts of high-quality data requires a pipeline, and the Allen Institute for Cell Science has created a team-driven model that takes cells from gene editing through assay development, microscopy, modeling and sharing with the entire community. **3**







Navigating Frontiers

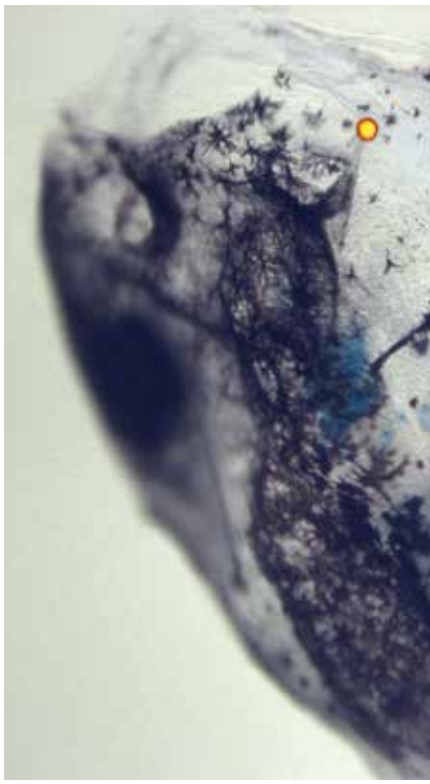
The Paul G. Allen Frontiers Group seeks out and supports pioneering ideas on the frontiers of science that have the potential to change our world for the better. Through events, travels and extensive conversations, the Frontiers Group is identifying researchers with breakthrough ideas and the passion and determination to pursue them.

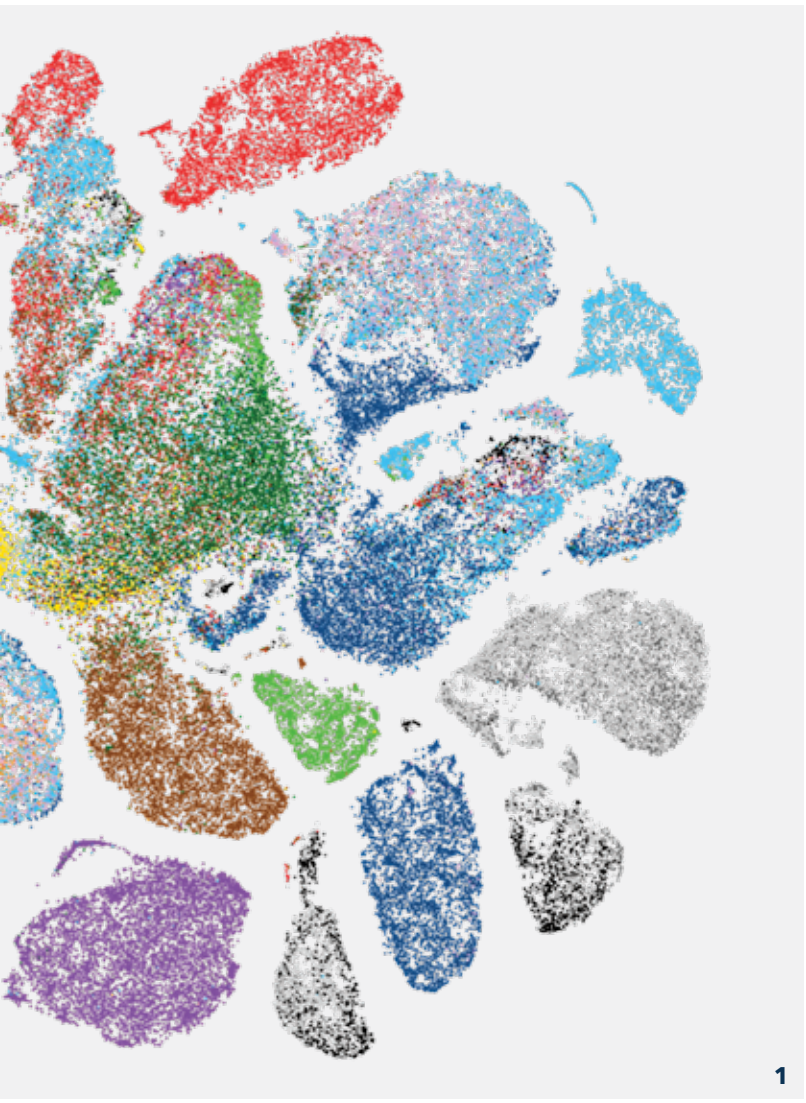
Two new Allen Discovery Centers
Two new centers, one at UW Medicine and another at Boston Children's Hospital and Harvard University, will explore the lineage of single cells as they develop into complex organisms, and evolutionary genomic changes that make the human brain capabilities distinct. **1**

Current Allen Discovery Centers continue their work to crack the morphogenetic code that controls body plan, and create whole-cell models of infectious agents and hosts. **2**

Five new Allen Distinguished Investigators
New investigators will investigate a wide range of pioneering topics, including epigenetics, aging and evolution. In addition, two joint awards with the American Heart Association will support investigation into the uncharted role of the extracellular matrix in heart disease.

Bringing thought leaders together
In addition to several scientific symposia, the Frontiers Group hosted the inaugural BioScience & Philanthropy Summit in Seattle, bringing together cutting-edge scientists with philanthropic and investment thought leaders to inspire new partnerships and create impact at the frontiers of science. **3**

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BIOSCIENCE &
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AT THE ALLEN INSTITUTE
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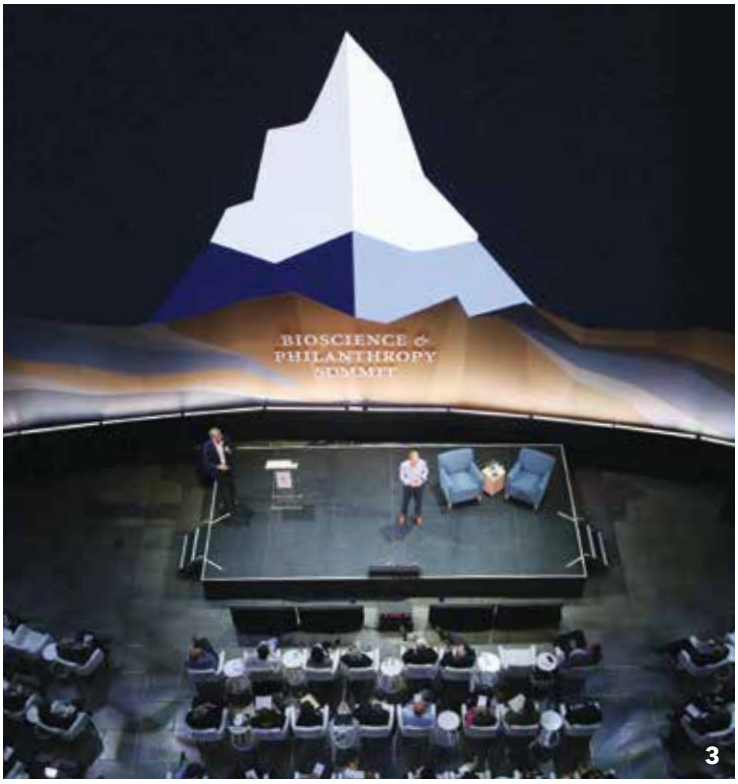
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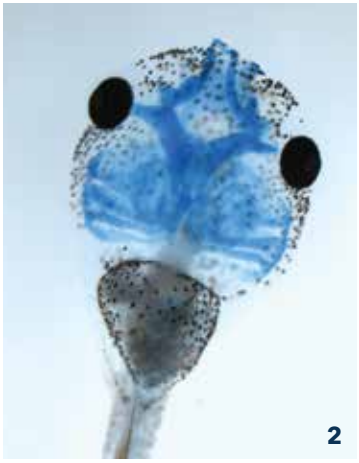
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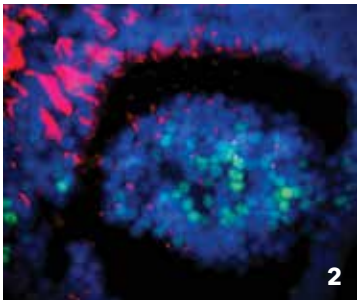
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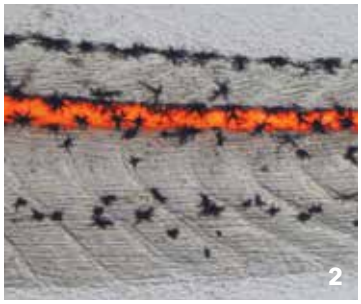
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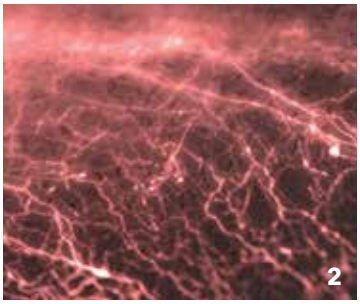
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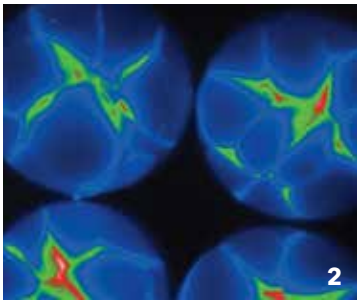
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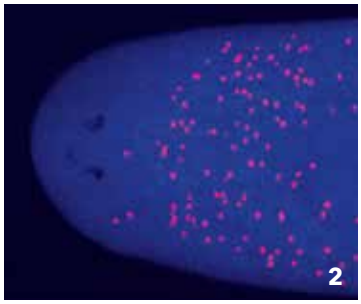
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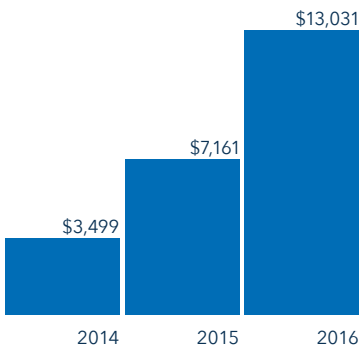
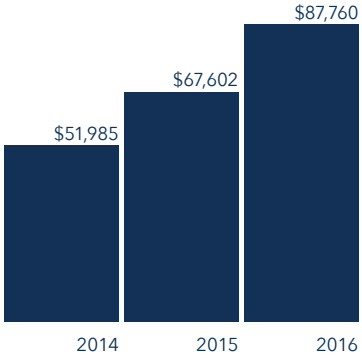
Financial Summary

The Allen Institute continues its rapid growth, supporting the research of the Allen Institute for Brain Science and Allen Institute for Cell Science, as well as the administrative costs of The Paul G. Allen Frontiers Group. We benefited from a large contribution in 2016 that will span multiple years, along with increased grant revenue.

Research Grant & Contract Revenue



Total Spending



Allen Institute Fiscal Years 2016 and 2015

(In Thousands)

	2016 (Audited)	2015 (Audited)
Support and Revenue		
Contributions	**$ 286,090**	$ 105,059
Research Grants and Contracts	**13,031**	7,161
Other	**(223)**	558
Total Support and Revenue	**298,898**	112,778
Expenses		
Program Services	**69,167**	55,891
Management and General	**18,593**	11,711
Total Expenses	**87,760**	67,602
Change in Net Assets	**$ 211,138**	$ 45,176
Net Assets, Beginning of Year	**216,309**	171,133
Net Assets, End of Year	**$ 427,447**	$ 216,309

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Jody Allen

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Chinh Dang
Chief Administrative Officer

Marjorie Thomas
Chief Financial Officer

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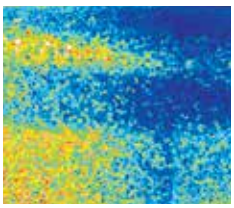

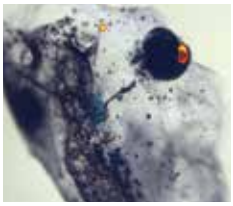

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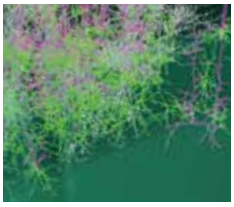

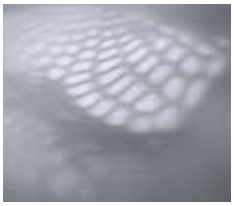

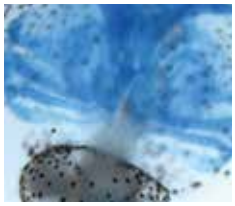

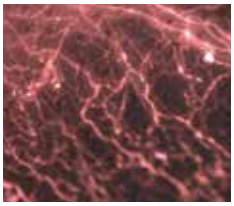

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