Short Report

**Multiplex targeted high-throughput sequencing for Mendelian cardiac disorders**

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Mendelian cardiomyopathies and arrhythmias are characterized by an important genetic heterogeneity, rendering Sanger sequencing very laborious and expensive. As a proof of concept, we explored multiplex targeted high-throughput sequencing (HTS) as a fast and cost-efficient diagnostic method for individuals suffering from Mendelian cardiac disorders. We designed a DNA capture assay including all exons from 130 genes involved in cardiovascular Mendelian disorders and analysed simultaneously four samples by multiplexing. Two patients had familial hypertrophic cardiomyopathy (HCM) and two patients suffered from long QT syndrome (LQTS). In patient 1 with HCM, we identified two known pathogenic missense variants in the two most frequently mutated sarcomeric genes \textit{MYH7} and \textit{MYBPC}. In patient 2 with HCM, a known acceptor splice site variant in \textit{MYBPC3} was found. In patient 3 with LQTS, two missense variants in the genes \textit{SCN5A} and \textit{KCNQ} were identified. Finally, in patient 4 with LQTS a known missense variant was found in \textit{MYBPC3}, which is usually mutated in patients with cardiomyopathy. Our results showed that multiplex targeted HTS works as an efficient and cost-effective tool for molecular diagnosis of heterogeneous disorders in clinical practice and offers new insights in the pathogenesis of these complex diseases.