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Class A scavenger receptors as novel autoantigens in SLE

The breakdown of self tolerance that leads to the characteristic production of autoantibodies in systemic lupus erythematosus (SLE) is thought to be partly mediated by increased apoptosis and impaired clearance of apoptotic cells, which results in a high level of autoantigen exposure to the immune system. In particular, the phagocytic capacity of macrophages—which is mediated by myriad receptors and ligands—seems to be impaired in patients with SLE. The class A scavenger receptors might have a role in the binding and clearance of apoptotic cells by macrophages: indeed, autoantibodies against two of these receptors, MARCO (macrophage receptor with collagenous structure) and SR-A (scavenger receptor A; also known as macrophage scavenger receptor 1 [MSR1]), have been found in SLE-prone mice and patients with SLE, and it is proposed that antibodies that block these receptors might impair macrophage activity. Chen *et al.* examined the prevalence of these autoantibodies in patients with various autoimmune diseases, and studied their effects on the clearance of apoptotic cells by macrophages.

Enzyme-linked immunosorbent assays (ELISA) were used to detect autoantibodies against SR-A and the ligand-binding, C-terminal scavenger receptor cysteine-rich (SRCR) domain of MARCO in the serum of patients with SLE ($n = 65$), rheumatoid arthritis (RA; $n = 65$) or primary Sjögren's syndrome ($n = 25$) and healthy controls ($n = 85$). A significantly greater proportion of SLE patients were positive for anti-SR-A antibodies (33.8%) or anti-SRCR antibodies (18.5%) compared with patients with RA (13.8% [$P = 0.007$] and 3.1% [$P = 0.005$], respectively) and Sjögren's syndrome (12.0% [$P = 0.038$] and 0% [$P = 0.032$], respectively). None of the healthy controls was positive for either autoantibody.

Flow cytometry analysis revealed that IgG isolated from the serum of SLE patients positive for both anti-SR-A and anti-SRCR autoantibodies inhibited ingestion of apoptotic cells by macrophages at a significantly higher rate than IgG from healthy controls ($P < 0.05$). IgG from serum positive for only one of the autoantibodies showed a significantly higher inhibition rate of macrophage binding to apoptotic cells ($P < 0.05$), but not of macrophage ingestion of apoptotic cells.

The results of this study demonstrate that class A scavenger receptors seem to represent autoantigens that have a potentially influential role in the breakdown of self tolerance in SLE. However, the *in vivo* effects of anti-SR-A and anti-SRCR autoantibodies on macrophage function will require further study in animal models.

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Original article Chen, X.-W. *et al.* Anti-class A scavenger receptor autoantibodies from systemic lupus erythematosus patients impair phagocytic clearance of apoptotic cells by macrophages *in vitro*. *Arthritis Res. Ther.* 13, R9 (2011)