Maria Traka, PhD - Research Project Summary, February, 2012

We have previously developed a genetic animal model of Canavan disease, the *Aspa*^{nur7} that allows us to investigate the mechanism that is responsible for the disease pathology, which specifically affects oligodendrocyes, the glial cells that produce myelin in the central nervous system (CNS). Our mouse model carries a mutation in the aspartoacylase gene that is mutated in Canavan disease patients and shows symptoms that significantly resemble the human disease. We have used this animal model to establish oligodendrocyte cell cultures in order to assess potential abnormalities in the mutant oligodendrocytes, which cannot express the aspartoacylase gene. We were able to demonstrate that mutant oligodendrocytes grown in cultures are normal as they showed absence of survival or developmental defects. Furthermore, we found that short-term or long-term exposure of the mutant oligodendrocytes to high levels of N-acetylaspartate (NAA) and the NAA glutamate derivative (NAAG) detected in the brains of the Canavan disease patients does not have a toxic effect in the mutant cells. Also, we have been able to identify a number of molecular changes that occur in the mutant oligodendrocytes. As a next step, the importance of these molecules in Canavan disease will be tested on the oligodendrocyte cell cultures. This approach is expected to help us identify candidate new molecules that could serve as therapeutic targets for treating Canavan disease patients.