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Ultrastructure and Function of Intercellular Adhesion Molecule-1 (ICAM-1): Involvement of ICAM-1 on Microvilli-Like Membrane Projection of Endothelial Cells upon Engagement of Leukocyte LFA-1

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Specific leukocyte/endothelial interactions are critical for immunity and inflammation, yet the molecular details of this interaction interface remain poorly understood. Thus we investigated, with confocal microscopy, the distribution dynamics of the central adhesion molecules, ICAM-1 and LFA-1 in this context. Monolayers of activated HUVECs stained with fluorescent anti-ICAM-1 Fabs, or CHO-K1 cells expressing ICAM-1-GFP were allowed to bind LFA-1-bearing monocytes, neutrophils or K562 LFA-1 transfectants. ICAM-1 was rapidly re-localized to newly formed microvilli-like membrane projections in response to binding LFA-1 on leukocytes. These ICAM-1-enriched projections encircled the leukocytes extending up their sides,and clustered LFA-1 underneath into linear tracks. Projections formed independently of VCAM-1/VLA-4 interactions, shear, and proactive contributions from the LFA-1-bearing cells. In the ICAM-1-bearing endothelial cells, projections were enriched in actin but not microtubules, required intraellular calcium and intact microfilament and microtubule cytoskeletons, and were independent of Rho/ROCK signaling. Disruption of these projections with cytochalasin-D, colchicine or BAPTA-AM had no affect on firm adhesion. These data show that in response to LFA-1 engagement the endothelium proactively forms an ICAM-1-enriched cup-like structure that surrounds adherent leukocytes but is not important for firm adhesion. Whether this structure plays a role in transmigration remains to be determined.