Stress management for mRNAs

A

n 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 phosphoryl-

ation 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

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he tyrosine kinase Src boosts protein glyco-
sylation 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.

GalNac-Ts add N-acetylgalactosamine sugars to serine and

threonine residues of secretory proteins—the initial step

in the O-glycosylation pathway. Src activation and enzyme

redistribution increased O-glycosylation levels, perhaps because

ER-localized GalNac-Ts have access to their protein substrates

for longer, or because they face less competition from other

glycosylation enzymes that remain in the Golgi.

Senior author Frederic Bard now wants to understand how

GalNac-Ts are specifically recruited into COP-I vesicles upon Src

activation—he suspects that the kinase phosphorylates an adaptor

protein that links the enzymes to the COP-I machinery. Another

question is how increased O-glycosylation affects cell behavior.

One possibility is that changing the glycosylation pattern of cell

surface proteins will alter their interactions with neighboring

cells or the extracellular matrix, suggesting a potential new way

for growth factors and Src to influence cell adhesion.

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

Nebulin doesn’t measure up

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appas et al. demonstrate that the giant disease-

related protein nebulin stabilizes actin filaments

to control their length in skeletal muscle.

Nebulin is big enough to stretch the entire length of muscle

filaments, binding individual actin subunits via a series

of repeated domains. Alternative splicing produces nebulin

molecules in various sizes that match the filament lengths

of different muscle tissues, suggesting that nebulin acts as a

“molecular ruler,” setting filament length by binding a defined

number of actin monomers. The protein’s size has hampered

efforts to test its function directly, so Pappas et al. synthesized a

truncated “mini-nebulin” to replace the longer version.

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.