

## Positive STAT5 protein and locus amplification status predicts prostate cancer recurrence after radical prostatectomy to assist precision medicine of prostate cancer

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**Background:** While radical prostatectomy (RP) for organ-confined prostate cancer (PC) has a curative intent, a significant fraction (30-60%) of patients experience post-RP biochemical recurrence (BCR). Markers to predict BCR are needed for optimizing the post-operative management of individual PC patients. *STAT5* is an oncogene in PC which undergoes gene amplification in 30% of PCs during progression to advanced disease.

**Methods:** In this study, we evaluated the importance of positive status for STAT5 protein expression vs *STAT5* locus amplification vs. combined positive status for both in predicting BCR after RP in a cohort of 457 PCs using immunohistochemistry and fluorescence *in situ* hybridization.

**Results:** Patients with combined *STAT5* gene amplification and protein overexpression suffered a 45% disadvantage in BCR in Kaplan-Meier survival analysis compared to patients with negative status for STAT5. Importantly, patients with Gleason grade group (GG) 2 and 3 PCs and combined positive status for STAT5 had even a more pronounced disadvantage of 55-60% at 7 years after RP in univariate analysis. In multivariate analysis including the CAPRA-S nomogram variables, combined positive STAT5 status was independently associated with a shorter BCR-free survival interval in all patients (HR=2.34, p=0.014) and particularly in patients with intermediate Gleason GG 2 or 3 PC (HR=3.62, p=0.021). The combined positive STAT5 status improved the predictive value of the CAPRA-S nomogram in both receiver operating characteristic area under the curve-analysis and in decision curve analysis for disease-free survival in all patients and in Gleason GG 2 and 3 patients. In conclusion, combined *STAT5* locus amplification and protein status identifies PC patients at elevated risk for BCR after RP.

**Conclusions:** Our results highlight potential for a novel precision medicine concept based on a pivotal role of STAT5 status in improving selection of PC patients who are candidates for early adjuvant interventions designed to reduce the risk of clinical recurrence.

**Conflict of Interest:** None

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