PROSTATE CANCER GENE EXPRESSION PROFILING FOR PERSONALIZED TREATMENT

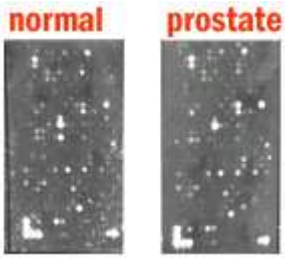
- Comparative Molecular Profiling Of Ffpe Prostate Tumor And Normal Tissue: New Differentially Expressed Genes Identified

- Recent Publication: Molecular Interactions Of Leptin And Prostate Cancer

- KLF6 Gene Polymorphism And Its Strong Association With Hormone Dependent Cancers

---

COMPARATIVE MOLECULAR PROFILING OF FFPE PROSTATE TUMOR AND NORMAL TISSUE:
NEW DIFFERENTIALLY EXPRESSED GENES IDENTIFIED.



- Archived FFPE tissues are easily available source material with well documented patient information that helps in conducting retrospective studies in relation to the type and stage of cancer, responsiveness to treatment and metastasis.

- A total of 139 differentially expressed genes were found suggesting the possible role of these genes in tumor formation or in malignacy.

- 30 differentially over expressed genes significant at $p<0.5$ were selected for further analysis. This gene panel with over expressed genes will be used for further clarification by quantitative PCR.

- Similarly 59 differentially under-expressed genes at a significance $p<0.05$ and 3 genes KLF6, LEP and RANTES from previous study will be included in the above panel to set up a 92 gene model for estimating the risk for cancer.

- This study clearly indicates the possible use of FFPE tissue to identify the relevant genes associated with the state of the disease. Comparisons with other cancers will be helpful to identify the specific genes that relate to their types.

- Studies are underway to establish these risk genes in Prostate and other types of cancer. Our future studies will be focusing in identifying new differentially expressed genes in patients with respect to responsiveness to treatment and metastasis.

RECENT PUBLICATION: MOLECULAR INTERACTIONS OF LEPTIN AND PROSTATE CANCER

Background:
Epidemiological studies have found obesity to be a risk factor for prostate cancer. Our prior independent studies in women have reported a strong relationship between variants of OB (leptin) gene, body mass index, and age at menarche and sporadic breast cancer. The current study investigates an association between genetic variants of the human obesity gene, serum leptin levels, and body mass index in subjects with prostate carcinoma and in age- and gender-matched normal subjects.

Methods:
Blood samples from 69 patients with prostate cancer and 137 age-matched control subjects were collected. Serum leptin level was investigated by radioimmunoassay, and body mass index was calculated. Allele sizes were determined via standard polymerase chain reaction. Statistical analysis was performed using SPSS10.0 computer software.

Results:
There was a strong association with significantly elevated serum leptin levels, high body mass index, and higher frequency of LEPR longer alleles in patients with prostate cancer than in control subjects. By contrast, a modest but not significant increase in the frequency of LEP short alleles was found in patients with prostate cancer as compared with control subjects Analysis within groups 1 (low leptin level and low body mass index) and 2 (other) showed a significant association only in group 2, with high frequency of OB gene variants (LEPR long alleles and LEP short alleles) in patients with prostate cancer but not in control subjects.

Conclusions:
These results represent the first report of a significant association between specific leptin gene alleles, serum leptin levels, and body mass index in subjects with prostate cancer. Consistent with prior reports, we also report a significantly elevated serum leptin level in patients with prostate cancer, suggesting a strong link with obesity as an increased risk factor.

Publication Types: Comparative Study
PMID: 16803678 [PubMed - indexed for MEDLINE].
Cancer J. 2006 May-Jun;12(3):201-6. Comment in: Cancer J. 2006 May-Jun; 12(3):178-81.

KLF6 GENE POLYMORPHISM AND ITS STRONG ASSOCIATION WITH HORMONE DEPENDENT CANCERS

Background:
Kruppel-like Zinc finger factor (KLF6) gene is functionally inactivated by allelic loss and initiates molecular mechanisms suggesting this gene to be a tumor suppressor gene. This inactivation may inhibit a number of key oncogenic signaling pathways raising the possibility of a generalized role in cancer pathogenesis. To identify the association of this gene polymorphism with hormone dependent cancers we included cases with breast (female) and prostate cancers and compared with gender and ethnic matched controls.

Methods:
This study includes 201 cancer patients (of which 134 have breast cancer, and 67, prostate cancer) with 192 normal healthy age, gender and ethnic matched subjects. DNA was isolated from peripheral blood drawn after an informed consent from all these subjects. PCR-RFLP based method was used to identify the genotype variation and SPSS software was used to analyze the data.

Results:
A significant association of this gene with both types of cancers was observed ($p<0.0001$) as compared to controls. Analysis of types of cancers in comparison to age-gender matched controls also showed this strong association (breast cancer – $p<0.0001$; prostate cancer-$p<0.001$).

Conclusions:
Our findings indicate the significant role of KLF6 gene polymorphism in hormone-dependent cancers. Our further investigations in tumor tissues in relation to gene expression and their responsiveness to drugs/therapy may help to better treatment.