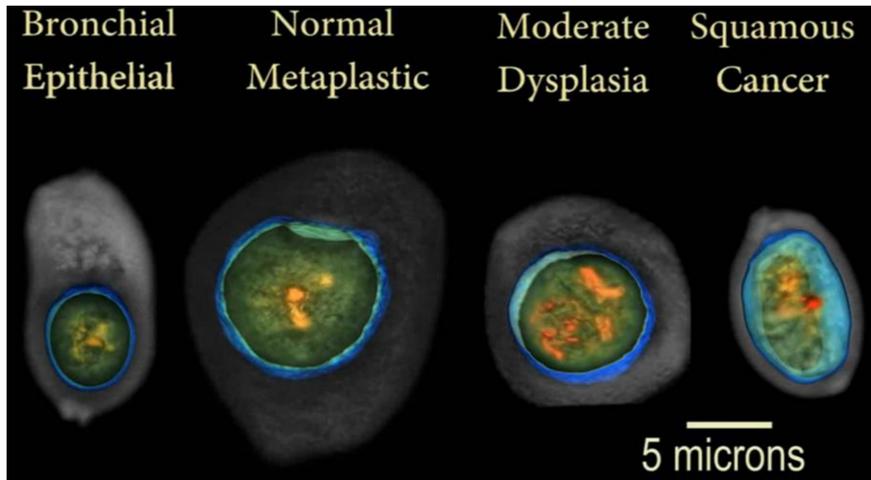


Morphometric Genotyping Identifies Lung Cancer Cells Harboring Target Mutations; Cell-CT[®] Platform Detects Gene Abnormalities

Abstract #9491: Nelson, Meyer, Sussman, Katdare, Presley, Lakers, Hamilton, Wilbur, Mastrangelo, Doherty

Background

Sputum Prep: Dissolves mucous, stains chromatin, enriches for bronchial epithelial cells
Cell-CT Processing: Automatically analyzes cells in true 3D with isometric, sub-micron resolution



Motivation: The advent of genotype-directed therapy in personalized medicine requires the identification of driver-mutations that are often under-diagnosed due to limitations in tissue biopsy and high false negative rates associated with genomic tests.

Studies have demonstrated that the mutation status of cancer cells correlates with changes in cellular morphology. The automated Cell-CT[®] platform produces isometric, high-resolution 3D images of cells in liquid biopsies, such as sputum, where published studies have demonstrated 92% sensitivity to biopsy confirmed lung cancer with 95% specificity. This study reports the development of cell classifiers for lung cancer cell lines that harbor known mutations, helping pave the way to driver-mutation targeted therapy.

Methods

Study Materials:

Non-invasive sputum specimens from patients without lung cancer (“normal cells”) and the following cell lines were analyzed using the Cell-CT[®] platform:

Small Cell Lung Cancer cell line

NCI-H69

Adenocarcinoma cell lines

A549 (EGFR wild-type, CDKN2A-c.1_471del471, KRAS- p.G12S)

NCI-H1650 (EGFR- p.E746_A750del, CDKN2A- c.1_471del471, TP53- c.673-2A>G)

NCI-H1975 (EGFR-T790M, CDKN2A- p.E69*, PIK3CA- p.G118D, TP53- p.R273H)

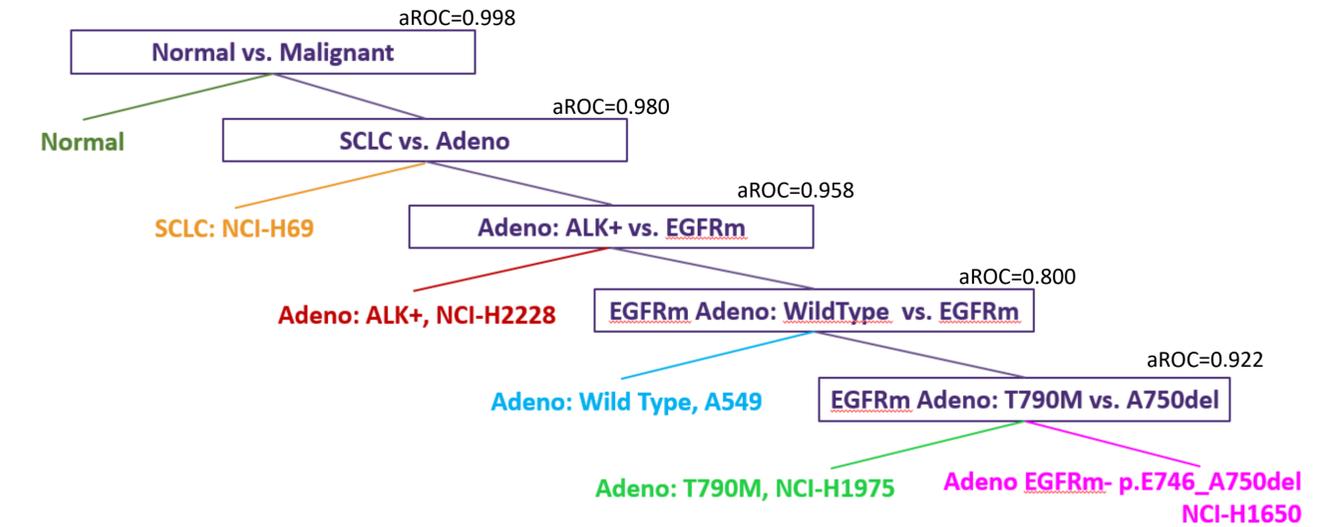
NCI-H2228 (EML4-ALK+, CDKN2A- c.1_471del471, RB1- p.E204fs*10, TP53- p.Q331* high PD-L1)

	#Cells	#Batches/ Patients
Normal vs. All Malignant	15000	125
(NCI-H69)	2000	6
ALK+ (NCI-H2228)	750	7
EGFR wild-type (A549)	750	7
EGFR – pE746_A750del (NCI-H1650)	750	5
EGFR -T790M (NCI-H1975)	750	5

Classifier Development:

- 704 morphometric biosignatures for each 3D cell image
- Ground truth defined by the cell line
- Ada-boost/Random Forest methods for classifier creation

Results and Conclusions



Cell Classifiers	Sensitivity (%)	Error Rate (%)
Normal vs. All Malignant	91.8	0.3
Small cell lung cancer (NCI-H69)	73.1	3.6
Adenocarcinoma, ALK+ (NCI-H2228)	69.1	5.0
Adenocarcinoma, EGFR wild-type (A549)	60.2	6.7
Adenocarcinoma, EGFR – pE746_A750del (NCI-H1650)	41.3	6.9
Adenocarcinoma, EGFR -T790M (NCI-H1975)	71.7	4.5

3D Cell morphology shows promise as a means of identifying mutations that define the growth of malignant tissue