Vinculin and Metavinculin Interact with Different Multiprotein Complexes, Associated with Integrin Adhesions

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Abstract

Focal adhesions (FAs) are large multi-protein complexes that act as transmembrane links between the extracellular matrix and the actin cytoskeleton. FAs were extensively characterized over the years, yet the molecular mechanisms underlying their mechanical and signaling functions remain unresolved. To address this question, protein complexes containing different FA components, were biochemically isolated from chicken smooth-muscle, and further characterized by combining cell biological approaches and mass spectrometry. Among the complexes found, were several vinculin and metavinculin-associated protein complexes. Vinculin is a ubiquitously expressed key focal adhesion component that serves as an adaptor protein, capable of binding more than eleven different partner proteins, as well as displaying an intra-molecular head-tail interaction, leading to the formation of a "closed conformation". Less is known about the molecular properties of metavinculin, a muscle-specific spliced isoform of vinculin that contains an extra stretch of 68 amino acids in the "neck region". Here we show that vinculin and metavinculin exhibit different dynamics within FAs of HeLa and vinculin-null mouse embryo fibroblasts. We also demonstrate that vinculin and metavinculin can be biochemically separated from one another, along with distinct sets of associated proteins, and that the open conformation of metavinculin is more prominent than that of vinculin.