Validation of GEMCaP as a DNA based biomarker to predict disease recurrence in patients with intermediate to high risk disease undergoing prostatectomy for prostate cancer

Hao G. Nguyen[1*], Christopher Welty[1*], Karla Lindquist[1], Vy Ngo[1], Elizabeth Gilbert[1], Henrik Bengtsson[4], Cristina Magi-Galluzzi[2], Jerome JeanGilles[3], Jorge Yao[3], Matthew Cooperberg[1], Edward Messing[5], Eric Klein[6], Peter Carroll[1], and Pamela L. Paris[1].

[1]Department of Urology, University of California at San Francisco (UCSF) Helen Diller Family Comprehensive Cancer Center (HDFCCC) San Francisco, CA. [2]Department of Anatomic Pathology, Cleveland Clinic, Cleveland, Ohio. [3]Department of Pathology, University of Rochester (UR), Rochester, NY. [4]Department of Epidemiology and Biostatistics, UCSF, San Francisco, California. [5]Department of Urology, UR, Rochester, NY. [6]Urological and Kidney Institute, Cleveland Clinic, Cleveland, Ohio.

*These authors contributed equally to this work.

Abstract:

Background and Objective: There are currently no validated DNA based biomarkers available for routine clinical use to predict prostate cancer recurrence after prostatectomy. The Genomic Evaluators of Metastatic Cancer of the Prostate (GEMCaP) assay is a tumor genotype using copy number for a set of genomic loci. We aim to validate the GEMCaP assay using an external cohort of intermediate and high risk patients.

Methods: We randomly identified 200 patients with intermediate to high clinical risk features who had undergone radical prostatectomy at the Cleveland Clinic (CC) and University of Rochester (UR) Cancer Centers from 2000-2005 and had tissue available for research. After pathology review (CMG, JY) cancer tissues were macrodissected and DNA extracted and subjected to high resolution array comparative genomic hybridization (aCGH) using Agilent's oligonucleotide microarray platform. A high GEMCaP score was defined as $\geq$20% of the genomic loci exhibiting copy number gain or loss in a given tumor, as in previous studies. Cox regression was used to evaluate associations between the GEMCaP score and risk of biochemical recurrence in univariate and multivariate analyses adjusted for the CAPRA-S score. The outcome was biochemical failure defined as PSA >0.2 or salvage radiation therapy. All analyses were adjusted for institution.

Results: We report the results from 140 patients, 54 from the CC cohort and 86 from the UR cohort. Median time to recurrence was 45.3 months and median follow-up among those who did not recur was 120.2 months. Based on the CAPRA-S score, 39.3% were low-risk, 42.2% were intermediate-risk and 18.5% were high-risk. 30.7% of the cohort had a high GEMCAP score (≥20%). A high GEMCaP score was associated with higher risk of biochemical recurrence (HR 2.69, 95%CI 1.51-4.77) and remained associated with biochemical recurrence after adjusting for the CAPRA-S score (HR 1.91, 95% CI 1.05-3.48). The C-index for GEMCaP alone was 0.64, and improved when combined with CAPRA-S (C-index = 0.76).

Conclusions: In this validation study, a high GEMCaP score was associated with biochemical recurrence in two external cohorts. This remained true after adjusting for clinical and pathologic factors as accounted for by the CAPRA-S score. The GEMCaP biomarker could be an efficient and effective clinical risk assessment tool to identify prostate cancer patients for early adjuvant therapy.

Funding: Prostate Cancer Foundation Young Investigator 2016 to H.N. and NHI RO1 to P.P.
Conflict of Interest: None