Neuroimmunology Group

Professor Trevor Owens

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The group's research interests

The Neuroimmunology group study pathogenic mechanisms of inflammatory diseases of the central nervous system (CNS), such as multiple sclerosis (MS) and neuromyelitis optica (NMO). We mainly focus to mouse models and we use histological, flow cytometric, molecular, (RNA-analysis) and tissue culture methods to evaluate immuno- and neuropathogenesis in genetically-modified mice. We study interactions between the immune system and glial cells of the nervous system, both those that lead to pathology as well as with regulatory and protective outcomes. We are particularly interested in translating clinical observations to experimental analyses and we collaborate with groups in Region Syddanmark to understand how innate and adaptive immune cells and mediators contribute to neurological disease.

Contact present / former students

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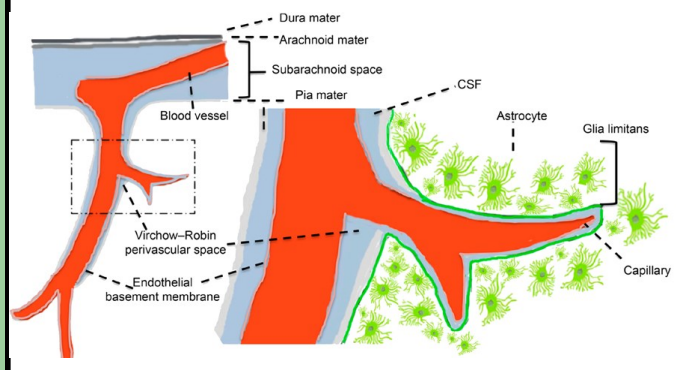
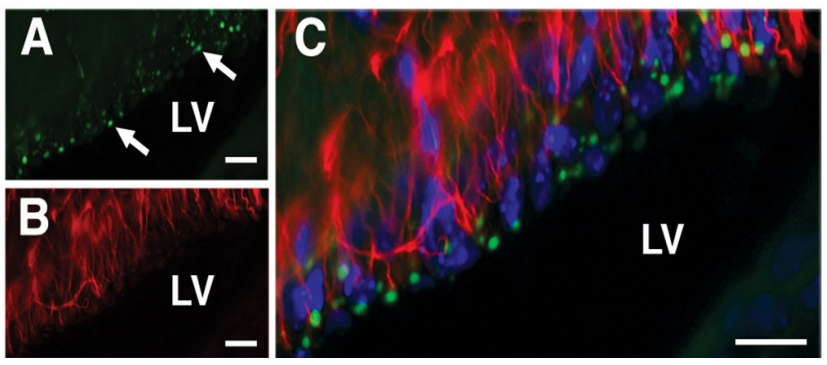
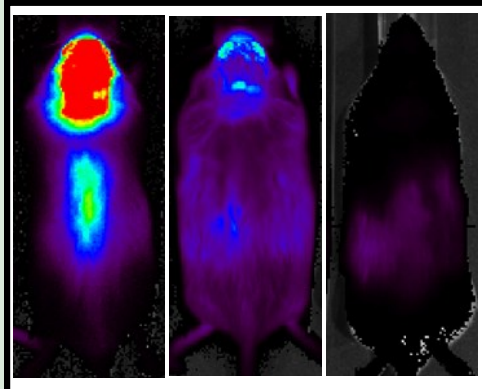


Schematic presentation of subpial vasculature in relation to subarachnoid space and brain parenchyma, showing relevant anatomical structures including the pial vessel, subarachnoid space, the Virchow-Robin space and the subpial glia limitans surrounding penetrating vessels into the brain (from Asgari et al, Annals Clin Trans Neurol 2:857 (2015)).



Fluorescent micrograph showing antibody-induced complement deposition (green) around the lateral ventricle (LV) of a mouse that had 7 days previously received immunoglobulin G purified from a patient with NMO. The red cells are astrocytes, the blue staining shows nuclei (from Asgari et al, J. Neuroimmunol 254:76 (2013))



In vivo imaging of transgnic mice that express luciferase at the interferon-beta locus. The mice are responding to injection to the brain of reagents that trigger signaling via innate receptors. (see Khorooshi et al, Acta Neuropathol (2015)).

Project examples

Glial signals in immune CNS interactions	Glial response to inflammation can both promote or modulate pathology. Both microglia and astrocytes are implicated in the pathogenesis of MS and NMO. Microglia are resident macrophage-like cells that can present antigen to T cells. Astrocytes contribute to integrity of the blood-brain barrier and of the synapse. Both cell types express receptors that recognize epitopes associated with tissue damage or infection, or endogenous hormones such as Angiotensin II, and can produce regulatory cytokines and chemokines. Projects are available to study signaling in microglia and astrocytes and how these signals contribute to pathological outcome. Cells will be isolated from mice or analyzed in situ by histology and signaling will be analyzed using molecular and histological methods.
Antibodies in neurologic diseases	Antibodies are a prominent feature of MS and are believed to directly cause pathology in NMO, where they recognize Aquaporin-4 expressed by astrocytes. Antibody+complement mediated cytotoxicity is implicated in demyelination in MS and NMO. We study how antibodies mediate demyelination and how this can be prevented. Other questions include how antibody accesses myelin within the central nervous system, and how complement expression is controlled in the CNS. We use animal models to assay effect of antibodies transferred from patients. Projects are available to study molecular and cellular mechanisms of antibody-mediated inflammation and demyelination using these experimental systems.
Regulation of autoimmunity in the CNS	Inflammatory T cells are implicated in induction of pathology in MS. CD4+ and CD8+ T cell subsets are defined on the basis of the cytokines they produce. Within the CNS interaction with DC or with microglia can modulate cytokine profiles. Microglia can produce immunoregulatory cytokines and we need to understand how this is controlled. Interactions between T cells and DC in the thymus can also abrogate autoimmunity. Projects in this area will exploit transgenic mice and viral vectors for selective expression and induction of cytokines, chemokines and their receptors in experimental autoimmune encephalomyelitis, a model for MS.