SUMMARY AND CONCLUSION

Our data from the co-infection studies suggest that one of the potential mechanisms by which helminth infections thwart the ability to respond to Mtb is by altering the antigen – specific immune responses of Th1, Th2 and Th17 cells, alterations that could have a profoundly detrimental effect by leading to reactivation of TB.

Our data from the HW/LTB study showed that, hookworm co-infection was associated with a significantly enhanced frequency of IL-10 expressing CD4+ Tcells, suggesting that adaptive Tregs might play the most important role in modulation of the T cell subsets observed. Hence this study clearly demonstrates the modulation of immune responses to Mtb by coincident helminth infection.

Our findings may have significant implications for vaccine efficacy in helminth-endemic countries and potentially for understanding how latency in Mtb is broken. Understanding the pathways that helminth infections utilize to mediate bystander suppression/modulation to exogenous antigens and infections should enable new strategies to antagonize suppression for controlling deleterious infections and optimal boosting of vaccine efficacy.

Our data also showed that, acute phase proteins, systemic immune activation markers and tissue remodelling enzymes more accurately reflect inflammatory pathology in chronic infections and may be considered as potent biomarkers of TB pathogenesis. Also, it was shown that these biomarkers significantly modulated by the presence of coincidental S.stercoralis infection. Hence, concomitant helminth infection has a secondary effect on systemic markers of disease severity/activity in pulmonary tuberculosis. We have also
observed a significant diminution in baseline and antigen-specific Th1 and Th17 cell responses in co-infected individuals. Thus, co-existent helminth infection is associated with profound inhibition of antigen-specific CD4\(^+\) T cell responses, thereby potentially promoting pathogen persistence and pathology.

**Future directions**

One of the major problems in terms of current TB research and clinical demands is the increasing number of cases of extensively drug resistant and treatment refractory TB. To combat this problem, a great deal of emphasis is now laid on host-directed therapies targeting inflammatory processes that can be deleterious and lead to immune exhaustion in TB. Candidates for such interventions may be biological agents or already approved drugs repurposed to interfere with inflammatory processes. Helminth immuno-modulators, if approved, could feasibly serve as another approach to tackle this issue.