182P: Multi-Modal Artificial Intelligence Outperforms Image-Based Approaches for Mutation Prediction from H&E Tissue Images in Colorectal Cancer

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Summary

We predict KRAS and BRAF mutational status in CRC end-to-end via deep learning on H&E slides. Using a multi-modal setup with available clinical data in addition to the images boosts predictive accuracy and **surpasses state-of-the-art image-based predictive models in diagnostic accuracy[1],[2],[3]**.

Background

Mutations in the MAPK/ERK pathway are frequently found across cancer entities, including colorectal cancer (CRC) where the accurate diagnosis of KRAS and BRAF mutational status is pivotal for treatment decisions. While the mutation analysis is usually done via genomic sequencing, the prediction of mutations from histological images using artificial intelligence (AI) could present a faster alternative with broad potential for diagnostic routine, research applications, and trial recruitment. However, to date, such algorithms typically do not meet the required accuracy criteria for real-world application in different institutions.

Data

Training data: 455 CRC cases from the TCGA database and from the University of Pennsylvania

Evaluation on TCGA hold-out cohort of n = 114 samples and an external cohort of n = 104 CPTAC samples

References

[1] Generalizable biomarker prediction from cancer pathology slides with self-supervised deep learning: A retrospective multi-centric study; Niehues et al; Cell Rep Med, 2023

[2] Transformer-based biomarker prediction from colorectal cancer histology: A large-scale multicentric study; Wagner et al; Cancer Cell; 2023

[3] Self-supervised attention-based deep learning for pan-cancer mutation prediction from histopathology; Saldanha et al; NPJ Prec Oncol; 2023

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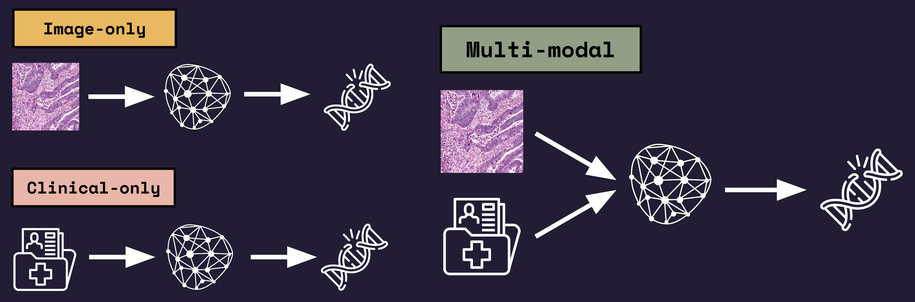
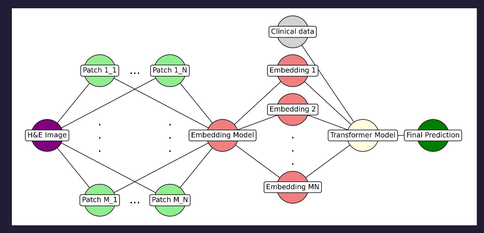
Methods

Since the frequency of both BRAF^{mut} and KRAS^{mut} is associated with easily available clinical patient parameters, we developed a multi-modal predictive AI model on n = 455 CRC cases from the TCGA database and UPenn. Besides H&E-stained tissue images and the corresponding BRAF^{mut} / KRAS^{mut} information, AI models were trained with readily-available patient data (e.g. age and sex), or a combination of both. We evaluated the models on an independent hold-out TCGA cohort of n = 114 samples and an additional external cohort of n = 104 CRC samples from the CPTAC database.

Models





Detailed multi-modal model architecture:
The H&E image is split into patches which are fed to an embedding model. A transformer model processes both the embeddings as well as the clinical data to predict the mutational status of BRAF/KRAS.

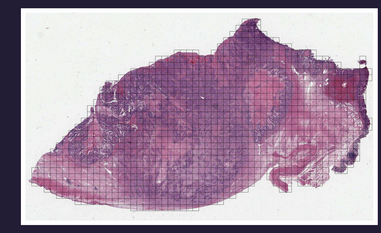
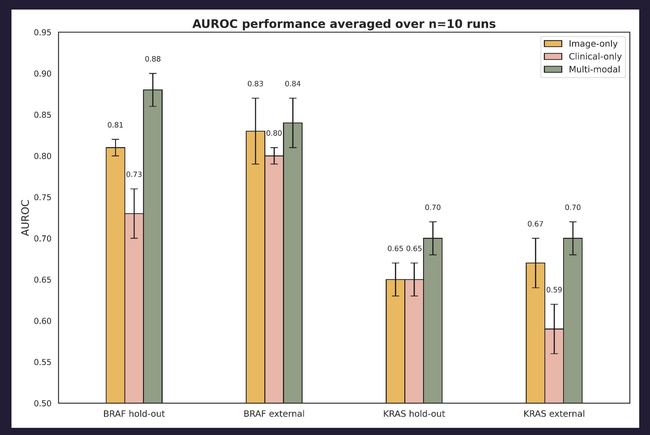
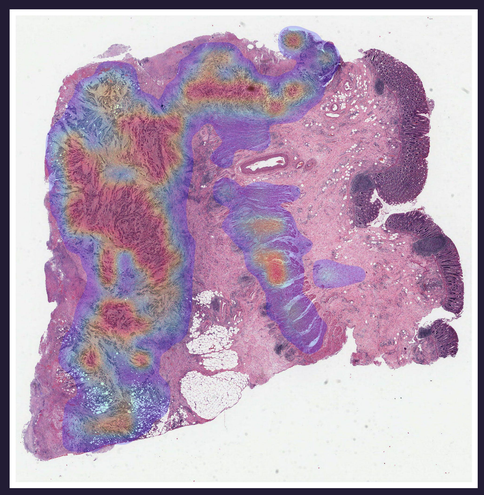


Illustration of the tiling of patches after detecting the tissue with a tissue detection model.

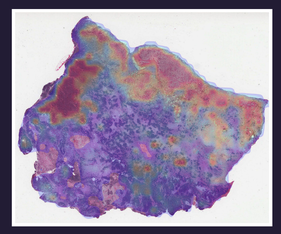
Results

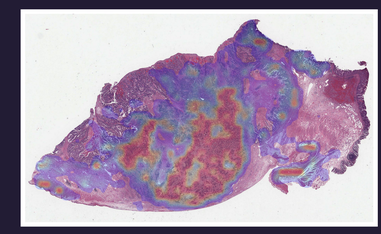


AUROC performance of the models with either only images, only clinical, or multi-modal input data used for training.



Attention maps demonstrate that the model focuses on tumor regions to make predictions.





With our multi-modal approach the AI model achieved an AUROC of 0.88 ± 0.02 and 0.70 ± 0.02 for BRAF / KRAS respectively on the TCGA hold-out test set. Accuracy levels were similar on the second external testing dataset indicating the model's ability to generalize across different cohorts. Notably, accuracy values obtained with the multi-modal training setup were higher than those from models that were trained with image data only. This improves on our previous model which reached AUROC scores of 0.84 and 0.67 for BRAF / KRAS respectively on the TCGA hold-out test set. **Our new model beats existing approaches with reported BRAF scores in the range 0.73 - 0.85[1],[2],[3].**

Conclusion

By analyzing mutations in two frequently mutated genes in CRC in two separate cohorts, we demonstrate that the inclusion of patient parameters in AI training can provide added value for predicting mutations from H&E images. Notably, with **AUROC scores of up to 0.88**, our multi-modal approach surpassed state-of-the-art image-based predictive models in diagnostic accuracy[1],[2],[3]. Our results also support previous findings that some mutations can be more accurately predicted from tissue than others. Altogether, these results show the potential of multi-modal deep learning to bring predictive AI towards real-world application in pathology.