

Evi Lends Wings to the Fly

Newly discovered protein triggers central signaling pathway of the cell

The Wnt signaling pathway regulates important steps in the embryonic development of all organisms. Defects in the control of this molecular communication pathway also contribute to tumor development. Scientists at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have discovered a new protein called Evi, which is required for Wnt secretion and, thus, for the start of the signaling cascade.

All important body functions are controlled by highly complex signaling chains, which instruct cells to stop growing, to divide or to specialize on individual tasks. Evolution has preserved many of these signaling chains with their molecules from fly to man – they are, in biological terms, highly conserved. A research group headed by Dr. Michael Boutros has now shown that the Evi (evenness interrupted) protein is required for Wnt growth factors to be released from the cell.

Many of the receptor molecules that receive or pass on the Wnt signal in the recipient cell are known. Yet little is known to date about how Wnt production and secretion is regulated. Evi is a newly discovered transmembrane protein which selectively triggers Wnt release, but has no influence on the secretion of other proteins. The researchers had individually switched off approximately 2,300 different transmembrane proteins using RNA interference. Then they had studied the effect of the loss of these proteins on the Wnt signaling cascade.

The Wnt signaling pathway controls development of body axes and limbs in the embryonic development of all multicellular organisms. In the fruit fly *Drosophila*, the homologous protein of vertebrate Wnt is called Wingless (Wg), because mutations in this gene lead to wingless flies. Hence, wing development is a suitable system for investigating the activity of the Wnt signaling pathway. In fly embryos in which Evi production had been shut down, recipient molecules of the Wg cascade were not activated, wing development was disturbed. If the homologous protein of Evi is switched off in human cells, the downstream stages of the Wnt signaling pathway are also no longer activated. Therefore, the scientists believe that Evi is another control mechanism designed to regulate this critical signaling cascade at the level of the Wnt producing cell.

Precise elucidation of the Wnt signaling pathway is important for cancer research, too, for it may thus become possible one day to selectively interfere with defective communication pathways of tumor cells using advanced drugs.

Secretion of Wnt Ligands Requires Evi, a Conserved Transmembrane Protein. Kerstin Bartscherer, Nadège Pelte, Dierk Ingelfinger and Michael Boutros, Cell Band 125, page 523, 2006

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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