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 pathogenic or likely pathogenic variant that is associated with an increased risk of developing numerous colon polyps, colon cancer, and certain other cancers 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 hereditary cancer?

DNA variants in the *APC* gene are associated with the hereditary cancer predisposition syndromes familial adenomatous polyposis (FAP) and attenuated FAP (A-FAP).[1,2] Clinical diagnosis of FAP or A-FAP may be made based on standard clinical criteria.[1,2]

- FAP is characterized by hundreds to thousands of adenomatous colon polyps. Left untreated, lifetime colon cancer risk approaches 100%[1]
- A-FAP is characterized by an average of 30 adenomatous colon polyps with approximate colon cancer risk of 70% by age 80 years[1]

Age of onset of colon polyps may vary, even within a family, and may appear in childhood.[1]

Variable extra-colonic manifestations may be present in individuals with *APC* variants.

Individuals with confirmed *APC* variants are recommended to undergo more frequent cancer screening, potentially starting as early as 10 years old.[2]

Management is best coordinated by a specialized care team.[1,2]

See the Management options section for more detail.

Patient conversation starters:

People with this DNA variant in the *APC* gene have a higher than typical chance of developing certain cancers, especially colon cancer.

DNA variants in the *APC* gene are linked to 2 different conditions: one called FAP and one called A-FAP. People with FAP have a higher risk of developing colon cancer than people with A-FAP.

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

What this result means for family members

There are 2 primary ways someone can have a DNA variant associated with FAP or A-FAP:

- The DNA variant can be inherited from a biological parent. At least 1 parent has the same DNA variant. Each full sibling and each child of someone with the variant has a 50% chance of having it
- The DNA variant can arise in someone for the first time (called a de novo variant). In this case, their children have a 50% chance of having the variant. Neither biological parent nor any siblings are likely to have the 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:

There are 2 ways someone can end up having a DNA variant linked to FAP or A-FAP.

First, it can be passed down from a parent. In this case, 1 parent would have that same DNA variant. Full siblings have a 50% chance (1 in 2 chance) of having the DNA variant too.

Second, it's possible that the DNA variant happens in someone in a family for the first time. In this case, parents and siblings are not likely to have the DNA variant.

However, in either case, each child of someone with the DNA variant has a 50% chance of having the same DNA variant.

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

Select extra-colonic clinical features in individuals with FAP or A-FAP[1,2]:

Clinical Feature	Approximate risk with *APC* variant	General population risk
Small bowel cancer	4-12% lifetime risk	<1%
Papillary thyroid cancer	1-12% lifetime risk	~1%
Stomach cancer	1% lifetime risk (may be higher in individuals of certain ethnic backgrounds)	<1%
*Osteomas (non-malignant)**	~20% of individuals	rare
*Desmoid tumors (non-malignant)**	~10-30% of individuals	rare
*Congenital hypertrophy of the retinal pigment epithelium (CHRPE)**	75% of individuals	rare

* Rare in A-FAP.
See references for full description of associated clinical features and risks. These risks may change over time as scientific research advances.

Management options

Clinical guidelines from the National Comprehensive Cancer Network® (NCCN®) for people with a confirmed DNA variant associated with FAP or A-FAP and no personal history of polyps or an associated cancer include[2]:

Cancer type	Guidelines for people with confirmed FAP or A-FAP
Colon	FAP: colonoscopy (preferred) or flexible sigmoidoscopy every 12 months beginning between the ages of 10-15 years old A-FAP: baseline colonoscopy in late teens, then repeat every 1-2 years Consider colectomy when polyps are present (FAP) or when there are too many polyps to remove via endoscope (A-FAP)
Extra-colonic	Varies with personal and family history

Patient conversation starters:

It's recommended that people with FAP or A-FAP 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.

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

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

1. Jasperson KW, Patel SG, Ahnen DJ. APC-Associated Polyposis Conditions. December 18, 1998. Updated February 2, 2017. In: Adam MP, Ardinger HH, Pagon RA, et al, editors. GeneReviews® [Internet]. University of Washington, Seattle; 1993-2020. Available from: www.ncbi.nlm.nih.gov/books/NBK1345/
2. National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Colorectal (Version 2.2022). NCCN Guidelines®. Accessed December 13, 2022. www.nccn.org

This information is not a substitute for medical advice, diagnosis, or treatment. The diagnosis or treatment of any disease or condition may be based on personal history, family history, symptoms, a physical examination, laboratory test results, and other information considered important by a healthcare provider.

Individuals should talk with a healthcare provider about the meaning of genetic test results and before stopping, starting, or changing any medication or treatment.

Genetic Insights is a test developed and performed by Quest Diagnostics. The test results are not diagnostic and do not determine overall chances of developing a disease or health condition. The tests are not cleared or approved by the US Food and Drug Administration.

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