# Dysregulation of GPR17, a new key actor involved in oligodendrogenesis, in a rodent model of Multiple Sclerosis: implications for re-myelination strategies

G.T.Coppolino[1], D. Lecca[1], D. Marangon[1], F.Viganò[2], G. Menichetti[1], M. Fumagalli[1], E. Bonfanti[1], R. Furlan[3], L. Dimou[2], M.P. Abbracchio[1]

[1]Dept. of Pharmacological and Biomolecular Sciences, University of Milan, Italy
[2]Physiological genomics, Institute for Physiology and Ludwig-Maximilians University Munich, Germany
[3]San Raffaele Scientific Institute, Milan, Italy

GPR17 is a membrane receptor activated by uracil nucleotides and cysteinyl-leukotrienes, mediators involved in inflammatory responses in the CNS (Ciana et., 2006). Under physiological conditions, GPR17 is expressed in Oligodendrocyte Precursor Cells (OPCs), with maximal levels in immature oligodendrocytes and progressive downregulated in terminally differentiating cells (Fumagalli et al., 2011). A marked GPR17 up-regulation has been found in rodent models of cerebral trauma, ischemia and in lysolecithin induced focal demyelination (Lecca et al., 2008, Boda et al. 2011). Little is known about GPR17 alterations in a primary demyelinating disease such as multiple sclerosis (MS). This work was aimed at characterizing GPR17 expression pattern in acute Experimental Autoimmune Encephalomyelitis (EAE) mice, a murine MS model. Immunohistochemical analysis revealed that, although the total number of $GPR17^+$ cells was reduced in spinal cord white matter (likely due to generalized tissue loss), numerous $GPR17^+$ cells accumulated around demyelinating lesions in close vicinity to activated inflammatory cells (microglia and blood-derived infiltrated monocytes/macrophages). Real-time PCR analysis confirmed GPR17 up-regulation suggesting disease-induced OPC recruitment and proliferation. The availability of an inducible reporter GPR17-iCreER$^{T2}$xCAG-GFP mouse line for fate mapping studies recently allowed us to directly visualize the behaviour of $GPR17^+$ cells in the acute EAE phase. Data confirmed a strong increase of $GFP^+$ cells at the sites of demyelinating lesions. Future studies in this mouse line will define the final fate of the GPR17 expressing $GFP^+$ cells, with implications for developing new remyelinating strategies for MS.

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