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Authors: Shumin Xia, Pakorn Kanchanawong

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Nanoscale mechanobiology of cell adhesions

Shumin Xia[1], Pakorn Kanchanawong[1,2,*]

[1]Mechanobiology Institute, Singapore. National University of Singapore, Republic of Singapore, 117411

[2]Department of Biomedical Engineering, Singapore. National University of Singapore, Republic of Singapore, 117411

*Correspondence: biekp@nus.edu.sg

Abstract

Proper physiological functions of cells and tissues depend upon their abilities to sense, transduce, integrate, and generate mechanical and biochemical signals. Although such mechanobiological phenomena are widely observed, the molecular mechanisms driving these outcomes are still not fully understood. Cell adhesions formed by integrins and cadherins receptors are key structures that process diverse sources of signals to elicit complex mechanobiological responses. Since the nanoscale is the length scale at which molecules interact to relay force and information, the understanding of cell adhesions at the nanoscale level is important for grasping the inner logics of cellular decision making. Until recently, the study of the biological nanoscale has been restricted by available molecular and imaging tools. Fortunately, rapid technological advances have increasingly opened up the nanoscale realm to systematic investigations. In this review, we discuss current insights and key open questions regarding the nanoscale structure and function relationship of cell adhesions, focusing on recent progresses in characterizing their composition, spatial organization, and cytomechanical operation.

Abbreviation

ECM: Extracellular matrices; FAs: Focal adhesions; NAs: Nascent adhesions; AJs: adherens junctions; PPIs: protein-protein interactions; EM: Electron microscopy; Cryo-ET: cryoelectron tomography; AFM: Atomic force microscopy; STED: stimulated emission depletion; SIM: structured illumination microscopy; PALM: Photoactivated localization microscopy; STORM: Stochastic optical reconstruction microscopy; FRET: Foster resonance energy transfer; ABS: Actin binding sites

Keywords: Nanoscale architecture; cell-cell adhesions; cell-matrix adhesions; super-resolution microscopy; mechanotransduction; integrin; cadherin; nanoclusters

1. Introduction

Forces interact with biological structures at multiple length scales to influence their forms and functions. This realization has propelled tremendous interest in the mechanobiology of diverse systems ranging from stem cells to tissues and organs[1-4]. The fundamental roles of mechanobiology is widely recognized in differentiation, developmental morphogenesis, homeostasis, immunity, and pathogenesis[5]. However, our understanding of the interplay between forces and biological structures has progressed unevenly at different length scales. In particular, mechanobiological processes are not as well understood at the nanoscale level, broadly defined as the 10-200 nm range, in between the length scales of structural biology techniques (~0.1-10 nm) and diffraction-limited light microscopy (200 nm and above)[6]. To understand mechanobiological processes at a predictive and quantitative level, an arguably useful conceptual framework is that of information processing[7]. Here, information is processed in units of individual molecules, through spatial-, temporal-, conformational-, and force-sensitive operations such as binding, unbinding, catalysis, degradation, cross-linking, clustering, and so on. All of these processes occur at the nanoscale. Hence, our ability to investigate mechanobiological processes at the nanoscale level is