To Detect and Explore Mechanism of CITED2 Mutation and Methylation in Children with Congenital Heart Disease

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Abstract

In this study we found four CITED2 coding region mutations (c.550G>A, c.574A>G, c.573–578del6) which led to alterations of amino acid sequence (p.Gly184Ser, p.Ser192Gly, p.Ser192fs) in 120 children with congenital heart disease. The CITED2 mutation associated with the dysregulation of HIF-1α, TFAP2c, and CITED2 methylation accompanied with its decrease in mRNA expression might be involved in the pathological process of congenital heart disease.

Keywords

CITED2 • Mutation • Methylation • Congenital heart disease

CITED2 mutation and methylation may be the cause of CHD. The purpose of this study was (1) to identify CITED2 mutation in children with CHD in China, (2) to analyze the mechanism of CITED2 mutation in cellular level if CITED2 gene mutation affects expression of HIF-1α and TFAP2c, and (3) to examine if CITED2 CpG island methylation exists in children with congenital heart disease.

1. Four CITED2 coding region mutations (c.550G>A one case, c.574A>G one case, c.573–578del6 two cases) exist in 120 children with congenital heart disease (Fig. 54.1) [1].
2. CITED2 mutation can inhibit TFAP2c expression. Our study also demonstrated that CITED2 has negative inhibition for HIF-1α. But this negative mechanism

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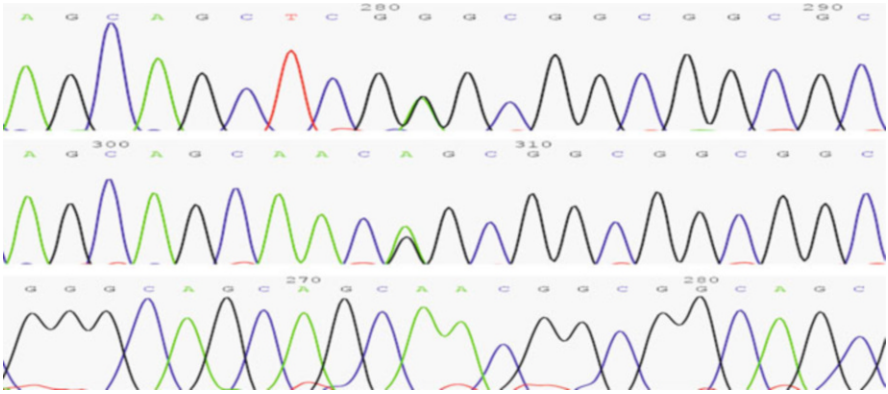

Fig. 54.1 The sequence of CITED2 mutation

will be weakened owing to CITED2 mutation in congenital heart disease; HIF-1α expression was elevated in CITED2 mutant group.

3. The CITED2 methylation is another mechanism of promoting congenital heart disease. CITED2 abnormal methylation was found in 26 of 31 congenital heart diseases. The abnormal methylation leads to decreased CITED2 mRNA expression [2].

CITED2 mutation and methylation may play an important role for the development of congenital heart disease.

References

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