**Effect of mechanical forces on the spatiotemporal organization of the b2-integrin receptor LFA-1.**

C. Manzo1, I. Piechocka1, A. Sosa-Costa1, K. Borgman1, T.S. van Zanten1, M.F. Garcia-Parajo1,2

*1ICFO- Institute of Photonic Sciences, Mediterranean Technology Park, 08860 Castelldefels, Spain*

*2ICREA- Institució Catalana de Recerca i Estudis Avançats, 08010 Barcelona, Spain*

[maria.garcia-parajo@icfo.es](mailto:maria.garcia-parajo@icfo.es)

Integrins are cell membrane adhesion receptors involved in morphogenesis, immunity, tissue healing and metastasis. A central, yet unresolved question regarding the function of integrins is how these receptors regulate both their conformation and dynamic nanoscale organization on the membrane to generate adhesion-competent microclusters upon ligand binding. Recent work has demonstrated that mechanical forces have a clear impact on integrin conformation [1] and that force transduction might lead to talin activation, in turn activating the actin polymerization machinery and linking integrins to the cytoskeleton [2,3]. These results highlight the impact of mechanical stimuli to regulate integrin conformation and function. Since integrin activation also depends on its lateral organization on the cell membrane, it is possible that changes in membrane physical properties and/or the membrane proximal actin cytoskeleton as a result of mechanical perturbations will have a major role in integrin activation. In our group, we exploit single molecule fluroescence techniques with high spatial (nanometer) accuracy and temporal resolution to investigate molecular conformation, lateral organization and dynamics of the b2-integrin LFA-1 on immune cells. Our overall results indicate that LFA-1 forms stable and non-mixable nanoclusters in the neighborhood of GPI-anchored protein nanodomains prior to ligand activation [4]. Mobility of LFA-1 on the cell membrane depends on its conformational state and anchoring to the cytoskeleton [4-6]. Furthermore, lateral mobility resulted crucial for microcluster formation upon ligand binding and for stable leukocyte adhesion under shear stress conditions [6]. Our ongoing investigations are centered on the role that mechanical stimuli (shear-stress and isotropic mechanical stretching) have on both activation and lateral mobility of LFA-1 on monocytes.

**References:**

[1] T. W. E, Trintchina et al, *Cell* **109**, 913, 2002.

[2] A. del Rio et al, *Science*, **323**, 638, 2009.

[3] E. M. Mace et al *Blood*, **116**, 1272, 2010.

[4] T.S. van Zanten et al *PNAS* **106**, 18557, 2009.

[5] R. Diez-Ahedo et al, *Small* **5**, 1258, 2009.

[6] G.J. Bakker et al *PNAS*,**109**,4869, 2012.