Cell-CT™ Differential Detection of Dysplastic Bronchial Epithelial Cells from Patient Explants

Abstract #10219: Sussman, Meyer, Katdare, Presley, Bell, Reyna, Lakers, Hamilton, Zulueta, Miller, Ghosh, and Nelson

Background

Chemoprevention could have a great impact on lung cancer prevention. While Iloprost treatment has shown a significant reduction of dysplasia in former smokers[1], the identification of patients who would benefit from the drug is seriously hampered due to the need to use invasive diagnostic procedures in patients who are typically asymptomatic.

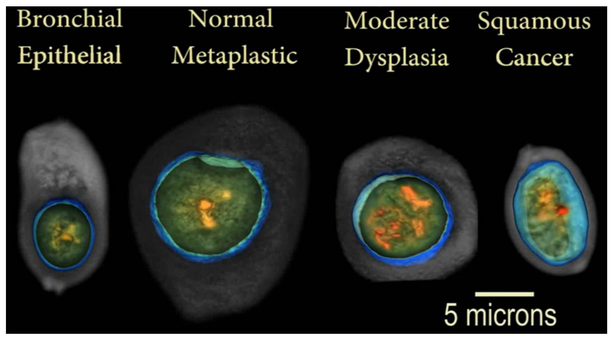
The VisionGate Cell-CT™ Platform automatically analyzes enriched sputum cells in true 3D with isometric, sub-micron resolution. Morphometric classifiers are trained to distinguish different cell types, resulting in a small gallery of abnormal cells forwarded for cytopathologist review. This Platform results in 92% sensitivity and 95% specificity for biopsy confirmed cancer that is independent of tumor histology and stage.[2]

This abstract reports the development of cell classifiers that, in conjunction with our Cell-CT™ Platform, distinguish dysplastic from normal and malignant cells in sputum samples.

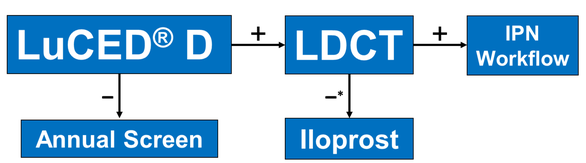
Methods

Cell training algorithms were developed using the AdaBoost classification technique along with feature value thresholding. For each cell, 704 structural biomarkers are measured to drive algorithmic classifiers that quantitatively assess the cell type. For the patient dysplastic explant sample classifier training, 246 progenitor cells were used against 473 malignant cells. For dysplastic cells in patient sputa, 830 pre-malignant cells were trained to be classified from 473 malignant cells. Pre-malignant cells included atypical squamous and atypical columnar cells. Malignant cells included adenocarcinoma, small cell, and squamous cancer cells. All cells used for training were classified by trained cytologists.

Results



Reconstructed images from Cell-CT™ pseudo-projections, with features highlighted based on gray-scale values.



Proposed screen for dysplasia in high-risk patients using the Cell-CT™ Platform and LuCED® D algorithm. Patients exhibiting dysplastic cells in their sputum will under go low-dose CT. Those patients with indeterminate pulmonary nodules (IPN) will undergo the standard workflow. Those that are negative will be treated with iloprost. *Patients will undergo bronchoscopy to rule out central occult cancer.

References

1. Keith, RL, et al., Cancer Prev Res. 2011, 4(6):793-802.
2. Wilbur, DC, et al., Cancer Cytopathol. 2015, 123(9):548-56.

Results

Three bronchoscopy biopsies from patients with moderate to severe dysplasia were enzymatically disaggregated and grown in culture on fibroblast feeder layers. 15,000 normal cells from sputum, 500 malignant cells from each of the five lung cancer cell lines and 264 cells from patient dysplastic explants were analyzed using the Cell-CT™ Platform.

Cell Classifiers	aROC	Sensitivity (%)	Specificity (%)
Lung cancer cell lines	0.999	93	99.99
Cells from patient dysplastic explants	0.995	86	99.99

Results obtained from classifier for dysplastic cells at a single cell level:

	Sensitivity (%)	Specificity (%)
Dyspalstic cells from patient sputa	30	98.1

Sensitivity of the LuCED® D test for dysplastic cells at a case level (For a given patient's sputum, sensitivity increases with the number of dysplastic cells in the sample):

Dysplastic Cell Number:	1	2	3	4	5	6
Case Level Sensitivity (%):	23	40	54	64	72	78

Conclusion

This study represents a first important step toward developing a non-invasive diagnostic test for detecting patients with moderate to severe bronchial dysplasia who may then be treated with chemopreventive drugs such as Iloprost.

VISIONGATE®
www.visiongate3d.com