Tuberculosis: Looking to the granuloma for answers

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When Mycobacterium tuberculosis bacilli enter the lung, cells are recruited to the site of infection and form a granuloma. This structure, composed of macrophages, lymphocytes, and sometimes neutrophils, can limit the replication and spread of M. tuberculosis. The early events in the lung, including granuloma formation and function, influence the outcome of infection. However, these early events and the functions and interactions of cells in the granuloma are not well characterized. Using a non-human primate model of tuberculosis, combined with serial PET/CT imaging, we have tracked granulomas during early events, dissemination, resolution, drug treatment and reactivation. Our studies indicate that each granuloma in a single host acts independently, in terms of inflammation and bacterial control. We have also characterized the macrophage and neutrophil populations in the granuloma, demonstrating both inducible nitric oxide synthase and arginase producing macrophages, suggesting that the balance of inflammation in the granuloma is controlled, at least in part, by the macrophage population. We have also characterized T cells and B cells in the granuloma to determine how they contribute to control or pathology in infection, as well as how T cells and cytokines contribute to control of latent infection. The non-human primate model recapitulates most of the aspects of human tuberculosis, making results from this model translatable to humans.

References:

