1084P - Predicting KRAS G12C subtype from non-small cell lung cancer H&E slides using deep learning

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Background

Biomarker testing in NSCLC is essential but can be held back by the cost, lack of access and turnaround time of molecular techniques. It also requires a sufficient amount of good quality DNA or RNA. Beyond EGFR, the emergence of new targeted therapies justifies the search for other biomarkers that are currently not tested for systematically in routine.

With a 13% prevalence in lung adenocarcinomas, and an effective targeted therapy available, KRAS G12C is an essential biomarker to be tested following ESMO recommendations. 1

Objective

Demonstrate that AI-based techniques applied to routine hematoxylin and eosin (H&E) stained whole slide images (WSI) can significantly predict KRAS G12C mutation status.

Method

330 biopsies
73 resections

403 metastatic NSCLC adenocarcinoma, naive of treatment, patients from a 1,076 local cohort gathered by Institut Bergonie and partner centers were included (patients with micro-biopsies smaller than 12mm² were excluded from experimentation).

Routine H&E slides without pathologist annotation were used to train an AI model to predict the KRAS G12C mutation status obtained by NGS.

Systematic analysis was performed by a senior pathologist to analyse the regions of interest identified by the model during its decision-making process.

Results: Mutation status prediction performance

843 patients

403 patients

Of the 403 patients analysed, 34% had a KRAS mutation.

Our AI-algorithm was able to predict the KRAS mutation within a NSCLC population with a significant performance of 66.7% ROC AUC score (average cross-validation score).

Model enriched population and sampled subsets (predicted a high probability) with a substantially higher prevalence of mutants.

Results: KRAS G12C mutation results

Of the 403 patients analysed, 16% patients had a KRAS G12C mutation.

Our AI-algorithm was able to predict KRAS G12C subtype mutation within a NSCLC population with a significant performance of 65.1% ROC AUC.

Considering restricted KRAS mutated population only (n=134) a performance of 63.7% ROC AUC was obtained for G12C subtype prediction.

KRAS G12C prediction external evaluation – TCGA LUAD

While not representative of clinical routine, our model has been tested on the TCGA LUAD cohort of 458 NSCLC patients – mainly based of large resections.

A significative ROC AUC of 57.8% confirmed that our model predicting KRAS was able to transfer on external cohorts.

Conclusion

Prevalence of KRAS mutation and G12C subtype of our series are in accordance with the literature.

In accordance with other studies, 2, 3, annotation-free deep learning-based approaches can significantly predict KRAS and G12C mutation subtypes from H&E routine biopsy data in metastatic lung adenocarcinoma.

While requiring further investigation and proof of robustness (such as robustness to very small tissue samples), these approaches could offer a fast and cheap mass patient screening solution, complementary to DNA testing, and improve access to targeted therapies.

Perspectives

In future, these innovative approaches could complete existing testing techniques and pave the way for a more systematic, early and potentially cost-effective mass screening approach of KRAS G12C mutations in clinical routine.


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