C.3. BRIEF DESCRIPTION OF THE RESEARCH IN LAYMAN'S TERMS, AIMED AT THE GENERAL PUBLIC

The four major brain-specific cell types are: (i) neurons, which transmit and process information via electrical signals, (ii) oligodendrocytes, which insulate neuronal axons with fatty sheets called myelin to ensure fast and complete electrical signal transduction, (iii) microglia, which provide defence against potential infections in the brain and, (iv) astrocytes, which provide metabolic support for neurons and ensure their proper functioning, are involved in immune defence and maintain healthy microenvironment in the brain. These cells, and indeed all living cells, have a wide range of proteins called receptors on their surface, which are activated by signalling molecules. EBI2 is one such receptor that plays very important roles in the biology of immune cells, where it regulates antibody production to fight infections[1, 2]. This research, aims to investigate whether the presence of EBI2 changes during maturation of oligodendrocytes. We will investigate whether EBI2 receptor is involved in regulation of physiological functions of oligodendrocytes, such as intercellular signalling or motility, and myelination of neurons.

So far studies on EBI2 receptor focused on its role in the cells of the immune system such as B cells/plasmocytes[1-3]. Significance of this receptor's presence and role in the brain has been unknown. Our recent studies suggest that EBI2 and its signalling molecule (oxysterol 7α25HC) may be involved in the onset and progression of neurodegenerative diseases of cerebrum and vertebral spine[4-7]. Therefore, it is important to learn how functional status of this receptor and its signalling pathway in the brain may modify the progress of these diseases. Its predictable application for the control of diseases will also be considered.

My research so far has shown that EBI2 is present on the surface of astrocytes[5] and oligodendrocytes *(unpublished data)* and that it does play a role in the immune function in the brain[4]. EBI2 activation promotes astrocytes migration[5] and attenuates release of harmful pro-inflammatory molecules called cytokines *(unpublished data)*. The EBI2 receptor is also capable of promoting astrocyte responses to infections, by releasing molecules that attract immune cells into the brain to help fight such pathologic conditions[4]. Our findings also indicate, that the EBI2 receptor may be necessary for appropriate and timely myelination of neurons by oligodendrocytes[7]. Activation of EBI2 receptor can also protect the neuronal cells against chemically induced demyelination[6]. The proposed research will allow us to further investigate the function of EBI2 in the brain, specifically in oligodendrocytes, and also, for the first time, will study the function of the receptor in live animals that have been subjected to demyelination.

Findings resulting from proposed project are important because they will provide new facts on the role of the EBI2 receptor in the brain, and particularly about its regulatory functions in oligodendrocytes. The experiments using the animal model will give us a unique insight into the pathomechanisms of demyelinating neurodegenerative diseases such as multiple sclerosis. Knowledge of these pathomechanisms may pave the path for development of new pharmaco-immunological approaches controlling oligodendrocyte function limiting or enhancing processes of myelinisation.

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