P21 Detectable biomarkers in urine for prostate cancer prognosis

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Introduction & Objectives: A major hurdle in today's prostate cancer (PCa) diagnostics and treatment is the high incidence rate accompanied by slow progression in most of the cases. Regarding the severity of highly aggressive forms of PCa, additional diagnostic tools to help with decision making during active surveillance are needed. Liquid biopsies such as urine are cost efficient, minimal invasive, and have a high compliance rate.

Materials & Methods: We analyzed urine samples of 50 fasting individuals (controls = 21; PCa = 29, collected prior radical prostatectomy [RP], 4 cases of recurrence [PSA ≥0.2 ng/ml after RP]) by LC-MS/MS (AbsoluteIDQ p180 Kit, Biocrates, Austria). This kit allows for quantification of a selection of acylcarnitines, amino acids, biogenic amines, glycerophospholipids, sphingolipids and hexose. Glycerophospholipids and sphingolipids were below limit of detection (LOD) or barely above LOD and were therefore excluded from the analysis.

Results & Discussion: Analyzing the grouped (PCa vs controls; normalized to creatinine) data with PLS-DA resulted in a poorly performing model with low accuracy. Grouping the data by using recurrence (rec. [n=4] vs. non-rec. [n=46]) we found that VIP scores (top-4, cut-off 1.5-fold above average VIP score) resulting from PLS-DA suggested kynurenine (KYN), dopamine (DOP), tetradecadienylcarnitine (C14:2), and serine (SER) as the strongest discriminants. Analyzing only PCa samples (rec. vs. non-rec.) led to similar results, with SER, KYN, DOP, and C14:2 being the strongest discriminants. Due to the limited number of patients with rec. both models overfitted with an accuracy of up to 100% dependent on the choice of test and train sets. Levels of KYN and C14:2 were 1.8-, 1.3-fold increased (p-values: 0.041 and 0.15, permutation test) while DOP and SER were 0.7- and 0.6-fold decreased (p-values: 0.057 and 0.0064) in patients with rec. compared to PCa patients. KYN is linked to immunosuppression enabling tumor progression and elevated levels in serum are associated with PCa[1,2]. Bromocriptine, a DOP D2 receptor agonist, enhanced the chemotherapeutic effect of docetaxel to treat bone metastatic PCa[3] explaining lowered DOP. Increased SER biosynthesis was observed in neuroendocrine PCa (NEPC) and served as carbon source to promote cell proliferation and the development of NEPC characteristics[4].

Conclusions & References: We could detect several metabolites in urine of which KYN, DOP, and SER are potential prognostic biomarkers for recurrence prior to RP and might also be of use as markers for PCa aggressiveness during active surveillance. Nevertheless, further data from targeted analysis of KYN, DOP, and SER in larger cohorts are required to confirm these findings.

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