2020 ANNUAL REPORT

ALLEN INSTITUTE
open for science

2020 has laid bare incredible challenges that face scientists and society alike. In what seemed like the blink of an eye, the virus we now call SARS-CoV-2 changed life as we know it around the world. COVID-19 is one of the most urgent scientific problems of our lifetimes; at the Allen Institute and around the world, research teams are pivoting from other fields to tackle it head-on. At the same time, we're undergoing a social reckoning of incredible scale as we respond to systemic racism.

These dual events show us how tightly science and society are connected. Our progress against the pandemic depends on many different societal factors and institutions, in addition to scientific research. And science is not immune to the biases that underlie every other facet of society; racism's integration into our lives and workplaces hampers our progress and must be addressed. At the Allen Institute, our leadership team is proud to support Diversity, Equity and Inclusion across our team – innovation requires diverse skills, backgrounds, and points of view: We are better together, and we are committed to making durable, lasting change.

I've never been so proud of my fellow scientists and so humbled by the tasks that face us at the same time. Globally, scientists are rising to 2020's unfolding crises. Locally, I continue to be amazed at the commitment of my Allen Institute colleagues to continue fulfilling our mission and to take on new complex problems, even in such an extraordinary year.

The events of 2020 underscore what we already knew: Science is foundational. Science is relevant. Science is for all of us.

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

This year has starkly illuminated why science is critical to the wellbeing of humanity. The unknowns of the novel coronavirus touch almost every corner of biomedical research, and also illuminate why foundational research is so important. There's so much we still need to understand about basic biological systems and the underpinnings of human health.

Neuroscientists Yi Ding, Ph.D. (left), and Anna Marie Yanny at work in an Allen Institute lab studying postmortem human brain samples to uncover the genetic mechanisms behind Alzheimer's disease.

ALLEN INSTITUTE *for* BRAIN SCIENCE

Science is a New Perspective

A fresh look at Alzheimer's disease

If scientists understood how Alzheimer's disease starts, they might have a better understanding of how to stop it. That's the premise behind a new National Institute on Aging-funded collaborative research center, headquartered at the Allen Institute for Brain Science with collaborations with UW Medicine and Kaiser Permanente Washington Health Research Institute. The research collaboration aims to build high-resolution maps of Alzheimer's patients' brains and identify how their neurons and other brain cells differ from those of healthy people.

By comparing brain cells across patients with different stages of the disease, the researchers will seek to pinpoint how and where the progressive disorder starts – and, ultimately, to find new targets for therapy. The research teams will use genes switched on in individual brain cells of patients with Alzheimer's disease to classify the cells into categories, or specific cell types, and then ask how those cell types and their active genes are affected as Alzheimer's disease progresses.

Using these methods to study brains from people across the spectrum of early- to late-stage Alzheimer's disease should reveal the specific kinds of neurons and other brain cells that are most vulnerable at the beginning of the disease. Such a detailed understanding of Alzheimer's origins is desperately needed, as many once-promising treatments have failed to benefit patients.

Like all resources generated at the Allen Institute, the data from this center will be openly available to the scientific community – and could catalyze progress in treating other neurodegenerative diseases as well.

Immunologist Charles Roll prepares blood samples from volunteers with COVID-19 for studies that will analyze the immune response to the novel virus.

ALLEN INSTITUTE *for* IMMUNOLOGY

Science is Critical

Researchers quickly pivot to study the novel coronavirus

A new study launched this summer in Seattle aims to tackle one of the most pressing questions about COVID-19: Why do some people infected with the novel coronavirus develop life-threatening symptoms, while others recover with few or even no symptoms at all?

Research teams from Fred Hutchinson Cancer Research Center and the Allen Institute for Immunology are tracking the details of individuals' immune responses as they are infected with, and recover from, SARS-CoV-2. The researchers are delving into the molecular and cellular details of how these patients' immune systems are responding to the virus, both shortly after infection and in the weeks and months following.

Scientific groups around the world are pivoting to focus on the novel coronavirus, but many studies to date have focused only on severe cases. This study is instead enrolling people with mild-to-moderate symptoms with the goal of understanding how their immune responses differ from those of severely ill patients.

The Allen Institute for Immunology research team is using their newly established deep immune system profiling pipeline for the study. The pipeline was built to integrate several different types of scientific data gleaned from a single blood or tissue sample and compare samples from the same person over weeks or months as their disease progresses, stabilizes or resolves. This process will allow them to zero in on the aspects of the immune response specific to SARS-CoV-2.

Their findings could ultimately inform better treatments and preventions for the novel virus. If scientists can understand the "successful" immune responses that accompany a mild or moderate case of the virus, and which aspects of those responses fail in severe illness, they might be able to design more effective vaccines and therapies.

Members of the Allen Institute serology team (left to right) Delissa McMillen, M.S., M.B.A., Kelli Burley, and Kaylee Oliva outside the lab.

Cardiologist Mukesh Jain, M.D., presents his research at the 2019 Allen Frontiers Symposium in Boston.

THE
PAUL G. ALLEN
FRONTIERS GROUP

Science is Life-Changing

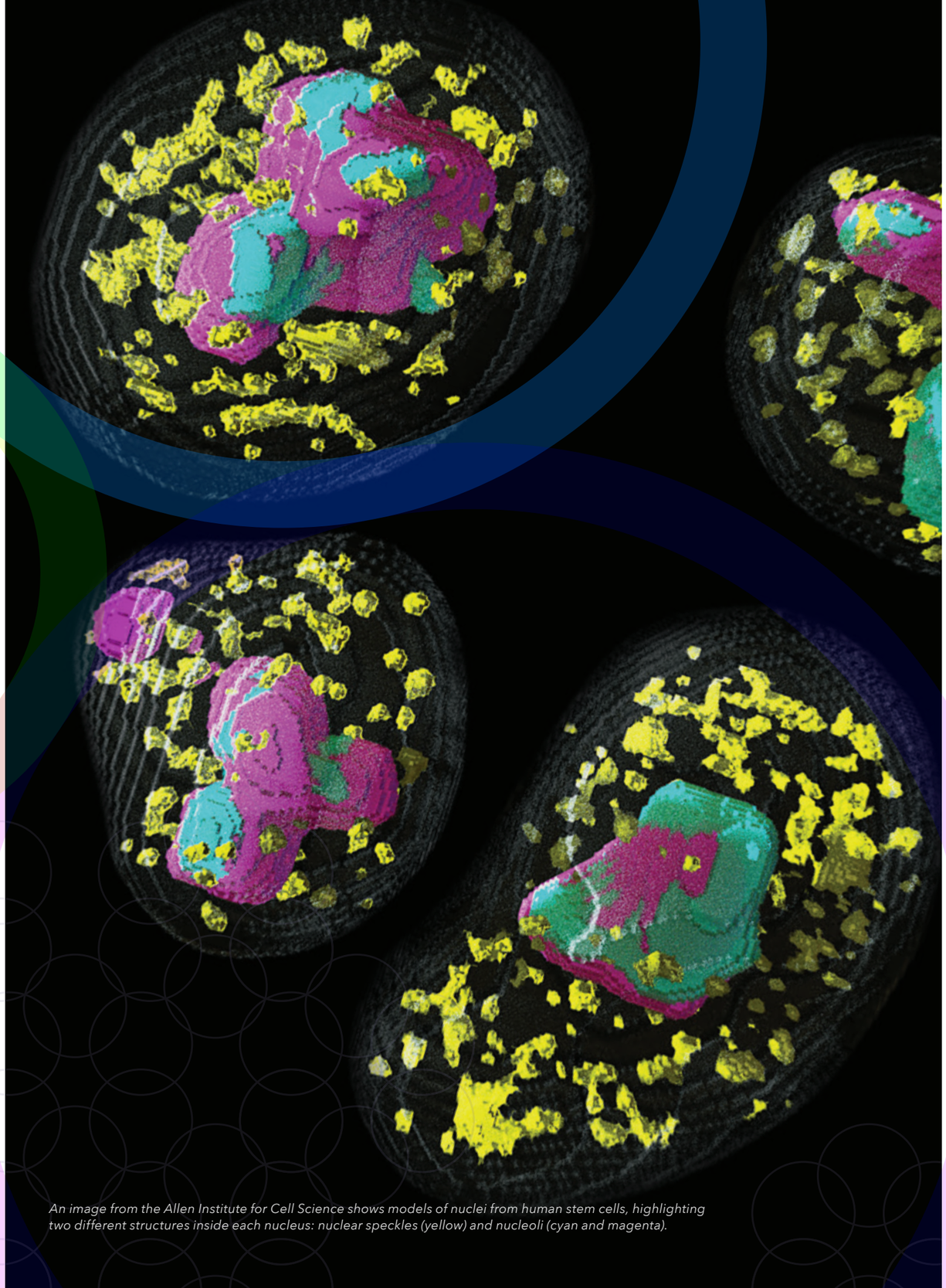
Frontiers-supported researchers' progress in translational science

The Paul G. Allen Frontiers Group awardees work across many emerging fields of bioscience; the implications of their research are equally far-reaching. Three recent projects from our awardees focus on important diseases.

Hodgkin lymphoma recruits and trains immune cells to help it thrive
A new study uncovered tricks Hodgkin lymphoma uses to hide itself from the immune system – and a possible new avenue for treatment. Allen Distinguished Investigator Christian Steidl, M.D., of BC Cancer and the University of British Columbia, and his colleagues sifted through lymphoma tumor biopsies, cell by single cell, to find a type of immune cell in tumors that is absent or rare in healthy people. Hodgkin lymphoma cells co-opt these immune cells to shield the cancers from the rest of the immune system. The researchers also found a molecular signature on these cells that could render them vulnerable to a certain experimental cancer treatment.

Adapting treatments aimed at Alzheimer's disease to combat COVID-19
When early reports came out about COVID-19's more bizarre effects – strokes, heart attacks, purple toes – University Hospitals and Case Western Reserve University cardiologist Mukesh K. Jain, M.D., spotted a common thread between the novel coronavirus and dementia: a link to blood clots and a dangerous lack of oxygen. With an award from the American Heart Association-Allen Initiative in Brain Health and Cognitive Impairment, Jain and his colleagues are developing a new class of treatments for dementia aimed at reversing that lack of oxygen and keeping blood flowing freely to the brain. Now, they're working to test this new class of therapies for severe COVID-19 patients.

Old age changes the way blood accesses the brain
A study in mice has found that contrary to longstanding dogma, many blood proteins easily cross into the brain. With funding from the AHA-Allen Initiative, a research team led by Stanford University School of Medicine's Tony Wyss-Coray, Ph.D., found that the blood-brain barrier is more dynamic and permeable than previously believed, but the way proteins cross that barrier changes with age. The researchers also found a drug that causes old mice to switch back to the young form of transport. Next, the team will test if this transport mechanism plays a role in cognitive decline.



An image from the Allen Institute for Cell Science shows models of nuclei from human stem cells, highlighting two different structures inside each nucleus: nuclear speckles (yellow) and nucleoli (cyan and magenta).

ALLEN INSTITUTE *for*
CELL SCIENCE

Science is Fundamental

A new project to map the nucleus, the information center of our cells

Researchers at the Allen Institute for Cell Science combine computational models and experimental data to answer big questions about how human cells work: How is a cell built? What rules govern its organization? Can scientists predict what a cell is going to do next based on what it looks like now?

The Allen Institute for Cell Science team.

This year, they've launched a new collaborative project to ask and answer these questions about our cells' largest internal structure: the nucleus. The information center of our cells, the nucleus houses all of our DNA – our genome – and its many associated proteins. If laid end-to-end, the entire string of a single human cell's genome would stretch about 6.5 feet long. But each of our cells has to fit all that DNA into the nucleus, a microscopic structure less than a fifth the width of a human hair.

It's not just a packing problem – the nucleus's organization needs to grant proteins access to DNA to read out its genes, to replicate the DNA every time the cell divides, to switch off genes that need to remain silenced. This organization also changes in different cell states, between cell types, and in disease. There's a whole city's worth of architecture inside each human nucleus, and scientists still understand very little about its rules and structure.

With new funding from the National Institutes of Health, Allen Institute for Cell Science researchers are teaming up with other scientific groups through the 4D Nucleome program to build realistic, predictive models of the human nucleus and genome. Their collaborators are constructing models of the human genome's physical structure within the nucleus, and then merging those with Allen Institute models of the nucleus and some of its internal compartments. This merging of models will help the researchers understand important details about how the genome fits into the actual 3D structure of the nucleus, how this varies in different cell states, and, ultimately, uncover new findings about how the nucleus and genome function in health and disease.

Neuroscientist Ximena Opitz-Araya, in the lab in 2019, working on new ways to label mouse and human brain cells.

Science is Forward-Looking

The next phase of neuroscience at the Allen Institute

This spring, we announced plans for new phases of research for the Allen Institute's neuroscience-focused teams.

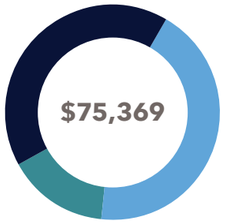
The Allen Institute for Brain Science, the Institute's largest and oldest division, is moving forward with a sole focus on brain cell types and connectivity research, while its MindScope research team transitioned to an independent research program. The Institute also announced a new neuroscience-related division, focused on neural computation and dynamics, that will launch in 2022.

These changes reflect a structural transition for the Allen Institute for Brain Science. They also represent a shift toward a new model for the future of the Allen Institute that was developed together with our late founder, Paul G. Allen, before his passing. Under this model, teams of researchers will coalesce around a discrete, challenging problem or set of problems in bioscience that can be solved in a set period of time.

The Allen Institute for Brain Science, with Hongkui Zeng, Ph.D. at the helm as its new Executive Vice President and Director, will move into a new 16-year phase that builds on the team's success in working toward a "periodic table" of brain cell types. The MindScope Program, which seeks to understand how the brain's neural circuits produce the sense of vision in behaving animals, has also moved onto a new phase of discovery and continues to be directed by Christof Koch, Ph.D.

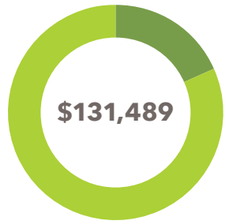
Financial Summary

Total Support & Revenue (In Thousands)



	2019 (Audited)	2018 (Audited)
Contributions	$31,242	$290
Research Grants & Contracts	$32,648	$30,244
Other	$11,479	$1,312

Total Expenses (In Thousands)

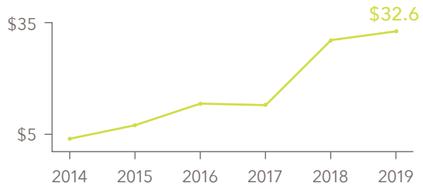


	2019 (Audited)	2018 (Audited)
Program Services	$107,666	$92,991
Management & General	$23,823	$20,831

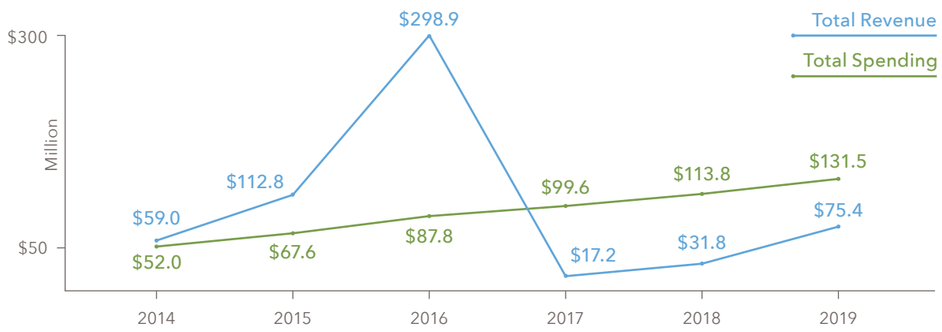
Change in Assets

	2019 (Audited)	2018 (Audited)
Change in Net Assets	(56,120)	(81,976)
Net Assets, Beginning of Year	263,038	345,014
Net Assets, End of Year	**206,918**	263,038

Research Grants & Contract Revenue (In Millions)



Revenue & Spending 5 Year Trend (In Millions)



The Allen Institute, comprising the Allen Institute for Brain Science, the Allen Institute for Cell Science, the Allen Institute for Immunology 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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