

## Gene blocks prostate cancer's journey

Like an insidious invader, cancer cells can spread through the bloodstream, spawning tumors at distant sites.

Prostate cancer, however, can be a reluctant traveler. Yet for an unlucky few men, this cancer can metastasize and kill. To date, doctors have had difficulty diagnosing prostate cancers likely to spread.

Now, a study reported in the May 12 *SCIENCE* suggests that prostate cancer patients with reduced expression of a particular gene may run the risk of metastasis.

J. Carl Barrett of the National Institute of Environmental Health Sciences in Research Triangle Park, N.C., and his colleagues had had hints that the KAI1 gene on chromosome 11 retards cancer's lethal movement. When working properly, such a suppressor gene carries the blueprint for a protein that slows the spread of cancer.

Would KAI1 thwart the movement of aggressive prostate cancer cells? To find out, the team first isolated KAI1 from human chromosome 11 and inserted it into prostate cancer cells taken from rats. Next, the researchers injected these treated cancer cells just under the skin of 58 mice. A group of 52 control mice received an injection of rat prostate cancer cells with no human KAI1 gene.

After about 4 to 5 days, the malignant rat cells took hold and produced a cancer at the injection site in both groups of mice. This indicates that KAI1, unlike a classic tumor suppressor gene, is powerless to stop a primary tumor's growth, says Jin-Tang Dong of Johns Hopkins University School of Medicine in Baltimore.

But KAI1 does seem to curb the cancer's spread. The researchers let the original tumor grow for about 43 days and then studied the lungs, a common site of metastasis.

All of the control mice showed malignant cells on the surface of the lung. The researchers noted an average of 30 to 47 metastases per untreated mouse.

Of the 58 treated mice, 53 developed malignancies in the lung. Yet mice with a high expression of the human KAI1 gene fared best in the race to beat the cancer's travel: The team found between six and seven metastases per mouse.

Those results hint that KAI1's protein product somehow prevents or slows prostate cancer's ability to journey through the bloodstream, comments David I. Kleinerman, a researcher at the University of Texas M.D. Anderson Cancer Center in Houston. Kleinerman and his colleagues have studied another gene involved in the suppression of prostate cancer.

"It's an excellent paper," Kleinerman says. He wonders whether such research may one day lead to a drug that will boost expression of KAI1 in prostate tumors, thus reducing a man's risk of metastatic cancer.

Barrett's team believes KAI1 may lead to a diagnostic test for travel-prone prostate tumors. He predicts that "cancers where the KAI1 gene is not expressed would have a higher probability of being metastatic."

Men who got such bad test results could undergo more aggressive therapy, Barrett adds.

— K. Fackelmann