

POSTER ABSTRACTS

Conclusions The presence of mutant p53 protein in ovarian cancer is associated with poor prognosis in patients with low grade tumors, an otherwise good prognostic sign.

64 ASSOCIATION BETWEEN BREAST CANCER PATIENT SURVIVAL AND LEVELS OF CREATINE KINASE BB IN TUMOR CYTOSOLS

Zarghami¹, N. Gial², M., Yu¹, H., Katsaros², D., Diamandis¹, E.P.,
¹Dept. of Pathology, Rm 600-16, Mount Sinai Hospital, Toronto, ON MSG IX5, Canada; ²University of Turin, Italy.

CK-BB activity is suspected to play a role in the development of breast cancer as CK-BB's transcription could be enhanced by estrogen and by oncogene products from adenoviruses. The disruption of CK metabolic pathway could result in a suppression of tumor growth.

Objectives To examine if CK-BB activity is associated with clinical and pathological features of breast cancer and the survival of the patients.

Methods Tumor tissues from 172 consecutive breast cancer patients were measured for CK-BB using a time-resolved immunofluorometric method. The associations between CK-BB level and clinicopathological variables were analyzed using the contingency table method, and the association between CK-BB level and survival was analyzed using the Cox proportional hazards regression model.

Results It was shown that younger (<50 yr.) or chemotherapy-treated patients belonged more frequently to the high CK-BB category (42% vs. 22%, $p < 0.01$; 28% vs. 12%, $p = 0.03$) respectively. No association was found between CK-BB and clinical stage, nodal status, histological grade and type, tumor size, or ER/PR status. Risks for relapse were not substantially different between patients with high and low CK-BB cancer, but the risk for death was significantly higher (Relative Risk=3.7, $p = 0.03$) in patients with high CK-BB cancer.

Conclusions The study may indicate the usefulness of CK-BB measurement in the future management of breast cancer patients.

65 PROSTATE SPECIFIC ANTIGEN GENE EXPRESSION IN OVARIAN CANCER POST-LIVER TRANSPLANTATION

Yu¹, H., Diamandis¹, E.P., Levesque¹, M.A., Asal, S., Monne², M., and Croce², C.M., ¹ Dept. of Pathology, Mount Sinai Hospital and University of Toronto, Ontario, Canada, M5G IXS, Canada; ² Thomas Jefferson University, Philadelphia, PA 19107, U.S.

Prostate specific antigen (PSA) is a serine protease and is believed to be produced exclusively by the prostate gland. We recently found PSA in female breast cancer.

Objectives To search for PSA in other tumors and to characterize its presence at a molecular level.

Methods PSA concentrations in various tumors' cytosols were measured with a time-resolved immunofluorometric PSA assay. The molecular form of PSA was analyzed with HPLC. PSA mRNA was characterized using RT-PCR, Southern Blot analysis, and DNA sequencing.

Results High level of PSA produced by an ovarian tumor was found in a patient who also had a liver transplantation before the development of the tumor. The patient was on glucocorticoid therapy for three years. Tumor PSA level was 5.6 ng/mg. PSA in the tumor was present in its 33 KDa form. Tumor RNA was amplified by the polymerase chain reaction using two sets of primers derived from exon 1 and 4, and exon 3 and the 3'-untranslated region. The two PCR products were hybridized specifically to a PSA cDNA probe on Southern blots. Sequencing analysis of the two PCR products revealed 100% homology with cDNA derived from prostatic tissue (Genbank accession #U17040).

Conclusions The study provides further evidence that PSA could be produced by tissues other than the prostate. Based on our previous findings, we speculate that the PSA gene expression in this patient's ovary is due to the administration of glucocorticoid.

66 THE MILK OF LACTATING WOMEN CONTAINS PROSTATE SPECIFIC ANTIGEN

Yu, H., Diamandis, E.P., Dept. of Pathology, Mount Sinai Hospital, Toronto, ON MSG IX5, Canada

Prostate specific antigen (PSA) was initially believed to be produced exclusively by the prostate. Recent studies demonstrated that PSA could also be produced by non-prostatic tissues. PSA was found in breast cancer and its presence was associated with steroid hormones and their receptors. Under the stimulation of certain steroid hormones, normal breast tissue could also produce PSA.

Objective To search for further evidence that the breast is capable of producing PSA.

Method PSA concentration in the milk of 38 lactating women was measured with a time-resolved immunofluorometric PSA assay.

Results PSA concentration in these samples measured ranges from less than 0.01 $\mu\text{g/L}$ (4 samples) to 350 $\mu\text{g/L}$, and the median is 0.47 $\mu\text{g/L}$. PSA level in milk is not associated with the age of lactating women and the gender of the newborn. PSA concentration in milk seems to decline with post-delivery time, but is still detectable until 2 weeks after delivery. PSA in milk is also measurable by other commercial methods (e.g. the IMx PSA kit from Abbott). HPLC and Western blot analysis demonstrated that the major molecular form of PSA in milk was free PSA (33kDa). Less than 25% of PSA immunoreactivity was due to the complex of PSA with alpha-1-antichymotrypsin (1 100kDa).

Conclusions This study further confirms the production of PSA by the breast and prompts the necessity for better understanding of the biological role of PSA in tissues other than prostate.

67 A POSSIBLE ASSOCIATION BETWEEN FETAL ABNORMALITIES AND LEVELS OF PROSTATE SPECIFIC ANTIGEN IN AMNIOTIC FLUID

Melegos, D.N., Yu, H., Allen, L.C., and Diamandis, E.P., Dept. of Pathology, Rm 600-16, Mount Sinai Hospital, Toronto, ON M5G IX5, Canada.

Prostate specific antigen (PSA) is thought to be produced only by the prostate and is used as a tumor marker of prostate cancer. Recently, we found PSA in female breast cancer and other tumors. Other studies suggest a role of PSA in growth factor regulation.

Objectives To search for PSA in non-prostatic tissue and its function in relation to fetal growth and development.

Methods PSA concentration in over 1400 amniotic fluids and maternal sera were measured using a highly sensitive PSA immunofluorometric procedure.

Results PSA concentration in amniotic fluid increases progressively from gestational week 11 (median PSA 0.001 $\mu\text{g/L}$) to gestational week 20 (median PSA 0.66 $\mu\text{g/L}$). The largest change of PSA concentration occurs between gestational weeks 13-14. PSA level stays unchanged from gestational week 20 to term. A similar change of PSA level was also seen in maternal serum, but PSA levels were 20-40 times lower in serum than in amniotic fluid. PSA levels were significantly higher in the serum of pregnant women than in those of non-pregnant women. No significant associations were seen between amniotic fluid PSA and fetal sex, maternal age, or length of mother's abstinence from sexual intercourse. PSA concentration in amniotic fluid was found to be significantly low (multiple of median MOM, PSA <0.15) in 4 fetuses with trisomy 18 or 21, in 4 fetuses with anencephaly (MOM <0.50), and in 2 fetuses with renal abnormalities (MOM <0.15).

Conclusions The study further confirms that PSA is not prostate specific. PSA may have functions similar to some growth factors or their regulators, and may play a role in fetal development.