A Live Cell Microfluidics Device Utilizing Biomarkers for Prostate Cancer.

Introduction: A novel tissue based biomarker panel was introduced to objectively assess disease aggressiveness and invasive potential of Prostate Cancer (CaP). The biomarker diagnostic platform incorporates both molecular and phenotypic data that may allow for an improved understanding of local growth and metastatic potential. Tissue-based diagnosis incorporates matrix biology, phenotypic biomarkers, microfluidics, and machine vision. This technology presents the opportunity to culture samples, and both determine and automate biomarker measurements from machine vision analysis. Data are presented towards clinical validation, the ability to risk stratify, and prediction of local aggressiveness and metastasis.

Methods: Conditions were optimized for reliably culturing prostate tumor samples ex vivo enabling automated imaging of the label free and label-based biomarkers.

Results: The validation study was IRB approved and performed in 20 consecutive CaP radical prostatectomy derived specimens collected between 03/2014 and 08/2015. Data was analyzed with receiver operating characteristic (ROC) generated Area-under-the-Curve (AUC) and specifically included capsule penetration, seminal vesicle invasion, as well as margin-positive disease. AUC Graphs are presented. The study further demonstrated that a normal set of biomarkers, confirmed with the Gleason score, are predictive of aggressive disease. AUCs greater than 0.9 for disease subtyping were observed.

Clinical Highlights:

- Only when biopsy samples are irrigated in a microscopic cellular analysis possible. However, the current state-of-the-art does not provide an objective or holistic analysis of tissue samples. Due to the lack of clear diagnostic tools, cancers of the prostate, kidney, and bladder are over diagnosed and over treated.
- There is an urgent need for quantifiable & actionable risk-stratification biomarkers for prostate, kidney, and bladder cancer.

Conclusion: 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 sample in a panel are input to (B) Cellanyx’s machine learning algorithm that generates a numerical score. These scores are linked to individual patient data and outcomes from cancers of a positive patient for a given pathological outcome. The decision trees are weighted to optimize alignment on pathological scores, specific to clinical morphology of the sample. This novel quantitative and actionable phenotypic biomarker panel has potential to be a robust input to risk stratification and predict adverse pathology from biopsies that do not contain tumor.

References:

- Proprietary phenotypic (biophysical and molecular) biomarker panel in live cells obtained from clinical tissue biopsies.
- A high throughput, cost effective approach to predict adverse pathology in prostate cancer.
- The goal of this blinded study was to demonstrate predictive capacity and complete sample characterization data of the device in prostate cancer. Further, an exploratory study was performed to predict biopsy grade in benign tissue.

Phenotypic, biophysical and molecular biomarkers are measured in a label-free microfluidic environment, analysis and predicted aggressive potential of prostate cancer. The models include but are not limited to: A) cell adhesion to device substrate, B) cellular morphology, C) rate of cell spreading on substrate, D) rapid dynamics of the microenvironment, E) gene expression, localization and phosphorylation state of subcellular protein complexes and individual proteins, and E) metabolic activity. Cellanyx’s novel DIC and fluorescence images were measured using a standard fluorescent microscope.

Live cells are harvested from fresh samples. A) Biopsy surgical samples are collected and processed into single cell cultures. B) Extracellular matrix (ECM) immunostain are used to produce a representative environment for cell survival. C) Microfluidic device, used in conjunction with ECM to form and culture a permissive and standardized biomarker measurement. D) Proprietary algorithms capture and analyze the quantifiable data (representative) into a diagnostic readout. The tissue based diagnostic incorporates matrix biology, phenotypic biomarkers, microfluidics, and machine vision. This technology presents the opportunity to culture samples, and both determine and automate biomarker measurements from machine vision analysis. Data are presented towards clinical validation, the ability to risk stratify, and prediction of local aggressiveness and metastasis.

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