Evaluation of a sensitive blood test for the detection of colorectal advanced adenomas in a prospective cohort using a multiomics approach

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INTRODUCTION

- Blood tests for colorectal cancer (CRC) with high sensitivity and specificity can improve adenoma detection, lead to earlier detection, and ultimately reduce mortality from CRC.
- As previously reported, our multiomics blood test detects early-stage (I/II) CRC at a sensitivity of 94% and specificity of 91% (Figure 1).
- The detection and subsequent removal of adenomas, especially advanced adenomas (AA), decreases CRC risk, prospectively collected study and achieved CRC-specific mortality reduction (%).
- Our novel multiomics blood test detected colorectal AAs from a predominantly average-risk, prospectively collected study and achieved sensitivity of 41% at a specificity of 90%.

OBSERVATIONS

- To date, blood tests that rely on tumor-derived cell-free DNA (cfDNA) methylation signatures alone have shown limited sensitivity for AAs.
- As previously reported, our multiomics blood test detects early-stage (I/II) CRC at a specificity of 94% (Figure 1).
- To compare the multiomics blood test to other single assay approaches (e.g., cfDNA methylation or CEA) alone have shown limited sensitivity for AAs.
- A multiomics approach that complements tumor-derived signals with non-tumor-derived signals predominate in earlier stages.
- While tumor-derived signals are abundant in later-stage disease, signals from non-tumor sources (e.g., immune) predominate in earlier stages.
- To train and evaluate a model, 10-fold cross-validation was performed. Each sample was tested once in a hold-out test set, and averaged by a model that had never seen that sample in training.

RESULTS

- AA sensitivity improved with increasing lesion size and was consistent across location and histology (except for serrated lesions).
- By combining signatures from both tumor- and non-tumor (e.g., immune) derived sources, our multiomics test detected approximately twice as many AAs as methylation-only or single-protein approaches.
- Sensitive AA detection at levels similar to or better than currently available stool tests is achievable in blood, which is necessary for effective early detection and prevention of CRC.

CONCLUSIONS

- Our novel multiomics blood test detected colorectal AAs from a predominantly average-risk, prospectively collected study and achieved sensitivity of 41% at a specificity of 90%.
- This AA performance is comparable to that of existing stool-based tests.
- AA sensitivity improved with increasing lesion size and was consistent across location and histology (except for serrated lesions).
- By combining signatures from both tumor- and non-tumor (e.g., immune) derived sources, our multiomics test detected approximately twice as many AAs as methylation-only or single-protein approaches.
- Sensitive AA detection at levels similar to or better than currently available stool tests is achievable in blood, which is necessary for effective early detection and prevention of CRC.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge:
- All participants enrolled in d-EMERGE®
- Members of the Fremen Clinical Development and Clinical Laboratory teams for securing and processing samples
- Richard Bourgeron, Adam Drake, Barbara Engelhardt, Sine Faeran, Julie Granke, John Higgins, Greg Hogan, Brian O’Driscoll, Nathan Won, Hayley Warsinske, and David Webdeg for scientific input and editorial support

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Presented at the 2021 Gastrointestinal Cancers Symposium