

BIOMEDICINE

Protein limits bladder cancer spread

People who have had surgery for bladder cancer can look forward to better survival prospects than those recovering from many other malignancies. Removal of a cancerous bladder can confer years of life.

Some of these patients get shortchanged, however, if their bodies fail to produce enough of a cancer-fighting chemical called p21 protein, researchers report in the July 15 *JOURNAL OF THE NATIONAL CANCER INSTITUTE* (JNCI).

In a study of 242 bladder cancer patients whose bladders had been removed, researchers analyzed tumor tissue taken during surgery. Samples from 86 patients lacked a full complement of p21 protein. Within this group, three-fourths suffered a recurrence of cancer within 5 years of the surgery, and three-fourths of those deficient in p21 died in that time. Of those patients with normal concentrations of p21 in their tumors, only 30 percent had a cancer recurrence and nearly two-thirds lived more than 5 years after surgery, according to study coauthor Richard J. Cote, a pathologist at the Norris Comprehensive Cancer Center at the University of Southern California in Los Angeles.

Inside cells, p21 can put the brakes on runaway cell growth, says Curtis C. Harris, a physician at the National Cancer Institute in Bethesda, Md.

The dearth of p21 protein observed in many of the patients doesn't appear to be caused by mutation of the gene that encodes it. Such a mutation is rare. Production of p21, an enzyme inhibitor, appears to depend in some cases on another cancer-suppressor protein, p53. Absence of p53 and mutations in its gene have been implicated in many other cancers.

In the new study, Cote and his colleagues explored the cascade of cellular events that begins with p53 production and leads to p21 formation. They were surprised at their findings. Although p53 is a key cell-cycle regulator, reduced p53 activity didn't pose a danger in bladder cancer patients who had normal p21 levels. On the other hand, patients with normal p53 in their tumors still faced a high risk of cancer recurrence if they lacked p21.

The unveiling of p21's importance may have clinical ramifications. Chemotherapy after bladder removal is common, but doctors face a difficult choice in deciding whether to give that harsh treatment to patients whose tumor cells haven't spread to other parts of the body. If a patient lacks p21 protein—and is therefore more susceptible to a cancer recurrence—chemotherapy might be more readily recommended.

"We can define a population within that group [of patients] that is at high risk of [cancer] progression," says Cote. "This could lead to a different way to manage cancer."

Indeed, Cote and his colleagues have already begun a study in which cancer patients' concentrations of p21 are measured and considered as part of the decision whether or not to administer chemotherapy after bladder removal.

The JNCI article "contributes to our understanding of factors involved in . . . bladder cancer," Harris says. The next step is to better define the role of p53, he adds.

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