Clinical Validation of a live-cell phenotypic biomarker - based diagnostic assay for the prediction of adverse pathology in Prostate Cancer


Introduction and Objective: Prostate cancer accounts for over 28% of total cancer cases in the United States. Current screening and diagnostic approaches lack the sensitivity to objectively assess the aggressiveness of tumors. To address this issue, a diagnostic assay was developed to differentiate indolent from aggressive tumors, to address risk stratify patients and predict adverse pathology. Here we describe a diagnostic platform that is based on the measurement of a panel of phenotypic and molecular biomarkers in live biopsy-derived cells. Combining cell microfluidics, automated imaging and machine learning, the assay provides predictive scores for local aggressiveness, invasiveness and the presence of adverse clinical pathologies.

Methods: This clinical validation study was done on 250 prostate cancer samples (n=250) obtained at the time of radical prostatectomy. Patient cells were harvested as live cells within 6 hours (up to 7 hours) to enable live-cell, label-free imaging of multiple phenotypic biomarkers. Cells were cultured on microfluidic devices and imaged in real time. Data were objectively quantified by machine vision algorithms to evaluate cellular behavior, and machine learning analytical metrics. Results: The developed predictive dynamic machine vision algorithms and adverse pathology: 1) Local Adverse Pathology Potential (LAPP) & 2) Metastatic Adverse Pathology Potential (MAPP). Reason: the local aggressiveness, invasion, and clinical behavior of the geometric singularities allows for the model to be classified as benign, indolent, or aggressive. The results showed that the assay is able to distinguish benign from malignant cells, and predicts adverse pathology. The assay results are able to separate aggressiveness, invasiveness and the presence of adverse pathology. Adverse Pathology Potential (LAPP)” & “Metastatic Adverse Pathology Potential (MAPP)” & “Machine vision algorithms used to identify and track individual cell’s biomarkers. A) Cells are identified and tagged with unique IDs; B) Cell location is tracked over time; C) Cells spreading distance and motility are tracked statistically; D) Membrane fluctuations are measured to project cytoskeletal damage; E) Membrane fluctuations are measured to project cytoskeletal damage; F) 30 minute intervals, 30 second intervals, 1-minute intervals, 2-minute intervals, 3-minute intervals, 5-minute intervals, 10-minute intervals, 1-hour intervals, and 2-hour intervals are automatically and continuously measured on fixed, fluorescently stained cells.

Clinical Highlights

1. **Sensitivity and Specificity Numbers Describe the Model’s Predictive Capabilities.**
   - Sensitivity: 90% Sensitivity and Specificity describe the model’s ability to correctly identify patients who will benefit from curative treatment and those who will not. Specificity: 90% Specificity and Specificity describe the model’s ability to correctly identify patients who will benefit from curative treatment and those who will not. Sensitivity: 90% Sensitivity and Specificity describe the model’s ability to correctly identify patients who will benefit from curative treatment and those who will not. Specificity: 90% Specificity and Specificity describe the model’s ability to correctly identify patients who will benefit from curative treatment and those who will not.
   - Sensitivity: 90% Sensitivity and Specificity describe the model’s ability to correctly identify patients who will benefit from curative treatment and those who will not. Specificity: 90% Specificity and Specificity describe the model’s ability to correctly identify patients who will benefit from curative treatment and those who will not.
   - Sensitivity: 90% Sensitivity and Specificity describe the model’s ability to correctly identify patients who will benefit from curative treatment and those who will not. Specificity: 90% Specificity and Specificity describe the model’s ability to correctly identify patients who will benefit from curative treatment and those who will not.

2. **Predictive Performance of Biomarkers and Adverse Pathology.**
   - Predictive Performance of Biomarkers and Adverse Pathology: The assay's predictive performance is evaluated using receiver operating characteristic (ROC) curves and area under the curve (AUC) calculations. The ROC curve is used to represent the trade-off between true positive rate and false positive rate at various threshold settings. The AUC is a measure of the test's overall discriminatory ability.

3. **Clinical Validation in Prostate Cancer:**
   - Clinical Validation in Prostate Cancer: The assay's clinical validation is demonstrated in prostate cancer patients. Patients are classified into two groups: those with low-risk prostate cancer and those with high-risk prostate cancer based on the assay's predictive scores.

4. **Conclusion:**
   - Conclusion: The assay's ability to predict adverse pathology in prostate cancer is demonstrated. The assay's predictive capability is validated using ROC curves and AUC calculations. The ROC curve shows the assay's ability to discriminate between low-risk and high-risk prostate cancer patients. The AUC is a measure of the assay's overall discriminatory ability.

**References:**


**Cellanyx:**

- **Cellanyx’s Machine Learning Algorithm Has the Ability to Process Multiple Biomarkers and Accurately Predict Various Pathological Outcomes.**
- A set of biomarkers measured for each cell in a patient are input to (B) Cellanyx’s machine learning algorithm that generates biomarker scores that predict disease progression.
- **Clinical Validation in Prostate Cancer:**
- This novel quantitative and actionable biomarker panel has potential utility in risk stratification and predicting adverse pathology from biopsies that do not contain tumor.
- **Conclusion:**
- This extended proof of concept clinical study in prostate cancer shows the potential utility of the panel in prostate cancer as well as other tumors (genitourinary and other).
- **Biomarker platform is applicable to predicting adverse pathologies in bladder and kidney samples.**