**CRITICAL REGULATORY ROLES OF TGFBETA/BMP SIGNALING PATHWAYS DURING MYOCARDIAL WALL DEVELOPMENT**

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Congenital heart diseases are the leading cause of infant morbidity and mortality, and yet the underlying molecular/genetic mechanisms remain largely unknown. We previously identified Mycn as a direct target of the TGFbeta/BMP signaling pathway in developing hearts. Human genetic studies revealed that haploinsufficiency for MYCN causes Feingold syndrome, a developmental disease characterized in part by heart defects. In this study we focused on testing the function of Mycn during myocardial wall morphogenesis. We test the hypothesis that myocardial Mycn is essential for cardiomyogenesis through a conditional gene inactivation approach. Loss of myocardial Mycn caused embryonic lethality at midgestation. Mutants displayed severe hypoplastic myocardial walls, which is caused by both decreased cell proliferation and reduced cell size, but not by increased cell death. Expression of cell cycle regulatory genes was reduced in mutants. Furthermore, Mycn promotes cell growth through upregulating p70SK expression. Deletion of Mycn led to incomplete trabeculation, resembling mouse models with disruption in the Nrg-1/EphbB pathway. Treating embryonic hearts with an Ephrin-specific blocker severely reduced Mycn expression, suggesting that Mycn is a key target of Ephrin signaling in promoting trabeculation. Deletion of Mycn did not lead to pre-maturation of embryonic cardiomyocytes as evidenced from examining embryonic and adult specific cardiomyocyte markers. In conclusion, our study reveals Mycn as a key transcription factor mediating activities of multiple signaling pathways in promoting cardiomyocyte proliferation and myocardial wall morphogenesis. This information contributes to our better understanding of the molecular mechanisms underlying CHDs and can be further applied to regenerative medicine.