Outwitting a brainy gene

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(Medical Xpress) -- The very first in the series of mutations causing colon cancer occurs in the beta-catenin gene; this gene is abnormally activated in about 90 percent of colorectal cancer patients, and in a much smaller percentage of people with almost every other type of cancer. Beta-catenin plays a dual role in the cell: it promotes adhesion, or stickiness, between cells, and regulates the expression of genes in the nucleus.

Research conducted in the laboratory of Prof. Avri Ben-Ze'ev of the Department of Molecular Cell Biology suggests that, in cancer, beta-catenin functions as an oncogene: when aberrantly activated, it spurs malignant transformation and causes the cell to proliferate abnormally. In one collaborative project with Institute colleagues, Prof. Ben-Ze'ev discovered that in normal cells, the p53 tumor suppressor gene keeps beta-catenin in check, but in malignant cells, p53 loses its grip on beta-catenin. In another collaborative project, a team led by Prof. Ben-Ze'ev isolated a short peptide (protein fragment) that blocks a vital portion of the beta-catenin molecule; the protein may thwart the development of cancer by preventing beta-catenin from acting as an oncogene.

More recently, Prof. Ben-Ze'ev's team unraveled several crucial elements in the signaling chain unleashed by the corrupt beta-catenin. One of these elements is Nr-CAM, a cell adhesion molecule not previously known to play a role in cancer.

In healthy people, the protein made by the Nr-CAM gene is present only in the brain and not at all in other tissues of the body, but the Weizmann

scientists showed that the Nr-CAM levels are dramatically elevated in colon cancer and melanoma cells; in fact, the more advanced the tumor, the higher the Nr-CAM level.

These findings could lead to the screening of large populations and early detection of cancer, based on the detection of the protein made by the Nr-CAM gene: this protein is likely to be present only in people with cancer caused by overly activated beta-catenin. Moreover, since the protein made by the Nr-CAM gene sticks out from the surface of cells, it is a convenient target for cancer therapy: by inactivating Nr-CAM, it may be possible to interrupt the chain of signals released by beta-catenin, thereby suppressing the development of prevalent malignancies such as melanoma and colon cancer.

Prof. Ben-Ze'ev's laboratory has also revealed that beta-catenin is involved in a key mechanism leading to the metastasis of colon cancer. By manipulating this mechanism, his team succeeded in reversing the metastatic properties of colon cancer cells in vitro. This research raises hopes that a target-specific therapy might be devised to prevent, or reverse, the invasive behavior of metastatic cells.

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