A genomic classifier to improve prediction of metastatic disease within 5 years after surgery in node-negative high-risk prostate cancer patients managed by radical prostatectomy without adjuvant therapy.

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Background: Surgery is a standard first line therapy for most intermediate-high risk men diagnosed with prostate cancer. While clinical factors such as tumor grade, stage and prostate specific antigen (PSA) are currently used to identify patients at risk of cancer recurrence, novel biomarkers that can improve risk stratification and distinguish local from systemic recurrence are needed. The Decipher Genomic Classifier (GC) is a validated model for predicting men at risk of metastasis. We evaluated its performance in predicting metastatic disease within 5 years after surgery (rapid metastasis, RM) in an independent cohort. **Methods:** Tumors and clinicopathologic data were obtained from a cohort of 2,641 RP patients treated between 1987-2008 at Cleveland Clinic. The final study cohort consisted of 15 RM patients and 154 patients as non-RM controls who met the following criteria: 1) preoperative PSA>20 ng/mL, stage pT3 or margin positive, or Gleason score ≥8; 2) pathologic node negative; 3) undetectable post-RP PSA; 4) no neoadjuvant or adjuvant therapy; and 5) minimum 5 year follow-up for the controls. **Results:** RM patients developed metastasis with a median of 2.3 (IQR: 0.8-5) years. In multivariable analysis, GC was a significant predictor of RM (OR=1.48, p=0.018) after adjusting for clinical risk factors. GC had the highest c-index, 0.77, compared to the Stephenson model (c-index 0.75) and CAPRA-S (c-index 0.72) as well as a panel of previously reported prostate cancer biomarkers unrelated to GC. Integration of GC into the Stephenson nomogram increased the c-index from 0.75 (95% CI: 0.65-0.85) to 0.79 (95% CI: 0.68-0.89). **Conclusions:** GC was independently validated as a genomic metastasis signature for predicting RM in a cohort of high-risk men treated with RP and managed conservatively without any adjuvant therapy. Integration of GC into clinical nomograms led to improvement in prediction of RM. GC may further allow identification of men most at risk for metastatic progression who should be considered for multimodal therapy or inclusion in clinical trials.