Ambry Genetics

RESEARCH FOR YOUR PRACTICE

Should We Be Testing the *PTEN* Promoter?

ARE WE INCREASING DETECTION RATES OR LEFT WITH UNCERTAIN RESULTS?

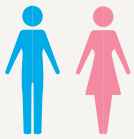
A recent collaboration between Ambry Genetics and The Ohio State University published in JCO Precision Oncology[1] illustrates the lack of association between variants in the *PTEN* promoter and cancer risk.

WHY THIS MATTERS TO YOU

The goal of genetic testing is to better understand a patient's risk for cancer so that we can personalize medical management. Through our study we found the significant number of variants of uncertain significance (VUS) identified in the *PTEN* promoter increases the likelihood of uncertainty for patients, without providing added clinical benefit.

BACKGROUND

- *PTEN* mutations account for about 35% of Cowden syndrome, which confers increased risks for breast, colon, endometrial, renal cell, and thyroid cancers[2]
- Evidence supporting the relationship between *PTEN* promoter variants and Cowden syndrome is limited and contradictory[3-6]
- Increased screening and management for cancer is typically not offered for patients who carry a VUS. Currently, all variants identified in the *PTEN* promoter are classified as VUS or benign[1]
- In this collaboration, researchers assessed 88,333 patients undergoing multigene panel testing (MGPT) to determine whether variants in the *PTEN* promoter were associated with breast and other cancers, as well as the age of onset compared to other pathogenic, non-promoter *PTEN* mutations, and controls.



88,333 patients assessed

– no cancer association observed

POINTS FOR YOUR PRACTICE

- Testing for the *PTEN* gene, including sequencing of the *PTEN* promoter region, is included on the majority of MGPT at Ambry Genetics and other labs.
- Inclusion of the *PTEN* promoter during genetic testing significantly increases the gene-specific VUS rate.
  - Exclusion of this region would result in > 80% decrease in *PTEN* VUS.
- Currently, all variants identified in the *PTEN* promoter region are classified as VUS or benign and are not clinically relevant; therefore, testing of this region may not be needed, as it does not increase the detection of patients with Cowden syndrome.

"PTEN promoter variants were not associated with cancer. These results do not support the inclusion of PTEN promoter sequencing in MGPT" – Study authors

SIGNIFICANT FINDINGS

- Patients with *PTEN* promoter variants were NOT significantly more likely than negative patients to have any of the studied cancer types.
- When compared to negative patients, individuals with pathogenic *PTEN* mutations outside of the promoter region were:
  - Significantly younger at breast cancer diagnosis

Learn more about our research here.

REFERENCES

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