EXPERIMENTAL ARTHRITIS

# A potential role for B-cell effects on lymph nodes in the pathogenesis of RA

A study exploring the pathogenesis of rheumatoid arthritis (RA) has revealed an unsuspected role of B lymphocytes in a well-characterized mouse model of the disease the disease, the tumor necrosis factor (TNF) transgenic mouse model, which was previously thought to be lymphocyte-independent. The work also provides insights into the effects of B cells on the structure, composition and function of the lymph nodes that drain joints affected by the disease, according to Andrea Bottaro, one of the study's key investigators.

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The study built on previous findings by Bottaro's collaborators Edward Schwarz and Steven Proulx, which demonstrated by use of sophisticated small-animal imaging techniques that the progression of arthritis in TNF-transgenic mice is accompanied by dramatic changes in the size and structure of joint-draining lymph nodes. "Together with [Schwarz and Proulx], we looked more closely at the cellular and histological composition of these lymph nodes, and found that B cells, and in particular a population with a unique surface phenotype characterized by high expression of the CD21 marker, have a prominent role in the observed changes," says Bottaro.

CD23$^{+}$CD21$^{hi}$ B cells were found to be involved in arthritis progression in TNF-transgenic mice from the earliest stages of the disease. Large numbers of these cells accumulated in the sinuses of lymph nodes that drain affected joints in these mice; a similar accumulation was also observed in aging mice with autoantigen-dependent arthritis (K/BxN mice). In the TNF-transgenic mice, B-cell-depletion therapy effectively cleared B cells, including the CD23$^{+}$CD21$^{hi}$ subset, from the lymph nodes and ameliorated disease.

The investigators suggest that these lymph node changes contribute to disease pathogenesis by altering the ability of the lymph node to carry out its normal immunological and drainage functions. "It is known that at least a subset of RA patients who respond positively to B-cell-depletion therapy do not show significant decreases of arthritis-associated autoantibodies in their blood," continues Bottaro. "Thus, B cells in these patients must contribute to disease through some other mechanism. Our findings provide a new example of antibody-independent pathogenetic function which could be important in arthritis."

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