Stress management for mRNAs

An enzyme involved in mRNA degradation turns into a transcript stabilizer during stress, Yoon et al. report. mRNA fates are determined by their association with regulatory proteins in ribonucleoprotein (mRNP) complexes. mRNPs can accumulate in large, cytosolic aggregates; P bodies, for example, contain translationally repressed mRNAs complexed with proteins that initiate mRNA destruction. One of these proteins is the enzyme Dcp2p, which removes the 5’ cap from mRNAs to spur their degradation. Yoon et al. found that budding yeast Dcp2p is phosphorylated during cell stress, when cells alter the fate of many of their mRNAs to aid their survival and recovery.

Dcp2p was phosphorylated by the stress-activated kinase Ste20p. Blocking this modification—either by mutating the phosphorylation site or deleting the kinase—prevented Dcp2p from accumulating in P bodies during stress and inhibited the formation of a second type of RNA–protein aggregate called stress granules. Yeast stress granules can depend on P bodies for their formation and contain repressed mRNAs that may be poised to re-begin translation. A Dcp2p mutant mimicking the phosphorylated form accumulated normally in P bodies and restored stress granules to yeast lacking Ste20p.

The phosphomimetic form of Dcp2p also stabilized a subset of yeast mRNAs, including a number of transcripts encoding ribosomal proteins. Senior author Roy Parker thinks that Dcp2p phosphorylation changes the fate of these transcripts by altering the decapping enzyme’s interactions with other regulatory proteins, promoting the mRNAs’ stable accumulation in stress granules instead of initiating their degradation. The mRNAs are thus poised to be translated once conditions improve, allowing the yeast to rapidly recover.

Yoon, J.-H., et al. 2010. J. Cell Biol. doi:10.1083/jcb.200912019.

The story of O-glycosylation

The tyrosine kinase Src boosts protein glycosylation by stimulating the transport of specific enzymes from the Golgi to the ER, Gill et al. reveal.

Src is activated downstream of growth factor receptors, but although a portion of the kinase localizes to the Golgi, little is known about its function at this organelle. Gill et al. discovered that growth factor stimulation induced a group of glycosylating enzymes called GalNac-Ts to relocate from the Golgi to the ER. This redistribution was blocked by inhibiting Src or by preventing the formation of COP-I transport vesicles. These vesicles only convey GalNac-Ts in response to Src activation: other glycosylation enzymes stayed put in the Golgi.

Gill, D.J., et al. 2010. J. Cell Biol. doi:10.1083/jcb.201003055.

Nebulin doesn’t measure up

Muscle cells expressing mini-nebulin contained filaments that were longer than mini-nebulin itself, indicating that the protein doesn’t measure out filament length directly. Instead, nebulin regulates thin filament size by stabilizing them: both full-length and mini-nebulin protected filaments from the depolymerizing drug latrunculin A. Filaments never depolymerized to lengths shorter than mini-nebulin, suggesting that the protein binds the filaments to set their minimum size. But photobleaching experiments revealed that mini-nebulin also stabilized filament ends not directly bound by the protein, allowing the filaments to grow longer still.

Senior author Carol Gregorio now wants to investigate how mini-nebulin stabilizes parts of the actin filament it has no contact with. The shortened protein will also enable studies of nebulin mutations that cause nemaline myopathy, a human disease characterized by protein aggregates and muscle weakness, and sometimes short, thin filaments.

Pappas, C.T., et al. 2010. J. Cell Biol. doi:10.1083/jcb.201001043.