Novel Live Tumor Cell Diagnostic Test Utilizing Biophysical and Molecular Biomarkers to Assess Local, Advanced, and Metastatic Prostate Cancer

Kevin S. Knopf1, Michael S. Manak2, Ashok C. Chander3, Kevin H. Raftery4, Michael R. Gomez2, Kevin B. Knopf2, 1

1California Pacific Medical Center, San Francisco, CA, 2Cellana, Inc., San Diego, CA, 3The University of Rochester Medical Center School of Medicine and Dentistry, Rochester, NY, 4University of Rochester Medical Center School of Medicine and Dentistry, Rochester, NY, 5Teallus University School of Medicine, Boston, MA.

Abstract: Over-treatment of prostate cancer affects 144,000 patients annually in the U.S. due to the lack of clinical tools for risk stratification. Combining functional molecular and biophysical biomarkers with clinically actionable diagnostic platforms may provide an assessment tool for the local invasiveness and metastatic potential of cancers derived from biopsy. Such a tool may improve patient outcomes, e.g. in low and intermediate grade prostate cancers (Gleason 3+3, 3+4, 4+3). This study describes the clinical data for a set of biomarkers measured with a proprietary live cell assay coupled with innovative machine vision and computational platforms for patient tumor samples using a unique microfluidic platform.

Methods: This proof of principle study was performed on 60 prostate cancer samples collected post radical prostatectomy. We report the details of this assay for culturing live tumor cells ex vivo, automated cell morphology, label-free and label-based, molecular and biophysical biomarkers. The test is designed to sustain adhesion and survival of primary prostate tumor cell populations associated with biomarkers/biopsy/surgical samples for up to three days prior to analysis of phenotypic characteristics.

Results: We show that this test distinguishes live normal and tumor cells via a set of phenotypic, molecular, and biophysical biomarkers. The primary biomarkers are predictive of disease characteristics when combined with machine vision algorithms and are used to derive secondary metrics termed “Metastatic Potential (MP)” and Oncoprogenetic Potential (OP). In comparing clinical measures with results of this assay, concordance analysis supports that OP and MP are statistically significant in distinguishing between Gleason 6 and Gleason 7 with 85% sensitivity and 66% specificity.

Conclusions: This novel phenotypic diagnostic test characterizes scoring metrics of MP and OP that correlate with 1) aggressive Gleason 6 vs. indolent Gleason 6, 2) seminal vesicle invasion and occurrence of margins after radical prostatectomy, 3) vascular invasion and 4) lymph node metastasis. These results will further help stratify patients to improve clinical decision-making among intermediate-risk prostate cancer populations, and potentially avoid unnecessary adjuvant radiation, ultimately leading to improved patient outcomes.

**Introduction:***

A novel diagnostic platform measures phenotypic, biophysical, and molecular biomarkers on five cells harvested from patient tumor samples. A) Flow diagram outlining the platform. B) Biomarker processing, biomarker measurement, analysis, and algorithmic interpretation of predictive measurement. C) Phenotypic, biophysical, and molecular biomarkers are measured on live and subsequently fluorescent samples. D) Diagram of Cellanyx’s biomarkers measured with single cell resolution.

**Clinical Study Design:***

Clinical collaboration is performed in a single patient cohort of Gleason 3+3 and Gleason 3+4 prostate cancers. Sample collection is performed via needle biopsy and surgical resection. All samples undergo immediately ex vivo fixed and archived analysis.

**Novel diagnostic platform measures phenotypic, biophysical, and molecular biomarkers on live cells harvested from patient tumor samples.** A) Flow diagram outlining the platform. B) Biomarker processing, biomarker measurement, analysis, and algorithmic interpretation of predictive measurement. C) Phenotypic, biophysical, and molecular biomarkers are measured on live and subsequently fluorescent samples. D) Diagram of Cellanyx’s biomarkers measured with single cell resolution.

**Combination:***

This initial proof of concept study in prostate cancer strongly supports future risk stratification validation studies in prostate cancer as well as other cancers (gastrointestinal, lung, and breast).

**References:**