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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%	*Surveillance*
		• No NCCN management guidelines have been established
		• The following surveillance strategy has been proposed by the Philadelphia Prostate Cancer Consensus 2017:[5]
		  ○ 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

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