

## POLD1

The *POLD1* 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 *POLD1* is to fix mutations that occur as the DNA in the cell copies itself.

Like most genes, each person has two copies of the *POLD1* gene: one inherited from each parent. A mutation in a single *POLD1* gene inherited from either parent causes Polymerase Proofreading-Associated Polyposis (PPAP), which is known to increase risks for colorectal cancer and polyps.

To date, studies on the *POLD1* gene have been focused primarily on one specific mutation. Research on the *POLD1* gene is ongoing, especially related to the exact cancers and cancer risks associated with other mutations in this gene.

### How common are mutations in the *POLD1* gene?

Mutations in the *POLD1* gene are rare—the exact frequency is not yet known. Studies to establish the frequency of *POLD1* mutations are ongoing.

## How mutations in this gene impact risk

### Women

If a woman has a mutation in the *POLD1* 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 95 | Average US woman <sup>1</sup> | With <i>POLD1</i> mutation  |
|------------------|-------------------------------|-----------------------------|
| Colorectal       | 4.2%                          | Elevated <sup>2,3,4,5</sup> |

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

<sup>1</sup> 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.

<sup>2</sup> Bellido F, Pineda M, Aiza G, et al. POLE and POLD1 mutations in 529 kindred with familial colorectal cancer and/or polyposis: review of reported cases and recommendations for genetic testing and surveillance. *Genet Med*. 2016;18(4):325-32.

<sup>3</sup> Palles C, Cazier JB, Howarth KM, et al. Germline mutations affecting the proofreading domains of POLE and POLD1 predispose to colorectal adenomas and carcinomas. *Nat Genet*. 2013;45(2):136-44.

<sup>4</sup> Church JM. Polymerase proofreading-associated polyposis: a new, dominantly inherited syndrome of hereditary colorectal cancer predisposition. *Dis Colon Rectum*. 2014;57(3):396-7.

<sup>5</sup> Valle L, Hernández-illán E, Bellido F, et al. New insights into POLE and POLD1 germline mutations in familial colorectal cancer and polyposis. *Hum Mol Genet*. 2014;23(13):3506-12.

## Men

If a man has a mutation in the *POLD1* 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 95 | Average US man <sup>1</sup> | With <i>POLD1</i> mutation  |
|------------------|-----------------------------|-----------------------------|
| Colorectal       | 4.6%                        | Elevated <sup>2,3,4,5</sup> |

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

## Additional information

### Not all *POLD1* mutations are linked to increased cancer risk.

For *POLD1*, only chr19:g.50909713 (including c.1433G>A) is analyzed, because other positions are not known to impact cancer risk.

## Screening guidelines

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).<sup>6</sup> They are for individuals who have a mutation in the *POLD1* 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<sup>7</sup>

- **Starting at age 25-30:** Colonoscopy every 2–3 years.
- **Depending on age and number of polyps:** Colonoscopy every 1-2 years and evaluation for colectomy (surgical removal of the colon and/or rectum).
- These recommendations may change if you have, colorectal cancer, inflammatory bowel disease (IBD), or family history of colorectal cancer.

<sup>6</sup> Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Colorectal. V.2.2016. © National Comprehensive Cancer Network, Inc 2016. All rights reserved. Accessed October 26, 2016. To view the most recent and complete version of the guideline, go online to NCCN.org. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, NCCN GUIDELINES®, and all other NCCN Content are trademarks owned by the National Comprehensive Cancer Network, Inc.

<sup>7</sup> National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Colorectal. NCCN Guidelines Version 2.2016. Available at [www.nccn.org](http://www.nccn.org). Published September 2016.

## Useful resources

### **Colon Cancer Alliance**

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

[www.ccalliance.org](http://www.ccalliance.org)

### **Hereditary Colon Cancer Foundation**

A nonprofit organization serving the hereditary colorectal cancer community.

[www.hcctakesguts.org](http://www.hcctakesguts.org)

### **Kintalk**

An educational and family communication site for individuals and their families with hereditary cancer conditions

[www.kintalk.org](http://www.kintalk.org)

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