Role of gut commensal translocation and molecular mimicry in autoantibody production in systemic lupus erythematosus

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Abstract

Objective. Gut commensals contribute to systemic lupus erythematosus (SLE) pathogenesis, though mechanisms are unclear. This study explored the role of gut bacterial translocation in molecular mimicry using lupus model mice and blood samples from untreated SLE patients.

Methods. Bacterial translocation to mesenteric lymph nodes (MLNs) was assessed in B6SKG lupus mice, known for expanded auto-reactive T cells due to a shift in thymic selection caused by ZAP70 point mutation. The pathogenicity of detected bacteria was analyzed through in vivo experiments, ELISA, immunoblotting, and epitope mapping.

Results. Lactobacillus murinus was enriched in MLNs of B6SKG mice with elevated anti-dsDNA IgG levels. Injection of heat-killed L. murinus increased anti-dsDNA IgG production without altering T- or B-cell subsets. The ATP-binding cassette (ABC) transporter of L. murinus was identified as a molecular mimicry antigen, confirmed through serological assays and in vivo immunization. This ABC transporter exhibited cross-reactive epitopes with sera from lupus mice and patients, similar to those found in Ruminococcus gnavus, a known pathogenic gut commensal in lupus patients.

Conclusion. ABC transporters from gut bacteria can act as molecular mimicry antigens, promoting anti-dsDNA antibody production in genetically predisposed mice. These findings suggest the involvement of molecular mimicry and bacterial translocation in lupus pathogenesis.