



Stromal gene expression predictive of metastatic primary prostate cancer

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Relevance. Clinical grading systems that use clinical characteristics, as well as nomograms, do not have the accuracy to guide treatment decisions for prostate cancer (prostate cancer). There is a critical need to identify biomarkers that can more accurately stratify men with primary prostate cancer.

The purpose of the study. To identify an effective prognostic signature that can better distinguish between indolent and aggressive prostate cancer (prostate cancer).

Design, conditions and participants of the study. To develop the signature, whole genome and whole transcriptome were sequenced on five prostate cancer models with xenographs from patients (PG) obtained from independent foci of a single primary tumor and demonstrating different metastatic phenotypes. Several independent clinical cohorts, including the intermediate risk cohort, were used to validate biomarkers.

Determination of results and statistical analysis Metastasis after radical prostatectomy was the outcome that determined aggressive prostate cancer. A general linear model with lasso regularization was used to construct a 93-gene stromal metastasis signature (SDMS). The association between SDMS and metastasis was assessed using the Wilcoxon rank sum test. Efficiency was evaluated using the area under the curve (AUC) for receiver performance and Kaplan-Meier curves. Univariable and multivariable regression models were used to compare SDMS with clinical histological variables and other signatures. AUC was evaluated to determine whether SDMS is additive or synergistic with respect to other previously defined signatures. **Results and limitations** There was a close association between stromal gene expression and metastatic phenotype. Accordingly, SDMS was modeled and validated in several independent clinical cohorts. Patients with high SDMS scores, as it turned out, had a worse prognosis. Moreover, SDMS was an independent predictive factor, was able to stratify the risk of intermediate-risk prostate cancer, and can improve the effectiveness of other previously presented signatures. **Conclusion** Profiling of stromal gene expression led to the development of SDMS, which has been validated as an independent prognostic factor for the metastatic potential of prostate tumors