Cleveland Clinic Innovations

PRODUCT

Method for Prediction of Clinical Outcomes in Patients with Germline *PTEN* Mutations

INDICATION

PTEN harmartoma tumor syndrome, Autism Spectrum Disorder, Neurodevelopmental Disorders, Cancer.

VALUE PROPOSITION

- Bioinformatics approach with high predictive index for diagnosis of NDD versus cancer in germline PTEN mutation carriers
- Available to develop into commercial genotyping arrays and CNV analysis tools

DEVELOPMENT STAGE

- Clinical validation complete

INTELLECTUAL PROPERTY

US Patent application filed.

RELATED PUBLICATIONS

Yehia *et al* 2020. "Copy Number Variation and Clinical Outcomes in Patients With Germline PTEN Mutations." JAMA network open

CONTACT INFORMATION

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Method to predict clinical outcome of *PTEN* mutation individuals

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UNMET NEED

Identifying gene mutations or variations in copy number have been one of the most powerful approaches to identify persons at high risk for a disease**.** *PTEN* germline alterations are among the most common causes of neurodevelopmental disorders (NDD), including autism spectrum disorder. Moreover, *PTEN* mutations have a well-established role in increasing lifetime risks of acquiring *PTEN* hamartoma tumor syndrome (PHTS). It is presently impossible to predict at an individual level precisely which *PTEN* mutation carrier will develop which cancer(s) and/or NDD. As such, why one gene contributes to such disparate disorders, even in patients with identical mutations, remains poorly understood.

SOLUTION

Researchers at Cleveland Clinic have developed a bioinformatics approach and method to predict cancer (PHTS) versus neurodevelopmental disorders (NDD) risk in *PTEN* mutation positive individuals. Copy number variation (CNV), a common type of structural variation in the human genome, is considered an important contributor to nonsyndromic idiopathic Autism Spectrum Disorder (ASD) and sporadic cancer. CNVs have also been associated with complex disorders, particularly those involving developmental delay, intellectual disabilities, and/or congenital anomalies. The invention described herein is based on the finding that specific CNV associations in individuals carrying germline *PTEN* mutations could predict for developing ASD/NDD versus cancer clinical phenotypes at an individual level. The presence of germline CNVs in conjunction with germline PTEN mutations may be determined using a variety of commercially available genotyping arrays and CNV analysis tools. Lastly, identifying an increased CNV burden and/or the presence of pathogenic or likely pathogenic CNVs offer a high predictive index for diagnosis of NDD versus cancer in germline PTEN mutation carriers.

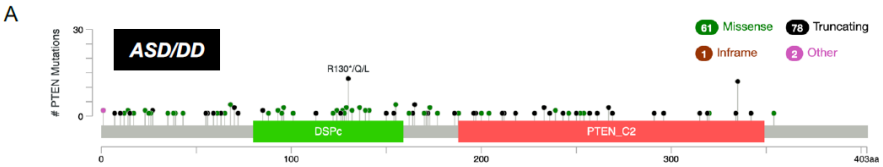

Fig 1: PTEN Mutation spectra across PHTS Clinical Phenotype Group