EGF growth factor accelerates cell division, study finds

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Biologists at Heidelberg University have discovered new approaches for the treatment of cancer. They investigated how a special signalling molecule, the epidermal growth factor (EGF), stimulates the separation of chromosomes in the cell. The researchers were able to demonstrate that EGF accelerates the division of the cell nucleus, i.e. mitosis, as well as boosts precision in chromosome segregation. "Because the regulation of the EGF pathway is radically altered in many types of cancers, the results of our research point to new approaches in cancer therapy", explains Prof. Dr. Elmar Schiebel from the Center for Molecular Biology of Heidelberg University (ZMBH). Together with scientists from the University of Leicester, the European Molecular Biology Laboratory and the German Cancer Research Center, Prof. Schiebel and his team have published their findings in the journal *Developmental Cell*.

"The duplication of cells is an extremely vital and highly regulated process that can lead to cancer if it goes awry", states Prof. Schiebel. During the mitosis phase of cell duplication, the genetic information is passed to the daughter cells by the spindle apparatus. The assembly of the spindle apparatus begins with the dissolution of the filamentous connection between the centrosomes. The centrosomes are responsible for the organisation of the spindle fibres, the microtubules. The microtubules, which control chromosome separation during mitosis, bind to the genetic material when mitosis begins and then slide the chromosomes toward the two spindle poles. The cell then splits into two daughter cells. "Our current study has shown that the centrosomes of cells stimulated by the growth factor EGF split apart earlier than in cells

with less EGF stimulation. This makes mitosis in EGF stimulated cells quicker and more precise", says Prof. Schiebel.

The results of this research are particularly significant for certain cancer therapy agents that block the spindle fibres and thereby prevent chromosome division during mitosis. These agents act on cancer cells, which divide more often than healthy ones, by selectively killing them. Prof. Schiebel indicates that cytostatics such as taxol have considerable side effects. Researchers are therefore endeavouring to find other drug targets with a function in mitosis for treating cancer.

According to Prof. Schiebel, the Eg5 motor protein is a target candidate since it is vital for mitosis. Eg5 orchestrates the separation of the two spindle poles, which correctly divide the chromosomes between the daughter cells. If synthetic substances such as monastrol or STLC inhibit Eg5, the cell cycle becomes arrested in mitosis. This causes programmed cell death; the "defective cells" are eliminated.

Prof. Schiebel's team has now discovered that cells stimulated by the EGF growth factor bypass the function of Eg5 during nuclear division and can proceed with mitosis without the motor protein Eg5. This means that substances like monastrol or STLC lose their effectiveness to kill cancer cells if they have high EGF regulation. "In terms of new approaches to cancer treatment, we see the need that not only the Eg5 protein is blocked, but the EGF pathway as well", explains Prof. Schiebel. "The efficacy of this new strategy in treating cancer patients must now be verified in clinical studies."

More information: Mardin, B. et al. EGF-Induced Centrosome Separation Promotes Mitotic Progression and Cell Survival, *Developmental Cell* 25, 229-240, May 13, 2013, doi: 10.1016/j.devcel.2013.03.012

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