Genetic Insights: quick reference guide for healthcare providers

This guide is intended to facilitate a discussion between a provider and their patient.

Genetic Insights test results: ***APC*-associated hereditary cancer**

Key results

A DNA variant, called c.3920T>A (p.Ile1307Lys), that is associated with an increased risk of developing colon cancer was found in the *APC* gene.

Next steps

Clinical recommendations	Resources
Genetic Insights is a screening test and not intended for diagnosis. A follow-up genetic test should be performed in a clinical setting before any other action is taken.	**Ready to order?** Check with your institution and/or patient's insurance about the preferred testing laboratory. Blueprint Genetics® offers hereditary cancer testing. To confirm this test result, **targeted variant testing** for the variant identified is available. You can order a confirmation test here: Blueprint Genetics/TVT **Have questions?** Call **1.866.GENE.INFO** (1.866.436.3463) to speak to a specialized Quest genetic counselor or geneticist available to healthcare providers to discuss test selection and results.
Refer your patient to a genetic counselor specializing in hereditary cancer. *Genetic counselors can provide counseling on the implications of this test result and next steps for your patient.*	Your patient can schedule a 1-on-1 remote genetic counseling session through their online Genetic Insights Cancer Risk Report at no additional cost. To find a genetic counselor with expertise in hereditary cancer genetics practicing in your patient's area for an in-person session, please visit FindAGeneticCounselor.NSGC.org

Patient conversation starters:

Patient conversation starters summarize the preceding information in plain language to support meaningful conversations between you and your patient.

FindAGeneticCounselor.NSGC.org

Your Genetic Insights test is a screening test. The next step is to have your result confirmed with a second genetic test.

It's also important that you talk with a genetic counselor. Genetic counselors are experts in genetics and can help you understand this result and potential next steps.

You can access a genetic counselor through your online Genetic Insights dashboard at no additional cost to you, and we can discuss a referral to a local genetic counselor.

Visit QuestDiagnostics.com/Genetic-Health-Screening for more information about this test.

What is *APC*-associated cancer risk?

The c.3920T>A (p.Ile1307Lys) DNA variant in the *APC* gene is associated with an increased risk of developing colon cancer.

The lifetime risk of colon cancer in people with the c.3920T>A (p.Ile1307Lys) *APC* variant is approximately 8%, or about twice the typical risk of 4%.[4,5] This risk may be higher if there is a family history of colon cancer.

This DNA variant is estimated to occur in 6%-8% of people of Ashkenazi Jewish ethnicity.[1,2] It is rarer in people of other ethnicities.[6] Therefore, the colon cancer risk linked to this DNA variant is best defined in people with Ashkenazi Jewish ethnicity.

Other DNA variants in the *APC* gene are associated with the hereditary cancer predisposition syndromes familial adenomatous polyposis (FAP) and attenuated FAP (A-FAP).[3,4] The colon cancer risk for people with these other variants is much higher than in people with the c.3920T>A (p.Ile1307Lys) DNA variant.

Individuals with a confirmed c.3920T>A (p.Ile1307Lys) variant in the *APC* gene are recommended to undergo more frequent cancer screening, typically starting at an earlier age than the general population.[4]

See the Management options section for more detail.

Patient conversation starters:

APC-associated cancer risk is caused by a DNA variant in a certain gene.

People with this DNA variant in the *APC* gene have a higher than typical chance of developing colon cancer. Not everyone with this DNA variant will develop colon cancer.

People with *APC*-associated cancer risk should have colon cancer screenings earlier in life and more often than typical. This increases the chance that if colon cancer develops, it's detected as early as possible.

What this result means for family members

Family members may have the same DNA variant. The DNA variant was most likely inherited from a parent, although in rare instances the patient could be the first person in the family to carry a variant. Full siblings and children have a 50% chance of having this variant.

In people with a confirmed DNA variant in the *APC* gene, cascade genetic testing for other family members may help inform their risks and screening protocols.

A genetic counselor can help determine the most appropriate testing options. Therefore, it is strongly recommended that people share their results with their biological relatives.

Patient conversation starters:

DNA variants run in families.

That means the DNA variant in the *APC* gene can be inherited or passed down from parents to their children. Your close relatives—like your parents, full siblings, and children—have a 50% (or 1 in 2) chance of having the same DNA variant. Other relatives might also have the same DNA variant.

Sharing this result with your family members is important so they can talk to a healthcare provider about genetic testing for this DNA variant.

Management options

Clinical guidelines from the National Comprehensive Cancer Network® (NCCN®) for people with a confirmed c.3920T>A (p.Ile1307Lys) variant in the *APC* gene and no personal history of colon cancer include[4]:

First-degree relative with colon cancer?	Guidelines for people with confirmed c.3920T>A (p.Ile1307Lys) *APC* gene variant
Yes	Colonoscopy screening every 5 years beginning at age 40 or 10 years prior to the age of the first-degree relative when diagnosed with colon cancer
No	Colonoscopy screening every 5 years beginning at age 40

Patient conversation starters:

It's recommended that people with this DNA variant have cancer screenings earlier and more often than typical. This way, cancer is more likely to be caught in the early stages when it's most treatable.

If your result is confirmed, it's important to work with the right specialists, like a medical oncologist and a geneticist, to find cancer screening and risk-reducing options that are right for you.

See NCCN for complete recommendations. Recommendations may change over time. If the test result is confirmed, local centers for excellence in hereditary cancer should be consulted for further clinical management.

Additional resources

The following advocacy groups have additional information and resources about hereditary colon cancer risk:

Facing Our Risk of Cancer Empowered (FORCE): FacingOurRisk.org
Colorectal Cancer Alliance: CCAlliance.org

References

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5. Liang J, Lin C, Hu F, et al. APC polymorphisms and the risk of colorectal neoplasia: a HuGE review and meta-analysis. *Am J Epidemiol*. 2013;177(11):1169-1179. doi:10.1093/aje/kws382
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