EuroSciCon

May 10-11, 2018
Frankfurt, Germany

JOINT EVENT
22nd Edition of International Conference on
Immunology and Evolution of Infectious Diseases
&
12th Edition of International Conference on
Tissue Engineering and Regenerative Medicine

Yawei Liu et al., J Transm Dis Immun 2018, Volume 2
DOI: 10.21767/2573-0320-C2-005

NEURONAL IFN-BETA–INDUCED PI3K/AKT-FOXA1 SIGNALING IS ESSENTIAL FOR GENERATION OF FOXA1^{+}TREG CELLS

Yawei Liu[1], Andrea Marin[1], Patrick Ejlerskov[1], Louise Munk Rasmussen[1], Marco Prinz[2, 3] and **Shohreh Issazadeh-Navikas[1]**

[1]BRIC - University of Copenhagen, Denmark
[2]Institute for Neuropathology - University of Copenhagen, Germany
[3]Centre for Biological Signaling Studies - University of Copenhagen, Germany

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

Yawei.liu@bric.ku.dk