

p22-FLIP Helps Tumor Cells to Survive

cFLIP stops cell death, its cleavage product additionally promotes growth

Among the major antagonists of programmed cell death, or apoptosis, are the proteins of the cFLIP family. cFLIPs are produced at elevated levels in many tumors. They prevent chemotherapy or radiotherapy from causing apoptosis in cancer cells to eliminate the malignant tumor.

It had been established previously that cFLIPs avert programmed cell death by inhibiting the procaspase-8 enzyme, a key molecule in the complex sequence of biochemical signals leading to apoptosis. Researchers **Dr. Inna Lavrik, Dr. Alex Golks and Dr. Dirk Brenner** of **Professor Peter Krammer's** division at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have now shown that cFLIP may help a cell to survive by yet another mechanism. A cleavage product of FLIP, called p22-FLIP, activates the NF-kappaB transcription factor. In cells of the immune system, NF-kappaB is a main switch that activates many growth-promoting processes. The investigators detected NF-kappaB activation in T cells, B cells and dendritic cells, and also in tumor cells. "It is possible that FLIP helps a tumor cell in two ways: It prevents cells death and, at the same time, its cleavage product p22 promotes cell growth," Inna Lavrik explains.

FLIPs, in whose discovery at the DKFZ Peter Krammer was instrumental, were first found in viruses ("vFLIPs"). The pathogens use these proteins to protect their host cells from being eliminated by apoptosis. Programmed cell death is part of an organism's protection program against viral infections. Later, scientists realized that FLIPs also belong to the equipment of human cells ("cFLIPS") where they contribute to the control of programmed cell death.

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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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