Prions by activation not amyloid

If conformational change can cause an infection—as appears to be the case with the amyloid-inducing prions—then perhaps the same is true for other protein modifications. B. Tibor Roberts and Reed Wickner (NIH, Bethesda, MD) now claim to have found an example of this latter case, and they suggest that the discovery of more cases is a matter of time.

Wickner says he knew “for 10 years” about work from Beth Jones (Carnegie Mellon University, Pittsburgh, PA), in which yeast cells lacking the upstream activator protease A (PrA) suffered a gradual disappearance of protease B (PrB) activity. This slow decline was always blamed on gradual dilution (even 106-fold dilution) of PrA and PrB mRNAs and proteins, and inefficient autoactivation by PrB.

But now Roberts and Wickner show that PrB activity can be maintained indefinitely in the absence of PrA, presumably based on PrB autoactivation. That process fails, however, when PrB expression is temporarily extinguished and then restored. The newly expressed PrB cannot activate itself, apparently because only the activated form of PrB can carry out this function. This rule also holds true between cells: the inactive PrB can be rescued via an “infection” with cytoplasm from cells with activated PrB.

This may seem like an oddity of one particular yeast mutant. But, says Wickner, “there are undoubtedly a lot of other examples, because there are so many proteins that have the ability to modify themselves. You just need the situation where you need the modified form to do the modification.” Transfer of these proteins in carriers such as exosomes could even spread such an infection to distant cell types.

Reference: Roberts, B.T., and R.B. Wickner. 2003. Genes Dev. 17:2083–2087.

Neurons that swell

Cells that passively swell and contract with changes in osmolarity are the key to detecting those changes, say Zizhen Zhang and Charles Bourque (McGill University, Montreal, Canada).

Most cells have at least two mechanisms for maintaining homeostasis in response to changes in salt concentrations. Without these mechanisms, osmotic forces take over: more water and thus less salt outside cells leads water to flood into a cell. But this swelling doesn’t occur in most cells because they pump ions out. Even if there is some swelling, the cells prevent membrane stretching by adding extra membrane to compensate.

The osmosensory neurons studied by Zhang and Bourque lack both of these responses, so they swell and contract with changes in salt concentration. “It’s a behavior you expect from passive diffusion across a membrane,” says Bourque.

The neurons have membrane reserves so that they do not pop as they swell. But channels in the membrane are affected: the ironing out of membrane folds, tension on underlying cytoskeleton, or both act to turn off the channels. The resultant hyperpolarization and lack of firing leads to less vasopressin release so that the kidney directs more water to be excreted.

Reference: Zhang, Z., and C.W. Bourque. 2003. Nat. Neurosci. 10.1038/nn1124.

Ready to replicate? So vesiculate!

Initiation of nuclear envelope breakdown may be controlled by regulating COP1 access to Nup153, which is primarily known for driving vesicle formation during intra-Golgi and Golgi-to-ER traffic, were also found to associate with Nup153 and to move from the Golgi to the nuclear periphery at the start of mitosis.

Vesicles have previously been isolated from cells in which nuclear envelope breakdown has occurred, but it was always possible that the vesicles were formed as part of extract isolation rather than normal physiology. Now, the Utah team has found that the nuclear pore protein Nup153, COP1 coatomer proteins, and ARF GTPase are needed for nuclear envelope breakdown in frog egg extracts. COP1 components, which are better known for driving vesicle formation during intra-Golgi and Golgi-to-ER traffic, were also found to associate with Nup153 and to move from the Golgi to the nuclear periphery at the start of mitosis.

Reference: Liu, J., et al. 2003. Dev. Cell. 5:487–498.