Researchers create 'scoring system' for PTEN mutation testing

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Researchers have discovered a method for more precise identification of individuals who should undergo testing for genetic mutations of the tumor suppressor gene PTEN, which associates with a variety of conditions including several types of cancers. The research has created a diagnostic scoring system that improves on established criteria.

Led by Charis Eng, M.D., Ph.D., Chair of the Genomic Medicine Institute at the Lerner Research Institute of Cleveland Clinic, the study – the largest clinical study to date on the identification of PTEN – involved 3,042 participants, including both adults and children. Dr. Eng and her team established a semi-quantitative diagnostic score as an evidence-based improvement over the existing National Comprehensive Cancer Network (NCCN) 2010 diagnostic criteria, resulting in more accurate diagnoses and, theoretically, better outcomes.

These results contribute to clinical practice recommendations. "The new criteria give non-genetics healthcare providers a guide of who should be referred to genetics evaluation, which includes genetic counseling," said Dr. Eng. "Knowing one's PTEN gene status will lead to personalized cancer screening, resulting in catching cancers earlier or even preventing them from coming at all."

In addition to the association between mutant PTEN and disease, the study's novel scoring system also incorporates the amount of PTEN protein as it relates to disease. A higher diagnostic score correlates with lower PTEN protein, substantiating previous laboratory studies that show

lower PTEN levels associate with carcinogenesis. "This is the first human evidence of a causal relationship between PTEN protein deficiency and disease manifestation, which had only been previously been shown in the laboratory dish or animal model," Eng remarked.

Researchers studied an international group of 290 patients who carry disease-causing PTEN mutations, which exceeds the total number of such patients reported in all published medical literature by 37 percent. The study also hails higher stringency, as only probands (the first family member to be affected by the disease) were included. This increases the study's ability to assess each disease feature, such as macrocephaly (larger-than-normal head size), various cancers and age at onset, as well as skin, neurologic, and gastrointestinal complications, without bias.

For the first time, the scoring system provides criteria for addressing important differences in assessing pediatric versus adult patients. Furthermore, autism, which was first linked to mutant PTEN by Dr. Eng and her team, is included in the clinical criteria. Although vascular malformations (altered blood vessels) have long been reported in adults with Cowden syndrome, the malformations are not part of NCCN criteria. In contrast, the newly discovered criteria specifically recommend these patients undergo further genetic testing for early diagnosis of other lurking complications, such as cancers, so that more careful screening can occur.

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