

Interpreting Machine Learning Algorithms To Understand Histological:Genomic Relationships in Kidney Cancer: TRACERx Renal

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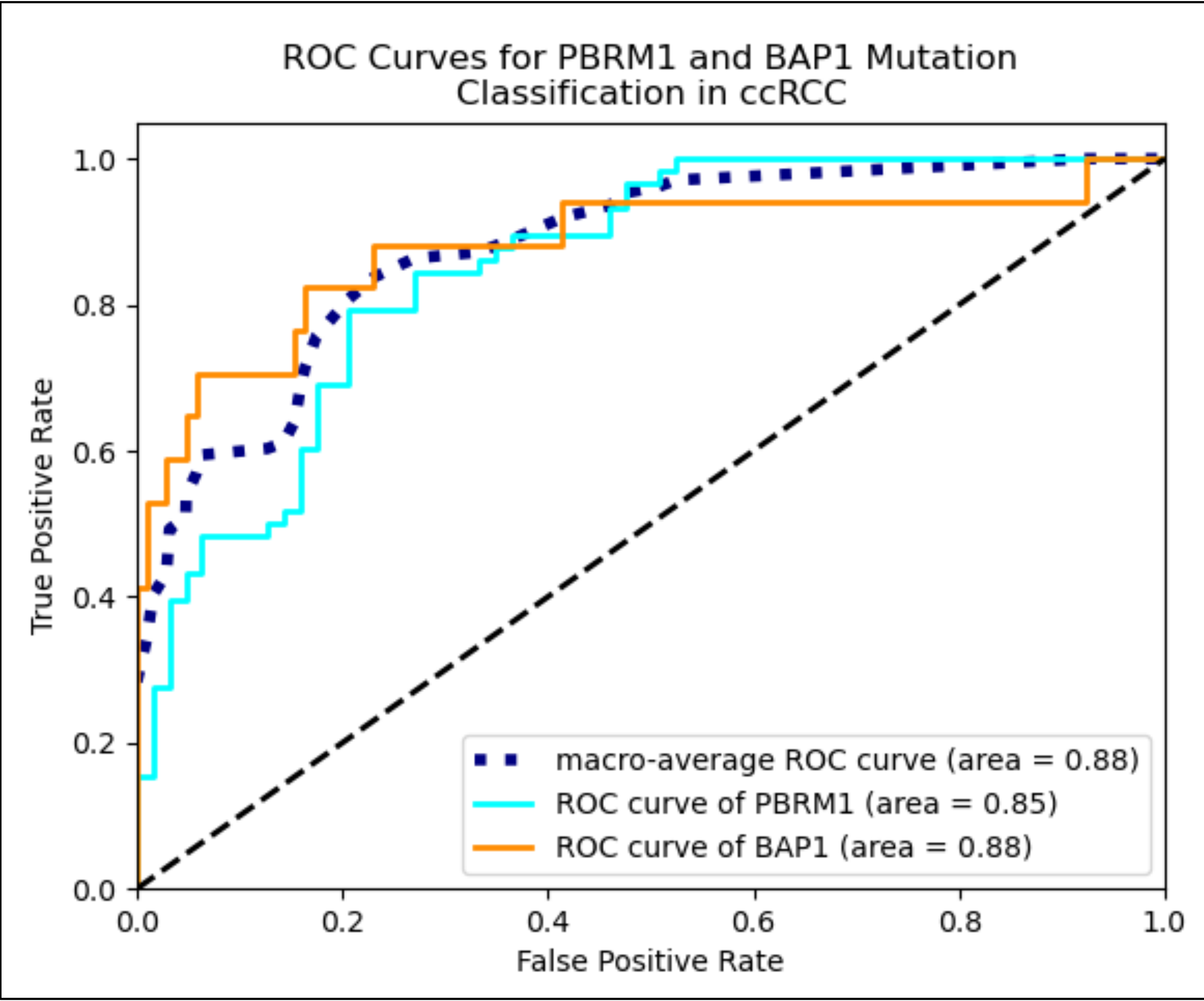
Background

- Histological analysis is the cornerstone of diagnosis for clear cell renal cell carcinoma (ccRCC)
- Genomic profiling provides prognostic information that could inform clinical management
- Intratumoural heterogeneity (ITH) necessitates multi-regional sampling, which is cost-prohibitive for genomic profiling but routine for histology in the clinical setting.
- Predicting genetic alterations from histology presents a cost-effective and implementable solution.
- Machine learning approaches can predict molecular alterations from histology in other cancer types but accurate prediction of important genetic events remains unachieved in kidney cancer.

Aim

- To develop a machine learning model to predict genomic alterations from histology in ccRCC. This will improve patient risk stratification in the stage III setting and enable personalised patient management.

Results



We predicted the mutational status of two ccRCC driver genes, *PBRM1* and *BAP1* from digital histological images.

- High region level hold-out prediction accuracy for both genes
- Accuracy:
 - *PBRM1*: 0.926
 - *BAP1*: 0.967
- F1-score:
 - *PBRM1*: 0.920,
 - *BAP1*: 0.867).

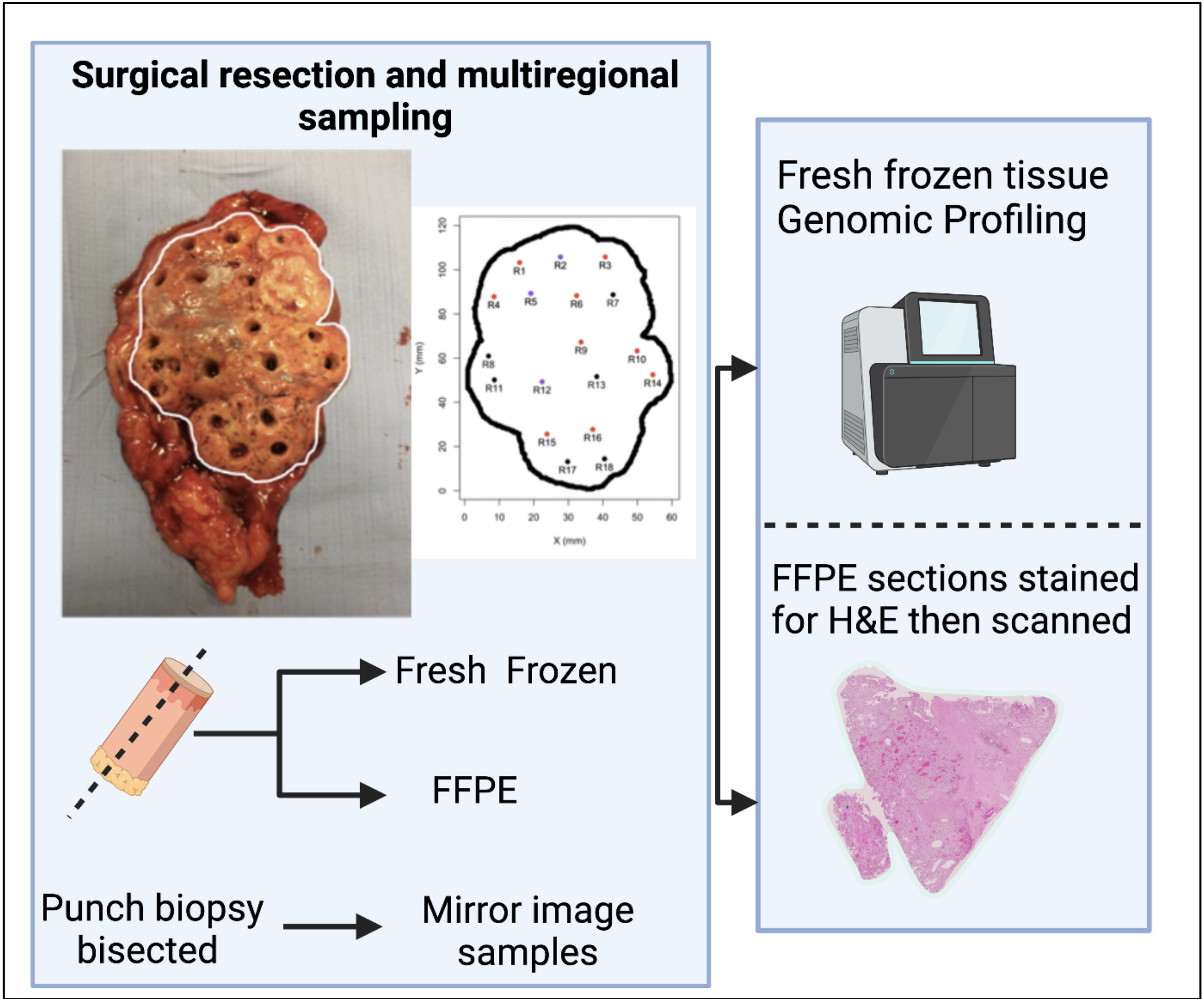
Conclusion

- Proof of principle that genomic alterations can be predicted with a high degree of accuracy from histology alone in ccRCC

Acknowledgments

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- Crick Support: Kenneth Ho, Donald Bell, Kurt Anderson, Emma Nye, Richard Stone

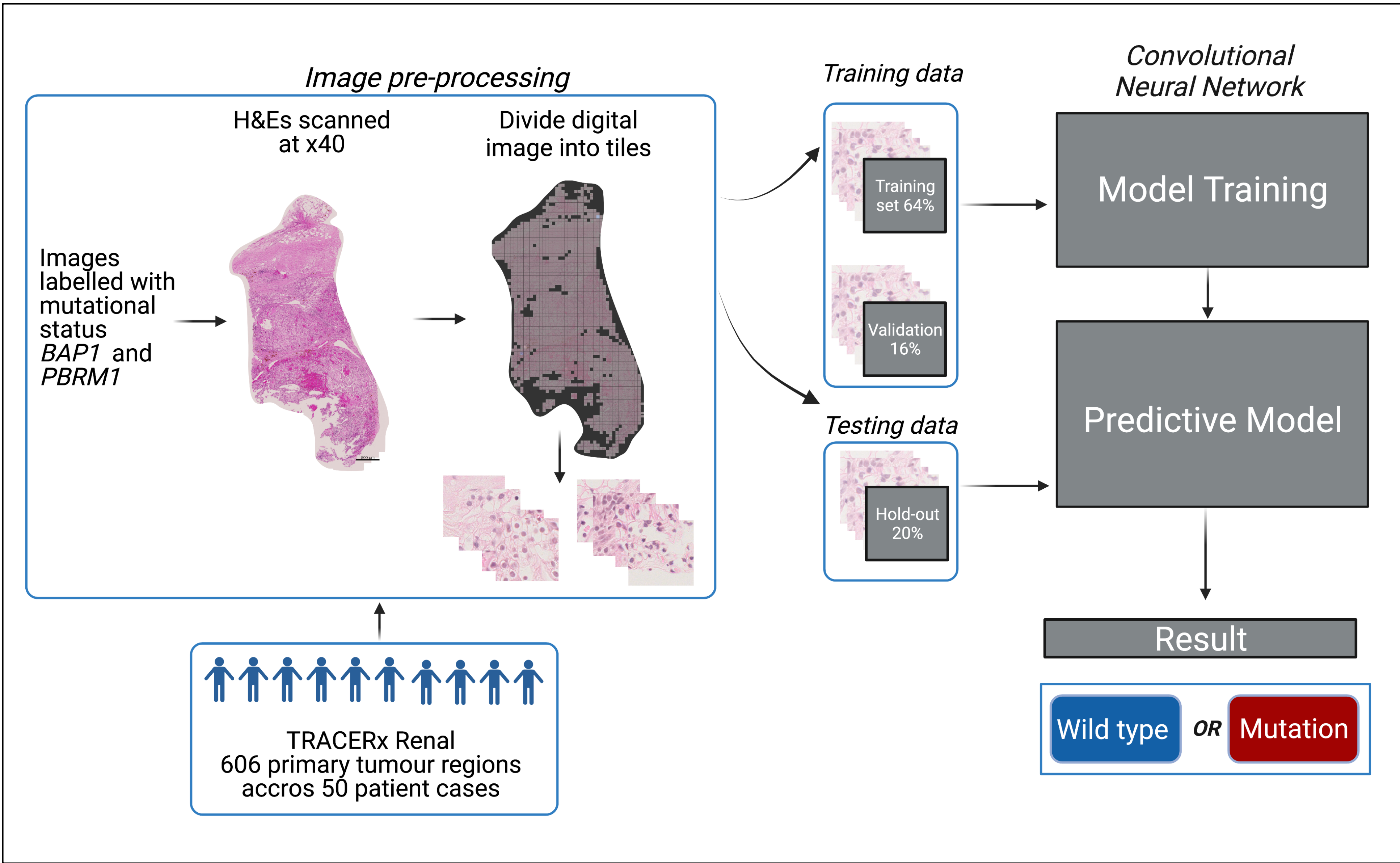
Discovery Cohort: TRACERx Renal*



*TRACERx Renal = TRACKing Renal Cell Carcinoma Evolution Through Therapy (Rx) NCT03226886

Methods

- We trained a convolutional neural network to classify histology of images by mutational status of *PBRM1* and *BAP1* on 606 tumour regions across 50 patient cases (64% training, 16% validation, 20% holdout).



Future work

- To validate results on an external cohort
- To explain the decision-making strategy of the algorithm for biological insights
- To train the CNN to predict other important molecular alterations