Exome Sequencing as a Rapid and Cost Efficient Diagnostic Method in Neurogenetic Disorders

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Introduction: Genetic heterogeneity is common in many neurological disorders. Mutations in a large number of genes have been implicated as causative for many neurological disorders. For example, mutations in 28 genes have been described for spinocerebellar ataxia. Traditional genetic testing involving such a large number of candidate genes is both time consuming and costly. In contrast, recently developed genomic techniques such as exome sequencing that focuses on the coding portion of the genome, offer an alternative strategy to rapidly sequence all genes in a comprehensive manner.

Here we investigate a large, four-generational British kindred with an autosomal dominant progressive cerebellar ataxia where conventional genetic testing had not revealed a causal mutation.

Methods and results: Exome sequencing was performed in one patient of the family. Known ataxia genes were investigated for mutations. This identified a novel Arg26Gly mutation in the PRKCG gene which is known to cause SCA14. The change was confirmed using Sanger sequencing and showed segregation with disease in the entire family.

Conclusion: Here we demonstrate the utility of exome sequencing to rapidly screen neurogenetic disorders. This method is more comprehensive, more time effective and above all more economical than conventional Sanger sequencing and thus has high potential as a diagnostic screening tool in clinical practice.