IMMUNE REGULATION

Worming away from TB immunity

The majority of helminth infections worldwide are concentrated in developing nations, where other diseases such as tuberculosis are endemic. It is known that a pre-existing helminth infection can impinge on immunity to *Mycobacterium tuberculosis* infection, but the underlying mechanism has yet to be described. Potian *et al.* now show that interleukin-4 (IL-4) production induced by infection with the helminth *Nippostrongylus brasiliensis* enhances the persistence of *M. tuberculosis* infection in mice, at least in part through the alternative activation of macrophages in the lung.

Infection of mice with *N. brasiliensis* (which transiently migrates through the lung during its life cycle) was found to induce a strong IL-4 response that impaired resistance to subsequent *M. tuberculosis* infection. Surprisingly, *M. tuberculosis*-specific T helper 1 (T_H1) cell responses were similar in the draining lymph nodes of mice with or without *N. brasiliensis* infection. So, the authors next examined the phenotype of macrophages in the lungs of co-infected mice and found an increase in the expression of markers of alternatively activated macrophages (which have been shown to be compromised in their ability to control *M. tuberculosis* infection).

Furthermore, in the absence of IL-4 receptor subunit-α (IL-4Rα), co-infected mice did not have an increased bacterial burden or an accumulation of alternatively activated macrophages in their lungs. Transfer of wild-type macrophages to *N. brasiliensis*-infected *Il4ra*$^{-/-}$ mice resulted in increased bacterial burden following *M. tuberculosis* infection, indicating that the IL-4-mediated alternative activation of macrophages contributes to reduced anti-tuberculosis immunity.

So, the IL-4Rα-dependent increase in the number of alternatively activated macrophages in response to helminth infections can, at least in part, compromise protection against *M. tuberculosis*.

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ORIGINAL RESEARCH PAPER Potian, J. A. *et al.* Preexisting helminth infection induces inhibition of innate pulmonary anti-tuberculosis defense by engaging the IL-4 receptor pathway. *J. Exp. Med.* 8 Aug 2011 (doi:10.1084/jem.20091473)

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