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A novel immune role for NgR on B-cell population localized in the central nervous system in a mouse model of multiple sclerosis

Despite clear evidence demonstrating that the deletion of Nogo-receptor 1 (NgR1) can protect against axonal degeneration and thus progression of experimental autoimmune encephalomyelitis (EAE), an immunological role for this receptor is yet to yield mechanistic evidence. However, recently NgR has been suggested as an alternate receptor for the B-cell activating factor (BAFF) in the central nervous system (CNS). Therefore, our strategic aim was to define whether NgR contributes in the modulation of the adaptive immune response during EAE by promoting maturation and differentiation of BAFF reactive B-cells within the follicles during the induction of disease. The results showed that CNS-infiltrating blood cells revealed an augmented response in the B-cells, which expressed NgR1 and NgR3, observed in *ngr1+/+* mice with the onset and progression of the disease that could not be demonstrated within the spinal cords of EAE-induced *ngr1-/-* mice. Remarkably, a cluster of B-cells-expressing NgR was present at the meninges of lumbosacral spinal cords of the *ngr1+/+* EAE-induced mice at clinical score 1. Furthermore, there was a significant increase of secreted immunoglobulins from these NgR1-expressing B-cells. Importantly, these cells could be directed into the synthesis phase of the cell cycle, after stimulating sorted cells by extracellular BAFF *in vitro*; however, when BAFF signaling was blocked using either rBAFF-R, or NgR1-Fc, or NgR3 peptides, the cells were observed to be into G0/G1 phase. As a consequence, when we blocked NgR1- ligand signaling using a novel hematopoietic stem cell based delivery of a therapeutic protein, immune lineage differentiated cells, including Zs green and fusion protein, were trafficking into the CNS during acute EAE. Collectively, these data indicate that the existence of an inducible expression of NgR1 and NgR3 in specific immune lineage cells upon the induction of EAE and that the follicular-like NgR1 and NgR3-positive B-cells in the meninges may play an active role during the induction of EAE. Thus, our data reinforce the idea that is blocking the interaction of BAFF and NgR1 and NgR3 may be vital for neuroprotection during inflammatory insults.

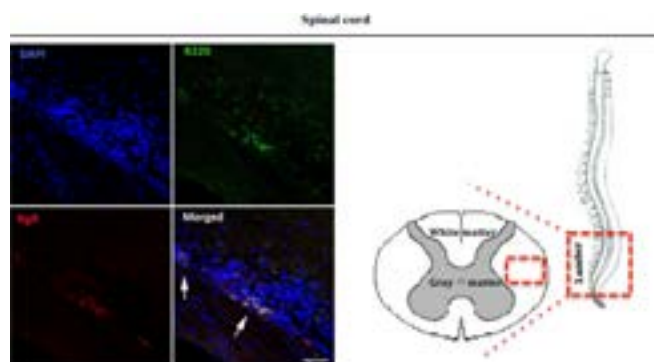


Figure1: Localisation of double-immunofluorescence staining (NgR1-positive B-cell clusters) on 10 µm-thick longitudinal spinal cord sections during EAE in *ngr1+/+* EAE-induced mice at clinical score 1. Anti- B220 and anti-NgR antibodies have been used to stain B-cells (green fluorescence) and NgR (red fluorescence) respectively. Infiltrate cells were present at the meninges of *ngr1+/+* mice during disease onset. Double-positive cells were aggregated and presented in follicles at the meninges (the white arrows), magnification 40x, scale bar= 50

Recent Publications

1. Bakhuraysah M M, Siatskas C and Petratos S (2016) Hematopoietic stem cell transplantation for multiple sclerosis: Is it a clinical reality? *Stem Cell Res Ther.* 7:12.
2. Alrehaili A, Lee J Y, Taghian K, Mahabakhuraysah, Thomas Speros and Petratos S (2014) Microglial mechanisms governing axonal degeneration in multiple sclerosis: a pathological perspective. *J Neurol Neurophysiol.* 5(3):1-8.
3. Mokhtar S H, Bakhuraysah M M, Cram D S and Petratos S (2013) The beta-amyloid protein of Alzheimer's disease: communication breakdown by modifying the neuronal cytoskeleton. *Int. J. Alzheimers Dis.* 2013:910502.
4. Litwak S A, Payne N L, Campanale N, Ozturk E, Lee J Y et al. (2013) Nogo-receptor 1 deficiency has no influence on immune cell repertoire or function during experimental autoimmune encephalomyelitis. *PLoS One.* 8(12):0e82101 .

Biography

Maha Bakhuraysah has her expertise in evaluation and passion in improving the health and wellbeing. Her research focuses on the role of the Nogo receptor in multiple sclerosis, and author is working with experimental autoimmune encephalomyelitis (EAE). Previous data has mentioned that there was no new role associated with Nogo receptor, thus she has focused on the immunological arm in this model and author has discovered the existence of B-cells expressing NgR in EAE. It has been published recently that in MS patients' B cells are localized in the brain, and we found it in mice. The studies haven't mentioned anything about the Nogo receptor but author has found them too.

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