The Diagnostic Utility of Exome Sequencing for Patients with Ataxias and Paraplegias

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Spinocerebellar Ataxia (SCA) and Hereditary Spastic Paraplegia (HSP) are neurodegenerative disorders with overlapping clinical features. The clinical and genetic heterogeneity of SCA and HSP historically made clinical differentiation between the two groups of disorders problematic. The ever-growing number of causative genes for SCA and HSP creates evident limitations in creating and maintaining targeted gene sequencing panels. Diagnostic Exome Sequencing (DES) has enabled interrogation of the entire coding region of the genome and thus can overcome these obstacles in a cost effective approach. Herein, we present a retrospective cohort analysis of 500 patients tested using diagnostic exome sequencing at Ambry Genetics. Among the 500, 59 patients (11.8%) had reported clinical features containing one or more of the following descriptors: ataxia, spasticity/ spastic, diplegia and/or paraplegia. This clinical category was found to have a diagnostic rate of 47.5% (28/59); a statistically significant increase from the exome cohort patients without symptoms of ataxia or paraplegia 124/441 (28.1%) ($p<0.005$). This finding, as well as the concentrations of phenotypes revealed in this analysis that were associated with ataxia and/or paraplegia, supports the diagnostic utility of exome sequencing as an additional tool in the molecular diagnosis of patients with these clinical features.