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Session Title : Regulatory T cells in transplantation

Interferon-beta and regulatory T cells in allograft rejection

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Type I interferons (IFNs) have immunosuppressive functions. We now know their underlying mechanism, which we could harness in transplantation. Type I IFNs are pleiotropic cytokines with potent antiviral properties that also promote protective T cell and humoral immunity. Paradoxically, type I IFNs, including the widely expressed IFNβ, also have immunosuppressive properties, including promoting persistent viral infections and treating T-cell-driven, remitting-relapsing multiple sclerosis. Although associative evidence suggests that IFNβ mediates these immunosuppressive effects by impacting regulatory T (Treg) cells, mechanistic links remained elusive to date. Our studies using genetic conditional deletion models and *in silico* computational models have found that:

- IFNβ enhances graft survival in a Treg-cell-dependent murine transplant model
- Extended allograft survival was Treg cell-mediated and required IFNβ signaling on T cells.
- IFNβ directly promoted Treg cell murine and human induction via STAT1- and P300-dependent Foxp3 acetylation

WHY IT MATTERS

- These findings identify a mechanistic connection between the immunosuppressive effects of IFNβ and Treg cells, with therapeutic implications for transplantation, autoimmunity, and malignancy.