Title of Presentation: Cerebral pathology in Glut1 DS model mice & effects on behavior

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Summary report:

Glucose Transporter-1 deficiency syndrome (Glut1 DS) is a debilitating neurodevelopmental disorder commonly caused by haploinsufficiency of the SLC2A1 gene and consequent low levels of its translated product, the Glut1 protein. Disrupting glucose supply to the brain has grim consequences, resulting in neuroglycopenia (low brain glucose) and cerebral energy failure. There is little to suggest how reduced Glut1 affects brain cells and causes cognitive dysfunction. Here we show that low Glut1 protein affects endothelial tip cells development and arrests cerebral angiogenesis, resulting in a profound diminution of the brain microvasculature. Moreover, Glut1 haploinsufficiency not only triggers a profound astrocytosis and microgliosis in the Glut1 DS brain, the neuro-inflammation occurring as early as 1 week old of age, but also reduces the number of neurons in the ventral posteromedial (VPM) thalamic nuclei of the mutant brain. Our studies also confirm that the learning and memory is impaired in Glut1 DS model mice. These observations emphasize the critical role of the Glut1 protein in early brain development. Identifying specific cell types and regions of the brain that are affected will shed important light on the spatial requirements for cerebral Glut1. Therefore, our results serve as an important step in the quest to effectively treat Glut1 DS.