TP53

The *TP53* 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 *TP53* is to make the critical decision of whether to repair damaged DNA or instruct the cell to die by a process known as apoptosis. The death of cells with significant DNA damage helps to prevent these cells from growing out of control and becoming a tumor.

Like most genes, each person has two copies of the *TP53* gene: one inherited from each parent. A mutation in a single *TP53* gene inherited from either parent is known to cause Li-Fraumeni syndrome, which leads to a high chance for cancers such as breast, brain, sarcoma, and others, at unusually young ages.

How common are mutations in the *TP53* gene?
Mutations in the *TP53* gene are extremely rare—found in approximately 1 in 20,000 individuals in the general population.[1]

How mutations in this gene impact risk

Women
If a woman has a mutation in the *TP53* gene, her chance of developing certain cancers, especially breast, brain, and sarcoma (cancer of the bone and soft tissue), is greater than that of the average US woman. Other Li-Fraumeni related cancers include adrenocortical carcinoma, colorectal, leukemia, liver, lung, lymphoma, melanoma, pancreas, and stomach. This does not mean that she has a diagnosis of cancer or that she will definitely develop cancer in her lifetime.

Because having a *TP53* mutation is rare, specific risk estimates for each cancer are not available.

Any cancer by age	Average US woman[2]	With *TP53* mutation[3]
20	<1%	18%
30	<1%	49%

[1] Gonzalez KD, Noltner KA, Buzin CH, et al. Beyond Li Fraumeni Syndrome: clinical characteristics of families with p53 germline mutations. J Clin Oncol. 2009;27(8):1250-6.
[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] Hwang SJ, Lozano G, Amos CI, Strong LC. Germline p53 mutations in a cohort with childhood sarcoma: sex differences in cancer risk. *Am J Hum Genet.* 2003;72(4):975-83.

40	2%	77%
50	5%	93%

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

Men

If a man has a mutation in the *TP53* gene, his chances of developing certain cancers, especially brain cancer and sarcoma, 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.

Because having a *TP53* mutation is rare, specific risk estimates for each cancer are not available.

Any cancer by age	Average US man[2]	With *TP53* mutation[3]
20	<1%	10%
30	<1%	21%
40	1.5%	33%
50	3.4%	68%

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

Additional information

Many cancers and tumors have a mutation in the *TP53* gene.

Genetic testing on tumor tissue is sometimes performed to provide information about prognosis and potential targeted treatments. These tests look for DNA changes that occurred while the cancer was forming, and often a mutation is found in the *TP53* gene. These changes are only in the cancer cells, not in any other cells of the body, and were not inherited from parents, nor can they be passed down to children. On the other hand, tests like the Color Test analyze the genetic makeup that was inherited from parents, which can be found in all cells of the body. The primary purpose of the Color Test is to find any potential inherited risk factors for cancer in order to provide detailed information about the risk of developing other cancers in the future, as well as to give important information to family members.

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) and other experts in Li-Fraumeni syndrome.[4] They are for individuals who have a mutation in the *TP53* 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. Additionally, promptly report any medical concerns or discomforts to your provider.

Women

Breast cancer[5]

- Starting at age 18: Breast awareness - Women should be familiar with their breasts and promptly report changes to their healthcare provider. Performing regular breast self exams may help increase breast awareness, especially when checked at the end of the menstrual cycle.
- Starting at age 20-25, or at the age of the earliest diagnosed breast cancer in the family, if below age 20 years: Breast exam by your provider every six months.
- Between ages 20-29: Breast MRI screening with contrast (preferred) every year or mammogram if MRI is unavailable.
- Between ages 30-75: Mammogram and breast MRI screening with contrast every year. Your provider may wish to alternate between these two screenings every 6 months.
- After age 75: Your provider may discuss an individualized management plan with you.
- Your provider may discuss the option of having a risk-reducing bilateral mastectomy (the surgical removal of both breasts).

Brain cancer and tumors[5,,6]

- Brain MRI every year, which may be part of a rapid total body MRI (recommended for sarcoma)

Sarcoma[5,6]

- Rapid total body MRI or equivalent every year, preferably as part of a long-term study
- Ultrasound of abdomen and pelvis every 6 months

Colorectal cancer[5]

- Starting at age 25, or 5 years before the earliest known colon cancer in the family: Colonoscopy every 2-5 years

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[4] 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. © 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. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, NCCN GUIDELINES®, and all other NCCN Content are trademarks owned by the National Comprehensive Cancer Network, Inc.

[5] National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Breast and Ovarian. *NCCN Guidelines Version 1.2017.* Available at www.nccn.org. Published September 2016.

[6] Villani A, Tabori U, Schiffman J, et al. Biochemical and imaging surveillance in germline TP53 mutation carriers with Li-Fraumeni syndrome: a prospective observational study. *Lancet Oncol.* 2011;12(6):559-67.

Leukemia and lymphoma[6]
- Blood tests (complete blood count, erythrocyte sedimentation rate, and lactate dehydrogenase) every 4 months

Melanoma[5,6]
- Skin examination by a dermatologist every year

Other cancers related to Li-Fraumeni syndrome[5]
- Annual physical exam by your provider, including a neurologic exam
- Avoid radiation therapy for treatment of cancer when possible
- Other screening may be recommended by your provider based on your family history of cancer

Men

Brain cancer and tumors[5,6]
- Brain MRI every year, which may be part of a rapid total body MRI (recommended for sarcoma)

Sarcoma[5,6]
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- Ultrasound of abdomen and pelvis every 6 months

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Useful resources

Li-Fraumeni Syndrome (LFS) Association
Provides a wide range of information, advocacy, and support services for individuals and families with Li-Fraumeni Syndrome.
www.lfsassociation.org

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

Bright Pink
Focused on the prevention and early detection of breast and ovarian cancer in young women, while providing support for high-risk individuals.
www.brightpink.org

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

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