SIMONS FOUNDATION

ANNUAL REPORT 2012

INVESTING IN PEOPLE

Progress depends on investment in the people who dedicate themselves to investigation, innovation and the pursuit of knowledge. This report highlights the importance of supporting people and their vision, including scientists, mathematicians and educators, all striving to uncover fundamental insights and to push the limits of what may be done.

CONTENTS

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

BOARD CHAIR JAMES H. SIMONS AND PRESIDENT MARILYN HAWRYS SIMONS

LETTER FROM THE PRESIDENT AND THE CHAIR

"Basic research leads to new knowledge. It provides scientific capital. It provides the fund from which all practical applications follow." These words, written by Vannevar Bush in his 1945 report to President Roosevelt, *Science, the Endless Frontier*, were intended to inspire a new direction for economic growth in the post-war U.S. economy.

The report led to an upsurge in support for fundamental research, and Bush's words proved true to their promise, fostering gains in innovation and technology that we are still realizing today. His words of vision are equally true today. Our society needs curiosity-driven, creative basic research if we want to sustain long-term growth and continue to make progress.

To the question, "How do we increase scientific capital?" Bush answers, "We must have plenty of men and women trained in science, for upon them depends both the creation of new knowledge and its application to practical purposes." The rest is history. The government's post-World War II investment in a higher-education system based on ability and merit resulted in an outstanding corps of scientific researchers that has grown in the years since. These people are a key component of our intellectual capital; their knowledge forms the foundation of our future.

Acknowledging the importance of fundamental research, we at the Simons Foundation have tried to develop grant programs to support the research community. Through our Mathematics and Physical Sciences, Life Sciences, and Simons Foundation Autism Research Initiative programs, we have given grants to support individual investigators, build institutes, archive materials, encourage interactions, ensure time to think and disseminate knowledge.

The goal of this annual report is to recognize and highlight some of the many talented men and women in science and mathematics doing research today. They are the people generating new ideas and striving to expand our knowledge base, providing the indispensable creativity and insight we need to advance.

Thinking beyond the present, there is a need to prepare students to become the next cohort of researchers. Training knowledgeable, skilled and passionate teachers of mathematics and science today will produce the visionaries and pioneers of tomorrow.

Through the Simons Foundation's support of Math for America — now expanding to include science teachers as well — we hope to contribute to the infrastructure necessary to produce tomorrow's creative thinkers. Through our outreach efforts, such as the Museum of Mathematics and the World Science Festival, we hope to inspire the next generation to deepen its appreciation of the importance and excitement of science and mathematics.

Support for science is the key to our development. "Today, it is truer than ever that basic research is the pacemaker of technological progress" were Vannevar Bush's inspiring words in 1945. They ring true today. Advancing basic science is a critical investment in our future. Let's hope that as a society we continue to make that investment.

"We must have plenty of men and women trained in science, for upon them depends both the creation of new knowledge and its application to practical purposes."

VANNEVAR BUSH

MATHEMATICS & PHYSICAL SCIENCES

2012 has been a busy and exciting year for the Mathematics and Physical Sciences (MPS) division, with the inauguration of new competitive, application-based programs designed to support extraordinary researchers by recognizing their accomplishments and giving them the resources they need to pursue their scholarship.

MPS launched its new flagship Investigator and Fellows programs. The Investigator program focuses on exceptional leaders in mathematics, theoretical physics and theoretical computer science, and it provides flexible funding for up to ten years. The Fellows program enables extension of sabbatical leave for up to 40 mathematicians and 20 theoretical physicists every year. In 2013, both programs will be open to Canadians as well as United States citizens.

2012 was the third year of our Collaboration Grants program. Each year, the foundation awards 140 of these popular five-year grants, which give researchers what they need to succeed, such as travel expenses, computer equipment or administrative help.

Another major highlight was the inauguration of the Simons Institute for the Theory of Computing at the University of California, Berkeley, with the distinguished computer scientist Richard Karp as founding director. The mission of this institute is to explore fundamental questions about the nature and limits of computations, with a long-term goal of designing novel algorithmic methods for virtually every area of science and technology.

The institute will bring together the world's leading theoretical computer scientists and experts in other disciplines interested in computational problems, accommodating about 40 visitors at any given time. The first semester-long programs show the breadth and range of potential impact. Their topics are: 'Real Analysis in Computer Science,' 'Theoretical Foundations of Big Data Analysis' and 'Quantum Hamiltonian Complexity.'

In August, the first three Africa Mathematics Program sites were chosen, led by Professors T. Ezome (Gabon), E.M. Lungu (Botswana), and D. Seck (Senegal), respectively. This program aims to extend the mathematical research community by supporting the establishment of a network of research collaborations in Sub-Saharan Africa.

While the vast majority of the MPS budget is allocated to direct support of scientists, MPS is also investing in research infrastructure, providing, for example, a matching grant for arXiv, the most important repository of prepublications in the theoretical sciences.

The MPS division is continuing its rapid growth. Among new projects is a program at the interface of mathematics and biology, to be established jointly with the foundation's Life Sciences division. This program will complement the foundation's contributions to the Simons Center for Systems Biology at the Institute for Advanced Study in Princeton, New Jersey, and to the Simons Center for Quantitative Biology at Cold Spring Harbor Laboratory in New York.

The initiatives described above were developed and launched by David Eisenbud. As his successor, it is my privilege to continue these efforts at the foundation.

Yuri Tschinkel
Director of Mathematics
and Physical Sciences

SIMONS INSTITUTE FOR THE THEORY OF COMPUTING


➤ Institute director Richard Karp and associate director Alistair Sinclair

In December 2009, the Simons Foundation gathered a group of leading computer scientists to discuss and prioritize the needs of their field. At the top of their list was the founding of a large-scale institute where researchers could exchange ideas on their most advanced and challenging problems. Twenty months later, after a competitive search among many leading universities, the Simons Institute for the Theory of Computing opened its doors at the University of California, Berkeley.

"Theoretical computer scientists study computation and information as fundamental concepts, much as physicists study matter and energy," says Sampath Kannan, professor of computer and information science at the University of Pennsylvania, and a member of the panel that tapped Berkeley. "But most of them are pursuing their research agendas in isolation. Bringing these top people together will lead to reexamination of these hard problems, providing opportunity for breakthroughs."

In the age of 'big data,' in which cloud computing and ubiquitous sensors are generating billions of gigabytes of information every day — more than was generated over entire millennia for most of human history — understanding the fundamental theory of computation matters more than ever.

But according to Richard Karp, the institute's director, this understanding applies to far more than computers themselves. "There are computational processes to be found in physics, biology, economics — even in human organizations," he says. Using this "computational lens," says Karp, scientists collaborating at the institute will push our understanding of the world forward in ways they never could have before, or could have done alone.

The Simons Institute is funded through the year 2022, and will support a series of semester-long programs to bring hundreds of senior scientists, post-docs and early-career researchers together to collaborate on multidisciplinary problems. "Arguably, the most exciting programs are those where people from different fields interact," says Alistair Sinclair, the institute's associate director.

For example, an evolutionary biology program scheduled for early 2014 will create collaborations between biologists, mathematicians and theoretical computer scientists; another meeting will draw together quantum-computation experts and theoretical physicists. "We'll have young scientists working alongside top people in these fields," Sinclair says, "and we hope those interactions will persist beyond these semester-long programs."

As for the institute's future goals, Karp intends to keep his outlook broad. "The computing environment is constantly changing, and we'll have to be proactive about identifying emerging trends," he says. In May, the Simons Institute hosted a symposium in which computer scientists, mathematicians, physicists, biologists, economists and nanotechnologists discussed the future of computation.

One thing that the institute is not likely to do over the next decade, though, is build any supercomputers of its own. "Supercomputers are wonderful for quickly calculating answers to certain questions," explains Kannan. "But theoretical computer science seeks entirely new methods to answer them orders of magnitude faster. Moreover, the theoretical computer science perspective can raise new questions that lead to insights not accessible by sheer computational power."

SIMONS SYMPOSIUM: ANALYSIS OF BOOLEAN FUNCTIONS

➤ Boolean Functions Symposium attendees, Caneel Bay, St. John

Computer scientists like to be efficient, and they like games. The two themes intertwined at the 2012 Simons Foundation's Analysis of Boolean Functions Symposium, held in February. The Simons Foundation's one-week Simons Symposia are intended to facilitate collaboration and open-ended discussion on specific, timely topics in mathematics, theoretical physics and computer science.

Boolean functions are like switchboards, converting a collection of incoming channels of 0's or 1's into a collection of outgoing channels of 0's or 1's. They are extremely useful in computer science, as the binary nature of variables in the Boolean universe allows for the ready coding of logical circuits.

Analyses of these functions are also used to solve constraint satisfaction problems, in which the characteristics, or 'states,' of a group of objects are limited by stated requirements or rules. Mathematicians often represent constraint satisfaction challenges as graph-coloring problems, where a graph represents the objects involved, and the rules by which the objects may be colored are governed by the constraints. Constraint satisfaction problems show up frequently in real life; freight shippers, for example, deal with constraint satisfaction when they try to move packages from many different origins to many different destinations using the fewest number of trucks, trains and planes.

In a symposium highlight, Parikshit Gopalan used Boolean function analysis to prove the existence of short code graphs. Because short code graphs are symmetrical mathematical objects, it is hard for a graph-coloring algorithm that is trying to maximize efficiency to pick a good starting point.

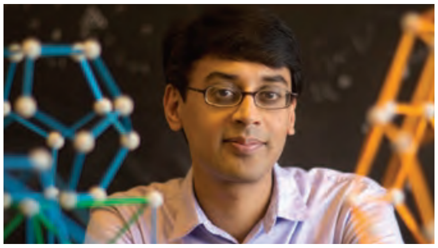
The just-proven existence of short code graphs threw a wrench into a highly regarded program by Sanjeev Arora, Boaz Barak and David Steurer, intended to disprove the famous Unique Games Conjecture. (The conjecture makes a guess about a certain type of constraint satisfaction problem: It posits that for problems that cannot be solved perfectly, it is just as difficult to find an approximately good solution as it is to find the very best solution.)

If Arora, Barak and Steurer's algorithm could solve short code graphs efficiently, it would demonstrate the Unique Games Conjecture to be false. But the very existence of short code graphs showed that this algorithm is not efficient enough.

Symposium organizers Ryan O'Donnell, Elchanan Mossel and Krzysztof Oleszkiewicz kept interested followers informed of these developments with a daily blog, and with videos of the presentations on Simonsfoundation.org; a core component of each symposium is the dissemination of the attendees' insights throughout the greater research community.

Whether the Unique Games Conjecture is true or false is still an open question — encouraging to some attendees because a great deal of intriguing mathematics has been derived from the conjecture. Yet, even if the conjecture were proven false, there is still new mathematics to be learned through it, because that would mean that some algorithm yet to be discovered can efficiently find good solutions to constraint satisfaction problems that arise in many applications.

SIMONS INVESTIGATORS



MANJUL BHARGAVA

Princeton University number theorist Manjul Bhargava considers the study of pure mathematics to have more in common with art than with science. "Most pure mathematicians like myself are guided by a feeling of creativity and beauty — we're not usually thinking of the applications that may arise," he says. "But it's also true that the really beautiful mathematics that mathematicians find is precisely what tends to find applications later on."

Bhargava focuses his explorations on the properties of cubic equations — for example, a conjecture that, for a certain class of cubic equations whose coefficients vary over the whole numbers, an equal proportion (50 percent) should have a finite number of rational solutions as have an infinite number of rational solutions. "There are heuristic reasons why this should be true, but until recently it wasn't known whether the probability that such an equation has finitely many rational solutions was even positive or not," Bhargava explains. He and his student Arul Shankar recently proved that the probability of finitely many rational solutions is, in fact, positive. "We want to move closer and closer to proving that 50-50 prediction," Bhargava says.

Bhargava has applied the techniques he used for deriving this proof to understanding the properties of higher-degree polynomials as well, such as hyperelliptic equations. For instance, he recently proved that as the degree of the polynomial approaches infinity, "the chance that the equation has a rational solution goes to zero," he says. "These problems are appealing because they're so simple to state, and yet we don't know the answer. How often does an integer polynomial take a square value? We should know that! It's similar to the feeling that an astronomer has when she looks up at the sky and wants to understand what is going on out there."

HIROSI OOGURI

As human beings expand our sphere of knowledge, we sometimes have to "invent new mathematics," says physicist Hirosi Ooguri of the California Institute of Technology. Ooguri is working in the area of superstring theory, the leading candidate for a unified theory of forces and matter, which aims to explain physical phenomena in our universe at its most fundamental level. His research has led to a new way to look at geometry in higher dimensions.

Superstring theory is defined in ten-dimensional space-time (nine in space, one in time), and it is postulated that six out of nine space dimensions are 'hidden' via a geometric concept called a 'Calabi-Yau space.' Ooguri says, "The beauty is that properties of elementary particles, such as the mass of the electron, are actually written in this six-dimensional space. I would like to find out how to read out such information from this space." The problem is that Calabi-Yau space is so complicated that "we don't even know how to measure distances between points in this space."

Ooguri found a way to circumvent this difficulty by developing a new mathematical method called topological string theory. "This method allows us to compute certain properties of elementary particles precisely using our limited knowledge about Calabi-Yau space," he says.

Ooguri's method has been used to elucidate mysterious properties of black holes pointed out by Stephen Hawking 40 years ago. "We need new mathematics to unify general relativity and quantum mechanics, and that is what I am working on," says Ooguri.

SANJEEV ARORA

'Non-deterministic polynomial-time hard' (NP-hard) problems are the hardest problems of them all: computationally intractable ones, in technical terms. As a Simons Investigator, Sanjeev Arora is continuing groundbreaking work that helps us understand when and how we can compute approximate solutions to them by using hierarchies of semidefinite programs. Arora has also applied this approach to the Unique Games Conjecture, resulting in an algorithm that could compute results in sub-exponential time.

His recent work identifies new approaches for dealing with computational complexity in machine learning applications, such as non-negative matrix factorization. Arora discovered that the matrix factorization problem, classified as NP-complete — and therefore intractable — is actually solvable in polynomial time when re-expressed in more parsimonious terms.

"The problem was phrased too broadly, which made it NP-hard," he explains. "We could reformulate the problem so that it still captures the aspects important in machine learning, and show that this reformulation is tractable.

"The human brain would seem to be proof that these sorts of seemingly intractable machine learning problems can be solved," Arora says. "Today we have enough computational power to match the brain; yet we still can't solve these problems. Figuring out such mismatches is why the study of computational intractability is so fascinating."

MICHAEL BRENNER

Harvard University physicist Michael Brenner is a theorist who loves applying his work wherever it may take him — whether that's modeling the fluid dynamics of splashing water droplets or understanding how the beak morphology of Darwin's finches might illuminate novel self-assembly processes in synthetic materials.

"I'm just interested in solving problems — the process of using calculations to make sense of the world," he says. "It's easy to get carried away to different places, but to me the topics I explore aren't as disconnected as they might seem."

As a Simons Investigator, Brenner explores "the interface between materials science and biology." For example, a colleague discovered a small number of genetic pathways in Darwin's finches that control the growth rate of skull bone and cartilage, thereby shaping the beak. Brenner became interested in how these growth rates are encoded in genes, and how they might be modeled mathematically so that the 'algorithm' might be applied elsewhere.

"Control of growth is of great interest in other fields," he says, "but there are many fewer 'knobs to turn' in man-made materials to create things. Yet the reverse is also interesting — can we impose a language borrowed from materials science to understand processes in biology?"

Brenner's own investigations of fluid dynamics have a similar cross-disciplinary bent. "It turns out that the events that lead to fluid splashing have never been well elucidated," he says. "We had this crazy idea that the critical event would happen before the droplet even contacted the solid surface."

Brenner modeled the effect using partial differential equations. "Science is organized around little calculations that tend to not be very complicated," he says. "I find it stimulating to combine things that are very well defined — where the question has been posed and it's a matter of figuring out the mathematics to solve it — with things that aren't well defined. In that way, I'm much more interested in trying to discover what the question really is than in trying to answer it."

SIMONS FELLOWS

TATIANA TORO

Most of us take measuring — defining an object in quantitative terms — for granted. But to University of Washington mathematician Tatiana Toro, measures are anything but mundane. "We intuitively know how to measure distance," she says, "but one can describe some very simple continuous curves so that the distance between any two points along the curve is infinite. We all know what length is, and we all know what surface area is. But there are more general types of these measures that can do very versatile, very weird and very beautiful things."

Toro researches geometric measure theory and its relation to variational problems that yield a partial differential equation and an associated free boundary (often the set where the solution to the equation is zero). If such a problem has a free boundary that is well approximated by planes — "there may be wiggles, but it's essentially plane-like," Toro explains — it is possible to prove that this set and the solution to the variational problem are smoother than would have been predicted *a priori*.

As a Simons Fellow, Toro has been using the same approach to prove results about the measures themselves, not just the sets. She is also working to relate geometric measure theory to the theory of optimal mass transport using Wasserstein metrics. "People have needed to move piles of things from point A to point B for a long time," Toro jokes, "but now the theory behind the most efficient ways to do this is proving to be useful in many fields."

PAUL STEINHARDT

Physicist Paul Steinhardt of Princeton University likes to keep his disparate research interests "out of phase" for convenience's sake, but over the past year, three of them were reaching fruition at the same time. Steinhardt is studying an alternative, cyclical model of the early universe that posits a 'big bounce' in lieu of the paradigmatic 'big bang.' He also investigates the properties of 'quasicrystals,' which are solids with symmetries that violate the conventional laws of crystallography.

Finally, Steinhardt's research on photonics — which seeks to build the light-based analogs of electronic circuits — has produced the photonic equivalent of an isotropic semiconductor, which was thought to be impossible.

"It's always a good idea to look in places where people say something is impossible," says Steinhardt. "That usually means one of two things: It's either truly impossible, like 1 + 1 = 3, or it means that it's 'impossible' given our standard assumptions. Those are the interesting cases, because you can make major breakthroughs if you can find a natural way to violate those standard assumptions."

Steinhardt and his collaborators have shown during this past year that there is a natural connection between the cyclic model of the universe and the recent detection of the Higgs boson at the Large Hadron Collider. Steinhardt also spent the past year analyzing the quasicrystal samples he gathered on an expedition to Russia's Far East. Quasicrystals were previously thought not to exist in nature, but Steinhardt launched a decade-long search and ultimately found the first example of a natural quasicrystal in a rare type of meteorite that formed in the early life of the solar system more than 4.5 billion years ago and landed in the Kamchatka Peninsula.

His work in the past year has clarified the processes through which the quasicrystal formed. His goal with the photonics project has been to miniaturize and test the isotropic semiconductor to function at the infrared wavelength scale, which could have applications in communications. "Getting a year to focus on these three projects really allowed me to move all of them forward quite a bit," says Steinhardt.

ASSAF NAOR

Suppose the 'distance' between two websites is the minimum number of clicks required to pass from one site to the other. Evaluating this distance is a complex computational task, but it would be easier if every website on the Internet could be mapped into a 'room' that obeyed simple geometrical rules: Computing the distance between two websites could then be as simple as drawing a straight line.

Assaf Naor specializes in translating abstract spaces with an intrinsic notion of distance, called metric spaces, into simpler mathematical 'rooms' called normed spaces. (A normed space is not necessarily as simple as a three-dimensional room, but even higher-dimensional normed spaces are simpler to analyze than most metric spaces.) "The minute you prove these geometric translations, you suddenly have a massive list of things you now know how to do, that before were invisible to you," Naor says. "This leads to non-obvious algorithms about many complex systems, such as similarity search in massive collections of proteins or images."

The long-term goal of mapping large abstract classes of metric spaces to normed spaces, called the Ribe program, has absorbed Naor for more than a decade already — "and I don't expect it to be completed in my lifetime," he says. But in his year as a Simons Fellow, Naor says he has been able to be "orders of magnitude" more productive. "There were many months where I was focused on one problem every day, from when I woke up until when I went to sleep and continued dreaming about it," he says.

"The Simons Fellowship makes it possible for researchers to work uncompromisingly on the most difficult and important questions that require extended periods of hard work and uninterrupted focus. In this respect, the Simons Foundation is a major catalyst of mathematical discovery."

CHUNG-PEI MA

Studying the properties of supermassive black holes at the centers of distant galaxies requires "a very intimate relation between theory and observation," says Chung-Pei Ma, a cosmologist and astrophysicist at the University of California, Berkeley. Ma uses hydrodynamical simulations of galaxy evolution to build new algorithms that model how these black holes exchange matter, energy and momenta with their host galaxies.

She is also studying how clouds of carbon monoxide gas in elliptical galaxies might be exploited as a new kind of 'tracer' for measuring the mass of these central black holes, each of which is one to ten billion times as massive as our sun. "We've been successful using the stars orbiting the black holes as indicators of mass," Ma says, "but ideally we would like to measure it with two different methods and compare the results."

In addition, Ma is surveying a group of about 30 galaxies within 300 million light years of the Milky Way to probe the statistical relationship between galaxy size and the mass of the black holes at their centers, as well as comparing the properties of these nearby black holes with those of distant quasars. "How do the biggest galaxies get to be this way? Do young quasars evolve into giant elliptical galaxies? These are very intriguing questions," Ma says. "Understanding these processes will help us understand the evolution of the universe as a whole."


O(3) × U

STONY BROOK UNIVERSITY

In 2012, the Simons Foundation continued its tradition of broad involvement in research at Stony Brook University in Long Island, New York. As ever, the foundation is pleased to play a role in facilitating the workings and growth of this fine public institution.

2012 saw the emergence of rich synergies at Stony Brook: between math and physics, art and math — and between philanthropists — looking to push life sciences research and medical care forward.

Stony Brook's Simons Center for Geometry and Physics (SCGP) enjoyed another year of fruitful collaboration between mathematicians and physicists. SCGP hosted many gatherings of scientists in 2012, including the Integrability of Modern Theoretical and Mathematical Physics program, which promoted discussion between gauge theorists and quantum integrable systems researchers.

Outside SCGP, the bronze sculpture "Umbilic Torus SC" was unveiled in November. This grand piece by artist and mathematician Helaman Ferguson was commissioned for, and installed in, the plaza between SCGP and the university's Math Building and Physics Building.

The largest sculpture of Ferguson's career, the piece embodies not only aesthetic elegance, but elegant mathematics.

The Simons Foundation's $50 million matching challenge grant for medical and life sciences research at the university aided in the creation of some 260 initiatives, spanning fields from cardiology to conservation to global health. Our gift, together with those of highly motivated donors, enabled real strides — on Long Island and the world over.

Through its support of Stony Brook University in varied ways and at various scales, the Simons Foundation supports researchers and departments in an array of fields.

HELAMAN FERGUSON

➤ Artist and mathematician Helaman Ferguson in his Baltimore, Maryland studio

Helaman Ferguson began the largest sculpture of his career while lying flat on his back with an injured leg. It was 2009, and the mathematician-sculptor had fallen and snapped his right quadriceps tendon while carrying a ladder down a flight of stairs in his Maryland home. "The upshot was that after surgery I had my leg in the air—and time on my hands," Ferguson says.

So when Jim Simons approached him soon after his accident to commission a 28-foot tall, 65-ton bronze sculpture called "Umbilic Torus SC" for the plaza outside the Math and Physics buildings at Stony Brook University, "I knew I'd have to put myself back together in order to do it," says Ferguson.

Ferguson has spent most of his life putting together what others have tried to separate: passion for mathematics and passion for art. After seeing his mother killed by lightning when he was 3 years old, Ferguson was adopted and raised by an Irish stonemason, from whom he learned to work with his hands.

In high school, Ferguson also became deeply interested in chemistry, but struggled to understand the mathematics he encountered in a physical chemistry textbook. "I had an excellent math teacher who was also interested in art, and she helped me get a grip on the equations," he recalls. "I thought, 'Aha, math: key to the universe.'"

He went on to a distinguished career in mathematical research. In 1977, Ferguson co-discovered an integer relation algorithm that was recently deemed one of the 20th century's most important algorithms, alongside the Monte Carlo method and fast Fourier transform. During that time, he worked continuously as a sculptor, visualizing complex equations in carved stone.

Ferguson found the umbilic torus, a mathematical object similar to a Moebius strip in three dimensions, especially inspirational. "I have a pretty good feel for what kind of math is worth a sculpture," he says. "I expect it to be beautiful and have a certain kind of elegance. The umbilic torus has a lot of exotic mathematical content, but you don't have to know that in order to appreciate it."

Carved and cast into the bronze surface of "Umbilic Torus SC" is a so-called 'space-filling curve,' which lets an observer trace a one-dimensional path over the entire surface of the sculpture and return to the same point. In order to produce the curve on the 144 unique metal plates that make up the sculpture, Ferguson built a 13 by 16 by 20-foot gantry robot out of 1980s leftover parts from the National Institute of Standards and Technology.

He programmed his specially designed 12-inch, diamond-coated cutting tool with more than 20,000 lines of code in a program language called Mathematica. "After I choreographed this robot and saw the cutting tool dance its surface-filling steps, it was like watching the convolutions of my brain," Ferguson says.

The sculpture was dedicated on October 25th at Stony Brook University after nearly three years of work by Ferguson and his collaborators. This tireless conviction has always been part of Ferguson's process as a sculptor and as a mathematician. "If I'm going to carve a 24-ton block of stone, I have to have this stubborn, driven sense of what it will be in the end," he says. "Doing mathematical research is like that. To discover something new, you have to be patient as a rock and have the sense of inevitability to say, 'Yes, somehow I know this can be done.'"

SIMONS CENTER FOR GEOMETRY AND PHYSICS

➤ Dr. Nikita Nekrasov, senior faculty member at the Simons Center for Geometry and Physics

In 2012, the Simons Center for Geometry and Physics at Stony Brook University continued to blaze the trail for interdisciplinary work between mathematicians and physicists.

"When you find connections between two domains in any science and you bring people together, you open windows of opportunity for both fields to benefit."

NIKITA NEKRASOV

Inaugurated two years ago with the goal of helping investigators in these fields communicate, the center strives to bring the Stony Brook mathematics and physics departments closer — physically and intellectually. In pursuit of this mission, the center hosts up to 40 visitors weekly and a variety of seminars and workshops, all designed to promote new synergies.

Nikita Nekrasov, one of four permanent members at the center and a mathematical physicist, along with Samson Shatashvili, a committee member at the center, organized a semester of such work last fall. The program, Integrability in Modern Theoretical and Mathematical Physics, connected gauge theorists, who study the interactions of elementary particles, and quantum integrable systems researchers, who focus on exactly solvable mathematical constructions that aid in understanding the physics of the natural world.

"There are things that are better understood in one language and things that are better understood in another, and once the two groups understand each other, they can advance both fields," says Nekrasov. "And that was precisely what happened with this program."

Nekrasov and Shatashvili's inspiration for organizing the program grew out of their own research, which focuses on the connection between quantum integral systems and supersymmetric gauge theory — idealized models of the universe that relate matter particles to particles that mediate the interactions of those matter particles.

Nekrasov and Shatashvili, along with Gregory Moore, also a committee member at the center, first discovered a theoretical connection between supersymmetric gauge theory and quantum integrable systems in 1997. Aided by a variety of collaborations over the years, their ideas have been evolving ever since.

"But," says Nekrasov, "the subject was clearly bigger and richer than what we could understand on our own, so we decided to bring more people, from both communities, to discuss, to learn and to advance."

And, according to Shatashvili, these disciplines are becoming increasingly important. "String theory, the most accepted candidate for the ultimate theory explaining how the universe works, cannot exist without supersymmetry." What's more, he says, "Quantum integrability in modern mathematics is probably one of the most active topics that incorporates many other subjects, such as geometry, algebra, analysis and others."

In the end, both consider the meeting to have been extremely successful, and it later gave birth to a smaller workshop "I believe this was one of the most successful programs I witnessed anywhere on the interface between mathematics and physics," says Shatashvili.

"When you find connections between two domains in any science and you bring people together, you open windows of opportunity for both fields to benefit," says Nekrasov.

MATCHING GIFTS AT STONY BROOK UNIVERSITY

➤ Matching gifts to Stony Brook from the Laurie Landeau Foundation and the Simons Foundation help to preserve the wildlife of Shinnecock Bay, Long Island.

In the 56 years since its creation, Stony Brook University has risen to become one of the nation's premier public universities. To solidify Stony Brook's position among the top research universities, in 2011 the Simons Foundation pledged a $50 million matching challenge grant to be invested in initiatives across the university, with an emphasis on medicine and the life sciences.

Combined with a $100 million personal gift from James and Marilyn Simons that year, these donations constitute the sixth-largest gift ever made to an American public university.

The Stony Brook Foundation anticipated that it would take three to five years to raise enough donations to fulfill the matching challenge. Instead, the university met its goal within a year, as the grant inspired a flurry of giving — much of it from first-time donors to the university — that will fund more than 260 initiatives.

The donations, including the five described below, provide for 13 endowed professorships and chairs, and student funds equivalent to 628 in-state full-tuition scholarships.

"These gifts will be transformational for Stony Brook," says Samuel Stanley, the university's president.

Marine Restoration. For more than a decade, scientists at Stony Brook's School of Marine and Atmospheric Sciences have been tracking the decline in water quality and shellfish populations in Shinnecock Bay on Long Island's South Shore. Now, a gift from the Laurie Landeau Foundation, matched by the Simons Foundation, will allow Stony Brook scientists to work over the next five years to restore this vital estuary. By restocking shellfish and expanding eelgrass beds, researchers hope to guide the habitat toward self-sustainability and revitalize the once-flourishing hard clam fishery.

Laurie Landeau and her husband Bob Maze run a thriving oyster farm on a tributary of Maryland's Chesapeake Bay, which has faced ecological devastation similar to that of Shinnecock Bay.

Landeau had committed seed money for the project prior to the creation of the Simons matching grant but hadn't initially planned to fund the entire project. "The match influenced me to stretch what I would commit, because I realized that we could make the entire budget for an ambitious, multi-year plan," Landeau says. "Had there been no match, I would have thought twice about giving that much because I would have wondered whether my gift alone would have enough impact."

Landeau and Maze hope the scientific approach to the Shinnecock Bay restoration will serve as a model for similar projects in the Chesapeake Bay and across the country.

The project helps fulfill one of Stony Brook's core missions, says Dexter Bailey, vice president for advancement at the university: "To be a good neighbor and a good steward of the community."

Pediatric Multiple Sclerosis. Multiple sclerosis is usually an adult-onset disease, but when it does strike children, the impact can be devastating: Symptoms include extreme fatigue, weakness and cognitive impairment. At the same time, unlike the adult form of the disease, pediatric multiple sclerosis sometimes mysteriously reverses itself completely.

Over the past decade, Stony Brook has been leading the charge to understand this little-studied form of the disease at its multidisciplinary Pediatric Multiple Sclerosis Center, the first of its kind in the United States. Now, a gift from Robert and Lisa Lourie will allow researchers at the center — renamed the Lourie Center for Pediatric Multiple Sclerosis — to bring advanced imaging tools to bear on the disorder. A matching gift from the Simons Foundation will create an endowment to support the center's activities.

The first purchase out of the gift, a combination PET/MRI scanner, will enable researchers to simultaneously apply two complementary imaging techniques, giving neurologists a view of the disease's effects at the level of individual brain cell types. The machine, which will also be made available to Stony Brook neuroscientists in other specialities, is only one of four such devices in the United States.

"We wanted to give Stony Brook the opportunity to be on the cutting edge" when it comes to neuroscience imaging, Robert Lourie says.

Being involved in significant scientific research "has been a huge source of satisfaction and intellectual interest for us," Lisa Lourie adds.

Madagascar Health Initiatives. For 26 years, Stony Brook primatologist Patricia Wright has been working to conserve the ecosystems of Madagascar, most of whose plants and mammals are found nowhere else on earth. As her work has progressed, Wright and Stony Brook have broadened this effort to include another goal: improving the lives of the Malagasy, Madagascar's indigenous people, who are among the most impoverished in the world.

A major gift from James and Robin Herrnstein offers a two-pronged approach toward achieving this goal. Their gift has enabled the completion of a state-of-the-art research facility in Madagascar, inaugurated in July 2012. The 15,000-square-foot building is the new home of Stony Brook's Centre ValBio, created in 2003 to promote research, conservation and projects to benefit the Malagasy people. The facility features a biosafety level 2 laboratory that will enable infectious disease research, plus several additional laboratories and a wide array of equipment.

The Herrnsteins' gift will also fund the creation of a new institution based on Stony Brook's Long Island campus: the Global Health Institute, whose mission is to conduct health science research for the benefit of the Malagasy. This interdisciplinary research center will work on projects such as infectious disease monitoring and prevention measures.

Cardiac Imaging. Stony Brook cardiologist Michael Poon is on the vanguard of efforts to incorporate noninvasive cardiovascular imaging into the diagnosis and treatment of heart conditions. Since joining the School of Medicine in 2009, he has reduced Stony Brook University Hospital admissions of patients with chest pain by using coronary computed tomographic angiography to quickly determine whether the chest pain indeed indicates heart disease.

Now, three gifts will allow Poon to expand his research. One, from Eugene and Carol Cheng, will create a cardiovascular imaging research endowment and enable Poon to buy an enhanced external counterpulsation (EECP) machine, which uses blood-pressure-like cuffs to increase blood flow into the coronary arteries of patients with angina or heart failure.

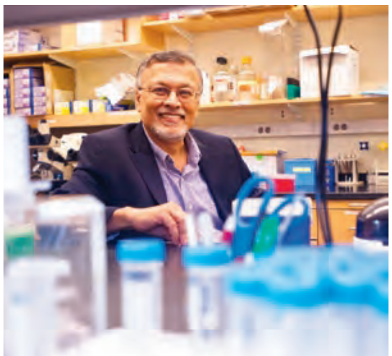
A second gift, from an anonymous donor, will allow Poon to perform clinical trials evaluating the EECP procedure. Matching funds from the Simons Foundation will establish the Dalio Center for Cardiovascular Wellness and Preventive Research, which will use imaging tools to study coronary artery disease, dementia and congestive heart failure.

A third gift, from Charles Gargano, will create a chair in advanced cardiovascular imaging at Stony Brook.

"These generous gifts provide the seed money to establish a world-class wellness research center," Poon says.

Diversity in Nursing. To help address the national nursing shortage, the Robert Wood Johnson Foundation has awarded Stony Brook a grant to fund ten scholarships for career changers to enroll in the university's Accelerated Baccalaureate Program, which offers a concentrated one-year nursing curriculum. Matching funds from the Simons Foundation will permit three of these scholars to progress to Stony Brook's Doctor of Nursing Practice Program, which affords students the leadership skills and expertise necessary to transform healthcare practices and train other nurses.

The Robert Wood Johnson Foundation's scholarships are part of its nationwide initiative to help nursing schools to prepare more students for advanced nursing practices. Stony Brook's School of Nursing has designated the funds to be used for students from economically disadvantaged backgrounds and from populations that are underrepresented in nursing.








SIMONS FOUNDATION AUTISM RESEARCH INITIATIVE (SFARI)

2012 was another successful year for SFARI in all areas of autism research, including understanding cells, understanding local circuits and the larger neural ensembles that are likely altered in autism spectrum disorder (ASD), and in the ongoing discovery of the genetic variants that impact all these cells and systems.

We achieved all this by funding new grants, holding meetings at the foundation and encouraging new collaborations through targeted projects. SFARI now supports the work of more than 150 excellent investigators in the United States and abroad.

And while one of SFARI's goals is to fund individual investigators in ASD research — and thereby improve the quality of life of those on the autism spectrum — these individuals, in turn and through us, form a community of ASD researchers.

It is this community that the foundation also endeavors to bolster: through meetings, interaction with foundation staff, and now, formally, through our website, SFARI.org, where we've created new forums and programming to probe questions that may require novel approaches.

In forging ahead, we will ask this community, "What is next?" in each area of investigation. How can we contact and evaluate large cohorts — on the order of 10,000 individuals — to validate and extend our early genetic findings? What environmental factors and life experiences influence the expression of genetic risk factors?

Will the analysis of gene networks point to new, approachable drug targets? What measures of behavior, brain activity or molecular function correlate best with autism severity? Is it best to focus on individual traits or on the entire clinical picture of autism in correlating genes and behavior?

When does the striking imbalance between synaptic excitation and inhibition observed in animal models of autism first appear? Is it accentuated in certain regions of the brain? This imbalance has been an important focus of current efforts to use GABA mimetics in therapeutic trials.

While collaboration between investigators and labs with different experimental expertise is essential in approaching these questions, mysteries will remain and new breakthroughs will undoubtedly still depend on creative insights by individuals.

Understanding this principle, we are steadfast in our investment in individual scientists. As I have stated in previous reports, many of these people come to autism research from other fields, but resources alone could not attract this level of talent; the science of autism is now ripe for approach with testable hypotheses, and for discovery.

It is through this multi-pronged approach involving staff, investigators and community that we hope and intend to make a difference in what is known about ASD and in the lives of people on the autism spectrum and their families.

Gerry Fischbach

Gerald D. Fischbach
Scientific Director

SFARI RESEARCH HIGHLIGHTS

More than 150 SFARI Investigators are currently conducting research into autism spectrum disorders at dozens of institutions across the country and abroad. The following pages represent some highlights of these researchers' achievements over the past year.

Signals and noise. Sensory input from the outside world generates unusually 'noisy' brain responses in people with autism, a new study suggests.

A research team including SFARI Investigator David Heeger of New York University used functional magnetic resonance imaging to scan the brains of 14 adults with autism and 14 controls as they performed vision tasks while being exposed to sensory stimuli such as beeping sounds and puffs of air on their hands.

The brain responses of individuals with autism showed much greater variability from one trial to the next than those of the controls, producing a lower signal-to-noise ratio, the researchers reported in the September 20, 2012 issue of *Neuron*[1].

The study may help account for the common observation that individuals with autism often notice small sensory details but miss the big picture, the researchers write. Unreliable responses to sensory stimuli might, for example, prompt a child to withdraw from an overly unpredictable social environment and focus instead on repetitive behaviors, the researchers speculate.

Most brain imaging studies of autism focus on deep regions of the brain involved in social behavior, but the noisy brain responses in the new study appear only in the cortex, calling new attention to this outer layer of the brain.

Branched chains. One rare form of autism may be treatable with a dietary supplement, a new study suggests, making it potentially the first form of autism to have a personalized treatment.

The study, led by SFARI Investigator Joseph Gleeson of the University of California, San Diego and published October 19, 2012 in *Science*, examined three families with children who have mutations in a gene called BCKDK[2].

This gene produces an enzyme preventing the breakdown of 'branched-chain' amino acids, protein building blocks that the human body can't synthesize. The children with the mutations, all of whom have both autism and epilepsy, have lower levels of branched-chain amino acids in the blood than other family members do, the researchers found.

Mutant mice that lack BCKDK have seizures and other neurological abnormalities, together with low levels of branched-chain amino acids. When the researchers fed the mice a diet enriched with these amino acids, their symptoms disappeared within a week, suggesting that the syndrome is reversible. The researchers are currently studying the effect of nutritional supplements on the human carriers of BCKDK mutations.

The mechanism by which BCKDK mutations may cause autism and seizures is unknown. The symptoms might be a result of low levels of branched-chain amino acids in the brain or of higher-than-usual levels of other amino acids. Both of these anomalies have been observed in the brain tissue of the mice that lack BCKDK.

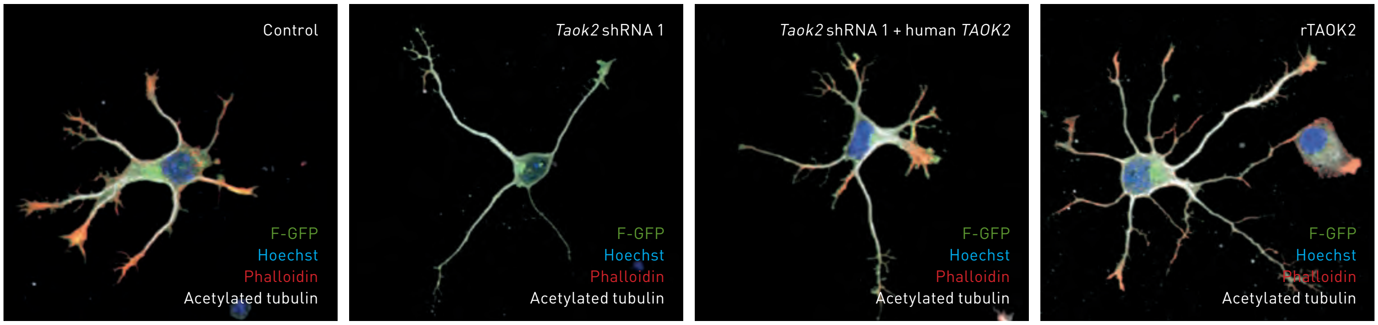
Worm signals. Mutations in two genes linked to autism may slow down neural signaling, a new study of worms suggests.

The two genes, which encode proteins called neurexin and neuroligin, have previously been shown to be involved the formation of synapses — the connections between neurons — during development. However, the new research, published August 2, 2012 in *Science*, suggests that mutations in these genes also affect how mature synapses function, altering the timing of signals in ways that may make it harder to process sensory information[3].

The research team, led by SFARI Investigator Joshua Kaplan of Harvard University, studied the cellular biology of the neurexin and neuroligin proteins in the nematode *Caenorhabditis elegans*. The researchers found that the two proteins work together to regulate a particular kind of reverse synaptic signal that halts the release of neurotransmitters at the junctions between neurons and muscle cells.

By eliminating either one of these two proteins in *Caenorhabditis elegans*, the researchers are able to turn this reverse signal off, which in turn results in a slower, more prolonged release of neurotransmitters.

While the cognitive implications of this slowdown are not yet elucidated, a muddying of the precise timing of signals might make it harder for an individual to figure out when a particular stimulus occurred. Brain images and sensory tests suggest that children with autism respond more slowly than other people to sounds, and have difficulty assessing the order in which events take place.



➤ **Neural disconnect.** Autism candidate gene TAOK2 is part of a signaling pathway that regulates the formation of neuronal projections, new research indicates. When the researchers shut down expression of TAOK2 in cultured cortical neurons (second from left), the cells show fewer branched projections compared with a control (left). Introducing into these TAOK2-shutdown cells a form of the TAOK2 gene that is resistant to the shutdown process (second from right) reverses these effects, indicating that they are indeed controlled specifically by TAOK2. Cells in which TAOK2 is overexpressed (right) show more primary neuronal projections than the control does.

Neural disconnect. An autism candidate gene called TAOK2 plays a role in the formation of neural connections during development, a new study suggests.

Published June 10, 2012 in *Nature Neuroscience*, the study identifies a new signaling pathway by which the TAOK2 protein interacts with several other proteins to regulate the formation of both axons and dendrites, neuronal projections that respectively send and receive signals[4]. Neurons with less TAOK2 than usual have fewer axons and dendrites than other cells, the researchers found, and for cells with excess TAOK2, the reverse is true.

The team, led by SFARI Investigator Li-Huei Tsai of the Massachusetts Institute of Technology, shut down the TAOK2 gene in certain neurons in prenatal mice. When the mice were a week old, the team found that the affected neurons had failed to produce axons crossing the midline of the brain in the corpus callosum, which connects the right and left brain hemispheres.

The TAOK2 gene resides in a chunk of the 16p11.2 chromosomal region, whose deletion is believed to be responsible for about 1 percent of autism cases. The new findings suggest that underdevelopment of neurons and disconnection of brain regions may underlie these cases of autism, the researchers write.

Blunted pruning shears. Sensory experiences sculpt the maturing brain by triggering the strengthening of some synapses and the elimination of others. The mechanisms behind this process, which is a crucial part of learning, are largely unknown. However, several studies have indicated that in autism spectrum disorders, the pruning of synapses seems to go awry.

Now, a research team led by SFARI Investigators Christopher Cowan of Harvard Medical School and Kimberly Huber of the University of Texas Southwestern Medical Center has turned a spotlight on one mechanism underlying this pruning process, and in doing so has uncovered a new connection between autism spectrum disorders and FMRP, the protein that is absent in fragile X syndrome. FMRP, the researchers report in the December 21, 2012 issue of *Cell*, works with three autism-related proteins to spark synaptic elimination[5].

FMRP works in concert with two of these proteins, MEF2 and PCDH10, the researchers found, to link a third autism-related protein — which sits at the ends of neurons — to the proteasome, the cellular body whose job is to break down unneeded proteins. In neurons that lack FMRP, the team found, this pathway toward synapse elimination is blocked.

Each of the three autism-linked proteins plays a unique and critical role in this synaptic elimination pathway. The findings, the researchers write, suggest that several different genetic causes of autism, involving one or another of these proteins, may produce the same end result: a deficit in synaptic pruning in response to stimuli from the outside world.

References:

1. Dinstein I. *et al. Neuron* **75**, 981-991 (2012)
2. Novarino G. *et al. Science* **338**, 394-397 (2012)
3. Hu Z. *et al. Science* **337**, 980-984 (2012)
4. de Anda F.C. *et al. Nat. Neurosci.* **15**, 1022-1031 (2012)
5. Tsai N.P. *et al. Cell* **151**, 1581-1594 (2012)

SFARI INVESTIGATORS

THOMAS BOURGERON

"Figuring out how to mimic ... protective [genetic] factors with drugs would provide another approach to autism drug development."

Nearly ten years ago, Thomas Bourgeron struck genetic gold. Scouring the X chromosome for clues to autism, the French scientist identified two mutations in genes called neuroligins, in two pairs of Swedish brothers with the disorder. These genes are essential for proper function of the synapse, the connection between neurons.

The study, published in *Nature Genetics*, garnered little attention at the time. But it was the first to link a rare mutation in a single gene with common forms of autism, and would ultimately change the face of autism research.

"[Bourgeron's] early work was the harbinger of an entire wave of rare-variant discovery that came after," says Matthew State, chair of the psychiatry department at the University of California, San Francisco. "I don't think there is anyone who had more a significant impact as an individual on where the field is."

About six years ago, Bourgeron received a phone call that would change the course of his career. He had met the mother of a 23-year-old man with autism at a student's Ph.D. thesis review, and the mother called Bourgeron after learning that her son carries a mutation in SHANK3, a gene that Bourgeron had linked to autism. "I told her what little we knew about the protein at the time," Bourgeron recalls. But there wasn't much that would be useful to a struggling parent. He recalls the mother saying, "If I knew at that time he had a genetic mutation, I would not have fought like this, because I don't think I could have fought the genome."

Her remark triggered a philosophical change in how Bourgeron viewed his work, and he set out to find practical applications for his research. Much of his recent work has focused on the study of sleep and the hormone melatonin. Although sleep is not considered one of the core symptoms of autism, many children with the disorder suffer from sleep problems, and Bourgeron says he believes studying it will bring important insight into the disorder. His team has confirmed that some people with autism have low melatonin levels, and found that this is linked to dampened activity of an enzyme needed for melatonin synthesis.

In the meantime, Bourgeron's team has not abandoned the synapse. He and his collaborators are sequencing the whole genomes of 15 families with multiple members who have autism. Apart from harmful mutations, Bourgeron says, he also hopes to find factors that protect from autism. Figuring out how to mimic such protective factors with drugs would provide another approach to autism drug development.

This profile was adapted from a longer version, written by Emily Singer and published October 25, 2012 on SFARI.org.

BETH STEVENS

A young child possesses a vastly overwired brain, with far more neuronal connections than an adult has. As the child matures, the brain gradually prunes away many of these connections, called synapses, while preserving the ones most useful for understanding the outside world. This sculpting process is crucial for learning and memory, but researchers are only beginning to understand just how the brain carries it out.

SFARI Investigator Beth Stevens' interest in the mechanisms behind synaptic pruning has led her to a seemingly unlikely participant in the process: microglia, the brain's dedicated immune cells. Microglia have been studied largely in terms of their role in injured or diseased brains, in which they act as both the brain's warriors and its garbage collectors, eating up enemies and pieces of cellular detritus.

About a decade ago, however, a second role for microglia began to surface. In healthy brains, studies have shown, microglia are constantly surveying neurons and touching their dendritic spines, neuronal projections that receive signals from other cells. This activity is most pronounced during the developmental window in which the most synaptic pruning occurs, a finding that led researchers to speculate that microglia play a key role in this process.

In a study of mice reported May 24, 2012 in *Neuron*, Stevens' lab at Children's Hospital Boston found that microglia do indeed prune synapses, literally eating unwanted neuronal connectors.

"Microglia were in exactly the right time and place, and we caught them in the act," Stevens says.

The team also uncovered a specific mechanism underlying this process — a receptor that, when knocked out, greatly diminishes microglia's consumption of synapses.

Several studies have suggested that microglia may be dysfunctional in individuals with autism. Brains of people with autism have been found to have more microglia than a typical brain does, and mouse models of autism suggest that the microglia are in an unusually activated state. Stevens is now using animal models to test whether microglia dysfunction may in fact be one of the causes of autism.

NATHANIEL HEINTZ

For more than two decades, Nathaniel Heintz, a SFARI Investigator at Rockefeller University in New York, has worked toward an ambitious goal: to understand the unique biochemistry of each of the hundreds of different types of cells in the central nervous system. That goal has led him in a direction he never anticipated — toward a connection between an autism-related disorder called Rett syndrome and the genomic markers that allow cells with identical genomes to mature into different types of brain cells.

Researchers have long known that cytosine — the genomic building block that provides the 'C' in the A, C, G, T of the genetic code — sometimes appears in a modified form called 5mC that seems to turn off certain genes. In 2009, Heintz's lab made an unexpected discovery: Cells in mammalian nervous systems also possess a second variant of cytosine, 5hmC, which had previously been observed only in the vastly different context of bacteria-infecting viruses.

New research from Heintz's lab, published December 21, 2012 in *Cell*, suggests that in the central nervous system, 5hmC and 5mC may act as genomic markers that play complementary roles in regulating genes. In three different types of brain cells, the team found, activated genes have much more 5hmC than 5mC; in deactivated genes, the reverse is true.

When Heintz's team searched for brain cell proteins that bind to 5hmC, the only protein that emerged was the one which, when mutated, causes Rett syndrome, which is characterized by language impairment and seizures, among other symptoms. The finding suggests that Rett syndrome may stem from faulty binding of the mutated protein to 5mC and 5hmC, which in turn could block the proper maturation of some types of brain cells.

After many years in science, Heintz says, research projects seldom result in true surprises. "But for me, the discoveries of 5hmC and the involvement of the Rett syndrome protein were both completely unexpected and fascinating," he says. "I think the next few years are going to be really interesting."

SIMONS CENTER FOR THE SOCIAL BRAIN AT MIT

The Simons Center for the Social Brain at the Massachusetts Institute of Technology (MIT), which launched in January 2012, has now completed its first full year of activity. With a mission to develop an infrastructure for autism research and to tackle 'grand but solvable' challenges in the field, the center is drawing on MIT's strengths in areas from neuroscience to engineering to foster a truly interdisciplinary community of autism researchers.

The center's grants fund scholars at all levels of their careers, from undergraduates to senior researchers — and in a wide variety of fields, including biology, engineering, mathematics and social sciences. To encourage cross-pollination between fields, each grant must have two co-investigators.

The center is also developing two large-scale, targeted projects that will each involve several different labs with complementary approaches, to study two genetic forms of autism in depth.

The center's colloquium series has quickly become the most widely attended series of talks on autism and developmental disorders in the Boston area, according to the center's director, Mriganka Sur. "We routinely have 80 to 100 people in the auditorium," he says.

MRIGANKA SUR

Mriganka Sur has spent more than two decades probing the brain's seemingly infinite capacity to reinvent itself. His landmark experiments 20 years ago, in which he rewired the brains of young ferrets, offer what is still one of the most dramatic examples of brain plasticity: When messages from ferrets' eyes get routed to the auditory cortex instead of the visual cortex, the auditory cortex transforms itself into a vision center, allowing the ferrets to see via brain regions normally used for hearing.

Since those early experiments, Sur's laboratory has uncovered many of the mechanisms underlying brain plasticity, explaining how electrical activity shapes and rewires the developing cortex. Using high-resolution imaging of individual neurons and synapses (the connections between neurons), Sur has identified a range of specific molecules that work together in a coordinated fashion to change neuronal activity.

Recently, Sur has turned these insights on mouse models of Rett syndrome, a rare, autism-related disorder that appears to involve faulty maturation and maintenance of synapses and brain circuits. Sur's lab has pinpointed a pharmacological substance called IGF1 that promotes this maturation, and the potential treatment is now in clinical trials.

"The hope is that with the right kinds of training and treatments in place, the brain's phenomenal capacity for plasticity can offset many of these disorders," Sur says.

While founding the Simons Center for the Social Brain has taken a great deal of effort, Sur is determined not to allow his new responsibilities to slow down the pace of research in his lab. "There are 24 hours in the day, and I've made a promise to myself to maintain a vigorous research lab," he says.

The center's goal of bringing together researchers from disparate fields is close to Sur's heart.

"I love to help researchers to collaborate, even if I'm not involved in the ultimate solutions they come up with," he says. "I believe that the most important advances often come at the intersection of different people and ideas. If I can help make that happen at the Simons Center, I will be deliriously happy."

YUN LI

When it comes to autism-related disorders known to be caused by a particular mutation — such as Rett and fragile X syndromes — animal models have offered key insights. Unfortunately, however, these animal models can take researchers only so far. Many aspects of these disorders are uniquely human, and to understand them, human tissues are needed.

Creating and studying such tissues is the central research focus for MIT postdoctoral fellow Yun Li, who works in the biology laboratory of Rudolf Jaenisch, where the first mouse model of Rett syndrome was developed in 2001. Together with her colleagues, Li — the recipient of a postdoctoral fellowship from the Simons Center for the Social Brain — has developed a technique for introducing the Rett and fragile X mutations into the genomes of human stem cells, and then growing those first into neural stem cells and then into neurons and other brain cells.

Li is now comparing neurons that have the Rett mutation with normal neurons. "We have some clues of what to look for, so it's not a total fishing expedition," she says. For example, individuals with Rett syndrome have unusually small heads, and postmortem examinations indicate that these individuals have as many neurons as in a typical brain, but smaller ones. And, indeed, the Rett mutation neurons Li has grown are significantly smaller than typical neurons. Li is also examining synapse formation and gene expression in the mutant cells.

Other researchers in Jaenisch's laboratory, in collaboration with researchers at the Broad Institute of Harvard and MIT, are planning to subject Li's Rett syndrome neurons to high-throughput drug screens that will hopefully identify candidate drugs to reverse or mitigate the disorder.

Just as the mouse model that emerged from Jaenisch's lab has proved a widely used platform for studying Rett syndrome, Li hopes that her work with stem cells will be useful "not just for us, but for any laboratory that wants to study Rett syndrome in human tissues," she says. "I would be very happy if this becomes a common resource for people to use."

BEVERLY COPE

As a child being homeschooled in Sudan, Beverly Cope always knew there was something unusual about her close friend and homeschooling classmate, who was later diagnosed with Asperger syndrome.

"I could tell she was different from the other kids I knew," Cope says. "At the time, there was no label on that difference — it was just who she was, and we were fine with that."

As Cope grew interested in psychology, she became eager to be part of the effort to understand autism spectrum disorders. As an undergraduate at MIT, she jumped at the chance to get involved in autism research.

With the support of an undergraduate research grant from the Simons Center for the Social Brain, Cope is now working in the laboratory of MIT neuroscientist Nancy Kanwisher to develop a more nuanced description of the variety of phenotypes that come under the umbrella of autism spectrum disorders.

Together with a team of faculty, postdoctoral fellows and students, Cope is testing children with autism as they perform various perceptual tasks, looking for subgroups whose behaviors and symptoms exhibit commonalities. Cope is also designing and conducting experiments herself, to examine how individuals with or without autism perceive arrays of shapes and colors.

Cope hasn't decided what her next step will be after college, but one thing is clear to her: Eventually, she wants to help people in developing nations to benefit from innovations in public health and medicine. In 2011, Cope spent a summer in India, examining why cataract patients in poor villages often don't avail themselves of free corrective surgery.

"I really like the challenge of figuring out how to make new technologies work for people overseas," she says. "I've always been interested in finding ways for people to help themselves."

SIMONS VARIATIONS IN INDIVIDUALS PROJECT

➤ Simons VIP Family Meeting, July 14, 2012, Chicago, Illinois

Attempts to devise treatments for autism have been hindered by the fact that 'autism' is no longer considered a single disorder. Variations between those diagnosed are widely acknowledged, and even at the genetic level, autism manifests itself through hundreds of different genetic variants.

These variants may or may not produce similar autism syndromes, and even when they do, it may be via completely different biological mechanisms. Treatments that work well for one genetic version of autism might not work at all for another, making it difficult to gauge just how promising any particular therapy is.

Because of this complexity, some researchers now advocate a 'gene-first' approach to studying autism — one that examines different genetic versions of autism separately, instead of lumping them all together.

One of the first such projects — the Simons Variation in Individuals Project (Simons VIP) — is starting to bear fruit. This multi-site collaboration collects psychological profiles, biospecimens and brain imaging data from about 200 individuals whose genomes show copy number variants (duplicated or deleted sections of DNA) in the 16p11.2 chromosomal region. About 1 percent of individuals with autism have copy number variants in this region, enough to make it one of the most common genetic variants associated with autism.

After three years, the Simons VIP is beginning to uncover commonalities among carriers of 16p11.2 deletions. Only about 15 percent of the individuals with deletions meet the diagnostic criteria for an autism spectrum disorder. However, about 80 percent have an identifiable psychiatric disorder, usually involving symptoms similar to those of autism, such as language delay and behavioral problems, the investigators reported in the *Journal of Medical Genetics*.

"The deletion creates a highly elevated risk for autism and neuropsychiatric disorders," says John Spiro, deputy scientific director of SFARI.

"Many researchers think of autism as a dichotomous trait — either you have it or you don't," says Wendy Chung of Columbia, the project's principal investigator. "But it seems that it's more a collection of qualitative traits, and once you get past a certain threshold, they are labeled as autism."

The *Journal of Medical Genetics* paper examined only a narrow swath of the collected data; now VIP researchers are examining full details of participants' psychological and genomic data, and perhaps most excitingly, their structural and functional brain scans. The latter scans, which show brain activity as the individuals perform activities such as language tasks, may help to pinpoint sources of the individuals' language difficulties, the most pronounced symptom associated with the 16p11.2 deletion.

The initial data, Chung says, suggest that individuals with the deletion may not be processing sounds quickly enough. The hope is that identifying the cause of these language difficulties will ultimately point the way toward therapeutic approaches, Chung says.

Already, the project has captured one feature of the disorder that could have immediate medical implications: Nearly one-quarter of individuals with the 16p11.2 deletion have had seizures. Given this relatively high frequency, and how subtle seizures can be, it is possible that some participants have had seizures that have not been diagnosed, Chung says. "If one of these individuals has something that looks even a little like a seizure, it is critical that they be tested to see whether it is indeed a seizure," she continues. "We should not miss the opportunity to treat seizures."

EXPLORING THE AUTISM GENOME

➤ Evan Eichler, Matthew State and Michael Wigler

Three large-scale genetic studies of families with autism have definitively established a role in the disorder for 'loss-of-function' point mutations — single-nucleotide glitches that likely render a gene nonfunctional.

The studies, led by SFARI Investigators Michael Wigler of Cold Spring Harbor Laboratory, Matthew State, now at the University of California, San Francisco, and Evan Eichler of the University of Washington, respectively, sequenced just the whole exomes — the protein-coding regions of the genome — of nearly 800 families.

The participants came from the Simons Simplex Collection, a repository of data from more than 2,700 autism families consisting of one child with the disorder and unaffected parents and siblings. State and Eichler's papers appeared April 4, 2012 in *Nature*, and Wigler's was published April 26, 2012 in *Neuron*.

Children with autism, the research teams found, are twice as likely as their unaffected siblings or controls to have spontaneous gene-disrupting point mutations — errors that occurred in a parent's germ line. Interestingly, such errors are more likely to come from the sperm than the oocyte, and are more common in older fathers, the researchers found.

The papers also showed that several genes exhibited mutations in more than one child with autism, providing robust evidence that these genes are implicated in the disorder.

A follow-up paper by Eichler's group, published December 21, 2012 in *Science*, turned up six such genes by performing a targeted search through the entire Simons Simplex Collection, looking for mutations in 44 candidate genes from his lab's whole-exome sequencing project. Loss-of-function mutations in one of these six genes, CHD8, appeared in eight children with autism, and that gene may underlie more than 0.3 percent of all autism cases, Eichler says.

However, despite the identification of a few strong candidate genes, the findings highlight the extreme genetic diversity of autism. The research teams estimate that mutations in several hundred to a thousand different genes probably confer high risk for the disorder.

The researchers are now carrying out whole-exome sequencing on the entire Simons Simplex Collection. That undertaking should bring to light many more autism mutations, the researchers agree, but a much larger collection would be needed to identify every autism gene. However, tracking down every last autism gene is not necessarily the most important goal, State says.

"There might be 1,000 spots in the genome linked to autism, but there is extremely strong evidence that they are converging on a much smaller set of networks and pathways that are going to be relevant to autism," he says. "The key things we want to understand are the biological processes, and it's very unlikely that there will be 1,000 of those. By the time we've identified maybe 50 to 100 genes, I would hope that we would have really strong leads for some specific biological processes, and then it's biology that will tell us how to treat our patients."

Already, evidence is emerging for the role of certain biological pathways in autism. For example, five of the six genes that Eichler's study turned up belong to the same highly interconnected protein-interaction network.

And Wigler's group turned up an unexpectedly strong link between autism candidate genes and FMRP, the protein whose function is disrupted in fragile X syndrome, a neuropsychological disorder in which autism traits are frequently observed. The fragile X protein appears to be a central player in neuroplasticity, Wigler says, and the observed links to autism genes bolster the theory that autism involves an impaired ability of the brain to adjust to changes in its environment.

"It's nice when theory is backed up with observation," Wigler says. "Then you know the ground is getting solid under your feet."

SFARI.ORG

➤ Stephan Sanders presented SFARI.org's webinar on whole-exome sequencing.

Since its launch in 2008, SFARI.org has become the central online resource for scientists studying autism and related disorders. The site provides authoritative news and opinion on autism research, with attention to the cross-disciplinary connections between genetics, cognition, behavioral psychology, neuroscience and clinical research.

This year, SFARI.org has begun to roll out new digital community tools for its users, such as webinars, blog posts from scientists, and an enhanced wiki and forum, all of which aim to get researchers from different fields to share and discuss their work.

"Autism research is especially well suited for online community tools, because there is this great need for awareness of complex discoveries and phenomena that are outside one's specialty," says SFARI.org community manager Greg Boustead. "So it's not just about having compelling chat questions on the site — it's also about asking researchers, 'How can we be of value to you in your work?'"

According to SFARI.org director Apoorva Mandavilli, offering researchers a personal stake in the news site's ongoing development is key. "We want them to feel like SFARI.org is theirs, and have a sense of ownership in where the site goes in the future," she says. "We're moving ahead from being a static, verbal content provider to something much more dynamic. It's SFARI.org 2.0 in every way."

The first webinar featured postdoctoral fellow Stephan Sanders from Matthew State's lab at the University of California, San Francisco. Sanders shared with participants the results from that lab's genetic analysis of 200 Simons Simplex Collection families.

The webinar described how whole-exome sequencing — a technique that allows researchers to target severe mutations in protein-coding base pairs — uncovered a specific gene, SCN2A, in which these mutations tend to cluster.

"There is no 'autism gene,'" Sanders explains, "but we already know that these mutations are important to determining the causes of autism." Prior to this research, SCN2A had not been implicated in any autism spectrum disorder.

SFARI.org's staff hope that the webinar series will not only highlight new thought leaders in autism research, but will define a new channel for cross-pollinating ideas across research specialties.

"We've had people telling us that the webinars are a good resource for digesting information and a place to begin asking follow-up questions for future collaborations," says Boustead. Sanders agrees: "It was wonderful to have an instant audience for the research, who all were fired up and ready to ask interesting questions."

Meanwhile, the robust news and opinion sections that SFARI.org is already known for continue to grow as autism research itself — and the number of papers the site covers each week — expands.

To that end, in the past year SFARI.org has hired another full-time reporter, and a web producer with experience creating multimedia presentations. The site will also continue recruiting researchers to write guest blogs about their own or others' research findings.

"The site has grown enormously — traffic has doubled every year since 2010," says Mandavilli. "But the ultimate goal is to form meaningful collaborations."










➤ The Fifteen Puzzle, at the newly opened National Museum of Mathematics, allows visitors to grapple with the mathematical concepts of parity, proof and impossibility.

EDUCATION & OUTREACH

Science and mathematics surround us, and their universal presence triggers curiosity and stimulates discovery over the course of a lifetime. A child's natural sense of wonder generates countless opportunities to explore the principles of our world. In the classroom, talented and engaged teachers can motivate and propel students beyond the boundaries of the curricula. Adults continue their explorations out of intellectual curiosity, or even in service of practicality: from thinking about what it means to be 'conscious' to understanding computer science and its applications.

At the Simons Foundation, we recognize the public's desire for high-quality, stimulating intellectual learning opportunities. Our education and outreach grants aim to encourage a deeper engagement with, and understanding of, science and mathematics among students, professionals and the interested public.

The foundation's sponsorship of public lectures, interdisciplinary forums and focused multimedia initiatives aims to amplify the voices of outstanding scientists and to connect them with the general public for discourse on the scientific topics of our times. It is often an exceptional teacher, scientist or thought leader who can best engage us with the stories they tell and the knowledge they impart. We meet them in the classroom, in public spaces and, nowadays, through the Web.

In 2012, our education and outreach programs sought to create and expand opportunities for both our students and the broader public to appreciate the richness and beauty of science and mathematics in our world.

MATH FOR AMERICA

Founded in New York City in 2004, the aim of Math for America (M*f*A) is to develop and support a corps of outstanding science, technology, engineering and math (STEM) educators in United States secondary schools. While its operations focus on sustaining excellent teachers in classrooms — and keeping them there — the organization's ultimate goal is to bolster United States math and science through better public education, ensuring that the United States remains a world leader in science and innovation.

Today, the M*f*A teacher corps includes nearly 600 exceptional math educators across seven United States cities. M*f*A offers fellowships that support these educators with financial incentives, top-quality professional growth experiences and a community of like-minded teachers. All of this is designed to keep the best teachers refreshed and inspired to stay in the classroom and to attract highly qualified, mathematically inclined college graduates into teaching in public schools.

Currently, M*f*A is planning to expand its New York program from 380 to 1,000 members across new disciplines — including biology, earth science, computer science and more. If this new growth is realized, the New York City M*f*A corps could come to represent some 10 percent of the city's math and science teachers.

Karina Liu and Cameron Cassidy are two New York City teachers who are working to fulfill the mission of M*f*A.

KARINA LIU

M*f*A FELLOW

Karina Liu is an M*f*A Fellow — an inspired and mathematically talented recent college graduate committed to teaching math in secondary schools. M*f*A Fellows participate in a five-year program, spending one year earning a master's degree in education, and four years teaching.

Liu has been drawn to the study of mathematics since childhood, when her calculus teacher inspired a deep and passionate enthusiasm for the field. After minoring in mathematics at Stanford University in California and later working with a nonprofit organization designed to help public-school students and teachers, Liu resolved to merge the two fields in her own career by moving into the classroom herself.

As part of M*f*A's mentoring and professional development program, Liu was paired with an M*f*A Master Teacher — an experienced math teacher who has shown demonstrable excellence in the classroom — and also with a more experienced M*f*A Fellow. "The M*f*A teachers are spectacular," says Liu. "It was great to start out in the classroom under their guidance. They appreciate the importance of teaching conceptually

> *"I am able to bring in new strategies to make an impact in my own classroom."*
>
> KARINA LIU

and enabling student discovery — which has enhanced my own teaching practice."

Liu's M*f*A advisors regularly observe her lessons, a practice that helps her hone her teaching skills and prioritize her time in the classroom. When she's not teaching, Liu frequently attends M*f*A's professional programs, including a recent series of middle school mathematics workshops. "M*f*A has helped me promote the importance of rigorous math for all students, and I am able to bring in new strategies to make an impact in my own classroom," she says.

Now a sixth grade math teacher at a school that focuses on preparing low-income students to graduate from college, Liu attributes much of her success in teaching to the support she receives through M*f*A.

"My students are happy when they come to my classes, and I help them develop a conceptual understanding of mathematics, as well as critical-thinking and problem-solving skills. I teach them to love math for the logic and creativity behind it, just as I do."

CAMERON **CASSIDY**

M*f*A MASTER TEACHER

Cameron Cassidy, an experienced New York City educator, joined M*f*A to revitalize his own teaching practice and to share his experiences with early-career educators — providing them with the guidance that he had missed when he began his own teaching career at a high-needs school in Brooklyn. He remembers having a passion for improving mathematics and science education for students from all walks of life, but receiving little support or guidance.

"I saw M*f*A as an opportunity to make a significant change in STEM education by bringing together high-caliber math and science teachers and leaders," says Cassidy, now an M*f*A Master Teacher who receives a four-year stipend, professional development and leadership opportunities within the organization. The fellowship's stipend gives him the financial stability to keep him in New York City classrooms.

Cassidy shares his experience by mentoring others in the M*f*A community and by holding workshops for M*f*A Fellows on topics ranging from classroom management to productive group work. "These workshops allow the Fellows to learn from veteran educators. They really appreciate the support system at M*f*A that is enabling them to become outstanding career educators," he explains.

But Cassidy also benefits from the M*f*A community himself, by attending workshops led by renowned mathematicians and exchanging ideas with other Master Teachers — opportunities that help him bring new concepts and practices to his classroom.

Now at a college preparatory high school, Cassidy improves his courses, which range from geometry to robotics, by employing tactics he learns through the M*f*A corps. "The way I teach is constantly changing due to new ideas I get from M*f*A activities and workshops," he says. His elective robotics course, for example, helps students understand the interconnectedness of mathematical disciplines and has distinguished him as a leader at his school.

> *"Education is so powerful because everyone truly wants to learn."*
> CAMERON CASSIDY

But most gratifying, says Cassidy, is his evolving ability to improve the educational process by engaging students with math in positive and exciting ways. "Education is so powerful because everyone truly wants to learn," says Cassidy.

NATIONAL MUSEUM OF MATHEMATICS

➤ A MoMath visitor enjoys the museum's now-famous square-wheeled tricycle.

On a winter evening last December, several hundred people in black tie filed into a large, dimly lit building in Manhattan's Flatiron District to witness the throwing of an enormous electrical switch. That switch was in the brand-new and not-yet-open National Museum of Mathematics, or MoMath, and the assembled crowd, which included such luminaries as Mathematica creator Stephen Wolfram and Harvard professor Noam Elkies, was gathered for a gala celebration of the museum's completion.

Accompanied by strains of "Pure Imagination" — the theme song from *Willy Wonka & the Chocolate Factory* — MoMath executive director Glen Whitney flipped the giant switch with associate director Cindy Lawrence and chief of design Tim Nissen. "The lights came up, the exhibits all powered up at once, and the museum was literally turned on," Whitney says. "It was a moment we had been working toward for quite some time, and it all came together almost magically."

Although MoMath opened its doors to the public three days later on December 15, 2012 to positive notices from national media outlets including *The New York Times*, *USA Today* and *The Wall Street Journal*, the wildly successful opening almost didn't happen. Hurricane Sandy's destructive swath through New York delayed construction and exhibit installation. Whitney and Lawrence briefly considered postponing the museum's opening until mid-January, but ultimately decided against it. "We'd been promising to open in December for a long time, and we felt there was credibility at stake," Lawrence says.

Although Whitney acknowledges that "some things came down to the wire," the risk paid off. Happily, says Lawrence, "a crowd had built up outside the door the morning we opened, and people were lined up waiting to come in."

The museum, supported by donors inside and outside New York state, has enjoyed robust attendance ever since. MoMath expected to bring in 60,000 visitors during the museum's first year, but surpassed that figure in the first four months of operation.

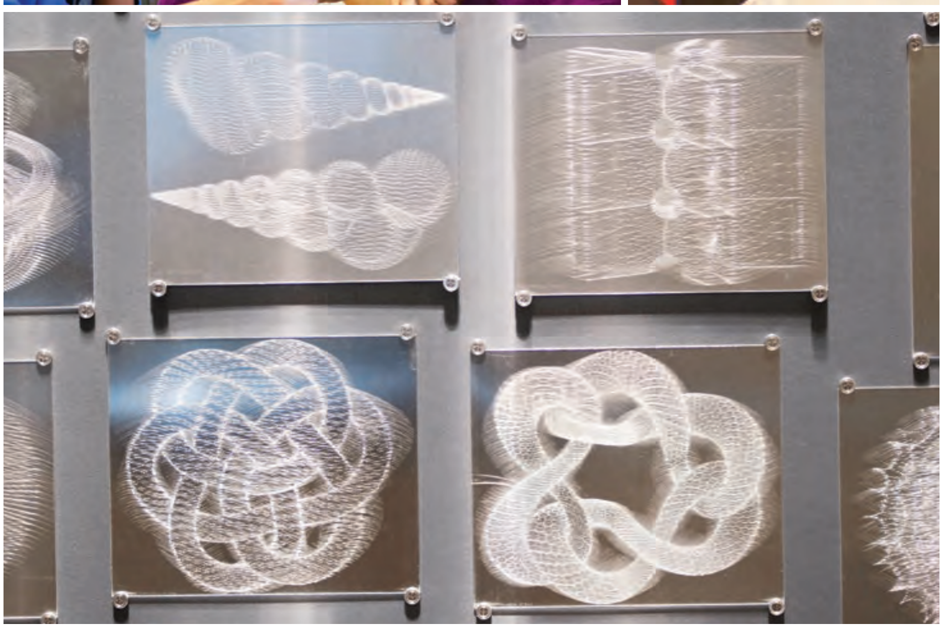
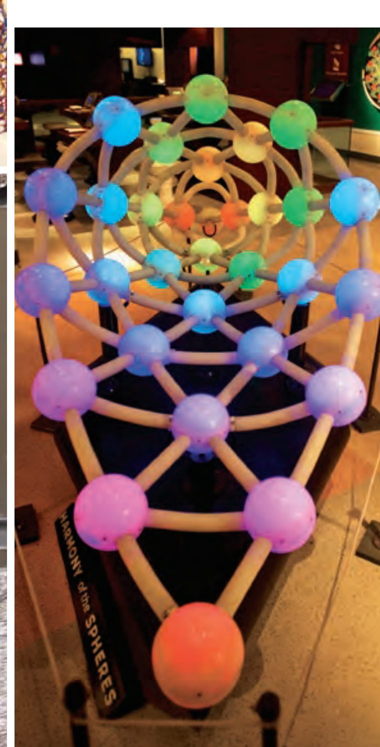
The museum has attracted visitors ranging from toddlers to senior citizens — a much wider demographic than Whitney and Lawrence expected. One regular visitor — a 2-year-old boy whose family lives near the museum — "walks around with a pentagon magnet in one hand and a hexagon in the other, telling anyone who cares to listen that a pentagon has five sides and a hexagon has six," Lawrence says. "The entire staff knows him by name. These are the kinds of wonderful relationships that you like to build in the community."

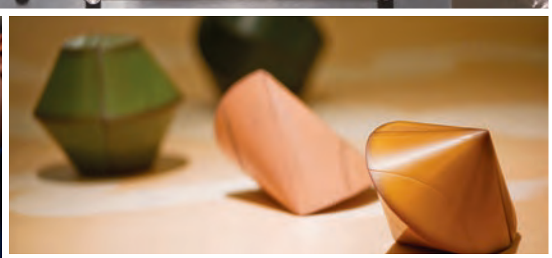
Creating new opportunities for that kind of in-person cultural engagement, says Whitney, is what the museum's mission is all about. Forthcoming programs in 2013 and early 2014 include an art gallery with rotating exhibitions, 'story-time' sessions and puzzle clubs for young children, a concert series and a recreational mathematics conference called MOVES, "where people prove theorems about topics that aren't so 'serious,' as it were," Whitney says.

"We're bubbling with ideas for mathematical activities, so that everybody can find something that's approachable — a hook to get them involved in the world of math."

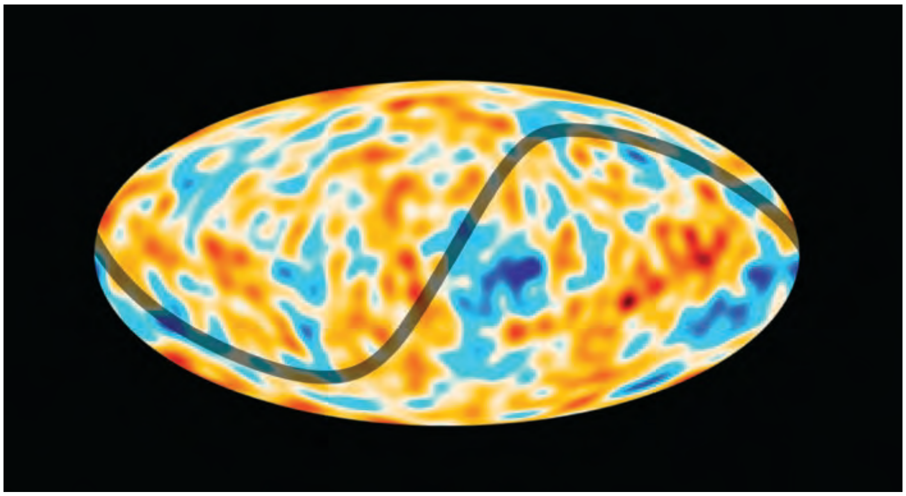




Wall of Fire
Tessellation Station
In Plane Sight
3-D Doodle






SIMONSFOUNDATION.ORG



➤ **European Space Agency and the Planck Collaboration**. A Planck satellite image of the early universe. At the largest scales, temperature fluctuations are more extreme in the half of the universe to the right of the gray line. From Simonsfoundation.org story, "In Lopsided Map of the Cosmos, a Glimmer of Its Origins"

In 2012, Simonsfoundation.org took visitors to the incinerating edge of a black hole, explained possible deep truths about the nature of our universe, and illuminated a major advance in the twin primes conjecture.

The Simons Foundation's new website — relaunched in October 2012 — aims to produce more content not only for the scientists and grant-seekers who traditionally frequent the site, but also for the ever-increasing number of students and scientifically literate laypeople who have begun to visit. With articles and videos designed to appeal to professional researchers and amateur enthusiasts alike, the early success of this site indicates that basic science and math topics — often seen as dry or overly abstract — are anything but.

In August 2012, with an eye toward improving the quality and quantity of its content and outreach, the foundation hired Thomas Lin, a former senior producer managing the science section of *The New York Times* website, as its new managing editor. Lin oversees all site operations and also leads a new, journalistically independent section of the site covering mathematics, the physical sciences, theoretical computer science and basic life sciences.

"We look forward to growing our readership, spreading scientific knowledge further, and thinking about how we can best use the site to advance our mission, which is to push the frontiers of research in math and science. The foundation itself is growing, and we wanted a website that reflects that."

MARILYN SIMONS

While information on all of the foundation's program areas and grant opportunities are clearly conveyed in an intuitive menu, "we also hope the site will become known as a place to learn about something fundamental or new in science," says Anastasia Greenebaum, communications director at the Simons Foundation.

The new site, and its venture into journalism, has already been successful. "It'd be fair to say that site visits have more than quadrupled," says Lin. The foundation has extended the reach of its articles by syndicating them to widely read outlets like *Scientific American* and *Wired*.

"But the real goal behind doing these journalistic pieces is to reach out to scientists and interested readers of all disciplines, and give them a fresh take on research that's not being covered by the mainstream media," says Lin. "A biologist recently commented on one of our articles that it 'helped me learn some physics without shedding any tears.' That makes me feel good, because we want to bring all these different communities together."

Foundation president Marilyn Simons says, "We look forward to growing our readership, spreading scientific knowledge further, and thinking about how we can best use the site to advance our mission, which is to push the frontiers of research in math and science. The foundation itself is growing, and we wanted a website that reflects that."

GERALD D. FISCHBACH AUDITORIUM

➤ Kerry Emanuel gives the first Simons Foundation Lecture, "Hurricanes: Present and Future."

In mid-November 2012, the new Gerald D. Fischbach Auditorium at the Simons Foundation opened its doors for the first time to host the SFARI Annual Meeting, a gathering in which approximately 150 Simons Investigators in the field of autism research convene every fall to share their work and even, on occasion, offer up some early findings. Construction had ceased just days before on this state-of-the-art, 172-seat facility, having kept ambitious pace since May (a brief-but-harrowing delay due to Hurricane Sandy notwithstanding).

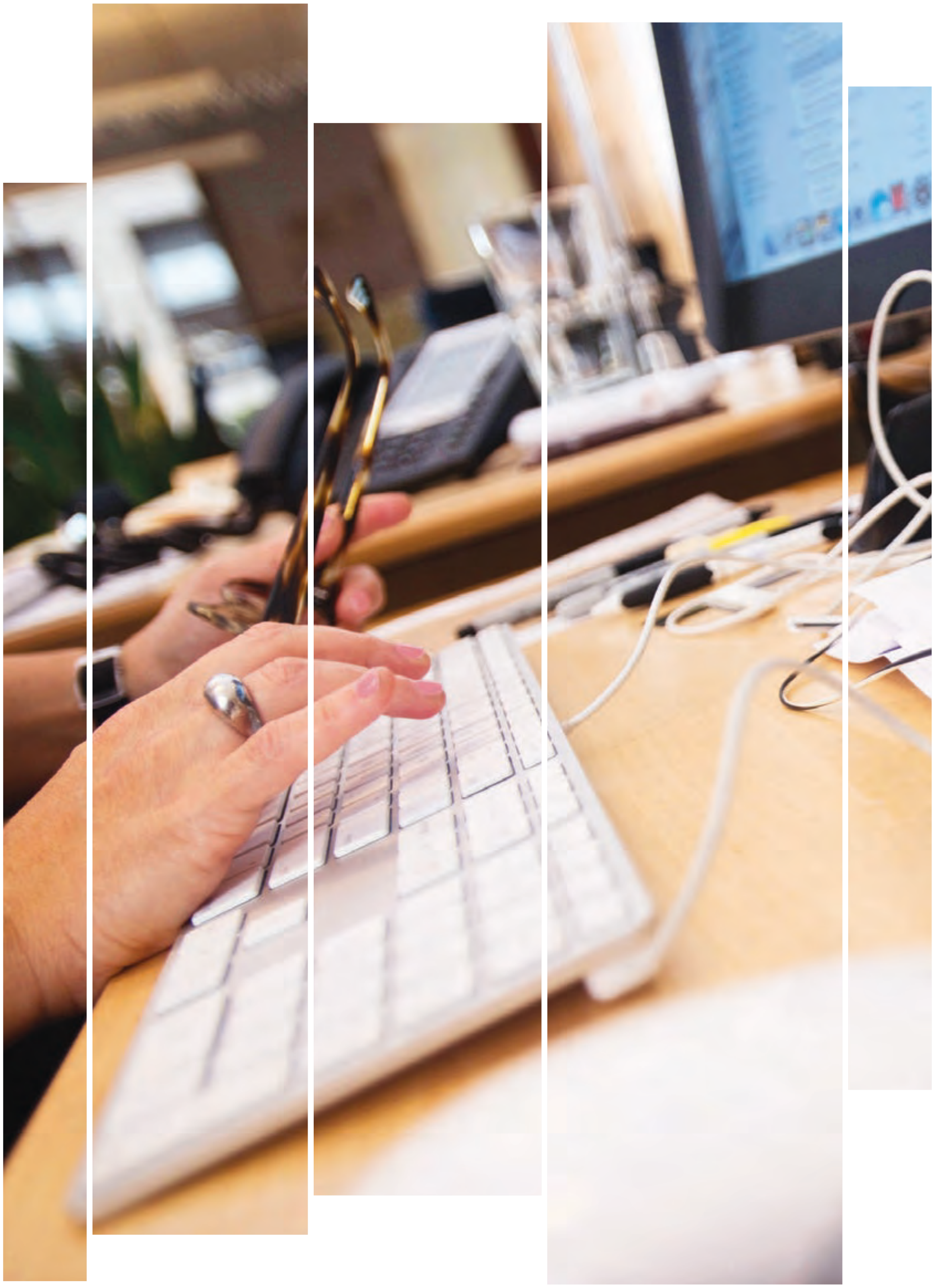
If a basic tenet of architecture is that 'form follows function,' and in biology that 'form determines function,' it might be said that 'form inspires function' in the case of the Gerald D. Fischbach Auditorium, named for the foundation's chief scientist and fellow — and former scientific director of SFARI — neurobiologist Gerry Fischbach. "Once it was decided to give a name to the auditorium, we thought that name should be reflective of our history. Gerry, who arrived to head our autism project, was the first scientist to join the foundation, and he has set a marvelous tone for all of our subsequent activities. It was the only choice and a perfect one," says Jim Simons, foundation board chair.

The auditorium and its surrounding facilities were designed by Ted Moudis Associates, who also designed the foundation's offices. Michael Sinkew and Mitchell Ross at Ted Moudis began discussing the project with Jim and Marilyn Simons in early 2011. "We could tell that this project was a precious element for them, so we played off of that," says Sinkew.

"From their submission of the first sketches, it was clear that they were onto something both highly original and highly functional, and so it has turned out. I believe the auditorium will play a brilliant role in helping the foundation achieve its goal of advancing basic scientific research. The Moudis organization did an outstanding job," says Jim Simons.

Because the Fischbach Auditorium was envisioned as a gathering place and enclave for the individuals and groups that take part in Simons Foundation programs, every feature of the auditorium was chosen to inspire exchange and collaboration among visitors. The young facility is already home to a broad spectrum of lectures, meetings and events supported by the foundation, including the Simons Science Series, a monthly interdisciplinary colloquium for scientists, the Simons Foundation Lectures series, the SFARI Annual Meeting and staff-based functions.

The conversation doesn't end with the lectures. Afterward, the learning enters a new mode as the audience flows into a surrounding space with tall windows that overlook Fifth Avenue. "The ancillary space became the natural breakout space," says Sinkew. Blackboards and whiteboards interspersed along the walls invite impromptu brainstorming sessions, and researchers from diverse fields gather at the café under the warm glow of hanging lamps, exchanging ideas and, hopefully, generating new collaborations.



FACTS AND PEOPLE

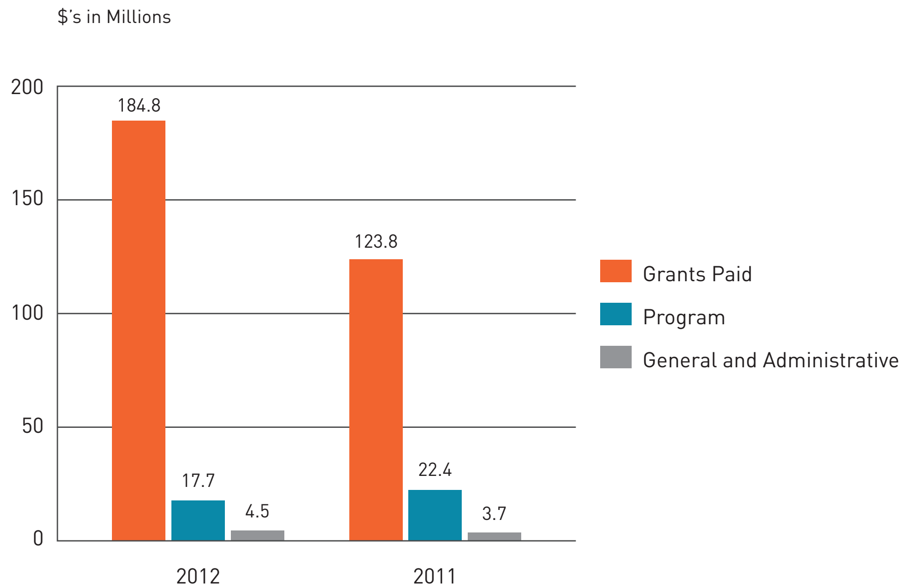
In 2012, the Simons Foundation continued to grow — expanding its programs, planning for new ones and offering more grant opportunities to practicing researchers around the globe. Total award amounts increased from approximately $120 million in 2011 to $180 million in 2012.

Expanded programming meant an increase in staff, both in New York City and remotely. The foundation expanded from 44 employees to 59 by the year's end. We also increased our facilities capabilities by inaugurating the Gerald D. Fischbach Auditorium, providing a ready site for the bloom of lectures, meetings and workshops we have begun to initiate and sponsor.

In short, we are happy to report another year of program-building at the Simons Foundation — and to confirm that all developments are firmly in the service of promoting advancements in mathematics and the basic sciences.

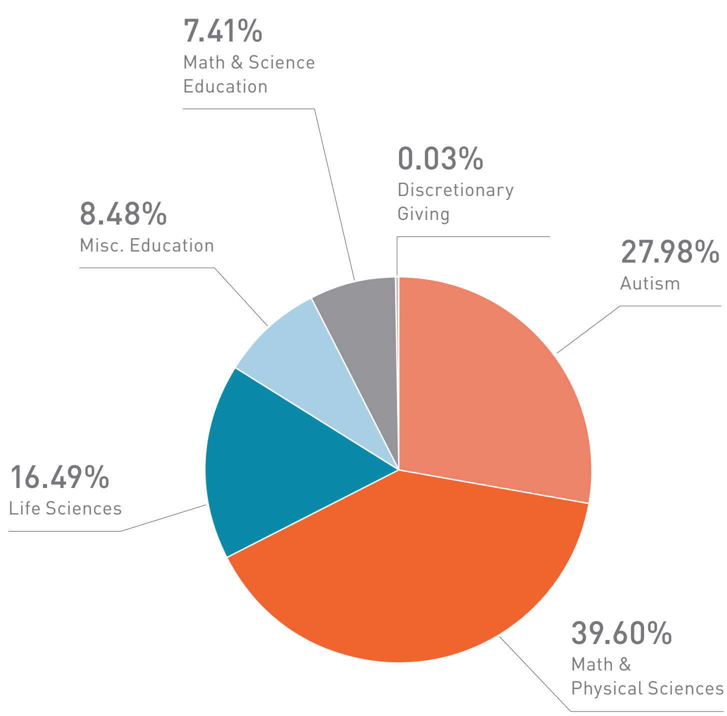
FINANCIALS

Proportions of Expenses



Grant Payment by Category

FOR YEAR ENDED 12/31/2012



FINANCIALS (UNAUDITED)

Balance Sheet

ASSETS	12/31/2012	12/31/2011
CASH AND CASH EQUIVALENTS	37,585,988	50,484,501
INVESTMENT PORTFOLIO	2,009,489,948	1,855,026,921
PROPERTY AND EQUIPMENT, NET	23,706,254	12,574,425
PREPAID EXCISE TAXES	14,398	-
OTHER	12,835,078	72,322,622
TOTAL	2,083,631,666	1,990,408,469

LIABILITIES		
ACCOUNTS PAYABLE	3,736,480	3,503,510
DEFERRED RENT LIABILITY	3,460,305	3,500,069
GRANTS PAYABLE	415,799,499	390,158,217
DEFERRED EXCISE TAX LIABILITY	12,166,503	9,840,354
OTHER TAXES PAYABLE	8,500,000	8,500,000
TOTAL	443,662,787	415,502,150

NET ASSETS		
UNRESTRICTED NET ASSETS	1,639,968,879	1,574,906,319

Income Statement

REVENUE	FOR 12 MONTHS ENDED 12/31/2012	FOR 12 MONTHS ENDED 12/31/2011
CONTRIBUTIONS	150,328,193	79,403,066
INVESTMENT INCOME	151,939,928	185,111,444
TOTAL	302,268,121	264,514,510

EXPENSES		
GRANTS PAID	184,781,415	123,802,345
CHANGE IN GRANTS PAYABLE	24,747,780	132,530,564
IN-KIND DONATION	775,581	-
PROGRAM	17,701,081	22,353,511
GENERAL AND ADMINISTRATIVE	3,193,927	2,785,564
DEPRECIATION AND AMORTIZATION	1,294,900	936,665
TAXES	3,989,432	10,700,840
OTHER (INCOME) EXPENSES	721,443	57,384
TOTAL	237,205,559	293,166,873
NET INCOME	65,062,562	(28,652,363)

SIMONS INVESTIGATORS

Mathematics & Physical Sciences

Igor Aleiner
Sanjeev Arora
Manjul Bhargava
Michael Brenner
Sharon Glotzer
Shafrira Goldwasser
Alice Guionnet
Christopher Derek Hacon
Matthew Hastings
Chris Hirata
Russell Impagliazzo
Charles Kane
Jon Kleinberg
Hirosi Ooguri
Frans Pretorius
Eliot Quataert
Paul Seidel
Amit Singer
Daniel Spielman
Terence Tao
Horng-Tzer Yau

SFARI

Ted Abel
Ralph Adolphs
Nadav Ahituv
John M. Allman
Mark Alter
Dora Angelaki
Dan Arking
Peter Barrett
Mark Bear
Arthur Beaudet
Marlene Behrmann
Yehezkel Ben-Ari
Deanna L. Benson
Stephen Bent
Michael Berk
Raphael Bernier
Manzoor Bhat
Thomas Bourgeron
Randy L. Buckner
Joseph Buxbaum
William Catterall
Chinfei Chen
Andrew Chess
Wendy Chung
Anis Contractor
Edwin H. Cook, Jr.
Giovanni Coppola
Eric Courchesne
Christopher Cowan
Jacqueline Crawley
Robert Darnell
Sandeep Datta
Pietro De Camilli
Karl Deisseroth
Bernie Devlin
Betty Diamond
Ricardo Dolmetsch
Evan Eichler
Noémie Elhadad
Mayada Elsabbagh
Craig Erickson
Michela Fagiolini
W. Andrew Faucett
Guoping Feng
Thomas Fernandez
Eric Fombonne
Thomas Frazier
Nicholas Gaiano
Jennifer Gentry
Dwight German
Daniel H. Geschwind
Jay Gingrich
Joseph Gleeson
Joseph Gogos
Robin Goin-Kochel
Mitchell Goldfarb
Michael Greenberg
Ralph Greenspan
Christina Gross
Adam Guastella
Abha Gupta
James F. Gusella
Danielle Hamra
Christian Hansel
Ellen Hanson
David Heeger
Nathaniel Heintz
Robert Hevner
Eric Hollander
Peter Howley
Valerie Hu
Kimberly Huber
Richard L. Huganir
John Jacob
Rudolf Jaenisch
Yuhong Jiang

Peng Jin
Mark Johnson
Eric R. Kandel
Joshua Kaplan
Maria Karayiorgou
Nicholas Katsanis
Raymond Kelleher
Tal Kenet
Young Shin Kim
Ami Klin
Eric Knudsen
Abba Krieger
Louis Kunkel
Gary Landreth
Paul A. Law
David Ledbetter
Christa Lese Martin
Pat Levitt
Gil Levkowitz
Xiaohong Li
Ellen Li
Paul Lombroso
Catherine Lord
Liqun Luo
Christian Lüscher
Robert C. Malenka
Tom Maniatis
Oscar Marín
Sarkis Mazmanian
Tiffany Mellott
Carolyn Mervis
Judith Miles
Alea Mills
Partha Mitra
Eric Morrow
Stephen Moss
Jeffrey Munson
Charles Nelson
Joel Nigg
Daniel Notterman
Ruth O'Hara
Karen O'Malley
Lucy Osborne
Pavel Osten
Opal Ousley
Theo Palmer
Luis Parada
Paul Patterson
Elior Peles
Kevin Pelphrey
Bradley Peterson
Donald Pfaff
Ben Philpot
Joseph Piven
Indira Raman
Vijaya Ramesh
James Rand
Wade Regehr
James Rehg
Louis Reichardt
Danny Reinberg
Tim Roberts
Celine Saulnier
Robert Schultz
Jonathan Sebat
Elliott Sherr
Maggie Shiffrar
Sagiv Shifman
Steven Siegel
Peter Sims
Alison Singer
Hazel Sive
Stelios Smirnakis
Jesse Snedeker
Noam Sobel
Vikaas Sohal
Hongjun Song
Sarah Spence
Matthew State
Beth Stevens
Thomas Südhof
David Sulzer
Mriganka Sur
James Sutcliffe
J. David Sweatt
Francis Szele
Michael Talkowski
Laurence Tecott
Li-Huei Tsai
Richard Tsien
Thomas Tuschl
Michael Ullman
Flora Vaccarino
Roger Vaughan
Jonathan Victor
Dennis Wall
Douglas Wallace
Christopher Walsh
Samuel Wang
Lauren Weiss
Michael Wigler
Jan Witkowski
Knut Wittkowski
Ofer Yizhar
Larry Zipursky
R. Suzanne Zukin
Lonnie Zwaigenbaum

GRANTS TO INSTITUTIONS

Mathematics & Physical Sciences

Albert Einstein College of Medicine
American University
Arizona State University
Ball State University
Bard College
Barnard College
Baruch College/CUNY
Baylor University
Binghamton University, SUNY
Boston College
Boston University
Brandeis University
Brigham Young University
Brown University
Bucknell University
California Institute of Technology
Carnegie Mellon University
Case Western Reserve University
City College of New York/CUNY
Claremont McKenna College
Clemson University
Cleveland State University
Colgate University
College of Staten Island/CUNY
College of the Holy Cross
Colorado State University
Columbia University
Connecticut College
Cornell University
Dartmouth College
Davidson College
Drexel University
Duke University
Euclid Lab
Florida Atlantic University
Florida International University
Florida State University
Furman University
George Washington University
Georgia Institute of Technology
Georgia Southern University
Harvard University
Harvey Mudd College
Howard University
Illinois State University
Indiana University
Institut des Hautes Études Scientifiques
Institute for Advanced Study
Johns Hopkins University
Kansas State University
Kennesaw State University
Kingsborough Community College/CUNY
Lafayette College
Lehman College/CUNY
Loyola University Chicago
Massachusetts Institute of Technology
Miami University
Michigan State University
Monmouth University
New Mexico State University
New York University
North Carolina State University
North Dakota State University
Northwestern University
Ohio State University
Oklahoma State University
Old Dominion University
Pennsylvania State University
Portland State University
Princeton University
Purdue University
Queens College/CUNY
Rider University
Rochester Institute of Technology
Rutgers, The State University of New Jersey
Saint Louis University
St. John's University
Stanford University
Stony Brook University
Syracuse University
Temple University
Texas A&M University
Texas Christian University
Union College
United States Naval Academy
University at Albany, SUNY
University of Alabama at Birmingham
University of Alaska Fairbanks
University of Arizona
University of Arkansas at Little Rock
University of California, Berkeley
University of California, Davis
University of California, Irvine
University of California, Los Angeles
University of California, Riverside
University of California, San Diego
University of California, Santa Barbara
University of Central Florida
University of Chicago
University of Cincinnati
University of Colorado, Colorado Springs
University of Colorado, Denver
University of Connecticut
University of Delaware
University of Denver
University of Florida
University of Georgia
University of Hawaii
University of Houston
University of Idaho
University of Illinois at Chicago
University of Illinois at Urbana-Champaign
University of Iowa
University of Kansas
University of Kentucky
University of Maryland
University of Massachusetts Amherst
University of Miami
University of Michigan

University of Minnesota
University of Mississippi
University of Missouri
University of Montana
University of Nebraska-Lincoln
University of Nevada, Reno
University of New Mexico
University of North Carolina at Chapel Hill
University of North Carolina at Charlotte
University of North Carolina at Greensboro
University of North Texas
University of Notre Dame
University of Oklahoma
University of Oregon
University of Pennsylvania
University of Pittsburgh
University of Rhode Island
University of South Alabama
University of South Carolina
University of Southern California
University of Tennessee
University of Texas at Arlington
University of Texas at Austin
University of Texas-Pan American
University of Toledo
University of Utah
University of Vermont
University of Washington
University of Wisconsin-Madison
University of Wisconsin-Milwaukee
University of Wyoming
Vanderbilt University
Virginia Commonwealth University
Wake Forest University
Washington University in St. Louis
Wayne State University
West Chester University
West Virginia University
Western Michigan University
Western Washington University
William Marsh Rice University
Wright State University
Yale University

SFARI

Albert Einstein College of Medicine
Autism Consortium
Autism Science Foundation
Baylor College of Medicine
Birkbeck, University of London
Boston Children's Hospital
Boston University
Brown University
California Institute of Technology
Carnegie Mellon University
Case Western Reserve University
Children's Hospital of Philadelphia
Cincinnati Children's Hospital Medical Center
Cleveland Clinic Foundation
Cold Spring Harbor Laboratory
Columbia University
Deakin University
Duke University
Emory University
Feinstein Institute for Medical Research
Geisinger Health System
George Washington University
Georgetown University
Georgia Institute of Technology
Harvard Medical School
Harvard University
Hebrew University of Jerusalem
Hugo W. Moser Research Institute at Kennedy Krieger, Inc.
Hunter College/CUNY
Institut Pasteur
International Society for Autism Research
Johns Hopkins University School of Medicine
Massachusetts General Hospital
Massachusetts Institute of Technology
McGill University Health Centre
McLean Hospital
Montefiore Medical Center
Mount Sinai School of Medicine
MRC National Institute for Medical Research, London
Neurochlore
New York State Institute for Basic Research in Developmental Disabilities
New York University
New York University School of Medicine
Northwestern University
Oklahoma Medical Research Foundation
Oregon Health & Science University
Pennsylvania State University
Princeton University
Research Foundation for Mental Hygiene, Inc. at New York State Psychiatric Institute
Rockefeller University
Rutgers, The State University of New Jersey
Seattle Children's Hospital
Stanford University
Stony Brook University
Tufts University
Universidad Miguel Hernández de Elche
Université de Genève, Faculté de Médecine
University of Alabama at Birmingham
University of Alberta
University of California, Davis
University of California, Los Angeles
University of California, San Diego
University of California, San Francisco
University of Chicago

GRANTS TO INSTITUTIONS

SFARI

University of Illinois at Chicago
University of Louisville
University of Michigan
University of Minnesota
University of Missouri
University of North Carolina at Chapel Hill
University of Oxford
University of Pennsylvania
University of Pittsburgh
University of Southern California
University of Sydney
University of Texas Health Science Center at San Antonio
University of Texas Southwestern Medical Center
University of Toronto
University of Washington
Vanderbilt University
Vanderbilt University Medical Center
Washington University in St. Louis
Weill Cornell Medical College
Weizmann Institute of Science
Whitehead Institute for Biomedical Research
Yale University

Life Sciences

Cold Spring Harbor Laboratory
Institute for Advanced Study
Marine Biological Laboratory
New York Genome Center
New York University School of Medicine
Rockefeller University
Stony Brook University

Education & Outreach

American Academy of Arts and Sciences
Columbia University
Cornell University
Lancaster University
Massachusetts Institute of Technology
Math for America
Mathematical Sciences Research Institute
Mathematics Foundation of America
Mathematisches Forschungsinstitut Oberwolfach
Museum of Mathematics
Queens College
Stony Brook University
Thirteen WNET
University of California, Berkeley
World Science Festival

SCIENTIFIC ADVISORY BOARDS

SIMONS FOUNDATION STAFF

Maria Adler
Leyla Ahari
Kate Augenblick
Rini Banerjee
Agnes Barszcz
Marta Benedetti
Lawrence Bianco
Aaron Biscombe
Greg Boustead
Alexandra Bowe
Elizabeth Brooks
Marian Carlson
Dennis Choi
Wendy Chung
Justin Creveling
Kori Devlin
Lisa Dicce
David Eisenbud
Timothy Eure
Meghan Fazzi
Pamela Feliciano
Jan Fernandez
Gerald Fischbach
Chris Fleisch
Neil Flood
Patrick Flood
Calissia Franklyn
Andrea Gallego
Laura Geggel
Katie Goodwin
Adrienne Greenberg
Anastasia Greenebaum
Leslie Greengard
Marion Greenup
Fang Han
Jessica Holthouser
Lydia Jung
Timothy Kane
Peggy Kaplin
Patricia Kim
Jack Kimura
Timothy Kissane
Abraham Lackman
Alex Lash

Monika Lenard
Thomas Lin
Alice Luo Clayton
Andrea Lynch
Apoorva Mandavilli
Julie Manoharan
Richard McFarland
Tanja Mrdjen
Elizabeth Mrozinska
Jessa Netting
Debra Olchick
Joette Orsini
Joanna Pacholarz
Alan Packer
Danielle Patch
Lauren Rath
Louis Reichardt
Elizabeth Roy
Kathleen Savarese
Krista Selasky
Alexandra Shaheen
Annaliese Sharkey
Emily Singer
Julia Sommer
John Spiro
Jennifer Tjernagel
MaryKate Trawinski
Yuri Tschinkel
M. Amedeo Tumolillo
Evan Tziazas
Sharon Valencia
Hope Vanderberg
Natalia Volfovsky
Patricia Weisenfeld
Casey White Lehman
John Whitfield
Natalie Wolchover
Jessica Wright

DIRECTORS

Marilyn Hawrys Simons, Ph.D. | President

Marilyn Hawrys Simons is president of the Simons Foundation. Under her leadership, the foundation has grown to become one of the country's leading private funders of basic scientific research. Simons is vice president of the board of Cold Spring Harbor Laboratory, treasurer of the board of the Learning Spring School and is a member of the board of trustees at the East Harlem Tutorial Program. She received a B.A. and Ph.D. in economics from Stony Brook University.

Gerald D. Fischbach, M.D. | Chief Scientist of the Simons Foundation and Fellow of the Simons Foundation

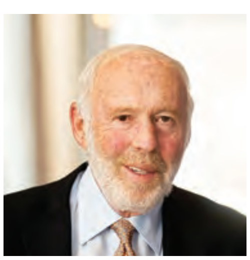
Gerald D. Fischbach joined the foundation in 2006 to oversee SFARI and is now the foundation's chief scientist and first fellow. He was formerly dean of the faculty of health sciences at Columbia University and director of the National Institute of Neurological Disorders and Stroke at the National Institutes of Health (NIH). Fischbach began his research career at the NIH and later served on the faculty of Harvard Medical School, where he became chair of the neurobiology department, a position he also held at Massachusetts General Hospital. Fischbach was also head of the department of anatomy and neurobiology at Washington University School of Medicine. He was a non-resident fellow of the Salk Institute for more than 20 years. Fischbach's research has focused on trophic interactions between nerve cells and the targets they innervate.

Mark Silber, J.D., M.B.A. | Executive Vice President and Chief Financial Officer, Renaissance Technologies

Mark Silber is executive vice president and chief financial officer of Renaissance Technologies LLC. Silber joined Renaissance in 1983 and is responsible for the overall operations of its finance, administration and compliance departments. He was formerly a certified public accountant with the firm of Seidman & Seidman, now BDO USA. He holds a B.A. from Brooklyn College, a J.D. and L.L.M. in tax law from New York University School of Law, and an M.B.A. in finance from New York University Graduate School of Business Administration.

David Eisenbud, Ph.D. | Director, Mathematical Sciences Research Institute

David Eisenbud is director of the Mathematical Sciences Research Institute in Berkeley, California. Previously, Eisenbud was director of the Mathematics and Physical Sciences division at the Simons Foundation. A former president of the American Mathematical Society, Eisenbud serves on the board of Math for America and is a member of the U.S. National Committee of the International Mathematical Union. In 2006, he was elected a fellow of the American Academy of Arts and Sciences. Eisenbud holds a Ph.D. in mathematics from the University of Chicago and has been on the faculty at the University of California, Berkeley since 1997.



James H. Simons, Ph.D. | Chairman

James Simons is chairman of the Simons Foundation and board chair and founder of Renaissance Technologies. Prior to his financial career, Simons was chairman of the mathematics department at Stony Brook University, taught mathematics at the Massachusetts Institute of Technology (MIT) and Harvard University, and was a cryptanalyst at the Institute for Defense Analyses. Simons holds a B.S. from MIT and a Ph.D. from the University of California, Berkeley. In 1976, he won the Veblen Prize for his work in geometry. He is a trustee of the Stony Brook Foundation, Rockefeller University, MIT, Brookhaven National Laboratory, the Mathematical Sciences Research Institute and the Institute for Advanced Study, and is a member of the American Academy of Arts and Sciences and the American Philosophical Society.

For more information on the
Simons Foundation and **SFARI**,
please visit our websites:

www.simonsfoundation.org
www.sfari.org

SIMONS FOUNDATION

160 Fifth Avenue
New York, NY 10010
Tel. 646 654 0066

www.simonsfoundation.org
www.sfari.org