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IN BRIEF

MECHANOTRANSDUCTION

Force-induced unfolding of fibronectin in the extracellular matrix of living cells.

Smith, M. L. *et al. PLoS Biol.* **5**, e268 (2007)

Fibronectin is a major component of the extracellular matrix (ECM) and forms fibrils that provide numerous binding sites for cell-surface and ECM proteins. Whether the mechanical forces imposed by cells on the ECM can mediate conformational changes in the fibronectin structure (model 1) or unfold fibronectin to regulate the exposure of numerous binding sites within fibronectin (model 2) has remained controversial. Viola Vogel and colleagues used fluorescence resonance energy transfer studies of fibronectin fibrils within a 3D matrix of human fibroblasts to show that mechanical force induces the unfolding of fibronectin, which potentially reveals cryptic binding sites while hiding others (model 2). Therefore, fibronectin unfolding could be important for mechanotransduction signalling.

DNA REPAIR

IgH class switching and translocations use a robust non-classical end-joining pathway.

Yan, C. T. *et al. Nature* **449**, 478–482 (2007)

Rag mutations reveal robust alternative end joining.

Corneo, B. *et al. Nature* **449**, 483–486 (2007)

The non-homologous end-joining (NHEJ) DNA-repair pathway rejoins DNA double-strand breaks (DSBs). The occurrence of DSBs can be programmed, for example, in processes that mediate antibody diversification (V(D)J recombination) and immunoglobulin expression changes (class switch recombination (CSR)) in B cells. Therefore, cells and mammals that are deficient in key components of the NHEJ pathway, such as XRCC4 and DNA ligase-4, are immunodeficient and are severely limited in NHEJ-mediated repair of DSBs, although evidence suggests that some rejoining can occur. The groups of Frederick Alt and David Roth now show in separate papers that an alternative NHEJ pathway can rejoin some DSBs, and that this mostly occurred when the 'classical' NHEJ pathway was non-functional. In addition, Alt and colleagues showed that the alternative NHEJ pathway was biased towards rejoining DNA ends with several base-pair homologies (microhomology) in CSR.

NUCLEAR TRANSPORT

Nanomechanical basis of selective gating by the nuclear pore complex.

Lim, R. Y. H. *et al. Science* 4 Oct 2007 (doi:10.1126/science.1145980)

Nucleocytoplasmic transport (NCT) across the nuclear envelope is regulated by nuclear pore complexes, which are supramolecular assemblies of numerous nucleoporins (Nups) surrounding a central pore. Nucleoporins involved in NCT contain FG domains (Phe-Gly repeats that are natively unfolded) that bind transport receptors (karyopherins) and selectively facilitate NCT. Roderick Lim, Birthe Fahrenkrog and colleagues used atomic force microscopy analyses to characterize how karyopherin-1β physically affects the FG domains of Nup153 to mediate transport through the nuclear pore. They showed that karyopherin-1β induced compaction of the FG domains that 'dangle' in the pore, allowing transit through it. The FG domains reverted back to a brush-like, entropic barrier conformation when the NCT inhibitor RanGTP was bound, providing a mechanical basis for NCT regulation.