



Protein Linked to Spinal Muscular Atrophy Identified

Libertyville, IL, Carlsbad, CA, Woodridge, IL October 8, 2008 - Families of Spinal Muscular Atrophy (FSMA, www.curesma.org), Invitrogen Corporation (NASDAQ:IVGN www.invitrogen.com), and deCODE chemistry & biostructures (www.decodechembio.com) announced today they have identified a protein that is a potential molecular target for the treatment of Spinal Muscular Atrophy (SMA). In its most severe form, SMA often leads to death in infancy, and there is currently no treatment or cure. Research published today in the journal *ACS Chemical Biology* of the American Chemical Society, entitled “*DcpS as a Therapeutic Target for Spinal Muscular Atrophy*,” details the identification and characterization of a protein that offers a novel biological mechanism for designing new SMA therapeutics.

SMA is an inherited genetic disorder that affects approximately one in every 6,000 births in the US. The molecular basis of the disease is a deficiency in production of a specific protein – Survival Motor Neuron (SMN) protein. Motor neuron function is acutely sensitive to lowered SMN protein levels. This cellular defect is the underlying basis for the loss of control of muscles in the limbs, neck and chest in these patients. Because the genetic capability to produce SMN protein is not completely eliminated in SMA patients due to the unique presence of a back-up gene, drugs that increase SMN protein levels in motor neurons are expected to modulate the severity of the disease and have done so in SMA mouse models.

Previously, researchers at deCODE chemistry & biostructures with funding from Families of SMA had developed a class of compounds called C-5 substituted quinazolines, which increased expression of SMN protein, potentially giving clinical investigators a new class of compounds to utilize for the treatment of SMA. However, the mechanism behind this increase in SMN production was unknown.

“While the identification of compounds that increase SMN expression represents significant hope to patients with SMA, we still did not understand the mode of action of these compounds in SMA,” noted Jill Jarecki, Ph.D., Research Director at Families of SMA. “The results outlined in the paper represent a new understanding of the physiological mechanisms that can increase SMN expression and will allow us to move forward in advancing potential treatments for SMA. This discovery gets to the level of really understanding how SMN deficiency can be corrected in the cells of the body, which in turn will open up many new ways of developing therapies.”

In the present study, researchers used a lead compound from the FSMA funded program, to probe Invitrogen’s high-density ProtoArray™ protein microarray for candidate proteins binding to the test compounds. The ProtoArray allowed researchers to rapidly identify a specific human protein called DcpS (human mRNA decapping scavenger enzyme) that interacted with the FSMA compounds. Additional functional experiments preformed by the laboratory of Dr. Megerditch Kiledjian at Rutgers, The State University of New Jersey confirmed that DcpS activity is modulated by the FSMA compounds.

“The identification of DcpS as a novel drug target for SMA is but one example of how Invitrogen technologies are on the forefront of research aimed at helping to find cures for disease,” said Brian Pollok, Ph.D., Chief Scientific Officer for Invitrogen. “In 2006, we started working with FSMA to define the biomolecular mechanisms for how these compounds up-regulate SMN production, and the successful outcome of this collaboration is very gratifying. Invitrogen is committed to creating advanced technologies which progress the understanding of disease biology and support the development of new therapies.”

Lance Stewart, Ph.D. President, deCODE biostructures explained further, “This demonstrates the value of protein structures in translational research. With the identification of DcpS as a candidate molecular target, we then synthetically engineered a novel DcpS gene for protein expression and crystallization with the aid of Gene Composer (www.genecomposer.net). Purified DcpS was then entered into co-crystallization trials with the FSMA molecules, which rapidly led to the high resolution X-ray structural elucidation of how the C5-substituted quinazolines specifically inhibit DcpS.” The DcpS structural information has been made publicly available through the Protein Data Bank (www.rcsb.org/pdb, PDB IDs: 3BL7, 3BL9 and 3BLA) with the hope that this information will inspire others to build upon these research discoveries to help SMA patients.

“We have long been involved in working with FSMA to try and find a cure for this disease,” said Mark Gurney, Ph.D. Sr. Vice President of Drug Discovery and Development at deCODE, and the paper’s corresponding author. “The work carried out by ourselves in collaboration with Invitrogen, Rutgers, and FSMA helps science understand the mechanisms of SMA.. While still in the discovery phase of drug development, the FSMA compounds represent novel potential treatments for SMA. We

look forward to continuing our work with FSMA to move the drug candidate forward so that patients may benefit from a potential new medicine to combat SMA.”

About Families of SMA

Families of SMA is a nonprofit organization that was founded in 1984 by a small group of parents for the purpose of raising funds to advance research to find a treatment and cure for Spinal Muscular Atrophy and to support all those affected by SMA.

Families of SMA has funded and directed the leading SMA research programs over the last 25 years: including the most advanced drug discovery programs and clinical trials to develop a treatment and cure for SMA. The organization is constantly looking to innovate and provide incentives for companies and the government to get involved and invest in SMA research.

Families of SMA is a network of families, researchers and clinicians who are determined to make a difference. To date FSMA has raised and invested \$43 Million towards SMA research. Support comes from generous individual donations and numerous fundraising events held by volunteer families and chapters. FSMA has 24 chapters throughout the United States and over 55,000 members and supporters. For more information visit the website www.curesma.org or call 1-800-886-1762.

About Invitrogen Corporation

Invitrogen Corporation (NASDAQ:IVGN) provides products and services that support academic and government research institutions and pharmaceutical and biotech companies worldwide in their efforts to improve the human condition. The company provides essential life science technologies for disease research, drug discovery, and commercial bioproduction. Invitrogen's own research and development efforts are focused on breakthrough innovation in all major areas of biological discovery including functional genomics, proteomics, stem cells, cell therapy and cell biology -- placing Invitrogen's products in nearly every major laboratory in the world. Founded in 1987, Invitrogen is headquartered in Carlsbad, California, and conducts business in more than 70 countries around the world. The company employs approximately 4,700 scientists and other professionals and had revenues of approximately \$1.3 billion in 2007. For more information, visit www.invitrogen.com.

About deCODE chemistry & biostructures

deCODE chemistry, Inc. & deCODE biostructures, Inc. provide contract research services to pharmaceutical companies, biotechnology companies, academic institutions, and government facilities. deCODE chemistry & biostructures takes a collaborative approach to pharmaceutical research services through a seamless integration of chemistry and biology capabilities including protein production, multifaceted structural studies, lead identification, *ex vivo* and *in vivo* assays, cGMP manufacturing and regulatory capabilities which furnishes accelerated timelines for moving molecules from the concept

and into the clinic. Visit deCODE chemistry & biostructures on the web at www.decodechembio.com.

deCODE gratefully acknowledges the funding from its partner FSMA, as well as the NIGMS-NCRR co-sponsored PSI-2 Specialized Center Grant U54 GM074961 which supports synthetic gene design work within the Accelerated Technologies Center for Gene to 3D Structure (www.ATCG3D.org).

Picture Image

The image shown here illustrates human DcpS (green and cyan ribbon) with D156844 (red) bound representing PDB ID:3BL7, together with m⁷GpppG (blue) bound as seen in PDB ID:1ST0, attached to the 5' end of an mRNA molecule (grey modeled).

Contacts:

deCODE chemistry & biostructures

Media:

Venkat Rajogopal

630-783-4858

VRajagopal@decode.com

Families of SMA

Kenneth Hobby

800 - 886-176

kenneth@fsma.org