TREM2 Presence in Margins of Ischemic Brain Lesions
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The microglia cell surface receptor, TREM2 (triggering receptor expressed on myeloid cells 2) has been identified as a marker for an "anti-inflammatory" state for microglia. Mutations of TREM2 are associated with polycystic disease states (PLOSL) and recently with a small subset of cases with Alzheimer's disease. Lack of TREM2 interferes with the phagocytic role of microglia in the removal of plaques in a mouse model of AD. In the role of TREM2 in the removal of apoptotic cells, the sequelae of events depart from those of "customary" inflammatory means. TREM2 is expressed on microglia cells surface ~300 times more than on astrocytes. In our study to evaluate available antibodies against markers of different activation states of microglia, an antiTREM2 antibody (Lifespan Biosci.) was applied to brain sections from rats in which the middle cerebral artery had been occluded for 2 hours and then allowed to survive 3, 7 and 14 days. At the margin of the ischemic area, where both astrocytes and microglia were prolific and highly hypertrophied, TREM2 positive staining was found as a fibrous meshwork, appearing more astrocyte-like than microglia. Double staining for GFAP and TREM2 displayed colocalization in the TREM2 positive meshwork. That is, TREM2 positive fibers were also positive for GFAP. No TREM2 staining was observed in unaffected regions. Double staining for TREM2 and Iba1 showed cohabitation, but no Iba1 positive profiles were fibrous or costained for TREM2. The location of TREM2 at the ischemic zone margin suggests, rather simplistically, a possible merging of phagocytic function of both astrocytes and microglia. In other studies the presence of TREM2 has already been noted in the margin of ischemia/infarction, but not with a costaining of astrocyte positive structures. For those studies the TREM2 antibody was from a different source. Other markers associated with TREM2 activation, reactive astrocytes, and microglia should be sought to elucidate this novel appearance of TREM2 immunoreactivity in this model of stroke.

Summary
- TREM2 staining colocalized with astrocyte structures but not with structures of microglia.
- Profiles that were only TREM2 positive were closer to the margin and in the center of the lesion.
- No obvious differences were perceived across the survival times.
- Shorter survival times might reveal the genesis of the staining patterns.

Contradiction in staining patterns: Different TREM2 antibodies against TREM2 yielded staining of different features. The antibody used here was goat polyclonal # LS C150090 LifeSpan Biosciences with epitopes in aa19-174 span. Other antibodies stained different structures including neurons. Regardless of human-rat epitope differences, the LS antibody against TREM2 reveals structures in damaged brain that, to our knowledge, have not been seen with other methods. Extending the application of this antibody to other forms of brain damage may yield insights for the identification of new therapeutic targets.