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## NEURONAL IFN-BETA—INDUCED PI3K/AKT-FOXA1 SIGNALING IS ESSENTIAL FOR GENERATION OF FOXA1<sup>+</sup>TREG CELLS

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**N**eurons reprogram encephalitogenic T cells (T<sub>enc</sub>) to become regulatory T<sub>reg</sub> cells FoxP3<sup>+</sup>T<sub>regs</sub> or FoxA1<sup>+</sup>T<sub>regs</sub>. We reported previously that neuronal ability to generate FoxA1<sup>+</sup>T<sub>regs</sub> was central to preventing neuroinflammation in experimental autoimmune encephalomyelitis (EAE). Mice lacking the cytokine interferon (IFN)β were defective in generating FoxA1<sup>+</sup>T<sub>regs</sub> in the brain. Neuron-induced FoxA1<sup>+</sup>T<sub>regs</sub> 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<sub>enc</sub> cells to FoxA1<sup>+</sup>T<sub>regs</sub>. Transfer of IFNβ competent encephalitogenic T cells to mice lacking IFNβ or its receptor; IFN AR in the brain (*Nes<sup>Cre</sup>:Ifnar<sup>fl/fl</sup>*) led to the absence of FoxA1<sup>+</sup>T<sub>regs</sub> 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<sup>+</sup>T<sub>regs</sub>. Our study identified crucial molecular player's central for neuronal ability to reprogram pathogenic T-cells and to generate FoxA1<sup>+</sup>T<sub>regs</sub>, 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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