

**Title of the project: Protein unfolding: a mechanical switch to control cell behaviour**

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**Project Description:** Cells attachment to the extracellular matrix (ECM) is mediated by macromolecular structures known as focal adhesion (FAs) complexes. The protein talin is a main player in FAs, and its interaction with other molecules orchestrates several cellular processes. Talin is strategically positioned in cells, it binds the cell membrane with the N-terminal head, and the actin cytoskeleton with the other end. As a consequence of this, during each cycle of acto-myosin contraction, the talin molecule is stretched and may expose previously cryptic sites to other molecules such as vinculin (one of its ligands). The degree of stretching depends on the compliance of the ECM. For example, in rigid substrates, talin is submitted to a greater tension, unfolds to a greater extend, and more vinculins can bind to its structure. Conversely, in soft substrates, talin might remain mostly unfolded; and in such condition, could only bind another FAs molecule, RIAM. The binding of talin to vinculin or RIAM brings opposite cell responses. Vinculin binding stabilizes the adhesion and triggers certain signalling cascades, while RIAM binding promotes cell protrusion, actin polymerization and lamellipodium formation. This project aims to investigate the interaction of talin with vinculin and RIAM in different substrate rigidities. The outcomes of this project will shed light on our understanding of how talin determines cell behaviour in physiological and pathological scenarios such as solid carcinomas, in which the rigidity of the substrates is significantly increased, making this disease highly influenced by mechanical cues.

**Key techniques:** Mutagenesis, cell transfection, cellular adhesion experiments, immunostaining.

Publications:

Haining AWM, von Essen M, Attwood SJ, Hytonen VP, del Río Hernández A. **All subdomains of the talin rod are mechanically vulnerable and may contribute to cellular mechanosensing** [ACS Nano 2016](#)

del Rio, A.; Perez-Jimenez, R.; Ruchuan, L.; Roca-Cusachs, P.; Fernandez, J. M. and Sheetz M.P. (2009) Stretching Single Talin Rod Molecules Activates Vinculin Binding. *Science*, **323**, 638-641.