THE ALS RESEARCH FORUM
Discovering a Common Goal, Discovering a Cure
PRIZE4LIFE ALS ASSOCIATION

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Research News

C9orf72 RNA foci: Much Ado About Nothing In ALS and FTD?

Neuronal RNA foci are a key hallmark of C9orf72 ALS and FTD. But according to a new study led by Mayo Clinic's **Rosa Rademakers** and **Marka Van Blitterswijk** in Florida, the number and/or distribution of these clumps of RNA in the brain do not explain why some people develop symptoms or what form of the disease. The study suggests that RNA foci do not play a major role in C9orf72-associated diseases. The results are published on May 19 in *Acta Neuropathologica*.

Check out our feature to learn more about the implication of these findings, including the testing of potential treatments approaching the clinic.

Pruning Spurious Genetic Links Clarifies Heritability in Sporadic ALS

About one out of six cases of sporadic ALS may be explained at least in part, by changes in genes previously linked to the disease according to a new study published on June 9 in *Neurology*. The whole exome sequencing analysis, led by **Stefan Pulst** and **Lynn Jorde** of the University of Utah, found that 17.2% of people with sporadic ALS harbored mutations and/or repeat expansions in 33 genes associated with the disease. 87 people with sporadic ALS participated in the study. The findings suggest in part, that emerging gene-targeted strategies may be of benefit to some people with sporadic disease.

When C9orf72 Silences U2, Spliceosomes Can't Find What They're Looking For

RNA processing defects may contribute to the most common form of ALS according to a report in the June 13 issue of *Cell Reports*. The study, led by **Robin Reed** at Harvard Medical School, found that C9orf72-associated dipeptide repeat proteins (DRPs) block spliceosome assembly by sequestering one of its key components, U2 snRNP, *in vitro*. What's more, according to RNAseq analysis, more than 40% of mRNAs missing exons in post-mortem brain tissue of people with C9orf72 ALS are spliced by a U2 snRNP-dependent mechanism. The results suggest that mis-splicing of key pre-mRNAs may contribute to motor neuron toxicity in C9orf72 ALS. Therefore, emerging "splice modulators" may help treat this form of the disease by facilitating the transcription and thereby, the synthesis of key proteins.

ALS/FTD Genes Reveal Pathways to Pathology

Mutations in mitochondrial protein CHCHD10 can lead to ALS/FTD. But according to a new study led by University of South Florida's **David Kang**, the drop in energy production in motor neurons alone may not cause the disease. The study found that CHCHD10 bound and retained TDP-43 in the nucleus of cultured hippocampal neurons. What's more, the transfection of ALS/FTD-linked mutant CHCHD10 increased levels of TDP-43 in the cytoplasm of these neurons by 30%. The results suggest that cytoplasmic mis-localization of TDP-43 may also contribute to motor neuron toxicity in CHCHD10-linked ALS. The study is published on June 6 in *Nature Communications*.

C9orf72 ALS Model Mice: Right On the Epigenetic Mark?

Chemical changes in the genome may contribute to ALS. But how to develop therapies that reset these genetic switches is tricky to do. Reprogramming motor neurons may alter and/or erase at least some of these epigenetic marks. And, animal models of ALS may not fully recapitulate them. Now, University of Miami's **Zane Zeier** in Florida reports that a mouse model of C9orf72 ALS exhibits key epigenetic changes in the brain associated with the disease. These modifications include increased levels of 5-hydroxymethylcytosine at the expanded promoter of the C9orf72 gene; key changes that may lead to more repeat-containing RNAs and dipeptide repeat proteins in motor neurons which may contribute to the disease. The study is published on June 12 in *Molecular Neurodegeneration*.

Check out our website to read more of the latest research advances in ALS.

Funding Opportunities:

AFTD is soon to be accepting applications for their early career awards, focusing on the basic science and treatment of FTD. Check their website for details.

July 2017

Rapid Response 2017. Weston Brain Institute. High-risk high reward translational research. FTD. Canada only. LOI due by **July 5, 2017.**

Harrington Rare Disease Scholar Award. In collaboration with Takeda Pharmaceuticals. Focus: Neurology and Gastroenterology. LOI due by July 19, 2017.

Accelerating Drug Discovery for FTD. Alzheimer's Drug Discovery Foundation and the Association of Frontotemporal Dementia. LOI due by July 31, 2017.

August 2017

Judith and Jean Pape Adams ALS Research Grants. Judith and Jean Pape Adams Foundation. Application due by August 4, 2017.

NEW! NeuroNEXT Clinical Trials. NIH, NINDS. Application due by August 3, 2017.

NEW! NIH Blueprint Neurotherapeutics Network: Small Molecule Drug Discovery and Development for Disorders of the Nervous System. Application due by August 9, 2017.

The Betty Laidlaw MND Research Prize. MND Australia. Applications due August 25, 2017.

MND Research Grants. MND Australia. Applications due August 25, 2017.

Postdoctoral Fellowships. MND Australia. Applications due August 25, 2017.

September 2017

MDA Venture Philanthropy Program. Muscular Dystrophy Association. LOI due by September 1, 2017.

Research Grants. Frick Foundation for ALS Research. Application due by September 30, 2017.

Check out our updated list of grants and awards.

Job Opportunities:

Director of Neurodegenerative Research, University of Pennsylvania. Philadelphia, PA.
Director, Institute of Biotechnology. University of Helsinki. Helsinki, Finland.
Research Scientist, Neurodegenerative Disease. University of California, San Francisco, CA.
Postdoctoral Fellow, Neurotherapeutics. KTH Royal Institute of Technology. Stockholm, Sweden.
Postdoctoral Fellow, Sareen Lab. Cedar Sinai Medical Center. Los Angeles, CA.
Postdoctoral Fellow, Vande Velde Lab. CRCHUM. Montréal, Canada.
Graduate Studentship, Vande Velde Lab. CRCHUM. Montréal, Canada.
Research Associate, ViTAL Consortium. University of Ulster. Belfast, Ireland.
Research Associate, University of California. San Francisco, CA.

Senior Associate Scientist, ALS and PD. Amgen. Cambridge, MA.
Postdoctoral Fellow, ALS. Sanofi. Framingham, MA.

Hiring someone onto your team? Contact us to add your listing to our updated job board: ALSjobs@prize4life.org.

Full List of Job Opportunities >>

Upcoming Meetings:

July 2017

July 8-11, 2017. Edinburgh, Scotland. European Meeting on Glial Cells in Health and Disease.

July 23-28, 2017. Stowe, Vermont. Gordon Research Conference on Amyotrophic Lateral Sclerosis (ALS) and Related Motor Neuron Diseases.

September 2017

NEW! September 4-5, 2017. Symposium Latsis: Degeneration of Neural Circuits. Lausanne, Switzerland. Abstracts due: July 31, 2017.

September 7-9, 2017. Ottawa, Canada. Ottawa International Conference on Neuromuscular Disease and Biology. **Abstracts due: July 15.**

September 16-21, 2017. Kyoto, Japan. World Congress on Neurology.

September 17-19, 2017. Sitges, Spain. Neuro-Immune Axis: Reciprocal Regulation in Development, Health and Disease.

October 2017

October 3-5, 2017. Clearwater Beach, Florida. The 16th Northeast ALS Consortium Meeting. Abstracts due: August 4.

Organizing an ALS meeting? Contact us to add your conference to our updated calendar: ALSmeetings@prize4life.org.

Full List of Upcoming Meetings>>

Download the Working with ALS Mice Manual Here

STAY CONNECTED: