Mechanism for invasion of tumorous cells discovered

April 11 2011

Researchers at the Hebrew University of Jerusalem have discovered a previously unknown mechanism whereby tumor cells invade normal tissues, spreading cancer through various organs.

The ability of tumor cells to invade adjacent structures is a prerequisite for metastasis and distinguishes malignant tumors from benign ones. Thus, understanding the mechanisms that drive malignant cells to invade and a possible avenue for halting that mechanism could have tremendous potential for enhancing early detection of malignant cells and for therapeutic treatment.

It has previously been assumed that tumor cells turn invasive upon accumulation of multiple mutations, each giving the cancer cell some invasive properties

Now, Prof. Yinon Ben-Neriah and Dr. Eli Pikarsky of the Institute for Medical Research Israel-Canada at the Hebrew University Faculty of Medicine and their colleagues are reporting an alternative mechanism through which tumor cells become invasive. They found a program that is operated by a concerted group of genes that, when activated together, confer invasive properties upon epithelial cells. (Epithelial tissues line the cavities and surfaces of structures throughout the body, and also form many glands.) An article reporting their work appeared in a recent issue of the journal *Nature*.

Interestingly, the expression of this entire gene group is normally

suppressed by a single gene – p53 – that is considered as the most important tumor suppressor but unfortunately is inactivated in the majority of human cancers. Some key properties of the protein produced by the p53 gene -- arresting cell growth and induction of cell death – were previously discovered by Dr. Moshe Oren of the Weizmann Institute of Science, another member of the current research team. These properties were thought to explain the main cancer protection activity of p53. However, the new research now described in *Nature* describes a different mechanism of action of p53 -- inhibition of cell invasion -- which may be the most critical means of cancer-protection in colon and rectal cancers and possibly other types of epithelial cancers.

Two Hebrew University doctoral students on the investigative team, Ela Elyada and Ariel Pribluda, developed a new mouse model in which they were able to demonstrate a process of genetically induced invasiveness of tumorous tissue and how that process could be prevented as long as p53 could be kept activated.

The new study may have important implications for cancer diagnosis and therapy.

The discovery of new invasion-activating genes could serve as diagnostic biomarkers for distinguishing malignant from benign lesions and the early detection of invasive cancer. This distinction is a critical determinant of therapeutic options, a judgment based today solely on microscopic study of tissue slides. With the availability of a prompt and exact molecular definition of invasive versus non-invasive lesions, lives could be saved by allowing the early implementation of curative treatments while withholding patient overtreatment, which often results in serious morbidity.

The reported findings may also indicate new measures for ways to maintain activation of p53 as a safeguard against malignant

transformation of epithelial tissues.

Provided by Hebrew University of Jerusalem