A87 INVOLVEMENT OF TOLL-LIKE RECEPTOR 2 IN PRISTANE-INDUCED LUPUS

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Background Autoantibodies against double stranded (ds) DNA and nucleosomes represent a hallmark of systemic lupus erythematosus (SLE).¹ However, the mechanisms involved in breaking the immunological tolerance against these poorly immunogenic nuclear components are not fully understood. Recent data indicate that toll-like receptors (TLRs) recognising endogenous ligands may be critically involved in the breaking of peripheral tolerance against nuclear autoantigens.² Results of this recent studies in non-autoimmune mice provide evidence of a important role of TLR2 in the anti-dsDNA and antihistone IgG autoantibody induction by high mobility group box protein 1-nucleosome complexes derived from apoptotic cells.³

Objective Using the pristane-induced mouse model of SLE, the authors further investigated the requirement of TLR2 signalling for induction of lupus-specific autoantibody production and SLE like disease.

Methods Female C57BL/6 wild-type (WT), TLR2-deficient mice were injected intraperitoneally with a single dose of 500 µl of the hydrocarbon oil pristane. The numbers of plasma cells were determined by flow cytometry. The concentrations of autoantibodies in sera were measured by ELISA. Autoantibody-secreting cells in the kidneys were detected by enzyme-linked immunosorbent spot assay. Renal disease was assessed by semiquantitative measurement of proteinuria in spot urine and quantified over 24 h after collection in metabolic cages as well as by histological analyses.

Results TLR2^{-/-} mice generated reduced numbers of splenic CD138/cytoplasmic κ/λ-L chain⁺/CD25 plasma cells in response to pristane treatment. Anti-dsDNA, antihistone, antinucleosome and some antinuclear antibody IgG responses were delayed and significantly reduced in pristane-treated-TLR2^{-/-} mice compared to pristane-treated WT controls. There were markedly lower numbers of total IgG-secreting and anti-dsDNA specific IgG-secreting cells in the kidneys of pristane-treated-TLR2^{-/-} mice in comparison to C57BL/6 mice. Importantly, pristane-treated TLR2-deficient mice developed significantly milder renal disease compared to the WT control group.

Conclusion TLR2 is specifically required for the lupus-specific autoantibody production as well as for development of renal disease in pristane-induced murine lupus model. Specific blocking of TLR2 signalling may therefore be a promising novel strategy for treatment of SLE.

REFERENCES

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