L-Selectin, an adhesion molecule : experimental measurement of its shedding and possible clinical implications /

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Monografía

L-selectin (CD62L) is a type I transmembrane glycoprotein and cell adhesion molecule that is expressed in most circulating leukocytes. L-selectin is broadly characterized as an anchor/bearing receptor. There is currently emerging evidence suggesting that L-selectin has a role in regulating monocyte protrusion during transendothelial migration (TEM). The lectin domain is Nterminal calcium-dependent (type C) interacts with numerous glycans, important to name sialyl Lewis X (sLex) for anchoring/coiling and proteoglycans for endothelial transmigration. The short cytoplasmic tail of 17 amino acids is responsible for adhesion. The ability of leukocytes to migrate from the periphery to tissues is a critical step in the immune response, with several adhesion molecules being involved in this process. This molecule is expressed on the surface of lymphocytes, neutrophils, monocytes, eosinophils, hematopoietic precursor cells, and immature thymocytes. L-selectin is a highly glycosylated protein of 95-105 kD in neutrophils and 74 kD in lymphocytes. It is involved in lymphocyte migration to peripheral lymph nodes through interaction with GlyCAM-110 and in the adhesion of lymphocytes, neutrophils and monocytes to the endothelium activated by cytokines at sites of inflammation. Several L-selectin ligands have been identified on endothelial cells, GlyCAM-1, CD34 and MAdCAM-1, all containing glycosylated mucin domains. The soluble form of L-selectin (sL-selectin) is present in plasma due to metalloproteinasemediated cleavage of L-selectin expressed on the cell surface. The soluble form retains bioactivity and at high concentrations can inhibit the binding of lymphocytes to the endothelium, suggesting their possible role in vivo. While sL-selectin can be detected in the circulation of healthy individuals from 0.7 to 1.5ug/ml, increased levels have been reported in patients with sepsis, inflammatory, autoimmune diseases and in leukemias. An indirect approach to measure sL-selectin is by means of the shedding of CD62L from the membrane of leukocytes. In this work we set up a method to measure it in vitro in order to apply it in the clinical management in patients with suspicion of immunodeficiency.

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