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

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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 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 lumbar spinal cords of the of ngr1−/− EAE-induced mice at clinical score 1. Furthermore, there were significant increases 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 ZsGreen 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 blocking the interaction of BAFF and NgR1 and NgR3 may be vital for neuroprotection during inflammatory insults.

Recent Publications


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, she and her team are working on Experimental Autoimmune Encephalomyelitis (EAE). Previous data has mentioned that there was no new role associated with Nogo receptor, thus she focused on the immunological arm in this model and discovered the existence of B-cells expressing NgR in EAE. It has been published recently that in MS patient’s B cells are localized in the brain, which she and her team found it in mice. The studies haven’t mentioned anything about the Nogo receptor, but she and her team found them too.