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MARYLAND RESEARCHER DR. JOHN HOLADAY

Prostate protein that flags cancer may fight disease

Antigen improves prognosis in other cancers, study finds

BY RANDOLPH E. SHMID
ASSOCIATED PRESS

WASHINGTON — A protein doctors test for as an indication of prostate cancer may actually be used by the body in battling the disease, a study indicates.

Millions of American men get blood tests every year to check for prostate specific antigen. Elevated levels of PSA can indicate the presence of cancer.

"God didn't put PSA as a marker of prostate cancer. There's got to be some biological function of this molecule and, in our mind's eye, it had not been defined adequately," said Dr. John Holaday, one of a team of Maryland researchers that found evidence PSA may slow cancer growth.

"There was data showing that women with advanced breast cancer, who had higher levels of PSA, had a better prognosis," Holaday said in a telephone interview. "That taught us two things: that prostate specific antigen is not prostate specific and, secondly, (that) it appears to be correlated with an improved outcome."

Some scientists have speculated it might be possible to slow prostate cancer by reducing PSA. There have been attempts to develop an anti-PSA vaccine. The findings of Holaday's group argue against that.

"No one had ever taken PSA... and added it to a bunch of prostate cancer cells, or other kinds of cancer cells, and made them grow more," he said. "No one really ever asked the question: what does PSA do."

The team concluded PSA may inhibit "growth of blood vessels associated with cancer progression" in a study in today's issue of the *Journal of*

the National Cancer Institute.

"As a man over 50, I know that when my prostate PSA levels are measured on an annual basis, I look to that as a measure of progressive disease or lack thereof," Holaday said.

"But I also realize that, when it reaches the later years, often people don't even treat prostate cancer in men 75 and older because it grows so slowly. We think it grows slowly because the PSA it makes keeps it in check."

Dr. Gerald Murphy of Northwest Hospital's Pacific Northwest Cancer Foundation in Seattle said he would need to know more about the type of PSA tested and how it operates, but said the report could help explain why PSA increases as cancer grows.

Scientists see two fronts in the battle against cancer: attacking tumour cells and battling endothelial cells that make up blood vessels needed to bring the tumour oxygen and nutrients.

The EntreMed scientists have been working on endostatin, a protein that blocks blood-vessel development in tumours. It is in the first phase of clinical trials on humans.

Many patients with growing tumours have increased levels of natural endostatin.

After lab tests indicated PSA added to cancer cells inhibited formation of new blood vessels, the team introduced cancer cells to mice susceptible to lung cancer and treated some with PSA.

Despite its name, and its value in diagnosing prostate cancer, PSA has been found as well in those with breast, lung and uterine cancers.

Mice treated with PSA averaged 62 to 78 tumour nodules in their lungs after 14 days.

By contrast, mice not given PSA averaged 99 to 131 tumours.

In similar tests using endostatin, treated mice averaged eight to 24 tumours.