

Prostate antigen also found in breast tumors

BY AMANDA KREIDIE

TORONTO — To their surprise, researchers have found that Prostate-Specific Antigen (PSA) production may not be exclusive to that gland.

Researchers at the University of Toronto recently detected traces of the glycoprotein in some breast tumor extracts.

"As the name of this compound suggests, PSA has not been found in any other tissue in either males or females," said chief investigator Dr. Eleftherios Diamandis, "so naturally its discovery in cancerous breast tissue comes as a real mystery and is a shock to people in the medical community."

The discovery, reported in the April 1994 issue of *Clinical Biochemistry*, was made when a graduate student investigating PSA production by cancer cell lines from prostatic tissue inadvertently switched prostate tumor extracts with those from breast tumors.

"Admittedly this thing happened completely by mistake but we capitalized on it and have since made some very promising findings," said Dr. Diamandis, an associate professor of biochemistry at the university and deputy biochemist-in-chief at The Toronto Hospital.

"This holds great promise for PSA being used in breast cancer prognosis, in selection of therapy and for devising new therapeutic interventions."

Following the initial discovery, the researchers decided to analyse 525 breast tumor cytosols for immunoreactive PSA (IR-PSA). Using a highly sensitive immunofluorometric procedure for PSA, they were surprised to find 30% of tumors tested positive for IR-PSA content. A subsequent analysis of a further 750 cytosols came up with similar results.

The finding has the researchers baffled. "We have no clue why PSA is being produced in the breast but

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Breast's receptors for sex hormones could be involved

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we are investigating," said Dr. Diamandis. "We know that the production of PSA (by cells lining the prostate) is mediated by the reaction of steroid hormone receptors so it could be that the breast's receptors for estrogen, progesterone and androgen are in some way involved. If we can understand why PSA is present it could be of great importance."

As to why the compound was found in some samples and not in others, he said it could be a function of some breast cancer tumors not having steroid hormone receptors, not having active receptors, or, the complete absence of a certain steroid hormone.

The U of T researchers have since tracked 200 patients whose tumors contained PSA to determine whether presence of the glycoprotein had an impact on prognosis. They found five years after surgery these patients were likely to live three times longer and were three times more likely to remain relapse-free than patients who test negative for the antigen.

"Again we do not know why this is happening," Dr. Diamandis said. "It may well be that actual benefit to the patient is not coming from the PSA but from the receptors or the steroid hormones that are stimulating its production."

To help answer all these nagging questions he has developed a tissue culture system which produces PSA *in vitro*. The culture system may also offer opportunities for screening agents that can be used to control or eliminate breast cancer cells. Dr. Diamandis is also attempting to devise methods for localizing early breast cancer tumors using their PSA content as a marker.

Discovered in 1980, PSA is believed to be the most specific cancer tumor marker ever found. The glycoprotein is widely used to diagnose and monitor prostate cancer patients.

Its recent detection in some breast cancer tumors holds tremen-

dous potential for improving detection and treatment of the disease since PSA presence may prove to be a better predictor than hormone receptor levels, of which patients will respond successfully to hormonal treatment.

Unknown

"Whether the IR-PSA production by breast tumors is associated with breast cancer initiation or prognosis is unknown," the researchers wrote.

"However, we have found that IR-PSA presence is preferentially associated with early stages of breast cancer, which may suggest that IR-PSA presence is a potentially favorable prognostic indicator in breast cancer."

They added that since the presence of the glycoprotein in breast cancer may be viewed as a marker of functional estrogen and progesterone

receptors, "IR-PSA may have a value of predicting which patients would respond to endocrine treatment that targets the estrogen and/or the progesterone receptor."

Given that tamoxifen—a widely used antiestrogen agent—was found to induce PSA production *in vitro*, Dr. Diamandis said it may be the best treatment for women whose tumors test positive for the molecule.

As for patients whose tumors do not contain PSA, he advised the prescription of more intense chemotherapy after surgery.

"In the long term, if we can understand why this thing is being produced and why it is good, then we could perhaps develop agents to stimulate production of PSA for localized treatment," Dr. Diamandis said.