Mechanical Activation of Talin, α-Catenin, and Vinculin

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Abstract

In tissue, cell adheres to extracellular matrix (ECM) through focal adhesion and to neighboring cells through cell-cell adhesion. Force-dependent regulations of focal adhesion and cell-cell adhesion have been shown crucial for shaping and maintenance of tissues. Talin and α-catenin, two cytoplasmic adapter proteins link the actin cytoskeleton to focal adhesion and cell-cell junction, respectively, which play central roles in regulation of the cell-ECM and cell-cell adherence. This regulation requires their binding to vinculin in a force dependent manner. By stretching single talin and α-catenin construct using magnetic tweezers, we find that force in physiological range can expose the vinculin-binding sites buried in them, drastically promoting subsequent binding of the head domain of vinculin with a nanoMolar affinity. The bound vinculin head can however be displaced at high forces > 30 pN, resulting in a biphasic force dependent binding of vinculin head to talin and α-catenin. Further, we find that full-length vinculin also binds to mechanically unfolded talin and α-catenin, implying release of the auto-inhibition conformation of full-length vinculin. Together, these results provide important insights into mechanosensing at cell-ECM and cell-cell adherence.

Biography

Yan Jie is currently an associate professor at the National University of Singapore (NUS). He is an principle investigator at Mechanobiology Institute (MBI) Singapore, NUS Centre for Bioimaging Sciences, NUS (Suzhou) Research Institute, and a faculty fellow at Singapore-MIT Alliance for Research & Technology (SMART). Professor Yan obtained two PhD. degrees: one in experimental biophysics from the University of Illinois at Chicago (2005; supervisor: Prof. John F. Marko), and the other in theoretical physics from Chinese Academy of Sciences (1998; supervisor: Prof. Ou-yang Zhong-can). His research areas involve investigating micromechanics of DNA, protein, and their interactions, at a single-molecule level using single-molecule force spectroscopy and single-molecule imaging method.