Macrophage migration inhibitory factor (MIF) is a pluripotent pro-inflammatory factor that acts as a mediator of innate immunity and is implicated in the pathogenesis of a number of autoinflammatory disorders, including Gout. Levels of serum MIF correlate with disease outcomes and clinical studies have shown correlations between elevated levels of IL-1β and MIF in serum of patients with autoimmune disorders. To date, it is unclear whether MIF specifically regulates the expression and secretion of IL-1 family cytokines. We show that depletion of MIF in macrophages significantly reduced IL-1 cytokine family release in response to NLRP3-activating stimuli, but has no effect on the secretion of TNF-α, IL-6 and MCP-1 (CCL2). Moreover, diminished IL-1 responses were independent of NF-kB function and production of pro-IL-1b. Instead, MIF depletion specifically inhibits NLRP3-mediated responses; IL-1 cytokine secretion was unaffected following activation of the AIM2 or NLRC4 inflammasomes. Our findings reveal a novel role for MIF in the modulation of IL-1-dependent inflammatory responses, linking MIF directly to NLRP3 inflammasome activation. This study for the first time implicates a specific role for MIF in the release of IL-1 family cytokines and highlights the potential of targeting MIF in IL-1-dependent pathologies.

Tali Lang commenced her current position as a Postdoctoral Research Fellow at the Centre for Inflammatory Diseases in 2014, with Dr. James Harris and Prof. Eric Morand. Tali is investigating the role of macrophage migration inhibitory factor (MIF) and interleukin-1 (IL-1) family cytokines in autoimmune diseases. Tali graduated from her PhD in 2011, under the supervision of Dr. Ashley Mansell at Monash Institute of Medical Research. Her PhD project investigated how “The Hepatitis B e antigen targets and suppresses activation of the Toll-like receptor signalling pathway”. In 2011, Tali joined Prof. Andreas Meinhardt’s group as a Postdoctoral Research Fellow at Justus-Liebig University in Giessen Germany, investigating the role of Uropathogenic E. coli and how they modulate innate immunity and the consequences on male fertility in the context of infectious epididymitis Tali has won numerous Australian and international awards, including the prestigious award “Young Investigator Grant of the German Society for Andrology” in 2012.