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Talin mediated force transmission and mechanosensing[1] JIE YAN, Department of Physics and Mechanobiology Institute, Natl Univ of Singapore, MINGXI YAO, Mechanobiology Institute, Natl Univ of Singapore, BENJAMIN GOULT, School of Biosciences, University of Kent, UK, MICHAEL SHEETZ, Department of Biological Sciences, Columbia University; Mechanobiology Institute, Natl Univ of Singapore — Cells adhere to extracellular matrix (ECM) through focal adhesion. Talin is a cytoplasmic adapter protein that links the actin cytoskeleton to focal adhesion, playing a central role in regulation of cell spreading and migration. Talin's functions depend on the binding of talin rod domains to a cytoplasmic protein vinculin in a force dependent manner. By stretching full-length talin rod using magnetic tweezers, we have determined the force-dependent unfolding and refolding rates of subdomains in talin rod. Kinetics simulations based on these rates have revealed that talin rod can serve as a force buffer, capable of maintaining tension in talin in a range of 5-10 pN over a wide range of extension change of talin rod from 50 nm to 400 nm. Further, this level of force is found able to expose the cryptic vinculin-binding sites, promoting subsequent binding of the head domain of vinculin with a nano Molar affinity. Such a force-sensitive interaction between talin rod and vinculin is described by a force-dependent dissociation constant derived based on the mechanical stability of the talin rod domains. Together, these results provide important insights into the mechanosensing at focal adhesion that is crucial for cells to sense and respond to their microenvironments.

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