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Unravelling the role of IL-10 in the development and function of the TB Granuloma

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Tuberculosis (TB), a deadly infectious disease caused by the bacterium Mycobacterium tuberculosis (Mtb). The disease is characterized by the development of granulomas consisting of immune cells that form a cluster around the bacteria to limit bacterial growth and disease outcomes. Control of the TB epidemic is limited by a complicated drug regimen, development of antibiotic resistance, and the lack of an effective vaccine against infection and disease.

There are a range of pro- and anti-inflammatory molecules associated with Mtb infection and it has been shown that depletion of a specific anti-inflammatory molecule, namely IL-10, is associated with improved vaccine efficacy in mice. However, there are conflicting results in both mice and monkeys as to the effects of IL-10 depletion on disease, with some studies showing that the depletion of anti-inflammatory factors improves disease outcome and others demonstrating that this depletion causes more severe disease. In previously published modelling studies, we suggest that depleting IL-10 can increase the probability that a granuloma is cleared in non-human primates (NHPs).

Using GranSim, our previously published hybrid, multiscale, agent-based model of granuloma formation following Mtb infection, we explore the role of IL-10, on granuloma development and function. In this exploratory study, we simulate the depletion of IL-10 from two discrete time points. The first time point coincides with the infection time of Mtb, and allows us to examine the role of IL-10 in granuloma formation. Elucidating the mechanisms by which IL-10 affects granuloma formation allows us explore whether the improvement in vaccine efficacy that has been identified in mice can also be observed in our model. The second time point is at 200 days post infection when a stable granuloma is already established to allow us to identify the mechanisms by which IL-10 is acting upon granuloma function and maintenance. Understanding the effect of IL-10 depletion on established TB granulomas is important to identify new therapeutic pathways for this disease.

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