

A Hedge-Fund Titan's Millions Stir Up Research

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thing he believes for sure is that genes play a big role.

It's a propitious moment to step into the field, observers say. Scientists have already mapped the complete human genome, the three billion units of DNA that define humans as a species. Combined with new high-tech tools, this makes gene searches easier and faster to perform, even for complex mental illnesses. Moreover, government funding for research into autism, while growing, still trails that for less-common diseases such as juvenile diabetes and pediatric AIDS. Dr. Insel predicts that genetic clues will begin spilling out quickly, giving scientists a beachhead from which they can begin thinking about tests or drugs.

Mr. Simons is well-known in mathematics circles for co-authoring a high-level piece of geometry known as Chern-Simons. It has since become important in string theory, the advanced branch of physics that posits a "theory of everything." He started young and earned a doctorate in mathematics at 23. He also proved to be a precocious investor. While in college, Mr. Simons persuaded his parents to mortgage their home so he could invest along with some college friends in a pipe-and-tile company in South America. Mr. Simons says the venture was "nicely successful."

By the mid-1970s, Mr. Simons moved from academia to Wall Street, with spectacular results. His hedge fund employs more than 60 top scientific specialists, including astronomers, physicists and mathematicians, who scour market data to uncover statistical relationships that could predict the price movements of commodities, currencies and stocks. His \$5 billion Medallion Fund has averaged 35% annual returns, after fees, since 1989. That beats even hedge-fund legends George Soros and Paul Tudor Jones, according to the U.S. Offshore Funds Directory.

Mr. Simons earned \$670 million last year, according to Institutional Investor's Alpha magazine. He declines to confirm the figure, which would rank him second among hedge-fund managers, behind Edward Lampert of ESL Investments, according to the Alpha survey. The Simonses live in a sprawling apartment on New York's Fifth Avenue filled with art by painters such as Milton Avery and Fairfield Porter.

Renaissance is now launching a fund designed to handle up to \$100 billion, which, if successful, could become the industry's largest. Like the \$100 million he says he'll spend on autism, it's an eye-popping figure. "I like big round numbers. The papers call me the \$100 billion guy," says Mr. Simons, between nuffs of

She has difficulty learning and misses social cues.

One hallmark of autism is having restricted or obsessive interests. Audrey's are attending synagogue and the rights of minorities and women.

"When she writes an essay for school, I usually just tell her to write one version all about Judaism and women to get it out of her system," Ms. Simons, her mother, says.

In an email, Audrey says of her autism that she does "not have as many problems because of it as some other people do." She says she wants to be a novelist and a painter as well as someone who can contribute to the Jewish world and work on behalf of Nepalese women and children.

After Ms. Simons gave a donation to a New York school for autistic children, "people began asking us for money" to pay for research, she says. With the help of a consultant, the Simonses hosted an autism workshop at New York's Plaza Hotel in June 2003, lining up a guest list of renowned academic figures.

Mr. Simons says his "take-away" from the meeting was that scientists had only one solid lead, and that was from studies on identical twins that began 20 years ago. Doctors have found that if one twin has autism, the other has a 90% chance of having some symptoms. For non-twin siblings, the chance falls to between 5% and 10%. That suggests genes play a key role, although not necessarily a simple one. Scientists believe dozens of different genes may be involved.

During a dinner party the same year, James Watson, the Nobel laureate who co-discovered the structure of DNA, told Mr. Simons about a recent finding made by French scientists that suggested a possible genetic link to autism. Mr. Simons recalls Dr. Watson calling it the first "really good" result in autism research. Dr. Watson, who also has a son with an autism-like mental disorder, couldn't be reached for comment.

"So it's genetic, plus people are beginning to find genes," Mr. Simons says. "As a scientist, I understand what it means for something to be ready. There is data."

At the suggestion of NIH's Dr. Insel, Mr. Simons met with the chief executive of deCODE genetics Inc. DeCODE is an Icelandic company that's mining health

make grafts directly to a profit-making institution.)

Scientists began to buzz about Mr. Simons. "He's had an electrifying impact on the thinking of researchers, knowing that kind of money is available," says Clarence Schutt, a Princeton University chemist whose son is autistic. "Everyone wants to talk to Jim."

Not everyone has been able to. Robert Hendren, executive director of the M.I.N.D. Institute, a center at the University of California, Davis, says his effort to get major funding from Mr. Simons has been unsuccessful. "They're not yet willing to hear our proposal," says Dr. Hendren.

Last spring, Dr. Hendren went to New York to visit several philanthropists, including Ms. Simons, who is president of the Simons Foundation, the family's charity. He says he's concerned that big-time private funding could overlook innovative approaches. He's also skeptical that genes alone will provide the answer. "If you are on the inside, you could get a lot of money...If you aren't, then you'd be left out."

John Shestack, a Hollywood producer who founded Cure Autism Now, one of the first advocacy groups to fund research, also hasn't talked to Simons about autism funding. He got a call a couple of years ago from the consultant employed by Mr. Simons, who at the time said only that he was working for a "reclusive billionaire." Mr. Shestack says he sent the consultant 15 pages of information, but "then I never heard from him again."

Groups such as Cure Autism Now have specialized in handing out small gifts and grants to get people interested in the field, funds that often aren't enough to pay for big-time research involving colonies of mice and costly equipment. Mr. Shestack's group, for example, gave a "genius grant" of \$100,000 to Huda



Marilyn Simons

Stir Up Research Into Autism

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Zoghbi of Houston's Baylor College of Medicine after she found the gene for Rett's Syndrome, a disorder similar to autism that affects girls.

In the end, it was \$2,246,817 from Mr. Simons that actually prompted Dr. Zoghbi's foray into autism research. "Without the funding from the Simons Foundation, we would never have embarked on this impactful project," wrote Dr. Zoghbi in a report to her patrons.

Mr. Shestack says Mr. Simons's approach is "smart" but also says the money manager is "very idiosyncratic" in how he spends his money. Mr. Simons, for example, hasn't given much money to parent's groups or scientists already working on autism.

Andy Shih, chief science officer for the National Alliance for Autism Research, in Princeton, N.J., says the 12-year-old nonprofit group has its own plans for a genetic screen but needs \$7 million. He doesn't know if Mr. Simons will fund the project and hasn't asked. He wants autism researchers to share results and says his experiment is a "collaborative" project involving the work of nearly 150 scientists.

"Hedge funds always want better performance than the Wall Street average," Dr. Shih says.

Many in the autism world welcome Mr. Simons's financial intervention regardless of where it's heading. Edwin Cook, a longtime autism researcher at the University of Illinois in Chicago, says he's happy the money manager is recruiting top scientists, even if that doesn't yet include him.

"Is that a view that puts my own research career in jeopardy? Well maybe, but the questions are too important not to bring everything to bear on it," says Dr. Cook.

This summer, Mr. Simons agreed to give \$7.5 million to MIT, on whose board of trustees he sits. The school's original proposal said it wanted funds for basic

research on the brain. "It was too general," Mr. Simons says. He and his wife asked for revisions, including a 200-page proposal showing how the research would specifically relate to autism. He also insisted that specific researchers who had impressed him be included.

The couple's demands were "very unusual," says Mriganka Sur, chairman of MIT's department of brain and cognitive sciences. "They had pretty clear views."

Mr. Simons says he's comfortable judging scientists, since he already runs



Audrey Simons

a "giant research project" studying financial markets. Says Henry Laufer, a Renaissance partner and its chief scientist: "In our non-money moments, we think of ourselves as doing science."

That impressed Nat Heintz, a star professor of genetics and brain development at Rockefeller University in New York. Dr. Heintz accepted a few million dollars from Mr. Simons after concluding that the hedge-fund manager "was someone you could deal with on an intellectual plane."

He also credits Mr. Simons with sparking his interest in autism, a disease to which he hadn't given much previous thought. Dr. Heintz now says autism is "fascinating." He's breeding mice that may help show how the disorder affects nerves in the brain.

Even with some of the world's most talented researchers involved, progress is likely to be slow. "In medical research, there are no people like Warren Buffett

or Jim Simons," says Steven Moldin, a senior manager at the NIH's mental health institute. "There is not some guy who can hit home runs every time and make it go suddenly faster."

Mr. Simons is betting otherwise. So far, the Simonses have handed out 15 grants to researchers, including two Nobel Prize winners. His largest gift so far—\$13.8 million—has gone to biologist Michael Wigler at Cold Spring Harbor Laboratory on Long Island. Dr. Wigler, a brilliant and reclusive scientist who played computer games during a recent interview, has come up with a new way to scan chromosomes in search of genetic errors. It's expensive, costing more than \$1,500 for every person's DNA examined.

Dr. Wigler and Jonathan Sebat, a colleague, say they've scanned the DNA of about 300 people with autism, plus some of their parents and siblings. The lab has turned up a possible problem on the male Y sex chromosome.

Dr. Wigler and Mr. Simons have become friendly. They vacationed together on a boat off Greenland and correspond via email about the research. Once they worked through some statistical problems on a blackboard in Mr. Simons's office.

The research center gets most of its DNA from anonymous blood banks. But Cold Spring Harbor staff also arranged special paperwork to initially handle the DNA of just three people—Mr. Simons, his wife and his daughter.

It's an unusual arrangement. Most people who give blood for research never get to know the results. Mr. Simons hopes to learn something that could help Audrey. "Our daughter has a long life ahead of her, so finding something for her would be the greatest thing for us," he says.

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Wealth Effect

A Hedge-Fund Titan's Millions Stir Up Research Into Autism

IRA

James Simons Taps Big Stars From Outside Field to Find A Genetic Explanation

Three Personal DNA Tests

By ANTONIO REGALADO

When their daughter Audrey was just a few months old, Jim and Marilyn Simons noticed that she wasn't making eye contact. It wasn't until the girl was 6 years old that she was diagnosed with autism. Ms. Simons scoured records from her pregnancy. Had something gone wrong? What caused her condition? In their quest for answers, the Simonses aren't just another family seeking comfort. Audrey's father, world-class mathematician James H. Simons, runs Renaissance Technologies Corp., one of the world's most successful hedge funds. With little notice, the family's charitable foundation has in the past two years committed \$38 million to find the causes of autism. The money manager says he and his wife will spend \$100 million more in what is rapidly becoming the largest private investment in the field.

The Simonses' philanthropy is stirring up the small community of autism researchers and advocates. Using his scientific background, Mr. Simons, 67, personally reviews grant applications. When the Massachusetts Institute of Technology asked him for money for brain research, he demanded that the project fo-

Deep Pockets

A sample of James Simons's \$38 million in donations to medical researchers seeking the cause of autism.

\$13.8 million: Cold Spring Harbor Laboratory, to search for the possible genetic roots of autism.

\$7.5 million: Massachusetts Institute of Technology, for genetic and other studies on autism.

\$2.6 million: Yale University, to fund a laboratory that uses eye-tracking equipment to diagnose autism in children.

\$750,000: Columbia University, salary support for a program that diagnoses autistic children.

Sources: Cold Spring Harbor Laboratory, MIT, Yale, Columbia

cus on autism and include scientists he liked. He has provided his family's DNA for study, pitched in to help solve research problems and is pushing scientists to probe a genetically based explanation for the disease.

Mr. Simons is picking star researchers from other specialties—"Nobel Prize winners and future Nobel Prize winners," he says—often passing over established autism groups or those with differing theories. Last month he lured a top Columbia University neurobiologist, Gerald Fischbach, to work part-time leading the foundation's scientific strategy.

In science, as with certain types of financial data, "past performance is the best predictor of success," Mr. Simons says.

For most in the autism field, the money manager remains a question mark, an idiosyncratic billionaire rarely seen or heard from, whose impact on the field is still unclear. Like many other wealthy donors these days, Mr. Simons is acting more like a venture capitalist, exerting extraordinary control over where and how his money is spent. Many are cheering this influx of cash, hoping Mr. Simons's riches can buy a breakthrough. Others complain that Mr. Simons isn't working with existing autism groups and that his focus on finding a genetic explanation could miss the disease's true cause.



James Simons

Autism is a developmental disorder that exhibits a range of perplexing symptoms, including failure to develop language skills and lack of empathy for others. According to the federal government's Centers for Disease Control and Prevention, between one and three of every 500 children are afflicted with some form of the disease.

It's an apparent epidemic for which experts have few explanations. In the highly charged atmosphere surrounding the subject, some parents insist childhood vaccines or mercury poisoning is to blame. They cite a startling rise in the number of children being diagnosed, up tenfold over the past decade. Many experts say this phenomenon is explained by the expanding use of the autism label by doctors and schools.

Another challenge: What doctors call autism is likely to be several related disorders. Some autistic children can't speak and throw violent tantrums, while others have relatively high IQ's. Some say that understanding the disease could be as difficult as understanding the brain itself.

Autism researchers lack a "good solid clue," says Thomas Insel, head of the mental-health institute at the government's National Institutes of Health. The doctor adds: "We have no lesion. We don't know what systems in the brain are involved. So we are at the very early stages. It's like cancer or diabetes research 25 years ago."

Mr. Simons thinks there's no compelling evidence for some parents' contention that autism is caused by vaccines or some other environmental factor. "People want an answer and people want a villain, the evil drug companies or whatever," says Mr. Simons. He says the only

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