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Assessment of Th1/Th2 immune response paradigm in *Mycobacterium avium subspecies paratuberculosis* infections.

Johne's disease, a persistent and slow progressing infection in ruminants such as cows and sheep is caused by *Mycobacterium avium subspecies paratuberculosis* (MAP) bacillus. Mycobacterial infections are associated with complex immune response mechanisms whose underlying biology is not clearly understood. Host immune response to MAP infection is associated with predominance of a cell mediated response in its early stages (Th1) and a switch to the dominance of antibody response (Th2) which is associated with rapid disease progression. How this switch is achieved during the infection and whether such switch can be regulated remains poorly understood. In this study, we develop several mathematical models to understand the driving causes for Th1 to Th2 switch in MAP infection. We specifically consider two hypotheses: 1) switch is driven by accumulation of extracellular bacteria that drive the development of Th2/antibody response which in turn suppresses the protective Th1 response, and 2) switch is driven due to loss of the protective Th1 response due to exhaustion/suppression, and concomitant rise in non-protective Th2/antibody response. We investigate the conditions under which these mathematical models give rise to the Th1 to Th2 switch. This approach provides novel insights into the underlying dynamics of the Th1 and Th2 responses during a chronic bacterial infection.

Keywords

Mycobacterium avium subspecies paratuberculosis, Johne's disease, mathematical modelling, immune response, Immunology, Population biology.