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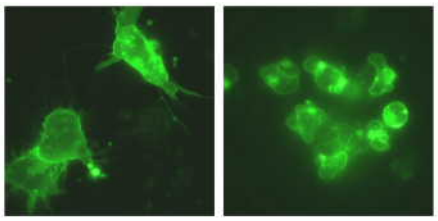
New important triggers for the migration of cancer cells

Embryonic cells and metastasising cancer cells are able to migrate and intrude into other tissues. Investigations of frog embryos have now provided scientists at the Karlsruhe Institute of Technology with the information that a well-known protein, cadherin-11, triggers cell migration. This glycoprotein is also responsible for the defective behaviour of cells that results in prostate cancer and arthritis.



The presence of cadherin-11 (left) triggers the cells to form long cellular protrusions; the absence of cadherin-11 (right) results in spherical cells.

Under normal circumstances, cadherins are crucial for the association of eukaryotic cells. "In principle, they work like a zip and interlock cells to each other to form associations of cells or tissue," said Professor Doris Wedlich, Director of the Institute of Zoology II at the KIT. These molecules prevent cells from being released from the cell association and migrating to other tissues or organs. Cadherin-11, one of the approximately 300 vertebrate cadherins known, behaves in a completely opposite way, particularly in tumour cells: it triggers the migration of the cells. "The presence of cadherin triggers the formation of cell protrusions, the "finger tips" of cells that find the most suitable migration path," said Wedlich. The KIT scientists focused on the question as to why cadherin-11 triggers tumour cell migration. They investigated the action of cadherin-11 in neural crest cells, i.e. early embryonic cells that enter the field of vision to form the face bones. "During early embryonic development, there are astonishing similarities with tumours," said the developmental biologist. Embryonic cells are therefore an interesting model system for the investigation of tumour development. The behaviour of embryonic cells is guided by the same principles that are used by tumours: uncontrolled growth, i.e. unlimited cell division. The tumour's cells are no longer able to do their original task and as a consequence alter their shape. They take on properties that they had had previously, for example the inclination to migrate and intrude into foreign environments. Recently there has been evidence that cadherin-11 plays a role in the metastasis of cancer and the induction of arthritis. However, the mechanism of function has so far not been understood. "It is now becoming clearer why cadherin-11 is found on prostate tumour cells, which preferentially metastasise bone tissue," said Wedlich. "A similar mechanism seems to be present in joint inflammations. Cadherin-11 causes cells that normally coat the joint capsule to grow on bones by mistake." Using molecular biology methods, the team led by Professor Wedlich found out that the binding of specific adaptor proteins to cadherin-11, i.e. Trio and beta-catenin, was necessary to trigger the formation of cell protrusions and hence the migration of the cell. Using genetically altered cadherin molecules that lacked certain segments, the scientists were able to localise the binding region of Trio in cadherin. "In the cell, Trio acts specifically on cadherin-11," said Doris Wedlich. "In order to prevent the defective behaviour of cells triggered by cadherin-11, it is worth analysing the effect of blocking the coupling of Trio to cadherin-11."

The junior research group led by Jubin Kashef at the KIT is currently working on questions relating to the structural properties of the binding sites of Trio and cadherin-11 and the activation of factors following the coupling of the two proteins. "If we succeed in answering these questions, then we might be able to interrupt the signalling pathway and suppress the migration of the cells," said Doris Wedlich outlining the long-term perspective of the researchers.

Karlsruhe Institute of Technology (KIT)

The Karlsruhe Institute of Technology (KIT) is a merger of the Karlsruhe Research Centre in the Helmholtz Society and the University of Karlsruhe. The KIT marks the establishment of an institution of excellent international research and teaching in the natural sciences and engineering. With around 8000 employees and an annual budget of approximately 700 million euros, the KIT focuses on the research triangle of research, education and innovation.

The KIT is a leading European energy research centre and has a high global profile in the nanosciences. The KIT sets new standards in education and the promotion of young scientists, attracting top-class researchers from around the world. In addition, the KIT is a leading innovation partner for industry.

The results have just been published in the June edition of the journal "Genes & Development" (issue 23 (12), 15th June 2009, DOI-No. 10.1101/gad. 519409).