

CDK4

The CDK4 gene is an oncogene. Oncogenes are involved in cell growth. When they don't work properly, cells can grow out of control, which can lead to cancer. The primary role of *CDK4* is to guide the cell through the process of copying its genetic material in order to divide.

Like most genes, each person has two copies of the *CDK4* gene: one inherited from each parent. A mutation in a single *CDK4* gene inherited from either parent is known to increase risk of melanoma.

Individuals with a *CDK4* mutation have an increased risk of developing dysplastic nevi (atypical moles) which must be monitored because they can change into melanoma. Certain factors can greatly increase risk of melanoma, including an individual's geographic region, ethnicity and sun exposure. For example, melanoma is 20 times more common in Caucasians than it is in African Americans.¹

How common are mutations in the *CDK4* gene?

Mutations in the *CDK4* gene are rare—the exact frequency is not yet known. Studies to establish the frequency of *CDK4* mutations are ongoing.

How mutations in this gene impact risk

Women

If a woman has a mutation in the *CDK4* gene, her chance of developing melanoma 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 ² | With <i>CDK4</i> mutation |
|------------------|-------------------------------|---------------------------|
| Melanoma | 1.6% | Elevated ^{3,4} |

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

¹ What are the risk factors for melanoma skin cancer? American Cancer Society Website.

<http://www.cancer.org/cancer/skincancer-melanoma/detailedguide/melanoma-skin-cancer-risk-factors> Updated February 01, 2016.

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 Goldstein AM, Chan M, Harland M, et al. High-risk melanoma susceptibility genes and pancreatic cancer, neural system tumors, and uveal melanoma across GenoMEL. *Cancer Res.* 2006;66(20):9818-28.

⁴ Puntervoll HE, Yang XR, Vetti HH, et al. Melanoma prone families with *CDK4* germline mutation: phenotypic profile and associations with MC1R variants. *J Med Genet.* 2013;50(4):264-70.

Men

If a man has a mutation in the *CDK4* gene, his chance of developing melanoma 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 ² | With <i>CDK4</i> mutation |
|------------------|-----------------------------|---------------------------|
| Melanoma | 2.6% | Elevated ^{3,4} |

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

Additional information**Not all *CDK4* mutations are linked to increased cancer risk.**

For *CDK4*, only chr12:g.58145429-58145431 (codon 24) is analyzed, because other positions are not known to impact cancer risk.

Screening guidelines

Below is a summary of screening guidelines from the American Cancer Society (ACS). Because there are no published screening guidelines specific to individuals with *CDK4* mutations, these guidelines are for individuals who have the same risk of melanoma as the average US individual. If you have a mutation in this gene, your healthcare provider may use these ACS Guidelines to help create a customized screening plan for you. They might also make additional recommendations to reduce the risk of melanoma.

Women and Men**Melanoma⁵**

- Your healthcare provider may discuss skin exams and eye exams for melanoma screening.
- To reduce the chance of developing melanoma, the American Cancer Society recommends limiting exposure to UV light by avoiding excess sun exposure, wearing a hat, sunglasses and long protective clothing, applying sunscreen with SPF of 30 or higher and avoiding tanning beds and sun lamps.
- Any new, unusual, or changing moles should be reported to your provider or dermatologist.

⁵ Skin Cancer Prevention and Early Detection. The American Cancer Society. Available at www.cancer.org. Updated 3/20/2015. Accessed April 2015.

Useful resources

American Melanoma Foundation

An organization supporting melanoma research, and providing advocacy and public awareness of melanoma.

www.melanomafoundation.org

Kintalk

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

www.kintalk.org

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