BIOMATERIALS

Forces in Biomolecular Systems SFB 863

Size-dependent protein sorting at membrane interfaces

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Abstract:

Membrane interfaces formed at junctions between cells are associated with characteristic patterns of membrane protein organization, such as E-cadherin localization to the edge of tight junctions and CD45 exclusion from the signaling foci of immunological synapses. While ligand-induced receptor clustering, lipid domain formation, and cortical cytoskeleton dynamics are important at cell-cell junctions, how the membrane itself contributes to spatial organization of membrane proteins at interfaces is unclear. Using an in vitro system of giant unilamellar vesicles and synthetic proteins, we recently showed that a fluid, deformable membrane interface linked by adhesion proteins drives segregation of non-adhesive proteins. This protein segregation can be sensitively tuned by modifying protein size and density, and membrane deformability. We hypothesize that these physical mechanisms underlie cell-surface protein sorting at all cellular junctions, and therefore influence downstream signaling. As a test case, we now ask if size-dependent protein sorting plays a role in Fc Receptor (FcR) driven phagocytosis. Interfacing macrophages with synthetic membranes containing size-controlled proteins with a site-specific IgG binding site, we show that the commitment to phagocytosis is critically dependent on the membrane-membrane distance imposed by the antibody-FcR complex. We further demonstrate that spatial segregation between large transmembrane phosphatases and the FcR underlies productive signaling. Our findings tempt us to speculate on implications of size dependence for the design of therapeutic antibodies directing macrophage effector activity against tumor cells.

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