Activated lymphocyte function-associated antigen-1 (LFA-1, $\alpha_L\beta_2$ integrin) found on leukocytes facilitates firm adhesion to endothelial cell layers by binding to intercellular adhesion molecule-1 (ICAM-1), which is upregulated on endothelial cells at sites of inflammation. Recent work has shown that LFA-1 in a preactivation, low-affinity state may also be involved in the initial tethering and rolling phase of the adhesion cascade. The ligand binding epitope of LFA-1 is contained entirely in the inserted (I) domain, and a conformational change in this region during activation increases ligand affinity. We have displayed wild-type I domain on the surface of yeast and validated expression using I domain specific antibodies and flow cytometry. Surface display of I domain supports yeast rolling on ICAM-1-coated surfaces under shear flow. I domain mutants were also expressed, and soluble ICAM-1 binding studies validated that these mutants have a range of affinities for the ligand. Expression of the locked open, high-affinity I domain mutant supports firm adhesion of yeast under shear flow, while yeast displaying intermediate-affinity I domain mutants exhibit a range of rolling phenotypes. Rolling behavior for these mutants fails to correlate with ligand binding affinity. These results indicate that unstressed binding affinity is not the only molecular property that determines adhesive behavior under shear flow.

For more information, please see:
Pepper LR, Hammer DA, Boder ET. J.Mol.Biol., 2006, 360, 1, 37-44.