ANDROGEN RECEPTOR EXPRESSION IN STROMAL AND EPITHELIAL PROSTATE CANCER TISSUE SPECIMENS

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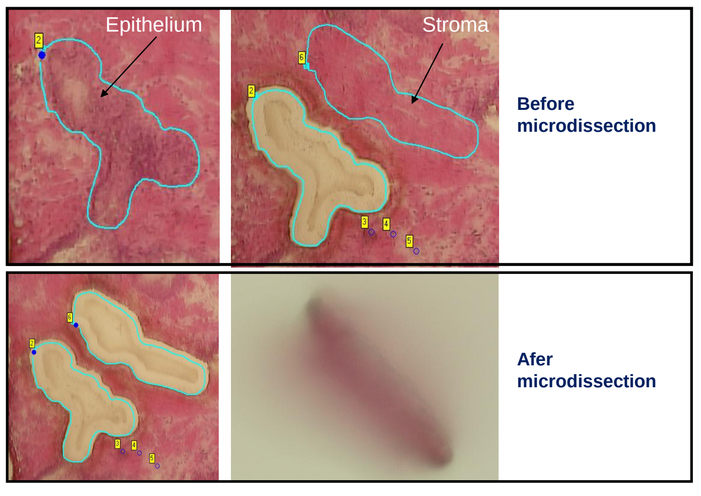
Prostate cancer (PCa) is one of the leading causes of tumor death in Western countries. Modifications in expression and functional alterations that involve the androgen receptor (AR) have been implicated in the progression of PCa and in the development of androgen independence; however, the role of AR in these processes is still debated, as contrasting results have been reported in several studies evaluating the relation between AR expression and disease progression (Tamburrino et al, 2012). Such evaluations are performed in PC specimens where, however, tumor tissue may be mixed to stromal and normal. There is now evidence in the literature that AR role in PCa may vary depending on its location. Indeed, studies performed in animal models (Niu et al, 2008) pointed out the different role of epithelial (protective toward a malignant phenotype) vs stromal (leading to tumor aggressiveness) AR in PCa. The present study was undertaken to evaluate AR expression in stromal and epithelial compartments of PCa specimens following careful microdissection.

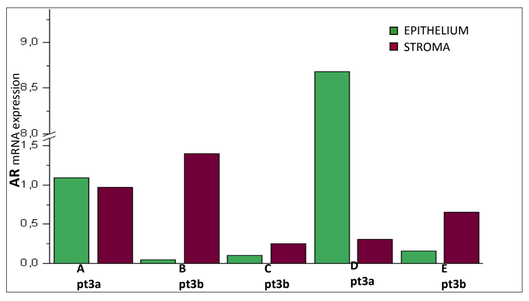
Material and Methods

Stromal and epithelial AR, EGFR, PSA and PTEN mRNA expression was analyzed in frozen PCa specimens after laser microdissection of the stromal and epithelial compartments. RNA was then extracted from 120 microdissected tissue samples and expression of genes was simultaneously evaluated after primer specific pre-amplification of cDNA. Microdissection has been performed collecting epithelial areas from the same specimens and the relative surrounding stromal tissue. As reference genes we used RPL13a (coding for a ribosomal protein). As positive and negative controls for AR we used mRNA extracted from LNCaP cells and HeLa cells, respectively.



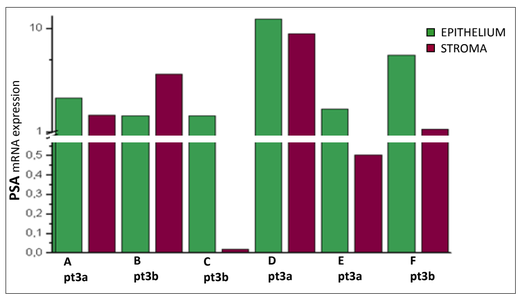
mRNA EXPRESSION

AR



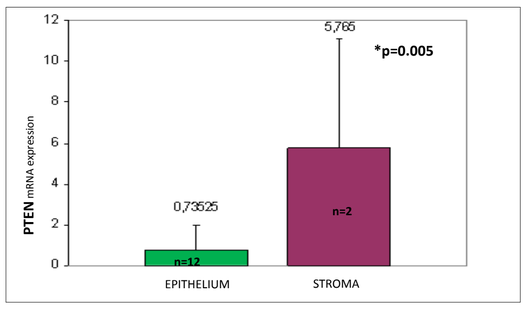
In few patients with tumor extension to seminal vesicles (PT3b) AR expression is higher in stromal respect to epithelial compartment

PSA



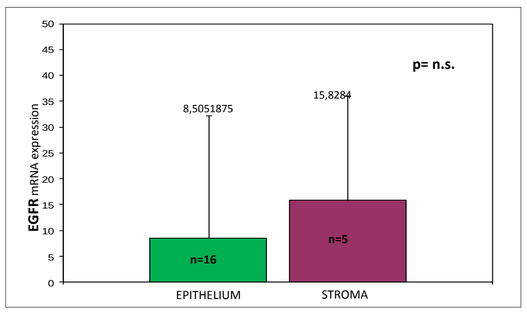
PSA expression is higher in epithelial respect to stromal compartment in most patients

PTEN



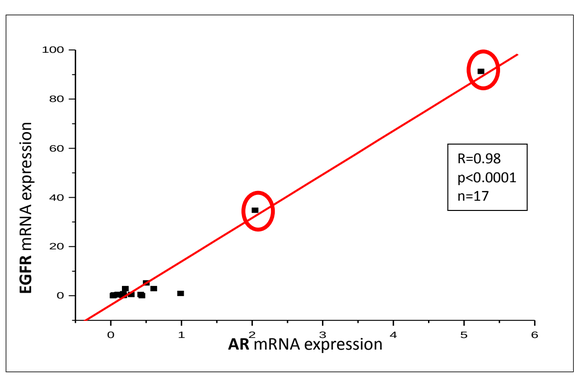
PTEN expression is significatively more expressed in stromal respect to epithelial compartment, in agreement with literature demonstrating loss of PTEN in PCa

EGFR



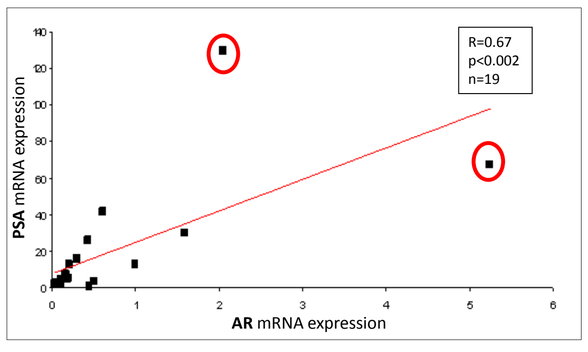
No significative differences in EGFR expression are found between stromal and epithelial compartments

CORRELATIONS



Preliminary results indicate that AR expression is correlated to that of EGFR in ***epithelial*** but not in ***stromal*** compartment (not shown)

Indicate two patients whose PSA serum levels did not dropped after surgery

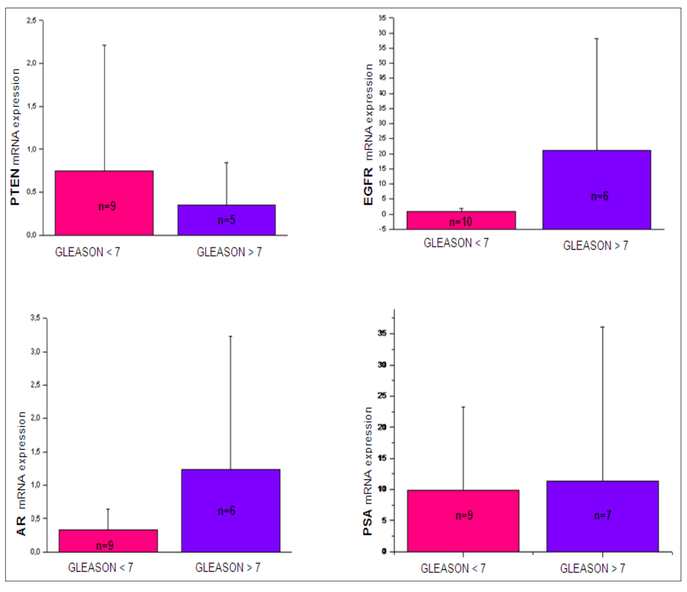


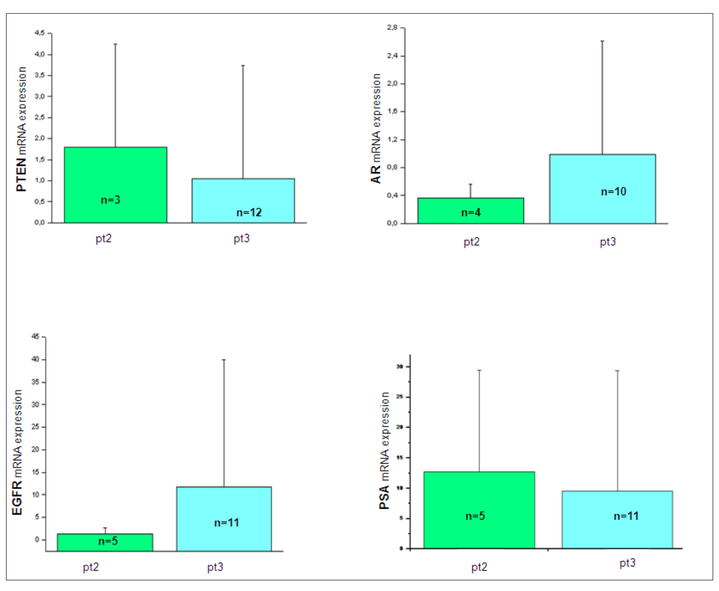
There is a significant correlation between AR and PSA in ***epithelial*** compartment

RELATION TO CLINICAL CHARACTERISTICS OF THE TUMOR

✓ **PTEN** expression tends to decrease and to become undetectable in high grade tumors

✓**AR** and **EGFR** expression appear to be higher in microdissected carcinoma areas with higher Gleason scores





✓ **PTEN** is more expressed in pt2 patients (pt2: Tumor confined to the prostate)

✓**AR** and **EGFR** are more expressed in pt3 patients (pt3: Tumor extends beyond the prostate)

CONCLUSIONS

- **Our preliminary data obtained on a limited number of patients (n=20) are in agreement with the literature concerning PTEN and EGFR expression, demonstrating the feasibility of the study.**
- **Occurrence of a highly significant correlation between AR and EGFR gene expression in the same microdissected area suggests that EGFR is under AR control at least in early phases of PCa.**
- **Evaluation of AR expression in microdissected PCa specimens may reveal new insights on the role of the steroid receptor in PCa progression in the two compartments.**