



RAF	CEA	ctDNA	DPYD	FAP	HER2	KRAS	Lyr
FAP: Familial Adenomatous Polyposis							NTR
K3CA	TMB	Tumor Location/Sidedness				UGT1A1	P

## Who should be tested for FAP?

All colorectal cancer (bowel cancer) patients with more than 20 total adenomatous polyps in their lifetime should be tested for FAP. Adenomatous polyps are abnormal growths in the lining of the colon and/or rectum. All biological family members (parents, siblings, children, cousins) of CRC patients with FAP should themselves be tested. An early FAP diagnosis can prevent colorectal cancer in family members.

## What is FAP?

Familial adenomatous polyposis is an inherited syndrome of very high colorectal cancer risk. FAP makes up fewer than 1% of CRC cases. There are three subtypes: classic FAP, attenuated FAP, and autosomal recessive FAP (also called MYH-associated or MUTYH-associated polyposis).

- Classic FAP and attenuated FAP are caused by mutations in the APC (adenomatous polyposis coli) gene.
- Autosomal recessive FAP is caused by mutations in the MYH gene.
- The lifetime risk of colorectal cancer in FAP is nearly 100%.

Patients with classic and attenuated FAP have hundreds to thousands of colorectal adenomatous polyps which are abnormal growths in the colon and rectum that are precancerous. If they are not removed, they will become malignant. APC is a gene involved in maintaining normal cell growth. When a mutation disrupts that function, abnormal growth occurs, leading to these polyps.

The timeline of polyp growth and cancer development is different in classic FAP and attenuated FAP. The average age of colorectal cancer is 39 years in patients with classic FAP. For attenuated FAP, the average age of CRC development is 55.

Patients with MYH-associated polyposis have fewer adenomatous polyps than classic or attenuated FAP patients, usually fewer than 100. MYH (also known as MUTYH) is a gene involved with repairing DNA damage in cells. When MYH is mutated, cells are unable to repair DNA damage and mutations build up in other genes that lead to abnormal cell growth and polyps. Most MYH-associated CRC occurs between 40 and 60 years of age.

Juvenile polyposis syndrome (JPS) is a related colorectal polyp syndrome with a lifetime risk of colorectal cancer of 34-38%. It is characterized by fewer polyps than FAP (5-100) and is caused by different gene mutations. 60% of JPS is caused by currently unknown mutations, 20% is caused by BMPR1A mutation, and 20% is caused by SMAD4 mutation. BMPR1A and SMAD4 are genes involved in cell growth control. Mutations in these genes allow abnormal growth, leading to polyps. The colorectal polyps in JPS are benign polyps. And like FAP polyps, if they are not removed they may become cancer. Colorectal cancer associated with JPS is treated with surgery, and additional treatments (chemotherapy, targeted therapy, immunotherapy) may be used based on cancer stage, tumor biomarkers, and other patient factors. JPS is inherited and biological family members need to know about your JPS diagnosis and have their own cancer screening and genetic testing. Like FAP, JPS is associated with several digestive system cancers, so talk to your medical team about screening and prevention of JPS associated cancers.

### **How is FAP tested? How are the results reported?**

Genetic testing is performed on a blood sample or on cells collected from your mouth or saliva. Testing for FAP is often accompanied by consultation with a genetic counselor, a health care provider with cancer genetics training. Genetic counselors provide risk assessment, education, and support for patients and families that may be affected by a genetic syndrome.

If you have FAP, your report will say “positive”, “pathogenic mutation detected”, or “variant detected, likely pathogenic” and will give the gene location of the specific mutation found. Pathogenic describes something that causes a disease.

If you do not have FAP, your results will be reported as “wild-type”, “negative” or “no pathogenic mutation detected”.

### **What do my FAP results mean for me? How do they impact my treatment?**

If you have no APC mutation (wild-type), your treatment options include traditional chemotherapy and targeted therapy and/or immunotherapy based on the results of your other biomarker testing.

If you do have a pathogenic APC mutation, you have FAP. Colorectal cancer caused by FAP is treated with colectomy. Additional treatments (chemotherapy, targeted therapy, immunotherapy) may be used based on cancer stage, tumor (tumour) biomarkers, and other patient factors. Patients with FAP who have not been diagnosed with cancer need to have increased colorectal cancer screening, and may have a preventive (prophylactic) colectomy.

Patients with all three types of FAP (classic, attenuated, and MYH-associated polyposis) are also at risk for other cancers, including cancer of the stomach (gastric), small intestine, pancreas, liver (hepatic) and biliary tract, adrenal glands, thyroid gland, and brain. These risks vary by the location of the mutation in the APC gene. If you have FAP, talk to your medical team about screening and prevention of other FAP associated cancers.

Because FAP is inherited, it is critical that your biological family members know about your FAP diagnosis and have their own genetic testing. If you have consulted with a genetic counselor in your FAP testing process, they can help you with information for your family members. Family members who are tested and subsequently diagnosed with FAP have earlier (starting at age 10) and more frequent (yearly) CRC screening, removal of precancerous polyps, and preventive (prophylactic) colectomy.

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Biomarker testing can give you and your medical team valuable knowledge about your cancer and help guide your treatment choices. For more information about colorectal cancer biomarkers, please visit [knowyourbiomarker.org](https://knowyourbiomarker.org) and talk to your medical team.