**Introduction**

Numerous studies have shown that the pathogenesis of multiple sclerosis (MS) is mediated by autoimmune inflammation, which results in oligodendrocyte degeneration, demyelination, gliosis and axonal damage. In line with this, genome-wide association studies (GWAS) in MS patients show an overrepresentation of immunologically relevant genes. Other studies, however, have proposed that brain intrinsic degeneration is the initial factor driving lesion formation. Thus, it is tempting to speculate that immunologically relevant genes are expressed not only by immune cells but also by brain cells. Their expression might contribute to immune cell recruitment and thus lesion formation.

**Results**

**Cuprizone-induced metabolic injury mirrors pathology of early MS lesions**

![Cuprizone-induced metabolic injury mirrors pathology of early MS lesions](image)

**Figure 1** Histopathological characteristics of inflammatory forebrain lesions in Cup/EAE mice. Immune cell invasion (shown by anti-CD4 stain and anti-CD3 stain) induces focal demyelination (shown by LFB/PAS stain), which is paralleled by breakdown of the glia limits perivascularis (shown by anti-GFAP stain (Rüther et al. 2017)).

**Intrinsic degeneration induces the expression of immunologically relevant genes**

![Intrinsic degeneration induces the expression of immunologically relevant genes](image)

**Figure 2** Gene transcription of immunologically relevant genes in cuprizone-treated mice. (A) Evaluation of Affymetrix GeneChip arrays shows that several immunologically relevant genes are upregulated in the corpus callosum after 1 week cuprizone intoxication. (B) Early Cd44 mRNA induction during cuprizone intoxication (p<0.001).

**CD44 expression during cuprizone-induced demyelination**

![CD44 expression during cuprizone-induced demyelination](image)

**Figure 3** Protein and mRNA expression of CD44 in cuprizone-treated mice. (A) CD44 expression correlates with treatment duration and peaks at the time of complete demyelination (5 weeks). (B) mRNA expression levels of Cd44 after 5 weeks cuprizone treatment. (C) CD44 is strongly induced at abluminal sites, but not by endothelial cells. Arrowhead marks the abluminal glia limits perivascularis; arrow marks the endothelium.

**Intrinsic degeneration triggers immune-cell recruitment**

![Intrinsic degeneration triggers immune-cell recruitment](image)

**Figure 4** Histopathological characteristics of inflammatory forebrain lesions in Cup/EAE mice. Immune cell invasion (shown by anti-CD4 stain and anti-CD3 stain) induces focal demyelination (shown by LFB/PAS stain), which is paralleled by breakdown of the glia limits perivascularis (shown by anti-GFAP stain (Rüther et al. 2017)).

**Discussion**

This study demonstrates that a classical immunologically relevant gene (CD44) is expressed by brain and immune cells in two different MS relevant models. Expression of immunologically relevant genes, such as CD44 by glia cells might explain their overrepresentation in GWAS and might regulate MS lesion formation.

**Literature**


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