CAL1 builds centromeres on the fly

Chen et al. reveal how Drosophila cells assemble the specialized histone CENP-A on centromeric DNA. Eukaryotic centromeres are defined by the histone H3 variant CENP-A, which is specifically incorporated into the nucleosomes that package centromeric chromatin. In mammalian cells, CENP-A is deposited at centromeres by a chaperone protein called HJURP. This protein is conserved in budding yeast but is missing from several eukaryotic lineages, including insects, nematodes, and fish. One candidate to fulfill HJURP’s function in flies is a protein called CAL1, whose depletion results in the loss of CENP-A from Drosophila centromeres.

Chen et al. found that mis-targeting CAL1 to noncentromeric sites (arrow) induces the ectopic incorporation of CENP-A (red).

A mutual interest in prostaglandin signaling

Binda et al. describe how the localization and activity of the prostaglandin receptor DP1 is regulated by its association with the enzyme that synthesizes its ligand. DP1 is a G protein–coupled receptor activated by the prostaglandin PGD₂. Much of the receptor is retained inside of the cell instead of being exported to the plasma membrane. Binda et al. discovered that the enzyme that synthesizes PGD₂, L-PGDS, binds to DP1 and colocalizes with the receptor in the endoplasmic reticulum and Golgi apparatus.

L-PGDS enhances DP1’s transport to the plasma membrane, the researchers found. Overexpressing the enzyme boosted DP1’s expression on the cell surface, whereas knocking down L-PGDS reduced the receptor’s export. L-PGDS promoted DP1 export by recruiting the chaperone Hsp90 into a complex containing both the receptor and the prostaglandin synthase. Abolishing the interaction between Hsp90 and L-PGDS, or inhibiting the chaperone with geldanamycin, prevented L-PGDS from stimulating DP1 export. The chaperone might help DP1 to fold correctly or regulate the vesicle transport machinery that delivers the receptor to the cell surface.

L-PGDS enhanced prostaglandin signaling by promoting DP1’s transport to the plasma membrane. But the receptor–enzyme interaction might also increase DP1 signaling inside the cell; DP1 stimulated L-PGDS’ enzymatic activity, generating PGD₂ that could potentially activate the receptor intracellularly. Indeed, L-PGDS and DP1 formed a complex with activated ERK kinases—downstream effectors of DP1—in the perinuclear region of cells. Senior author Jean-Luc Parent now wants to distinguish the effects of intracellular and cell surface DP1 signaling pathways.

Rouvinski, A., et al. 2014. J. Cell Biol. http://dx.doi.org/10.1083/jcb.201304015.

Prion infections come with strings attached

Misfolded prion proteins form extended amyloid strings on the surface of infected cells, Rouvinski et al. reveal. The endogenous prion protein, PrP, is attached to lipid rafts on the plasma membrane by a C-terminal glycosylphosphatidylinositol (GPI) anchor. Infectious prion particles convert PrP to a misfolded conformation, PrPSc, that is subsequently trimmed down to a protease-resistant C-terminal fragment. PrPSc forms amyloid fibers when detergent-extracted from infected cells, but whether it aggregates on membranes in vivo and where it localizes in the cell are still uncertain, in part because antibodies to the protein’s C-terminal region fail to recognize PrPSc under physiological conditions.

Rouvinski, A., et al. 2014. J. Cell Biol. http://dx.doi.org/10.1083/jcb.201308028.