Implication of autoantibodies against lactosylceramide in a neuroinflammatory disorder, EMRN

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Previous studies have shown that encephalomyeloradiculoneuropathy (EMRN) involves both central and peripheral nervous systems. The detailed molecular mechanisms of this disorder, however, still remain to be elucidated. Our previous study has demonstrated that EMRN patients exhibit autoantibodies against neutral glycosphingolipids, especially lactosylceramide (LacCer) in the acute phase of the disease and these autoantibodies disappeared after extensive immunomodulatory therapies, suggesting these autoantibodies can be an excellent biomarker for EMRN (Neurology, 2014). Intriguingly, a recent report indicated that astrocytes in plaque lesions of MS model mice extensively produce LacCer and its content was significantly upregulated in the lesions of both mice model and MS patients (Nat Med, 2014). In the present study, with LC/MS/MS analyses of cerebrospinal fluid (CSF), we found statistically significant increase of LacCer levels in CSF from EMRN patients than neurologically free individuals. Moreover, anti-LacCer antibodies induced the upregulation of inflammatory cytokines mRNA expression from cultured astrocytes. These data strongly suggest the same story as recently reported by Grabowsky's group on Gaucher disease also hold on EMRN, where they demonstrated that increased amount of glucosylceramide induced the production of autoantibodies against glucosylceramide and these autoantibodies in turn induce neuroinflammatory reactions (Nature, 2017). Thus, there should be some abnormalities in neutral glycosphingolipids metabolism, especially LacCer in EMRN patients and these abnormalities result in an alteration of the tuning in immune system of the patients, provoking neuroinflammatory reactions.