

Accelerated Cure Project for MS

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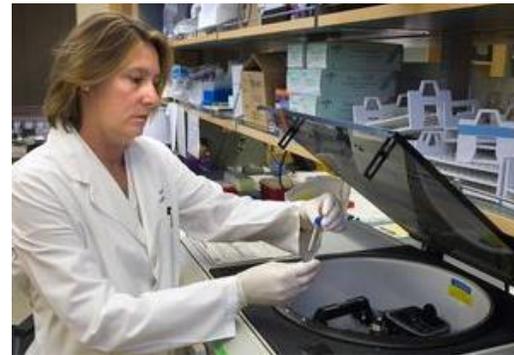


A Highlight from ACTRIMS 2019

by David Gwynne

Last month, members of the ACP team ventured to [ACTRIMS Forum 2019](#), in Dallas, Texas. This annual meeting focuses on the presentation of cutting edge research in MS and related demyelinating diseases.

Dr. Rhonda Voskuhl gave a wide-ranging presentation on several areas of the research from her lab at UCLA. This work included [transcriptome](#) (genetic) studies in an MS animal model, experimental autoimmune encephalomyelitis (EAE). The work used [RNA sequencing](#) to look at specific brain regions and tissues. This approach could be very useful for the discovery of pathways associated with disease, a potential source of new drug targets. Different tissues and cell types in the brain show significant [heterogeneity](#) with respect to gene expression changes during disease. A focus on [astrocyte](#) (a type of glial cell) gene expression showed differences between areas of the brain, such as cerebral cortex, cerebellum, hippocampus, and spinal cord. Pathway associated genes that showed disease related changes included genes encoding cholesterol synthesis proteins (decreased expression) and genes encoding immune response pathway components. Cholesterol is used in the synthesis of myelin and synapses. Dr. Voskuhl is extending her work into post-mortem samples from MS patients. This work also has the potential to provide novel disability and brain atrophy-associated biomarkers.



In the second part of her presentation, Dr. Voskuhl spoke about sex differences in disease and the urgent need to examine experimental results in both males and females, from preclinical animal models to studies in clinical subjects. Steroid hormones play a significant role in these differences. This is very relevant to MS where, to quote Dr. Voskuhl, “pregnancy is good for MS” (a 70% decrease in relapses is observed in pregnant women in their third trimester). She described some experimental results where the [estriol](#) pathways were examined in gene knockout EAE mice. Estriol has neuroprotective and anti-inflammatory effects. The estriol effects are lost when the estriol receptor (beta) gene is knocked out. There are several clinical trials ongoing to look at the effects of estriol in MS, in men and women. Continuing the sex differences theme, Dr. Voskuhl made the



observation that men are more likely to show a progressive disease course when compared to women. Her research results in EAE mice showed that EAE mice with an XY sex chromosome (male), vs. XX (female), showed greater clinical disease severity with more neuropathology. Her current research is looking at the mechanisms of this observation.

Interested in reading more from ACTRIMS? Dr. Farren Briggs and his team at Case Western Reserve University presented [four posters](#) at the conference. Each summarized interesting new information on such topics as the relationship between MS and comorbid autoimmune conditions, as well as risk factors for depression and disability in MS.