Mechanotransduction in Vascular Smooth Muscle: FAK-Rac as mediators of stiffness-induced responses

Yongho Bae, PhD

Abstract:

Extracellular matrix (ECM) stiffness is transduced into intracellular stiffness, signaling, and changes in cellular behavior. Integrins and several of their associated focal adhesion proteins have been implicated in sensing ECM stiffness. We investigated how an initial sensing event is translated into intracellular stiffness and a biologically interpretable signal. We found that a pathway consisting of focal adhesion kinase (FAK), the adaptor protein p130Cas, and the guanosine triphosphatase Rac selectively transduced ECM stiffness into stable intracellular stiffness, increased abundance of the cell cycle protein cyclin D1, and promoted S phase entry. Our findings establish that mechanotransduction by a FAK-p130Cas-Rac signaling module converts the external information encoded by ECM stiffness into stable intracellular stiffness and mechanosensitive cell cycling.