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A novel variant in *TBX20* (p.D176N) identified by whole-exome sequencing in combination with a congenital heart disease related gene filter is associated with familial atrial septal defect

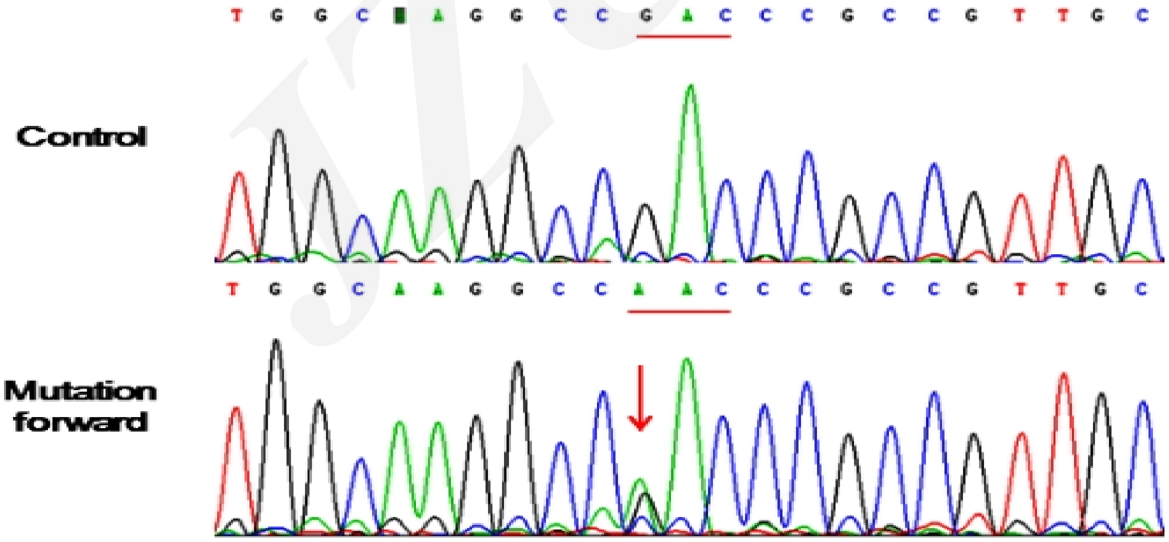
Key words: Congenital heart disease (CHD), Atrial septal defect (ASD), Whole-exome sequencing, CHD-related gene filter, *TBX20*

Research Summary

*We reported a novel *TBX20* mutation (p.D176N) in a three generation family with three ASD patients.

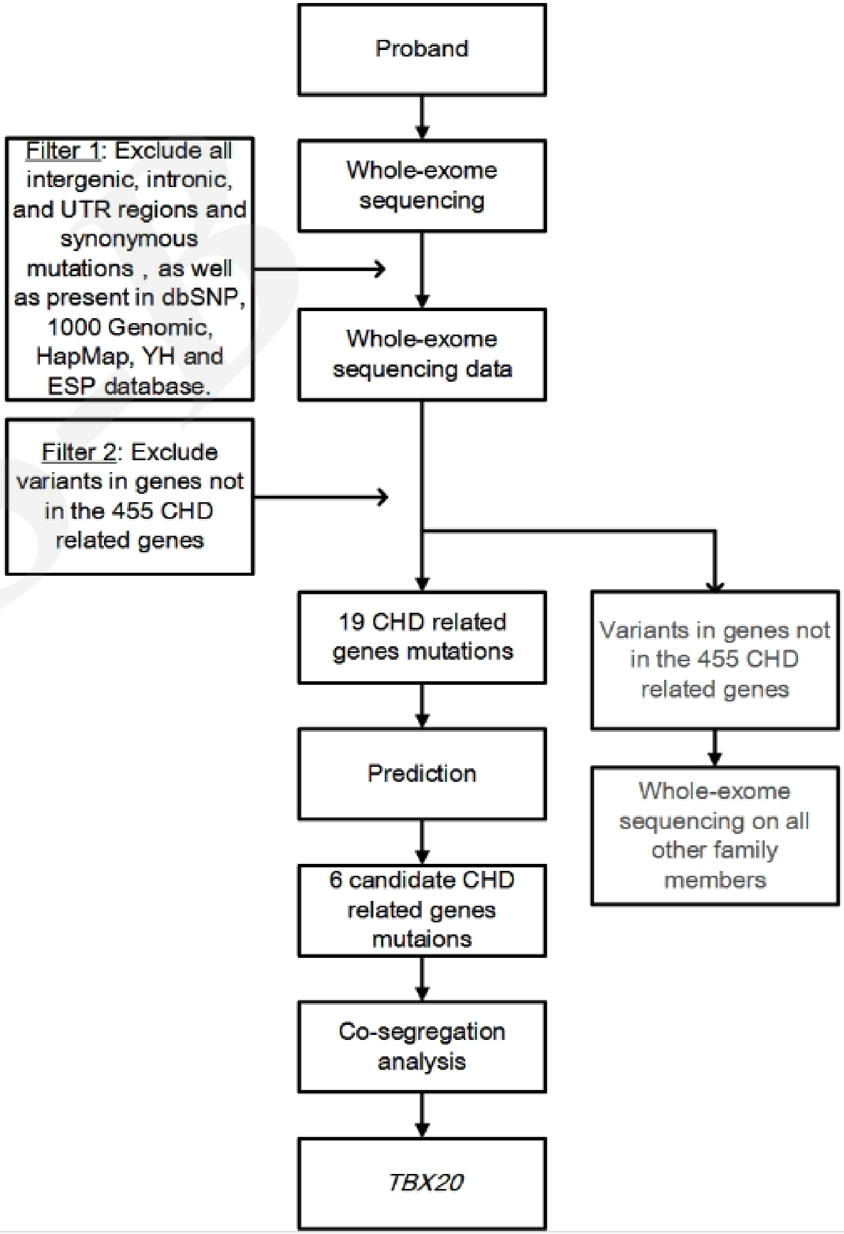
* The present identification of a novel mutation not only further supports the important role of cardiac transcription factor TBX20 in congenital ASD, but also expands the spectrum of *TBX20* mutations and will contribute to genetic diagnosis and counseling of families with CHD.

* Our study provided a new and cost-effective analysis strategy for genetic study in small CHD pedigree.



Innovation points

- In our study, the pedigree is really small, it is difficult to discover a new causative gene. Therefore, we initially hypothesized that the causative gene is in the list of related genes for CHD after analysis of whole-exome sequencing data.
- According to prediction by three bioinformatics programs (SIFT, Polyphen 2 and Mutationtaster), six candidate causative genes were highly suspicious.
- Co-segregation analysis demonstrated that only *TBX20* gene mutation (c.526G>A/p.D176N) was segregated in all affected family members.
- If the variant is not in the 455 CHD related genes, much more work needs to be done, such as whole-exome sequencing on all other family members.



Proband

Whole-exome sequencing

Filter 1: Exclude all intergenic, intronic, and UTR regions and synonymous mutations , as well as present in dbSNP, 1000 Genomic, HapMap, YH and ESP database.

Whole-exome sequencing data

Filter 2: Exclude variants in genes not in the 455 CHD related genes

19 CHD related genes mutations

Variants in genes not in the 455 CHD related genes

Prediction

Whole-exome sequencing on all other family members

6 candidate CHD related genes mutaions

Co-segregation analysis

TBX20

Research highlight

A novel mutation of TBX20 (D176N) in a Chinese family with ASD.

Whole-exome sequencing in combination with congenital heart candidate genes filter provided a new and cost-effective analysis strategy for genetic study in small CHD pedigree.

T-box DNA binding domain of TBX20 (109aa-288aa) are associated with CHDs.