Ataxia MJD Research Project, Inc.

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Three scientists awarded MJD/SCA3 research grants

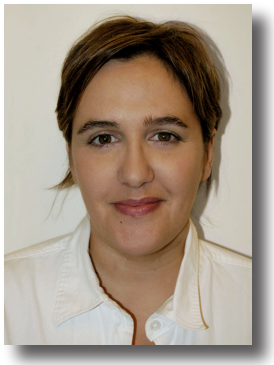
Randall Pittman, Ph.D.

Randall Pittman, Ph.D. professor at the University of Pennsylvania Medical School has been awarded $50,000 to conduct a study entitled, *Cell Penetrating Peptides as Vectors for Disrupting Pathogenic Interactions of Ataxin-3*. (Ataxin-3 is the protein responsible for MJD/SCA3.)

Dr. Pittman's goal is to use a cell penetrating peptide carrier to deliver peptides or protein domains into neurons of normal mice and rats to disrupt select interactions of ataxin-3 with proteins that may cause pathogenesis in MJD. Transgenic mice neurons will be used once Dr. Pittman has worked out the paradigms.

The specific focus will be the disruption of the interaction of ataxin-3 and VCP.

Characterizing cellular functions of ataxin-3 is critical for understanding pathogenesis and developing therapeutic interventions.



Patricia Maciel, Ph.D.

Patricia Maciel, Ph.D., assistant professor at the University of Minho in Braga, Portugal has been awarded $49,500 for research entitled, *Role of neuroinflammation in the pathogenesis and progression of Machado-Joseph disease: study of a mouse model*.

The goal of this study is to determine the role of the brain's immune system in Machado-Joseph disease. The hypothesis she is testing is that neurons expressing mutant ataxin-3 may send inappropriate signals to a specific type of cells named microglia, that are very important in the brain's response to insults. If these cells are inappropriately activated, as an attempt of the brain to respond to this insult, they may cause some damage to the neurons, thus contributing to their dysfunction and degeneration.

An additional aspect is that these activated cells may also be too sensitive to signals from the rest of the body, particularly when infections occur, and they could respond in an excessive manner to this situation, leading to brain inflammation. In this case, a usually "harmless" infection could in MJD patients be contributing to the faster progression of disease. This has been seen in other neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease.

They will test this hypothesis in a mouse model of Machado-Joseph disease they generated, which recapitulates several aspects of the human disease, including the loss of coordination of movements. If the hypothesis is true, then anti-inflammatory agents could be useful to delay the progression of this disease.

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Ilya Bezprozvanny, Ph.D., Associate Professor at The University of Texas Southwestern Medical Center has been awarded a $50,000 grant for his study, *Evaluation of dantrolene as therapeutic for SCA3/MJD1*.

Ilya Bezprozvanny, Ph.D.

Dr. Bezprozvanny's project is based on the discovery that mutant ataxin-3 protein has a direct effect on neuronal calcium signaling. Calcium is a universal messenger that plays a critical role in brain function.

He and his team reasoned that abnormal calcium signaling resulting from ataxin-3 mutation may cause degeneration of neurons in SCA3/MJD1 patients. To test this hypothesis they will evaluate the calcium inhibitor dantrolene in SCA3/MJD1 mouse models.

Results obtained from these experiments will provide insight into the connection between calcium signaling and neurodegeneration in SCA3/MJD1. Furthermore, their results may provide important information about the clinical efficacy of dantrolene for treating SCA3/MJD1.

Ataxia MJD Research Project, Inc. is a nonprofit organization operated by volunteers.

Since the formation of Ataxia MJD Research Project, Inc. in 1997, we have funded scientific research that includes: biochemical analysis of ataxin-3 misfolding, creation of an MJD transgenic mouse model, MJD zebra fish and MJD mouse model research, other mouse model work, and RNAi research.

Our funding has helped scientists learn more about MJD/SCA3 and helped them acquire critically important mouse models which they are working with today.

Because of your support, we are able to offer three grants this year. These grants will help highly-regarded MJD researchers move science towards finding a treatment or cure for MJD/SCA3.

Please help us continue funding this vital research by making a tax-deductible donation through PayPal on our website or by sending a check to the address below. Thank you.

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