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 locus. 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.


M Almond

Correspondence to: Dr M Almond, ST1 Oncology, Royal Marsden Hospital, London, UK; mhalmond@gmail.com

Provenance and peer review: Commissioned; not externally peer reviewed.

The sst1 locus controls granuloma necrosis in tuberculosis

M Almond

Thorax 2009 64: 949
doi: 10.1136/thx.2009.122879

Updated information and services can be found at:
http://thorax.bmj.com/content/64/11/949

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/