5368 AI-enabled Prediction of lung cancer specific hot spot gene alterations from histology images

Gowhar Shafi[1], Shiva Shivamurthy[2], Anand Ulle[2], Chongtham Cha Chinglemba[1], Sumit Haldar[2], Fauzul Moubeen[2], Mohan Uttarwar[1]

OneCell Diagnostics
OncoPredikt
Predicting Genomic Signatures

BACKGROUND

Lung cancer, one of the most common cancers worldwide, has traditionally relied on molecular testing of major biomarkers. However, this type of testing can be expensive and time-consuming, resulting in infrequent testing and suboptimal treatment decisions. To address this issue, the National Comprehensive Cancer Network (NCCN) provides guidelines for lung cancer treatment, which include recommendations for molecular testing.

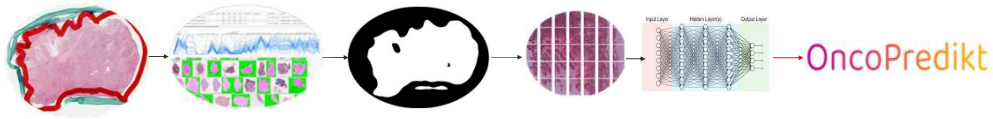
PROBLEM STATEMENT

- Effective cancer management requires accurate molecular profiling to guide treatment decisions.
- Limited access to molecular testing, high costs, and long turnaround times can hinder frequent testing, despite NCCN guidelines.
- We developed an AI-enabled platform to predict gene hot spot genomic alterations from a single H&E slide, aligning with NCCN guidelines.
- The platform's approach is rapid, precise, and cost-effective.
- This approach has the potential to improve cancer management through targeted therapy decisions.

METHODS

- The H&E-stained histological images of the tumor having matching pathogenic mutations were downloaded from TCGA database for the training and testing purpose.
- The input image was segmented into 65 x 10^3 tiles, each of 64 μm^2 in size for an individual pathological class.
- 80% of the data set was used for training the engine, while validation and blinded study were respectively performed on the remaining 10% of the data.
- Resnet AI algorithm was trained to predict lung specific hot spot genomic alterations.
- Program extracted histopathological features, followed by pattern mapping to predict genomics status based on the results of NGS testing from 480 samples.

Schematic Representation of training the OncoPredikt's back-end algorithm

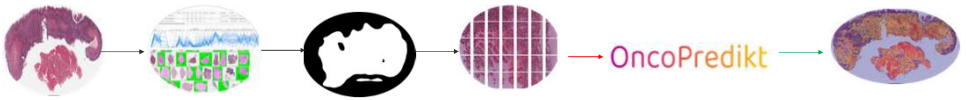


H&E WSI | QC | Tissue Region Detected | Small Tiles (265x256)c | ResNet 50 | AI Model

TABLE 1

Gene	Sample (n = 480)		Evaluation parameters for tested samples					
	Training	Testing	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	F1-score (%)	Accuracy (%)
KRAS	248	62	100	94	94	100	97	97
ALK	16	4	100	100	100	100	100	100
EGFR	72	18	88	100	100	90	94	94
MET	16	4	50	100	100	66	66	75
ROS	16	4	100	100	100	100	100	100
STK11	88	22	82	73	75	80	78	77
RET	24	6	50	100	100	60	50	67

Schematic Representation of OncoPredikt's inference Engine and reporting process:



H&E WSI Test Image | QC | Tissue Region Detected | Small Tiles (265x256)c | AI Model | Heatmap with Final Prediction

[1]OneCell Dx Inc, Cupertino, CA, USA and India;
[2]Indx.AI Inc, Cupertino, CA, USA and India.
Correspondence: Dr. Gowhar Shafi
gowhar.shafi@indxtechnology.com, gowhar@onecelldx.com

RESULTS

- Using single blinded clinical samples, our AI model analyzed whole slides and predicted for the presence of major hot spot genomic alterations, with a high sensitivity, specificity, and accuracy.
- Table 1 summarizes the parameter matrix for the following clinically significant variants: KRAS, ALK, EGFR, MET, ROS, STK11 and RET.
- A high sensitivity and specificity was observed for variants encoding mutated cell surface proteins compared to variants encoding intracellular mutant targets when compared on similar training and testing parameters (e,g, ALK to MET and ROS to MET).
- The prediction efficiency of AI engine will improve with training with a large, better quality data set.

AI process development

CONCLUSIONS

- AI-enabled prediction of hot spot genomic alterations can yield results comparable to next generation sequencing technology with much lower turnaround time, cost and resources.
- Based on pattern associated with H & E slides, the AI engine predicted presence of actionable gene alterations with a high positive and negative prediction values.
- The AI based digital pathology methods hold great potential for prediction of actionable mutations and offer better treatment options for lung cancer patients.