MUTYH

The *MUTYH* gene is a tumor suppressor gene. Tumor suppressor genes slow down cell division, repair DNA mistakes, or tell cells when to die. When they don't work properly, cells can grow out of control, which can lead to cancer. The primary role of *MUTYH* is to work together with other genes, including *MSH2* and *MSH6*, to recognize DNA mistakes and signal other genes to make repairs.

Like most genes, each person has two copies of the *MUTYH* gene: one inherited from each parent. Having two *MUTYH* mutations, one from each parent, causes a condition called MUTYH-associated polyposis (MAP). MAP is associated with a significantly increased risk for colorectal cancer and polyps, and potentially other cancers.

A mutation in a single *MUTYH* gene inherited from one parent slightly increases the risk for colorectal cancer.

How common are mutations in the *MUTYH* gene?

A single mutation in the *MUTYH* gene is found in 1-2% of people with Caucasian ancestry.[1] Further research is needed to clarify the frequency of mutations in the *MUTYH* gene in other populations.

How mutations in this gene impact risk

How a single *MUTYH* mutation affects women

If a woman has a single mutation in the *MUTYH* gene, her chance of developing colorectal cancer is greater than that of the average US woman. This does not mean that she has a diagnosis of cancer or that she will definitely develop cancer in her lifetime.

Cancer by age 80	Average US woman[2]	With single *MUTYH* mutation
Colorectal	2.8%	Elevated[3,4]

Elevated: Risk is increased, but further research may clarify the exact risk figure.

[1] Cleary SP, Cotterchio M, Jenkins MA, et al. Germline MutY human homologue mutations and colorectal cancer: a multisite case-control study. Gastroenterology. 2009;136:1251–60.
[2] Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute. 2010-2012. DevCan software (http://surveillance.cancer.gov/devcan) V 6.7.0, Accessed June 2015.
[3] Win AK, Dowty JG, Cleary SP, et al. Risk of colorectal cancer for carriers of mutations in MUTYH, with and without a family history of cancer. Gastroenterology. 2014;146(5):1208-11.e1-5.
[4] Theodoratou E, Campbell H, Tenesa A, et al. A large-scale meta-analysis to refine colorectal cancer risk estimates associated with MUTYH variants. Br J Cancer. 2010;103(12):1875-84.

How a mutation in each copy of the *MUTYH* gene affects women

If a woman has a mutation in each copy of the *MUTYH* gene, her chances of developing colorectal and small bowel cancer (especially in the duodenum) are greater than that of the average US woman. This does not mean that she has a diagnosis of cancer or that she will definitely develop cancer in her lifetime.

Cancer by age 80	Average US woman[2]	With mutation in each copy of *MUTYH*
Colorectal	2.8%	86%[3,5]
Small Bowel (Duodenal)	<1%	Elevated[6]

Elevated: Risk is increased, but further research may clarify the exact risk figure.

How a single *MUTYH* mutation affects men

If a man has a single mutation in the *MUTYH* gene, his chance of developing colorectal cancer is greater than that of the average US man. This does not mean that he has a diagnosis of cancer or that he will definitely develop cancer in his lifetime.

Cancer by age 80	Average US man[3]	With single *MUTYH* mutation
Colorectal	3.4%	Elevated[3,4]

Elevated: Risk is increased, but further research may clarify the exact risk figure.

How a mutation in each copy of the *MUTYH* gene affects men

If a man has a mutation in each copy of the *MUTYH* gene, his chances of developing colorectal and small bowel cancer (especially in the duodenum) are greater than that of the average US man. This does not mean that he has a diagnosis of cancer or that he will definitely develop cancer in his lifetime.

Cancer by age 80	Average US man[3]	With mutation in each copy of *MUTYH*
Colorectal	3.4%	88%[3,5]
Small Bowel (Duodenal)	<1%	Elevated[6]

[5] Nieuwenhuis MH, Vogt S, Jones N, et al. Evidence for accelerated colorectal adenoma–carcinoma progression in MUTYH-associated polyposis?. Gut. 2012;61(5):734-8.
[6] Vogt S, Jones N, Christian D, et al. Expanded extracolonic tumor spectrum in MUTYH-associated polyposis. Gastroenterology. 2009;137(6):1976-85.e1-10.

Elevated: Risk is increased, but further research may clarify the exact risk figure.

Additional information

Like most genes, our understanding of *MUTYH* has evolved with time.
The *MUTYH* gene was initially thought to be important only if a person had a mutation in each copy, causing MAP. Only in the last several years have researchers discovered having a single mutation is also associated with an increased colorectal cancer risk, though to a much milder extent.

Screening guidelines for individuals with a single *MUTYH* mutation

Below is a summary of screening guidelines from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) established by experts at the National Comprehensive Cancer Network (NCCN).[7] They are for individuals with a mutation in the *MUTYH* gene. If you have a mutation in this gene, your healthcare provider may use these NCCN Guidelines® to help create a customized screening plan for you.

Women and Men

Colorectal cancer[8]

- Beginning at age 40 or 10 years younger than the earliest diagnosis of colorectal cancer in a parent, sibling, or child (whichever is earlier): Colonoscopy every 5 years.
- These recommendations may change if you have polyps, colorectal cancer, inflammatory bowel disease (IBD), or family history of colorectal cancer.

Screening guidelines for individuals with a mutation in each copy of *MUTYH*

Below is a summary of screening guidelines from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) established by experts at the National Comprehensive Cancer Network (NCCN).[7] They are for individuals who have a mutation in each copy of the *MUTYH* gene. If you have a mutation in each copy of this gene, your healthcare provider may use these NCCN Guidelines® to help create a customized screening plan for you.

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[8] National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Colorectal. NCCN Guidelines Version 2.2016. Available at www.nccn.org. Published September 2016.

Women and Men

Colorectal cancer[8]

- Starting at age 25-30: Colonoscopy every 2-3 years if no polyps are found.
- Depending on age and number of polyps: Colonoscopy every 1-2 years and evaluation for colectomy (surgical removal of the colon and/or rectum).
- If colectomy is necessary: Speak to your provider about recommended follow up, which may include surveillance with endoscopy, and medications to reduce the risk of polyps and cancer.

Small bowel cancer (duodenal and other sections)[8]

- Starting at age 30-35 years: Baseline upper endoscopy (including complete visualization of the ampulla of Vater). Frequency of the endoscopy depends on the number and size of polyps identified.

Other MAP-related conditions[8]

- Physical exam annually.

Useful resources

Colon Cancer Alliance

An organization dedicated to colon cancer prevention, funding colon cancer research and providing support to patients.
www.ccalliance.org

Hereditary Colon Cancer Foundation

A nonprofit organization serving the hereditary colorectal cancer community.
www.hcctakesguts.org

Kintalk

An educational and family communication site for individuals and their families with hereditary cancer conditions
www.kintalk.org

Last updated May 15, 2017