RESEARCH ALS TODAY

THE ALS ASSOCIATION | VOLUME 3 | SPRING 2008

INSIDE

Opportunities for Drug Discovery in ALS by Richard Robinson

A four-day research meeting brought together neurologists, bench scientists, and CEOs; non-profits, government agencies, academics, and the private sector; Big Pharma and biotech startups; Ph.D.s, M.D.s, and M.B.A.s—almost 80 people in all, to brainstorm how to discover and bring to clinical trials drugs treatments for ALS. "It was unlike any other meeting I've been to," said one participant. "It was unique for the field of ALS," said another.

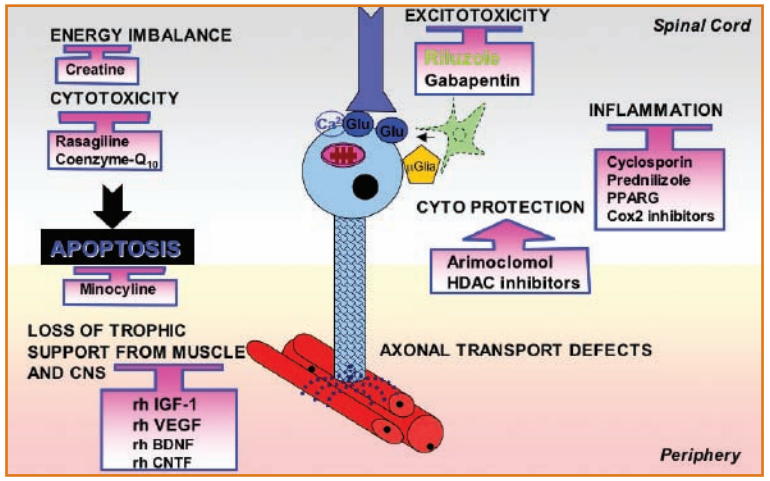
The meeting, held in January, was sponsored by The ALS Association as part of its TREAT ALS initiative, with funding provided by the Association; the National Institute of Neurological Disorders and Stroke and The Office of Rare Diseases, National Institutes of Health; and The Linden Foundation in memory of Suzanne V.A. Kelsey.

TREAT ALS Translational Research Advancing Therapy for ALS (TREAT ALS) is an Association initiative to increase the pace and prospects for success of drug discovery and clinical trials in ALS. The program identifies, solicits, and funds approaches with the highest likelihood of success, based on criteria established by its multidisciplinary steering committee. More details about TREAT ALS are available at out website, www.alsa.org.

"Several developments in the ALS field have come together to make this an ideal time to push the drug discovery process forward," according to Lucie Bruijn, Ph.D., science director and vice president of The ALS Association, including commitment from government funding agencies, new interest from large drug companies in less common diseases, and progress in cell and animal models for high-throughput drug screening

Despite slower growth in federal research funding, ALS ranks high "for where we can make a difference," said lead speaker Story Landis, Ph.D., director of the National Institute for Neurological Diseases and Stroke (NINDS). And ALS is becoming a more attractive target for Big Pharma, according to Andrew Wood, Ph.D., of Wyeth Neuroscience, on the heels of Genzyme's success with a treatment for Gaucher disease. "They realize there is a market in smaller diseases for which current treatments are either unavailable or unsatisfactory," Wood said.

"We need to draw on the full range of potential partnerships," Dr. Bruijn said. The largest companies may be interested, but academia and small biotechs are still taking the big risks early on in the search for new drug leads, with the larger companies funding the most promising ones closer to the clinic.



Clinical trials in ALS have targeted multiple mechanisms. See article on page 4 for a detailed overview of clinical trials in ALS.
–Image courtesy of Wyeth Research

Drug discovery in ALS must be moved forward along parallel pathways, speakers agreed, using multiple disease models and assays. According to Robert Pacifici, Ph.D., of the Cure Huntington's Disease Initiative, which is a model for TREAT ALS, "the goal in a drug screen is to get rid of as many candidates as fast as possible," and to replicate any successes in multiple models. Only then, he said, can you devote the resources to the few promising ones.

The most advanced screening programs in ALS focus on drugs to counteract the

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ALS Association
TREAT ALS
Translational Research Advancing Therapy for ALS

Recent Studies Open New Pathways for Hope

Promising new discoveries provide new opportunities for ALS research. The identification of mutations in the protein TDP-43 linked to some cases of sporadic and familial ALS confirm that this protein is directly involved in the disease process. This enables the development of new model systems for ALS, crucial not only to understanding disease mechanism but important as tools for drug development. There is an increasing interest in the academic and biotech sector to develop therapies for ALS. One of the limitations has been the focus on one animal model, the G93A SOD1 transgenic mice, representing only a small percentage of the disease.

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

The discovery of variations in the gene DPP6, that controls an enzyme found mostly in the brain and associated with spinal cord injury in rats, in two different studies and populations provides early evidence that the whole genome association studies have the potential to uncover gene changes linked to sporadic ALS. Recent advances in stem cell technology provide opportunities to develop cell lines from people with ALS so that we can more closely mimic the human disease in the laboratory.

As highlighted in this issue's article titled *"New Treatments for ALS 2008"* on pages 4 and 5, there are many challenges to clinical trails for ALS, but with a growing number of potential compounds for the disease and networks to move trials forward, we are better positioned now to bring potential therapies to patients. Through the growing interest in translational efforts, there is an increasing interaction between clinicians, research scientists and the industry and an enthusiasm to move research from the lab to the clinic.

It is indeed a promising time for researchers to be focused on ALS research, and with commitment and collaboration, we look forward to new therapeutic approaches for people with ALS.

- Lucie Bruijn, Ph.D.

Robberecht honored with Essey Award

The ALS Association joins the American Academy of Neurology in presenting the 2008 Sheila Essey Award for ALS Research to Wim Robberecht, M.D., during the Academy's 60th Annual meeting in Chicago, April 12-18, 2008.

"...his leadership and collaborative approach to research efforts are invaluable to the ALS community."

*–**Lucie Bruijn**, Ph.D.*

Robberecht, Chairman of the Department of Neurology, University Hospital Gasthuisberg, University of Leuven, Leuven, Belgium is a highly respected clinician and researcher in the ALS field. His research aims to contribute to the understanding of the disease mechanism of ALS and to the development of a treatment for this disorder. To this end, the clinical team he directs is actively involved in clinical trials, genetics of ALS and epidemiology. In addition, his team provides multi-disciplinary care for ALS patients.

Wim Robberecht, M.D.

His laboratory has used in vitro cultures of motor neurons and glial cells to determine the role of excitotoxic and calcium-mediated motor neuron death, the involvement of heat shock proteins in neurodegeneration and the biology of vascular endothelial growth factor (VEGF) in ALS. More recently his laboratory has focused on using a zebrafish model for ALS and has observed some interesting early changes in axon outgrowth that may be exploited to develop a novel screen for ALS.

"Our work on excitotoxicity, VEGF and glial

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Essey Award cont.

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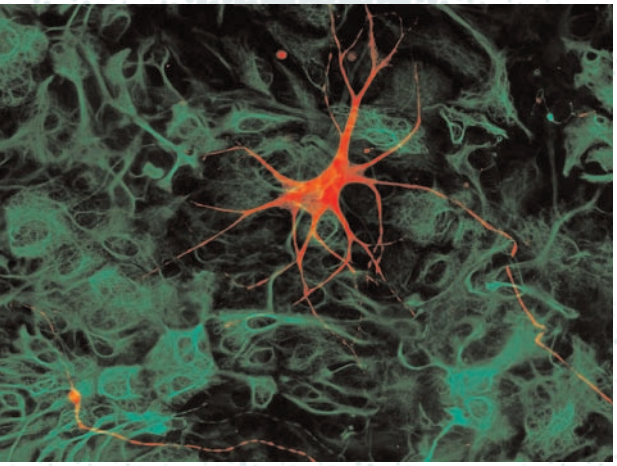
cells will hopefully contribute to the understanding of the sporadic form of ALS accounting for the majority of ALS patients. In addition, the genetic screen of the zebrafish model we recently developed may complement the results obtained in human studies. Such combined approach of basic and clinical research is, at least in my mind, what is needed in order to advance the understanding and treatment of ALS. The participation of ALS patients in molecular, genetic and therapeutic studies is pivotal." commented Robberecht.

"As clinician and research scientist, Robberecht has contributed significantly to the ALS field, and his leadership and collaborative approach to research efforts are invaluable to the ALS community," commented Lucie Bruijn, Ph.D.

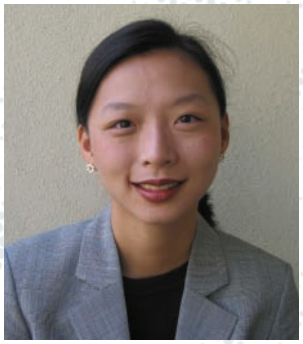
The $25,000 prize honors the memory of Sheila Essey and was made possible through the generosity of the Essey Family Fund. Past recipients have often used the funds to support research of promising young scientists on their teams.



In vitro culture of motor neurons (red) and glial cells (green) derived from the G-93A SOD1 mouse model. *–Image courtesy of Wim Robberecht*

Clinician Scientist Receives Award

The ALS Association and the American Academy of Neurology (AAN) are pleased to announce that Alice S. Chen-Plotkin, M.D., from the University of Pennsylvania School of Medicine, Philadelphia, PA, is this year's recipient for the AAN/ALS Association Clinician Scientist Development Award as part of TREAT ALS (**T**ranslational **Re**search **A**dvancing **T**herapy for ALS). The purpose of the award is to recruit talented and promising young clinicians to the ALS research field, who propose innovative clinical research, and to foster their development to make significant contributions to ALS clinical research. Dr. Chen-Plotkin's study will focus on the suggested role of TDP-43 in regulating the expression of genes.



Alice S. Chen-Plotkin, M.D.

TDP-43 (TAR DNA binding protein 43) has been previously identified as a major component of the "inclusions," or protein clumps, found in the motor neurons of ALS patients. Scientists have recently identified mutations in the gene encoding TDP-43 linked to familial and sporadic ALS confirming that in at least some cases of ALS TDP-43 is integral to the disease process. "We hope that by understanding the genome-wide expression of genes in ALS and the contribution of TDP-43 to regulating this process, we can find early clues to the causes of disease. This, in turn, might lead to the development of effective therapies," commented Dr. Chen-Plotkin. "I feel extremely honored to be receiving the AAN/ALS Foundation Clinician Scientist Development Award. Not only does it provide crucial support for my research, but it also serves as a vote of confidence and, as such, is very encouraging to a fledgling neurologist-neuroscientist."

Opportunities for Drug Discovery in ALS cont.

Continued from Page 1

effects of mutant superoxide dismutase 1 (SOD1), and the protein aggregation it causes. SOD1 mutations account for 20% of familial ALS, or about 2% of all ALS cases. Efforts are also underway to develop a vaccine against the mutant protein, to stabilize it in its normal form, and to silence it with antisense. But SOD1 is only a small part of the ALS picture, and targeting it is only part of the solution, speakers agreed. Other potential targets include improving axonal transport, rescuing mitochondria, and reducing neuroinflammation. Drug screens for each of these targets are contemplated.

High-throughput screening requires fast and simple assays, which are best done in individual cells not whole animals. New developments in stem cells will soon allow rapid production of billions of human motor neurons, perfect for the task (mouse neurons can already be made in such abundance). Partnering between academic researchers, who have identified potential targets, and biotech companies with expertise in central nervous system drug development will improve the chances of success by drawing on the specialized strengths of each group, Dr. Bruijn said.

Clinical trials are the goal of all this effort, of course. The full picture of ALS clinical trials is covered elsewhere in this issue, in a special article by Merit Cudkowicz, M.D., of Massachusetts General Hospital.

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

The ALS Association Research Staff
Lucie Bruijn, Ph.D.
Science Director and Vice President
Research ALS Today *Editor*
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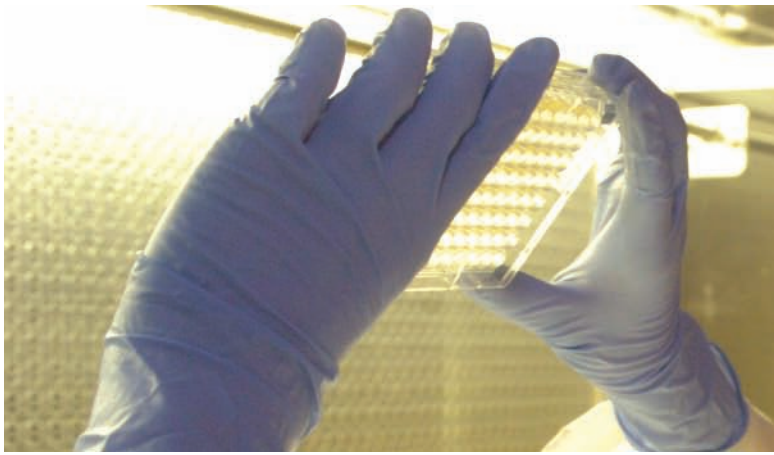
Director, Operations and Programs

New Treatmen

Merit Cudkowicz, M.D. Harvard Medical



In recent years, scientists have learned much about disease mechanisms underlying ALS and have identified a wide range of new pathways where targeted treatment may be effective. Although results from such studies have not as yet influenced patient care, other advances have improved both the quality and duration of life for people with ALS. Recent studies have shown that early nutritional and respiratory support is extremely effective; it is also clear that riluzole, approved in 1993 for treatment of ALS, prolongs life, though modestly. In the same time span, multidisciplinary ALS centers have proliferated, fostered by funding from both The ALS Association and the Muscular Dystrophy Association. The increased availability of such centers has further improved quality of life for ALS patients and has also likely contributed to improved survival.

In approximately 90% of people with ALS, there is no apparent family history of ALS (sporadic ALS); 10% of people do have a positive family history for ALS (familial ALS). Discovery of several genes that cause familial ALS and others that might increase the risk of developing sporadic ALS has provided new and exciting insights into disease mechanisms, which may lead to new treatments both for patients with familial and sporadic disease. There are currently seven active therapy trials in North America, Europe and Asia, five upcoming trials (see table 1 and www.clinicaltrials.gov); and many more therapies are in the early drug development. Three treatments, talampanel, tamoxifen and lithium have encouraging data from small, pilot studies in people with ALS.

The Northeast ALS consortium (NEALS), founded in 1995, is an independent, non-profit consortium of clinical and scientific investigators who conduct research at their affiliated institutions. The goal of NEALS is to translate research advances rapidly into clinical trials for patients with ALS. The membership of NEALS has grown to 72 sites throughout the United States and Canada (www.alsconsortium.org). The ALS Association recently awarded a TREAT ALS grant to NEALS to support a network of high-quality, well-trained ALS clinical trial sites that can rapidly test new treatments for ALS in a collaborative, efficient manner.

"Recent studies have shown that early nutritional and respiratory support is extremely effective; it is also clear that riluzole, approved in 1993 for treatment of ALS, prolongs life, though modestly."

–Merit Cudkowicz, M.D.

Currently, five studies are being conducted through the TREAT ALS NEALS ALS Association network. Three are clinical drug studies; the new drug arimoclomol is being investigated separately in the larger population of ALS patients, as well as in patients with a specific ALS causing mutation in the gene for superoxide dismutase 1 (SOD1). The third study utilizes the exciting new strategy of developing antisense oligonucleotides to inhibit mutant SOD1 gene activity in patients with this mutation. The other two studies have as their goal the discovery of sensitive markers for diagnosis and assessment of disease progression.

The identification of sensitive and specific ALS biomarkers would greatly aid further ALS research. There are several different types of biomarkers that are important to develop for ALS. These include biomarkers of disease that can aid in earlier diagnosis, biomarkers of disease progression, that can shorten clinical drug development time, and biomarkers of the biological effects of treatments. Using the TREAT ALS NEALS network, a new study will soon be underway to build a Biomarker Sample Repository. The goal of this repository is to identify diagnostic biomarkers and therapeutic targets for ALS. Blood and cerebrospinal fluid will be collected at 18 centers from people with ALS, other motor neuron disorders, ALS mimic disorders and people without neurological disorders.

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

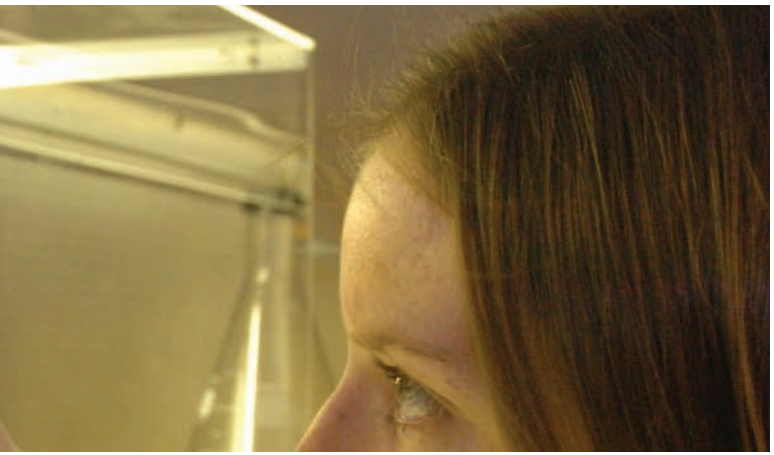
1989: The ALS Association funds search for a common genetic link to ALS

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

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

ts for ALS 2008

School, Massachusetts General Hospital



"The identification of sensitive and specific ALS biomarkers would greatly aid further ALS research."

–Merit Cudkowicz, M.D.

Much has also been learned about how to improve clinical ALS trials, and what challenges must be overcome to rapidly study a steadily increasing number of hopeful therapies. Challenges for the community are to improve enrollment and participation of people with ALS in treatment trials. The fastest and only way to effectively develop good treatments to slow down and ultimately cure ALS is through clinical trials. Development of biological markers will speed therapy development. Increased appreciation of the importance of small studies to determine dosage and activity of new therapies at specific targets will also speed therapy development. These studies will ultimately decrease the size and costs of studies, and most importantly, lead to the development of the second, third and fourth treatments for ALS.

During the past decade, significant progress has been made in our understanding of pathogenesis of ALS. We have gained tremendous experience in the conduct of clinical trials and have developed a large and dedicated group of trained clinical trial sites. However, there remains an unmet need to find treatments that effectively slow the progression of ALS, or to cure it completely. Key areas for future ALS clinical research include better understanding of riluzole mechanisms with the hope to develop more potent riluzole analogs. Preclinical studies that help identify dosage, pathways and pharmacodynamic markers will allow design of better early studies in humans. These will result in better-designed efficacy studies. To accomplish this, more investment is needed by industry, foundations and government funding agencies in early therapy development in animals and humans. Understanding barriers to participation and retention in clinical studies will improve study conduct and speed development of better treatments. A more sensitive ALS outcome measure that can detect small but important responses could revolutionize therapy development. With coordinated effort combined with increased knowledge of the disease pathology and the therapeutic challenges, effective therapies are now, more than ever, within reach.

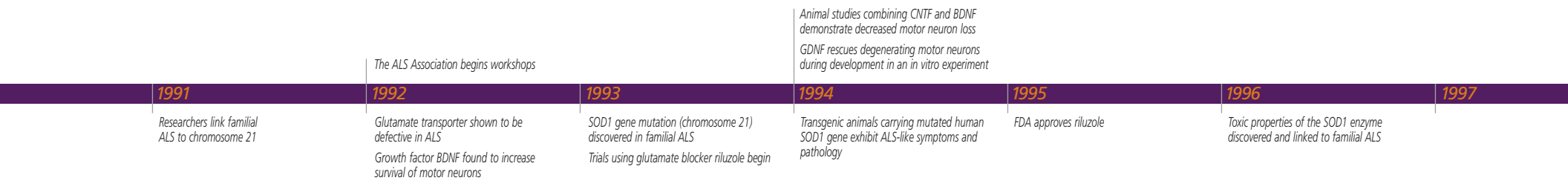
TABLE 1: CURRENT AND FUTURE ALS TREATMENT TRIALS

CURRENT

Compound	Proposed mechanisms of action
Ceftriaxone	Glutamate antagonisms (Increases EAAT2/GLT1 activity), antioxidant
ONO-2506	Prevents reactive astrocytosis; glutamate antagonism
Co-enzyme Q-10	Antioxidant; facilitates mitochondrial respiration
Memantine	N-methyl D-aspartate (NMDA) receptor antagonist
MCI-186	Antioxidant, facilitates mitochondrial respiration; anti-apoptotic
Diaphragm Pacing	Provide respiratory support and muscle training
Arimoclomol	Heat shock protein inducer

FUTURE

Antisense Oligonucleotide SOD1	Decrease production of SOD1 protein. Trial for people with familial ALS secondary to mutations in the gene for superoxide dismutase 1.
Talampanal	α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA) receptor modulator (glutamate antagonist)
TRO19622	facilitates mitochondrial respiration; glutamate antagonist; anti-apoptotic
R+ Pramipexole	Antioxidant
Arimoclomol – FALS	Heat shock protein inducer; Trial for people with familial ALS secondary to mutations in the gene for superoxide dismutase 1.
Lithium	Increased autophagy, anti-apoptotic, glutamate antagonist



Investigator-Initiated Research Grants

The ALS Association's INVESTIGATOR-INITIATED RESEARCH GRANT PROGRAM supports innovative research of high scientific merit and ALS in areas of ***stem cell research, disease mechanism, therapeutic approaches, model systems and genetics.*** *The ALS Association encourages international applications.*

Multi-year Grants are offered *to ESTABLISHED ALS INVESTIGATORS. The ALS Association will support research that is projected for periods of one (1) up to three (3) years. Funding is committed for one (1) year only, with noncompetitive renewals conditioned upon receipt of satisfactory interim progress reports. Awards will be in an amount of* ***$80,000 per year****.*

Starter Grants are offered *for NEW INVESTIGATORS ENTERING THE FIELD OF ALS, proposing innovative and novel projects likely to provide important results relevant to ALS research. Alternatively, they can be PILOT STUDIES BY ESTABLISHED ALS INVESTIGATORS or STUDIES BY SENIOR POST-DOCTORAL FELLOWS IN THE ALS FIELD. These applications do not require strong preliminary data but must emphasize novelty, feasibility, innovation and relevance to ALS. The maximum amount awarded is* ***$40,000 for one year****.*

The Milton-Safenowitz Post-Doctoral Fellowship for ALS Research is awarded annually *each spring. The call for abstracts is part of the Investigator Initiated Research call announced each December. The award is* ***$40,000 annually for two years****. Applicants who are eligible are new post-doctoral fellows or those that have been a fellow for no more than one year.*

The ALS Association sponsors a Clinical Management Research Grant Program *to improve care and quality of living with ALS. The program funds starter grants for research into the clinical, psychological and/or social management of ALS. The projects are funded in the range of a total of* ***$40,000 - $50,000 for up to two years****.*

CONTACT *For Clinical Management Research Grant Program (only), contact Sharon Matland, vice president, Patient Services at (818) 587-2217. For all other grant information or to be added to our mailing list, please contact researchgrants@alsa-national.org.*

active Research Projects cont.

Continued from Back Cover

Harrison, PhD, Jeffrey / *University of Florida, Gainesville, FL*
Hoogenraad, PhD, Casper / *Erasmus MC, Rotterdam, NETHERLANDS*
Jaarsma, PhD, Dick / *Erasmus MC, Rotterdam, NETHERLANDS*
Kasarskis, MD, PhD, Edward / *University of Kentucky, Lexington, KY*
Lander, PhD, Eric / *Massachusetts Institute of Technology, Cambridge, MA*
Nicholson, PhD, Garth / *ANZAC Research Institute, Concord, AUSTRALIA*
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Siddique, MD, Teepu / *Northwestern University, Chicago, IL*
Simmons, MD, Zachary / *Pennsylvania State University, PA*
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Streit, PhD, Wolfgang / *University of Florida, Gainesville, FL*
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Traynor, MD, Bryan / *National Institute on Aging, Baltimore, MD*
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Yang, MD, PhD, Yanmin / *Stanford University, Stanford, CA*

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Schubert, PhD, Dave / *Salk Institute, La Jolla, CA*
Van Broeckhoven, PhD, DSc, Christine / *University of Antwerp, NETHERLANDS*

INFLAMMATION

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Cunningham, PhD, Timothy / *Drexel University, Philadelphia, PA*
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Gordon, MD, Paul / *Columbia University, New York City, NY*
Heiman-Patterson, MD, Terry / *Drexel University, Philadelphia, PA*
Moeller, PhD, Thomas / *University of Washington, Seattle, WA*
Prather, PhD, Paul / *University of Arkansas, Little Rock, AR*

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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

The ALS Association holds scientific workshop on "Environmental Factors and Genetic Susceptibility"

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

Study shows that human embryonic stem cells can be stimulated to produce motor neurons

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

nts

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LABORATORY MODELS OF ALS

Barrett, PhD, Ellen / *University of Miami, FL*
Beattie, PhD, Christine / *Ohio State University, Columbus, OH*
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Kirsch, PhD, Donald / *Cambria Biosciences, Woburn, MA*
MacLeod, PhD, Angus / *BioFocus Discovery Limited, Saffron Walden, UNITED KINGDOM*
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Pushett, PhD, David / *PsychoGenics, Inc., Tarrytown, NY*
Raoul, PhD, Cedric / *INMED, FRANCE*
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Siddique, MD, Teepu / *Northwestern University, Chicago, IL*
Silverman, PhD, Richard / *Northwestern University, Chicago,IL*

MITOCHONDRIA

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Da Cruz, PhD, Sandrine / *Ludwig Institute for Cancer Research, La Jolla, CA*
Gunther, PhD, Michael / *West Virginia University Research Corporation, Morgantown, WV*
Liu, PhD, Jian / *California Pacific Medical Center, San Francisco, CA*
Tanguay, PhD, Robert / *University Laval, Quebec, CANADA*

RNA THERAPY

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Cudkowicz, MD, Merit / *Massachusetts General Hospital, Boston, MA*
Miller, MD, PhD, Timothy / *Washington University, Sr. Louis, MO*
Raoul, PhD, Cedric / *Ecole Polytechnique Federale de Lausanne, SWITZERLAND*
Samulski, PhD, Richard / *University of North Carolina, Chapel Hill, NC*

SOD1 (COPPER ZINC OXIDE DISMUTASE 1)

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Beattie, PhD, Christine / *Ohio State University, Columbus, OH*
Beckman, PhD, Joseph / *Oregon State University, Corvallis, OR*
Borchelt, PhD, David / *University of Florida, Gainesville, FL*
Bosco, PhD, Daryl / *Massachusetts General Hospital, MA*
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Gunther, PhD, Michael / *West Virginia University Research Corporation, Morgantown, WV*
Haines, PhD, Jonathan / *Vanderbilt University, Nashville, TN*
Hart, PhD, P John / *University of Texas Southwestern Medical Center, Dallas, TX*
Hayward, MD, PhD, Lawrence / *University of Massachusetts, Worcester, MA*
Julien, PhD, Jean-Pierre / *Laval University, Quebec, CANADA*
Kirsch, PhD, Donald / *Cambria Biosciences, Woburn, MA*
Lansbury, Jr, PhD, Peter / *Brigham and Women's Hospital, Cambridge, MA*
Lin, MD, PhD, Jonathan / *University of California, San Francisco, CA*
McLaurin, PhD, JoAnne / *University of Toronto, Ontario, CANADA*
Ray, PhD, Soumya / *Brigham and Women's Hospital, Cambridge, MA*
Robertson, PhD, Janice / *University of Toronto, Ontario, CANADA*
Roos, MD, Raymond / *University of Chicago, IL*
Tennore, PhD, Ramesh / *Ohio State University, Columbus, OH*
Thomas, PhD, Philip / *University of Texas Southwestern Medical Center, Dallas, TX*
Tiwari, MD, PhD, Ashutosh / *University of Massachusetts, Worcester, MA*
Urushitani, MD, PhD, Makoto / *Laval University, Quebec, CANADA*
Walter, PhD, Peter / *University of California, San Francisco, CA*
Xu, MD, PhD, Zuoshang / *University of Massachusetts, Worcester, MA*

STEM CELLS

Boulis, MD, Nicholas / *Emory University, Atlanta, GA*
Carrasco, PhD, Monica / *Harvard University, Cambridge, MA*
Goldstein, PhD, Lawrence / *University of California, San Diego, CA*
Guillemot, PhD, Francois / *National Institute for Medical Research, London, UNITED KINGDOM*
Kerr, MD, PhD, Douglas / *Johns Hopkins University, Baltimore, MD*
Li, PhD, Xue-Jun / *University of Wisconsin, Madison, WI*
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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, MD, Nicholas / *Emory University, Atlanta, GA*
Carmeliet, MD, PhD, Peter / *University of Leuven, BELGIUM*
Feldman, MD, PhD, Eva / *University of Michigan, Ann Arbor, MI*
Kalb, MD, Robert / *Children's Hospital of Philadelphia, PA*
Keshet, PhD, Eli / *The Hebrew University, Jerusalem, ISRAEL*
Longo, MD, PhD, Frank / *Stanford University, Stanford, CA*
Mitchell, PhD, Gordon / *University of Wisconsin, Madison, WI*
Moons, PhD, Lieve / *University of Leuven, BELGIUM*
Svendsen, PhD, Clive / *University of Wisconsin, Madison, WI*

2004

Study implicates smoking as likely risk factor in sporadic ALS
Study releases evidence that mitochondrial malfunction may play an important role in ALS
Study funded by The ALS Association to find biomarkers in cerebrospinal fluid and blood

2005

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
Early data suggests that mutant SOD1 may be secreted by and may activate microglia
*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

2006

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

2007

Stem cell study shows SOD1 mutant support cells can kill any motor neuron
ALS U.S. registry efforts gaining ground in Congress
Fish model of ALS: Progress reported
SOD1 in altered form common to both sporadic and inherited ALS
Engineered stem cells making GDNF help motor neurons survive in SOD1 mutant rats
First genome screening data published based on NINDS ALS Repository

2008

Discovery of DPP6 in two genome wide association studies in ALS
Mutations in TDP-43 linked to familial and sporadic ALS
Induced Pluripotent Stem Cell Technology opens up new avenues for ALS

active

Research Projects of The ALS Association Spring 2008

ALS Association

National Office

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AXON DYNAMICS

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Holzbaur, PhD, Erika / *University of Pennsylvania, Philadelphia, PA*
Hoogenraad, PhD, Casper / *Erasmus MC Rotterdam, NETHERLANDS*
Jaarsma, PhD, Dick / *Erasmus MC Rotterdam, NETHERLANDS*
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COGNITIVE CHANGE WITH ALS (FRONTOTEMPORAL DEMENTIA)

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GENETICS OF ALS

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