

Discovery of New Target for Papillomavirus Oncogene

Scientists of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) and the University of Jena have discovered that cancer-causing papillomaviruses accelerate cell growth by a previously unknown mechanism. Substances intervening at this point might check the process.

In the 1980s, this year's winner of the Nobel Prize for Medicine, Harald zur Hausen, and his co-workers discovered that specific types of human papillomaviruses (HPV) cause cervical cancer. Shortly after, scientists were able to elucidate how these pathogens cause cell transformation and promote cancer. The main culprits, as is known today, are the two viral oncogenes, E6 and E7, which switch off two key cancer brakes in infected mucosal cells. Oncogene E6 prevents cells from undergoing programmed cell death, or apoptosis, while E7 blocks a protective mechanism of cells which normally inhibits replication of the genetic material and, thus, slows down cell growth.

Scientists of the German Cancer Research Center and the University of Jena, under the leadership of Professor Felix Hoppe-Seyler, have now discovered another mechanism by which E7 fuels uncontrolled cell growth. E7 activates the switch that controls the production of regulatory enzyme EZH2 in a cell so that large amounts of this protein are produced. EZH2 is a key molecule of many central regulatory pathways of the cell.

If EZH2 production is blocked using a genetic trick, the growth of HPV infected cancer cells in the culture dish slows down. Researchers have also investigated the EZH2 level in tissue samples of cervical tumors and in precursors of cancer. Whenever the two viral oncogenes, E6 and E7, are active, they found particularly high levels of EZH2 in transformed tissue.

It has also been shown in other tumors such as breast, prostate and kidney cancers that EZH2 accelerates tumor cell growth. Felix Hoppe-Seyler thinks that the role of EZH2 in cancer might be an Achilles' heel of the tumor. "Substances that block the activity of EZH2 have been developed just recently. Thus, we have the possibility of developing these into drugs that might also be effective against cervical cancer."

Daniela Holland, Karin Hoppe-Seyler, Bettina Schuller, Claudia Lohrey, Julia Maroldt, Matthias Dürst, and Felix Hoppe-Seyler: Activation of the Enhancer of Zeste Homologue 2 Gene by the Human Papillomavirus E7 Oncoprotein. *Cancer Research* 2008, DOI:10.1158/0008-5472.CAN-08-1134

The German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) is the largest biomedical research institute in Germany and is a member of the Helmholtz Association of National Research Centers. More than 2,000 staff members, including 850 scientists, are investigating the mechanisms of cancer and are working to identify cancer risk factors. They provide the foundations for developing novel approaches in the prevention, diagnosis, and treatment of cancer. In addition, the staff of the Cancer Information Service (KID) offers information about the widespread disease of cancer for patients, their families, and the general public. The Center is funded by the German Federal Ministry of Education and Research (90%) and the State of Baden-Württemberg (10%).

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