REFERENCE GUIDE

Ambry Genetics®

Testing for Hereditary Colorectal Cancer

Hereditary Cancer Risk Assessment and/or Testing Are Recommended By:

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[1-2]

American College of Gastroenterology (ACG)[3]

American College of Medical Genetics and Genomics (ACMG) & National Society of Genetic Counselors (NSGC)[4]

GUIDELINES RECOMMEND GENETIC TESTING FOR ALL PATIENTS WITH PERSONAL OR FAMILY HISTORIES OF THE FOLLOWING SIGNS OF HEREDITARY CANCER:

CLINICAL RISK FACTORS

› 10 or more colorectal polyps in a person's lifetime

MULTIPLE CANCERS

› 2 or more primary cancers in the same person

› 3 or more cancers on the same side of the family

EARLY-ONSET CANCERS

› Colorectal cancer diagnosed before 50

› Gastric cancer diagnosed before 50

ABNORMAL TUMOR SCREENING

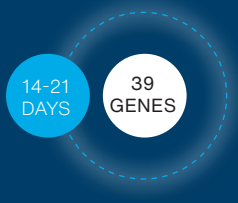
› Tumors with microsatellite instability (MSI) or loss of immunohistochemical (IHC) staining

RARE CANCERS

› Ovarian cancer, male breast cancer, pancreatic cancer, metastatic prostate cancer

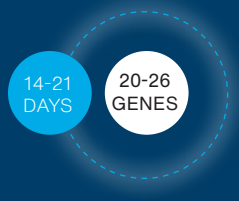
** Adapted from published genetic testing guidelines*

HEREDITARY CANCER TESTING OPTIONS*



CancerNext®

39-gene test addressing the most common hereditary cancers; National consensus management guidelines provide recommendations regarding risk management for **all genes** on the panel[1,2]



ColoNext®

20-gene base panel addressing colorectal cancer, gastric cancer, and polyposis risk; National consensus management guidelines provide recommendations regarding risk management for **all 20** genes.[1]

Option to add 6 additional limited evidence genes.**

*Additional testing options available
**Genes are considered "limited evidence" if association with cancer has been suggested but not confirmed due to limited evidence. Management guidelines are not available regarding risk management.

Add +RNAinsight® for More Accurate Results[5-9]

- **Identifies more positive results**
- **Reduces variant of uncertain significance (VUS) rate**
- **Helps address evidence gaps in non-White populations**

+RNAinsight Product Overview

- Has no impact on turnaround time or out-of-pocket cost to patient
- Is available for all tests except for BRCAPlus®
- Kit includes 1 EDTA tube (DNA) and 1 PAXgene® tube (RNA)

5%

Patients Impacted[8]

RNA evidence has been useful for 5% of hereditary cancer testing patients at Ambry.

~1/25

Positive Patients Would Be Missed Without +RNAinsight®[9]

Results without +RNAinsight would be missed or inconclusive

References
1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric. V2.2024 ©National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed October 19, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. V1.2025. ©National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed September 13, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
3. American College of Gastroenterology et al. The American Journal of Gastroenterology. 2015
4. Hampel H, ACMG, NSGC, et al., Genetics in Medicine. 2014
5. Landrith T et al. npj Precision Oncology. 2020.
6. Karam R et al. JAMA Network Open. 2019.
7. Horton C et al. NPJ genomic medicine. 2022.
8. Horton C et al. JAMA Oncology. 2023
9. Horton C et al. Expanding the reach of paired DNA and RNA sequencing: Results from 450,000 consecutive individuals from a hereditary cancer cohort; (Oral Presentation Session 84 - Strategies to Interpret Germline Variants in Cancer Predispostion Genes). Presented at the Annual Meeting of The American Society of Human Genetics, November 68, 2024, in Denver, CO.

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