HIGHLIGHTS

WEB WATCH

A genome goldmine

- <http://wit.integrated-genomics.com/GOLD/>

It is almost impossible these days to keep track of all the organisms whose genomes are being fed through sequencing machines, so I take my hat off to the curators of this web site who have put together an impressive array of information on the many sequencing projects that are out there. The Gold — Genomes Online Database — web site provides continuously updated information on both ongoing and completed sequencing projects, with links through to relevant sequence databases and additional information where available. The site is sponsored by Integrated Genomics, Inc., who are involved in sequencing several prokaryotic genomes.

There are several ways in which to search through the information that is available on this web site. One way is to use a search query form to take you through to genome sequencing information on a specific organism of interest. A feature of the Gold database that I particularly like is the scrollable pages of ongoing prokaryotic and eukaryotic sequencing projects — there are just under 450 of them in total. You can browse through these pages to see what genomes are being sequenced, where the sequencing is being done and who is funding the sequencing of an organism. These pages also provide useful links to taxonomic information on each organism, and links through to some of the main sequencing centres. All in all, it's a golden resource for the genetics and genomics communities.

Jane Alfred

RNA PROCESSING

Nonstop destruction

How do you deal with mRNAs 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 an 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 when an mRNA has no stop codons? Frischmeyer and colleagues generated 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. Moreover, their destruction required translation, which indicates that this process occurs through a different pathway.

The most obvious candidate for this is the exosome, a collection of proteins with a 3'–5' exoribonuclease activity that processes RNAs, such as ribosomal RNA and small nuclear RNA. Van Hoof *et al.* showed that a yeast mutant for *Ski4* — which encodes one of the core exosome subunits — in which cytoplasmic 3'–5' mRNA degradation is disrupted, stabilized the nonstop-PGK1 transcripts at least sixfold. The nonstop transcripts were also stabilized by mutant forms of

Ski7, which is related to the translation elongation factor EF1A and to the translation termination 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 indicated that the mechanism used to degrade the non-stop 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 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 necessary mechanism — for example, for processing mRNAs that contain a 3'-end processing signal upstream of the termination codon (as is found in 1.2% of expressed sequence tags from *S. cerevisiae*).

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Nature Reviews Molecular Cell Biology

References and links

ORIGINAL RESEARCH PAPERS Frischmeyer, P. A. *et al.* An mRNA surveillance mechanism that eliminates transcripts lacking termination codons. *Science* **295**, 2258–2261 (2002) | Van Hoof, A. *et al.* Exosome-mediated recognition and degradation of mRNAs lacking a termination codon. *Science* **295**, 2261–2264 (2002)
FURTHER READING Macquart, L. E. Skiing toward nonstop mRNA decay. *Science* **295**, 2221–2222 (2002)