

HOXB13 Mutations

Cancer Risks and General Management Recommendations

Currently only one known pathogenic variant is well-established in *HOXB13*, the G84E variant. Multiple studies have shown that the c.251G>A (p.Gly84Glu) variant in *HOXB13*, also known as G84E, is associated with an increased risk of prostate cancer.^{1,2} This variant is associated with earlier-onset prostate cancer (<55 years). Individuals with this variant are more likely to have a family history of prostate cancer.

| HOXB13 Mutation Carrier Cancer Risks | General Population Lifetime Cancer Risks | Surveillance/Management Recommendations |
|---|---|---|
| Prostate ^{3,4} 33-60% | 11.2% | <p><i>Surveillance</i></p> <ul style="list-style-type: none"> • No NCCN management guidelines have been established • The following surveillance strategy has been proposed by the Philadelphia Prostate Cancer Consensus 2017:⁵ <ul style="list-style-type: none"> ○ Baseline PSA at age 40 years, or 10 years prior to the youngest prostate cancer diagnosed in the family ○ PSA testing to be performed annually, or as dictated by the baseline PSA • Consult with physician to determine appropriate prostate cancer risk management options |

Other Cancer Risks: While there has been suggestion of the potential for other cancers to be associated with *HOXB13*, none are currently well-established. As *HOXB13* was recently identified, the cancer risks and management recommendations for mutations carriers may evolve over time.

Implications for Family Members/Reproductive Considerations

- First-degree relatives (i.e., parents, siblings, and children) have a 50% chance to have the familial *HOXB13* mutation. Second-degree relatives (i.e., nieces/nephews, aunts/uncles, and grandparents) have a 25% chance to have the familial mutation.
- For carriers of a known mutation, assisted reproduction (with or without egg or sperm donation), pre-implantation genetic testing, and prenatal diagnosis options exist.
- All family members are encouraged to pursue genetic counseling to clarify their risks. Family members can visit www.FindAGeneticCounselor.com to find genetic services near them.

References

1. Huang H, Cai B. G84E mutation in HOXB13 is firmly associated with prostate cancer risk: a meta-analysis. *Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine*. 2014;35(2):1177-1182.
2. MacInnis RJ, Severi G, Baglietto L, et al. Population-Based Estimate of Prostate Cancer Risk for Carriers of the HOXB13 Missense Mutation G84E. *PLOS ONE*. 2013;8(2):e54727.
3. Cai Q, Wang X, Li X, et al. Germline HOXB13 p.Gly84Glu mutation and cancer susceptibility: a pooled analysis of 25 epidemiological studies with 145,257 participants. *Oncotarget*. 2015;6(39):42312-42321.

4. Witte JS, Mefford J, Plummer SJ, et al. HOXB13 mutation and prostate cancer: studies of siblings and aggressive disease. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*. 2013;22(4):675-680.
5. Giri VN, Knudsen KE, Kelly WK, et al. Role of Genetic Testing for Inherited Prostate Cancer Risk: Philadelphia Prostate Cancer Consensus Conference 2017. 2018;36(4):414-424.