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Assessment of prostate cancer aggressiveness using metabolomics evaluation of urine by NMR spectroscopy

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Introduction: Prostate cancer (PCa) is the most common non-skin cancer type among men and one of the leading causes of cancer deaths worldwide. The introduction of prostate-specific antigen (PSA) testing resulted in a substantial increase in the number of diagnosed cases. However, a significant fraction of PCa cases detected solely on the basis of an increased serum PSA are indolent, i.e. non-aggressive, slow-growing tumors with 10-year survival rates above 90% even without treatment. The inability to discriminate clinically relevant aggressive PCa from indolent forms results in over-diagnosis and over-treatment highlighting the urgent need for novel biomarkers indicating aggressive PCa.

Materials & Methods: We obtained urine samples of 524 patients with PCa before prostatectomy. Post-Op Gleason score (GS) was used as a definition for aggressiveness (indolent GS <= 6 vs. aggressive GS >= 7). We conducted a high resolution urine metabolomics analysis using NMR spectroscopy combined with logistic regression analysis for the validation of previously reported biomarkers from literature, and the identification of additional biomarkers for the assessment of PCa aggressiveness.

Results: We obtained a list of models (composed of NMR signals) that show promising performance (AUC up to 0.73) in discriminating indolent from aggressive PCa in a training cohort (238 cases, 64 controls). Results were validated on an independent cohort (183 cases, 39 controls) leading to an AUC up to 0.67.

Conclusions: The study of urinary metabolomics alterations associated with PCa progression using NMR offers a promising approach for validating reported biomarkers and also for discovering novel clinical biomarker constellations. Further work will investigate metabolic pathways affected by PCa using systems medicine approaches in conjunction with genomics and proteomics data sets.