Project Title: Quantitative MRI of myelin integrity in a mouse model of toxic demyelination
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An increasing understanding of the molecular processes regulating oligodendrogenesis and myelination raises the exciting possibility of regenerating myelin in MS. But biomarkers for remyelination trials are not sufficiently available, which greatly limits the potential success of translational studies. This is especially apparent in a lack of myelin-specific MRI endpoints that support translation between animal models and clinical trials. The quantitative MRI measures in this study allow direct translation to human MRI, where the same sequences are available and used by the principal investigator. Previously we have identified a physiological pathway for regulating oligodendrogenesis by increasing N-glycan branching of the platelet derived growth factor receptor (PDGFR) on oligodendrocyte precursor cells (OPC). The rate-limiting metabolite N-Acetylglucosamine is deficient in MS patients with severe disease, and blocking this pathway prevents myelin repair after acute inflammatory demyelination. If successful, MPM will allow seamless interpretation of effects between models and disease preclinical animal MRI and human clinical trial MRI, thereby greatly supporting translation of this pathway and other remyelinating therapies. The project will be instrumental to establish animal MRI for neurologic research at UCI, including a history of collaboration between the investigators.