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Lung alert

The *sst1* locus controls granuloma necrosis in tuberculosis

There is broad variation in susceptibility to *Mycobacterium tuberculosis* (MTB), and mouse models play a key role in elucidating the underlying mechanisms. The authors tested the hypothesis that caseation within pulmonary lesions is a specific effect of the *sst1* (supersusceptibility to tuberculosis 1) locus on chromosome 1.

Typical mouse lesions described in the literature lack central caseation. However, the C3HeB/FeJ strain of mouse develops large necrotising granulomas after exposure to MTB. The authors compared the course of infection in an MTB-resistant mouse strain (B6) with an *sst1*-susceptible congenic strain (B6.C3H-*sst1*) which was genetically identical except for the interval containing the *sst1* locus.

They found that, although initial dissemination was similar, bacterial loads, clinical disease, lung necrosis and mortality were considerably worse in the strain containing the *sst1*-susceptible allele. In addition, relapse after 3 months of isoniazid was faster and more rampant in this group. After demonstrating significantly slower disease progression and milder histopathology in the B6.C3H-*sst1* strain compared with the C3HeB/FeJ strain, the authors concluded that the effect of the *sst1* locus is modified by the genetic background of the host. Enhanced pro-inflammatory cytokine production by macrophages was observed in the susceptible strains; however, this appears to be controlled by loci other than *sst1*.

Further characterisation of *sst1*-encoded molecular mechanisms may not only shed light on a key aspect of the pathogenesis of tuberculosis, but may also suggest therapeutic interventions to reduce lung pathology and transmission of the pathogen.

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