

**THE ROLE OF CD44 AND L-SELECTIN IN LEUKOCYTE-ENDOTHEL
INTERACTIONS IN DIFFERENT MURINE MODELS OF INFLAMMATION**

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Using mice deficient in CD44, L-selectin, or both we developed two different inflammatory models. In the model of allergic dermatitis, that shows similarities to the acute phase of atopic dermatitis (elevated Ag-specific IgE level, Th2 type cell activation), the mice were sensitized intraperitoneally with chicken ovalbumin (OVA) injection. The local reaction was elicited by intradermal administration of OVA. In the model of antigen induced arthritis (AIA) mice were immunized with methylated BSA, and their right knees were injected with the same antigen. Despite comparable immune responses to OVA and mBSA, the morphological features of allergic dermatitis and AIA were different in WT and gene-deficient groups. In the absence of CD44 (or both CD44 and L-selectin) expression, CD44 and double KO mice demonstrated significant reductions in leukocyte influx and ear swelling after local challenge with OVA, whereas inflammation in mice lacking L-selectin only was comparable to WT, suggesting that CD44, but not L-selectin, was required for the entry of effector cells into the inflamed skin. Joint swelling was strongly reduced throughout the 5-day observation period in mice lacking L-selectin or both L-selectin and CD44. Histopathology of the knees and flow cytometric analysis of the joint infiltrating cells revealed a delay in leukocyte extravasation, with a slower accumulation of granulocytes in the joints in the absence of L-selectin.

Extravasation of granulocytes, but not the recruitment of T cells, was diminished in the joints of mice lacking L-selectin at the early phase of AIA. Using intravital microscopy (IVM), in CD44 KO animals the rolling velocity and frequency was higher, the adherence of leukocytes was diminished as compared with the WT mice. In the model of AIA, L-selectin-deficient and double KO mice rolling leukocytes were more frequent than in WT mice, while the ability of these cells to adhere to the vessel wall was reduced.