

MSc DEFENCE Thursday, July 5th, 2018

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Title: CD1D LIPID ANTIGEN PRESENTATION IN THE CENTRAL NERVOUS SYSTEM OF MULTIPLE SCLEROSIS

Time and location: 10:00 am PST; Blusson Spinal Cord Center (iCORD), Room 1220-1230 (Ground Floor), 818 West 10th Avenue, Vancouver, BC

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ABSTRACT

Background: Research into the diffusely abnormal white matter (DAWM) in archival MS brain tissue has shown that there is a lipid-specific depletion with preservation of myelin proteins within DAWM, implicating a response against myelin lipids in multiple sclerosis (MS). CD1, the Class I major histocompatibility complex (MHC)-like protein family, present lipid antigens to the immune system. CD1a, b, and d have been found in the central nervous system (CNS) of MS patients, yet to date no studies have quantified the presence of CD1d in tissues of the CNS.

Methods: Archival formalin-fixed, paraffin-embedded MS and healthy control brain tissues were sectioned and stained with luxol fast blue (LFB) for myelin, and HLA-DR (class II MHC). Lesions were categorized as either active, or chronic active, based upon the HLA-DR and LFB staining characteristics. Sections were stained for CD1d, ionized calcium-binding adapter molecule 1 (Iba-1, microglia), glial fibrillary acidic protein (GFAP, astrocytes), 4',6-diamidino-2-phenylindole (DAPI, nuclei), and Sudan Black B for myelin. Tissues were imaged using an epifluorescent microscope and lesions were outlined based on absence of myelin staining. CD1d-positive cells were quantified per mm² and the number of cells double labeling with Iba-1 or GFAP were noted.

Results: CD1d immunoreactivity was significantly increased in MS compared to healthy control tissue. CD1d-positive cells were more prevalent in areas of active demyelination in MS lesions, and colocalized primarily with GFAP-positive reactive astrocytes. The active edges of lesions contained CD1d-positive cells in similar numbers to active lesions but had significantly more CD1d-positive cells than the quiescent lesion centers. CD1d was also found occasionally within Iba-1 positive cells.

Conclusions: Our findings show increased CD1d in the CNS of MS patients, and demonstrating greatest expression in areas of active demyelination is novel and supports a lipid-targeted autoimmune process contributing to the pathogenesis of MS. CD1d is primarily localized to GFAP-positive astrocytes and highlights a role for these cells compared to only occasional CD1d-positive microglia.