**Complement Activation Leads to Worse Cognitive Outcomes Following Germinal Matrix Hemorrhage in a Chronic Mouse Model**

**Introduction**

Germinal matrix hemorrhage (GMH) is a common neonatal neurologic pathology that results in sequalae such as post-hemorrhagic hydrocephalus (PHH) and periventricular leukomalacia (PVL), likely secondary to post-hemorrhagic scarring and gliosis. The complement cascade has been established as a major player in secondary injury and subsequent development of gliosis. Here, we discuss the progressive cognitive and motor decline in animals following GMH and the protective role of a novel complement inhibitor, CR2Crry.

**Methods**

A neonatal mouse GMH model was created by injection of collagenase into the subventricular zone of post-natal day four (P4) pups. A control (injured) group was compared to animals treated with a complement inhibitor (CR2-Crry). Neurocognitive motor function and survival analysis was obtained on all animals up to 90 days of life. Histologic comparisons were performed at various time points up to 90 days, with a focus on inflammation and neuroprotection.

**Results**

A significant reduction in proportion of high-grade infarcts, bilateral ventricular involvement, and PHH (grade 5) was observed in CR2Crry-treated mice compared to control at the various time points up until 90 days. MR imaging was used at various time points (every 30 days) until 90 days, and revealed significant brain tissue sparing in animals treated with CR2Crry compared to controls. Barnes maze testing (behavioral) and CATWalk tests (motor) showed a higher rate of functional preservation in the treated animals. Histologic analysis of tissue showed reduced overall scar formation and inflammation in the treated animals.

**Conclusion**

There are currently no treatments for GMH targeting the inflammatory pathway leading to gliosis and PVL. A better understanding of the inflammatory pathway associated is essential for the development of a treatment to reduce the effects of the secondary injury. Our results show that complement activation is detrimental to brain development, CSF absorption, and functional development in a chronic GMH model.