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SYSTEMIC LUPUS ERYTHEMATOSUS

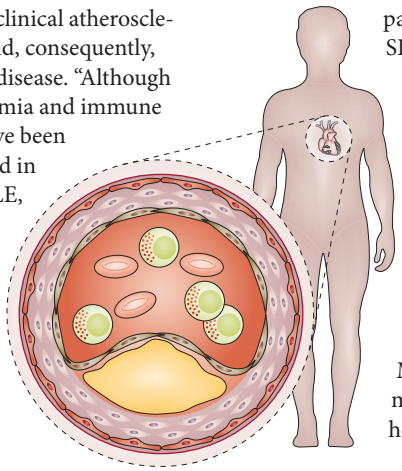
iNKT cells guard the heart against disease

> iNKT cells from patients with [SLE and atherosclerotic plaques] had a distinctive phenotype

Invariant natural killer T (iNKT) cells might have an atheroprotective role in patients with systemic lupus erythematosus (SLE) who have asymptomatic atherosclerotic plaques, according to new research. "For the first time, we describe a link between dyslipidaemia detected by metabolomics analysis, altered cytokine responses in iNKT cells and an atheroprotective immune response in patients with SLE who have preclinical atherosclerosis," states Elizabeth Jury, corresponding author of the study.

Atherosclerosis is an important comorbidity for patients with SLE, who have an increased risk of developing subclinical atherosclerotic plaques and, consequently, cardiovascular disease. "Although both dyslipidaemia and immune dysfunction have been widely described in patients with SLE, their role in the development of atherosclerosis is not clear," explains Jury. "We questioned whether iNKT cells, which respond specifically to lipid antigens presented by CD1d on antigen-presenting cells, have a key role in linking the immune system, lipids and cardiovascular disease in patients with SLE," she continues.

Jury and colleagues found that patients with SLE and atherosclerotic plaques (SLE-P) had increased numbers of iNKT cells compared with patients with SLE and no plaques (SLE-NP). iNKT cells from patients with SLE-P had a distinctive phenotype, producing increased levels of IL-4 compared with iNKT cells from both healthy individuals and patients with SLE-NP.



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Serum from patients with SLE-P was sufficient to cause iNKT cells to expand *in vitro* and produce IL-4, and, in the presence of iNKT cells, to induce an M2 phenotype in monocytes from healthy individuals, suggesting a role for serum lipids in iNKT activation. Metabolomic analysis of serum lipids revealed increased levels of VLDL cholesterol with an altered composition of cholesterol and phospholipids in patients with SLE-P compared with patients with SLE-NP.

The researchers identified a strong correlation between serum lipids and iNKT cell frequency and IL-4 production in patients with SLE-P, suggesting that a combination of iNKT cell phenotyping and serum lipid analysis could predict the development of atherosclerosis in patients with SLE. "Understanding iNKT cell heterogeneity and its link to dyslipidaemia is an important step towards stratifying patients with increased cardiovascular risk, both in SLE and other at-risk patient groups, and potentially harnessing iNKT cells for therapeutic benefit," concludes Jury.

Joanna Collison

ORIGINAL ARTICLE Smith, E. *et al.* Cross-talk between iNKT cells and monocytes triggers an atheroprotective immune response in SLE patients with asymptomatic plaque. *Sci. Immunol.* **1**, eaah4081 (2016)

FURTHER READING Exley, M. A. *et al.* What rheumatologists need to know about innate lymphocytes. *Nat. Rev. Rheumatol.* **12**, 658–668 (2016)