

## ATM

The *ATM* 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 *ATM* is coordinating a response to damaged DNA so it can be repaired by other genes, including *BRCA1*, *NBN*, *TP53*, and *CHEK2*.

Like most genes, each person has two copies of the *ATM* gene: one inherited from each parent. A mutation in a single *ATM* gene inherited from either parent is known to increase risk of certain cancers over a lifetime, including breast, pancreatic, prostate, and possibly others.

Some studies have suggested that individuals with *ATM* mutations have a higher sensitivity to ionizing radiation, such as that used in treating cancer. Women with *ATM* mutations who were treated for breast cancer with radiation therapy have been shown to develop new breast cancers more often than women with *ATM* mutations who were not treated with radiation therapy or women without *ATM* mutations.<sup>1,2</sup> More research is needed to clarify these risks further. We recommend discussing this with your provider.

In very rare cases, a person can inherit two *ATM* mutations, one from each parent. This causes a condition called Ataxia-Telangiectasia, which is associated with increased risk for childhood cancers, as well as impairments of the nervous and immune systems.

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

Mutations in the *ATM* gene are rare—found in approximately 0.5-1% of people of Caucasian ancestry.<sup>3</sup> Studies to establish how common *ATM* mutations are in other populations are ongoing.

## How mutations in this gene impact risk

### Women

If a woman has a mutation in the *ATM* gene, her chances of developing breast and pancreatic cancer 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.

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<sup>1</sup> Broeks A, Braaf LM, Huseinovic A, et al. Identification of women with an increased risk of developing radiation-induced breast cancer: a case only study. *Breast Cancer Res.* 2007;9(2):R26.

<sup>2</sup> Cardis E, Hall J, Tavtigian SV. Identification of women with an increased risk of developing radiation-induced breast cancer. *Breast Cancer Res.* 2007;9(3):106.

<sup>3</sup> Swift M, Morrell D, Cromartie E, Chamberlin AR, Skolnick MH, Bishop DT. The incidence and gene frequency of ataxia-telangiectasia in the United States. *Am J Hum Genet.* 1986;39(5):573-83.

Cancer by age 70	Average US woman <sup>4</sup>	With ATM mutation
Breast	7.1%	Elevated (16-26%) <sup>5</sup>
Pancreatic	<1%	Elevated <sup>6</sup>

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

## Men

If a man has a mutation in the ATM gene, his chances of developing pancreatic and prostate 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 70	Average US man <sup>4</sup>	With ATM mutation
Pancreatic	<1%	Elevated <sup>6</sup>
Prostate	7.2%	Elevated <sup>78</sup>

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

## 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>9</sup> They are for individuals with a mutation in the ATM 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.

<sup>4</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>5</sup> Easton DF, Pharoah PD, Antoniou AC, et al. Gene-panel sequencing and the prediction of breast-cancer risk. *N Engl J Med*. 2015;372(23):2243-57.

<sup>6</sup> Roberts NJ, Jiao Y, Yu J, et al. ATM mutations in patients with hereditary pancreatic cancer. *Cancer Discov*. 2012;2(1):41-6.

<sup>7</sup> Pritchard CC, Mateo J, Walsh MF, et al. Inherited DNA-Repair Gene Mutations in Men with Metastatic Prostate Cancer. *N Engl J Med*. 2016;375(5):443-53.

<sup>8</sup> Na R, Zheng SL, Han M, et al. Germline Mutations in ATM and BRCA1/2 Distinguish Risk for Lethal and Indolent Prostate Cancer and are Associated with Early Age at Death. *Eur Urol*. 2017;71(5):740-747.

<sup>9</sup> Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast and Ovarian V.1.2017 and Breast Cancer Screening and Diagnosis V.1.2016. © National Comprehensive Cancer Network, Inc 2016. All rights reserved. Accessed September 20, 2016. To view the most recent and complete version of the guideline, go online to [NCCN.org](http://NCCN.org). NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, NCCN GUIDELINES®, and all other NCCN Content are trademarks owned by the National Comprehensive Cancer Network, Inc.

**Women**Breast<sup>10</sup>

- **Starting at age 40:** Your provider may discuss mammogram and breast MRI with contrast every year.
- Your provider may discuss the option of having a risk-reducing bilateral mastectomy (the surgical removal of both breasts) based on family history.

Pancreatic cancer<sup>11</sup>

- Currently, there are no pancreatic cancer screening guidelines from the NCCN specific to ATM mutation carriers. Your provider may discuss screening or referral to a specialist.

**Men**Pancreatic cancer<sup>11</sup>

- Currently, there are no pancreatic cancer screening guidelines from the NCCN specific to ATM mutation carriers. Your provider may discuss screening or referral to a specialist.

## Prostate cancer

- Currently, there are no prostate cancer screening guidelines from the NCCN specific to ATM mutation carriers. Your provider may discuss screening or referral to a specialist.

**Useful resources****FORCE**

Providing support, education, research, and resources for survivors and people at increased risk of cancer due to an inherited mutation or family history of cancer.

[www.facingourrisk.org](http://www.facingourrisk.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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<sup>10</sup> National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Breast and Ovarian. *NCCN Guidelines Version 1.2017*. Available at [www.nccn.org](http://www.nccn.org). Published September 2016.

<sup>11</sup> Canto MI, Harinck F, Hruban RH, et al. International Cancer of the Pancreas Screening (CAPS) Consortium summit on the management of patients with increased risk for familial pancreatic cancer. *Gut*. 2013;62(3):339-47.

**Susan G. Komen**

Dedicated to reducing deaths from breast cancer by funding breast cancer research, ensuring access to care through community programs worldwide and supporting public health policies that help people facing breast cancer.

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

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