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Family link: Danielle and Jon Draut with fraternal triplets Hunter, left, Blake and Easton. Blake and Easton have autism. Hunter has some autistic traits.

Science gets to roots of autism

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Project collects DNA samples from families to find associated genes

By Kim Painter
Special for USA TODAY

Cover
story

When Blake Draut was 2½ years old, a specialist told his parents that their son's speech delays and odd habits, his fears of dirty hands and grassy feet, were part of a bigger problem: autism.

When the specialist learned that Blake was part of a set of fraternal triplets, all with developmental quirks, "she wanted to see all three," recalls Blake's mother, Danielle Draut.

Several months and several evaluations later, the Anaheim, Calif., family had the news: Two of the three boys were autistic. The third, who turned out to have a hear-

ing problem, didn't qualify for an autism diagnosis but did show some of the rigid behaviors associated with the disorder.

What might sound like an extraordinary run of bad luck was actually nothing of the sort. Scientists have known for some time that autism often runs in families. Studies suggest that if one child is autistic, there's a 5% to 10% chance any sibling will be autistic and a 30% to 40% chance the sibling will have milder, but related, problems. If the sibling is an identical twin, the risk for autism shoots to between 60% and 90%, says Andy Shih, research director of the National Alliance for Autism Research.

Please see COVER STORY next page

Autism's full spectrum

When researchers study autism today, they are studying a more broadly defined spectrum of disorders than was once recognized.

People with autism spectrum disorders can be severely impaired — mute, retarded, caught up in a world of obsessive, seemingly meaningless behaviors — or they can be so intelligent and verbal that they appear merely quirky to an untrained observer.

There are three major disorders on the autism spectrum. All are listed in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV) under an even broader category called Pervasive Developmental Disorders (PDD).

The three disorders are:

► **Autistic disorder.** Hallmarks are impaired social and communication skills, repetitive behaviors and limited interests. Many people with autistic disorder do speak but have trouble keeping up a conversation or playing an imaginative game.

► **Asperger's disorder.** People with Asperger's learn to speak at a normal pace and have normal intelligence. But they have stunted social skills, engage in repetitive behaviors, have limited, often obsessive interests and are impaired enough to have significant difficulties with school, work or social activities.

► **Pervasive developmental disorder not otherwise specified.** Someone with severely impaired communication or social skills or some of the atypical behaviors associated with autism or Asperger's may be given this label if he or she doesn't meet the criteria for the other diagnoses.

Continued from 7B

Though environmental factors clearly play a role, "autism is the most genetic of neuropsychiatric syndromes," more strongly linked to genes than schizophrenia or bipolar disorder, says Dan Geschwind, a genetics researcher at the University of California-Los Angeles.

And now researchers are poised to learn which genes are involved in autism, how they work and how their effects might be blunted. It's all part of a new push for autism answers, fueled by new technology, new funding and, perhaps most important, a heightened public awareness of an increasingly diagnosed disorder.

"It's a very exciting time," Geschwind says.

Geschwind was among researchers who spoke recently at a summit in Washington, D.C., on autism sponsored by the federal government. At the meeting, government officials laid out a 10-year plan for improving services for autistic people and for studying its causes and possible treatments.

High on the list of priorities is finding the genes associated with autism. At the meeting, the private autism research alliance and the public National Institutes of Health announced a partnership to do just that. The NIH is contributing \$2.5 million and the alliance is contributing \$2 million to start the project that will help to link the work of 170 researchers around the world, Shih says.

Actually running it over the next five years will cost up to \$25 million, money that has not yet been committed, Shih says.

And finding the genes will be a complex task.

Preliminary research suggests 15 to 20 different genes may contribute to autism susceptibility — and that different combinations of those genes may cause different variations in different people.

"In child A, it may be genes number 2, 4 and 6; child B may have 1, 3 and 6 interacting," Shih says. "Ideally, this project should be able to identify all of the possible combinations."

Finding so many genes in so many combinations will require many DNA samples from affected families, experts say. "The power is in the numbers," says Thomas Insel, director of the National Institute of Mental Health (NIMH).

That's where families like the Drauts come in. About a month ago, Danielle, her husband, Jon, and the boys got a visit from a medical technician who took several tubes of blood from each family member. Sometime soon, specialists will visit the family home to observe the boys, who are now almost 5, and take detailed histories

of their development. They'll also interview Danielle and Jon about their family histories, looking not only for a history of autism but also for a history of related disorders and traits — everything from language delays to obsessive-compulsive disorder.

The project in which the family is participating is called the Autism Genetic Resource Exchange. It started in the late 1990s as a private effort, financed by Cure Autism Now Foundation. At that time, the Los Angeles advocacy group was begging scientists to do more research on autism genes and finding that a major obstacle was a lack of genetic samples, says foundation founder Jon Shestack. "There wasn't much of it, and most of it was in the hands

balance, something about the womb environment," Shih says. Vaccines, suspected by some, have not been shown to be a factor in several large studies, he says. Infections or toxins might play roles. But, Shih says, "the bottom line is that we just don't know."

Learning more will mean bringing in more scientists with expertise in brain development, Foote says. "Right now, there is a shortage of investigators" to do that kind of work, he says. "They are largely busy with normative developmental issues, just understanding the basics of how any brain gets put together."

But if the pieces do ever come together, some researchers and advocates envision a day when fetuses or babies could be tested for autism risks and treated before the damage was done. The treatments might include drugs, diets or more refined versions of the teaching methods already helping many autistic children.

While the work goes on, families hit hard by autism will struggle on.

of scientists who didn't necessarily want to share," says Shestack, himself the father of an autistic boy.

Over five years, the project collected blood samples and histories from 450 families with multiple cases of autism or other disorders on the so-called autism spectrum. The blood has been turned into renewable cell lines, available to any researcher for a small fee.

A few months ago, the project got a \$3.9 million grant from NIMH to recruit 400 more families by 2007. And the private group has agreed to pool its samples with others available for free from the federal agency.

"The numbers of samples in (the repository) will increase dramatically over the next few years," says Steve Foote, who directs neuroscience and basic behavioral science at the institute.

Researchers are fairly confident that with enough genetic material, money and manpower, they will find the most important autism genes in the next few years, UCLA's Geschwind says.

But finding the genes won't mean instantly understanding autism. Scientists will have to learn what the culprit genes do and how they can go wrong.

Then they'll need to learn how environmental factors, before or after birth, interact with genes to produce autistic traits. "It could be as simple as a hormonal im-

balance, something about the womb environment," Shih says. Vaccines, suspected by some, have not been shown to be a factor in several large studies, he says. Infections or toxins might play roles. But, Shih says, "the bottom line is that we just don't know."

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— Jean Yates, speaking of her 10-year-old autistic son

"If you ask Robert 'What is the capital of South Africa,' he'll tell you. If he goes to the dentist and he's desperate, he'll yell 'Fire!' But he cannot say to you, 'I want to leave the dentist's office.'"

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trums. Robert Robert, 10, can read and speaks a little, but mostly just to show off his arcane knowledge of geography.

"If you ask Robert 'What is the capital of South Africa,' he'll tell you," his mother says. "If he goes to the dentist and he's desperate, he'll yell 'Fire!' But he cannot say to you, 'I want to leave the dentist's office.'"

Maybe the research will help the boys' older brother or their four half-siblings, none of whom has children yet. If the family does carry autism susceptibility genes, "I'd like for them to know about it," Jean says.

In any case, she says, "when you are a parent of children like this, there are so many ways you feel helpless. But this is empowering. You know that somewhere down the line this is going to help someone."

Says Geschwind: "We are going to find the major pathways that cause the disease. ... The bridge to treatment may be hard to cross. But you can't get there without the genes."

For more information on autism research

- The National Institute of Mental Health, www.nimh.nih.gov
- The Cure Autism Now Foundation, www.canfoundation.org
- The National Alliance for Autism Research, www.naar.org
- The Autism Society of America, autism-society.org