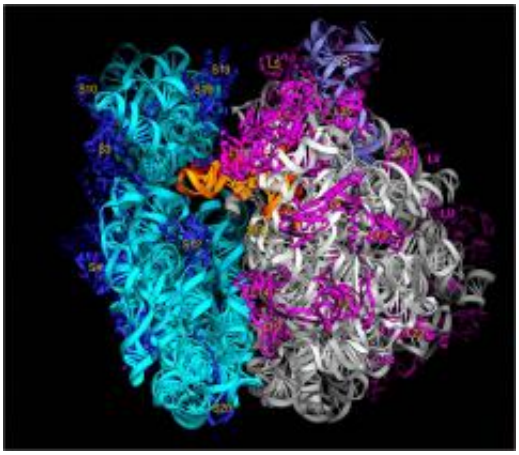
Cell's protein-making machines shift modes under stress

April 23 2015, by Krishna Ramanujan



ribosome

Similar to a hybrid car that switches from gas to electric as it drives on major highways and secondary roads, Cornell researchers have discovered that the cell's protein-making machinery, called ribosomes, exists in a hybrid form to meet different needs encountered under normal and stressed conditions.

The traditional view of ribosomes was that they operate in only one mode. But a study published April 13 in the journal *Nature Structural and Molecular Biology* finds that ribosomes actively change their structure depending on whether a cell is in a normal and stressed state.

While the study advances our understanding of basic cell biology, it also has relevance for countless diseases related to cell stress, including cancer.

"In normal conditions, the ribosome is mainly responsible for [making] housekeeping proteins" that facilitate regular cell functions, said Shu-Bing Qian, associate professor of nutritional sciences and the paper's senior author. Xingqian Zhang, a research associate in Qian's lab, is the paper's first author.

But when a cell becomes stressed, these housekeeping jobs must slow down so errors don't occur. At the same time, "there are certain survival proteins that need to be promoted to deal with the stress," Qian said. "A long-standing mystery is how the ribosome knows to switch their targets" between normal and stressed conditions, Qian added.

The researchers discovered that a protein, called MRPL18, attaches to ribosomes during cell stress, which changes the ribosomes composition and function. MRPL18 is normally localized in the cell's powerhouse, an organelle called the mitochondria. But in the event of stress, MRPL18 loses a signal that helps facilitate its movement into the mitochondria, and it stays in the cytoplasm, the cell's fluid-filled main compartment inside the cell wall and a central site for protein production. In the cytoplasm, MRPL18 attaches to ribosomes and facilitates the creation of stress proteins, Qian said.

Cells may experience stress as a result of temperature shifts, accumulation of misfolded proteins and from oxidative damage, all of which lead to disease if the stress response is faulty.

Basic understanding of such cellular processes provides new targets for drugs to treat diseases related to cell stress.

More information: Translational control of the cytosolic stress response by mitochondrial ribosomal protein L18, *Nature Structural & Molecular Biology* (2015) DOI: 10.1038/nsmb.3010