Newman H[1], Powis Z[1], Yussuf A[1], Wang J[1]
[1]*Ambry Genetics, Aliso Viejo, CA, 92656*

Phenotype is not Always a Positive Predictor of Detection Rate in Epilepsy Panels

OBJECTIVE:

To present the initial mutation spectrum and investigate whether phenotype influences detection rates in targeted NGS (next generation sequencing) epilepsy panels.

BACKGROUND:

Comprehensive NGS panels are being used as first tier testing to confirm or identify molecular diagnoses in individuals with broad epilepsy phenotypes.

DESIGN/METHODS:

Retrospective analysis was performed on 166 unselected individuals tested on multi gene epilepsy panels using a combination of NGS sequencing and targeted microarray analyses.

RESULTS:

We identified mutations in 22% of individuals tested (36/166), while the remaining 51% (85/166) and 27% (45/166) of individuals were inconclusive and negative, respectively. The three most commonly mutated genes were *SCN1A* (8 individuals), *KCNQ2* (6 individuals), and *PRRT2* (5 individuals). In addition, mutations were found in multiple individuals in *PCDH19, TPP1*, and *CDKL5.* Interestingly, there were no significant differences between percentages of individuals with certain phenotypic presentations in specific test result categories. 96% of all individuals tested (160/166) had seizures; similarly, 97%, 95%, and 98% of individuals with positive, inconclusive, and negative results had seizures. The total percentage of individuals with abnormal EEG findings was 61% (101/166); similarly, 56%, 59%, and 69% of individuals with positive, inconclusive, and negative results had abnormal EEG findings. 52% of all individuals tested (86/166) had DD/ID, whereas 50%, 52%, and 53% of individuals with positive, inconclusive, and negative results had DD/ID. The total percentage of individuals with regression/plateau was 14% (23/166), similarly, 6%, 16%, and 16% of individuals with positive, inconclusive, and negative results had regression/plateau.

CONCLUSIONS:

While these data show that phenotype may not be a good positive predictor of detection rate in epilepsy panels, they also demonstrate the utility of panel testing for individuals with broad spectrum epilepsy phenotypes. This finding is clinically relevant as it suggests that it is not

possible to determine beforehand which epilepsy phenotypes should be considered most appropriate for genetic testing.