

Laboratoire de Biochimie Théorique
Institut de **Biologie Physico-Chimique**
13, rue Pierre et Marie Curie
75005 PARIS

S E M I N A I R E

Sergi Garcia-Manyes

Department of Physics, Randall Centre for Cell and Molecular Biophysics, and London Centre
for Nanotechnology, King's College London, UK
The Francis Crick Institute, 1 Midland Road, London, UK

‘The mechanical stability of proteins regulates their translocation rate into the cell nucleus »

The translocation of mechanosensitive transcription factors (TFs) across the nuclear envelope is a crucial step in cellular mechanotransduction. Yet the molecular mechanisms by which mechanical cues control the nuclear shuttling dynamics of TFs through the nuclear pore complex (NPC) to activate gene expression are poorly understood. Here, we show that the nuclear import rate of myocardin-related transcription factor A (MRTFA) — a protein that regulates cytoskeletal dynamics via the activation of the TF serum response factor (SRF) — inversely correlates with the protein's nanomechanical stability and does not relate to its thermodynamic stability. Tagging MRTFA with mechanically-stable proteins results in the downregulation of SRF-mediated gene expression and subsequent slowing down of cell migration. We conclude that the mechanical unfolding of proteins regulates their nuclear translocation rate through the NPC and highlight the role of the NPC as a selective mechanosensor able to discriminate forces as low as ~ 10 pN. The modulation of the mechanical stability of TFs may represent a new, general strategy for the control of gene expression.

Mardi 28 mai 2019
11h00

Bibliothèque