Characterization of brain T cells in multiple sclerosis

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Research question and background

Genome-wide association studies and disease-modulating treatments strongly implicate a role of T cells in the pathogenesis of multiple sclerosis (MS). In striking contrast, the biology of T cells in the MS brain is poorly understood. We recently completed a first flow-cytometric analysis of lymphocytes derived from the human brain. We found that the human brain contains a unique local population of T cells with an effector-type phenotype and a low expression of cytolytic enzymes (Smolders et al, Acta Neuropathol 2013; 126(4):525-35). We hypothesize that dysregulation of the physiological surveillance of the central nervous system by T cells not only increases the odds of developing MS but also favors the formation of new MS lesions in patients. Currently, we aim to establish the phenotypic and functional profiles of T cells in normal-appearing white matter (NAWM) and white matter containing lesions of MS patients and in NAWM of control donors.

Methods and tissues used

Mononuclear cells isolated from white matter and paired peripheral blood of brain donors with MS (n=2) and without MS (n=7) were isolated by density gradient centrifugation and cryopreserved. Next, we analyzed the expression of markers for T cell differentiation, activation, proliferation, homing, tissue-residence, effector function and transcription factors by multi-color flow cytometry.

Results and conclusion

We found that T cells isolated from NAWM express markers of tissue-residence (CD69, CD103) and a selective set of chemokine receptors (CCR5, CXCR5). Furthermore, brain T cells are neither exhausted nor senescent, in a resting state, and contain moderate levels of transcription factors that direct effector molecules (T-bet, EOMES). Preliminary findings suggest that active MS lesions contain T cells, which have full cytotoxic function but a high expression of the co-inhibitory receptor PD-1. Inclusion of additional MS brains is required to confirm this possible correlation between T cell function and MS lesion activation state. In conclusion, we found that the human brain contains a specific pool of tissue-resident memory T cells, which are in a resting state but functionally equipped to respond upon antigen encounter.