

CBIMMS Invited Seminar
**Co-Sponsored by the Center for Biomolecular and Tissue
Engineering**

*“Neutrophil Adhesion and Signaling Within
the Inflammatory Synapse”*

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ABSTRACT

Two adhesive events critical to efficient capture of neutrophils at vascular sites of inflammation are upregulation of endothelial selectins that bind sLex-ligands and activation of 2-integrins that support neutrophil arrest by binding ICAM-1.

E-selectin binding alone can signal the transition from neutrophil rolling to arrest, but the mechanism is unresolved. Here we show that multivalent binding of E-selectin to sLex on L-selectin and PSGL-1 drives their colocalization into caps at the trailing edge of rolling neutrophils. Co-clustering of L-selectin/PSGL-1 was mimicked in neutrophil suspensions treated with E-selectin-IgG and soluble blockers of MAPK phosphorylation inhibited ligand capping.

Transition to arrest on endothelium involved redistribution of active 2-integrin to high avidity clusters within the contact region. Integrin mobility, but not the shift to high affinity, was also reduced by blocking MAPK. Taken together, the data reveal that multivalent binding of sLex ligands between a rolling neutrophil and endothelium via E-selectin drives the assembly of a macromolecular signaling complex denoted the inflammatory synapse.