

Contact Disorder Makes Cancer Cells Mobile

The loss of the protein VMP1 in cancer cells increases their tendency to detach from the initial tumor – the first step towards metastasis. The reason for this, as scientists of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have shown, is that a loss of VMP1 causes cells to lose their capacity to establish contacts with their neighbors.

What causes tumor cells to leave the tissue and start traveling through the body via lymph or blood? As a rule, it is this change of behavior that turns cancer into a deadly disease, because it is a first seed of dangerous secondary tumors (metastases). Scientists of Professor Annemarie Poustka's division at the DKFZ, collaborating with colleagues in Göttingen and Graz, have shown that a disruption of contact formation between neighboring cells is among the causes why tumor cells become mobile.

In renal cell cancer the researchers discovered that the gene coding for VMP1 is read significantly less in metastases of the tumor than in cells of the primary tumor. Subsequently, the VMP1 gene activities of various breast cancer cell lines were examined. The investigators found that the VMP1 gene is read less in cells with "invasive potential", which may invade other tissues, than in cells without a tendency to migrate or in cells from healthy breast tissue.

The VMP1 protein, as was shown by special dyeing, is responsible at the cell surface for the formation of specific contact sites between neighboring cells. When the researchers switched off the production of VMP1 in living cells, these rounded up and stopped forming their typical contacts among each other, which normally hold the tissue together. The results obtained by the Heidelberg researchers suggest that VMP1 is responsible for establishing the initial contact, but it is not permanently inserted at the site of physical contact between neighboring cells.

If VMP1 is experimentally switched off in non-invasive renal cancer cells, the cells develop a tendency to migrate. Thus, in a test that simulates the invasion of tissues in the culture dish, VMP1-negative cells showed a significantly more invasive behavior.

"Whether VMP1 production is actively switched off by the tumor or lost by mutations is something we do not know yet," explains Annemarie Poustka. "We are now investigating whether the VMP1 content of tumor cells may be used as a reliable marker for metastasis."

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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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