Neuronal IFN-beta–induced PI3K/Akt-FoxA1 signaling is essential for generation of FoxA1+Treg cells

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Neurons reprogram encephalitogenic T cells (T(enc)) to become regulatory Treg cells FoxP3+Treg or FoxA1+Treg. We reported previously that neuronal ability to generate FoxA1+Treg was central to preventing neuroinflammation in experimental autoimmune encephalomyelitis (EAE). Mice lacking the cytokine interferon (IFN)β were defective in generating FoxA1+Treg in the brain. Neuron-induced FoxA1+Treg were capable of preventing chronic and demyelinating EAE in mice lacking IFNβ. Here we show that lack of neuronal IFNβ-signaling was associated with lack of neuronal expression of program death-ligand1 (PDL1), which also prevented their ability to reprogram T(enc) cells to FoxA1+Treg. Transfer of IFNβ-competent encephalitogenic T cells to mice lacking IFNβ or its receptor IFNAR in the brain (NesCre:Ifnarfl/fl) led to the absence of FoxA1+Treg generation and aggravated neuroinflammation. We identified that IFNβ activated neuronal PI3K/Akt signaling. Phosphorylated Akt consequently bound to transcription factor FoxA1, which upon translocation to the nucleus induced neuronal PDL1 expression. Conversely, inhibition of PI3K/Akt, or FoxA1 and PDL1 knock-down blocked neuronal ability to generate FoxA1+Treg. Our study identified crucial molecular player's central for neuronal ability to reprogram pathogenic T-cells and to generate FoxA1+Treg, which could be a therapeutic target to prevent neuroinflammation.

Biography

Yawei Liu has a medical doctor background and has been doing medical research for more than 10 years. Since her Ph.D., she mainly focused on the role of neurons in the regulation of auto-reactive T cells and central nervous system (CNS) inflammation. We reported a novel function for neurons as being highly immune-competent cells, based on their crucial role in the regulation of T-cell responses and CNS inflammation in models of multiple sclerosis

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