GERMAN CANCER RESEARCH CENTER
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New Prospects for Treating Ovarian Cancer

Antibodies against the L1 cell adhesion molecule inhibit tumor cell growth in cell cultures and tumor spread in the murine model.

The L1 cell adhesion molecule may prove to be a suitable target for treating ovarian cancer. This was confirmed by a research group headed by Professor Dr. Hans-Peter Altevogt of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ), in collaboration with scientists from Munich Technical University under the leadership of Professor Dr. Achim Krüger, and the Swiss Paul Scherrer Institute. Positive results have been obtained in cell lines of human ovarian cancer both in the culture dish and in the murine model. Treatment with anti-L1 monoclonal antibodies led to an inhibition of cell growth and considerable reduction of the tumor mass. The amount of abdominal fluid production was also reduced substantially. The researchers are planning to develop an analogous antibody for humans and to conduct clinical trials with humans in the near future.

Ovarian cancer is a malignant transformation of the ovaries which affects about 8,000 women, typically between the ages of 45 and 65 years, in Germany each year. Disease risk is increased by familial predisposition, childlessness, and giving birth at a later age. Since the symptoms of ovarian cancer are unspecific, by the time tumors are detected, in most cases metastatic tumors and abdominal fluid have already formed in the abdominal cavity. Ovarian cancer is treated by surgery and adjuvant chemotherapy, with moderate success in advanced stages.

The promising target for a new treatment approach is the membrane-bound L1 protein, a cell adhesion molecule that interacts with other cell adhesion molecules and receptors. The signaling cascade thus triggered leads to cell differentiation, cell proliferation, and – in the case of transformed cells – to migration and invasion. The protein caught the researchers' attention when a connection between L1 overexpression and tumor spread was established in ovarian cancer. Other cancers, including kidney and colon cancers, were also found to overproduce L1 during tumor growth and metastatic spread. Dissolved L1, which is released into the serum and abdominal fluid in uterine and ovarian cancers, in its turn, promotes cell mobility and tumor development.

Altevogt's group studied the effects of monoclonal antibodies directed against L1 on the development of L1-positive tumor cell lines in the culture dish and the spread of ovarian cancer in infected, immunodeficient nude mice. In both cases, tumor cell growth slowed down. In the living organism, antibody treatment resulted in a reduction of tumor mass by up to 63.5% and of abdominal fluid formation by up to 75%. The health of the treated mice improved noticeably compared to the controls. The antibodies bind to both the membrane-bound and the dissolved form of the cell adhesion molecule, slow down the growth of tumor cells and prevent migration by networking among each other.

In their article published in Cancer Research, the scientists anticipate that this study is the first step towards developing new strategies to treat ovarian cancer based on efficient inhibition of tumor growth and metastasis by L1 antibodies.

Matthias J.E. Arlt et al.: "Efficient Inhibition of I.p. Tumor Growth and Dissemination of Human Carcinoma Cells in Nude Mice by Anti-L1-Cell Adhesion Molecule Monoclonal Antibody Treatment", Cancer Res; 66(2), 15. Jan 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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