

Dissecting Integrin-Mediated Mechanotransduction by Optogenetics

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Abstract

Integrin-based focal adhesions are essential for cellular attachment to the underlying tissue microenvironment, mediating cell migration, rigidity sensing, and the transmission of forces to the cell exterior. Recent studies suggest that the core mechanical linkage in focal adhesions may consist primarily of three indispensable components – integrin, talin, and actin. Since chemo/opto-genetic control offers a powerful approach for on/off switching of mechanical linkages that are prevalent at biological intermolecular interfaces, to enable systematic investigation of integrin-mediated mechanotransduction with high spatiotemporal precision, we generated a suite of chemo- and optogenetically modified talin to enable on-demand control of integrin/actin linkage by small molecule or light, respectively. I will discuss the development, characterization, and application of these molecular tools to interrogate different aspects of integrin-mediated mechanotransduction, with recent examples on multiplexing super-resolution microscopy with optogenetics.

Biography

Pakorn (Tony) Kanchanawong received his Ph.D. in Biophysics from Stanford University, followed by a postdoctoral training at the National Institutes of Health (NIH). He was recruited to the National University of Singapore as a recipient of the National Research Foundation Fellowship in 2011. He is currently an Associate Professor and Associate Head (Postgraduate Program/Research) in the Department of Biomedical Engineering as well as serving as Deputy Director of the Mechanobiology Institute. Research activities in his group spans from the development and application of super-resolution microscopy and advanced imaging techniques to mechanistic dissection of adhesion- and cytoskeleton-mediated mechanotransduction processes, particularly in integrin- and cadherin-based cell adhesions. His recent works include the development and application of 3D interferometric PhotoActivated Localization Microscopy to map the nanoscale architecture of integrin-based focal adhesions and determine the molecular basis of their organization in various cell types (Shtengel et al., PNAS 2009; Kanchanawong et al., Nature 2010; Liu et al., PNAS 2015; Xia et al. ACS Biomaterials Sci.&Eng. 2019). He has also been active in utilizing chemo- and optogenetic tools to control molecular-scale force transmission in cell-matrix adhesions (Wang et al., Nano Letters 2019; Rafiq et al., Nature Materials 2019; Yu et al., Phys Rev. X 2020). Beyond integrin-based cell-matrix adhesions, he also has a strong interest in applying super-resolution microscopy to study nanoscale molecular organization in cadherin-based cell-cell interactions (Wu et al., Developmental Cell 2015; Bertocchi et al., Nature Cell Biology 2017) or the actin cortex (Sakamoto et al., PLoS Biology 2018; Xia et al., Cell Reports 2019).