

Cadherin dynamics and the cytoskeleton

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(Introduced by Pierre Moens)*

Classical cadherin adhesion receptors are major determinants of tissue organization both in health and disease. They have long been thought to function in close cooperation with the actin cytoskeleton. Despite this, the molecular mechanisms responsible for cadherin-actin cooperation are poorly understood and lack, indeed, a clear over-arching conceptual framework. A major analytic challenge is to develop approaches to encompass both the dynamics of adhesion receptor organization and the intrinsic dynamics of actin polymer assembly/disassembly and organization. We are tackling this problem by using lentiviral shRNA systems to “replace” endogenous proteins with XFP-tagged transgenes; and then combining live cell imaging (including FRAP and photactivation) with mathematical modelling in order to quantitatively characterize cadherin and cytoskeletal dynamics. This multimodal approach is yielding a picture of functional cytoskeletal modules that cooperate, in a context-dependent fashion, to regulate the stability and turnover of cell-cell junctions.