# Design and Implementation of a Clinical Study to Validate a Multiomics Blood Test for Colorectal Cancer Screening

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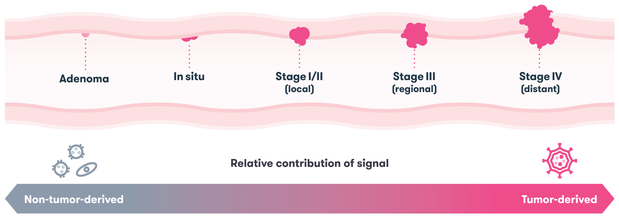
## BACKGROUND

- 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] and it will likely be more challenging to screen younger people
- Certain populations have even lower screening rates, specifically individuals aged 50-54 years (48%), those on Medicaid or other state plans (53%), and Hispanic individuals (59%)[5]
- These same groups with lower screening rates often comprise a large percentage of the screen-eligible population. For example, ~24% of individuals eligible for CRC screening are Medicaid recipients.[6]
- 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.[5]
- Here, we describe our validation study 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 the development of a blood-based test for CRC screening. Our multiomic approach uses both DNA and protein assays to evaluate tumor- and non-tumor signals to detect CRC.
- To describe the recruitment processes used for our large validation study: Prevention of Colorectal Cancer Through Multiomics Blood Testing (the PREEMPT CRC® study)

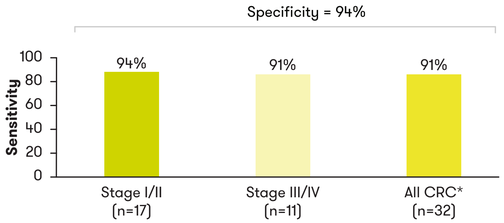
### Figure 1. Biological signals change as cancer evolves




- 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 test combines tumor- and non-tumor signals from DNA and proteins and uses machine learning to detect CRC

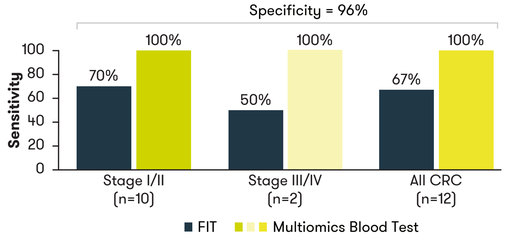

### Figure 3. Our CRC blood test detected early-stage CRC (I/II) with a sensitivity of 94% and specificity of 94%[7]




*14 samples with unknown stage were tested

- Samples from our AI-EMERGE® study, consisting of average-risk screening and case-control cohorts, were used in this study, and included CRCs and colonoscopy-confirmed negatives
- Positive and negative likelihood ratios were calculated (PLR = 15.2; NLR = 0.1)

### Figure 4. Our CRC blood test outperforms FIT[7]




1. Polymedco OC-Auto® FIT results are reported per manufacturer's specification at a cutoff of 100 ng/ml

- In AI-EMERGE, stool collection was optional. Only 52% of participants who provided a blood sample provided stool for FIT testing.
- FIT results are consistent with published data from DeeP-C (74% sensitivity and 95% specificity)[8]

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

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

**Study Population**

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

**Recruitment**


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

**Study Endpoints**

- **Secondary:** Sensitivity for advanced adenomas and negative and positive predictive values for CRC detection
- **Compared to colonoscopy** with histopathology as the reference method

Sensitivity for CRC

Specificity

- Initial enrollment target of 14,000 was achieved ahead of schedule
- However, during the COVID -19 pandemic, fewer Medicare-aged participants enrolled, contributing to a lower event rate. Therefore, to ensure adequate representation of this population and a sufficient number of events, the study will continue, with an estimated target enrollment of 25,000.

### Figure 6. Key elements of success include increasing diversity and accessibility to 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:**
- 12.8% Black individuals
- 11.6% Hispanic individuals

**Key sites:**
- HBCUs
- 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 CRC screening at home

Hybrid recruitment has brought in participation from 40 states

HBCU = historically black college or university; FQHC = federally qualified health center
*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

- Here we describe the development and validation of a multiomics blood test for the detection of early-stage (I/II) CRC
- 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
- Results from the AI-EMERGE study demonstrated sensitivity of 91% for CRC and a specificity of 94%
- The test is currently being validated in a 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 PREEMPT CRC study has both traditional and virtual recruitment arms to facilitate access and enable enrollment of a diverse and representative clinical trial population

## REFERENCES

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