SelfDecode™

ACMG-Based Predisposition Report

Report date: 04 Feb 2026

Client Information

Name: John Doe
Age: 55
Sex: Male
Height: 5ft 11” / 182cm
Weight: 192lb / 87kg

Report Provider

Name: Jane Doe
Company: Company name
Email: email@companyname.com
Web: www.companyname.com
Phone: (000) 00 000 0000
Address: Address address address, City, Zipcode, State, Country

Table of Contents

About This Report

ACMG SF v3.2 Secondary Findings

This report analyzes your Whole Genome Sequencing (WGS) data using the **ACMG Secondary Findings (SF) list, version 3.2.** The ACMG SF list is developed by the **American College of Medical Genetics and Genomics**, and is internationally recognized as one of the most authoritative frameworks for returning medically actionable genetic information.

The ACMG recommends a curated list of gene–condition pairs that should be evaluated when sequencing is performed, even if not directly related to the reason for testing. These findings are known as **secondary findings** — genetic variants that may increase the likelihood of developing certain medical conditions, independent of your current symptoms or clinical indication.

The v3.2 list includes genes linked to:

✓ hereditary cancer syndromes
✓ cardiovascular conditions (including sudden cardiac death risk)
✓ metabolic conditions
✓ other clinically actionable genetic disorders

As described in the publication, this list is **maintained, evaluated, and updated regularly** by a working group of experts in medical genetics, genomics, cardiology, oncology, and bioinformatics . The purpose of the list is to identify genetic findings where **early detection, surveillance, or treatment may prevent or significantly reduce morbidity and mortality**.

What This Report Shows You

Your genome was analyzed specifically for **pathogenic or likely pathogenic variants** in the genes included in the ACMG SF v3.2 list. Variants classified as pathogenic or likely pathogenic according to ACMG criteria are returned. **Variants of Uncertain Significance (VUS) are not included**, per ACMG recommendations.

How to Interpret Your Results

Summary Table

You will first see a summary of all ACMG v3.2 conditions. For each condition, you can see:

Variant Detected
You carry a variant known to increase risk for the condition

Variant Not Detected
No actionable variant was found in this gene

Inheritance Model
Explains how risk is expressed genetically

Detailed Variant Pages (Only if a Risk Variant Is Found)

If a harmful variant is identified, you will receive a detailed explanation including:

ACMG clinical summary for the condition:

Background, medical implications, intervention relevance

Your specific variant(s):

SNP ID(s), genotype, pathogenicity classification

Population frequency:

How common the variant is in large populations

Risk interpretation:

Clarifies how likely the variant is to cause disease

Inheritance explanation:

Whether 1 or 2 variants increase risk and expected penetrance

Interpretation example:

Your Variant Scenario:	Meaning:
1 pathogenic variant in an **autosomal dominant (AD)** gene	Increased risk — may develop condition
1 pathogenic variant in an **autosomal recessive (AR)** gene	Carrier only — typically not at risk unless two variants present
2 pathogenic variants in an **AR** gene	High risk of condition expression
Variant in **X-linked** gene	Risk may differ for males vs females

Presence of a variant **does not guarantee** disease. Risk depends on inheritance, penetrance, age, lifestyle, and clinical management options.

Summary Overview

Detected Variants

Condition	Gene(s)	Inheritance	Status
Familial adenomatous polyposis (FAP)	**APC**	**AD**	**Variant detected**
Familial hypercholesterolemia	**LDLR**	**SD**	**Variant detected**
Biotinidase deficiency	**BTD**	**AR**	**Variant detected**

Cancer

Condition	Gene(s)	Inheritance	Status
Familial adenomatous polyposis (FAP)	**APC**	**AD**	**Variant detected**
Multiple endocrine neoplasia 2	RET	AD	Variant not detected
Hereditary breast and/or ovarian cancer	BRCA1	AD	Variant not detected
	BRCA2		
	PALB2		
Hereditary pheochromocytoma/ paraganglioma syndrome	SDHA	AD	Variant not detected
	SDHB		
	SDHC		
	SDHD		
	SDHAF2		
	MAX		
	TMEM127		
Juvenile polyposis syndrome (JPS)	BMPR1A	AD	Variant not detected
	SMAD4		
Li-Fraumeni syndrome	TP53	AD	Variant not detected
Lynch syndrome (Hereditary Nonpolyposis Colorectal Cancer; HNPCC)	MLH1	AD	Variant not detected
	MSH2		

Condition	Gene(s)	Inheritance	Status
Lynch syndrome (Hereditary Nonpolyposis Colorectal Cancer; HNPCC)	MSH6	AD	Variant not detected
	PMS2		
	EPCAM		
Multiple endocrine neoplasia type 1	MEN1	AD	Variant not detected
MUTYH-associated polyposis (MAP)	MUTYH	AR	Variant not detected
NF2-related schwannomatosis	NF2	AD	Variant not detected
Peutz-Jeghers syndrome (PJS)	STK11	AD	Variant not detected
PTEN hamartoma tumor syndrome	PTEN	AD	Variant not detected
Retinoblastoma	RB1	AD	Variant not detected
Tuberous sclerosis complex	TSC1	AD	Variant not detected
	TSC2		
von Hippel-Lindau syndrome	VHL	AD	Variant not detected
WT1-related Wilms tumor	WT1	AD	Variant not detected

Cardiovascular

Condition	Gene(s)	Inheritance	Status
Familial hypercholesterolemia	**LDLR**	**SD**	**⚠ Variant detected**
	APOB	AD	Variant not detected
	PCSK9		
Loeys-Dietz Syndrome (LDS)	TGFBR1	AD	Variant not detected
	TGFBR2		
	SMAD3		
Heritable thoracic aortic disease (HTAD)	ACTA2	AD	Variant not detected
	MYH11		
Arrhythmogenic right ventricular cardiomyopathy	PKP2	AD	Variant not detected
	DSP		
	DSC2		
	DSG2		
	TMEM43		

Condition	Gene(s)	Inheritance	Status
Catecholaminergic polymorphic ventricular tachycardia	RYR2	AD	Variant not detected
	CASQ2	AR	
	TRDN		
Dilated cardiomyopathy	TNNT2	AD	Variant not detected
	LMNA		
	FLNC		
	TTN		
	BAG3		
	DES		
	RBM20		
	TNNC1		
Hypertrophic cardiomyopathy	MYH7	AD	Variant not detected
	MYBPC3		
	TNNI3		
	TPM1		
	MYL3		
	ACTC1		
	PRKAG2		
	MYL2		
Ehlers-Danlos syndrome, vascular type	COL3A1	AD	Variant not detected
Long QT syndrome type 1	KCNQ1	AD	Variant not detected
Long QT syndrome type 2	KCNH2	AD	Variant not detected
Long QT syndrome 3; Brugada syndrome	SCN5A	AD	Variant not detected
Calmodulinopathy	CALM1	AD	Variant not detected
	CALM2		
	CALM3		

Inborn Errors of Metabolism

Condition	Gene(s)	Inheritance	Status
Biotinidase deficiency	**BTD**	**AR**	**⚠ Variant detected**
Fabry disease	GLA	XL	Variant not detected
Ornithine transcarbamylase deficiency	OTC	XL	Variant not detected
Pompe disease	GAA	AR	Variant not detected

Miscellaneous

Condition	Gene(s)	Inheritance	Status
Hereditary hemochromatosis	HFE	AR	Variant not detected
Hereditary hemorrhagic telangiectasia syndrome	ACVRL1	AD	Variant not detected
	ENG		
	SMAD4		
Malignant hyperthermia	RYR1	AD	Variant not detected
	CACNA1S		
Maturity-Onset of Diabetes of the Young	HNF1A	AD	Variant not detected
RPE65-related retinopathy	RPE65	AR	Variant not detected
Wilson disease	ATP7B	AR	Variant not detected
Hereditary TTR (transthyretin) amyloidosis	TTR	AD	Variant not detected

Condition Details

Familial Adenomatous Polyposis (FAP)

Category: Cancer | **Gene: APC**

Familial Adenomatous Polyposis (FAP) is an autosomal dominant disease caused by pathogenic **variants in the APC gene**. FAP is characterized by the development of **numerous adenomatous polyps in the colon and rectum**, significantly increasing the **risk of colorectal cancer**, as well as upper intestinal and extraintestinal tumors.

Classic FAP is characterized by the presence of 100 or more colorectal adenomas. An **attenuated form of FAP (AFAP)** is characterized by fewer colorectal adenomas (>10 to 99) with a later age of onset.

The incidence of FAP varies from 1 in 7,000 to 1 in 22,000 individuals.

Detected Variant (SNP) Table

Gene	SNP	Genotype	Inheritance	Chromosome	Position	Classification
APC	rs515726215	CT	AD	chr19	11089615	Pathogenic

Screening & Surveillance

- **Colorectal Monitoring.** Individuals with a known pathogenic APC variant and classic FAP, should begin colonoscopy annually, starting at age 10 to 12. Surveillance following colectomy should include annual endoscopic examination of the rectum or ileal pouch, or examination of an ileostomy every two years. Individuals at risk for AFAP should have colonoscopy every one to two years, starting in the late teenage years. Patients with colorectal polyps should undergo polypectomy when feasible, followed by annual colonoscopy for surveillance
- **Upper endoscopy** using a forward-viewing endoscope for gastric polyps and a side-viewing duodenoscope for duodenal polyps at the time of onset of colonic adenomas or around age 20 to 25 years, whichever comes first. Subsequent upper endoscopic surveillance and management is guided by the severity of duodenal polyposis. Annual upper GI screening also involves H. pylori testing and eradication if positive (to reduce gastric cancer risk)
- **Thyroid ultrasound** starting in late teenage years, repeating every two to five years, due to a ~2% risk of thyroid carcinoma
- No routinely screening of all patients with FAP for intra-abdominal desmoids, but perform an abdominal computed tomography scan to assess for desmoids:
- Prior to colectomy in patients at increased risk for desmoids
- When there is a palpable abdominal mass on physical examination
- When symptoms are suggestive of abdominal organ obstruction
- Hepatoblastoma screening in at-risk young children can be considered with liver ultrasound and AFP every 3–6 months until age 5

Lifestyle Modifications

While no specific lifestyle changes have been proven to prevent polyp formation, maintaining a balanced diet rich in fruits, vegetables, and fiber, along with regular physical activity, while avoiding smoking and excess alcohol is sensible, supports overall health and may aid in cancer prevention.

Medical Therapy

There is limited evidence that chemopreventive agents, such as aspirin or NSAIDs (sulindac or celecoxib), may suppress the recurrence of larger colorectal polyps in patients with FAP. However, no single agent or combination of agents has convincingly been shown to delay disease progression or obviate the need for surgery.

Surgery

- Due to the high risk of colorectal cancer, **prophylactic colectomy** is often recommended once polyps are detected. The timing and extent of surgery depend on individual factors, including polyp burden and patient health. Indications for colectomy in FAP patients include:
  - documented or suspected CRC
  - adenoma with high-grade dysplasia
  - significant symptoms related to colonic neoplasia (e.g. GI bleeding)
  - marked increases in polyp number on consecutive exams
  - inability to adequately survey the colon because of multiple diminutive polyps
- Colectomy is eventually necessary in all patients with classic FAP
- Patients with AFAP can often be managed with **colonoscopic polypectomy** and may possibly never need colectomy
- Avoid delaying recommended surgery longer than necessary – prolonged retention of the colon elevates cancer risk, but surgery should be timed to balance polyp burden and desmoid risk. Because surgical trauma can trigger desmoid tumors, colectomy is often deferred as long as safely possible in young patients with a family history of desmoids

Family Planning & Genetic Counseling

- Since FAP is inherited in an autosomal dominant pattern, each child of an affected individual has a 50% chance of inheriting the condition. Genetic counseling and testing are crucial for at-risk family members to facilitate early detection and management
- Prenatal testing and preimplantation genetic diagnosis (PGD) are options for affected individuals who wish to avoid passing on FAP

References

- Kim, H. M. & Kim, T. I. Screening and surveillance for hereditary colorectal cancer. Intest Res 22, 119–130 (2024). doi: 10.5217/ir.2023.00112
- Kanth, P., Grimmett, J., Champine, M. et al. Hereditary Colorectal Polyposis and Cancer Syndromes: A Primer on Diagnosis and Management. Am J Gastroenterol 112, 1509–1525 (2017). doi: 10.1038/ajg.2017.212. PMID: 28786406.
- Menon, G. & Kasi, A. Familial Adenomatous Polyposis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538233/
- Syngal, S., Brand, R. E., Church, J. M. et al. ACG clinical guideline: Genetic testing and management of hereditary gastrointestinal cancer syndromes. Am J Gastroenterol 110, 223-62; quiz 263 (2015). doi: 10.1038/ajg.2014.435. PMID: 25645574.
- Vasen, H. F., Möslein, G., Alonso, A et al. Guidelines for the clinical management of familial adenomatous polyposis (FAP). Gut 57, 704-13 (2008). doi: 10.1136/gut.2007.136127.136127. PMID: 18194984.
- Ishikawa, H., Mutoh, M., Sato, Y. et al. Chemoprevention with low-dose aspirin, mesalazine, or both in patients with familial adenomatous polyposis without previous colectomy (J-FAPP Study IV): a multicentre, double-blind, randomised, two-by-two factorial design trial. Lancet Gastroenterol Hepatol 6, 474-481 (2021). doi: 10.1016/S2468-1253(21)00018-2. PMID: 33812492.
- Kemp Bohan, P. M., Mankaney, G., Vreeland, T.J. et al. Chemoprevention in familial adenomatous polyposis: past, present and future. Fam Cancer 20, 23-33 (2021). doi: 10.1007/s10689-020-00189-y. PMID: 32507936.

Familial Hypercholesterolemia

Category: Cardiovascular | **Genes: LDLR, APOB, PCSK9**

Familial Hypercholesterolemia (FH) is the most common autosomal dominant genetic disease. It is characterized by **extremely elevated low-density lipoprotein cholesterol (LDL-C)** levels and a **propensity to early-onset atherosclerotic cardiovascular disease.**

FH usually is caused by a functional **mutation of one of three genes: LDLR, PCSK9 and APOB**. Mutations in these genes interfere with the breakdown of LDL particles. They have additive gene dosing effects, such that patients with two pathogenic mutations (homozygotes or compound heterozygotes) are more adversely affected than those with one pathogenic mutation (heterozygotes).

In general, **homozygotes** manifest the disease at a much earlier age and the disease is more severe. They are **at risk of childhood onset CVD**, with an untreated LDL-C > 500 mg/dL (> 13 mmol/L). **Heterozygotes** have an **increased risk of premature CVD in early middle age**, with an LDL-C >160 mg/dL (> 4.1 mmol/L). In the absence of aggressive lipid lowering therapy, life span is significantly shortened.

Prevalence of heterozygous FH is estimated at 1 in 300 people worldwide. Homozygous FH has an estimated prevalence of 1 in 300,000 - 400,000.

Detected Variant (SNP) Table

Gene	SNP	Genotype	Inheritance	Chromosome	Position	Classification
LDLR	rs515726215	CT	SD	chr19	11089615	Pathogenic

Screening & Surveillance

- **Physical examination with detailed personal and family history.** The patient should be evaluated for the presence of other major risk factors for atherosclerotic CVD.
- **Annual fasting lipid profile.**
- Some recommend testing for **lipoprotein(a)** and **apoE** variants.
- **Imaging** may be performed for atherosclerosis.
- Adult homozygous patients and heterozygous patients who have not achieved their LDL-C goal with commonly used lipid-lowering agents or have evidence of CVD should be referred to a lipid specialist with expertise in FH.

Lifestyle Modifications

- Focus on a healthy diet that emphasizes the intake of vegetables, fruits, nuts, whole grains, lean vegetable or animal protein, and fish and minimizes the intake of trans fats, red meat and processed red meats, refined carbohydrates, and sweetened beverages.
- Maintaining a healthy weight is important. Most patients may benefit from referral to a dietitian or nutritionist.
- Regular physical activity (at least 150 minutes per week of accumulated moderate-intensity physical activity or 75 minutes per week of vigorous-intensity physical activity).
- Smokers should be assisted and strongly advised to quit smoking.

Medical Therapy

- High-potency statin, e.g. rosuvastatin, atorvastatin, is the first-line therapy for FH.
- Second-line therapy, e.g. ezetimibe or a PCSK9 inhibitor, is recommended for patients with heterozygous FH whose LDL-C remains above their goal despite the use of a high-potency statin, or who are unable to tolerate a high-potency statin.
- Refractory FH should be referred to a lipid specialist if the patient is not already under a specialist's care. Possible therapies for refractory disease include: colesevelam, bempedoic acid, evinacumab, lomitapide (for homozygous FH) and weekly or biweekly LDL apheresis.
- Aspirin is suggested for patients who have FH and clinically evident atherosclerotic CVD (75 - 100 mg/day). Some also recommend it to those with uncontrolled LDL-C.
- More intensive interventions are recommended for other CVD risk factors, such as hypertension and diabetes.

Surgery

For rare patients who have exhausted other options, liver transplantation or partial ileal bypass surgery may be considered.

Family Planning & Genetic Counseling

- FH is autosomal dominant, with a 50% inheritance risk.
- Lipid profiles are recommended for all first-degree relatives to identify other individuals at risk, including children beginning at age 2.
- For patients with FH attempting to conceive, lipid-lowering medications are generally paused from 6 to 12 weeks before the attempt, and throughout the duration of pregnancy and breastfeeding. In rare cases (e.g. a patient with homozygous FH and CVD), a statin might be continued during pregnancy. LDL apheresis is a possible therapeutic option for pregnancy with severe hypercholesterolemia.

References

- EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC), Global perspective of familial hypercholesterolaemia: a cross-sectional study from the EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC). Lancet. 398, 1713-1725 (2021). doi: 10.1016/S0140-6736(21)01122-3. PMID: 34506743.
- McGowan, M.P., Hosseini Dehkordi, S.H., Moriarty, P.M. et al. Diagnosis and Treatment of Heterozygous Familial Hypercholesterolemia. J Am Heart Assoc. 8, e013225 (2019). doi: 10.1161/JAHA.119.013225. PMID: 31838973.
- Di Taranto, M.D., Giacobbe, C. & Fortunato, G. Familial hypercholesterolemia: A complex genetic disease with variable phenotypes. Eur J Med Genet. 63, 103831 (2020). doi: 10.1016/j.ejmg.2019.103831. PMID: 31883481.
- Sturm, A.C., Knowles, J.W., Gidding, S.S. et al. Clinical Genetic Testing for Familial Hypercholesterolemia: JACC Scientific Expert Panel. J Am Coll Cardiol. 72(6), 662-680 (2018). doi: 10.1016/j.jacc.2018.05.044. PMID: 30071997.
- Arnett, D.K., Blumenthal, R.S., Albert, M.A. et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 140(11), e563-e595 (2019). doi: 10.1161/CIR.0000000000000677. PMID: 30879339.
- Harada-Shiba, M., Arai, H., Ohmura, H. et al. Guidelines for the Diagnosis and Treatment of Adult Familial Hypercholesterolemia 2022. J Atheroscler Thromb. 30(5), 558-586 (2023). doi: 10.5551/jat.CR005. PMID: 36682773.
- Benn, M., Watts, G.F., Tybjærg-Hansen, A. et al. Mutations causative of familial hypercholesterolaemia: screening of 98 098 individuals from the Copenhagen General Population Study estimated a prevalence of 1 in 217. Eur Heart J. 37(17), 1384-94 (2016). doi: 10.1093/eurheartj/ehw028. PMID: 26908947.
- Pearson, G.J., Thanassoulis, G., Anderson, T.J. et al. 2021 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in Adults. Can J Cardiol. 37(8), 1129-1150 (2021). doi: 10.1016/j.cjca.2021.03.016. PMID: 33781847.
- Grundy, S.M., Stone, N.J., Bailey, A.L. et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 139(25), e1082-e1143 (2019). doi: 10.1161/CIR.0000000000000625. PMID: 30586774.
- Stone, N.J., Robinson, J.G., Lichtenstein, A.H. et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 129(25 Suppl 2), S1-45 (2014). doi: 10.1161/01.cir.0000437738.63853.7a. PMID: 24222016.
- Khera, A.V., Won, H.H., Peloso, G.M. et al. Diagnostic Yield and Clinical Utility of Sequencing Familial Hypercholesterolemia Genes in Patients With Severe Hypercholesterolemia. J Am Coll Cardiol. 67(22), 2578-89 (2016). doi: 10.1016/j.jacc.2016.03.520. PMID: 27050191.
- Trinder, M., Li, X., DeCastro, M.L. et al. Risk of Premature Atherosclerotic Disease in Patients With Monogenic Versus Polygenic Familial Hypercholesterolemia. J Am Coll Cardiol. 74(4), 512-522 (2019). doi: 10.1016/j.jacc.2019.05.043. PMID: 31345425.
- de Ferranti, S.D., Rodday, A.M., Mendelson, M.M. et al. Prevalence of Familial Hypercholesterolemia in the 1999 to 2012 United States National Health and Nutrition Examination Surveys (NHANES). Circulation. 133(11), 1067-72 (2016). doi: 10.1161/CIRCULATIONAHA.115.018791. PMID: 26976914.
- Hu, P., Dharmayat, K.I., Stevens, C.A.T. et al. Prevalence of Familial Hypercholesterolemia Among the General Population and Patients With Atherosclerotic Cardiovascular Disease: A Systematic Review and Meta-Analysis. Circulation. 141(22), 1742-1759 (2020). doi: 10.1161/CIRCULATIONAHA.119.044795. PMID: 32468833.
- Thompson, G.R., Blom, D.J., Marais, A.D. et al. Survival in homozygous familial hypercholesterolaemia is determined by the on-treatment level of serum cholesterol. Eur Heart J. 39, 1162-1168 (2018). doi: 10.1093/eurheartj/ehx317. PMID: 29106543.

Biotinidase Deficiency

Category: Inborn Errors of Metabolism | **Gene: BTD**

Biotinidase deficiency is a rare autosomal recessive metabolic disorder, caused by **mutations in the BTD gene**, that **affects the body's ability to recycle biotin** (vitamin B7). The deficiency can be **partial or profound**. Without treatment, individuals with this condition can develop various neurological and skin-related symptoms and profound deficiency can be fatal.

Prevalence of clinical biotinidase deficiency is estimated to be 1 in 40,000 - 60,000 births. Carrier frequency in the general population is approximately 1 in 120.

Detected Variant (SNP) Table

Gene	SNP	Genotype	Inheritance	Chromosome	Position	Classification
BTD	rs515726215	CT	AR	chr19	11089615	Pathogenic

Screening & Surveillance

- Biotinidase deficiency is often detected through newborn screening, required in many countries. Early diagnosis is crucial because treatment can prevent or minimize symptoms.
- Once diagnosed, regular monitoring of biotinidase enzyme activity is recommended: annual for those with profound deficiency and every two years for those with partial deficiency.
- Follow-up visits might include assessment of clinical symptoms and neurocognitive development, with ophthalmology and audiology evaluations annually for those with profound deficiency and every two years for those with partial deficiency.

Lifestyle Modifications

- Patients must take daily biotin supplements for life. If symptoms such as skin rashes, hair loss, or neurological issues are present, treatment with biotin supplements typically improves or resolves them.
- Raw eggs should be avoided because they contain avidin, an egg white protein that binds biotin, thus decreasing its bioavailability. However, thoroughly cooked eggs present no problem because heating inactivates the protein.

Medical Therapy

- The cornerstone of treatment is lifelong biotin supplementation. The typical dose ranges from 5 to 10 mg per day, depending on the severity of the deficiency. In some cases doses up to 40 mg are warranted.
- In cases where treatment is delayed, some neurological symptoms may become irreversible. If neurological or other symptoms are present, additional treatments might be required, including physical therapy or hearing aids if hearing loss occurs.
- Skin rashes and hair loss, which are common symptoms of untreated biotinidase deficiency, can be managed with appropriate dermatological care.

Family Planning & Genetic Counseling

- Since biotinidase deficiency is inherited in an autosomal recessive manner, both parents need to carry one copy of the defective gene for a child to be affected. Genetic counseling is recommended for families with a history of the disorder or for those who have a child with the condition. The risk of having another child with the same condition is 25%.
- Carrier testing is available for at-risk relatives
- Prenatal (PND) and preimplantation genetic testing (PGD) are possible if the pathogenic variant in the family is known.

References

- Saleem, H. & Simpson, B. Biotinidase Deficiency. [Updated 2023 Feb 9]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560607/ PMID: 32809442.
- Wolf, B. Biotinidase Deficiency. 2000 Mar 24 [Updated 2023 May 25]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1322/


Cancer


Cardiac


Endocrine


Gastrointestinal


Hematologic


Metabolic


Neurologic


Renal


Vascular


Other

Condition Details

Familial Adenomatous Polyposis (FAP)

Category: Cancer | Gene: APC

Familial Adenomatous Polyposis (FAP) is an autosomal dominant disease caused by pathogenic **variants in the APC gene**. FAP is characterized by the development of **numerous adenomatous polyps in the colon and rectum**, significantly increasing the **risk of colorectal cancer**, as well as upper intestinal and extraintestinal tumors.

Classic FAP is characterized by the presence of 100 or more colorectal adenomas. An **attenuated form of FAP (AFAP)** is characterized by fewer colorectal adenomas (>10 to 99) with a later age of onset.

The incidence of FAP varies from 1 in 7,000 to 1 in 22,000 individuals.

Detected Variant (SNP) Table

Gene	SNP	Genotype	Inheritance	Chromosome	Position	Classification
BTD	rs515726215	CT	AR	chr19	11089615	Pathogenic

Screening & Surveillance

- **Colorectal Monitoring.** Individuals with a known pathogenic APC variant and classic FAP, should begin colonoscopy annually, starting at age 10 to 12. Surveillance following colectomy should include annual endoscopic examination of the rectum or ileal pouch, or examination of an ileostomy every two years. Individuals at risk for AFAP should have colonoscopy every one to two years, starting in the late teenage years. Patients with colorectal polyps should undergo polypectomy when feasible, followed by annual colonoscopy for surveillance
- **Upper endoscopy** using a forward-viewing endoscope for gastric polyps and a side-viewing duodenoscope for duodenal polyps at the time of onset of colonic adenomas or around age 20 to 25 years, whichever comes first. Subsequent upper endoscopic surveillance and management is guided by the severity of duodenal polyposis. Annual upper GI screening also involves H. pylori testing and eradication if positive (to reduce gastric cancer risk)
- **Thyroid ultrasound** starting in late teenage years, repeating every two to five years, due to a ~2% risk of thyroid carcinoma
- No routinely screening of all patients with FAP for intra-abdominal desmoids, but perform an abdominal computed tomography scan to assess for desmoids:
  - Prior to colectomy in patients at increased risk for desmoids
  - When there is a palpable abdominal mass on physical examination
  - When symptoms are suggestive of abdominal organ obstruction
- Hepatoblastoma screening in at-risk young children can be considered with liver ultrasound and AFP every 3–6 months until age 5

Lifestyle Modifications

While no specific lifestyle changes have been proven to prevent polyp formation, maintaining a balanced diet rich in fruits, vegetables, and fiber, along with regular physical activity, while avoiding smoking and excess alcohol is sensible, supports overall health and may aid in cancer prevention.

Medical Therapy

There is limited evidence that chemopreventive agents, such as aspirin or NSAIDs (sulindac or celecoxib), may suppress the recurrence of larger colorectal polyps in patients with FAP. However, no single agent or combination of agents has convincingly been shown to delay disease progression or obviate the need for surgery.