Protein engineering strategy to design and develop a photo-responsive ICAM-1 domain

Shardul Bhusari[1], *Priyanka Dhakane*[1], *Shrikrishnan Sankaran*[1], *Aránzazu del Campo*[1,2]

[1]INM Leibniz Institute for New Materials, Saarbruecken, Germany

[2]Chemistry Department, Saarland University, Saarbruecken, Germany

Shardul.Bhusari@leibniz-inm.de, Priyanka.Dhakane@leibniz-inm.de

The immunological synapse forms by tight apposition of Antigen Presenting Cells and T-cells. This structure is a complex assembly of spatially organized concentric rings of multiple proteins.[1] The functional role of molecular clustering in the center of immunological synapse is debatable. Numerous reports have shown that the spatiotemporal organization of the ligands, along with the APC's mechanical properties, are vital for the IS to form and function effectively.[2] The aim of our current research work is to establish artificial models of APCs based on hydrogel surfaces that allow light-regulated patterning of IS receptors. In particular, we have synthesized a photoswitchable Intracellular Cell Adhesion Molecule (ICAM). ICAM is an APC transmembrane protein which binds to LFA-1 on T-cells during early adhesion events of IS formation. For making it light switchable, we fused the Light-Oxygen-Voltage (LOV) domain from Avena Sativa to the N-terminus of extracellular domain 1 (D1) of ICAM.[3] This light switchable fusion protein is inactive in the dark, and can be reversibly activated using blue light, thereby allowing the possibility to dynamically modify the spatial distribution of active ICAM when immobilized on hydrogel surfaces. To analyze the dark and light state binding affinities of the photo-switchable D1 fusion proteins (PS-D1) towards LFA-1 αI, a new technique combining quartz crystal microbalance with dissipation monitoring (QCM-D) and nanoplasmonic resonance (NPS) is used.

References:

1. M. L. Dustin, Cancer Immunol. Res. 2014, 2, 1023–1033.
2. D. M. Davis, M. L. Dustin, Trends Immunol. 2004, 25, 323–327
3. Y. I. Wu, D. Frey, O. I. Lungu, A. Jaehrig, I. Schlichting, B. Kuhlman, K. M. Hahn, Nature 2009, 461, 104–108.