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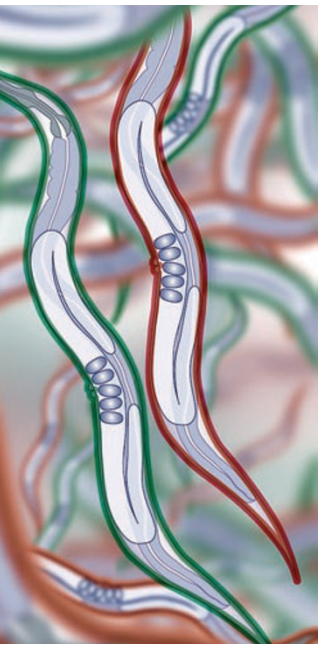
TECHNOLOGY

Colour-changing worms



Observing the real-time changes in gene expression that occur during the development of a living worm is now possible owing to a recent study by Ohno and colleagues. Using fluorescent proteins, the team visualized developmentally regulated changes in live nematodes during alternative pre-mRNA splicing, the process that produces proteome diversity from a finite number of genes.

Alternative splicing of the *Caenorhabditis elegans lethal 2* (*let-2*) gene — which encodes collagen α2(IV) and is expressed in the body wall muscles — is strictly regulated and changes during the worm's lifetime: embryos express only exon 9, whereas adults express only exon 10; thus, these two exons are mutually exclusive. A transgenic worm reporter system revealed the tissue-specific expression profiles of each developmentally regulated *let-2* exon using a GFP cDNA linked to exon 9 and a red fluorescent protein (RFP) cDNA linked to exon 10. Under the control of the body-wall-specific promoter *myo-3*, expression of the *let-2* reporters almost completely switched from GFP to RFP during development from the embryo to the adult stage, in parallel with endogenous *let-2* mRNAs. By visualizing the splicing patterns of exons 9 and 10 in this way, the authors identified splicing mutants, an intronic sequence that is required for developmental switching and their partially spliced pre-mRNAs as other processing intermediates.

The advantages of this technique are that it can be used in higher metazoans such as mice, and that the relative abundance of two different mRNA isoforms can be reliably analysed in each cell with only a minimal effect on the transcription level in living organisms.

Deregulated alternative splicing is thought to have a role in cancer and inherited neurodegenerative diseases; thus, achieving a greater understanding of how pre-mRNAs are developmentally regulated through the use of alternative splicing reporter proteins will help in elucidating this proposed role.

Anne Blewett, Copy Editor, Nature Reviews Molecular Cell Biology

ORIGINAL RESEARCH PAPER Ohno, G., Hagiwara, M. & Kuroyanagi, H. STAR family RNA-binding protein ASD-2 regulates developmental switching of mutually exclusive alternative splicing *in vivo*. *Genes Dev.* **22**, 360–374 (2008)