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The Normal Female and the Male Breast Epithelium does not Express Prostate-Specific Antigen. Preliminary Immunohistochemical Observations of Autopsy Breast Tissues

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Abstract. In the normal female and male breast epithelial structures any prostate-specific antigen (PSA) immunohistochemical positivity was observed Variable PSA expression, which often borders the positivity, was observed in membranes of adipocytes of fat tissue and in the endothelium of small vessels in a female and a male breast Based on these initial observations, tissue of the normal breast, male or female, can not be considered to be the principal source of PSA

Key words: Prostate-specific antigen (PSA) — Immunohistochemistry — Normal female breast — Normal male breast

Introduction

Some investigators consider the female breast to be the principal source of PSA In female, not only the pathological breast tissue especially benign (hyperplastic) breast disease and cancer, but also the normal female breast tissue is assumed to be the principal source of

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PSA (Yu et al 1996, Diamandis 1998) This assumption is based on the immunochemical quantification of PSA in the serum and breast fluids as well as extracts of women with normal, benign and malignant breast disease (Mannello *et al* 1996, Borchert *et al* 1997, Diamandis 1998 and references therein) However, no immunohistochemical data concerning the expression of PSA in the normal female and normal male breast have been reported up to date Since in healthy women serum PSA values cover the range from nondetectable to high concentrations (up to 0 9 ng/ml), and a value approaching the normal male reference ranges of PSA (1–2 ng/mL according to Borchert et al 1997), it appeares to address the question Which organ or tissue of the healthy female is actually responsible for the production of this prostate marker? Therefore, aims of this preliminary study were (1) Is the female breast the principal source of PSA in the healthy female and (2) besides the male prostate, what role does the normal male breast tissue play in the production of PSA?

Materials and Methods

Using immunohistochemical methods, PSA was examined in normal breast tissue obtained by autopsy from 29 men and 23 women, of which 11 subjects were less than 50 years of age and 41 subjects were above 50 years of age Histological examination of normal female breast revealed only age-dependent involutionary postmenopausal atrophic changes, characteristic of female subjects over 50 years of age and resting female breast tissue seen in younger female patients Normal male breast histology revealed only ducts and no lactiferous sinuses and lobule formation in the samples examined Immunohistochemical staining was carried out by the biotin – streptavidin – peroxidase technique with aminoethylcarbasole development, using the Universal Kit (Dako, Corp , Carpinteria, CA, USA) Primary antibodies – rabbit polyclonal and mouse monoclonal anti-prostate-specific antigen antibody (Dako Corp , Carpinteria, CA, USA) were diluted 1 100–200 The study invariably involved negative controls (slides processed without primary antibodies)

Results

PSA expression was not observed in any epithelial structures of the 29 normal male or 23 normal female breast tissues evaluated Fig 1 shows no positivity of PSA in normal postmenopausal breast epithelial tissue of 64 years old female Occasional bordeline expression of PSA was observed in membranes of adipocytes of fat tissue and in the endothelium of small vessels of the female and male breast Fig 2 indicates PSA positivity in membranes of adipocytes of fat tissue in resting normal female breast of 44 years old female

Discussion

Results of our preliminary immunohistochemical study appear to provide a clear answer concerning the role of normal female and normal male breast tissue in the production of PSA In contrary to the conclusion of Diamandis's group (Yu *et al* 1996, Diamadis 1998) we have found that normal female breast epithelia do not produce PSA (Fig 1) Differences between the quantified immunochemical results of Diamandis and our findings may by explained by the fact that despite the higher sensitivity of quantifiable immunochemical compared to immunohistochemical methods, the former yield data on the heterogeneous homogenate, containing not only female breast glands, but also adipose tissue (Fig 2) and small vessels, in which positivity was observed on immunohistochemical examination The

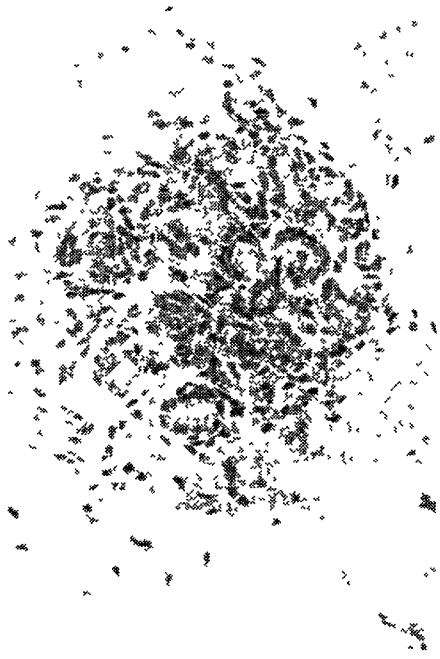

Figure 1. Normal post-menopausal breast tissue of 64-year-old female No positivity of PSA in breast epithelial structures (Autopsy No 980451, atherosclerotic heart disease) Magnification 180×

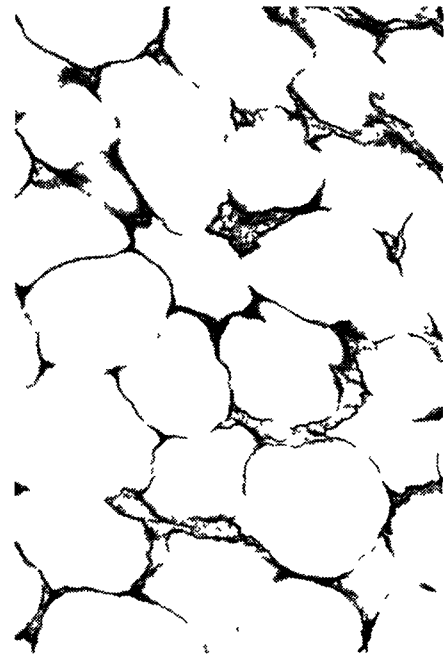

Figure 2. PSA positivity in membranes of adipocytes of breast fat tissue The resting normal female breast of 44-year-old female (Autopsy No 980291, adenocarcinoma of lung) Magnification 180×

hypothesis of Diamandis's group suggesting PSA production in the normal female breast has not been confirmed by these preliminary studies and cannot be explain by the source of PSA in the normal healthy female Therefore, pending further investigations, the tissue of the normal breast, male or female, can not be considered to be the producer of PSA Our studies of the female prostate (Zaviačič *et al* 1985, Zaviačič 1987, Zaviačič and Whipple 1993, Zaviačič and Ablin 1998 a, b, c) suggest that in the male, the female prostate (Skene's gland) is the normal and the principal source of PSA However, in consideration of recent reports of the anomalous expression of PSA in extraprostatic tissues, inclusive of the pathological female breast, one may envisage, as suggested by Ablin (1997), the existence of a regulatory gene network controlling ist expression Under such circumstances, a given tissue may, depending on the state of cellular differentiation, express repressed genes after neoplastic transformation Additionally, somatic mutations may contribute to specific changes in PSA genes in cancer cell clones

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The Role of Adenylate Cyclase in Ischemic Preconditioning in the Rat Heart: A Cytochemical Study

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Abstract. Using catalytic cytochemistry the AC activity was studied during ischemic preconditioning (IP) (5 min occlusion of LAD and 10 min reperfusion) followed by 30 min regional ischemia in isolated Langendorff-perfused rat heart In controls the specific precipitate of AC reaction was found on the sarcolemma (SL) and the junctional sarcoplasmic reticulum (JSR) of cardiomyocytes After prolonged ischemia the reaction product was absent, whereas IP followed by prolonged ischemia protected the AC activity on SL and JSR IP-induced enhancement of AC activity in this model was accompanied by significant reduction of ischemia/reperfusion fibrillation The results suggest involvement of AC system in mechanisms of IP

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