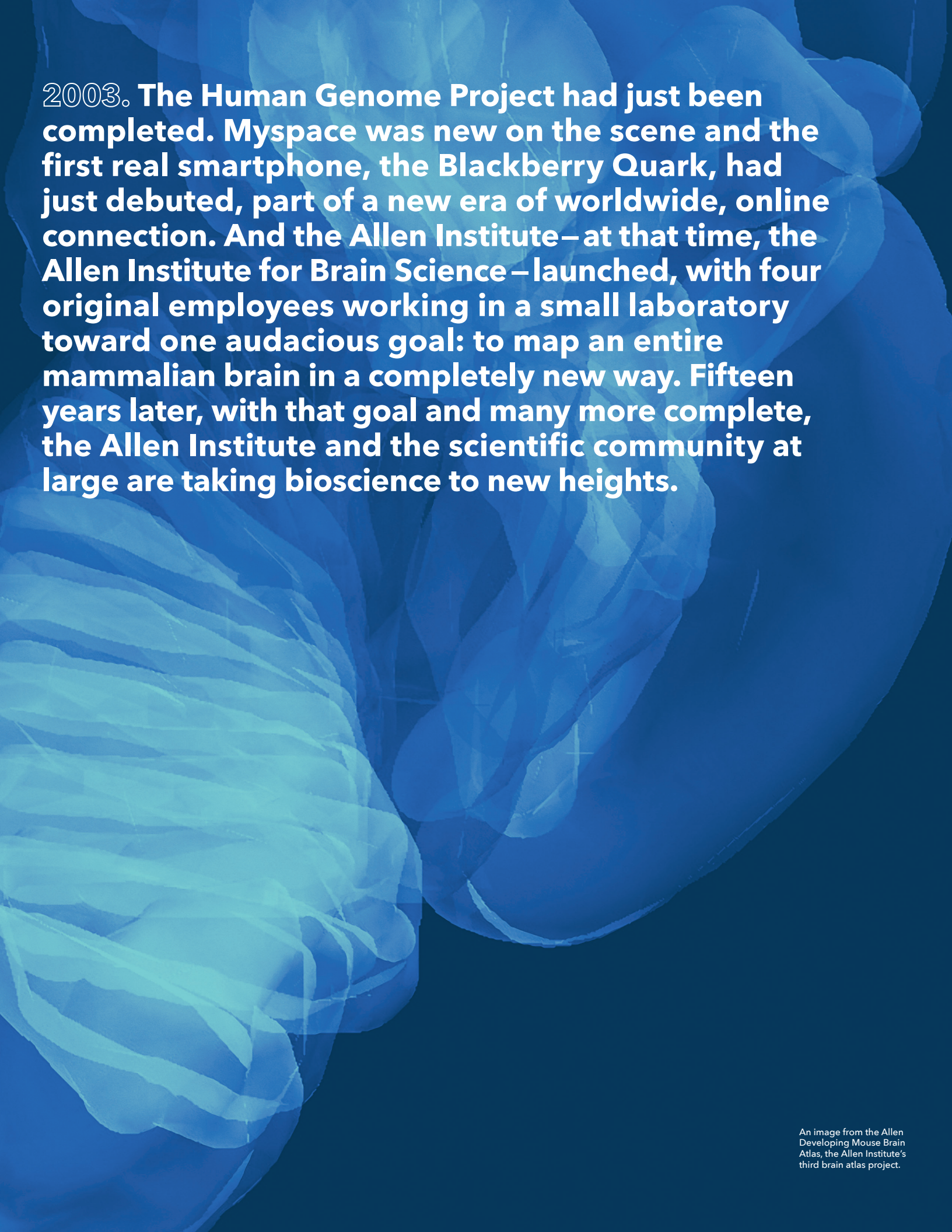
ALLEN INSTITUTE

2018
Annual Report

15 YEARS OF IMPACT

2003. The Human Genome Project had just been completed. Myspace was new on the scene and the first real smartphone, the Blackberry Quark, had just debuted, part of a new era of worldwide, online connection. And the Allen Institute—at that time, the Allen Institute for Brain Science—launched, with four original employees working in a small laboratory toward one audacious goal: to map an entire mammalian brain in a completely new way. Fifteen years later, with that goal and many more complete, the Allen Institute and the scientific community at large are taking bioscience to new heights.



An image from the Allen Developing Mouse Brain Atlas, the Allen Institute's third brain atlas project.

The Allen Institute was founded to tackle hard problems in brain science. In 2003, we started from scratch to build both a new model of carrying out neuroscience research and a new brain atlas, one which would map every gene's expression pattern in the entire mouse brain. That initial project, the Allen Mouse Brain Atlas, required us to think about neuroscience in a new way, applying an industrial-scale approach to a very foundational problem in bioscience. Our first atlas was completed in 2006, and it draws more users today than it did 12 years ago, a testament to its lasting power as an essential resource for the community.

In 2004, we shared our first dataset openly and publicly. Open science has been our credo ever since: We share our data, our transgenic mice, our cell lines, our know-how with the world. This allows us to have global impact from our Seattle base – our data is accessed and consumed thousands of miles away. We were at the vanguard of open science, a movement that's now growing and one which benefits all scientists and humanity.

This year, we're celebrating 15 years since our launch. In 2003, we were a handful of scientists and engineers with a start-up mentality and a singular focus on completing one imperative project. Today, we're three divisions, nearly 500 employees from 34 different scientific disciplines, catalyzing and building myriad projects and platforms, all with the scale, urgency and innovation of our initial atlas.

It's been an exciting and humbling 15 years, watching the growth and transformation of both the Allen Institute and the broader field of bioscience. What will the next 15 years bring? It's impossible to say, but I know for certain that we are just getting started.

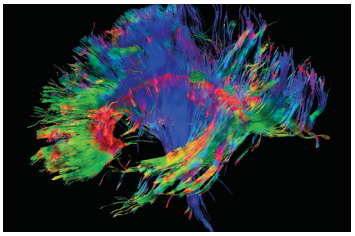
Allan Jones, Ph.D.
President & Chief Executive Officer

Left Allen Institute researchers and founder Paul G. Allen in 2007. *Photo by Bryce Duffy.*

Right The Allen Institute team in early 2018.

In 15 years we've **evolved**

2011



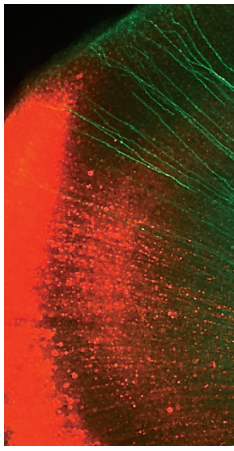
Human brain mapped Four years in the works, the Allen Human Brain Atlas is completed. The most comprehensive characterization of the human brain up to that point, the atlas marries precise gene expression with anatomical information.

2012

A 10-year plan launched Mr. Allen commits an additional $300M to expand the Allen Institute for Brain Science, setting it on a new 10-year course to tackle the most challenging questions facing the field of brain science: building a new observatory to record activity of thousands of nerve cells and to obtain a census of all cell types in the brain.

2014

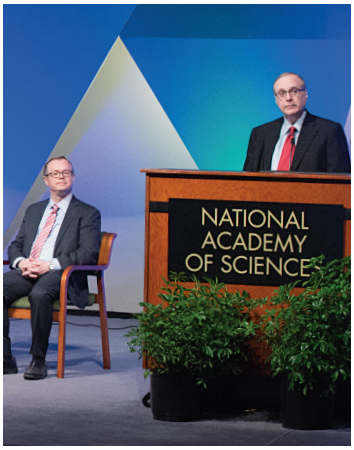
Wiring diagram of the brain published The Allen Institute completes and publishes the Allen Mouse Brain Connectivity Atlas, a "connectome" map of the mouse brain, the most comprehensive wiring diagram of a mammalian brain to date.

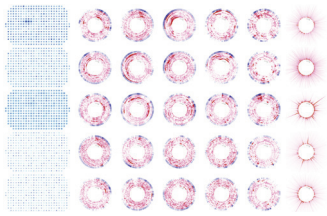


A new home Allen Institute staff move from several different buildings around Seattle to their new dedicated facility in Seattle's South Lake Union neighborhood.

2016

New frontiers Mr. Allen launches The Paul G. Allen Frontiers Group with an initial commitment of $100M to identify and fund pioneering, transformative bioscience around the world. At the launch, the Frontiers Group also announced the first two Allen Discovery Centers, new collaborative research groups headquartered at Stanford University and Tufts University.



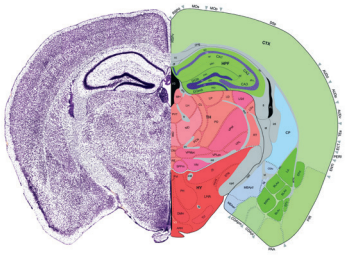


The brain in action The Allen Brain Observatory, the first tool of its kind to capture standardized data about cellular activity of the mouse visual system, launches.

2003

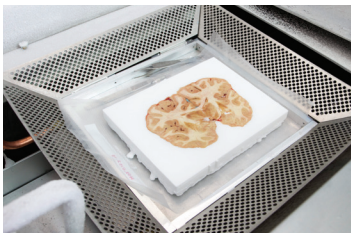
September 16, 2003
Our beginnings Investor and philanthropist Paul G. Allen commits $100M in seed money to launch the Allen Institute for Brain Science.

2006

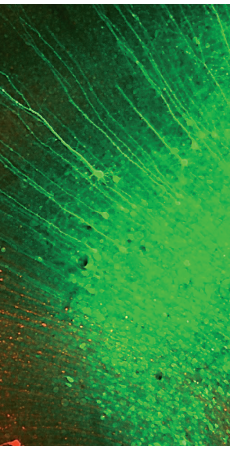


A map completed The Institute's inaugural project, a map of genome-wide gene expression over the entire brain of the adult laboratory mouse known as the Allen Mouse Brain Atlas, is released to the public.

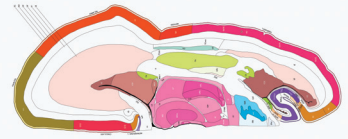
2008

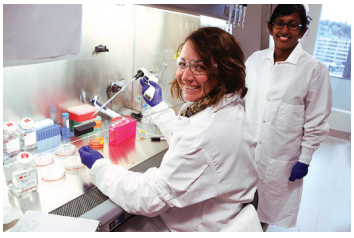


First human brain project The Allen Institute for Brain Science turns to the human brain, announcing an unprecedented project to map more than a thousand genes' expression in the human brain.



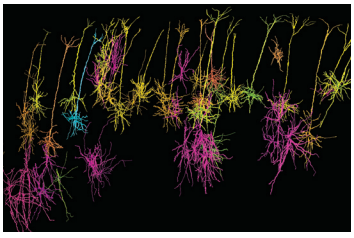
A chronicle of the growing human brain The BrainSpan Atlas of the Developing Human Brain is published in Nature, developed by a consortium of several research organizations including the Allen Institute for Brain Science. The atlas reveals how genes are turned on and off in the developing human brain during pregnancy and sheds light on how autism and other developmental disorders arise at their earliest stages.





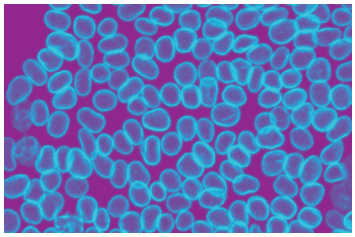
A new institute for cell science is born Mr. Allen commits $100M to launch the Allen Institute for Cell Science, dedicated to creating integrated, predictive models of the human cell and sharing tools and data publicly.

2015



A "periodic table" of brain cell types The first data from the Allen Cell Types Database, a census of cell types in the mouse brain, is released. This ongoing project aims to better understand the brain by characterizing its base elements, the cells.

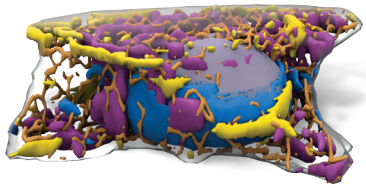
Glowing cells for science The Allen Cell Collection is announced, giving researchers around the world access to the Allen Institute for Cell Science's gene-edited, fluorescently tagged human stem cell lines.



2017

New centers of discovery Two new Allen Discovery Centers are announced: The Allen Discovery Center at Boston Children's Hospital and Harvard Medical School studies the evolution of the human brain, and the Allen Discovery Center at UW Medicine creates global maps of cell lineage. *Photo by Celia Muto.*

2018



An integrated human cell The Allen Institute for Cell Science announces the Allen Integrated Cell, the first predictive and comprehensive 3D model of a live human stem cell, allowing researchers to see multiple structures inside living cells at the same time.

In 15 years we've **transformed**

As the Allen Institute has grown, so has the surrounding scientific landscape. In 2003, sharing data and scientific publications openly was relatively rare in life sciences. Today, open science is a strong and growing movement in bioscience.

4	Allen Discovery Centers
30	Gene-edited stem cell lines produced that are used by labs around the world, targeting 27 cellular structures
69	Allen Distinguished Investigators, past and present
80	Genetically engineered mouse lines in use in labs around the world
2,133	Scientific articles that have cited the original Allen Mouse Brain Atlas publication
24,928	Curated images of human stem cells shared with the community
943,303	High-resolution images shared with the community from the Allen Institute's first completed project, the Allen Mouse Brain Atlas
2,758,943	High-resolution images shared with the community to date, across all Allen Institute for Brain Science resources

In 15 years we've impacted the field

From kidney and heart disease to human language to cutting-edge tools to explore the brain, research building off the Allen Institute's data, resources and support is generating important findings across bioscience and biomedical research.

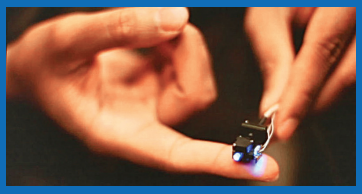
Exploring the potential for organ regeneration
Benjamin Freedman, Ph.D., is studying kidney disease and regeneration at the University of Washington. Freedman is using cell lines from the Allen Institute for Cell Science to grow mini kidneys, or organoids, to better understand the kidney regeneration process and what goes wrong in kidney disease. One day, he hopes to be able to use pluripotent stem cells to grow a functioning kidney in the lab for patients in need of organ transplants.

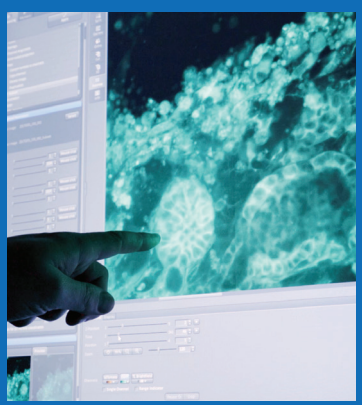
Eight years of distinguished investigators
Many of the ideas sparked through the Allen Distinguished Investigator program are now proving their merit and impact in bioscience. Anthony Zador, M.D., Ph.D., professor of neuroscience at Cold Spring Harbor Laboratory, received an inaugural Allen Distinguished Investigator Award in 2010 to support his outside-the-box idea to map the brain's entire suite of neural connections using a unique RNA-barcoding technique, now being used to draw detailed wiring maps of the mouse brain. Mark Schnitzer, Ph.D., associate professor of biology and applied physics at Stanford University and HHMI Investigator, was also funded in 2010 and used the distinguished investigator support to catalyze an idea for a novel research tool: a tiny, implantable microscope to watch animal brain activity in real time. Today, those microscopes are the basis for the Palo Alto startup company, Inscopix Inc. They are used by hundreds of labs worldwide, including the Allen Institute, and have led to multiple recent insights into brain function and disease.

Allen Institute resources inform speech and language research
Computational neuroscientist Emma Myers, Ph.D., used the Allen Human Brain Atlas in her doctoral research working with Jason Bohland, Ph.D., Associate Director of the Cognitive Neuroimaging Center at Boston University, where she studied the genetic roots of speech and language disorders. The atlas helped her marry the list of genes she identified from previous studies as implicated in speech and language with their expression pattern, a key step toward the researchers' goal to better understand how speech disorders arise in the brain and, ultimately, how to better diagnose and treat them.

Top An implantable microscope developed by Allen Distinguished Investigator Mark Schnitzer, Ph.D. and collaborators. *Ghosh et. al Nat Methods 2011*

Bottom Cell lines developed at the Allen Institute for Cell Science are being used in kidney regeneration research.





Today we're capturing the big picture

The Allen Institute for Brain Science is now making headway into understanding the brain at a scale and depth not possible anywhere else.

A custom-built microscope for Allen Brain Observatory researchers to capture real-time activity of cells in the mouse brain.

A parts list of the brain

Building on their 2016 catalog of 49 different types of cells in the mouse visual cortex, Allen Institute researchers have vastly expanded the project to sort brain cells into categories using the suite of genes each individual cell turns on or off. In this landmark undertaking, they've profiled more than 23,000 different brain cells from the mouse visual cortex and motor cortex and identified more than 130 distinct cell types. Thanks to a unique partnership with Seattle-area neurosurgeons, Allen Institute researchers are also making headway into cataloging human brain cell types using similar techniques.

The 'observatory of the mind'

The Allen Brain Observatory, debuted to the public just two years ago, takes the Allen Institute's large-scale, standardized approach to neuroscience to the level of understanding the brain in action. Scientists are now able to watch—and ultimately to understand—how the mouse brain works in real time. As of this year, the observatory team has generated and shared data from more than 63,000 neurons in action, including 13 different types of inhibitory and excitatory neurons, in the mouse visual cortex across six different regions. They have also begun a new pipeline using Neuropixels probes, a technology co-developed by the Allen Institute with collaborators, that will allow researchers to record electrical activity from more than 1,000 neurons across nine different areas of the brain at once.

25,000 tiny slices to reconstruct a massive neuroscience puzzle

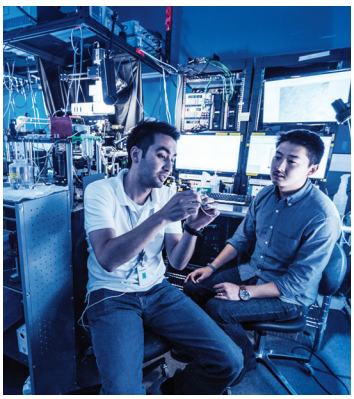
This year, Allen Institute researchers reached a milestone in their part of a large collaborative effort, funded by IARPA, to digitally reconstruct the cells and connections of a cubic millimeter of mouse visual cortex. The team has now completed making 25,000 microscopically thin, precise slices of the speck-sized piece of mouse cortex, which will be the largest piece of brain tissue to be reconstructed in its entirety once the project is complete.

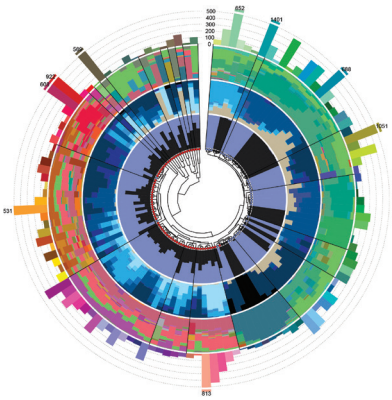
Far left Christof Koch, Ph.D., Chief Scientist & President of the Allen Institute for Brain Science, welcomes attendees to a computational neuroscience conference at the Allen Institute.

Left The Allen Institute for Brain Science scanning lab. Researchers in this lab image brain cells and whole brain slices.

Right Allen Institute electrophysiology researchers establishing new methods to characterize brain cell types.

Far right Allen Institute researchers found more than 130 types of cells in the mouse brain. Shown here, a "dendrogram," or relationship tree, of the cell types based on the genes they express.





Today we're **putting it all together**

The integrated cell
This year, the Allen Institute for Cell Science team debuted the Allen Integrated Cell, the world's first predictive and comprehensive model of a live human stem cell. The new visualization tool builds from the team's large collection of stunning microscopy images taken of their gene-edited, fluorescently tagged human stem cell lines, adding two different computational models that can accurately predict the shape and location of cellular structures.

Pinpointing cellular structures from black and white
The team published a signature paper in the journal Nature Methods describing one of those models, a label-free prediction method, that can accurately recognize cellular structures in cells without fluorescent labels, using only black and white images generated by an inexpensive form of microscopy known as brightfield microscopy.

Heart cell lines join the Allen Cell Collection
The Allen Cell Collection debuted the first gene-edited stem cell lines that carry a fluorescent tag specific to heart muscle cells, or cardiomyocytes. One of those cardiomyocyte-specific lines has labeled the largest known human protein, Titin, a muscle protein.

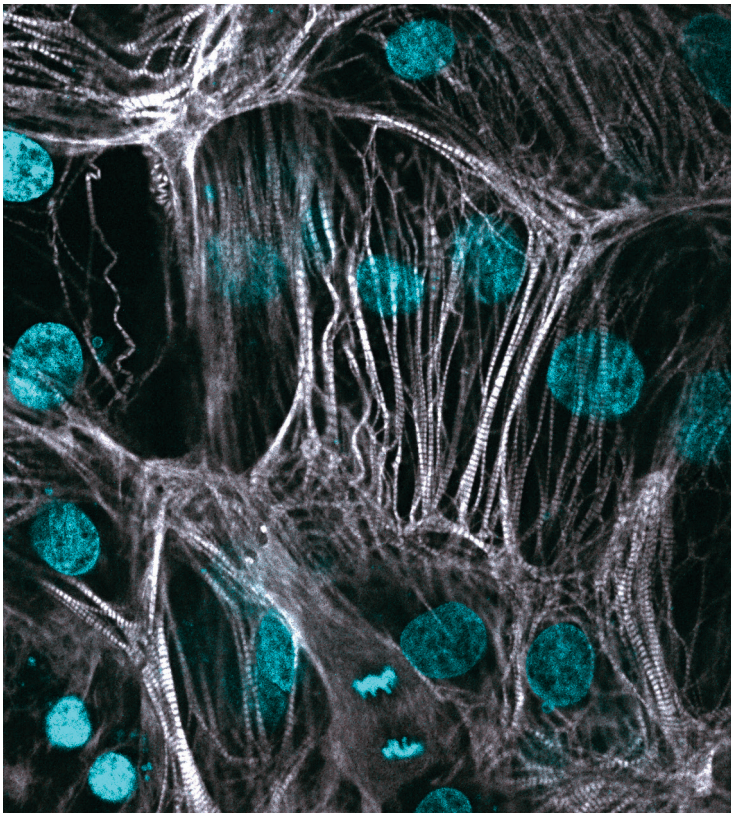
Scientists at the Allen Institute for Cell Science are working toward a cohesive, holistic picture of what a human cell truly looks like.

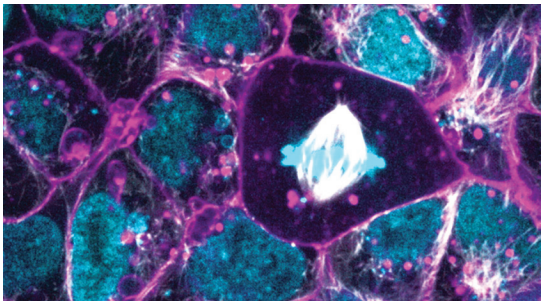
Left An Allen Institute for Cell Science researcher in the lab.

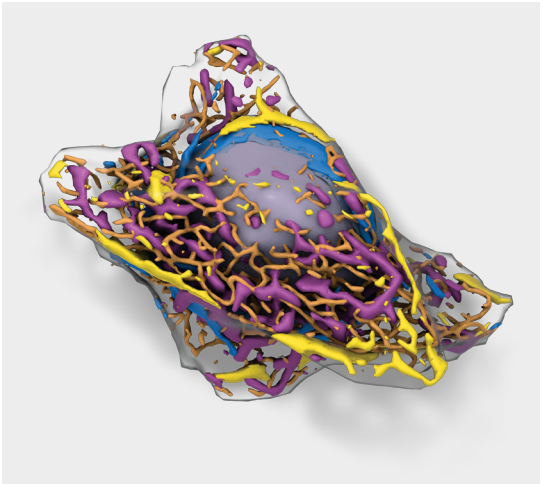
Middle Cardiomyocytes, or heart muscle cells, genetically engineered by Allen Institute for Cell Science researchers to light up under a fluorescent microscope.

Top right An image of fluorescently tagged human stem cells shows one cell in mitosis, or division, taken by researchers at the Allen Institute for Cell Science.

Bottom right A reconstruction of a human stem cell made by Allen Institute for Cell Science researchers.







Today we're sparking new beginnings

Through new research projects launched this year, The Paul G. Allen Frontiers Group is taking concrete steps to accelerate biomedical research to benefit human health.

Rodent astrocytes, a type of brain cell, glowing under the fluorescent microscope. These cells are the focus of a newly launched Allen Distinguished Investigator award project.

An alliance against Alzheimer's disease
The Paul G. Allen Frontiers Group and the American Heart Association/ American Stroke Association announced a new initiative to support research projects on age-related cognitive impairment, including Alzheimer's disease. The unique initiative – committing $43 million over eight years – will bridge an historic divide between studies of cerebrovascular disorders, such as stroke, and neurodegenerative disease.

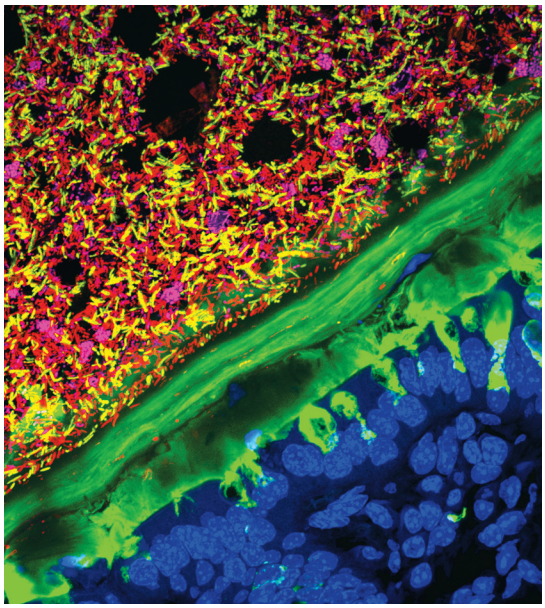
New Allen Distinguished Investigators focus on disease, aging
New Allen Distinguished Investigators announced this year will receive a total of $13.5 million in funding over three years to further their studies into lymphoma, aging, neuroimmunology, how astrocytes are altered in Alzheimer's disease, and nuclear biophysics, an emerging field of bioscience that tackles the unique physics inside cells.

Allen Discovery Centers' progress continues apace
Leaders at Allen Discovery Centers are continuing to tackle complex problems whose solutions have the potential to significantly impact humanity. Researchers at the Allen Discovery Center at Stanford University made an exciting discovery about the biophysics of certain bacteria that could point to a whole new avenue for antibiotic development. The Allen Discovery Center at UW Medicine published several studies describing new approaches to profiling cell lineages of different organisms. The Allen Discovery Center at Boston Children's Hospital and Harvard University, which focuses on human brain evolution, celebrated its official grand opening this fall; and the Allen Discovery Center at Tufts University uncovered new findings about how frog bodies signal injuries through electricity.

Left Stained sections from the distal colon of a mouse, with various bacteria shown in yellow and red, mucus in green, and epithelial cells in blue. The Allen Discovery Center at Stanford University is modeling infections with the pathogenic bacteria *Salmonella. Image by Kristen Earle, Gabriel Billings, Kerwyn Casey Huang and Justin Sonnenburg.*

Top right Markus Covert, Ph.D., leader of the Allen Discovery Center at Stanford University, speaks at the 2017 Allen Frontiers Symposium in San Francisco.

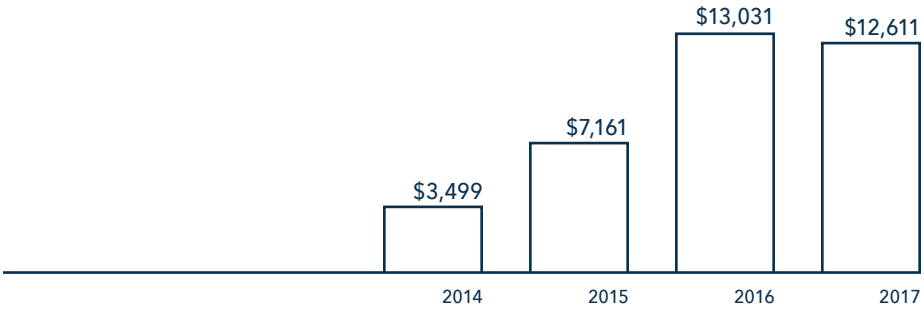
Bottom right Neurodegeneration panel speakers at the 2017 Allen Frontiers Symposium in San Francisco.



Financial summary

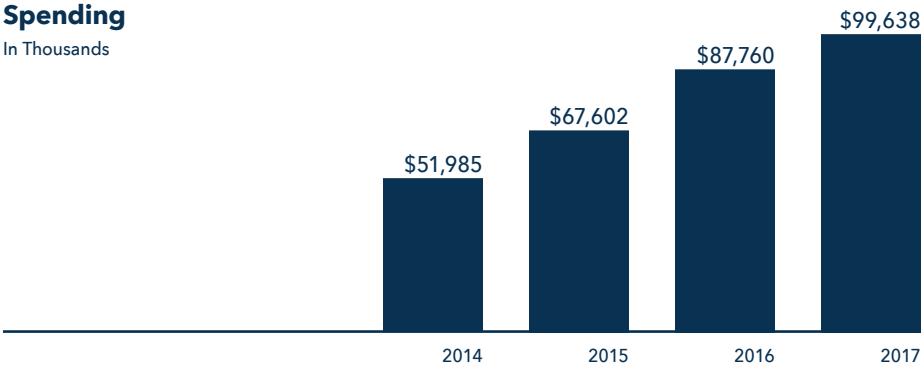
Research Grants & Contract Revenue

In Thousands



Total Spending

In Thousands



Allen Institute Fiscal Years 2017 and 2016

(In Thousands)

	2017 (Audited)	2016 (Audited)
Support and Revenue		
Contributions	**$ 109**	$286,090
Research Grants and Contracts	**12,611**	13,031
Other	**4,485**	(223)
Total Support and Revenue	**17,205**	298,898
Expenses		
Program Services	**80,082**	69,167
Management and General	**19,556**	18,593
Total Expenses	**99,638**	87,760
Change in Net Assets	**(82,433)**	211,138
Net Assets: Beginning of Year	**427,447**	216,309
Net Assets: End of Year	**$345,014**	$427,447

The Allen Institute, comprising the Allen Institute for Brain Science, the Allen Institute for Cell Science and the administrative portion of The Paul G. Allen Frontiers Group, continues to grow. A large contribution in 2016 will support the Institute for multiple years.

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Paul G. Allen

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Marjorie Thomas
Chief Financial Officer

Christof Koch, Ph.D.
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In memory of our founder
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Paul's vision and insight have been an inspiration to me and to many others both here at the Institute that bears his name, and in the myriad of other areas that made up the fantastic universe of his interests. He will be sorely missed. We honor his legacy today, and every day into the long future of the Allen Institute, by carrying out our mission of tackling the hard problems in bioscience and making a significant difference in our respective fields.

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