RESEARCH ALS TODAY

THE ALS ASSOCIATION | VOLUME 1 | SPRING 2007

INSIDE

TREAT ALS: Accelerating Translational Research

TREAT ALS, a drug discovery and clinical trials process initiated by The ALS Association, is supporting clinical pilot studies that offer novel clinical approaches for ALS.

With advances in technology, a better understanding of the disease process in ALS, and models systems now available, the time is right to translate research ideas into possible therapies. TREAT ALS (**T**ranslational **Re**search **A**dvancing **T**herapy for ALS), a drug discovery and clinical trials process initiated by The ALS Association, is supporting clinical pilot studies that offer novel clinical approaches for ALS. Several studies are already underway and investigators are encouraged to respond to the request for additional proposals offered in this publication.

It is unlikely that a single compound will be able to effectively treat a complex disorder such as ALS. Paul Gordon, M.D., of Columbia University, and colleagues in a currently funded study are testing celecoxib together with creatine, as well as creatine and minocycline. Both combinations were additively beneficial in the SOD1 mutant mouse, prolonging survival. By design, the combination clinical trial allows investigators to detect which combination might be better in a small number of patients. This pilot study paves the way to more rigorous testing: any treatment emerging from such a study would have to prove itself in a larger clinical trial with placebo to know that it is indeed changing the clinical course of the disease.

Using a novel therapeutic approach for ALS, researchers led by Don Cleveland, Ph.D., demonstrated that antisense oligonucleotides synthesized against SOD1 (copper-zinc superoxide distmutase 1) successfully downregulated the expression of the protein and increased survival in rats modeling ALS. The investigators are currently testing the safety of this approach. Clinical trials in inherited ALS patients carrying mutations in this protein are planned in the coming year. Several efforts are underway to develop a similar approach using RNAi.

Other patient trials funded through TREAT ALS seek reliable measures to follow progression and gauge treatment impact. These include comparison of a new measure of muscle function, electrical impedance myography, to a more established test, motor unit number estimation. The drug memantine is also in a TREAT ALS pilot trial that will monitor an MRI signal related to integrity of neurons for changes with disease progression, and compare with a more traditional marker, the ALS functional rating scale.

In an effort parallel to clinical trials, investigators through TREAT ALS are exploring comprehensive molecular and cellular approaches to finding new therapies for ALS. These partnerships forged with biotech and with academia are described inside.

ALS Association
TREAT ALS
Translational Research Advancing Therapy for ALS

Progress in ALS Genetics

The identification of new genes linked to ALS will provide new clues for drug targets. To this end, a search through the entire set of human genes for any possibly involved in the disease is proceeding rapidly, as published on line in *Lancet Neurology* in February and updated at the Boston AAN meeting in May. The DNA repository established in partnership with the National Institute of Neurological Disorders and Stroke and other organizations has collected well over a thousand patient samples and the data are in the public domain. "Contributions from patients and the collaboration among funding organizations have enabled the genome search that is bringing clues to which genes might be involved in ALS," said Lucie Bruijn, Ph.D., science director and vice president of The ALS Association.

Henderson Honored with Essey Award - page 2 | Call for Clinical Pilot Trial Proposals - page 4

Collaboration, Innovation and Commitment

Lucie Bruijn, Ph.D.
Science Director and Vice President
The ALS Association

Welcome to our first volume of *Research ALS Today*, marking an exciting time for ALS research. The goal of this new publication is to challenge and inform scientists to become ALS investigators. With the availability of model systems both in vivo and in vitro mimicking aspects of the disease, and advances in technology, new partnerships among academia, industry, government and not-for-profit groups allow experts from diverse fields to collaborate toward new treatments.

ALS (Amyotrophic Lateral Sclerosis), also known as motor neuron disease or Lou Gehrig's disease, is a complex fatal disorder affecting motor neurons and neighboring glia in the brain and spinal cord, leading to cell death and muscle paralysis. This complexity invites innovation and collaboration. TREAT ALS (**T**ranslational **Re**search **A**dvancing **T**herapies for ALS), an initiative of The ALS Association, is targeted to take advantage of and lead research and funding partnerships, to advance drug discovery, pre-clinical development and clinical trials.

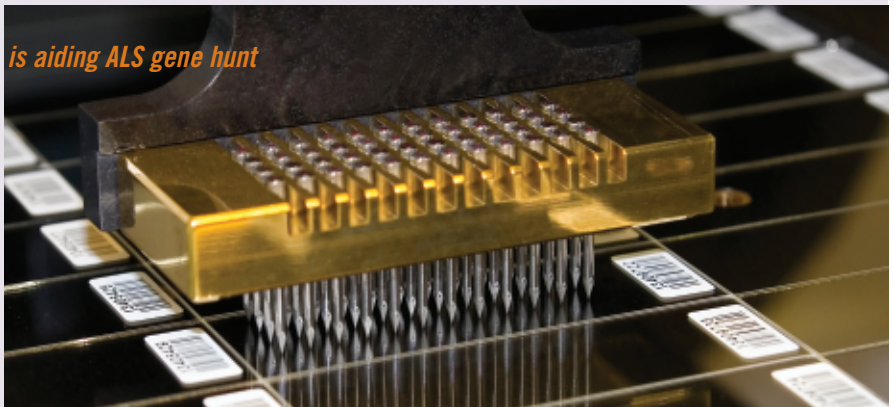
The ALS Association has been a driving force behind the collection of DNA samples from ALS patients enabling an international collaboration to begin to identify the causes of sporadic ALS accounting for 90% of the disease. Together with modern gene-chip technology and published maps of human genetic variants, the DNA repository sponsored in partnership with the National Institute of Neurological Disorders and Stroke enabled one of the first whole genome association studies for ALS.

As we link new genes to the disease, new avenues for research open toward new model systems and point to new targets for therapy. Patients and their families are ready to participate in and remain informed of ALS research.

I believe that through continued collaboration, innovation and commitment we will find effective therapies for ALS. I invite you to take up the challenge and *Research ALS Today*.

–Lucie Bruijn, Ph.D.

Microarray technology is aiding ALS gene hunt



Henderson Honored with Essey Award

The ALS Association joins the American Academy of Neurology in presenting The 2007 Sheila Essey Award for ALS Research to Christopher E. Henderson, Ph.D., during the Academy's 59th Annual Meeting in Boston, April 30 through May 4.

Henderson, formerly at INSERM (France's Institut National de la Santé et de la Recherche Médicale), and now at Columbia University in New York City, studies the way that nerve cells die in a process called programmed cell death, and how that process interacts with the inflammation that accompanies the cell loss in neurodegenerative diseases. Many of his investigations have been funded by The ALS Association and have yielded important insight into why the disorder kills motor neurons.

"I see our work as one example of how studying the basic mechanisms of development and cell death can lead to findings that are relevant to late-onset diseases such as ALS," Henderson said. "The role of patient-related organizations such as The ALS Association, has been critical: supporting the basic work needed for discovery, while encouraging and facilitating the translation toward more direct applications."

The cell death process is triggered when a death receptor is activated by nitric oxide.

Continued on Page 3

"The role of patient-related organizations such as The ALS Association has been critical: supporting the basic work needed for discovery, while encouraging and facilitating the translation toward more direct applications."

–Christopher Henderson, *Columbia University*

Identification of New Targets for ALS

"We are very pleased to be collaborating with The ALS Association and Galapagos on this discovery project."

*–**James Kelly,** Ph.D. / Stem Cell Innovations*

In a focused drug discovery effort funded by TREAT ALS, proprietary stem cells and gene manipulation technologies will be combined in a search for targets for candidate therapies for the disease.

Partnering with The ALS Association are the companies Galapagos NV and Stem Cell Innovations, Inc. The three million dollar milestone driven project will be directed by a team of experts with a goal to find new targets for the disease in the next two years.

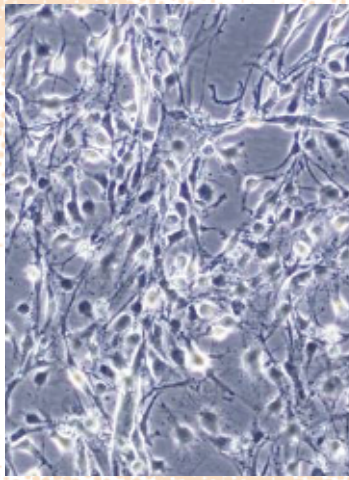
The unique ability provided by SCI to screen human motor neurons on a large scale, and Galapagos' target discovery technology will open new approaches to developing therapies for ALS. This alliance is an important initiative within The ALS Association's mission to find a cure for and improve living with ALS.

Stem Cell Innovations has a proprietary stem cell technology based on cells that are exempt from the President's ban. The stem cells are able to produce human motor neurons that can grow robustly in the lab.

"The human motor neuron cultures derived from our PluriCells will form the basis of this exciting alliance," said Stem Cell Innovations CEO James Kelly, Ph.D. "We are very pleased to be collaborating with The ALS Association and Galapagos on this discovery project."

Galapagos has developed high-throughput technology that inserts or deletes genes in cells in vitro using siRNA libraries. If manipulating these genes rescues the cells when they are challenged by stimulation with toxic factors such as excessive levels of glutamate or by withdrawal of trophic factors, then the genes should represent targets at which to aim drugs.

"We are proud to work with The ALS Association in the fight against ALS," said Onno van de Stolpe, CEO of Galapagos. "This alliance builds on both our CNS expertise and on our strong franchise in working with non-profit health organizations to identify disease-modifying drug targets for unmet medical needs."



Human stem cell culture
Photo: Stem Cell Innovations

Henderson cont.

Continued from Page 2

Christopher Henderson Ph.D.
Photo: Columbia University Medical Center

Henderson and colleagues detected an amplified nitric oxide response in mice expressing mutant SOD1 (copper-zinc superoxide dismutase 1– a mutation linked to some forms of ALS) well before symptoms could be detected in these mice.

In keeping with a growing appreciation of the role of glial cells in the demise of motor neurons in ALS, neighboring astrocytes and microglia appear to secrete nitric oxide as well, Henderson found.

"As co-founder of Trophos, Henderson is an excellent example of a scientist who sees the bigger picture," noted Lucie Bruijn, Ph.D. "His expertise helped drive the development of motor neuron assays for drug discovery, which has led to a lead compound currently in clinical trials for ALS."

The $25,000 prize honors the memory of Sheila Essey and was made possible through the generosity of the Essey Family Fund. Past recipients have often used the funds to support research of promising young scientists on their teams.

***TO KEEP CURRENT** with the ALS field, read the monthly journal news reports at www.alsa.org under the research tab.*

RESOURCES

Visit **www.alsa.org** and click on the blue research tab for these resources:

- SOD1 mutations database **www.alsod.org**
- Coriell NINDS DNA repository **http://ccr.coriell.org/ninds/**
- ALS Epidemiology **http://aces.stanford.edu/ForRes.html**
- SOD1 mutant rats, Taconic, **http://www.taconic.com/wmspage.cfm?parm1=258**
- SOD1 mutant mice, The Jackson Laboratory **http://jaxmice.jax.org/models/als.html**

ALS Association
TREAT ALS
Translational Research Advancing Therapy for ALS

CONTACT

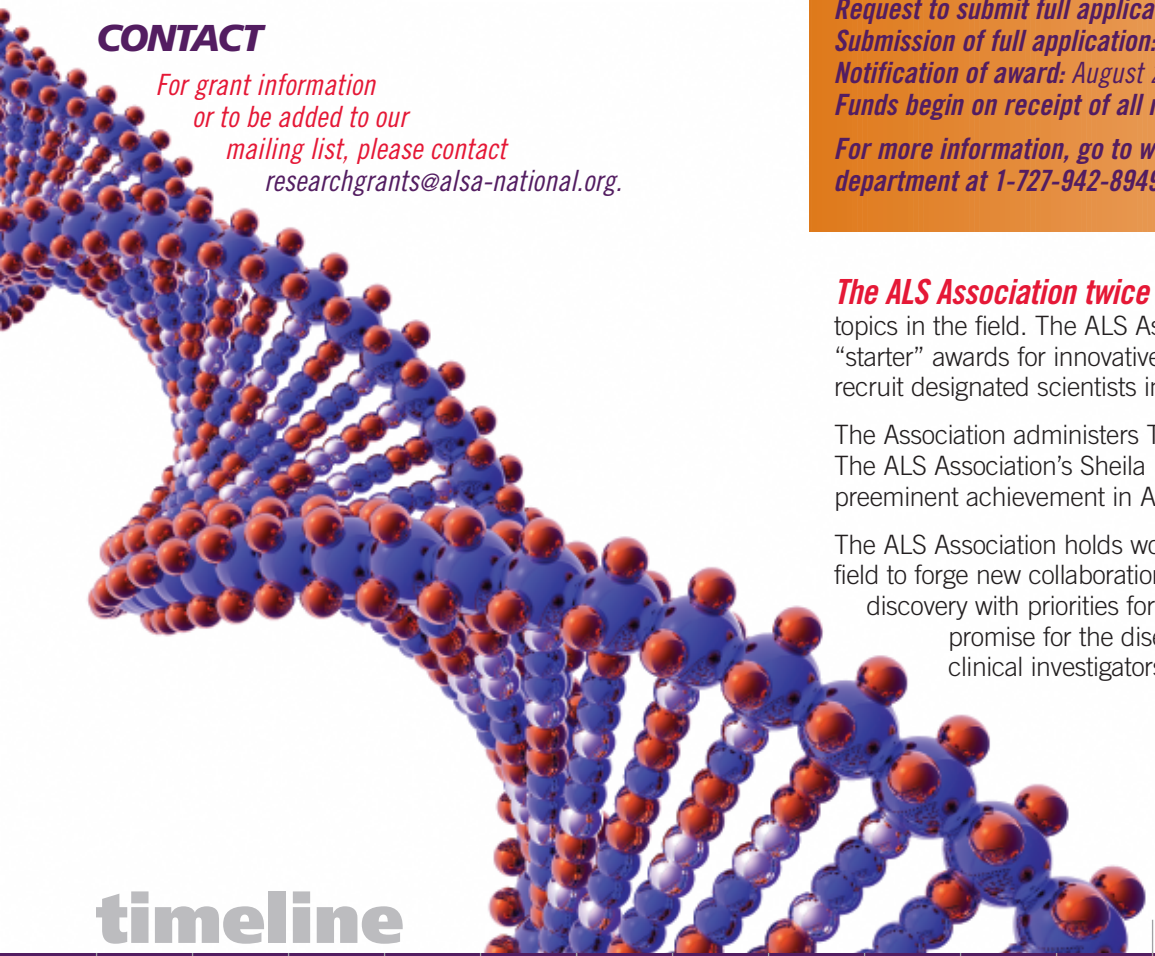
For grant information or to be added to our mailing list, please contact researchgrants@alsa-national.org.

Clinical Research Pilot Study Request for Proposals
Deadline for brief study outline: May 14, 2007
Email researchgrants@alsa-national.org for forms

*The ALS Association's initiative TREAT ALS (**T**ranslational **Re**search **A**dvancing **T**herapy for ALS) focuses specifically on drug discovery and pilot clinical studies. This call for proposals seeks to fund pilot studies to obtain preliminary clinical data which will support applications to the National Institutes of Neurological Disorders and Stroke for subsequent larger clinical trials of an intervention to treat or prevent ALS. The research proposal should directly address how to provide specific data that will be essential to design the subsequent definitive efficacy trial. A control group is not necessary to achieve these objectives.*

Brief study outline: *May 14, 2007*
Request to submit full application: *May 31, 2007*
Submission of full application: *July 6, 2007*
Notification of award: *August 2007*
Funds begin on receipt of all relevant signatures: *September 2007*

For more information, go to www.alsa.org and click the blue research tab or contact the research department at 1-727-942-8949.



The ALS Association twice yearly invites "investigator-initiated" proposals covering a broad array of topics in the field. The ALS Association offers multi-year grants to established investigators, as well as one-year "starter" awards for innovative research. It also spearheads projects generated by a committee of experts to recruit designated scientists in the field to specific aims.

The Association administers The Milton Safenowitz Post-Doctoral Fellowship for ALS Research. In addition, The ALS Association's Sheila Essey Award, partnering with the American Academy of Neurology, recognizes preeminent achievement in ALS research.

The ALS Association holds workshops each year that bring together scientists inside and outside the ALS field to forge new collaboration and fresh insight. In addition, the TREAT ALS initiative combines efficient drug discovery with priorities for existing drug candidates to accelerate testing in patients of compounds with promise for the disease. This funding includes a clinical researcher award to recruit promising clinical investigators to the field in partnership with the American Academy of Neurology.

timeline

1840 | 1850 | 1860 | 1870 | 1880 | 1890 | 1900 | 1910 | 1920 | 1930 | 1940 | 1950 | 1960 | 1970 | 1980 | 1990

1869: *French neurologist Jean-Martin Charcot identifies ALS*

50s: *DNA structure solved*

50s: *Nerve growth factor (NGF) identified—protective, growth promoting factor for nerve cells*

1968: *SOD1 enzyme identified*

70s: *Programmed cell death in motor neurons demonstrated*

1985: *The ALS Association funds study of inherited motor neuron disease*

1986: *Genes for muscular dystrophy identified*

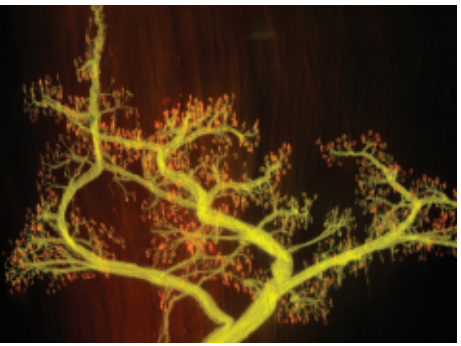
1989: *The ALS Association funds search for a common genetic link to ALS*

1990: *Congress declares the 1990s the "Decade of the Brain"*

1990: *Growth factor CNTF is found to increase survival of motor neurons*

Axonal Dynamics and the Synaptic Junction

The ALS Association each year hosts focused workshops on emerging topics to promote advances and new collaborations. Dynamics within the axon, increasingly implicated in neurodegenerative diseases was the topic of the workshop held at Cold Spring Harbor, New York last September. The focus of the program, organized by Don Cleveland, Ph.D., Erika Holzbaur, Ph.D., and Lucie Bruijn, Ph.D, included the role of axonal trafficking in ALS and similar disorders, changes at the neuromuscular junction, and the potential of therapeutic interventions to target these abnormalities in ALS.



Ending of nerve fiber as it contacts muscle

Photo: Jeff Lichtman Lab

Researchers described findings that the earliest event in the disease is a retreat of the axon terminals from their junction at muscle, well before symptoms appear. Pico Caroni, Ph.D., of the Miescher Institute in Basel, showed that early changes in gene expression are associated with damage to specific motor neurons in a mouse model of ALS even before the first axons detach. Whether the earliest events arise at the neuromuscular junction or the cell body was the subject of lively debate.

Key players involved in axonal transport include the molecular motor proteins, which move crucial cell materials along the cytoskeleton. Erika Holzbaur, Ph.D., of the University of Pennsylvania and Phillip Wong, Ph.D., of John Hopkins described how mutations to the motor proteins, dynein and dynactin, produce changes in motor neuron functions similar to ALS. Christopher Miller, Ph.D., of University of London showed that many different mutant SOD1 molecules—more than 117 to date are known to cause ALS—can slow axonal transport. Gerardo Morfini, Ph.D., of the University of Illinois, Chicago, has evidence that certain compounds can ameliorate slowing of axonal transport produced by SOD1 (copper-zinc superoxide dismutase) mutations in vitro in preparations of squid axon, a beginning step for novel ALS therapeutics.

Several investigators presented their work on the role of mitochondria in axons relating to neurodegeneration. Delivery of mitochondria to the synapse is essential for refining the connection to muscle. Thomas Schwarz, Ph.D., of Children's Hospital, Boston, showed that particular proteins (miro and milton) may hook mitochondria to the motor molecules and may be required for their axonal transport.

As technologies improve to model these abnormalities in vitro, and if new animal models can show similar axonal changes related to the disease, a path to treatment may become evident.

More details are available at www.alsa.org, under the blue research tab, see workshops. Workshop was sponsored by The Greater New York Chapter of The ALS Association.

"We are grateful for the continual support, both financial and more importantly, intellectual, that we have received from The ALS Association. This support has been a catalyst for our continual interest and progress in this area. While an effective cure for this terrible disease may not yet be in view, I strongly feel that the far-sighted approach of The Association is the most effective driving force in moving the work forward, marked by a willingness to pursue basic cellular mechanisms as well as potential therapeutic interventions. This interest in attacking the problem on all fronts is the strategy that is most likely to lead to significant synergies and rapid progress in our understanding of ALS."

–Erika Holzbaur, Ph.D.

Erika Holzbaur, Ph.D.

University of Pennsylvania

Photo: Miriam Chua, Cold Spring Harbor Laboratory

1991

Researchers link familial ALS to chromosome 21

1992

The ALS Association begins workshops

Glutamate transporter shown to be defective in ALS

Growth factor BDNF found to increase survival of motor neurons

1993

SOD1 gene mutation (chromosone 21) discovered in familial ALS

Trials using glutamate blocker riluzole begin

1994

Animal studies combining CNTF and BDNF demonstrate decreased motor neuron loss

GDNF rescues degenerating motor neurons during development in an in vitro experiment

Transgenic animals carrying mutated human SOD1 gene exhibit ALS-like symptoms and pathology

1995

FDA approves riluzole

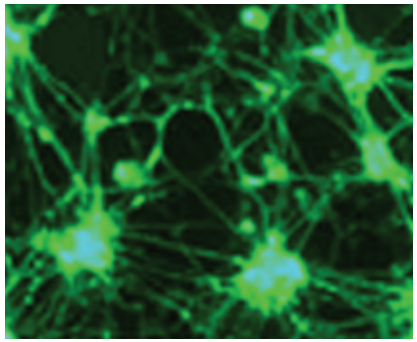
1996

Toxic properties of the SOD1 enzyme discovered and linked to familial ALS

1997

Stem Cell Derived Motor Neurons to Screen for Novel Compounds

Through its translational research initiative, TREAT ALS, The ALS Association is funding a method to find new small molecule candidates to slow or halt the disease. The screening technique will harness motor neurons derived from mouse embryonic stem cells and will be led by Lee Rubin, Ph.D., of the Harvard Stem Cell Institute.



Motor neurons from mouse stem cells
Amy Sinor, Ph.D. & Lee Rubin, Ph.D.

"We are very excited about working together with The ALS Association to contribute to finding a cure for this devastating disease," said Rubin. "Our approach is a new one and is focused on setting up a large scale screen in motor neurons generated in virtually unlimited numbers from mouse embryonic stem cells."

These investigators have been successful in using this approach to find potential candidates for another motor neuron disease, spinal muscular atrophy. Bruijn said, "we are encouraged to have their expertise applied to a search for effective ALS treatments in actual motor neurons."

Motor neurons, the cells that die in the disease, are challenging to obtain and grow in the lab in order to create an optimal automated screening assay aimed at candidate discovery for ALS. Standard tissue culture demands thousands of labor intensive dissections of mouse spinal cords to provide the targeted cells in sufficient numbers.

Rubin and collaborating Harvard stem cell scientist Kevin Eggan, Ph.D., now can generate billions of mouse motor neurons per week. Two different stressors for the growing motor neurons will be validated with initial TREAT ALS funding. One is withdrawal of growth factors. The other is to produce excess stimulation with a compound that mimics the messenger molecule, glutamate. These insults represent mechanisms thought to be involved in the disease process.

"We are very excited about working together with The ALS Association to contribute to finding a cure for this devastating disease."

*–**Lee Rubin,** Ph.D.*
Harvard Stem Cell Institute

timeline cont.

1998
- RNAi discovered by Craig Mello and Andrew Fire

1999

2000
- The ALS Association co-sponsors workshop on high-throughput drug screening with NINDS
- NINDS issues first ever RFA (request for applications) specifically for ALS research

2001
- A transgenic rat is designed; efforts start on fly model
- Attention turns to support cells of nerve tissue to find role in ALS
- Inflammation and programmed cell death gather research interest
- ALS2 gene (alsin protein) linked to juvenile ALS
- The ALS Association/NINDS collaborative effort begins screening drugs

2002
- Aggressive search for new ALS genes funded by The ALS Association
- Scientists complete map of mouse genome
- Agency of Toxic Substances and Disease Registries awards 5 grants focused on ALS
- Department of Defense approves funding for ALS-specific research

2003
- Study shows surrounding support cells play key role in ALS
- Gulf War study shows that vets deployed to Persian Gulf in 1991 developed ALS at twice the rate of those not deployed there
- IGF-1 gene therapy study proves beneficial in mice with ALS
- VEGF gene abnormalities shown to be potential factor in ALS
- The ALS Association collaborates with U.S. Department of Veterans Affairs to enroll all vets with ALS in registry
- Early tests of ceftriaxone appear to increase survival in mice with ALS
- Combination of creatine and minocycline prove more effective together in mouse model than either drug alone

active

Research Projects cont.

Continued from back cover

INFLAMMATION

Beattie, PhD, Eric / *California Pacific Medical Center, San Francisco, CA*
Carroll, PhD, Michael / *CBR Institute for Biomedical research, Inc., Boston*
Cunningham, PhD, Timothy; Heiman-Patterson, MD, Terry / *Drexel University, Philadelphia*
Enikolopov, PhD, Grigori / *Cold Spring Harbor Laboratory, New York*
Gordon, MD, Paul / *Columbia University, New York City*
Moeller, PhD, Thomas / *University of Washington, Seattle*
Prather, PhD, Paul / *University of Arkansas, Little Rock*

LABORATORY MODELS

Beattie, PhD, Christine; Burghes, PhD, Arthur / *Ohio State University, Columbus*
Broom, PhD, Wendy; Brown, Jr, DPhil, MD, Robert / *Massachusetts General Hospital, Boston*
Callaerts, PhD, Patrick; Norga, PhD, Koen / *University of Leuven, BELGIUM*
Cox, PhD, Gregory; Seburn, PhD, Kevin / *The Jackson Laboratory, Bar Harbor, ME*
de Belleroche, MD, PhD, Jackie / *Imperial College, London, UK*
Jansen, PhD, Richard / *Stem Cell Innovations, B.V. and Affiliates, Leiden, NETHERLANDS;*
MacLeod, PhD, Angus / *BioFocus Discovery Limited, Saffron Walden, UK*
Johnson, PhD, Jeffrey / *University of Wisconsin, Madison*
Kirsch, PhD, Donald / *Cambria Biosciences, Woburn, MA*
Kottman, PhD, Andreas / *Columbia University, New York City*
McCabe, PhD, Brian / *Columbia University, New York City*
Pushett, PhD, David / *PsychoGenics, Inc., Tarrytown, NY*
Silverman, PhD, Richard / *Northwestern University, Chicago, IL*
Taconic Farms Inc., / *Germantown, NY*

MITOCHONDRIA

Burgess, PhD, Robert / *The Jackson Laboratory, Bar Harbor, ME*
Gunther, PhD, Michael / *West Virginia University, Morgantown*
Liu, PhD, Jian California / *Pacific Medical Center, San Francisco, CA*

RNA THERAPY

Aebischer, MD, Patrick; Raoul, PhD, Cedric / *Ecole Polytechnique Federale de Lausanne, SWITZERLAND*
Cleveland, PhD, Don; Miller, MD, PhD, Timothy / *University of California, San Diego*
Cudkowicz, MD, Merit / *Massachusetts General Hospital, Boston*
Lin, PhD, C Glenn / *Ohio State University, Columbus*
Samulski, PhD, Richard / *University of North Carolina, Chapel Hill*

SOD1 (copper-zinc superoxide dismutase 1)

Atkin, PhD, Julie / *Howard Florey Institute, The University of Melbourne, AUSTRALIA*
Borchelt, PhD, David / *Johns Hopkins University, Baltimore, MD*
Durham, PhD, Heather / *McGill University, Montreal, CANADA*
Haines, PhD, Jonathan / *Vanderbilt University, Nashville, TN*
Hart, PhD, P John / *University of Texas Southwestern Medical Center, Dallas*
Hayward, MD, PhD, Lawrence; Tiwari, MD, PhD, Ashutosh / *University of Massachusetts, Worcester*
Julien, PhD, Jean-Pierre; Urushitani, MD, PhD, Makoto / *Laval University, Quebec, CANADA*
Kay, PhD, Brian / Argonne National Laboratory; IL; Roos, MD, Raymond / *University of Chicago*
Lansbury, Jr, PhD, Peter / *Brigham and Women's Hospital, Cambridge*
Lin, MD, PhD, Jonathan / *University of California, San Francisco*
McLaurin, PhD, JoAnne; Robertson, PhD, Janice / *University of Toronto, CANADA*
Thomas, PhD, Philip / *University of Texas Southwestern Medical Center, Dallas*
Walter, PhD, Peter / *University of California, San Francisco*

STEM CELLS

Anderson, PhD, David; Lukaszewicz, PhD, Agnes / *California Institute of Technology, Pasadena, CA*
Carrasco, PhD, Monica / *Harvard University*
Goldstein, PhD, Lawrence / *University of California, San Diego*
Guillemot, PhD, Francois / *National Institute for Medical Research, London, UK*
Kerr, MD, PhD, Douglas / *Johns Hopkins University, Baltimore, MD*
Li, PhD, Xue-Jun / *University of Wisconsin, Madison*
Maniatis, PhD, Tom / *Harvard University*
Mitchell, PhD, Gordon; Svendsen, PhD, Clive / *University of Wisconsin, Madison*
Studer, MD, Lorenz; Tabar, MD, Viviane / *Sloan Kettering Institute for Cancer Research, New York City*
Zhang, MD, PhD, Su-Chun / *University of Wisconsin, Madison*

TROPHIC FACTORS—DISEASE PROCESS

Nguyen, PhD, Minh Dang / *University of Calgary, Alberta, CANADA*

TROPHIC FACTORS—GENE THERAPY

Bartus, PhD, Raymond / *Ceregene Inc., San Diego, CA*; Boulis, PhD Nicholas / *Cleveland Clinic Foundation, Cleveland, OH;* Feldman, MD, PhD, Eva / *University of Michigan, Ann Arbor*
Carmeliet, MD, PhD, Peter; Moons, PhD, Lieve / *University of Leuven, BELGIUM*
Keshet, PhD, Eli / *Hebrew University, Jerusalem*
Kalb, MD, Robert / *Children's Hospital of Philadelphia*
Longo, MD, PhD, Frank / *Stanford University, CA*

grants

Study implicates smoking as likely risk factor in sporadic ALS
Study releases evidence that mitochondrial malfunction may play an important role in ALS

2004

Study funded by The ALS Association to find biomarkers in cerebrospinal fluid and blood

Ceftriaxone increases levels of the glutamate transporter GLT1 in a mouse model of ALS
RNAi treatment to silence the mutant SOD1 gene yields increased survival in mice
First international workshop on frontotemporal dementia discusses link to ALS
Stem cells engineered to make GDNF survive when transplanted into rats modeling ALS
Publication identifies potential biomarkers for ALS

2005

*Launch of TREAT ALS initiative (**T**ranslational **Re**search **A**dvancing **T**herapies for ALS) to accelerate clinical trials in ALS*
VEGF increases survival in a rat model of ALS while improving motor performance

ALS patient samples collected to NINDS ALS Repository
Repository samples allow genome analysis for sporadic ALS
First TREAT ALS clinical trials funded
First TREAT ALS clinical trials begun

2006

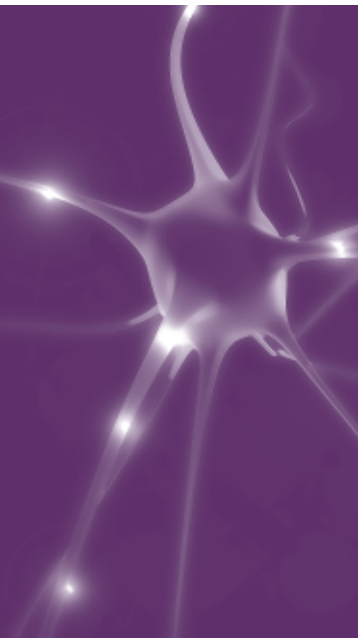
TDP-43 discovered as a common link in FTD, ALS; chromosome 9 region intense focus for FTD, ALS

2007

First genome screening data published based on NINDS ALS Repsoitory

active

Research Projects of The ALS Association Spring 2007



AXON DYNAMICS

Goldstein, PhD, Lawrence / *University of California, San Diego*
Holzbaur, PhD, Erika / *University of Pennsylvania, Philadelphia*
Meisler, PhD, Miriam / *University of Michigan, Ann Arbor*
Schmitt-John, PhD, Thomas / *Aarhus University, DENMARK*
Fisher, PhD, Elizabeth, and Greensmith, PhD, Linda / *University College London, UK*
Davis, PhD, Graeme / *University of California, San Francisco*
Nguyen, PhD, Minh Dang / *University of Calgary, Alberta, CANADA*
Hoogenraad, PhD, Casper, and Jaarsma, PhD, Dick / *Erasmus MC, Rotterdam, NETHERLANDS*
Perlson, PhD, Eran / *University of Pennsylvania, Philadelphia*

BIOMARKERS

Cudkowicz, MD, Merit / *Massachusetts General Hospital, Boston*
Bowser, PhD, Robert / *University of Pittsburgh, Pennsylvania*
Brown, Jr, DPhil, MD, Robert / *Massachusetts General Hospital, Boston, (with Metabolon, Inc., Durham, NC)*
Paige, PhD, Lisa, Metabolon, Inc. / *Durham, NC, Metabolites of ALS progression*
Katz, MD, Jonathan / *California Pacific Medical Center, San Francisco*, and Michael Weiner, MD, *San Francisco VA Medical Center*
Roland, PhD, Henry, and Lomen-Hoerth, MD, PhD, Catherine, / *University of California San Francisco*
Shaw, PhD, Gerry, and Borchelt, PhD, David / *University of Florida, Gainesville*
Kalra, MD, Sanjay, and Choi, PhD, Changho / *University of Alberta, Edmonton, CANADA*
Rothstein, MD, PhD, Jeffrey / *Johns Hopkins University, Baltimore, MD*
Rutkove, MD, Seward / *Beth Israel Deaconess Medical Center, Boston, MA* and Shefner, MD, PhD, Jeremy / *Upstate Medical Center, Syracuse, NY*

CELL DEATH

Enikolopov, PhD, Grigori / *Cold Spring Harbor Laboratory, NY*
Burgess, PhD, Robert / *The Jackson Laboratory, Bar Harbor, ME*
Xu, MD, PhD, Zuoshang / *University of Massachusetts, Worcester*
Pasinelli, PhD, Piera, Trotti, PhD, Davide / *Farber Institute for Neurosciences, Philadelphia, PA*
Dangond, MD, Fernando / *Brigham and Women's Hospital, Cambridge, MA*
Lin, MD, PhD, Jonathan, Walter, PhD, Peter / *University of California, San Francisco*
Rhee, PhD, Jinseol / *University of California, San Francisco*

CELL TARGETS

Burden, PhD, Steve / *Skirball Institute, New York City*
Roos, MD, Raymond / *The University of Chicago*
Carroll, PhD, Michael / *The CBR Institute for Biomedical Research, Inc., Boston*
Kasischke, MD, Karl, and Nedergaard, MD, PhD, Maiken / *University of Rochester, NY*
Maragakis, MD, Nicholas and Rao, MD, PhD, Mahendra / *National Institute on Aging and Johns Hopkins University, Baltimore, MD*
Davies, DPhil, Kay and Turner, Bradley, PhD / *University of Oxford, UK*
Ko, PhD, Chien-Ping / *University of Southern California, Los Angeles*

CLINICAL TRIALS

Cudkowicz, MD, Merit / *Massachusetts General Hospital, Boston*
Bennett, Jr., MD, PhD, James / *University of Virginia, Charlottesville*
Methner, MD, Axel / *University Hospital Dusseldorf, Germany*, and Schubert, PhD, Dave / *Salk Institute, La Jolla, CA*
Chan, MD, K Ming and Kalra, MD, Sanjay / *University of Alberta, Edmonton, CANADA*
Gordon, MD, Paul / *Columbia University, New York City*
Brown, Jr, DPhil, MD, Robert / *Massachusetts General Hospital, Boston*

COGNITIVE CHANGE

Strong, MD, FRCPC, Michael / *Robarts Research Institute, London, Ontario, CANADA*
Lomen-Hoerth, MD, PhD, Catherine / *University of California, San Francisco*
Leigh, MD, P Nigel / *King's College London, UK*

ENVIRONMENTAL FACTORS

Stellman, PhD, MPH, Steven / *Columbia University, New York, NY*
Nelson, MS, PhD, Lorene / *Stanford University, Stanford, CA*
Schmidt, PhD, Silke / *Duke University, Durham, NC*
Lomen-Hoerth, MD, PhD, Catherine / *University of California, San Francisco*
Shaw, PhD, Christopher A / *University of British Columbia, Vancouver, BC, CANADA*

GENE THERAPY

Cunningham, PhD, Justine, Bartus, PhD, Raymond / *Ceregene Inc., San Diego, CA*
Drachman, MD, Daniel, and Lu, PhD, Yang / *Johns Hopkins University, Baltimore, MD*
Rothstein, MD, PhD, Jeffrey / *Johns Hopkins University, Baltimore, MD*

GENETICS

Cox, PhD, Gregory, Seburn, PhD, Kevin / *The Jackson Laboratory, Bar Harbor, ME*
Kasarskis, MD, PhD, Edward / *University of Kentucky, Lexington, KY*
Sorenson, MD, Eric / *Mayo Clinic, Rochester, MN*, and Tandan, MD, FRCP, Rup / *University of Vermont, Burlington, VT*
de Jong, PhD, Pieter / *Children's Hospital Oakland, CA*
Pericak-Vance, PhD, Margaret / *Duke University, Durham, NC*
Shaw, MD, Christopher E. / *Institute of Psychiatry, King's College London, London, UK*
de Belleroche, MD, PhD, Jackie / *Imperial College, London, UK*
Lander, PhD, Eric / *Massachusetts Institute of Technology, Cambridge, MA*
Osoegawa, PhD, Kazutoyo / *Childrens Hospital Oakland, CA*, and Siddique, MD, Teepu / *Northwestern University, Chicago, IL*
Hardy, PhD, John, Traynor, MD, Bryan / *National Institute on Aging, Baltimore, MD*
Nicholson, PhD, Garth, and Blair, PhD, Ian / *ANZAC Research Institute, Concord, AUSTRALIA*
Rouleau, MD, PhD, FRCP(C), Guy / *CHUM Research Centre, Notre-Dame Hospital, Montreal, QC, CANADA*
Al-Chalabi, PhD, FRCP, Ammar / *Institute of Psychiatry, King's College London, London, UK*
Haines, PhD, Jonathan / *Vanderbilt University, Nashville, TN*
Harrison, PhD, Jeffrey, Streit, PhD, Wolfgang / *University of Florida, Gainesville, FL*
Yang, MD, PhD, Yanmin / *Stanford University, Stanford, CA*
Hedlund, PhD, Eva, Isacson, Dr. Med Sci, Ole / *Harvard University, Cambridge, MA*
Hardiman, MD, Orla / *Beaumont Hospital, Dublin, IRELAND*
Bonifati, MD, PhD, Vincenzo, Oostra, PhD, Ben / *ErasmusMC, Rotterdam, NETHERLANDS*

GLUTAMATE

Beattie, PhD, Eric / *California Pacific Medical Center, San Francisco, CA*
Chan, MD, K Ming; Kalra, MD, Sanjay / *University of Alberta, CANADA*
de Belleroche, MD, PhD Jackie / *Imperial College, London, UK*
Kalb, MD, Robert / *Children's Hospital of Philadelphia*
Methner, MD, Axel / *University Hospital Dusseldorf; Schubert, PhD, Dave / Salk Institute, La Jolla, CA*
Niu PhD, Li / *State University of New York, Albany*
Robberecht, MD, PhD, Wim / *University of Leuven, BELGIUM*
Rothstein, MD, PhD, Jeffrey / *Johns Hopkins University, Baltimore, MD*
Seeburg, PhD, Peter / *Max Planck Institute for Medical Research, Heidelberg, GERMANY*
Van Broeckhoven, PhD, DSc, Christine / *University of Antwerp, BELGIUM*

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ALS Association

National Office
27001 Agoura Road, Suite 150
Calabasas Hills, CA 91301-5104
www.alsa.org

The ALS Association Research Staff

Lucie Bruijn, Ph.D.
Science Director and Vice President

Nathalie Kayadjanian, Ph.D.
Associate Director of Biomedical Research

Mark Yard
Manager, Operations and Programs

Roberta Friedman, Ph.D.
Research Information Coordinator