**Characterization of Brain Morphology in Mucopolysaccharidosis Type IIIB Affected Mice Using Magnetic Resonance Imaging**

Gilkes, J.; Gibney, J. (Division of Hematology and Oncology, University of Florida); Sands, M. (Division of Oncology, Washington University in St. Louis, St. Louis, MO) and Heldermon, C. (Division of Hematology and Oncology, University of Florida)

**Introduction**

Mucopolysaccharidosis Type IIIB, a lysosomal storage disorder, results in the retention of heparan sulfate. This retention is associated with chronic brain inflammation and abnormal neuropathology, ultimately leading to severe neurodegeneration in affected individuals [1,2]. Characteristic features include increased permeability of the blood brain barrier and activated microglia. The focus of this project is to conduct a longitudinal study to assess changes in brain morphology of MPSIIIB mice with the 4.7 T and 11 T magnets in an attempt to determine what changes are measurable and which magnet produces optimal imaging results and will therefore be used in future studies. This research will not only provide new insight into morphological changes occurring in the brains of these affected mice over time, but it will also fill a long standing void in qualitative and quantitative analysis in this particular animal model.

**Experimental**

The MPSIIIB mouse model (-/-), provided in collaboration with Mark Sands, and control (+/-) will be employed in this study. Five mice from each genotype will be subject to MRI analysis using the 4.7 T magnet and the 11 T magnet. MRI analysis will be conducted when mice are two, five and eight months of age. Diffusion weighted-MRI is a preferential method of imaging since it is more sensitive to early changes in brain morphology after neuronal damage. In order to improve image detection and resolution, and assess for inflammation and blood brain barrier permeability, a gadolinium chelate based contrast agent will be used. Mice will be injected with 100 µl of 0.5 mol/L gadolinium chelate via tail vein catheter [3]. MRI images will also be take pre and post gadolinium chelate administration. Additional factors associated with MRI such as T1 and T2 relaxation time will also be evaluated during the procedure.

**Results and Discussion**

We have completed the scans for our mice but have not finished data analysis.

**Conclusions**

The experiment is feasible and the proper settings have been determined. We await final data analysis.

**Acknowledgements**

A portion of this work was performed at the National High Magnetic Field Laboratory, which is supported by National Science Foundation Cooperative Agreement No. DMR-1157490, the State of Florida, and the U.S. Department of Energy.

P01777-E001-AMRIS

**References**

1. Ausseil J, Desmaris N, Bigou S, Attali, R, Corbineau S, et al. (2008) Early Neurodegeneration Progresses Independently of Microglial Activation by Heparan Sulfate in the Brain of Mucopolysaccharidosis IIIB Mice. PLoS ONE 3(5): e2296. doi:10.1371/journal.pone.0002296
2. Garbuzova-Davis S, Louis MK, Haller EM, Derasari HM, Rawls AE, et al (2011) Blood-Brain Barrier Impairment in an Animal Model of MPS III B. PLoS ONE. 6(3): 16601. doi:10.1371/journal.pone.0016601
3. Petit A, Santin M, Bertrand A, Wiggins C, Petit F, et al (2011) Gadolinium-staining reveals amyloid plaques in the brain of Alzheimer’s transgenic mice. Neurobiology of Aging. Article in Press. doi: 10.1016/j.neurobiolaging.2011.03.009