

## **Plant Constituent with Selective Effect on Cancer Cells**

**The substance wogonin triggers the death program apoptosis in tumor cells, while it has virtually no effect on healthy cells. Scientists of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have discovered the molecular mechanism underlying this selectivity.**

Defects in genes that control growth can turn a cell into a threat for the whole organism. Defective cells that might get out of control are driven into suicide by a protective mechanism called apoptosis. However, this life saving mechanism is no longer working in most tumor cells, since numerous molecules regulating apoptosis are defective.

This is why researchers have been trying for some time to restore the capability of controlled suicide in tumor cells. However, this is a risky venture, because it involves the danger of damaging healthy tissue, too, by cell death. Therefore, scientists have urgently been searching for substances that induce cell death selectively in tumor cells.

**Dr. Min Li-Weber** of the Division of Immunogenetics headed by **Prof. Dr. Peter Krammer** has been concentrating on pure substances from herbs that are used in traditional Chinese medicine. Investigating their ability to trigger apoptosis, the scientist has recently come across an interesting candidate: the substance wogonin, a plant flavone from Baikal skullcap. Wogonin causes apoptosis in leukemia cells in the culture dish, while it has virtually no damaging effect on healthy blood cells. Wogonin also led to reduced cancer growth in mice that had been transplanted human leukemia cells.

The mechanism underlying the selective effect of this plant constituent had still been unclear. There are two different ways by which the apoptosis program can be started in a cell: by external stimuli or by signals from within the cell as a response to factors such as radioactive radiation or reactive oxygen compounds such as hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>). Li-Weber has now shown that wogonin leads to highly increased formation of hydrogen peroxide in tumor cells compared to healthy cells. The peroxide, in turn, produces a calcium response which triggers the apoptosis reaction cascade. In addition, tumor cells contain a higher number of those membrane channels through which calcium flows from its intracellular storages into the cytoplasm.

Min Li-Weber's results so far are based on experiments in the culture dish and in the animal model. The scientists rate the data as convincing enough to continue testing the suitability of wogonin as a therapeutic agent for leukemias.

Sven Baumann, Stefanie C. Fas, Marco Giarsi, Wolfgang W. Müller, Anette Merling, Karsten Gülow, Lutz Edler, Peter H. Krammer and Min Li-Weber: Wogonin Preferentially Kills Malignant Lymphocytes and Suppresses T-cell Tumor Growth by Inducing PLC $\gamma$ 1- and Ca<sup>2+</sup>-dependent Apoptosis.

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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

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