Development and Validation of a Prognostic Molecular Cell Cycle Progression Signature for Decentralized Testing of Men with Localized Prostate Cancer

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INTRODUCTION

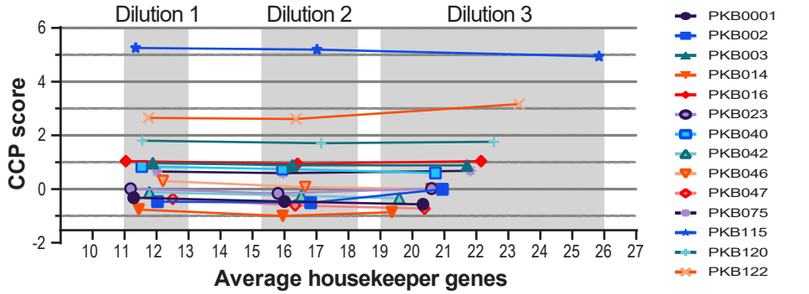
- The Prolaris cell-cycle progression (CCP) test is a validated 46-gene assay which informs individual risk of disease progression (disease specific mortality or metastasis) for men with localized prostate cancer.
- This study developed and validated a 16-gene kit-based version of Prolaris® for decentralized testing in localized facilities.

METHODS

- Kit test gene selection was performed by correlating the genes of the 46-gene panel with the CCP score. Genes with the lowest expression rate and lower correlation with CCP score were excluded. The number of CCP and housekeeper genes required to produce a robust CCP score was assessed. The final 16-gene set was optimized using analytical data.
- RNA was extracted from formalin-fixed, paraffin-embedded prostate cancer tissue. CCP scores were calculated as the expression of CCP genes normalized to housekeeper genes.
- Amplification efficiency, minimum tumor content, repeatability, and reproducibility were evaluated.
- Scores from the 46- and 16-gene tests were compared to verify that the 16-gene test could be applied in a similar clinical manner to the 46-gene test.

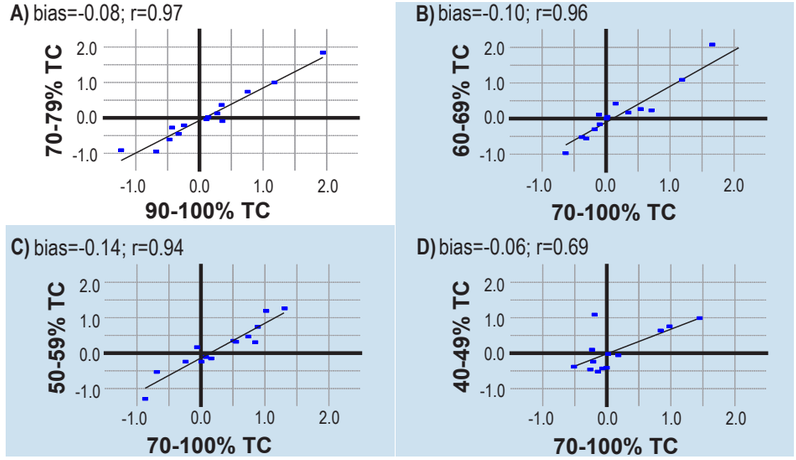
RESULTS

Figure 1. CCP scores across the validated measurement range.



Different colors/shapes represent different patient samples (n=14), Each were analyzed with 3 different dilutions (represented by average of housekeeper genes).

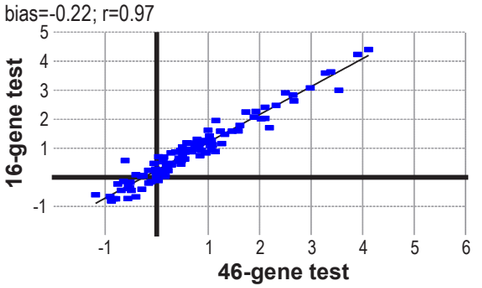
Figure 2. CCP scores calculated from paired RNA samples isolated from patient biopsy samples with different tumor contents.



CCP scores were compared to those calculated from samples with following tumor contents (TC): (A) 90-100% TC (white background) or (B-D) 70-100% TC (blue background).

- The 16-gene test showed reproducible results over a wide range of RNA input concentrations (Figure 1).
- Amplification efficiency of all CCP and housekeeper genes in the 16-gene test fell within an acceptable range of 92-105%.
- Samples with at least 60% tumor content were determined to be appropriate for testing with the 16-gene kit (Figure 2).
- Test results were highly repeatable (SD in CCP score 0.085) and reproducible (SD 0.115), with instrument used, test operator, and kit lot all having minimal impact on test result variation (SD 0.000, SD 0.016, and SD 0.114, respectively).
- The CCP scores generated from the 46- and 16-gene tests were highly correlated (r=0.97, bias=0.22) (Figure 3).

Figure 3. Correlation of CCP scores from 16-gene test with scores from 46-gene test (n=100).



CONCLUSIONS

- The 16-gene test, which consists of 10 CCP and 6 housekeeper genes, results in similar scores when compared to the 46-gene test, showing the 16-gene test can be used in a similar clinical manner.
- Kit lot, test instrument, and operator had minimal impact on the CCP score results from the 16-gene test, indicating it is appropriate for use in a decentralized testing setting.
- The validation of this 16-gene based CE-marked test will allow access to a version of the Prolaris® test for patients in areas where testing in local laboratories is required or desired.