NUCLEAR TRANSPORT

Barring faulty exports

Reporting in *Cell*, Vincent Galy *et al.* have begun to unravel the molecular mechanisms underlying a process that has been largely inaccessible to experimentation — nuclear retention of unspliced mRNAs.

Building on previous work on the yeast structural proteins Mlp1 and Mlp2, the authors made a surprising discovery: Mlp1 and Mlp2 are distributed asymmetrically in the nuclear envelope, adjacent to chromatin. This prompted them to investigate what processes might take advantage of this unusual Mlp distribution.

Galy *et al.* found that inactivation of the splicing factor Prp18 was synthetically lethal with *MLP1* deletion. Deleting *MLP1* or *MLP2* had no detectable effect on splicing; instead, *mlp1Δ* and *prp18Δ* mutant strains both 'leaked' intron-containing mRNAs (*MLP2* deletion had no such effect), and combining both mutations was additive.

But how does Mlp1 function to retain RNAs in the nucleus? Galy *et al.* found that, on Mlp1 overexpression, intranuclear Mlp1 clusters trap specifically intron-containing mRNAs, and identified SF1 as an RNA-dependent Mlp1-binding partner. SF1 is known to bind specifically to the branchpoint region of intron-containing RNAs, so the RNA-dependent interaction between SF1 and Mlp1 demonstrates a physical link between Mlp1 and unspliced mRNAs. Further data indicates that the 5′ splice site mediates Mlp1-dependent retention.

Finally — building on evidence that the nucleoporin Nup60 docks Mlp1 and Mlp2 into position, and that its deletion mislocalizes them both — *nup60Δ*-dependent release of Mlp1 was shown to result in more severe (but less specific) pre-mRNA leakage and a splicing defect, which indicates that Nup60 is also involved in pre-mRNA retention.

So, Galy *et al.* have shown, for the first time, that splicing and pre-mRNA retention are functionally distinct processes, and propose that in its asymmetric distribution "…Mlp1 implements a quality control step prior to export, physically retaining faulty pre-mRNAs".

Natalie Wilson

References and links

ORIGINAL RESEARCH PAPER Galy, V. *et al.* Nuclear retention of unspliced mRNAs in yeast is mediated by perinuclear Mlp1. *Cell* **116**, 63–73 (2004)

PROTEOMICS

Interacting maps

Understanding protein–protein interactions within complex molecular networks can help us to understand many biological processes. A eukaryotic protein–protein interaction, or interactome, mapping effort has been initiated for *Saccharomyces cerevisiae*. However, many of the protein–protein interactions that are relevant for understanding human biology, disease and development only take place in multicellular organisms. Now, the interactome maps of two multicellular model organisms have been reported.

From a draft map of 7,048 proteins and 20,405 interactions, Jonathan Rothberg and colleagues have produced a high-confidence *Drosophila melanogaster* interactome map of 4,679 proteins and 4,780 interactions — to do this, they developed a computational method (a statistical model that incorporates experimental data) to assign confidence to the interactions. These authors found that the interactome map not only recreated known pathways, but that it also extended them and identified new pathway components. They also found that the protein–protein interactions were organized on both a local and a global level — this organization is thought to represent the formation of multiprotein complexes and intercomplex connections, respectively.

For *Caenorhabditis elegans*, Marc Vidal and colleagues identified 4,027 interactions, which they validated using a second, independent protein interaction assay. They then combined these interactions with previously identified interactions (found for specific processes, such as vulval development and germline formation) and those predicted by *in silico* searches for interactions that are known to exist for orthologues in other species. The result, Worm Interactome version 5 (WI5), contains 5,534 interactions and connects 15% of the *C. elegans* proteome. Interestingly, by showing that ancient, multicellular and worm-specific proteins interact with each other equally well, these authors also add weight to the theory that evolution creates new structures by modifying pre-existing ones.

The availability of these two different interactome maps is good news, because they not only provide "…functional hypotheses for thousands of uncharacterized proteins…" but are also "…a starting point for the systems biology modeling of multicellular organisms, including humans". And, in an effort to make these interactomes public resources, Rothberg, Vidal and colleagues have deposited the interactions in various databases, including FlyBase, GRID (general repository of interaction datasets), BIND (biomolecular interaction network database) and DIP (database of interacting proteins).

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References and links

ORIGINAL RESEARCH PAPERS Giot, L. *et al.* A protein interaction map of *Drosophila melanogaster*. *Science* **302**, 1727–1736 (2003) | Li, S. *et al.* A map of the interactome network of the metazoan *C. elegans*. *Science* 2 Jan 2004 (doi:10.1126/science.1091403)