Cells communicate in a host of fascinating ways, including cell-to-cell adhesion, in which one cell directly binds to another cell. Cell adhesion is what makes all tissue formation in the body possible. Adhesion proteins play a role in nearly all disease processes, including infection, neoplasia, immune deficiency, and autoimmunity. One of the most well-studied cellular adhesion molecules is intracellular adhesion molecule-1 (ICAM-1). ICAM-1 is a glycoprotein found in leukocytes, vascular endothelium, dermal fibroblasts, and mucosal (including corneal and conjunctival) epithelium.

One of ICAM-1’s most prominent roles involves mediation of leukocyte transmigration, the process in which white blood cells leave the circulatory system in an area of inflammation. Here’s how it works. Inflammatory mediators known as chemokines (e.g., IL-1, IL-8, TNF-α) are released from the site of inflammation into the surrounding tissue. These enter the capillary bed in the area of inflammation stimulating expression of ICAM-1 on the vascular endothelial surface while also increasing expression of lymphocyte function associated antigen-1 (LFA-1) on the leukocyte surfaces. As a leukocyte approaches the endothelium in the area of inflammation, ICAM-1 and LFA-1 bind, causing the leukocyte to “roll” along the surface until it “stops” and adheres to the endothelial cells with an affinity strong enough to withstand the bloodstream. Once fully adherent, the cytoskeleton of the leukocyte changes to form “pseudopods,” blobs of cellular matter that are then projected through gaps in the endothelial lining. Surface proteins on both the endothelial cells and the leukocytes then help “pull” the leukocyte through the vascular wall into the site of inflammation. This ICAM-1/LFA-1 interaction is known to play a major role in vasculitis, thrombosis, and graft rejection.

The importance of ICAM-1 in inflammation has made it a popular drug target. Many therapeutics for uveitis, diabetic eye disease, Sjögren’s syndrome, and melanoma are thought to work in part through modulation of ICAM-1. Antihistamine eye drops such as azelastine are known to decrease expression of ICAM-1. The anti-ICAM-1 antibody efalizumab holds promise for the treatment of uveitis.

Aside from its role in transmigration of leukocytes, ICAM-1 affects the eye in several ways. ICAM-1 has an established role in dry eye syndrome, in which ICAM-1 expressed on conjunctival epithelium and acinar cells adhere to proliferating T-cells, leading to disruption of the tear film and cytotoxicity. A more recent example is ICAM’s role in super-selective intra-ophthalmic artery chemotherapy for retinoblastoma, in which vascular toxicity is a known complication. Two of the agents used in this selective chemotherapy, carboplatin and melphalan, increase expression of ICAM-1 in retinal arterial endothelium with resultant dose-dependent retinal arteriole occlusion.

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