B cell repertoire expansion occurs in meningeal ectopic lymphoid tissue.

Abstract:

Ectopic lymphoid tissues (ELT) can be found in multiple sclerosis (MS) and other organ-specific inflammatory conditions. Whether ELT in the meninges of central nervous system (CNS) autoimmune disease exhibit local germinal center (GC) activity remains unknown. In an experimental autoimmune encephalomyelitis model of CNS autoimmunity, we found activation-induced cytidine deaminase, a GC-defining enzyme, in meningeal ELT (mELT) densely populated by B and T cells. To determine GC activity in mELT, we excised meningeal lymphoid aggregates using laser capture microscopy and evaluated B cell repertoires in mELT and secondary lymphoid organs by next-generation immune repertoire sequencing. We found immunoglobulin heavy chain variable region sequences that were unique to mELT and had accumulated functionally relevant somatic mutations, together indicating localized antigen-driven affinity maturation. Our results suggest that B cells in mELT actively participate in CNS autoimmunity, which may be relevant to mELT in MS and ELT in other chronic inflammatory conditions.