

Journal club

Host genotype-specific therapies for tuberculosis

This paper suggests that therapies for tuberculosis (TB) will, in the future, be tuned specifically to the patient's genotype. Using zebra fish and human models, Tobin *et al* demonstrated that susceptibility to TB can be caused by both reduced and increased inflammatory activity, which in turn is governed by the patient's genotype. The increased inflammatory pathway begins with increased leukotriene A4 hydrolase (LTA4H) activity, which leads to increased production of a proinflammatory eicosanoid (LBT4) and tumour necrosis factor. The decreased inflammatory pathway begins with reduced LTA4H activity resulting in increased anti-inflammatory activity and increased production of lipoxins. Both mechanisms cause lysis of macrophages.

These findings suggests that by identifying whether a patient infected with TB is in a high or reduced inflammatory state, as dictated by their LTA4H genotype and the detrimental effects of each extreme countered, patient morbidity and mortality would be improved. Blindly used 'scatter-gun' therapies may be either beneficial or detrimental, depending on the inflammatory state of the patient. In the increased inflammatory state produced by increased LTA4H activity, targeted therapies, such as aspirin, may be useful as this inexpensive drug inhibits tumour necrosis factor activity. Similarly, in those with a reduced inflammatory state (the low-activity LTA4H genotype) limiting the increased anti-inflammatory activity may be beneficial.

The development of genotype-directed treatment strategies for TB and other serious infections will be an interesting area of future research.

► **Tobin DM**, Roca FJ, Oh SF, *et al*. Host genotype-specific therapies can optimize the inflammatory response to mycobacterial infections. *Cell* 2012;**148**:434–46.

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