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Short communication

GPCRs in Oligodendrocyte Differentiation and Myelin Regeneration

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Introduction

Multiple sclerosis (MS) is an autoimmune disease that results in inflammatory damage to the central nervous system and causes disability in young adults. The pathogenesis of MS is characterized by a cascade of pathological events, involving the activation of the immune system, infiltration of lymphocytes, activation of microglia, focal inflammatory demyelination and axonal damage. Currently available treatments for MS all target the immune system with mechanisms of action including general immunosuppression/immunomodulation and blockade of immune cell infiltration into the CNS. Although effective in reducing the relapse rate and the formation of new lesions, these drugs, however, have very limited effects in preventing the progression of disability. Promoting oligodendrocyte progenitor cell (OPC) differentiation, remyelination and subsequent functional recovery of the neurons have been proposed to be the new direction of MS therapy. To identify targets and pathways that regulate myelin regeneration is of great interest.

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In our early studies, we've discovered that two G protein-coupled receptors (GPCRs), CysLT1 and A2B (Wang et al., 2011; Wei et al., 2013), are critically involved in the development of MS by regulating the differentiation or function of immune cells. Blocking these receptors alleviates clinical symptoms of EAE, a mouse model of MS, indicating these receptors are potential drug targets for MS. Recently, we screened a number of GPCRs in OPC to oligodendrocytes differentiation, and demonstrated that several GPCRs, including KOR and GPR149, are important for oligodendrocyte-mediated remyelination in demyelinating disease models, suggesting KOR and GPR149 (Du et al., 2016; Suo et al., 2022) might be a target to develop new MS therapies from a regenerative point of view.

Conclusion

GPCR may regulate OPC differentiation and myelin formation, they might be useful targets to develop drugs in treating MS from a regenerative point of view.

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