ADAMs and ectodomain proteolytic shedding in leucocyte migration
Focus on L-selectin and ADAM17

Leucocyte recruitment from the bloodstream into tissues depends on a coordinated sequence of adhesive interactions between leucocytes and vascular endothelial cells. It is tightly regulated, both spatially and temporally, such that leucocyte recruitment is efficient and the integrity of the blood vessel wall is not impaired. Although the cell adhesion molecules and chemokines that mediate adhesion have been identified, the signalling events that control leucocyte extravasation are just starting to be understood. Ectodomain shedding by the ADAMs (A Disintegrin And Metalloproteinase) family of metalloproteinases is emerging as an important regulatory step in leucocyte-endothelial cell interactions. In addition to their proteolytic activities, ADAMs have the potential to regulate leucocyte recruitment by binding to, or modulating the affinity of, leucocyte integrins. The evidence for ADAMs involvement in leucocyte recruitment will be reviewed with particular emphasis on L-selectin and ADAM17. The regulation of ADAM catalytic activity is complex and controlled by intracellular signaling pathways and cellular localization. ADAM activity is also regulated by substrate availability and the roles of extracellular and intracellular domains of L-selectin in regulating ADAM dependent ectodomain shedding will also be reviewed.