Alterations in plasmablasts in the cerebrospinal fluid of patients with multiple sclerosis support a relation to Epstein Barr virus

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Abstract

Multiple sclerosis (MS) is the most common chronic autoimmune disease of the central nervous system. The prevalence of MS in Finland is one of the highest in the world, in the range of 100-200/100,000. Antibody production inside the central nervous system is a key finding in MS. By far the most important risk factor for MS is an infection with Epstein Barr virus (EBV) with an increase in the risk of MS by 32-fold. EBV is a common herpesvirus that after the primary infection remains latent in a subgroup of B cells. EBNA1 is the key protein responsible for the upkeep of latency of EBV in B cells. Here, we studied cerebrospinal fluid (CSF) samples collected from active MS patients at the diagnostic phase (n=4) and healthy controls (n=4) with 10X Genomics Chromium Single Cell Immune Profiling. Single cell level gene expression profiles were obtained after preliminary data processing and analysis by 10X Genomics Cell Ranger pipeline. Further analysis was performed in R with Seurat. Single cell RNAseq data was obtained for 7087 cells from all samples, with an average of 1018 (range: 709 - 1291) cells from MS patients, and 754 (range: 669 - 926) cells from controls. We evaluated cell type abundance differences after cell type annotation with SingleR. Here, plasmablasts (Wilcoxon Signed Rank Test, $P = 0.03$) were significantly more prevalent in MS patients than in controls. In the differential expression analysis, the expression of EBNA1 binding protein 2 was higher in the plasmablasts of the CSF of the patients compared to the controls ($P=0.03$). This suggests that the excessive proliferation of plasmablasts in the CSF of MS patients is related to alterations in the capability of B cells to facilitate EBV latency.