Probing Nanoscale Architecture of Cell Adhesion Complexes by Superresolution Microscopy

Summary
Many complex biological functions are performed by supramolecular assemblies self-organized from a diverse ensemble of proteins. Cell adhesion structures such as the integrin-based focal adhesions and cadherin-based cell-cell junctions are multi-protein complexes known to transmit, sustain, sense, and respond to mechanical force. The knowledge of their physical organization is therefore essential for molecular mechanistic insights into their mechanobiological functions. Due to the nanometer size scale of the adhesion protein building blocks, the nanoscale is the functionally salient length scale for the spatial organization of these molecular complexes. Here, interference-based techniques in superresolution microscopy have been particularly useful for achieving sub 20-nm resolution amenable for deciphering protein organization. I will discuss our recent studies whereby such superresolution strategies have been employed to elucidate the nanoscale architecture of cell adhesion complexes and to probe molecular orientation and conformational transitions of key mechanotransducer proteins, providing structural frameworks for understanding how mechanical forces and biochemical signals may be integrated at cell adhesion sites.