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Actin Muscles In on DNA Transcription

Overturning a scientific stereotype, researchers at the University of Illinois at Chicago have discovered a new role for a key protein involved in muscle contraction and shown it is present not just in the cytoplasm of cells but in the nucleus as well.

Actin has been pigeonholed as a molecular motor, explains Primal de Lanerolle, professor of physiology and biophysics at UIC. "Whenever cells move or divide, actin is involved, like its partner myosin."

"But in the nucleus," de Lanerolle said, "actin acts instead like a binding protein. It recruits other proteins in the very complicated process our bodies use to transcribe DNA segments into messages made of RNA." These messages travel out to the cytoplasm, where they serve as templates for building proteins, including actin itself.

"If actin is blocked, transcription can't begin," de Lanerolle said.

The finding is published in the current issue of Nature Cell Biology and follows an earlier discovery by de Lanerolle and his colleagues that actin's cohort, myosin, the other compound involved in muscle contraction, is also present in the nucleus.

Transcription occurs in the nucleus in enzyme factories composed of up to 100 proteins -- huge complexes through which lengthy segments of DNA move as each nucleotide is read off to create an RNA strand. The factories are partly rebuilt each time a gene needs to be transcribed.

"If the factory were the size of Grand Central Station, then the DNA would stretch from New York to San Francisco, back to New York again, and on to Kansas City," said de Lanerolle.

Part of the factory is a group of proteins that, once assembled, jump-starts transcription. While scientists know a great deal about this pre-initiation complex, as it is called, they still have much to learn about its components and the sequence in which those components are assembled.

As de Lanerolle and his co-workers discovered, actin is one of the proteins in this complex. Its job is to recruit RNA polymerase II, the enzyme that will later detach itself from the complex and proceed on down the DNA string, stitching together the RNA message.

"We were looking for a motor, but we found something completely different," de Lanerolle said. He suspects that actin does act as a motor once RNA polymerase II begins transcription, but that has yet to be proved.

"Learning about the precise components and sequence of events in DNA transcription is important because the process is essential to all cellular activity, whether in normal healthy tissues or in diseases like cancer," de Lanerolle said. "The knowledge we gain will one day open up opportunities for

intervening when genetic transcription goes awry."

Other authors of the study are Wilma Hofmann, Ljuba Stojiljkovic, Beata Fuchsova, Gabriela Vargas, Evangelos Mavrommatis and Thomas Hope, from UIC; Vlada Philimonenko, Katarina Kysela, and Pavel Hozak from the Institute of Experimental Medicine in the Czech Republic; James Goodrich, from the University of Colorado; and James Lessard, from the Children's Hospital Research Foundation in Cincinnati, Ohio.

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