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 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.
- Evidence supporting the relationship between *PTEN* promoter variants and Cowden syndrome is limited and contradictory.
- 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.
- 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.

**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

- **2.3X** more likely to have breast cancer
- **7.23X** more likely to have bilateral/multiple primary breast cancer
- **7.56X** more likely to have uterine/endometrial cancer

Learn more about our research [here](#).

**REFERENCES**

1. Black MH, Li S et al. *PTEN* Promoter variants are not associated with common cancers: implications for multigene panel testing. JCO Prec Onc. October 2017