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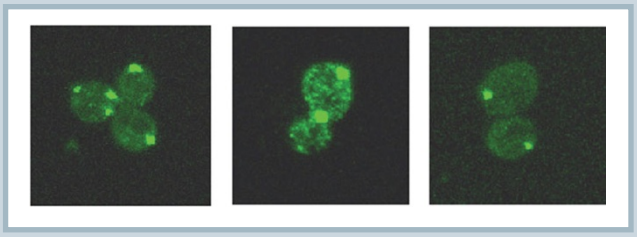
Visualizing an mRNA destruction line

When it comes to the fate of mRNA, location *is* everything. mRNA is transcribed and processed in the nucleus, then transported to the cytoplasm where it is translated into protein. Quality control processes that are encountered along the way are believed to destroy a substantial amount of mRNA before it leaves the nucleus, and cytoplasmic mRNA decay—which determines the half life of the message—is a key factor in determining the ultimate amount of protein produced. Now, a report by Ujwal Sheth and Roy Parker in the May 2 issue of *Science* (**300**, 805–808; 2003) presents the most recent example of the subcellular compartmentalization that occurs during the lifecycle of mRNA.

In yeast, the mRNA decay process can be broken down into three distinct steps. The first step, deadenylation, involves removal of the poly(A) tail from the 3′ end of the mRNA. This triggers cleavage of the structure that caps the 5′ end of the mRNA (decapping), which paves the way for 5′ to 3′ degradation.

By constructing green fluorescent protein (GFP) fusions of yeast mRNA decay factors, Sheth and Parker were able to determine the localization of these proteins within live cells. And their observations were striking. Both subunits of the decapping enzyme, Dcp1p (left) and Dcp2p, were found to concentrate to specific cytoplasmic locations, as were the decapping activators Lsm1p (right), Pat1p (not shown) and Dhh1p (center). And, studies that incorporated GFP-tagged Dcp1p or Dhh1p together with red fluorescent protein–tagged Lsm1p showed that these proteins were co-localizing.

The authors term these subcytoplasmic structures processing bodies, or 'P bodies', and suggest that they are specific sites of



mRNA decapping and degradation (Ccr4p, a subunit of the major deadenylating enzyme, was much more uniformly dispersed throughout the cells, suggesting that the deadenylation step takes place outside of P bodies). Their proposal is buoyed by several points of evidence. Inhibition of the mRNA turnover process at different points along the decay pathway had a predictable effect on the number and size of the P bodies. Blocking either decapping or degradation led to increases in the size and number of P bodies, whereas blocking deadenylation markedly reduced the number and size of P bodies.

The authors also used GFP-tagged mRNA that contained specific RNA sequences that were known to block degradation, stalling the decay process after the decapping step. The decay intermediates, too, accumulated in the P bodies, localizing mRNA decay to the P bodies. And, although the P-body decay pathway is by no means the only mRNA decay pathway, there is evidence that a similar pathway may exist in mammalian cells. Thus, the results of Sheth and Parker offer new and valuable insight into the controlled and compartmentalized lifecycle of mRNA.

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