Novel live tumor cell diagnostic test using biophysical and molecular biomarkers for assessment of tumor burden and metastatic potential in prostate cancer.


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Abstract:

Introduction:

- Prostate specific antigen (PSA) is a non-specific biomarker for prostate cancer (PCa).
- Widespread use of PSA screening has led to significant over diagnosis and over-treatment of non-metastatic PCa.
- The lack of reliable risk-stratification biomarkers has resulted in approximately 80% of low risk patients receiving unnecessarily aggressive treatment.
- There is a clear need for quantifiable and actionable risk-stratification biomarkers for PCa.

Methods:

An analytical validation study was performed on fresh prostate cancer samples (n=100) obtained at the time of radical prostatectomy (RP). The diagnostic platform enables: 1) growth of patient cells in vivo on extra cellular matrix formulations supporting adhesion/survival for 72 hours 2) high-throughput imaging of multiple phenotypic biomarkers such as morphology, cytoskeleton dynamics, and protein subcellular localization & modification states and 3) objective quantification of biomarkers via machine vision analysis. Patient samples were imaged over a three hour period capturing live-cell biological biomarkers. After three hours cells were fixed and stained for molecular biomarkers. Machine vision technology was then utilized to analyze phenotypic biomarkers to yield specific metrics that quantified local tumor growth (Oncogenic Potential-OPs) and invasive potential of the tumor to other tissues (Metastatic Potential- MP) that correlated with RP specimen pathologic findings.

Results:

Abstract:

Background: Due to the inconsistencies of existing molecular, genomic, and pathophysiological markers for pathological stratification, effective prostate cancer diagnosis and treatment remains a challenge in clinical practice. Therefore, the development of a diagnostic platform that differentiates cancer patients who will clinically significant disease from those who have a low risk of progression is an important area of interest. In this study, we tested a diagnostic platform that combines a scalable microfluidic device, automated live cell assay, and objective machine vision algorithms to measure phenotypic biomarkers [defined here as functional biophysical and molecular biomarkers], which evaluate both local growth and metastatic potential of prostate cancer.

Clara's Machine Learning has the ability to process multiple biomarkers and accurately predict various pathological outcomes. (A) A set of biomarkers measured for each cell in a patient is input to (B) Clara’s machine learning algorithm that generates multiple decision trees stratifying cells of a patient from cells of a positive patient for a given pathological outcome. The decision trees are then weighted to optimize a prediction algorithm (C) representing a stratifying score for each patient. Using this stratifying score, the patient is then classified into one of the following risk categories: (D) A representative plot demonstrating stratification of patients for a given predicted pathology.

Conclusion

-Proprietary* phenotypic, molecular and biophysical biomarker panel in living cells obtained from fresh tumor tissue is strongly predictive of Gleason grade in radical prostatectomy (RP) specimens.
-Proprietary* predictive metrics, Oncogenic Potential (OP) and Metastatic Potential (MP), differ significantly between prostate cancer patients with low and intermediate risk disease and tumors.
-Proprietary* biomarkers were predictive of adverse pathologic findings in RP specimens. OP was predictive of tumor burden and MP of metastatic potential.

This novel quantitative and actionable phenotypic biomarker panel has potential utility in risk stratification in men with Gleason 6 and Gleason 7 (3+4, 4+3) prostate cancer.

*Clara's Machine Learning, a trademark of Cellanyx Inc.

Clinical Highlights

1. Sensitivity and specificity numbers describe the capability of proprietary* prostate cancer diagnostic test to predict pathologic Gleason (Gleason and other) findings.
2. The Oncogenic Potential (OP) describes the extension of tumor in the prostate capsule and seminal vesicles, and the Metastatic Potential (MP) describes the tumor's potential to spread to peripheral systems such as blood, lymph and/or bone. The OP & MP calculation is made with a proprietary* algorithm.
3. OP and MP values in the adjacent table represent predictive thresholds of disease status.
4. Gleason 6 or Gleason 7 denotes predicting Gleason 7 patients from a set of Gleason 6 & 7 patients.
5. Gleason 3+4 vs. 4+3 denotes predicting Gleason 4+3 patients from a set of Gleason 3+4 patients.
6. Biomarker platform is currently being applied to bladder, kidney, and lung tumors.

References: