Blood. 2006 Oct 1;108(7):2275-9. Epub 2006 May 30.

# ADAM17 deficiency by mature neutrophils has differential effects on L-selectin shedding.

Li Y, Brazzell J, Herrera A, Walcheck B.

**Source**

Department of Veterinary and Biomedical Sciences, University of Minnesota, St Paul, MN 55108, USA.

## Abstract

L-selectin directs neutrophils to sites of inflammation, and upon their activation, surface expression of the receptor is rapidly down-regulated by ectodomain shedding. Tumor necrosis factor-alpha-converting enzyme (TACE, or ADAM17) is a sheddase of L-selectin; however, Adam17 gene targeting (ADAM17(DeltaZn/DeltaZn)) in mice is perinatal lethal and its role in L-selectin shedding by mature neutrophils has not been determined. This was addressed here by using radiation-chimeric mice reconstituted with ADAM17(DeltaZn/DeltaZn) fetal liver cells. ADAM17-deficient neutrophils, monocytes, and lymphocytes failed to shed L-selectin in response to PMA, as did neutrophils infiltrating the inflamed peritoneum. In addition, the absence of functional ADAM17 resulted in significantly increased levels of L-selectin surface expression by peripheral-blood leukocytes, indicating the sheddase also plays a role in the constitutive cleavage of L-selectin. Interestingly, not all manners of L-selectin turnover required ADAM17. Plasma L-selectin levels were similar between ADAM17(DeltaZn/DeltaZn)-chimeric and control mice, as was the shedding of L-selectin by neutrophils undergoing spontaneous apoptosis. The latter process, however, was diminished by a metalloprotease inhibitor, indicating the role of a sheddase other than ADAM17. Together, our data reveal that L-selectin's surface density on neutrophils is regulated by ADAM17, but homeostatic L-selectin cleavage is not.

PMID: 16735599 [PubMed - indexed for MEDLINE]