The CEO of ALS Research

COMMANDING PRESENCE In 2006, ALS robbed Nieto of speech. "But he is louder than ever," says his son Austin. "His passion and drive can be heard around the world."

JOHN MEDINA/GETTY IMAGES

Fitness mogul Augie Nieto is applying his passion and business acumen to the fight against amyotrophic lateral sclerosis.

BY JAMIE TALAN

A team of scientists has recently uncovered a new and surprising pathway involved in amyotrophic lateral sclerosis (ALS), commonly referred to as Lou Gehrig's disease after the famous Yankee baseball player. The series of events that led to this discovery began in the spring of 2004, when a 47-year-old fitness buff in southern California noticed a twinge in his right bicep. Augustine ("Augie") Nieto chalked it up to a strenuous workout. The co-founder of Life Fitness, a successful exercise equipment company, Nieto was the model of physical prowess. But the prickling feeling in his arm spread to his chest. His muscles seemed to take on a life of their own.

A few months later, doctors at the Mayo Clinic in Scottsdale, AZ, diagnosed Nieto with ALS. No one in his family had the disease. He learned that there were no medicines to stave off the relentless degeneration of his motor neurons, nerve cells located in the brain and spinal cord that directly or indirectly control muscles. The result would be paralysis and a single-digit life expectancy. Most patients never celebrate their sixth year post-diagnosis.

For the first few months a depression gripped him with more force than the disease itself. On the eve of Memorial Day in 2005, Nieto swallowed enough antianxiety pills to plunge himself into a coma. When he awoke a few days later, surrounded by his wife and children—who were scared, distraught, and loving—he realized he had an obligation to fulfill. To them. To himself. And to thousands of other people living with ALS.

THE AUDACITY OF HOPE

Nieto approached the puzzle of ALS in the same way he approached the marketing of the first stationary bicycle he peddled to gyms—and gave away when no one seemed inter-

The science that is emerging from the ALS-Therapy Development Institute, which Nieto promotes, may change the **trajectory of research**.

ested—during his college years in the 1970s. His tenacity and business acumen kept that dream alive, enabling him to build Life Fitness into the multimillion dollar company it is today.

Soon after his diagnosis, Nieto learned of a non-profit biotech company called the ALS-Therapy Development Foundation (ALS-TDF), started by Jamie Heywood, a young man whose brother was diagnosed with ALS in 1998. Heywood's idea was to bypass the big pharmaceutical companies and build an organization with a research lab that could test every federally approved drug—in fact, any molecule being used worldwide for any disease—for the treatment of ALS. At the time, there was only one lab model that mimicked the human familial form of the disease, using a mouse with the same gene deficiency found in humans with ALS. Heywood wanted to find a cure for his brother, Stephen, who would succumb to his disease in 2006 at the age of 37, despite the family's Herculean efforts.

Many in the scientific community bristled at the audacity of a patient advocacy group hiring researchers. Critics argued that such groups would only slow research down by adding another layer. They also argued that advocates may be so intent on producing health benefits that they impede the research process. But proponents of advocacy groups as research organizations countered that they are less encumbered by bureaucracy, able to take more risks (especially in the search for treatments for rare diseases), and unhampered by the profit motive of private industry.

Nieto and his wife Lynne first met Heywood when he was teaching a course called ALS 101, designed to teach people how to cope with the disease. When Nieto and Lynne entered the meeting room, they saw men and women of all ages and in all stages of ALS.

"The first time I saw another person with ALS was at Jamie's seminar," Nieto recalls, communicating by voice through a computer controlled by his foot. "He was in a wheelchair in the back of the room. All I could see was his chair. All I could hear was his respirator."

"Augie kept looking at these people knowing that someday soon he would be where they were," Lynne says. "He couldn't believe it. This was ALS."

THINKING BIG

By the summer of 2005, ALS-TDF had tested every drug in development for ALS against the genetically engineered mouse model that was the gold standard in the field. Not one of the drugs had an impact on the disease process, they found, despite the fact that millions of federal and pharmaceutical industry dollars had been poured into these potential treatments.

That fall, Nieto was to receive the fitness industry's Lifetime Achievement Award. He decided to use the event to raise awareness and money for ALS research. His colleagues thought it was a great idea, as did the Muscular Dystrophy Association (MDA, **mda.org**), who had been supporting ALS research for decades. The MDA gives about $7 million (20 percent of its $35 million research budget) to ALS researchers each year.

A few days before Nieto's first weekend fundraiser, Lynne christened their organization Augie's Quest. At the end of the event, Nieto walked away with his Lifetime Achievement Award, and the ALS research community became a million dollars richer. It was the start of something big.

Around this same time, the MDA was talking to Sean Scott, a young film producer whose mother had died of familial ALS and who was overseeing the research at ALS-TDF. Although Scott didn't have a science background, he learned everything he could about the disease. The MDA, an organization that understood how patients drive the funds for research, was impressed with the science underway at ALS-TDF. So was Nieto,

ATSDR wants to strike out Lou Gehrig's Disease

Because learning more about ALS is an important step in the battle to defeat it, the Agency for Toxic Substances and Disease Registry (ATSDR) is developing a national registry to gather information from people who are living with disease. The goal of the registry is to gather and organize information that can be used to:

- **Estimate the number of new cases of ALS identified each year**
- **Estimate the number of people who have ALS at a specific point in time**
- **Better understand who gets ALS and what factors affect the disease**
- **Examine the connection between ALS and other motor neuron disorders that can be confused with ALS, misdiagnosed as ALS, and in some cases progress to ALS**
- **Improve care for people with this disease**

To learn more about the National ALS Registry, visit www.cdc.gov/als.

EYES ON THE PRIZE Using the EyeMax and VMax, two new devices from DynaVox, Nieto is able to speak to his wife, Lynne, by blinking.

COURTESY DYNAVOX INC., WWW.DYNAVOXTECH.COM

who recognized the organization's potential but also the absence of a good business plan. He decided that the money he raised would go directly to ALS-TDF.

To do it right, though, they needed to up the ante by hiring a scientist to direct research. They brought on Steve Perrin, Ph.D., a scientist at the pharmaceutical company BioGen Idec. Within a few months of Perrin's touchdown at the small organization in Cambridge, MA, the number of scientists working there to find a treatment for ALS doubled, from 14 to 28.

GETTING DOWN TO BUSINESS

During his impressive tenure at ALS-TDF, Scott discovered that the family legacy of ALS had passed to him. He died within a year of his diagnosis, at the age of 39.

But Scott passed on a legacy of hope. The science that is emerging from the organization may alter the trajectory of research. Realizing that none of the potential ALS drugs showed benefits in animals, Dr. Perrin and his colleagues decided to go back to the drawing board and erase everything that had been written on it. They needed to better understand the variables that led to false positives in the animal model in order to be more effective at drug screening. There were hundreds of possibilities as to why the treatments in development had failed to impact the disease process.

They decided to look for abnormal gene expression profiles (the activity measurement of thousands of genes at once, which helps determine how cells react to particular treatments) in the spinal cord, skeletal muscle, and peripheral nerves (outside the brain and spinal cord), both in the blood of humans with ALS and in the animal model. What they found, and recently published in the prestigious journal *Nature Genetics*, was the involvement of a key regulator of the body's immune response. Not only was it off-kilter in animals, but the pathway was overactive in the blood of 56 percent of the ALS patients they tested.

Upon finding out that a drug was available targeting this pathway, they immediately designed a study to test its effectiveness in slowing the disease process. The experimental drug slowed the characteristic weight loss of the disease, delayed paralysis, and extended survival in the ALS mouse by nine days. This was more than they had seen with any drug they ever tested, Dr. Perrin says. Whether that discovery will translate into a clinical trial remains to be seen. ALS is still a devastating disease with a bad outcome for most patients. The hope is to gain federal approval to test the drug in patients. The only other drug approved for ALS is riluzole, which works modestly to improve some of the symptoms in some patients.

A NEW MODEL FOR RESEARCH?

Meanwhile, Augie's Quest became the primary promoter of ALS-TDF, committed to raising $18 million with a matching grant from MDA over five years. It is now called ALS-Therapy Development Institute. The model of an organization developing its own research core is slowly being adopted by other non-profit patient and advocacy groups, including the Scleroderma Foundation, the Myelin Repair Foundation, Autism Speaks, Michael J. Fox Foundation, and CHDI, an organization searching for medicines to treat Huntington's disease.

In 2008, Nieto was given the President's Award by the

ONGOING CONVERSATION Nieto can use his TypeRight software to type 40 words a minute with his feet. His ability to communicate his thoughts quickly is key to his productivity and well being.

National Association of Hispanic Journalists. Then-President Rafael Olmeda honored Nieto as someone who put a "Latino face on an American story." In 2009, the group Five for Fighting wrote a song called "Augie Nieto" to help raise money for Augie's Quest. And this year, Nieto celebrated the fifth anniversary of his diagnosis. He is now on the other side of the survival curve.

"It was an odd anniversary," Lynne says. "I asked Augie whether he thought that he would get here, and if he could have known he'd be happy here." She pauses and adds, "There have been horrible things and wonderful things." They recently renewed their vows for their 10th wedding anniversary. And Nieto continues to feel an energy that he has felt since his realization that he can make a difference in the ALS world. "I am excited every day that I get up," he says. "I wake up every morning and redefine normal."

"Even if it won't help me, it will help generations of people like me," Nieto says. In 2006, Nieto's damaged motor neurons led him into a wheelchair. The next year, he lost the ability to move his arms; last year, his ability to talk. "But he is louder than ever," says his son Austin. "His passion and drive can be heard around the world." Augie's Quest has now raised more than $23 million—and every dime goes to research.

Augie's Quest has now raised more than $23 million—and **every dime** is applied to finding a cure for ALS.

GOING MOBILE

In addition to his passion for a cure, Nieto is figuring out ways to improve the day-to-day lives of people who have ALS. Most people with the disease lose motor neurons in their peripheral nerves. Depending on the type of ALS, they may also lose their ability to talk. Because of his knowledge of the disease, Nieto was ahead of the curve when his voice began to falter. A young man named Troy Jurgensen, who was rebuilding Nieto's house to make it wheelchair-friendly, happened to be a computer wiz. Nieto has a knack for identifying the talents of people all around him. The two began developing TypeRight software, which allows people with ALS to type with their feet. Nieto can type 40 words a minute using TypeRight.

Nieto is also testing a device that reads brain waves and translates them into data that can be read by a computer, which then uses a voice-activated program to decipher the code and say what Nieto is thinking. Nieto's dedication is shared by his eldest son: Austin works for DynaVox, a company that is developing the next generation of devices to help disabled patients speak without uttering a word.

Not surprisingly—given the amount of work he does in a typical day—Nieto relies on his iPhone, which he accesses with the help of software called iControl that he developed. More than 200,000 applications are already accessible. He uses Facebook, DirecTV, Bank of America, and occasionally Atomic Fart. Of the noises created by the last app, he says, "No one could be upset with a guy in a wheelchair!"

His wife laughs. She is not surprised by the difference her husband has made in the ALS world. "If Augie's efforts, and the efforts of those working with him, can save any one of these families from this heartache, then it will be worth it. It hasn't come without a cost. But this quest has kept Augie alive longer than we expected. He has used his talents in business to deal with something much bigger." NN

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STEVE COHN