

## **The Role of Mesodermal-Produced TGFbeta2 in Congenital Heart Defect**

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**Abstract:** Congenital heart defect (CHD) is abnormalities in the structure of the heart at birth which can change the way blood flows to the heart. Some common areas of the heart where CHD can be seen are the walls, valves, and arteries and veins of the heart. The most common types of CHD are ventricular septal defect (opening between two ventricles) and abnormal heart valves development (thick or fused valves) that make it difficult for the heart to function properly. CHD is the most common type of birth defect in the world with a total of more than 35,000 babies born with CHD in the US each year. Because CHD is such a prevalent disease in the human population and the genetic mechanisms underlying the disease are poorly understood, it is important to study it and find new cures for it to help those who are affected by these heart defects. Transforming growth factor beta (TGFβ) is homodimer signaling protein of three TGFβ isoforms and it is important for heart development. TGFβ regulates cell proliferation, differentiation, apoptosis and other functions in embryonic and adult cells. Loss of function mutation in TGFB2 observed in human with congenital heart defects, however, little is known about the cell-source of TGFB2 involved in heart development. The aim of this study is to determine how the heart will develop in the absence of the TGFβ2 produced by cardiac progenitor or mesodermal cells with a particular focus on its impact on heart valves and the right side of the heart. For this study, genetically engineered mice model with Tgfb2 gene deletion in the mesodermal cells was generated. Genotyping was performed to sort control and experimental group and histological staining was used to characterize the heart defects in this mouse model. The results show that mesodermal deletion of Tgfb2 resulted in ventricular septal defect (VSD), overriding aorta, and thickening of heart valves (mainly pulmonary and aortic valve stenosis). In addition, these mice developed thicker, more muscular, and small right ventricle. CHD patients with Tetralogy of Fallot (TOF) exhibit these clinical abnormalities in the heart. In conclusion, our results indicate an important cell-specific function of TGFβ2 in the pathology of TOF.