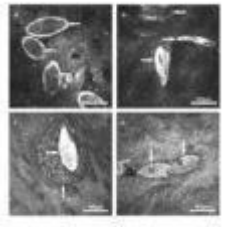
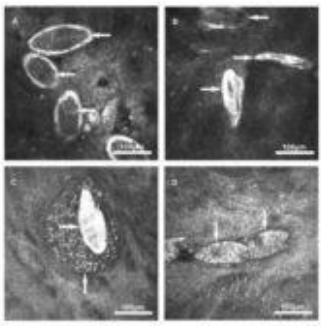
Type I interferons are important in anti-helminth Th2 immunity





Confocal images of Schistosoma eggs (Holtfreter et al., 2011. PlosOne)

Type I interferons (IFN) have been traditionally associated with innate immune defences against viruses and bacteria which ultimately result in Th1/17-type adaptive immune responses. Although a Type I IFN signature has been detected in immune cells responding to pathogens other than viruses and bacteria, the significance of these observations is not fully understood. Recently, Webb and co-authors showed that Type I IFN signaling is also a critical component of the Th2-type immune response against helminth *Schistosoma mansoni (Sm)* eggs.

Sm is the cause of intestinal schistosomiasis, a chronic disease prevalent in many tropical regions. Adult *Sm* parasitize blood vessels of the large intestine, where for a long time they can dwell and produce eggs remaining unnoticed by the immune system. The *Sm* eggs induce inflammation in the gut mucosa and surrounding organs, which ultimately results in organ damage.

In 2004, Trottein and colleagues found that *Sm* eggs induce a Type I IFN signature in dendritic cells, the sentinels of the immune system. More than a decade later, Webb et al. explored this finding further using murine bone marrow-derived dendritic cells, grown in the presence of Flt3 ligand to represent the three major sub-types of DCs resembling the *in vivo* DC repertoire.

Web and co-authors found that upon exposure to *Sm* eggs/egg-derived compounds, DCs produced ample quantities of different TI IFNs. Upon closer investigation, it was found that IFNα a major type I IFN, was mainly produced by class 2 conventional DCs, but not plasmacytoid DC- the main source of IFNα in antiviral responses. The researchers further performed adoptive transfer experiments to confirm that *Sm*-activated DCs migrated to mouse draining lymph nodes, where they promoted Th2 polarization by inducing production of Th2-associated cytokines. Through a series of subsequent experiments, Webb and co-authors established that effective DC migration triggered by *Sm* eggs was also dependent on functional IFNα receptor signaling. Finally, by injecting *Sm* egg antigens directly into a mouse, the authors demonstrated that exposure to *Sm* eggs induces up-regulation of IFN-stimulated gene expression in DCs across different tissues *in vivo*.

In summary, the study by Webb et al. elucidates for the first time the role of Type I IFN signaling in helminth egg-driven Th2-type immunity and highlights the context-dependent nature of Type I IFN signaling triggered by different pathogens. On a broader scale, these findings have important implications for

ongoing studies on anti-helminth vaccines and research focusing on co-infections of helminths and other pathogens, such as HIV.

Journal article: Webb et al., 2017. Type I interferon is required for T helper (Th) 2 induction by dendritic cells. *EMBO J*

References: Trottein et al., 2004. A type I IFN-dependent pathway induced by Schistosoma mansoni eggs in mouse myeloid dendritic cells generates an inflammatory signature. *J Immunol*

Article by Sergey Yegorov (PhD Student, University of Toronto)