The role of microglia in Sandhoff disease pathology

Submitted by Prof. Tony Futerman, Weizmann Institute of Science, Israel

Microglia play key roles in brain development, and physiology during life and aging, and act as the immune cells in the brain. There is accumulating evidence that neuroinflammation plays critical roles in Tay Sachs and Sandhoff Disease pathologies and we have recently studied the roles of microglia in Sandhoff disease, in work funded generously by the NTASD.

We isolated microglia from the brains of a Sandhoff disease mouse model and in order to determine how these microglia function in disease, we examined their gene expression profile using a technique known as ‘RNAseq’. By doing so, we were able to identify profiles of gene expression in young mice which do not show overt disease symptoms, and in old mice, which are close to the end-stage of the disease. The figure below shows some of the pathways that are activated in the older mice. Whether any of these pathways are targets for therapeutic intervention awaits further analysis of the pathways.

Our findings indicate that different pathways are induced in microglia at the early stage compared with the late stage of the disease and pave the way for further study of the precise role of microglia in the development of Sandhoff disease. Further study of these pathways is ongoing and data will soon be collated for inclusion in one or two manuscripts.