

## **ADHESION MECHANO-SENSITIVITY: A BIOCHEMICAL STUDY OF THE FORCE-DEPENDENT TALIN-RIAM-VINCULIN COMPLEX**

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Adherent cells and phagocytes are constantly submitted to similar changes in the mechanical properties of their environment and intracellular tension. They sense and transduce these parameters into an appropriate biochemical response. In these cells, the actin cytoskeleton plays a central role by transmitting force towards the mechano-sensitive focal adhesions or the phagocytic cup. These two structures couple the the actomyosin cytoskeleton to the extracellular matrix (ECM) or to the particle to phagocyte, via integrins and actin-binding proteins (ABP). The ABP talin controls integrin activation and actin anchoring, by recruiting the ABP vinculin in response to force. The talin-binding protein RIAM is thought to antagonize vinculin action. (1, 2) However, the molecular mechanism underlying this force-dependent antagonism has never been studied. We developed a novel in vitro system, made of pure proteins, to demonstrate that the actomyosin force unfolds talin to expose cryptic vinculin-binding sites (VBS) (3,4). We use this approach to characterize the effect of actomyosin force on the talin-vinculin-RIAM complex. The first data suggests that RIAM prevents force-dependent association of vinculin to talin. The effect of vinculin on RIAM association to talin in response to force will also need to be addressed.

### **References:**

- (1) Benjamin Goult, Thomas Zacharchenko, Neil Bate, Ricky Tsang, Fiona Hey, Alexandre Gingras, Paul Elliott, Gordon Roberts, Christoph Ballestrem, David Critchley, Igor Barsukov. RIAM and vinculin binding to talin are mutually exclusive and regulate adhesion assembly and turnover. *J. Biol. Chem.* (2013) 288:8238-8249
- (2) Ho-Sup Lee, Praju Anekal, Chinten James Lim, Chi-Chao Liu, Mark Ginsberg. Two modes of integrin activation form a binary molecular switch in adhesion maturation. *Mol Biol Cell.* (2013) May; 24(9):1354-62.
- (3) Corina Ciobanasu, Bruno Faivre, Christophe Le Clainche. Actomyosin dependent formation of the mechanosensitive talin-vinculin complex reinforces actin anchoring. *Nature Communications* (2014) 5:3095
- (4) Corina Ciobanasu, Bruno Faivre, Christophe Le Clainche. Reconstituting actomyosin-dependent mechanosensitive protein complexes in vitro. *Nature Protocols* (2015) Jan;10(1):75-89