GENE EXPRESSION

The nonsense police

RNA transcripts that encode truncated proteins are eliminated from eukaryotic cells by a process known as mRNA surveillance. In yeast and *Caenorhabditis elegans*, classical genetic approaches have identified some of the genes required for this surveillance. A puzzle, however, is why mRNA surveillance exists at all. What are the natural targets? Mitrovich and Anderson provide some possible answers.

The authors reasoned that, in a *C. elegans* mRNA surveillance mutant (*smg-2*), RNA transcripts that are targets for mRNA surveillance will tend to be present at higher levels, relative to wild-type strains. This was the basis for an RNA subtraction experiment and, sure enough, transcripts were identified that were enriched in the surveillance mutant.

Gene transcripts for four ribosomal proteins were repeatedly represented in the selected pool and, in all cases, the transcript was aberrant, containing part of an intron that would normally have been removed by splicing. The intronic sequence also contained in-frame stop codons. Overall, it seems that these ribosomal protein genes produce two types of transcript — a productive and an aberrant transcript — and the aberrant transcript is normally removed by mRNA surveillance.

Mitrovich and Anderson found that the intronic sequences present in the aberrant transcripts are highly conserved among a group of nematodes, suggesting that the sequences have functional significance, despite not encoding protein. The authors speculate that this function helps to ensure the tight regulation of ribosomal protein levels. When ribosomal protein levels rise, one way of reducing new protein synthesis is to bias splicing towards the aberrant transcripts, and the authors provide data to support this view. But then the cell has a problem — the aberrant transcript could encode a truncated, and possibly deleterious, protein. At that point, the surveillance mechanism steps in and removes the offending transcripts.

Mark Patterson

References and links

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WEB SITES Phil Anderson's homepage

EVO-DEVO

A head with no torso

When we think of *Drosophila*, it's often in terms of the genes and processes that it has in common with higher animals. The well scrutinized pathway of how a fly embryo tells its head from its tail (and everything inbetween) has laid the paradigm for the patterning function of morphogens in development. But it is puzzling that many other insects — never mind ourselves — don't undergo patterning in quite the same way. The fly uses two different pathways to specify the anterior tip of its head. Now Schaeffer *et al*. show that these two pathways, whose function in anterior development has been acquired recently in evolution, converge on similar targets and that removal of one of them can be compensated by boosting the other.

The *Drosophila* body plan is set up by the action of three sets of maternally contributed genes: the anterior, posterior and terminal systems. The terminal system requires local signalling through the Torso (Tor) receptor tyrosine kinase, which specifies the extreme tips of the head and tail. The anterior and posterior systems consist of localized mRNAs that, once translated, form gradients that regulate target genes in a concentration-dependent manner. The homeoprotein Bicoid is the most notable among the anterior-group genes, and embryos born to *bcd*$^-$ mothers lack a head, thorax and part of the abdomen.

Schaeffer *et al*. show that, in the anterior of the fly embryo, *bcd* and *tor* are part of two independent pathways that share common target genes. What's more, a deletion mutant of *bcd* that is expressed 3–4 times higher than the wild-type protein can rescue the phenotype of the *tor* pathway, to give embryos with normal anterior structures. Indeed, increased doses of wild-type Bicoid protein suffice to rescue the anterior defects of terminal-pathway mutants. This argues that one function of Tor is to potentiate the anterior system, as the rescue occurs by upregulating downstream targets, such as *huckebein*.

The additive effect of the terminal system on *bcd* had already been suspected: hypomorphic mutants of *bcd*, or mutations in the genes that localize *bcd* mRNA, look virtually identical to embryos with terminal phenotypes, with double mutants being much more severe. In addition, correct *huckebein* expression can be induced by either Tor or Bcd activity alone.

Bicoid seems to be a recently acquired gene in fruitflies, and the use of *bcd* and *tor* at the anterior is an eccentricity of *Drosophila*.

If, as is proposed, Tor antagonises repressors of Bcd targets then, in insects that lack *bcd*, the anterior terminal system could assist other genes (e.g. orthodenticle, thought to be one of the ancestral head determinants). The fact that *tor* is dispensable for head development might explain why most insects (e.g. with short germband development) can form a head even if it develops further down the egg.

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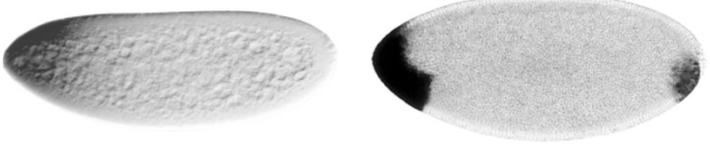
LAB PAGES Claude Desplan's lab page at NYU
WEB SITES Flybase, the *Drosophila* database



Bicoid protein is expressed at the anterior of the embryo (left), where it reinforces the expression of *crocodile*, a target of the Torso terminal pathway (right).
Courtesy of Valérie Schaeffer and Ernst Wimmer.