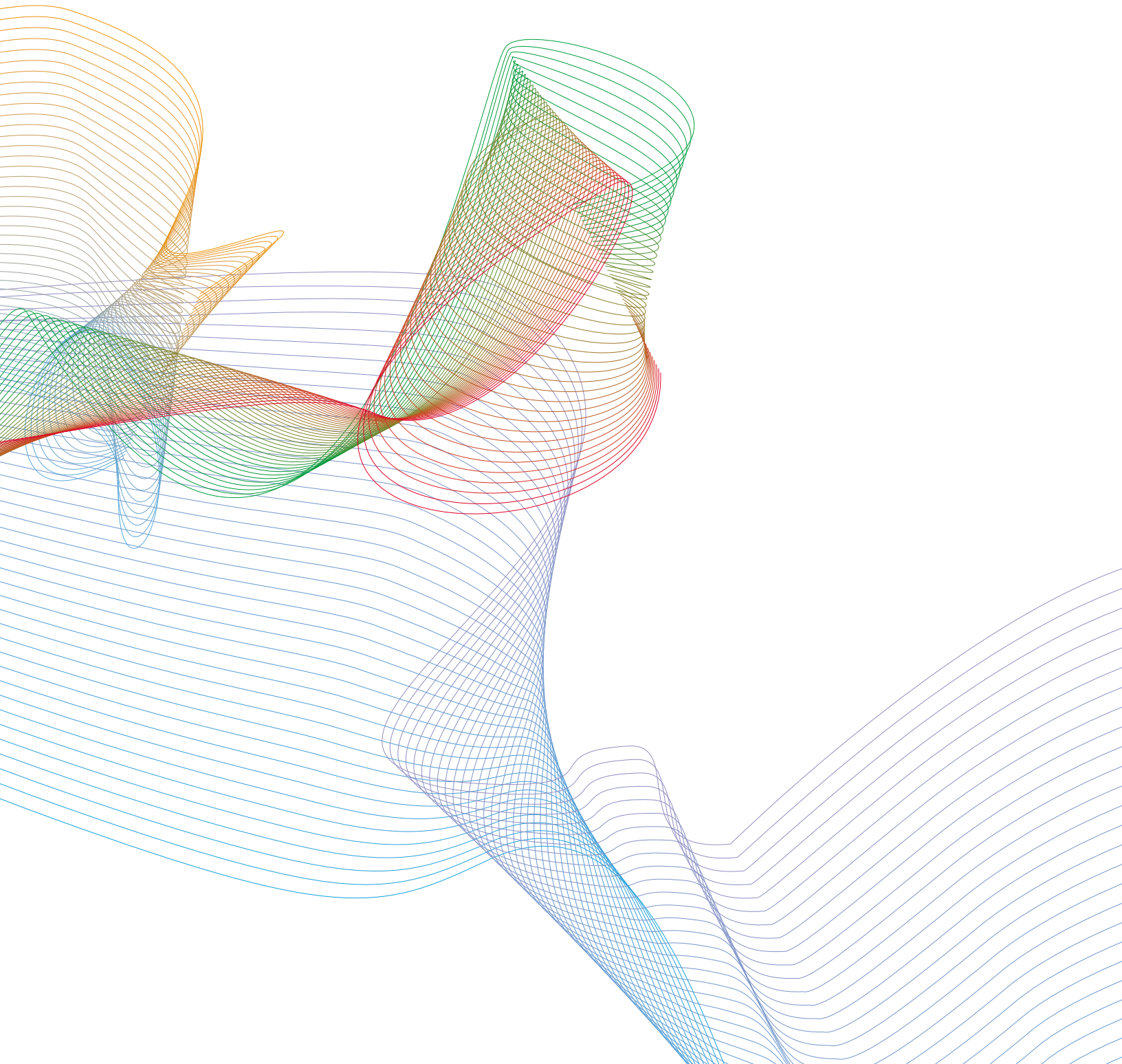




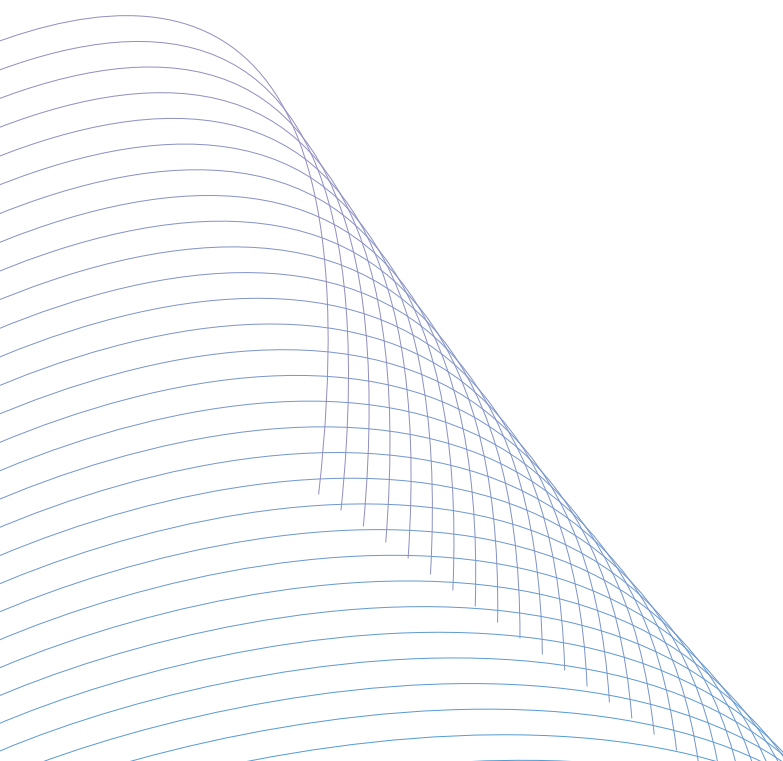
**SIMONS FOUNDATION**

Annual Report 2.007 x 10<sup>3</sup>



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## The primary mission of the Simons Foundation is to advance the frontiers of research in the basic sciences and mathematics.

### **Letter from the President** June 30, 2008

Two years have passed since my last letter, two years marked by increased grant making, an expanded staff, and a stronger sense of direction. Though our funding interests span the broad reach of physical sciences, mathematics and life sciences, our commitment to our core mission remains focused, and our strategy of leveraging our funding continues to be key to our decision making.

In the area of Math and the Physical Sciences, the Simons Foundation continues its support of fine research institutions around the world. Under the direction of trustee and founder Jim Simons, the foundation seeks to catalyze donations to these organizations through challenge grants and pledged contributions to their seed programs.

In the Life Sciences too, the Simons Foundation offers institutional grants as well as more targeted research support. Our grant making has been diverse and includes such topics as systems biology, human evolution and math in biology, all of which probe important questions at the leading edges of knowledge.

Perhaps the most significant change in the foundation over the past two years has been a more proactive approach taken in our Autism Research Initiative. Under the leadership of Dr. Gerald D. Fischbach, we have been able to open up and expand our application process.



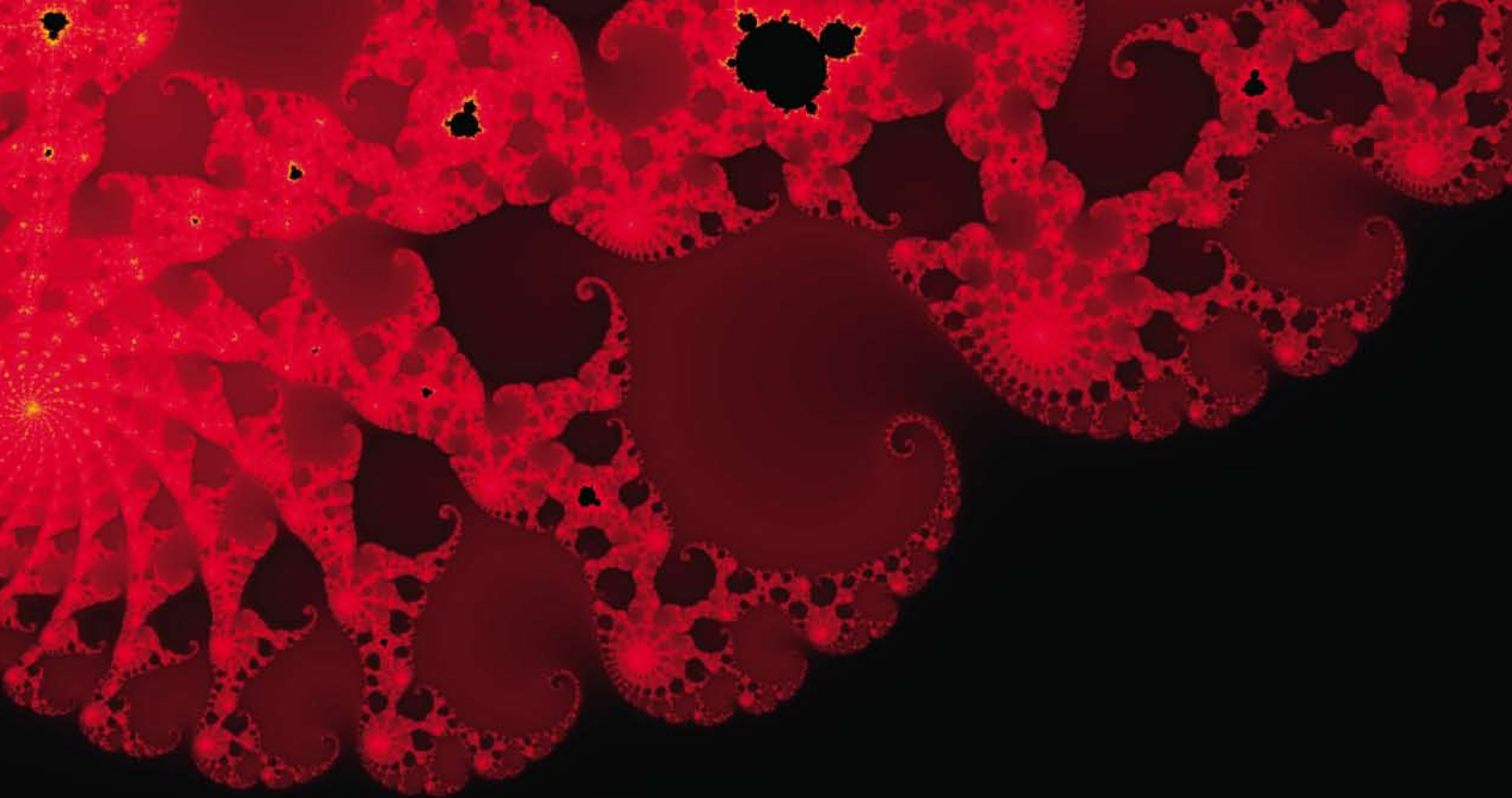
Grants, made to individual researchers through their institutional affiliations, are directed toward answering important questions in genetics and neuroscience in the hope that this work will lead to an understanding of the causes of autism.

A final small, but important, part of the Simons Foundation is stimulating math and science education to help prepare tomorrow's scientific researchers and technicians. Through such efforts as Math for America and the World Science Festival, we hope to see our children better prepared for the challenges ahead.

In looking back on the past two years, we are all proud of our expansion in support of more research projects, and the ongoing accomplishments and fulfilling sense of purpose of all of our grantees. I look forward to more of the same in the upcoming year.

Marilyn Simons  
President  
Simons Foundation

# Enable



## Progress through Math and Science

From Archimedes to Newton to Einstein, much of the most profound work in physics has been deeply intertwined with the geometric side of mathematics. Since then, and with the advent of such areas as quantum field theory and string theory, developments in geometry and physics have become if anything more interrelated.

The Simons Foundation supports the work of institutions and organizations that give many of the world's best mathematicians and physicists the opportunity to work and interact

in environments designed to enhance progress. Through symposia, visiting lectureships and the support of under-served communities of scientists, these institutions are broadening the reach of these important disciplines.

The principles of physics and mathematics are the bedrock of the universe, and yet they often go unappreciated by the public. Part of our mission is also to train students and educators in these disciplines, and to organize programs that can introduce the wonders of these fields to children and to the general public.

## The foundation of progress in science and technology is through basic research.

### Institute for Advanced Study (IAS)

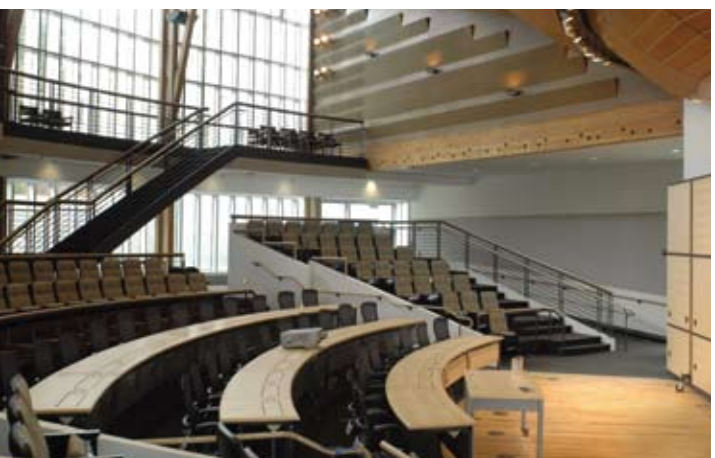
The Simons Center for Systems Biology at the Institute for Advanced Study (IAS) is a leading center for theoretical research in the sciences, and its work is at the interface of molecular biology and the physical sciences.

Led by Arnold J. Levine, Ph.D., the center hosts a wide range of distinguished members and visitors each year, and fosters original research in the field of systems biology. The use of newer technologies has generated large amounts of as yet unseen biological and genetic data. The tools of modern physics, mathematics and computer science enable integration of this data, allowing scientists to make progress toward a fundamental understanding of evolution and basic molecular biology, and leading to significant breakthroughs in personalized approaches to the diagnosis and treatment of cancer, viruses, and other diseases.

Researchers at the center include a diverse group of theoretical physicists, cancer biologists, mathematicians and computational biologists of extraordinary promise who are conducting detailed analyses of the large genomic, structural and clinical databases that have been created over the past few years. The center uses this information to explore and understand how genes are expressed in time (fetus, adult, the progression of old age), space (location within a cell, an organ, a neuron), and in different human conditions (disease, aging, embryonic development).

The postdoctoral training model that the center has developed includes frequent conferences, symposia and seminars, and encourages collaborations with other academic, clinical and industrial groups, both locally and around the world, to test information and confirm theoretical models.

[www.ias.edu](http://www.ias.edu)



## Mathematical Sciences Research Institute (MSRI)

The Mathematical Sciences Research Institute (MSRI), founded by three Berkeley professors in 1982 in Berkeley, CA, is dedicated to advancing fundamental knowledge in mathematics and the mathematical sciences, and to cultivating human capital in these areas. Each year more than 1,700 mathematical scientists visit MSRI, one of the world's leading mathematical science research centers, to do research and participate in workshops and conferences. There are also ongoing public events and programs designed for educators and students.

### Annual grants from the Simons Foundation support:

#### Simons Visiting Professors

Leaders in the field are invited to meet and work with peers and mentor postdoctoral fellows.

#### MSRI Biology Colloquium

Mathematicians are encouraged to learn about and engage in problems related to biology, with week-long visits by innovators from around the U.S.

#### MSRI Museion Dinner Lectures

A speaker series that convenes mathematical scientists and others interested in the field.

#### Shiing-Shen Chern Hall and Simons Auditorium

MSRI facilities were expanded and greatly improved, adding state-of-the-art capabilities.

In 2007 MSRI received a \$10 million gift from the Simons Foundation, the largest single cash pledge in the institute's history and the largest gift of endowment made to a U.S.-based institute dedicated to mathematics. The Eisenbud Endowed Professorship has been established (in the name of Dr. David Eisenbud, former Director of MSRI) to support senior MSRI scholars. And a challenge grant helped establish an endowment to ensure excellence and the long-term survival of MSRI.

[www.msri.org](http://www.msri.org)

## The principles of physics and mathematics are the basis of the universe, and yet they often go unappreciated by the public.

8

### Institut des Hautes Études Scientifiques (IHÉS)

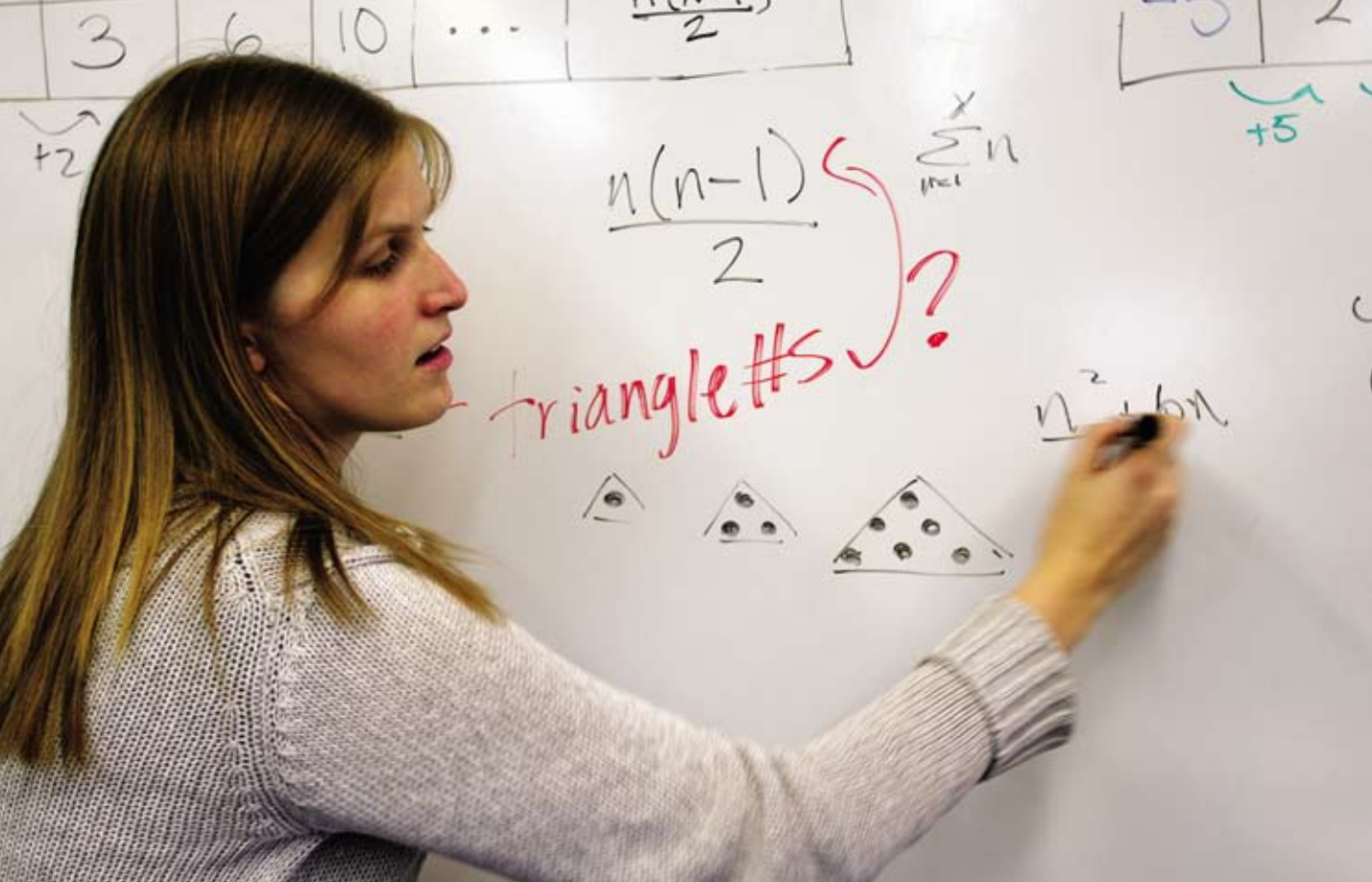
With its core of permanent professors and over 250 visiting researchers from around the world, the mission of the Institut des Hautes Études Scientifiques (IHÉS)—located in Bures-sur-Yvette, France—is to foster fundamental research at its highest level, theoretical research in mathematics, physics, human sciences methodology and any other related theory-based discipline. Since 1998, the Simons Foundation has been instrumental in supporting this work.

The foundation was a major donor to the first IHÉS international “Invest in the Power of the Intellect” fundraising campaign, out of which came the institute’s first endowment and the construction of a 130-seat conference center. The conference center enables IHÉS to assemble leading experts in a wide variety of disciplines for discussion and sharing.

As it celebrates its 50th anniversary, IHÉS recently launched its second international fundraising campaign. The goal is to ensure the success of research in new scientific fields, such as biology, medicine and high technology, recruit research talent, and reach out to young scientists and under-represented researchers—those from developing countries, and women. In support of this effort, the foundation has provided IHÉS with a €6 million challenge grant, half of which is intended to reinforce the institute’s activities at the interface with biology. To meet this challenge the institute must raise €3 million in France and €3 million in the rest of the world.

This challenge grant represents the largest ever gift in IHÉS history and contributes significantly to the development and financial stability of one of the world’s leading independent research institutes.

[www.ihes.fr](http://www.ihes.fr)



### Math for America (MfA)

Since its inception in 2004, Math for America (MfA), a nonprofit organization with a mission to improve math education in our nation's public schools, has recruited, trained and retained nearly 200 mathematically knowledgeable individuals to become teachers in New York City.

The MfA Fellowship is a five-year program for mathematically talented individuals who are new to teaching. After a rigorous selection process, fellows spend their first year earning a Master's degree in education with a partner college or university - Bard College, NYU or Teachers College at Columbia University - followed by a four-year commitment to teach in public schools. The fellowship includes a full tuition scholarship, annual stipends, mentoring and professional development services.

The MfA Master Teacher program selects and rewards exceptional high school math teachers who are currently working in public schools with a four-year fellowship. Master Teachers receive annual stipends and participate in professional development and leadership opportunities.

MfA's New York City program was designed as a pilot for a national program. In 2007 Congress passed, and the President signed into law, legislation to create a new National Science Foundation Teaching Fellowship Program to substantially increase the corps of highly qualified science, technology, engineering and mathematics (STEM) teachers. The NSF program and an enhanced Robert Noyce Teaching Fellowship program was modeled on MfA's New York City programs.

MfA has expanded to Los Angeles and San Diego, California, and actively seeks partnerships with state governments, educational institutions and foundations.

[www.mathforamerica.org](http://www.mathforamerica.org)

The goal is to ensure the success of research in new scientific fields, such as biology, medicine and high technology, recruit research talent, and reach out to young scientists.

### The Vehicle Design Summit (VDS)

The Vehicle Design Summit (VDS) is an international, student-led initiative with the mission of innovation in the area of sustainable transportation technologies. VDS began in 2006 with an eight-week design-build session that brought 55 of the world's top engineering students together at the Massachusetts Institute of Technology (MIT) to build concept cars. The all-volunteer student team (from 21 universities in 13 countries) designed and built four full-scale driving prototypes from scratch that summer! This unprecedented endeavor drew national media coverage, including a Discovery Channel documentary.

A Simons Foundation's contribution early on led the way for over 30 other individuals, companies and foundations to pledge support, with almost \$500,000 in total. There are now teams at 20 universities worldwide collaborating on building a series electric hybrid car within three years, with the equivalent of 100 mpg efficiency and paving the way for a future version of 200 mpg.

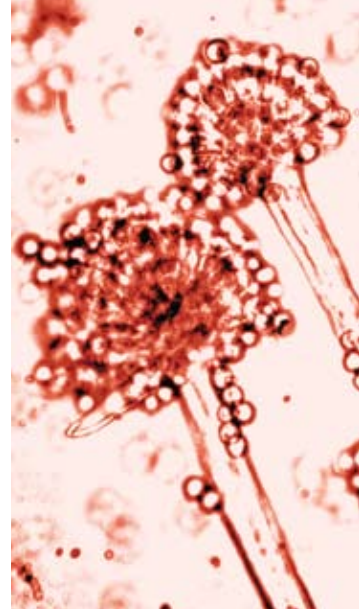
"The opportunity for students to work with international colleagues on a topic of global import (energy efficiency) while still in school is a tremendous educational experience, with the potential to yield both new ideas and new innovators who can lead research across the energy sector," said Robyn Allen, Executive Director. "We are very grateful to the Simons Foundation for enabling us to leverage the talent and passion of university students toward this crucial challenge."

Robyn Allen co-founded VDS while she was an MIT undergraduate studying aerospace engineering.

[www.vehicledesignsummit.org](http://www.vehicledesignsummit.org)

# NY08

# World<sup>TM</sup> Science Festival



## Art and Science join together in reaching the public

The first annual World Science Festival (WSF) took place at 15 venues around New York City from May 28 to June 1, 2008. Co-founders Dr. Brian Greene, a Columbia University professor of physics and mathematics and Pulitzer Prize-winning author of *The Elegant Universe*, and Tracy Day, an Emmy Award-winning television journalist, envisioned the event as a way to help make advanced science accessible, interesting and even inspirational to more people, children and adults.

WSF brought together over a dozen Nobel laureates, leading researchers, educators and high-level policy makers with creative, award-winning artists, filmmakers and performers in over 40 unique lectures, debates, film, music, theater and interactive events. All were designed to bring science to the forefront and explore how science discovery and innovation shape modern life. Among the programs: a discussion of quantum mechanics with actor and television host Alan Alda; a talk on human perception with neurologist Oliver Sacks; an exploration of robotics, pyrotechnics and virtual reality by Walt Disney technologists; a lecture on longevity by Pulitzer Prize-winning author Robert N. Butler; gallery talks at the Metropolitan Museum of Art and a dance performance at the Guggenheim Museum, as well as a street fair in lower Manhattan.

The WSF was made possible by the support of a number of foundations, including the Simons Foundation, corporate sponsors and program partner organizations, and was co-hosted by Columbia University, New York University, Cooper Union, Rockefeller University and the City University of New York.

[www.worldsciencefestival.com](http://www.worldsciencefestival.com)

## The Turkana Basin continues to provide dramatic new evidence concerning human evolution.

### Turkana Basin Institute

A new and exciting research program addressing the entire span of human evolution is planned in the Omo-Turkana Basin of northern Kenya and southern Ethiopia.

Extending back in time from modern humans, through the first pastoralists and pottery makers, the earliest members of our species, *Homo sapiens*, early diversity in the genus *Homo*, and back to our earliest ancestors, the geological deposits in this large lake basin span an exceptionally long stretch of time.

Older sediments extend this record even farther back to the origin of monkeys and apes, including the earliest known apes, and even to a time, unknown elsewhere in Africa, when dinosaurs dominated the fauna.

Nearly four decades of research have resulted in a good understanding of the lake basin's geological history and the distribution and age of the extensive exposures. Sediments from the past 10,000 years are particularly well exposed at Turkana, but to date this important phase of human evolution has been little investigated. Until recent times, a waterway directly connected the Lake Turkana Basin to the civilizations in the Upper Nile and the Sudan. It is therefore likely that excavations of the extensive Turkana Holocene sites will provide evidence of links with these cultures and may even show that the origins of the ancient Egyptian cultures came as much from Africa as from farther north. The past 10,000 years are critical in disclosing these links.



Until now, research in the Turkana Basin had largely been led by Europeans and Americans who have access to substantial government funding. Limited access to research funds, as well as scarce research opportunities in government institutions had, until now, presented a major deterrent to Africans who wish to continue Africa-based research in paleontology and paleoanthropology. This new initiative will provide the opportunity to involve indigenous Africans as key members and leaders of the research efforts. Through private funding, they will have the ability to develop a career in this field, based in their home continent, but with strong links to academic institutions in the rest of the world.


In addition, this initiative will provide financial and material benefits to the local communities. Now, all the recovered fossils and artifacts are taken to a central institution in Kenya's capital city, where local communities have minimal participation in the research activities. The creation of permanent research stations will result in the direct involvement of local people, and will generate sustainable employment opportunities as well as improved local infrastructure. These activities and benefits will increase appreciation of their natural heritage and will give a better understanding of the importance of these research activities in the international arena.

Stony Brook University has a long tradition of involvement and initiatives in human evolution. As the academic center of the institute, Stony Brook will ensure sustainability of the Turkana Basin Institute and the future of its research programs. The institute will provide opportunities for field training for both African and American students that will stimulate further research and educational programs being developed using the Internet.

[www.stonybrook.edu/tbi](http://www.stonybrook.edu/tbi)

# Explore





## SFARI: Simons Foundation Autism Research Initiative

Autism is a developmental disorder that was first described more than 70 years ago. Clinical descriptions have become more precise with time, and new diagnostic instruments have quantified cardinal clinical features across the entire spectrum of autism disorders.

Due in part to these improvements in diagnosis, the number of children identified as having autism has steadily risen over the past two decades. Despite the increasing awareness of autism, however, the disorder's causes remain mysterious.

However, we have good reasons to hope that, in the near future, we will understand much more about what causes autism. Recent advances in genetics and neuroscience have led to new hypotheses, and to the discovery of molecular, anatomical and functional 'biomarkers' that will facilitate research.

- The rapid development of genetic technologies, including high-resolution comparative genome hybridization and high-throughput DNA sequencing, has intensified the search for risk genes. It is clear that no single gene causes all manifestations of autism, but the identification of genetic risk factors will turn attention to relevant

biochemical pathways, regions of the brain and critical times during development.

- New methods for characterizing neural circuits and for manipulating genes that alter circuit function can help understand learning, memory and the 'social brain'. They also offer the exciting possibility of preventing or even reversing errors in development that predispose to autism.
- High-resolution brain imaging and new methods for recording electromagnetic signals from populations of nerve cells have led to testable hypotheses about social cognition, language delay and repetitive behaviors.

SFARI, the Simons Foundation Autism Research Initiative, is funding research in each of these areas. We have also initiated an unprecedented effort to characterize 2,000 'simplex' families (see page 20).

There is a growing excitement in the autism research community. New, talented investigators have been attracted to the field, and hopes are high that major advances are on the horizon.

Gerald D. Fischbach  
SFARI Director

Christopher  
Walsh



*“Autism is a disorder that seems to be telling us something very important about how the brain works.”*

### Clues to the brain’s mysteries, courtesy of the Middle East

Over the past 14 years, neurologist **Christopher Walsh** has been studying families in the Middle East—including in Turkey, Saudi Arabia and Jordan, where marriage between first and second cousins is a common social custom.

In these families, recessive genetic disorders occur more frequently and are easier to identify because the genetic culprit can be traced to a single shared grandparent or great-grandparent.

Based on this work, Walsh’s team has identified a dozen genes that when disrupted result in gross malformations of the brain, leading to epilepsy, mental retardation and other symptoms.

The same approach is proving useful in studying the genetic basis of autism.

“Autism is a disorder that seems to be telling us something very important about how the brain works,” says Walsh, who is the Hamilton Kuhn professor of biological chemistry and molecular pharmacology at Harvard Medical School.

Like the more severe developmental disorders Walsh has studied, autism is a heterogeneous disorder thought to arise from a multitude of genetic variations. “The more we learn about it, the more evident that becomes,” Walsh says. “We already know about a dozen genes that account for only a small fraction of all the kids with the disorder.”

With funding from the Simons Foundation, he and his collaborators have already identified a number of genetic variations linked to autism, and expect to publish their results soon.

There are no treatments yet for the disorders—such as a form of microcephaly or an abnormally small brain—for which Walsh has identified a genetic basis. But scientists can offer genetic tests and counseling to affected families, and help them decide whether to marry or have additional children.

Thomas  
Südhof



*“Can we behaviorally improve this mouse by simply attenuating inhibitory synaptic function?”*

### Mouse model mimics autism’s unique features

Scientists working on autism have had few choices for animal models that mimic the distinct social and behavioral abnormalities reminiscent of autism.

That changed in September 2007, when **Thomas Südhof** and his group at the University of Texas Southwestern Medical Center debuted a mouse model that carries a mutation linked to autism.

Südhof’s team introduced a single-letter mutation in the gene encoding a protein called neuroligin-3, a member of a family of proteins known to be important in helping nerve cells communicate across synapses. The mutation had been identified in 2003 in two Swedish brothers, one with autism and one with the related Asperger syndrome.

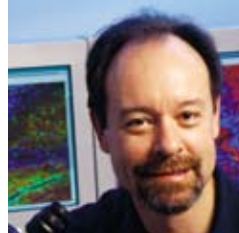
The mutant mice are just as coordinated and mobile as, and no more anxious than, their unaffected litter mates. But they show impaired social behavior, spending less time than their normal litter mates interacting with a novel, caged mouse.

In an interesting twist, the mutant mice have better spatial learning and memory abilities than their wild type counterparts. They also show an increase in both the frequency and strength of the inhibitory—or dampening—messages sent across synapses.

Autism is thought to be associated with an imbalance of excitatory and inhibitory signaling across brain synapses, though the exact mechanisms involved are unknown.

The finding presents an immediate possibility that Südhof is testing: “Can we behaviorally improve this mouse by simply attenuating inhibitory synaptic function?” he asks. “A lot of anti-anxiety drugs do that.”

Luis  
Parada



*“I think we know very little about autism and it would be a huge mistake to think that we [know more]. Everything is of interest; all bets are on.”*

### Detour from cancer leads unexpectedly to autism

At the University of Texas Southwestern Medical Center, **Luis Parada** holds the Southwestern Ball Distinguished Chair in Basic Neuroscience Research.

Here's the rub: Parada has never taken a course in neuroscience—not in college, not in graduate school, not in all the years of his scientific training.

He is in fact best known for research on cancer, systematically examining the role of cancer-causing genes in embryonic development.

One such 'proto-oncogene' he identified, *Trk*, later turned out to be the much sought after receptor for proteins that induce neurons to grow and survive.

“At that point, when I saw this and I realized what it meant, I didn't just want to hand it off,” Parada recalls. “So I started working on developmental neurobiology, and sort of learned by the seat of my pants.”

When Parada discovered that some cancer genes have been linked to autism, his lab immediately set about making mice in which one of those genes, *PTEN*, has been deleted from neurons.

These mice are anxious and unsocial, and they have seizures and big heads—all features of autism. With funding from the Simons Foundation, his lab is examining whether deleting other genes in the *PTEN* pathway has similar effects.

These unusual detours in his own research have made Parada a big believer in keeping an entirely open mind.

“I think we know very little about autism and it would be a huge mistake to think that we [know more],” he says. “Everything is of interest; all bets are on.”

Huda  
Zoghbi



*“With more basic research and understanding really what this protein is doing in the brain, we can come up with a treatment.”*

### A return to basics in the search for a cure

It took **Huda Zoghbi** more than 15 years from the time she saw her first patient with Rett Syndrome to cloning the *MECP2* gene, a mutation in which causes the disease.

No one, not her colleagues, and not those reviewing her grants or publications, believed that she could solve the puzzle. For years, Zoghbi worked with the help of just one lab member, painstakingly excluding parts of the X chromosome that did not contain the culprit gene. She is now trying to develop mouse models that mimic features of autism.

Since she zeroed in on *MECP2* in 1999, girls with Rett syndrome, who also have many of autism’s features, are being diagnosed earlier, and learning through physical therapy to be mobile, active and interactive.

“Yes, it’s true, we haven’t found a treatment yet for Rett syndrome, but things are much better,” Zoghbi says. “And one would hope that with more basic research and understanding really what this protein is doing in the brain, we can come up with a treatment.”

In the quest for cures, the importance of basic research is often lost, she says.

Zoghbi is dedicated to her patients, so much so that when she cloned the gene for spinocerebellar ataxia in 1993, she called each one of the 200 study participants, explaining what the results meant.

Still, her time is better spent working in the lab than seeing patients, she says. “For long term, enduring, transforming help, you need basic research,” Zoghbi says. “The results may be slow, but they’ll come.”

## Studying autism is really studying the essence of what it means to be an individual.

### 'Simplex' collection seeks to find origins of autism

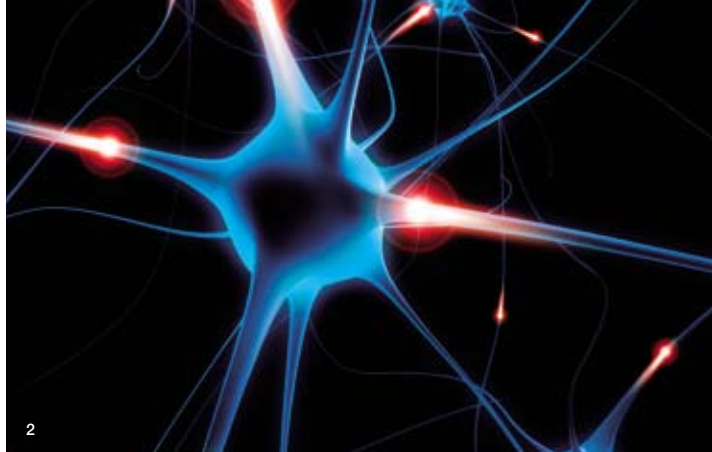
In February 2005, more than a dozen leading scientists met for an unusual 'Autism Think Tank' in New York City. Over the course of two days, they brainstormed ways to enhance our understanding of autism through studies of genetics, brain imaging and neurophysiology.

Among other recommendations, these researchers emphasized the need to identify genetic risk factors for autism. The discussions led to our current effort to study "simplex" families in which one child (aged 4 to 15) has been determined to be on the autism spectrum but neither parent nor any other sibling is similarly affected.

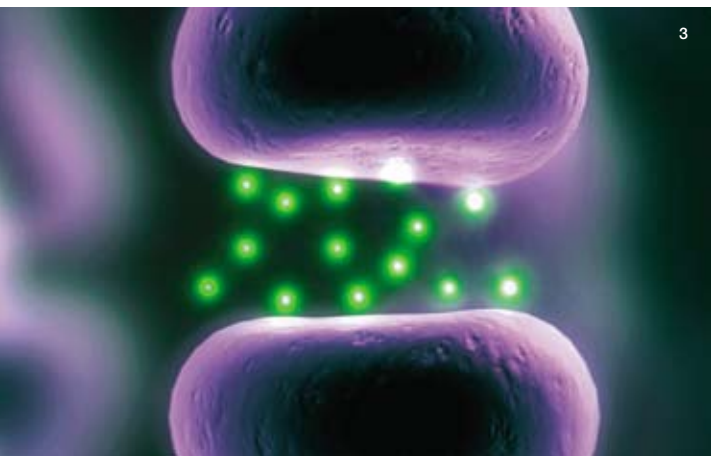
The Simons Simplex Collection (SSC) is based, in large part, on the work of Michael Wigler and Jonathan Sebat and their colleagues at the Cold Spring Harbor Laboratory (CSHL). In a groundbreaking paper published in early 2007, the CSHL group reported that roughly ten percent of children with autism were found to have small deletions or duplications of DNA segments. Such Copy Number Variants (CNVs) were ten times more common in children with autism than in unaffected children. Strikingly, the CNVs were usually not present in the somatic cells (blood cells or other tissues) of either parent. They probably arise as new mutations in the germ cells of one or the other parent. Such "*de novo*" mutations are rare and they are usually not passed on from generation to generation. That is, they are not inherited. The authors predict that higher resolution genome scans for CNVs will show that most cases of autism arise in this manner.



1



2



3



4

1. Nerve cells
2. Neuron cell body with numerous synapses.
3. Microscopic view of a synaptic cleft, the gap where communication from one neuron flows to another neuron.
4. Chromosomes

The SSC is an unprecedented effort to study 2,000 families (8,000 individuals) with rigorous and uniformly applied phenotyping procedures. Precise phenotype descriptions are of paramount importance in our search for autism genetic risk factors.

Thirteen medical centers across North America are now involved. The selection of diagnostic instruments, and training in their use is under the direction of Catherine Lord, director of the University of Michigan Autism and Communication Disorders Center. In addition to the rigor of the initial phenotyping effort the SSC offers the opportunity to follow individuals over time.

Standard instruments such as the Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview – Revised (ADI-R) are supplemented with other measures of cognitive and emotional function, extensive medical histories, and teacher-interviews. Phenotype data will be correlated with genetic data obtained by analysis of DNA obtained from each participant in the study. Two groups funded by the Simons Foundation are poised to perform high-resolution genome scans for CNVs and to follow up with additional genetic analyses. The Wigler group at the CSHL lab will take one approach, and a group of geneticists from SSC sites led by Matthew State at Yale will take a complementary approach. Data from these and all subsequent studies will be stored in a central database that is available on line to all researchers worldwide.

As Lord says, “We’re all contributing to something that’s bigger than what any of us could do as individuals.”

If we can identify what genes characterize autism, and we know what those genes do, then we can develop treatments.

### SFARI Scientific Advisory Board

**Wendy Chung M.D., Ph.D.**

Assistant Professor of Pediatrics, Columbia University

**Thomas M. Jessell Ph.D.**

Professor of Biochemistry & Molecular Biophysics, Columbia University

**Nancy Kanwisher Ph.D.**

Ellen Swallow Richards Professor of Cognitive Neuroscience,  
Massachusetts Institute of Technology

**Arnold J. Levine Ph.D.**

Professor, Institute for Advanced Study

**Richard P. Lifton M.D., Ph.D.**

Professor of Medicine, Yale University School of Medicine

**Catherine E. Lord Ph.D.**

Professor of Psychiatry and Psychology, University of Michigan

**J. Anthony Movshon Ph.D.**

Silver Professor; Professor of Neural Science and Psychology,  
Adjunct Professor of Physiology and Neuroscience, New York University

**Martin Raff M.D.**

Professor, MRC Laboratory for Molecular Cell Biology (LMCB) & Cell Biology Unit  
and Biology Department at University College, London



## Straight talk from Cathy Lord, Principal Investigator of the Simons Simplex Collection

### How did the idea for the SSC develop?

The Simons Foundation was interested in working with simplex families that were not so genetically loaded; where something might have happened that's unique to the child with autism.

### What is the main purpose of the SSC?

Initially in the field we thought there was going to be one autism gene, but that's clearly not true. If we can identify what genes characterize the disorder, and we know what those genes do, then we can develop treatments.

### What does the Autism Diagnostic Observation Schedule entail?

We make a diagnosis by doing a long, standardized parent interview, which describes the medical history of the child and also what the child is like at home. Then we have a formal observation and psychological, cognitive and language testing.

### Why do all the SSC sites use the same tests?

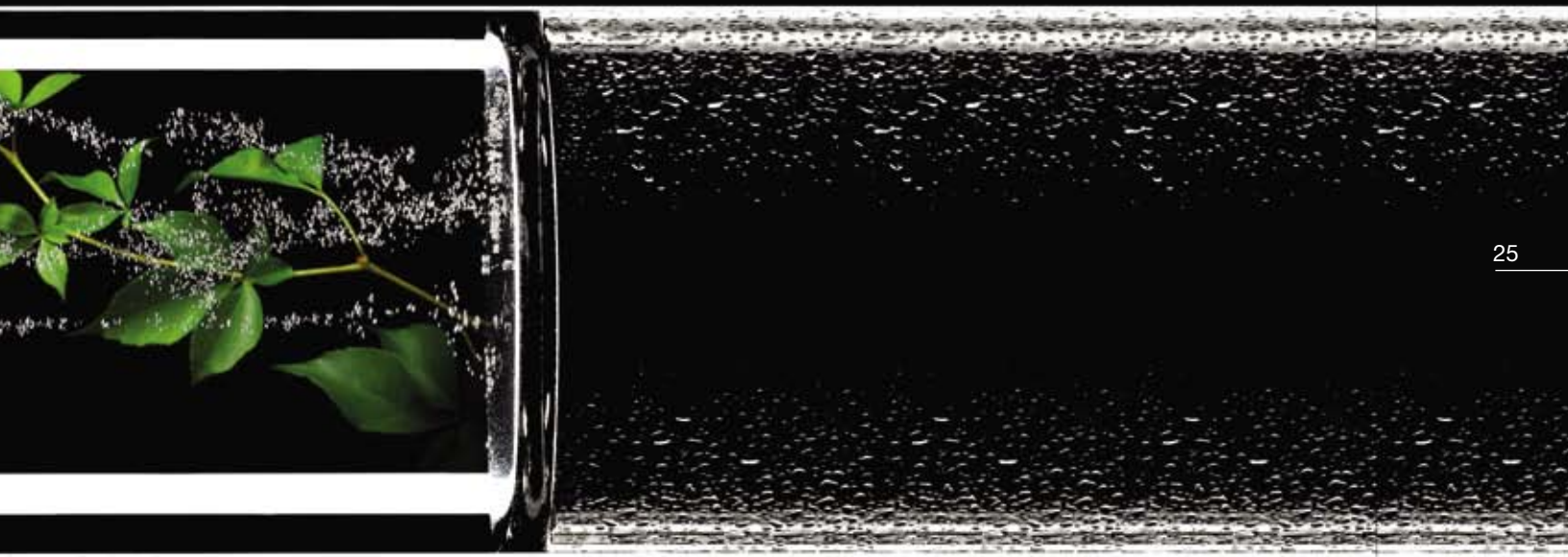
For many years, autism studies had great difficulty in replicating across labs, and one concern was that they were actually studying children with very different characteristics, but all diagnosed with autism. Because at this point autism is defined purely by behavior, we must be very careful in our descriptions of behavior.

### What's the long term plan for the SSC?

Ideally, once we begin receiving the genetic findings we will be able to review the data and look across all the sites for particular kids. We could, for example, follow up on only the girls with a diagnosis of autism; go back and say how were they doing in school, or do further medical tests like imaging studies.

# Sustain





## Balance Sheet

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<b>ASSETS</b>	June 30, 2007	June 30, 2006
Cash and Cash Equivalents	\$815,022	\$246,262
Investment Portfolio	693,764,890	475,655,816
Property and Equipment, net	514,561	614,886
Other	886,350	521,728
<b>Total</b>	<b>695,980,823</b>	<b>477,038,692</b>

<b>LIABILITIES</b>	June 30, 2007	June 30, 2006
Grants Payable	76,690,635	29,341,600
Taxes Payable	2,245,374	0
Deferred Excise Tax Liability	7,071,983	5,714,983
Other	265,548	0
<b>Total</b>	<b>86,273,540</b>	<b>35,056,583</b>

<b>NET ASSETS</b>	June 30, 2007	June 30, 2006
<b>UNRESTRICTED NET ASSETS</b>	<b>\$609,707,283</b>	<b>\$441,982,109</b>

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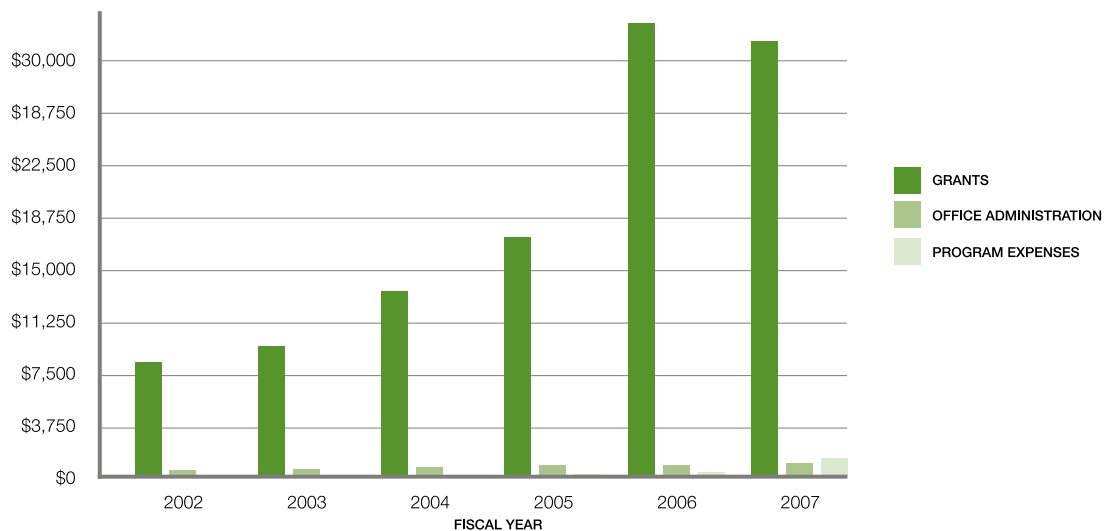
## Income Statement

REVENUE	June 30, 2007	June 30, 2006
Contributions	\$70,923,570	\$64,749,656
Investment Income	182,565,644	121,370,244
<b>Total</b>	<b>253,489,214</b>	<b>186,119,900</b>
<b>EXPENSES</b>		
Grants Paid	32,607,522	33,027,511
Change in Grants Payable	47,349,034	(8,274,890)
General and Administrative	817,816	596,575
Program	1,102,637	132,240
Depreciation and Amortization	164,939	151,134
Federal Excise Taxes	3,633,092	2,387,500
Other	89,000	0
<b>Total</b>	<b>85,764,040</b>	<b>28,020,070</b>
<b>NET INCOME</b>	<b>\$167,725,174</b>	<b>\$158,099,830</b>

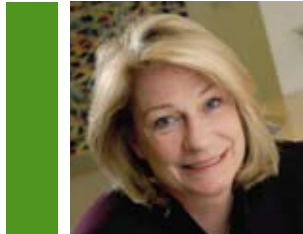
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## Proportions of Expenses

(\$'s in Thousands)



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### **Marilyn H. Simons Ph.D.** President

Marilyn Hawrys Simons has worked primarily in the non-profit sector as a volunteer for the past 20 years, focusing on education. She has served as President of the Simons Foundation since 1994. Dr. Simons is currently President of the Board of LearningSpring Elementary School, a school for children diagnosed with autism spectrum disorders. She received a B.A. and a Ph.D. in Economics from the State University of New York, Stony Brook.



### **Mark Silber J.D., M.B.A.** Vice-President

Mark Silber, J.D., M.B.A., is Vice-President and General Counsel at Renaissance Technologies, where he has held responsibility for finance, administration and compliance since joining the firm in 1983. Prior to joining Renaissance, he was a Certified Public Accountant with the accounting firm of Seidman & Seidman, now BDO Seidman. Mr. Silber holds a Bachelor's degree from Brooklyn College, a J.D. and L.L.M. in tax law from the New York University School of Law, and an M.B.A. in finance from the New York University Graduate School of Business Administration.



### **James H. Simons Ph.D.** Secretary and Treasurer

James H. Simons, Ph.D. is Secretary and Treasurer of the Simons Foundation. Dr. Simons is President and founder of Renaissance Technologies Corp. Prior to his financial career, Dr. Simons served as chairman of the Mathematics Department at the State University of New York, Stony Brook, taught mathematics at Massachusetts Institute of Technology and Harvard University, and was a cryptanalyst at the Institute of Defense Analyses in Princeton, N.J. Dr. Simons' scientific work was in the area of geometry and topology, and his most influential work involved the discovery and application of certain measurements, now called Chern-Simons Invariants, which have had wide use, particularly in theoretical physics. James Simons holds a B.S. from the Massachusetts Institute of Technology, a Ph.D. from the University of California, Berkeley, and won the American Mathematical Society's Veblen Prize for his work in geometry in 1975. He is a former Chairman of the Stony Brook Foundation, and is currently a trustee of Rockefeller University, Massachusetts Institute of Technology and the Institute for Advanced Study.



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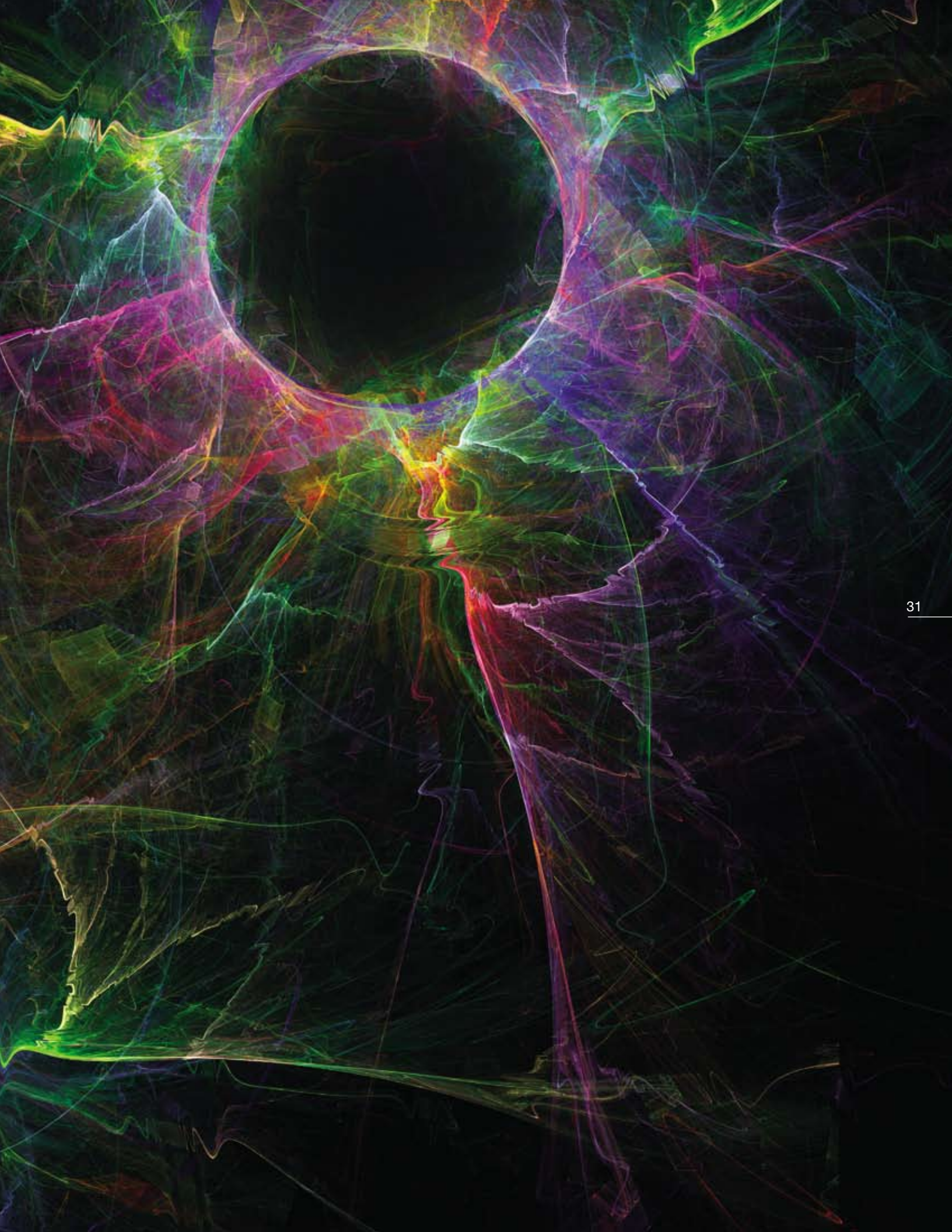
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Historically, the Simons Foundation has accepted only solicited grant proposals. All grant decisions are made by the trustees of the foundation and the foundation staff. The foundation does not make awards to individuals, except through their institutions.

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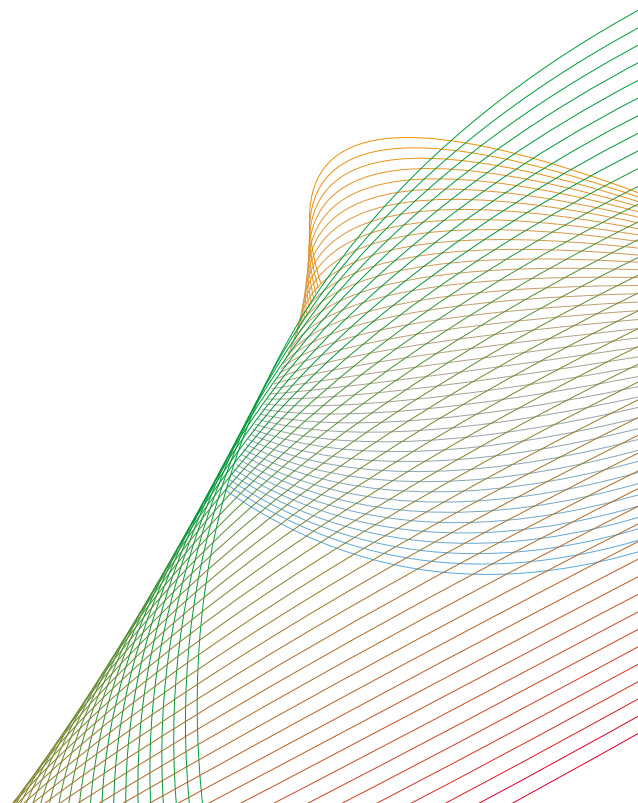
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Nashville, Tennessee

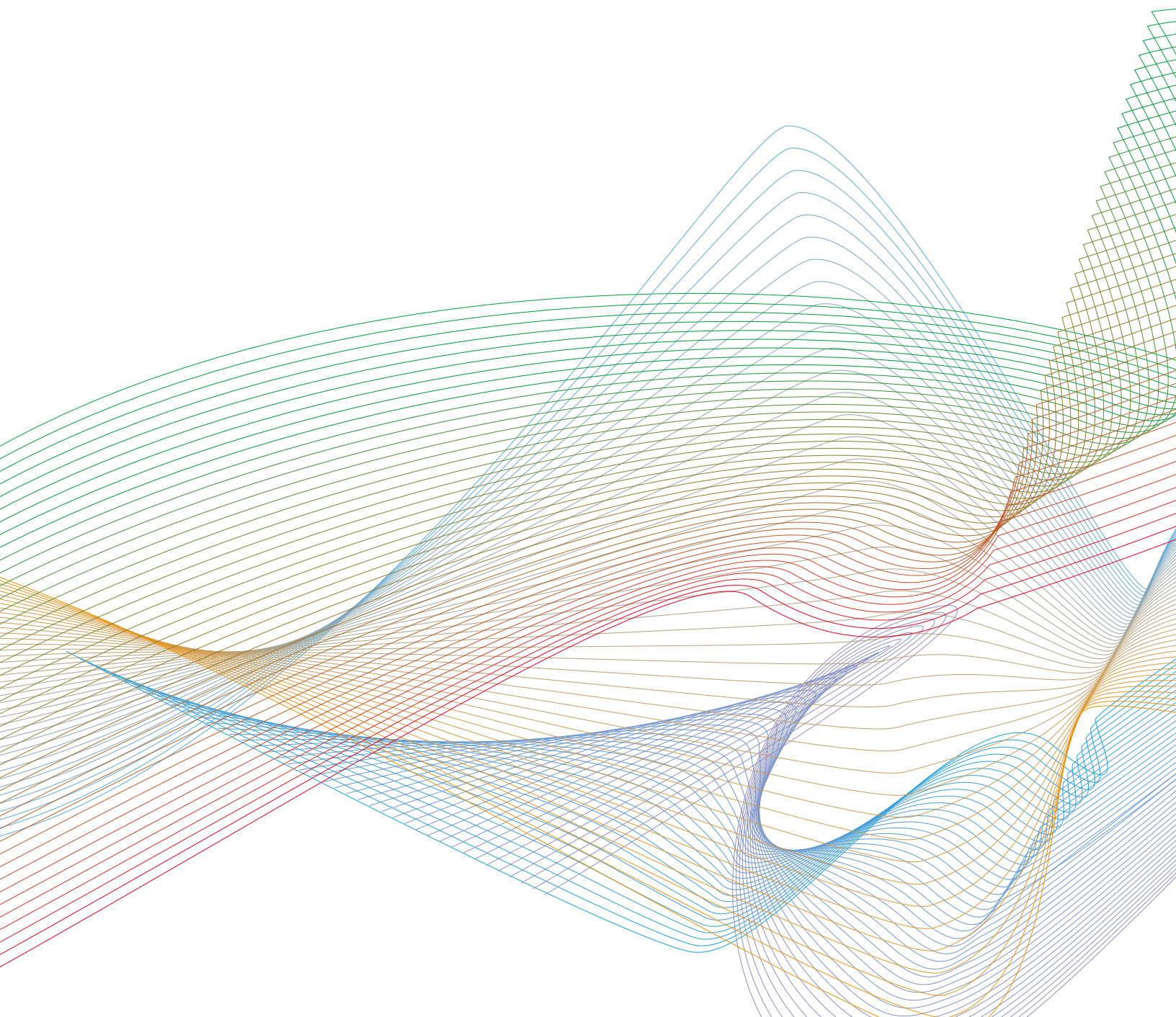
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Yale University  
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