

What Are Muscle Proteins Doing in the Nucleus?

The proteins actin and myosin have a firm place in the muscles where they are responsible for contraction. While recent investigations have shown that they are also found in the nucleus, it has been unclear to date just what they are doing there. Now an international team of investigators headed by Professor Dr. Ingrid Grummt, head of the Division of Molecular Biology of the Cell II of the Deutsches Krebsforschungszentrum (German Cancer Research Center, DKFZ), has shown that the muscle proteins in the nucleus are actively involved in transcription, i.e. the reading of genetic information.

“This is a breakthrough in molecular biology that revolutionizes our thinking about the transcription process,” said Ingrid Grummt. Jointly with investigators from Chicago, Prague, and Heidelberg, the scientist recently published an article in *Nature Cell Biology** which has shattered a biological dogma that restricted the physiological role of the proteins actin and myosin to muscle contraction and their function as intracellular supporting elements.

The results are of fundamental relevance for cancer research, since the reading of genetic information and its translation into the cellular protein machine are essential for cell growth. In cancer cells, transcription activity is abnormally high, the cells are dividing uninhibited.

“Once we learn to understand how this process is regulated in a normal cell, we will be able to investigate specifically what is going wrong in tumor cells and on this basis identify targets for therapeutic approaches,” Grummt explained.

While researchers had experimentally proven the presence of actin and myosin in nuclei before, a gene-regulatory function of these molecules has been fiercely debated. Grummt’s team has now been able to show that actin and myosin play an active role in the reading of genetic information called transcription. Using antibodies directed specifically against these proteins, the investigators blocked the transcription of genes that are needed for the production of ribosomes – the cellular protein synthesis devices. The antibody-induced blockage of transcription was reversed by adding the proteins. “The results suggest that the muscle proteins are associated directly with the key enzyme of transcription, RNA polymerase, and serve as a motor providing the energy required for RNA polymerase to dock to the right site and read the gene sequences.” Grummt favors the hypothesis that a complex of myosin and an essential transcription factor binds to RNA polymerase and thus causes a structural change in the polymerase. Actin seems to influence both the start and the further process of transcription. Altogether, actin and myosin appear to be central switching elements of transcription in the nucleus.

*“Nuclear actin and myosin I are required for RNA polymerase I transcription”. *Nature Cell Biology*, Vol. 6 / Number 12 / December 2004, pp. 1165 – 1172 / Vlada V. Philimonenko, Jian Zhao, Sebastian Iben, Hana Dingová, Katarina Kyselá, Michal Kahle, Hanswalter Zentgraf, Wilma A. Hofmann, Primal de Lanerolle, Pavel Hozák and Ingrid Grummt.

The task of the Deutsches Krebsforschungszentrum in Heidelberg (German Cancer Research Center, DKFZ) is to systematically investigate the mechanisms of cancer development and to identify cancer risk factors. The results of this basic research are expected to lead to new approaches in the prevention, diagnosis and treatment of cancer. The Center is financed to 90 percent by the Federal Ministry of Education and Research and to 10 percent by the State of Baden-Wuerttemberg. It is a member of the Helmholtz Association of National Research Centers (Helmholtz-Gemeinschaft Deutscher Forschungszentren e.V.).

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