151

Steroid hormone receptors are differently expressed in prostate cancer depending on Gleason grade and presence of disease recurrence

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INTRODUCTION & OBJECTIVES: Steroid hormone receptors (SHR) are abundantly expressed in the prostate and are known to play important roles in the onset and progression of prostate cancer (PCa). The androgen receptor (AR) is well known to play an active role in the onset and progression of PCa, but it becomes apparent that other SHR like progesterone receptor (PR) and estrogen receptor (ER) are also important in PCa, partially by modulating the role of AR. Here we investigated the impact of Gleason grade and clinical failure (CF, i.e. disease recurrence) on the expression profiles of AR, PR and ER in PCa.

MATERIAL & METHODS: Matched patient cohorts were composed for different Gleason grades (6-7-8, n=30/group) and for presence/absence of CF 5 years post-prostatectomy (n=25/group). Tissue micro-arrays (TMA) with 6 samples/patient were composed (both PCa and non-PCa tissue) and subsequently processed for immunohistochemistry (IHC) with clinically validated antibodies on a calibrated autostainer within a standardised time frame. Stained slides were digitalised using a calibrated scanner, stroma and epithelium were selectively annotated, and all selected areas were analysed for percentage of (nuclear) expression with standardized and validated image analysis. Paired and independent groups of quantitative data were compared using appropriate non-parametric tests (sign test, Kruskall Wallis test and associated post-hoc tests and Spearman correlation analysis).

RESULTS: In all studied groups (both controls and PCa) we observed significantly higher expression of AR and lower expression of ER in epithelium compared to stroma (PR was only expressed in stroma) ($p<0.05$). High Gleason grade (7-8) was associated with an increased expression of ER in tumour cells compared to stroma ($p<0.05$). No further significant changes were found in epithelial and/or stromal expression of AR, PR and ER between the different Gleason grade groups. CF was associated with a significant decrease in AR expression in tumour cells compared to normal prostate epithelial cells, whereas in the non-CF group the opposite was observed ($p<0.05$). No other significant changes in epithelial and/or stromal expression of AR, PR and ER were observed between the CF and non-CF-groups. We found significant positive correlations in the non-CF group between stromal AR and ER expression in non-PCa tissue and in the CF-group for stromal AR and PR expression in the PCa-tissue.

CONCLUSIONS: The present study reveals different SHR expression profiles in normal prostate versus PCa with specific changes depending on the Gleason grade and on the presence or absence of CF.

151

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Most remarkably, decreased AR expression in the primary tumour was correlated with a worse clinical outcome, while increased ER expression in tumour cells was associated with a high grade PCa phenotype. A better knowledge of PCa-related changes in the complex SHR physiology is pivotal in the search for new anti-androgen therapies; modulating the changed SHR expression might then be a promising therapeutic approach.