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IN BRIEF

CELL SIGNALLING

Notch under tension

Notch signalling is a conserved pathway that regulates cell fate decisions and is initiated by binding of a transmembrane ligand (Jagged (JAG) or Delta-like (DLL)) to a Notch receptor. This binding is followed by proteolytic cleavage of the receptor, which requires molecular tension. Building on previous studies of DLL4–Notch1 interactions, Luca *et al.* applied *in vitro* protein evolution to generate a high-affinity JAG1 variant, and, using crystallography and affinity analysis, demonstrated that different ligands interact with Notch in clearly distinct ways. DLL4 binds to Notch with higher affinity than does JAG1, and lower tension was required for the activation of Notch by DLL4 or high-affinity JAG1 than by wild-type JAG1. These results suggest that mechanical tuning of Notch signalling occurs through the modulation of ligand–receptor affinity, which is determined by their intermolecular interactions.

ORIGINAL ARTICLE Luca, V. C. *et al.* Notch-Jagged complex structure implicates a catch bond in tuning ligand sensitivity. *Science* http://dx.doi.org/10.1126/science.aaf9739 (2017)

CHROMOSOME BIOLOGY

Trimethylation of CENP-A supports mitotic fidelity

Centromeres are chromosomal sites for kinetochore assembly, which supports the attachment of spindle microtubules and chromosome segregation. The centromere is specified by the incorporation of the histone H3 variant CENP-A into nucleosomes. CENP-A interacts with components of the constitutive centromere-associated network (CCAN), which forms the foundation for kinetochore assembly. Sathyan *et al.* now show that the first amino-terminal Gly residue of CENP-A is trimethylated and that this modification is important for interactions between CENP-A and CCAN in human cell lines. Chromosome segregation defects were observed in CENP-A-depleted cells that express CENP-A mutants that cannot be methylated, which most likely result from aberrant kinetochore assembly. Upon concomitant p53 depletion, the cells exhibited increased proliferative potential, both *in vitro* and when transplanted into mice, indicating that loss of CENP-A methylation may promote tumorigenic growth.

ORIGINAL ARTICLE Sathyan, K. M., Fachinetti, D. & Foltz, D. R. α-Amino trimethylation of CENP-A by NRMT is required for full recruitment of the centromere. *Nat. Comms.* http://dx.doi.org/10.1038/ncomms14678 (2017)

MEMBRANE DYNAMICS

PERKs of plasma membrane–ER communication

PRKR-like endoplasmic reticulum kinase (PERK) is an ER protein that regulates the unfolded protein response, but it has also been implicated in other cellular processes, including calcium (Ca^{2+}) signalling. van Vliet *et al.* identified actin regulators as important PERK interactors in mammalian cells. Knockout of *Perk* in mouse embryonic fibroblasts results in abnormal accumulation of filamentous actin (F-actin) at the cell cortex. Depletion of ER Ca^{2+} stores (or increase in cytosolic Ca^{2+}) normally induces the formation of plasma membrane–ER contact sites, which promote transport of Ca^{2+} to the ER. However, the cortical F-actin accumulations in $Perk^{-/-}$ cells interfered with the establishment of these contact sites, indicating that PERK — through its involvement in modulating actin organization — has an important function in regulating plasma membrane–ER contact site formation and Ca^{2+} homeostasis.

ORIGINAL ARTICLE van Vliet, A. R. *et al.* The ER stress sensor PERK coordinates ER-plasma membrane contact site formation through interaction with Filamin-A and F-actin remodeling. *Mol. Cell* **65**, 885–899 (2017)