Molecular machine turns packaged messenger RNA into a linear transcript

February 11 2009

For RNA, the gateway to a productive life outside the nucleus is the nuclear pore complex, an amalgamation of 30 kinds of proteins that regulates all traffic passing through the nuclear membrane. New research from Rockefeller University shows that one of these proteins magnetically couples with a special molecule — a helicase — to form a machine that unpacks balled-up messenger RNA particles so that they can be translated.

The work illuminates a previously unknown stage in the process by which genetic information is read and converted to proteins. In humans and other higher organisms, the genetic information that is encoded in the DNA is stored inside the nucleus, while the factories that convert DNA instructions into proteins are located in the surrounding cytoplasm. As those instructions — messenger RNA particles — pass through the nuclear membrane, numerous proteins that cover and protect the delicate messenger RNA molecules must be stripped off.

André Hoelz, a research associate in John D. Rockefeller Jr. Professor Günter Blobel's Laboratory of Cell Biology, and his colleagues solved the crystal structure of a complex located on the cytoplasmic side of the nuclear pore — nucleoportin Nup214 coupled with helicase Ddx19. They then performed a series of biochemical experiments to further parse the interactions between these two molecules and to elucidate their mechanism of action. "We found that the messenger RNA protein package and Nup214 competitively bind to the helicase, one after the other," Hoelz notes. Each time the helicase binds the ball of messenger

RNA and protein, it strips one protein molecule off. “The process is akin to a ratchet mechanism for messenger RNA export.” The result, Hoelz speculates, is a linear messenger RNA transcript that travels on to the ribosome, where it delivers instructions for building proteins.

The work may also clarify a cause underlying acute myeloid leukemia, which is associated with mutations to Nup214. “Patients with mutations in Nup214 that remove the docking site for the helicase are likely to have a messenger RNA export defect,” Hoelz says.

More information: *Proceedings of the National Academy of Sciences*: February 10, 2009

Provided by Rockefeller University