And the winner is …

the phosphatase!

Signaling pathways can be a dizzying confusion of interlacing kinases, phosphatases, activators, and inhibitors. But with mathematical models, Reinhart Heinrich (Humboldt-University, Berlin, Germany), Benjamin Neel, and Tom Rapoport (Harvard Medical School, Boston, Massachusetts) have injected some transparency into these murky waters. And they have discovered that phosphatases have more influence than previously thought.

Until now, kinases appeared to be the powerhouses of signal transduction, and phosphatases were almost an afterthought. But when Heinrich derived analytical expressions for steps in an idealized kinase/phosphatase cascade, he found that phosphatases are in control of both the time it takes a signal to travel from the cell surface to its intracellular target and the duration of the signal. Kinases, however, have more influence over the strength of the signal.

Although the group started their work using simplified, idealized pathways, the models hold up in more complex pathways, and the outcomes are consistent with the behavior of kinases and phosphatases in vivo. Modeling, says Rapoport, enables scientists to see the relative contributions of a system’s components. This information can help to focus future efforts on critical points in a pathway. “My hope is that this paper may stimulate more research on the phosphatases, which must be as tightly regulated as the kinases,” says Rapoport.

Reference: Heinrich, R., et al. 2002. Mol. Cell. 9:957–970.

The nuclear pore as a chromatin boundary

Exportins are nuclear transport proteins associated with the nuclear pore complex (NPC). Evidence from Ulrich Laemmli (University of Geneva, Switzerland) and colleagues suggests the proteins act as chromatin boundaries, blocking the spread of heterochromatin by tethering the DNA to the NPC.

Laemmli’s group constructed a boundary-trap yeast strain to screen for proteins that can stabilize a reporter gene from the silent mating-type HML locus flanking it on either side. A large number of genes came out of the screen, says Laemmli, but the exportins, including Cse1p, Mex67p, and Los1p, are the first to be characterized.

Their boundary activity (BA) depends on a small COOH-terminal region in each of the proteins, a domain distinct from the Ran/GTP-binding domain required for transport activity. The exportins’ BA relies on interaction with Nup2p, a protein primarily associated with the nuclear pore. In yeast strains lacking Nup2 or the NPC-interacting Nup2 domain, the exportins lack BA. Thus, the exportin BA seems to rely on a physical bridge between the DNA and the NPC.

This sort of physical tethering, especially to the NPC, is not the only way chromatin boundaries are formed, and the physiological role of the interaction is not yet established, stresses Laemmli. But, he says, this unexpected turn “gives us a new view of something we don’t know that much about.”

Reference: Ishii, K., et al. 2002. Cell. 109:551–562.

Cajal body finds its function

The Cajal body (CB, formerly coiled body) is a prominent nuclear structure, yet its function remains obscure. Now, Xavier Darzacq, Tamás Kiss (CNRS, Université Paul Sabatier, Toulouse, France), and colleagues speculate that the CB is where small nuclear RNAs go for modification.

Last year, Kiss’s team identified a small guide RNA, U85, that directs both 2’-O-methylation and pseudouridylation of the spliceosomal component U5 snRNA. This year, they’ve identified six more RNAs, U87–U92, dubbed small Cajal body–specific RNAs, or scaRNAs.

The new scaRNAs resemble U85 in structure, and they contain sequences complimentary to pol II–transcribed UsnRNAs, suggesting that the scaRNAs may be guides for posttranscriptional modification of the UsnRNAs. The scaRNAs are immunoprecipitated by antibodies against fibrillarin and GAR, proteins that are likely to be involved in these modification reactions.

Most important, says Kiss, is the fact that these RNAs localize entirely to the CB, even when heavily overexpressed, making them unique in the world of CB biology. Previously, the best marker for the structure was p80-coilin, but only a fraction is in the CB—the rest floats free in the nucleoplasm.

This implies that the scaRNAs are functioning in the CB, not just being stored there. Add in the fact that both snRNAs and snoRNAs seem to transit through the CB, and Kiss thinks he’s found the elusive CB function. “This strongly, strongly indicates that at least one function of Cajal bodies is the posttranscriptional modification of the snRNAs,” he says.

Reference: Darzacq, X., et al. 2002. EMBO J. 21:2746–2756.