GERMAN CANCER RESEARCH CENTER
IN THE HELMHOLTZ ASSOCIATION

No. 45 17. September 2012 (Koh)

Discus throw with cancer signals

The Wnt signaling protein plays an important part in embryonic development and also in the development of diseases such as cancer. It has been unknown until now just how Wnt is carried from cell to cell. Scientists of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) and Medical Faculty Mannheim of Heidelberg University have now discovered that the protein is shipped on small discus-shaped vesicles called exosomes. The researchers are now investigating whether Wnt exosomes are relevant for the development of cancer.

At the cellular level, fly, frog and man all speak a common language. Cells communicate via signals such as “Wnt” proteins. They use this universal means of communication to transmit important information such as about the basic plan of the body pattern. Transmission errors in the communication of such messages usually have fatal consequences. During embryonic development, they result in severe malformations, while later in life wrong Wnt signaling frequently results in cancer.

Cells receive Wnt messages via matching receptor proteins on their surface. However, it has been unknown so far just how these important signaling proteins are carried. Wnt directs body pattern formation and needs to be sent via long distances in an organism. “But since it is a hydrophobic protein, this cannot be done without appropriate packaging”, says Prof. Dr. Michael Boutros, who leads a joint department of DKFZ and Medical Faculty Mannheim of Heidelberg University.

Scientists in Boutros’ team have now uncovered the secrets of Wnt transport. Inside of Wnt-secreting cells, small bubbles of cell membrane are formed. Their wall, in turn, folds inwards to form what are called exosomes – tiny ferries containing the Wnt protein. These ferries are then sent on their way by being thrown – like a discus – out of the cell.

However, transport via exosomes is not the only way to mediate the Wnt signal. When the investigators suppressed bubble formation in the cells, the Wnt signal did not subside completely. “We therefore suppose that different ways of signal transmission have different biological functions. Thus, it could make a difference for the target cell whether it receives the biological signal via individual Wnt molecules or whether a whole, fully loaded exosome is incoming,” speculates Dr. Julia Gross, co- author of the publication.

The Wnt signaling protein has been shown to play an important part in the development of cancer in humans; it has even been discovered in malignant tumors for the first time. Many tumor cells produce too much Wnt, which induces other cells to divide too frequently or to become resistant to chemotherapy. Wnt turns off important tumor suppressor proteins which act as growth brakes. In this way, it fuels tumor growth.

Scientists have been discovering more and more details about the role of exosomes in many biological processes. Thus, US researchers have recently been able to demonstrate in malignant melanoma that tumor cells release exosomes full of cancer-promoting proteins which make the surrounding tissue susceptible for colonization by tumor metastases. Boutros and his co-workers suspect that Wnt exosomes, too, may play a role in the development of cancer. Furthermore, they intend to investigate whether Wnt exosomes, which are easy to detect in blood, may serve as new tumor markers for medical purposes.

This research work was carried out as part of the DFG-funded Research Group 1036 and the CellNetworks excellence cluster at the Medical Faculty Mannheim of the University of Heidelberg and the German Cancer Research Center (DKFZ).

Julia Christina Gross, Varun Chaudhary, Kerstin Bartscherer and Michael Boutros: Active Wnt proteins are secreted on exosomes. Nature Cell Biology 2012, DOI: http://dx.doi.org/10.1038/ncb2574

A picture for this press release is available at:
www.dkfz.de/de/presse/pressemitteilungen/2012/images/Exosomen.jpg
Caption: Wnt exosomes are being thrown from the cell on the left (electrone microscope images)
Source: Michael Boutros, DKFZ

Dr. Stefanie Seltmann
Head of Press and Public Relations
German Cancer Research Center
Im Neuenheimer Feld 280
D-69120 Heidelberg
T: +49 6221 42 2854
F: +49 6221 42 2968
presse@dkfz.de