Live Cell Phenotyping Test Predicts Prostate Cancer Pathology with High Precision

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NEW YORK (360Dx) – A platform using automated machine learning and machine vision to phenotype single live cells can effectively risk-stratify prostate cancer patients when compared to post-surgical adverse pathology evaluations, according to a recent proof-of-concept study in the journal *Urology*.

Notably, the assay — called STRAT-AP, from Boston-based startup Cellanyx — has the potential to detect cells that have phenotypic biomarkers indicating metastatic potential from tissue that are classified as low risk based on gold standard methods.

The trial involved culturing prostate cells from 237 patients who had undergone radical prostatectomy for prostate cancer. Samples were obtained from five university hospitals, three large urology group practices, and two biobanks. At the time of each surgery, a bit of fresh prostate sample was shipped to a central lab where it was analyzed with the Cellanyx technology in a double-blinded fashion, and then compared to the post-surgical adverse pathology features of the Gleason score and Prostate Cancer Grading Group score.

In the study, the test predicted adverse pathologies with an area under the curve greater than 0.80 and also predicted Gleason pattern, stage, and adverse pathology with the same high precision.

The STRAT-AP technology measures more than 600 dynamic and fixed phenotypic biomarkers in cancer cells. In cultures of single prostate cancer cells visualized with standard differential interference contrast microscopy, STRAT-AP uses machine vision to automatically measure features like cell shape, how fast and how far a cell moves, how much it adheres to the culture dish, and dynamic changes in the nucleus' area over time.

Single cells are observed for a period, then subsequently fixed, immunofluorescently stained, and automatically imaged again in order to obtain information on phenotypic markers like microtubule organization, intensity of different proteins, and presence of focal adhesions.

Then, the data is analyzed using a machine learning paradigm. In the study, 70 percent of the live cells collected were used to train the machine learning algorithms. The remainder of the cells were then studied using the algorithms.

Automated phenotypic testing can potentially take less time than standard genomic or histopathology tests, according to a recent perspective article in *Precision Oncology* written by clinicians evaluating the technology who are also members of the Cellanyx scientific advisory board. Faster turnaround times may have psychological benefits for patients, and could potentially have health economics benefits, as well.

The method may also provide information, not obtainable with genetic or static testing, that could show whether a patient with slow-growing cancer was at risk of more aggressive disease, and guide future

treatment. This is important because risk stratifying patients with indolent disease remains a big challenge, according to David Albala, the lead clinical investigator on the *Urology* study and an advisor to Cellanyx.

"I have been taking care of prostate cancer patients for over 28 years, and currently there is not an accurate way to risk-stratify patients with low and intermediate grade disease," Albala said in an email with 360Dx. "The goal of this test is to identify the 'wolf in sheep's clothing' so to speak, to catch those patients at risk of aggressive disease and provide assurance to those who are not" at risk, he said.

Cellanyx's CEO Ashok Chander said in an interview that the *Urology* results support an earlier proof-of-concept *Nature Biomedical Engineering* study that had a smaller sample size, but that the artificial intelligence is also learning and refining the groupings compared to post-surgical adverse pathology results, as well as optimizing the biomarkers that are most important.

Single-cell phenotyping may address problems of tumor heterogeneity better than other methods, Chander suggested. "Even if there is a small cluster of cells that maybe the pathologist didn't stain properly, or didn't see, or it didn't really register in the fixed cell setting because the biomarkers aren't even relevant, because we are using different biomarkers, we can say, actually, this patient is going to have metastasis," he said.

The *Urology* results were presented at The American Urological Association national meeting in the spring, where Cellanyx's work "was selected as the best biomarker study in prostate cancer," Albala noted, adding he sees growing interest among colleagues regarding phenotypic testing and how it may be applied to prostate cancer patients.

Now, Cellanyx will take the next step with a prospective, randomized study demonstrating tumor cell behavior at prostate biopsy. Chander said he thinks the results are likely to support what was seen with prostatectomy patients.

"Theoretically, it should result in similar success, in as much as we are still taking samples from the prostate, and given the nature of MRI-guided biopsies and even trans-rectal ultrasound-guided biopsies … the ability to understand where the tumor is in the case of these MRIs is greater than 85 percent," he explained. Chander estimated that the trial and subsequent data analysis should take about 18 months with a publication following soon after.

"There is a possibility for having the first live cell diagnostic for the risk stratification of prostate cancer — which one is indolent, which one is aggressive — in our reach within two years," Chander said. Meantime, the firm will continue talking with clinicians, investors, and potential strategic partners interested in precision diagnostics, he said.

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