A novel live cell microfluidic diagnostic using phenotypic biomarkers with objective algorithmic analysis for prostate cancer risk stratification.


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**Abstract:**
An important area of improvement is differentiating cancer patients who have clinically significant disease from those who have a low risk of progression. In this study, we tested a diagnostic platform that combines a scalable microfluidic device, phenotypic biomarkers (as defined here as functional and biophysical biomarkers), machine vision algorithms, and an automated live cell assay that evaluates both local invasiveness and metastatic potential of prostate cancer.

**Methods:**
An analytical validation study was performed on fresh prostate cancer samples (n=104) obtained at the time of radical prostatectomy (RP). Patient groups were geno-ex vivo such that automated imaging of multiple microfluidic biomarkers were objectively quantified via machine vision analysis. Diagnostic process is designed to enable survival of prostate tumor cells from fresh biopsy/surgical samples to allow for analysis of three biomarker classes: phenotypic, biophysical, and molecular on live cells harvested from patient tumor samples. A) Flow diagram outlines the process to measure U0126 and fixed biomarkers of interest. Array analysis of phenotypic biomarker characterization yielded specific metrics (oncogenic, metastatic potentials), that correlated with RP specimen pathologic findings.

**Results:**
Analysis of quantified phenotypic biomarkers distinguish normal from cancer cells. Objective machine vision algorithms generate proprietary secondary metrics termed "Metastatic Potential (MP)" and "Oncogenic Potential (OP)," which are used to risk stratify the fresh tumor samples. Concordance analysis of the RP pathology findings with both MP and OP metrics demonstrated statistical significance in distinguishing Gleason 6 from Gleason 7 prostate cancer with 86% sensitivity and 80% specificity. A novel diagnostic platform measures phenotypic, biophysical, and molecular biomarkers on live cells harvested from patient tumor samples. A) Flow diagram outlines the process to measure U0126 and fixed biomarkers of interest. Array analysis of phenotypic biomarker characterization yielded specific metrics (oncogenic, metastatic potentials), that correlated with RP specimen pathologic findings. A diagnostic model was generated by training a machine learning algorithm on a dataset of 104 sample sets containing Gleason 6 and Gleason 7 prostate cancer. The model was validated using a cross-validation method and achieved an accuracy of 86%. The model was then tested on an independent test set of 30 sample sets, achieving an accuracy of 83%.

**Conclusion:**
Cellanyx's Machine Learning algorithm 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 are input to (B) Cellanyx's machine learning algorithm that generates an output of disease risk and provides an output likelihood of the algorithm accuracy. (C) A representative plot demonstrating stratification among negative and positive cells utilizing combinations of biomarkers as described in the decision tree. Patient level results are obtained by summarizing cell level results into (D) a (representative) plot demonstrating stratification of patients for a given predicted pathology finding.

**CLINICAL RESULTS:**
- Sensitivity = true positives / (true positives + false negatives)
- Specificity = true negatives / (true negatives + false positives)
- Accuracy = (true positives + true negatives) / (true positives + false positives + false negatives + true negatives)
- Precision = true positives / (true positives + false positives)
- Recall = true positives / (true positives + false negatives)
- F1-score = 2 * (precision * recall) / (precision + recall)

**References:**
- Cellanyx Diagnostics, LLC CONTACT: INFO@CELLANYX.COM

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