WEB WATCH

• http://www.biocompare.com

Buyer's guide

Do you ever want to buy an enzyme or kit but end up being bewildered by which one to choose from the increasingly large range on offer? Well, Biocompare — a company based in California, United States — aims to help by being "The buyer's guide for life scientists". It was started a few years ago by life scientists who wanted better information in order to compare reagent purchasing, and on this web site you can browse products that relate to cell biology, molecular biology and tissue culture, to name just a few. The company's mission is "to facilitate scientific discovery by providing objective product information to the life science community".

And this site is not just about browsing products — it has evolved to include several other useful and freely accessible sections, including New Technologies, News, Professional Reviews and Technology Spotlights. You can view News as either 'Top Stories', or perhaps more conveniently under categories relating to your research interests. The Professional Reviews contain a synopsis, which succinctly summarizes the review information under the headings 'Product', 'The Good', 'The Bad' and 'The Bottom Line'.

The web site is easy to use and navigate, and is consistently and frequently updated. There is a simple search facility on the home page, and the search results are listed under the sections mentioned above. By stopping scientists having to search through print catalogues to find the product they need, Biocompare aims to give them more time to focus on their valuable work.

Rachel Smallridge

RNA PROCESSING

Nonstop destruction

How do you deal with messenger RNAs that just don't know when to quit? Cells can create transcripts that contain no stop codons for the translation machinery to recognize, which can lead to the synthesis of abnormal and potentially harmful proteins. But according to two reports in *Science*, cells recognize these so-called 'nonstop' mRNAs and can destroy them using a mechanism called nonstop decay.

The cell has evolved a remarkable array of quality-control mechanisms to ensure gene expression occurs correctly, such as nonsense-mediated mRNA decay (NMD), which detects mRNAs that contain premature termination codons and stops the formation of truncated proteins.

But what happens in the opposite case, when no stop codon exists? Frischmeyer and colleagues constructed a nonstop-PGK1 construct — in which all in-frame termination codons were removed — and found that these 'nonstop' transcripts were just as unstable in *Saccharomyces cerevisiae* cells as a nonsense form of the gene.

However, the nonstop transcripts were still unstable in yeast mutants that lacked factors required for both the NMD pathway and for the destruction of normal mRNAs, yet required translation of the mRNA for the decay to occur (as shown by cycloheximide treatment, which inhibits protein synthesis, or by depletion of charged transfer RNAs) — so the destruction of nonstop transcripts had to be occurring through a different pathway.

The most obvious candidate is the exosome, a collection of proteins with a 3′–5′ exoribonuclease activity that processes RNAs, such as ribosomal RNA, small nuclear RNA and small nucleolar RNA. Van Hoof *et al.* showed that a yeast mutant for Ski4, one of the core exosome subunits that specifically disrupts cytoplasmic 3′–5′ degredation of mRNA, stabilized the nonstop-PGK1 at least sixfold. The nonstop transcripts were also stabilized by mutant forms of Ski7, which is related to the translation elongation factor EF1A and the translation temination factor eRF3, and is one of two other factors that are also required for exosome-mediated degradation. Transcriptional pulse–chase studies using transcripts with differing lengths of poly(A) tails suggested that the mechanism used to degrade the nonstop mRNAs starts at the 3′ end of the poly(A) tail.

Together, these data provide a model for how the cell detects and destroys nonstop mRNAs. When the ribosome reaches the end of the nonstop mRNA strand, the exosome homes in on the stalled ribosome. Ski7 associates with the cytoplasmic form of the exosome, which then degrades the mRNA, starting from the 3′ end of the poly(A) tail. Given the similarity of Ski7 to EF1A and eRF3 — which interact with the A site of ribosomes that contain a sense or nonsense codon, respectively — Ski7 might distinguish nonstop from normal mRNAs by binding to the empty A site of ribosomes that have reached the 3′ end of mRNAs.

Many questions remain but the authors say that nonstop decay might be a valuable and necesssary mechanism. It could be required for mRNAs containing a 3′-end

CELL POLARITY

Building site

Multi-domain scaffolding proteins are important for cell polarity because they target proteins to precise subdomains. Margolis's group has now identified a new multiprotein complex that localizes to tight junctions and is therefore a strong candidate for regulating epithelial cell polarity.

The authors found that Pals1, a membrane-associated guanylate kinase (Maguk) scaffolding protein with several protein-interaction domains, localizes to tight junctions, and then identified one potential protein — Pals1-associated tight junction protein (PATJ) — that might target it there. PATJ binds to a distinct domain (L27N) of Pals1 through a new protein–protein interaction domain that the authors called a Maguk recruitment (MRE) domain.

PATJ was shown to be part of a ternary complex that binds not only Pals1, but also CRB1, the human homologue of *Drosophila melanogaster* Crumbs. But PATJ and CRB1 don't bind directly to each other, which indicates that Pals1 probably functions as an adaptor. Similarly, in *Drosophila*, Crumbs binds the Pals1 orthologue, Stardust, but doesn't bind the PATJ homologue, Discs Lost.

Discs Lost and Crumbs are both essential for cell polarity and have also been implicated in the localization of adherens junctions. So, although the exact function of the Pals1 complex needs further clarification, its conservation from fly to human indicates the importance of this complex.

Katrin Bussell

References and links

ORIGINAL RESEARCH PAPER Roh, M. H. *et al.* The Maguk protein, Pals1, functions as an adaptor, linking mammalian homologues of Crumbs and Discs Lost. *J. Cell Biol.* **157**, 161–172 (2002)

FURTHER READING Rashbass, P. & Skaer, H. Cell polarity: Nailing Crumbs to the scaffold. *Curr. Biol.* **10**, 234–236 (2000)

WEB SITE

Ben Margolis' laboratory: http://www.med.umich.edu/cmb/margolis.htm