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PREEMPTCRC™
PREVENTION OF COLORECTAL CANCER THROUGH MULTIOMICS BLOOD TESTING

Blood-based CRC Screening Using Multiomics and Artificial Intelligence/Machine Learning

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WEO CRC Screening Committee

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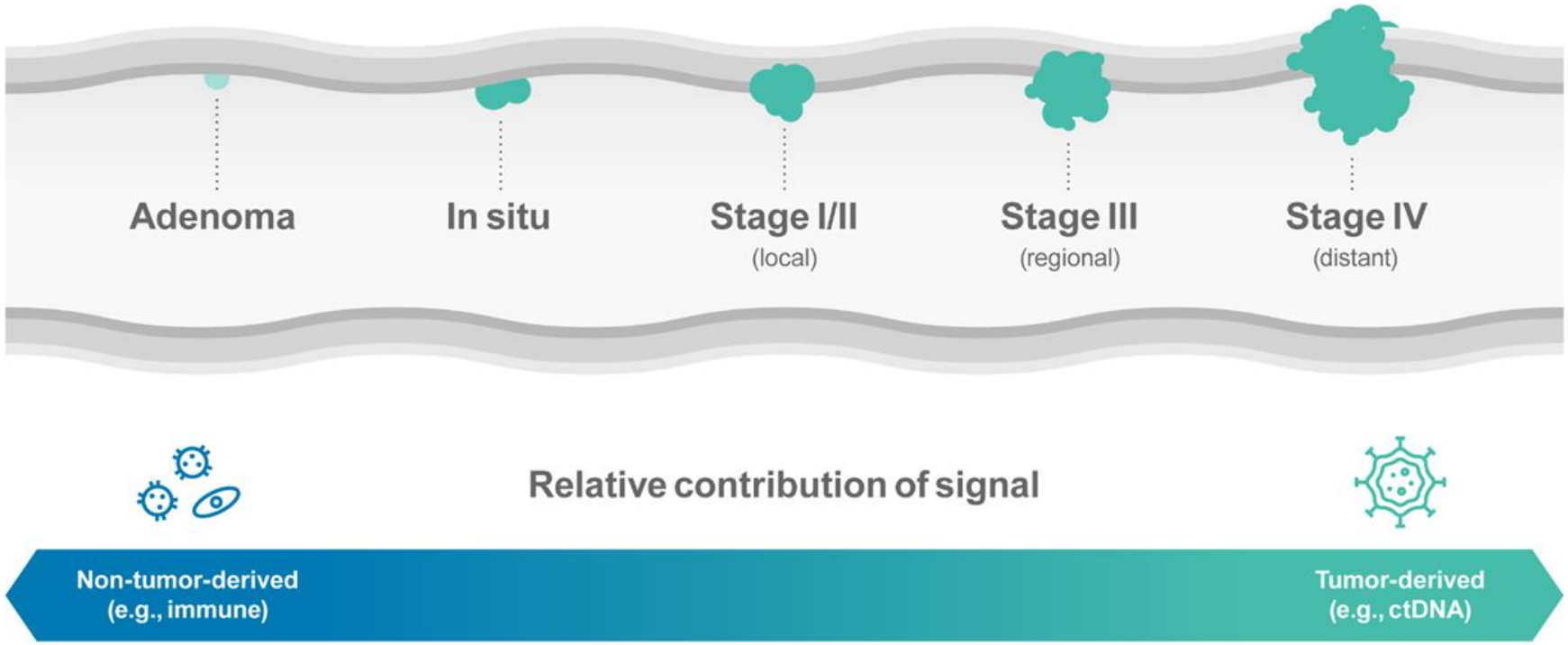
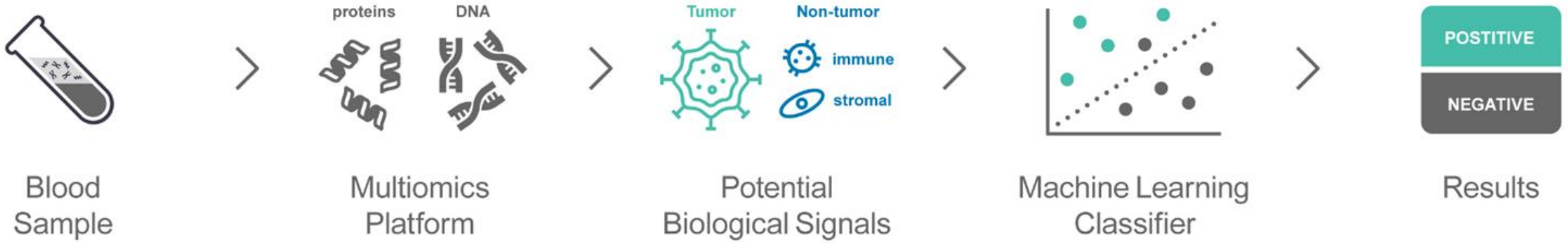
Detection of earlier stages of colorectal neoplasia in blood can be difficult



- Tumor-derived signals are detectable in late-stage disease
- Non-tumor-derived signals (e.g., immune system's tumor response) are detectectable in earlier stages
- A multiomic approach could address the limitations of a strategy focused on a single assay

Multiomic test combines tumor- and non-tumor signals from DNA and proteins and uses an AI/ML-enabled classifier



AI-EMERGE Study Design:

Prospective multi-center clinical study to iteratively train and test the classifier

Screening Cohort
N=3217

- Scheduled for screening colonoscopy
- Average risk
- 50-84 yrs of age
- Blood collected pre-colonoscopy, prior to bowel preparation

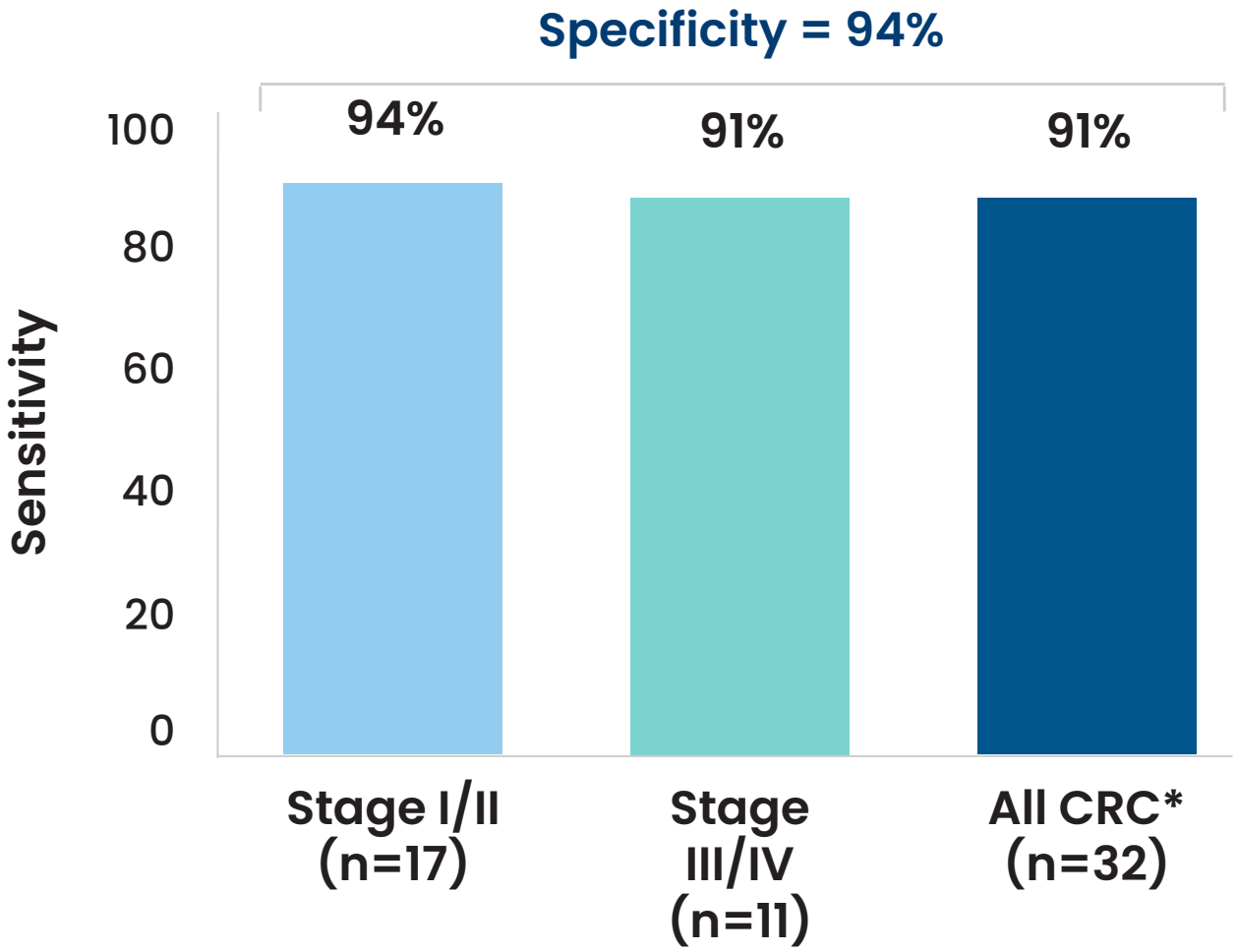
Post-Colonoscopy Cohort
N=250

- Recent diagnosis of CRC or AA
  - Average risk
    - 50-84 yrs of age
  - Average and high risk
    - ≥ 18 yrs of age
- Blood collected post-colonoscopy, prior to bowel preparation and treatment

30 study sites (NCT#03688906)

- 2 academic tertiary care centers
- 28 community practices

AI-EMERGE: CRC results

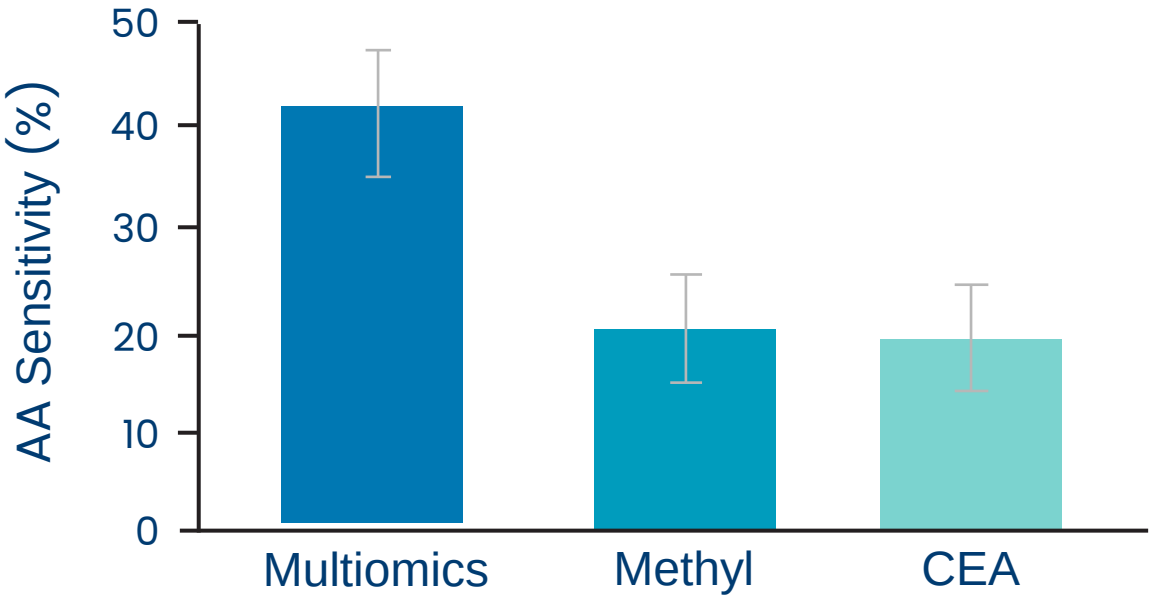


*4 samples with unknown stage were tested

- A statistically-based subset of samples from AI-EMERGE, including CRCs and colonoscopy-confirmed negatives, were used in this study
- 4-fold cross validation

AI-EMERGE: Advanced Adenoma Results

Multiomics vs cfDNA methylation or CEA alone



	Multiomics	Methyl	CEA
Sensitivity	41	20	19
Specificity	90	91	90

Whiskers show 95% confidence interval for sensitivity

- By combining signatures from both **tumor- and non-tumor- (e.g., immune) derived sources,** the multiomics test detected twice as many AAs as methylation-only or single-protein approaches
- 122 adenomas from screening and case-control arms
- 10-fold cross-validation was performed

Presented at ASCO GI 2021

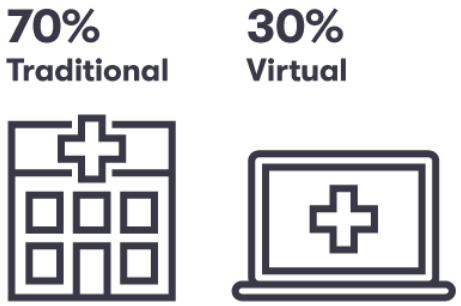
The PREEMPT CRC® study: Prevention of Colorectal Cancer Through Multiomics Blood Testing

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

Hybrid Recruitment



Traditional and Virtual: mobile phlebotomy available to all participants, enabling recruitment from 49 states

Study Endpoints

- Sensitivity for CRC
- Specificity for advanced colorectal neoplasia

Secondary: Sensitivity for advanced adenoma and negative and positive predictive value for CRC detection

Colonoscopy reference standard

Initial enrollment target of 14,000, increased to 25,000 based on lower than expected disease event rate

Highlights

PREEMPTCRC™
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Co-lead PIs

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Diversity

Focus on the inclusion of a diverse and representative population

Enrollment to date:

- **12.8% Black participants**
- **11.6% Hispanic participants**

180 sites from 35 states:

- **Academic**
- **Community practices**
- **HBCUs* *(Morehouse, Meharry*)**
- **FQHCs***

Partnerships:

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

Accessibility

- **Traditional recruitment enables in-person study enrollment**
- **Virtual recruitment has enabled enrollment from 49 states and allows participants to use their preferred, local healthcare providers, reflecting real-world clinical care**
- **Mobile phlebotomy enables blood collection at home (or any preferred site)**

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

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Conclusions

- A multiomics approach, combining analysis of cell free DNA and proteins with an AI/ML classifier, may overcome traditional barriers to the detection of advanced adenomas and early stage CRC in blood.
- PREEMPT CRC, a validation study for this approach, has a target enrollment of >25,000, representing the largest registrational study to date for a non-invasive test for CRC in an average-risk population
- A hybrid virtual and site-based recruitment model is being used to recruit a diverse population and to help overcome barriers encountered during the COVID-19 pandemic.
- The population prevalence of CRC will likely decrease with ongoing screening efforts.
- To keep CRC screening affordable, creative solutions are needed to enable validation of modified or newly developed tests to proceed in a cost-efficient manner.

Thank You!

K-fold cross validation: A Machine Learning Technique