NOVEL STOOL-BASED NON-INVASIVE EARLY DETECTION OF COLORECTAL CANCER AND PRECANCEROUS LESIONS BY CLASSIC FIT COMBINED WITH NUCLEIC ACID-BASED BIOMARKER SIGNATURES

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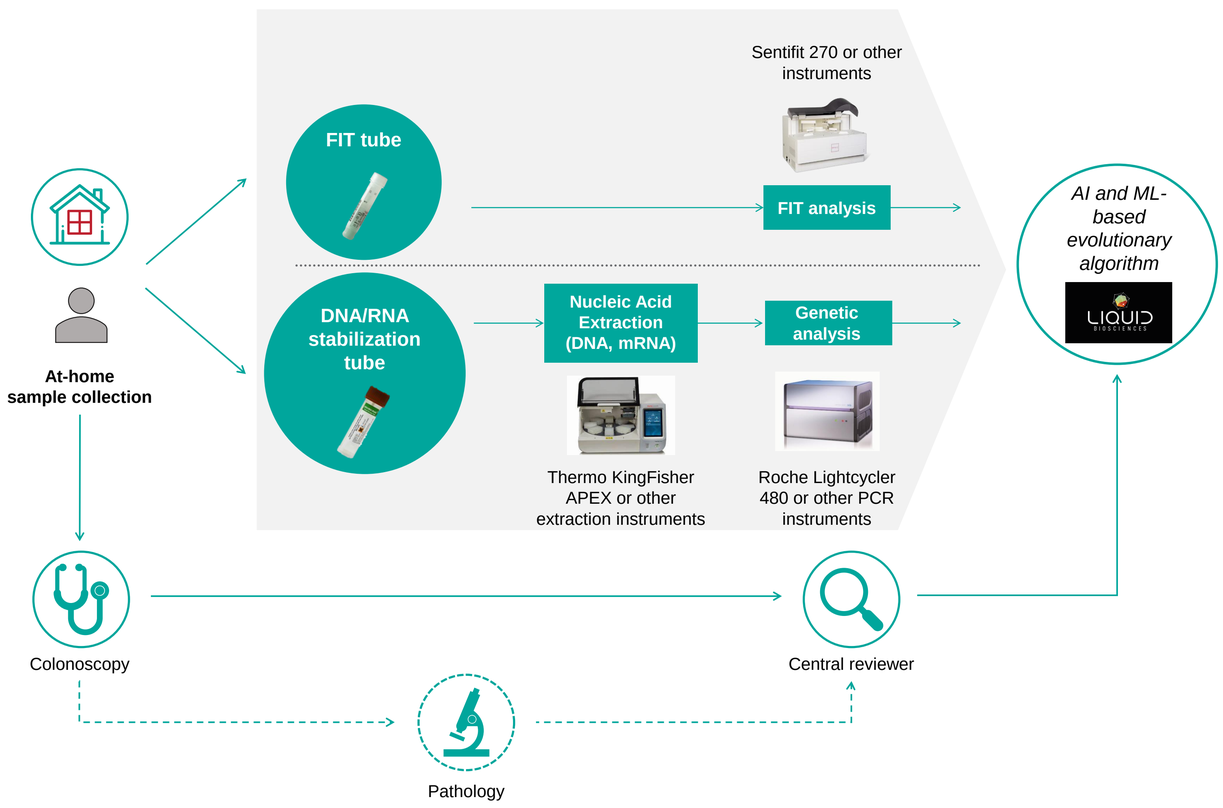
INTRODUCTION

Colorectal cancer (CRC) ranks as the second leading cause of global cancer mortality, with rising incidence among younger populations. Early detection of CRC and advanced precancerous lesions (APL) such as advanced adenoma (AA) is crucial for successful treatment. The most recommended screening method is colonoscopy, which is only accepted by and accessible to a subset of the targeted screening population due to its invasive nature. Thus, reliable non-invasive screening measures are urgently needed to address the growing challenge of CRC-related deaths. The fecal immunochemical test (FIT) is currently the most utilized non-invasive screening test for CRC screening, even though it lacks sufficient sensitivity. Here, we describe a newly established advanced multimodal screening strategy combining human DNA and mRNA signatures with FIT.

METHODS

Data Evaluation insights



- Occult blood was determined by hemoglobin quantification.
- Automated silica-bead based extraction method followed by (RT)-qPCR for novel mRNA and DNA biomarkers were used.
- The artificial intelligence/machine learning algorithm was developed in partnership with Liquid Biosciences of Aliso Viejo, California.

eAArly DETECT Demographics

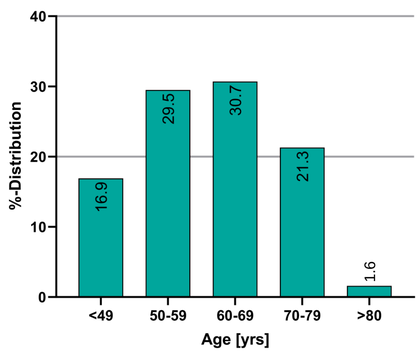
Study Population

333 subjects enrolled.

21 US study sites.

254 evaluable data sets.

Age Distribution



Distribution of Pathological Results

Total n=254 evaluable subjects

Gender Distribution

RESULTS

Clinical Performance

Performance of advanced nucleic acid screening for APL and CRC combined with classical FIT. Performance is displayed as sensitivity and specificity for CRC, APL and a combined group of diseased subjects with two-sided 95% Clopper-Pearson confidence intervals (CI).

Category	Sensitivity (%)	Specificity (%)
CRC vs. Normal + non-AA (95% confidence interval)	**97.1%** (85.1-99.9)	**97.3%** (93.3-99.3)
APL vs. Normal + non-AA (95% confidence interval)	**82.3%** (70.5-90.8)	**97.3%** (93.3-99.3)
CRC+APL vs. Normal + non-AA (95% confidence interval)	**88.0%** (80.0-93.6)	**94.8%** (90.0-97.7)

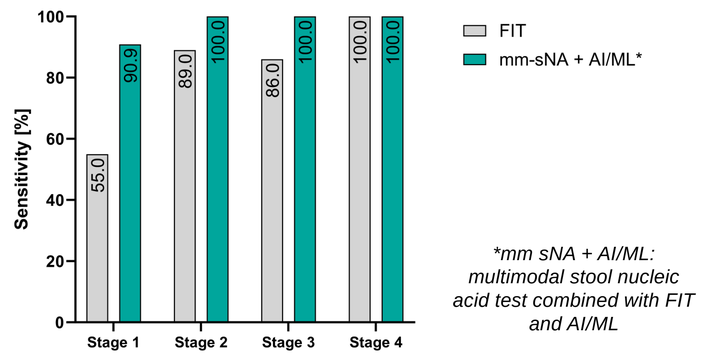
Clinical Performance by APL Pathological Result/CRC Stage

Pathological Result for CRC

CRC staging	No. of patients
Stage I	11
Stage II	9
Stage III	7
Stage IV	4
Sum	31

[x] *Four CRC samples without staging information.*

CRC-Sensitivity by Stage



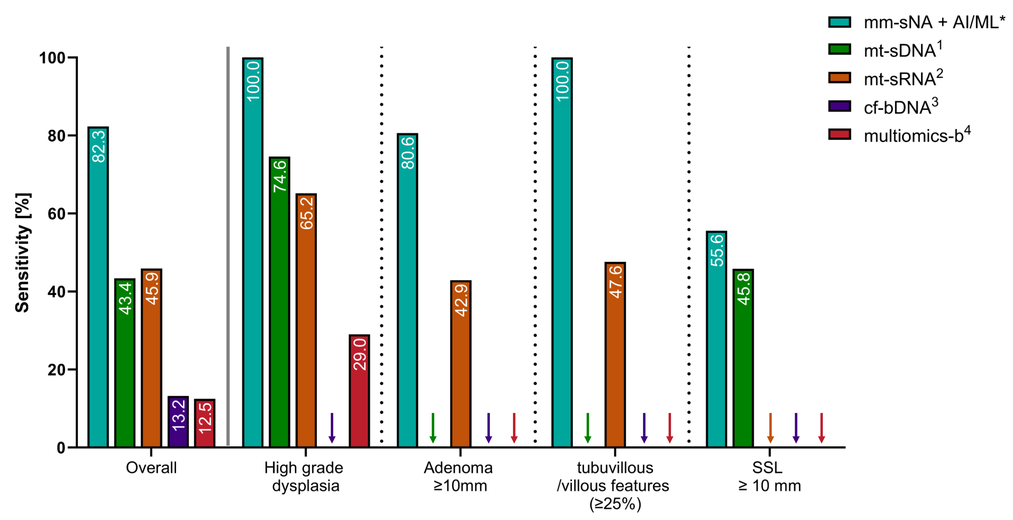
**mm sNA + AI/ML: multimodal stool nucleic acid test combined with FIT and AI/ML*

Pathological Result for APL

APL pathological result[&]	No. of patients
Sessile Serrated lesion, ≥ 1.0 cm in size or with cytological dysplasia	9
Adenoma ≥ 1.0cm in size	32
Tubuvillous/villous growth pattern (≥ 25%), any size	12
High-grade dysplasia	11
Sum	64

[&] *One samples without subtype information.*

APL-Sensitivity by Pathological Group – Comparison to Other Approaches



**data generated in this study; [1]Imperiale et al. (2024): multitarget stool DNA test, [2]Barnell et al. (2023): multitarget stool RNA test; [3]Chung et al. (2024): cell-free DNA blood test, [4]PREEMPT CRC study, press release Freenome Holdings, Inc.: multiomics blood test*
↓ data not reported.

CONCLUSION

The combination of mRNA, DNA and FIT with an AI/ML generated algorithm is a s**ubstantial and meaningful improvement** as a non-invasive strategy, that enables not only colorectal cancer and advanced precancerous lesion detection, but above all the **prevention** of **colorectal cancer.**

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References:
[1]Imperiale TF, Porter K, Zella J, Gagrat ZD, Olson MC, Statz S, et al. Next-Generation Multitarget Stool DNA Test for Colorectal Cancer Screening. N Engl J Med. 2024 Mar 14;390(11):984–93.
[2]Barnell EK, Wurtzler EM, La Rocca J, Fitzgerald T, Petrone J, Hao Y, et al. Multitarget Stool RNA Test for Colorectal Cancer Screening. JAMA. 2023 Nov 14;330(18):1760–8.
[3]Chung DC, Gray DM 2nd, Singh H, Issaka RB, Raymond VM, Eagle C, et al. A Cell-free DNA Blood-Based Test for Colorectal Cancer Screening. N Engl J Med. 2024 Mar 14;390(11):973–83.
[4]press release Freenome Holdings, Inc.; Apr 02,2024; https://www.prnewswire.com/news-releases/freenome-announces-topline-results-for-preempt-crc-to-validate-the-first-version-of-its-blood-based-test-for-the-early-detection-of-colorectal-cancer-302105203.html