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ALS Therapy Development Institute Links Gene Expression Profiling to Identification of Potential Treatment for ALS

Novel Therapeutic Slows Progression and Extends Survival in Preclinical Model of Disease

CAMBRIDGE, Mass. – March 28, 2010 – In an article published in *Nature Genetics* today, scientists at the ALS Therapy Development Institute (ALS TDI) describe how they have linked an unbiased gene expression profiling effort to the identification and successful preclinical testing of a potential novel therapeutic for amyotrophic lateral sclerosis (ALS).

The work adds to the body of evidence for immune system involvement in ALS, and focuses new attention on immune system modulation as an approach for treatment. The authors report that blocking the interaction between two immune system molecules can significantly slow disease progression in a mouse model of ALS.



The therapeutic, *ALS TDI 00846*, blocks activation of a cell surface protein, CD40 ligand, and modifies a key immune system response not previously known to be associated with the progression of amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease). In their research, the authors show that the pathway used to identify *ALS TDI 00846*, is also increased in 56% of the ALS patient samples analyzed by the Institute. Although ALS is commonly thought of as a disease of the central nervous system, this novel disease-modifying treatment was shown to directly affect the activity of classes of immune cells responsible for maintenance and repair of the peripheral nervous system.

"Of the five pathways we found, two are associated with T cell activation, two with macrophage activation and one pathway contains genes involved with co-stimulatory regulation of the immune systems. Because we could slow the disease, at least in the mice, when we blocked the co-stimulatory pathway with *ALS TDI 00846*, we believe that we have implicated an immune process that may drive the degeneration of neurons. It is our hope that this work will open up a new class of therapeutic strategies for ALS," said John Lincecum, Ph.D., associate director of research biology at ALS TDI and co-author on the paper with the Institute's director of *in vivo* operations, Fernando Vieira, M.D.

Specifically, the report entitled, "From transcriptome analysis to therapeutic anti-CD40L treatment in the *SOD1* model of amyotrophic lateral sclerosis," details the characterization of the co-stimulatory pathway, which is a key regulator of immune system response, and the development of *ALS TDI 00846* as a therapeutic biologic. The preclinical development of this potential treatment for ALS was made possible by multi-year grants from the Muscular Dystrophy Association, the Department of Defense, and the RGK Foundation, as well as from donations received from hundreds of people living with this devastating neurodegenerative disease.

"ALS TDI was built to overcome the drug development gap for ALS, meaning the lack of connections between target discovery and therapeutic development. Our infrastructure, which is paid for entirely by the ALS community, is specifically designed to bridge this gap. With this paper we begin to show the full potential of this approach," said Steve Perrin, Ph.D., chief executive officer and chief scientific officer of ALS TDI.

Prior to publishing in *Nature Genetics*, ALS TDI scientists presented early results and data to the field at several high-profile scientific conferences throughout 2009, including the annual meeting of the

Society of Neuroscience in Chicago, the BIO International Conference in Atlanta, the first annual Partnering for Cures conference in New York, and the annual International Symposium for MND/ALS Research in Berlin, Germany.

“What the team in the lab has accomplished in terms of discovery and development is unprecedented, and something that the entire ALS community can be proud of. We believe that the next logical step for this molecule, *ALS TDI 00846*, is that it be advanced into the clinic for trial as soon as possible, and that is exactly what the executive team is focused on doing. However hopeful we are that this drug will be successful in slowing disease down, we know that we must continue to discover and build additional therapeutics so that all those affected by ALS have the chance to fight,” remarked Augie Nieto, chairman of the board at ALS TDI, via email. Nieto was diagnosed with ALS in 2006 and has raised more than \$21 million for ALS research. In addition to leading the ALS TDI board, Nieto is a national vice president of MDA and co-chairs its ALS Division along with his wife, Lynne.

About ALS TDI

The mission of the ALS Therapy Development Institute (ALS TDI) is to develop effective therapeutics that slow or stop amyotrophic lateral sclerosis (ALS, Lou Gehrig’s disease), as soon as possible. Focused on meeting this urgent unmet medical need, ALS TDI executes a robust discovery program, while running the world’s largest efforts to pre-clinically validate potential therapeutics; including small molecules, protein biologics, gene therapies and cell-based constructs. The world’s first nonprofit biotech, ALS TDI has developed an industrial-scale platform that allows for the development and testing of dozens of potential therapeutics each year. Built by and for patients, the Institute is the world's only nonprofit biotechnology company with more than 30 professional scientists. In addition, the Cambridge, Massachusetts based research Institute collaborates with leaders in both academia and industry to accelerate ALS therapeutic development. For more information, please visit us online at www.als.net.

About MDA

MDA (www.mda.org) is the world’s largest nonprofit provider of ALS services and funder of ALS research. Over the years, MDA has invested \$250 million specifically fighting ALS. MDA operates more than 200 clinics at hospitals across the country, 36 of which are ALS-specific research and care centers. The Association’s unparalleled health care services, research, advocacy and education programs provide help and hope to more than one million Americans affected by ALS and 42 other neuromuscular diseases. MDA was the first nonprofit organization recognized by the American Medical Association with a Lifetime Achievement Award “for significant and lasting contributions to the health and welfare of humanity.”

About Augie's Quest

Fitness pioneer Augie Nieto started *Augie's Quest* (www.augiesquest.org) in conjunction with MDA's ALS Division. Nieto is co-founder and former president of Life Fitness of Chicago, and chairman of Octane Fitness. He and his wife, Lynne, serve as co-chairpersons of MDA's ALS Division. Nieto received a diagnosis of ALS in March 2005, and *Augie's Quest* raises money primarily through a variety of special events, including “Fight Night” in Tustin, CA; *Augie's Quest* Bash in San Diego, CA; “Tradition of Hope” in Los Angeles, CA; “Celebrity Golf Classic” in Phoenix, AZ; “Gift of Time: St. Patty’s Day Bash” in Denver, CO; “Field of Hope Gala” in New Jersey; “Secure A Cure Golf Classic” in Purchase, NY; “Big Canyon Golf” in Newport Beach, CA; The ClubCorp Charity Classic at golf clubs nationwide; plus “Clubs for A Cure” special visitation benefits for *Augie's Quest* at LA Fitness and Bally Total Fitness locations across the country, as well as at scores of other independent and regional health clubs.

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