Nature Reviews Rheumatology **7**, 497 (2011); published online 9 August 2011; doi:10.1038/nrrheum.2011.113

CONNECTIVE TISSUE DISEASES

SAP-induced macrophage polarization: a potential therapeutic option for SLE?

A number of studies have associated reduced serum amyloid P component (SAP)—a serum DNA binding and opsonizing protein—with the pathogenesis of systemic lupus erythematosus (SLE). New evidence from Zhang *et al*. suggests that SAP supplementation could enhance clearance of autoantigenic apoptotic material and ameliorate this disease.

In this study, immunization of mice with DNA led to the development of SLE-like disease. However, SAP binding to DNA increased phagocytic uptake of this material by macrophages and caused them to switch from a proinflammatory M2b phenotype observed with unbound DNA to an anti-inflammatory M2a phenotype. This was associated with decreased production of anti-DNA antibodies, IgG deposition in glomeruli, proteinuria and lupus nephritis. Furthermore, adoptive transfer of *in vitro* polarized M2a, but not M2b, macrophages attenuated disease to a similar extent as immunization with SAP bound DNA.

Zhang and co-workers also showed that IL-10 released by M2a cells is responsible for the inhibition of polarization to the M2b phenotype. Correspondingly, *in vivo* antibody blockade of IL-10 inhibited the protective effect of SAP binding to DNA.

"SAP supplements could complement insufficient DNA phagocytosis ability and regulate macrophage M2b-to-M2a switch in SLE ... which reveals a possible molecular mechanism for the modulation of macrophage differentiation and opens a new potential therapeutic avenue for SLE disease," concludes Sidong Xiong, lead investigator of the study.

David Killock

Original article Zhang, W. *et al*. Macrophage differentiation and polarization via phosphatidylinositol 3-kinase/Akt–ERK signaling pathway conferred by serum amyloid P component. *J. Immunol*. doi:10.4049/jimmunol.1002315