UROTENSIN II RECEPTOR PREDICTS THE CLINICAL OUTCOME OF PROSTATE CANCER PATIENTS AND IS INVOLVED IN THE REGULATION OF MOTILITY OF PROSTATE ADENOCARCINOMA CELLS

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Introduction and Objective
Urotensin II (UT-II) is a potent vasoconstrictor peptide and its receptor (UTR) was correlated with human cortico-adrenal carcinoma proliferation. In this retrospective study, we have evaluated the correlation between UTR expression and Gleason score of human prostate adenocarcinoma.

Materials and Methods
In order to investigate UTR changes occurring in human prostate tumorigenesis, we have evaluated the expression of UTR in 143 human prostate tissue samples of patients affected by prostate adenocarcinoma and underwent prostate biopsy and then radical prostatectomy between 2007 and 2011. All patients had a minimum follow up of 5 years.

Univariate associations between Gleason Score upgrading and clinical and tumour characteristics were assessed using either the chi square test or the Mann-Whitney U test. Multivariable logistic regression models were used to explore the independent role of UTR expression in predicting Gleason upgrading with respect to a set of base prognostic factors including PSA, primary and secondary Gleason score and muscle invasion. The predictive accuracy of the models was evaluated by ROC curve analysis and measured using the area under the curve (AUC). Comparison among the different AUCs was carried out computing the bootstrap sampling distribution of the difference in the two AUCs.

Results
55 (38.5%) patients showed a Gleason score upgrading from biopsy on final pathology. The most frequent pattern (n=20, 36.4%) of upgrading was from a biopsy score of 3+4 to a RPP score of 4+3.

At univariate analysis, lower primary Gleason, presence of muscle invasion ad higher UTR expression showed a significant association (p<0.001) with Gleason upgrading. Although patients with GS upgrading were characterized by higher PSA values (median [range] PSA: 6.6 [4.8 to 9.5] vs 5.8 [4.4 7.8]), this difference did not reach statistical significance (p=0.215). In a multivariable logistic model including both primary and secondary Gleason score, PSA, muscle invasion and UTR expression levels, patients with an high UTR expression showed a more than ten-fold increase in the odds of upgrading (O.R. 13.77, C.I. 3.1 to 62.5, p<0.001) with respect to patients with low UTR expression.
In ROC analysis, this model predicted Gleason Upgrading with an AUC equal to 0.88 (95% C.I. 0.79 to 0.96, p<0.001). With respect to base model not including UTR, the absolute gain in predictive accuracy of the complete model was equal to 9% (p=0.042).

**Conclusion**
These data suggest that UTR can be considered a prognostic marker in upgrading human prostate adenocarcinoma patients from biopsy to radical prostatectomy.