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50 Years – Research for
A Life Without Cancer

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Enough is enough: How tissues regulate their growth

Scientists from the German Cancer Research Center (DKFZ) have discovered a previously unknown mechanism that cells can use to control their growth. This mechanism plays a role in development, and its failure can result in cancer. The DKFZ researchers headed by Aurelio Teleman, jointly with colleagues in the group of Kent Duncan at Hamburg-Eppendorf University Hospital, have now published their results in Nature.

Before a cell divides, it must duplicate all its components. To boost the production of the various proteins that are required for this, their blueprints, the genes, have to be read at increased levels. Thus, many messenger RNA (mRNA) molecules are formed and are subsequently translated into proteins in the protein factories of the cell known as ribosomes. On this level, the protein production may be further fuelled by increasing the levels of mRNA translation. Special proteins that promote the binding of the mRNA to the ribosome play an important role in this process. “For some time now, we have suspected MCT-1 to be a candidate for this role,” says Aurelio Teleman, department head at the DKFZ, “because it binds mRNA and is found with particularly high frequency in leukemia cells, which divide very rapidly.” However, up to now the exact mechanism by which it accomplishes this task had remained in the dark.

Sibylle Schleich, first author of the article, found out in studies on fruit flies (*Drosophila*) that MCT-1 teams up with a partner called DENR to make particular mRNA molecules stay bound to the ribosome long enough to facilitate their translation into proteins. The mRNAs for proteins that are required for cell division – and which are therefore also involved in cancer – particularly depend on the assistance by the MCT-1-DENR couple. “Without the help from the MCT-1-DENR complex, these mRNAs drop off from the ribosome after a short time and are not translated into protein,” Schleich explains. Flies whose cells lacked either MCT-1 or DENR did not develop beyond the pupal stage and were not viable afterwards. “So we have discovered a universal control mechanism of the cell that affects the total production of proteins that are relevant for cell division,” says Aurelio Teleman, explaining the relevance of this work. Teleman and his co-workers have also found the MCT1-DENR complex in human cells. This means that it might represent an interesting target for new anti-cancer drugs.

Sibylle Schleich, Katrin Strassburger, Philipp Christoph Janiesch, Tatyana Koledachkina, Katharine K. Miller, Katharina Haneke, Yong-Sheng Cheng, Katrin Kuechler, Georg Stoecklin, Kent E. Duncan and Aurelio A. Teleman “DENR•MCT-1 Promotes Translation Reinitiation Downstream of uORFs to Control Tissue Growth“, Nature, 13401, DOI: 10.1038/nature13401

the remaining ten percent from the State of Baden-Württemberg.

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