Prevention of Colorectal Cancer Through Multiomics Blood Testing: The PREEMPT CRC Study

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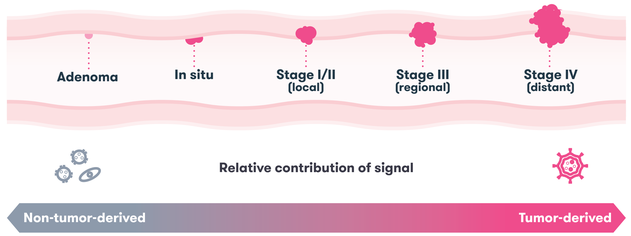
BACKGROUND

- Recent guidelines recommend initiating colorectal cancer (CRC) screening at age 45[1,2], increasing the number of screen-eligible individuals by >19M[3]
- Only 67% of average-risk individuals over the age of 50 years are up-to-date on CRC screening[4] despite the availability of multiple non-invasive screening options
- This will likely become even more challenging with the addition of 45-49 year-olds[5] since younger individuals have even lower screening rates[5] and younger patients now comprise a large percentage of the new screen-eligible population
- Further, participation by minorities in clinical trials remains challenging, and this is unfortunate since such groups are often at increased risk for CRC. For example, CRC prevalence is ~20% higher in Black individuals compared to White individuals.[4]
- Blood tests can help overcome at least some of these barriers through ease of sample collection and integration into routine clinical care
- Here, we describe our registrational study for the clinical validation of a blood test for the early detection of CRC using a multiomics approach, which is a combination of DNA and protein assays. We also highlight adaptations to our recruitment processes to increase representation of historically underserved populations and broaden access to our clinical trial.

OBJECTIVES

- To describe our multiomic approach that uses both DNA and protein assays to evaluate tumor- and non-tumor signals to detect CRC and advanced adenomas (AAs)
- To describe the recruitment processes used for our clinical validation study: Prevention of Colorectal Cancer Through Multiomics Blood Testing (PREEMPT CRC®)

Figure 1. Biological signals change as cancer evolves



- While tumor-derived signals are abundant in late-stage disease, non-tumor-derived signal, such as that from the immune system's tumor response, may contribute more significantly in earlier stage disease
- A multiomics approach that complements tumor-derived signals with non-tumor-derived signals can better address the inherent limitations of a strategy only focused on a single assay

Figure 2. Our multiomics blood test combines tumor- and non-tumor signals from DNA and proteins and uses machine learning to detect CRC and advanced adenomas

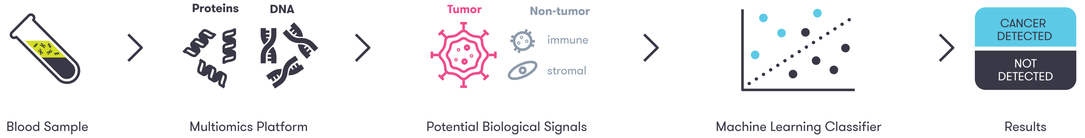
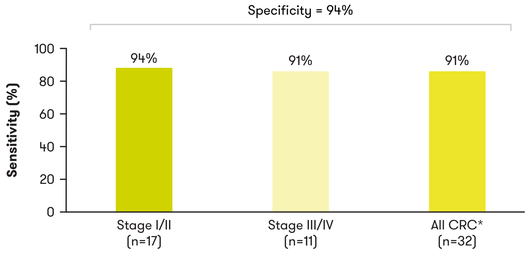


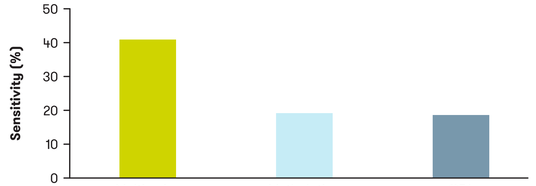
Figure 3. Our multiomics blood test achieved 94% sensitivity and 94% specificity for early-stage (I/II) CRC in AI-EMERGE[6]



*14 samples with unknown stage were tested

- Samples from AI-EMERGE®, a prospective, multi-center study that included average-risk screening patients, were used in this study. Both CRCs and colonoscopy-confirmed negatives were included.

Figure 4. Multiomics detected twice as many advanced adenomas as methylation or CEA alone in AI-EMERGE[7]

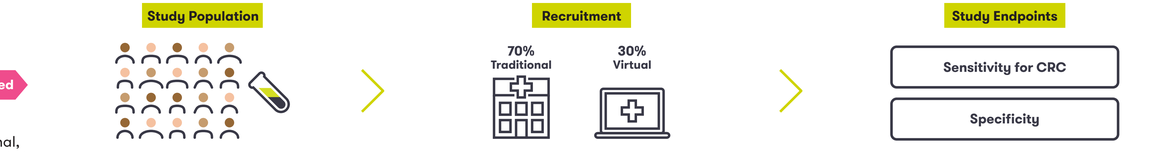


	Multiomics	Methylation	CEA
Sensitivity (n=122)	41	20	19
Specificity (n=420)	90	91	90

- By combining signatures from both tumor- and non-tumor- (e.g., immune) derived sources, our multiomics approach detected twice as many AAs as methylation-only or single-protein approaches

Figure 5. The PREEMPT CRC® study: Prevention of colorectal cancer through multiomics blood testing

Prospective, Blinded, Multi-center Registrational Study (NCT04369053)



Targeting >25,000 participants:
45-85 years of age, at average risk for CRC and willing to undergo a routine screening colonoscopy

Hybrid traditional and virtual recruitment:
Mobile phlebotomy available to all participants and enabling recruitment from every ZIP code in the continental US

Secondary: Sensitivity for advanced adenomas and negative and positive predictive values for CRC detection

Compared to colonoscopy with histopathology as the reference method

Figure 6. Increasing diversity and accessibility of our clinical study

>25,000 participants, 45-85 years

Largest prospective registrational trial studying CRC screening in the average-risk population

Diversity

Focus on the inclusion of a diverse and representative population

Enrollment to date:
11.3% Black participants
10.3% Hispanic participants

Study sites:
- >200, US and ex-US
- Includes HBCUs and FQHCs

Partnerships:
- Colorectal Cancer Alliance
- Dia de la Mujer Latina*

Accessibility

- Traditional recruitment enables in-person study enrollment
- Virtual recruitment enables enrollment from any ZIP code in the continental US
- Enables participants to use their preferred, local healthcare providers, reflecting real-world clinical care
- Mobile phlebotomy enables blood testing at home

Hybrid recruitment has enabled participation from 49 states

HBCUs = historically black college or university; FQHC = federally qualified health centers
*We have partnered with Dia de la Mujer Latina to build a culturally competent CRC education training curriculum for over 4,000 community health workers in Texas serving a predominantly medically underserved Hispanic community.

CONCLUSIONS

- Our multiomics test combines tumor- and non-tumor signals from DNA and protein biomarkers and uses machine learning to detect complex patterns of disease from blood
- The test is currently being validated in a large, prospective, multi-center, registrational study called PREEMPT CRC®, which will likely be the largest study of a blood-based test in the average-risk CRC screening population
- The study includes both traditional and virtual recruitment arms to facilitate access and enable enrollment of a diverse and representative clinical trial population, even in the midst of the COVID-19 pandemic
- For additional information
  - clinicaltrials.gov - NCT04369053
  - preemptcrc.com
  - clinicalstudies@freenome.com

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