Project B3: MMP-2 and MMP-9 in penetration of the CNS parenchymal in murine EAE; functional analyses and molecular *in vivo* imaging

Research areas: Neuroinflammation, Molecular imaging

Project summary: During leukocyte infiltration of the CNS, immigrating cells must transmigrate the endothelial cell monolayer and its underlying basement membrane (BM) and the subjacent parenchymal BM with its associated ensheathing layer of astrocytes endfeet before they gain access to the CNS parenchyma. Studies on murine MOG35-55 induced EAE have shown that these are distinct steps that are independent of each other and that disease symptoms become apparent only upon penetration of the parenchymal border, indicating that it is a crucial disease-limiting step. MMP-2 and MMP-9 activity correlate with sites of leukocyte penetration of the parenchymal border and MMP-2/MMP-9 DKO mice are resistant to EAE (Agrawal et al., 2006); MMP-2/MMP-9 activity is therefore a good indicator of active leukocyte migration into the CNS and the extent of ongoing inflammation in the CNS. However, the precise source of MMP-2/MMP-9 and their modes of action remain poorly studied. The aims of this project are therefore (1) to define the cellular source/s of MMP-2/MMP-9 and their relative contribution to EAE and (2) to exploit the MMP-2/MMP-9 data for development of PET- and SPECT-based imaging strategies for identification of active lesions in living mice and, eventually, patients.

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