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# AS2.3 CD62L (L-selectin) cluster report

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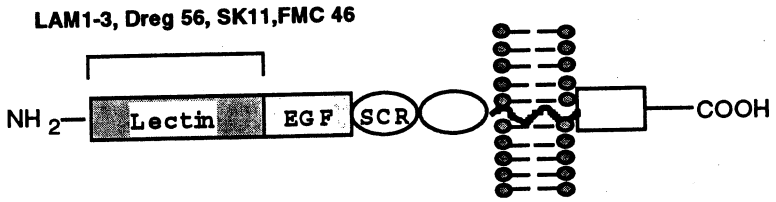


CD62L (L-selectin)

CD62L (L-selectin, LAM-1, Leu 8, TQ1) (introductory figure), a member of the selectin family of adhesion receptors, functions in leucocyte binding to activated endothelium as well as in lymphocyte homing to high endothelial venules (HEV) [1]. The expression of this leucocyte antigen was initially described in the mouse by Gallatin *et al.* [2] using the monoclonal antibody (mAb) mel-14. In the human, L-selectin was characterized with mAb Leu 8 [3] and TQ1 [4]. L-selectin was clustered in the Fifth Workshop as CD62L with four mAb, S054 (LAM1–3), S056 (Dreg 56), S059 (SK11), and S061 (FMC46).

## Molecular characterization

The L-selectin molecule is 76 kDa $M_r$ in sodium dodecyl sulfate-polyacrylamide gel (SDS-PAGE) [5,6]. cDNA clones encoding the L-selectin molecule have been reported [7–9]. The *lyam-1* gene spans more than 30 kb pairs of DNA and is composed of at least 10 exons [10]. The protein encoded by this gene contains an amino-terminal lectin-binding domain, an endothelial growth factor (EGF)-like domain, two short consensus repeat (SCR) sequences similar to those found in complement-binding proteins, a transmembrane region, and a short cytoplasmic region. Seven potential N-linked carbohydrate attachment sites are found in the extracellular region. The human L-selectin protein is 77 per cent identical to mouse L-selectin [7]. It shares considerable amino acid sequence and structure homology with E- and P-selectin and has been mapped to the same region on chromosome 1 (bands q23–25).

## Epitope analysis and transfectant studies

The specificity of the four mAb to CD62L was demonstrated using selectin transfectants [Diacovo and Springer, AS2, Table 1]. Epitope analysis using selectin chimeras localized the binding of all of these mAb to the lectin domain of the molecule [Saunders and Tedder, AS2.8].

## Cellular expression

L-selectin expression is limited to lymphoid tissues [Autschbach *et al.*, AS2.5; Zola *et al.* and Rizzo *et al.*, unpublished Workshop reports]. CD62L is expressed on neutrophils, monocytes, NK cells, and subpopulations of B and T lymphocytes [3,4,11]. Phorbol myristate acetate (PMA) stimulation of purified peripheral blood lymphocytes [12] and neutrophils [13] results in downmodulation of L-selectin expression.

## Function

Functional studies evaluated the ability of the selectin mAb to inhibit receptor–ligand interactions. Rolling interactions between L-selectin transfectant L1-2 cells and purified peripheral node addressin were completely inhibited by mAb S056 (Dreg 56) and partially by mAb S059 (SK11) and S061 (FMC46) [Andrew *et al.*, AS2.9]. In addition, these three mAb significantly reduced the binding of fluorescein-conjugated PPME (phosphomannan monoester core polysaccharide) to these cells and to peripheral blood lymphocytes, monocytes, and neutrophils.

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# AS2.4 Approaches to *in vivo* blocking of adhesion molecules

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The responses of neutrophils to inflammatory stimuli, resulting in neutrophil transmigration, accumulation of neutrophils in tissues, and subsequent injury, is a complex process that features an array of mediators as well as events that result in an altered (and 'activated') endothelium. As a result of molecular biological techniques and the development of monoclonal antibodies (mAb) that have become useful probes, it has been possible in some inflammatory models to characterize relevant adhesion molecules both on endothelial cells as well as on leucocytes. In this report we describe approaches that can be used *in vivo* to define the role of adhesion molecules in neutrophil transmigration and accumulation in tissues.

## Sequence of events in neutrophil transmigration

It is now beyond doubt that the transmigration of neutrophils into extravascular sites requires the participation of a variety of adhesion molecules and