Characterization of tissue Transglutaminase expression in active white and grey matter MS lesions

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Background and Research question

Multiple sclerosis (MS) is a chronic neuroinflammatory disease which manifests with neurological deficits caused by inflammation, demyelination and axonal damage. A pathological hallmark is the infiltration of leukocytes into the central nervous system, which subsequently serve as a source of inflammatory mediators contributing to local activation of glial cells and further production of inflammatory mediators. Tissue Transglutaminase (TG2) is a multifunctional enzyme whose expression and activity is enhanced during inflammatory processes. Furthermore, TG2 is known to act as a beta-integrin co-receptor involved in cell-extracellular matrix (ECM) interactions (Akimov et al, JCB, 2000; Akimov and Belkin, Blood, 2001; Wang et al, JBC, 2012), and to be involved in cell adhesion and migration. We have previously shown that the expression of TG2 is increased in post-mortem material of MS patients, especially in active white matter lesions. Double labelling indicated co-localization with MHC-II expression, presumably of infiltrated monocytes/macrophages (manuscript submitted).
We now would like to further characterize the phenotype of these TG2 positive cells in active white matter lesions.

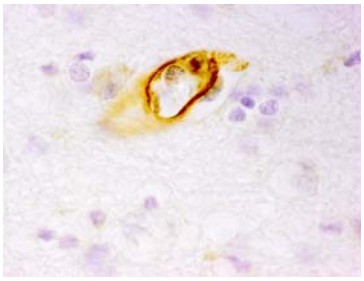
Methods and tissues used

The material used in this study is fresh frozen brain tissue (white matter) from Multiple sclerosis patients and healthy control donors. The tissue was used in immunohistochemical stainings for various markers present or potentially present in Multiple sclerosis.

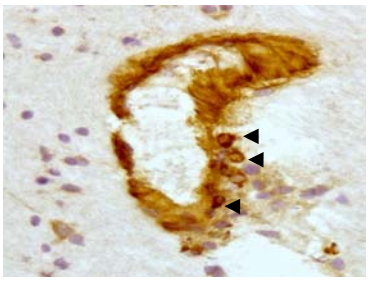
Results and conclusion

So far we worked on the confirmation of cellular TG2 immunoreactivity in active white matter lesions in addition to blood vessel expression, which is also shown in control patient derived tissue. We also stained T lymphocytes present in MS lesions and showed no co-expression of CD3 marker with TG2. Further experiments such as TG2 double staining with B cell and monocyte/macrophage/microglia markers will characterize TG2 positive cells in MS lesions in more detail.

TG2 in blood vessel white matter of control subject



Additional TG2 in white matter MS lesion (arrowheads)



TG2 (red) not in CD3 (T cells, green) in white matter MS lesion