

Wednesday, March 5th, 2014

LSC 3 - Life Sciences Centre

2350 Health Sciences Mall

12-1pm



Dr. Mark Scott

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“Resetting the Immune System via miRNA-Based Therapeutics: Therapeutic Efficacy in Murine Type 1 Autoimmune Diabetes”

Autoimmune diseases affect virtually all tissues and organ systems and encompass such diverse diseases as type 1 diabetes (T1D), Crohn’s disease, multiple sclerosis and rheumatoid arthritis. A key cellular mediator of autoimmune diseases is the T lymphocyte. Extensive autoimmune disease research has demonstrated that T Regulatory (Treg) cells are downregulated while T Effector cells (Teff; e.g., Th1 and Th17 cells) are upregulated (i.e., reduced Treg:Teff ratio) leading to a chronic pro-inflammatory state. While current therapeutic interventions partially target this imbalance in the Treg:Teff cell ratio, these drugs are characterized by significant toxicity. Using a cellular bioengineering approach, we have generated an exogenously sourced microRNA (miRNA) based therapeutic (CBS-TA1) that effectively, persistently and safely modulated the Treg:Teff cell ratio yielding a tolerogenic/ anergic state both in vitro and in vivo. In both normal and autoimmune murine models, the miRNA-based CBS-TA1 systemically increased Treg, while concurrently downregulating Teff, T cell subpopulations. In the NOD mouse model of Type 1 autoimmune diabetes, a single treatment of TA1 at 7 weeks of age significantly reduced both disease incidence and age of onset and was correlated with a significant increase in the Treg:Teff cell ratio.

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