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Nuclear Co-repressor 1: A Potential Candidate Gene in the Manifestation of Congenital Heart Diseases

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ABSTRACT The heart is the first organ formed during embryogenesis. The development of the heart is controlled by a network of pathways involving various transcription factors and signalling. Disruptions of these factors lead to the manifestation of congenital heart disease (CHD). The ventricular septal defects (VSD) of CHD are more frequent in the Indian population, particularly in Mysuru. In view of this, to identify defective genes in ventricular septal development, whole-exome sequencing was performed in seven cases of non-syndromic VSDs and three cases of Tetralogy of Fallot. The exome data analysis revealed that of all the defective genes identified, *Nuclear Co-repressor* 1 (*NCoR1*) is the prominent gene. It showed four non-synonymous damaging single nucleotide variants, that is, G244A, C241T, G207C and G121A. These mutations were present in the GPS2 protein domain, an integral part of NCoR1-HDAC complex involved in myogenesis. Further, pathway enrichment and network analysis indicated that NCoR1 interacts with HEY1, HEY2, MEF2A, NOTCH2 and HDAC3 proteins involved in heart development. Hence, defects in NCoR1 are responsible for VSD in heart development.