The blood-brain barrier (BBB) maintains homeostasis within the central nervous system (CNS) to safeguard neuronal function. In multiple sclerosis (MS) the function of the BBB is disturbed which contributes to neuroinflammation. Under normal conditions, astrocytes closely interact with the BBB to maintain barrier properties. Neuroinflammation in MS results in a reactive astrocyte phenotype that can both contribute to, and dampen inflammatory signalling.

We sought to elucidate the protective properties of reactive astrocytes. We previously showed the importance of the Vitamin A metabolite retinoic acid (RA) in BBB function during CNS development. Our recent analyses reveal that RA counteracts the deleterious effects of inflammatory cytokines on BBB function in vitro, and induces general immune quiescence in brain endothelium. To investigate the role of RA in neuroinflammation, we analysed the synthetic pathway of RA in MS. Our data indicate that reactive astrocytes in MS lesions re-express the enzyme responsible for RA synthesis. Using primary human astrocytes, we were able to reproduce inflammation-induced RA release, and show that this is an endogenous response to inflammation. Ongoing research focuses on the mechanism by which astrocyte-derived RA can protect the inflamed BBB, pointing to antioxidant pathways as downstream mediators.

Understanding the regulation of RA levels in the CNS by astrocytes and the effect on the BBB may lead to the development of therapies that restore the BBB and reduce the inflammatory cascade in MS lesions.