

# Induction of Cardiac Progenitor Cells by Targeting Wnt Pathway and TGF- $\beta$ -2 Receptor in the Remodeling of Injured Myocardium

Shumaila Shafique<sup>1\*</sup>, Mahanoor Nisar<sup>1</sup>, Irfan Khan<sup>1,2</sup>, Asmat Salim<sup>1</sup>

<sup>1</sup>Dr. Panjwani Center for Molecular Medicine and Drug Research, ICCBS, Karachi 75270, Pakistan.

<sup>2</sup>Center for Regenerative Medicine and Stem Cell Research, The Aga Khan University, Karachi, Pakistan.

\*E-mail: shumaelashafique@gmail.com

## ABSTRACT

**Introduction:** Myocardial infarction (MI) is the leading cause of death globally. Conventional pharmacotherapy and surgical interventions often improve cardiac function but current therapeutic strategies have limitations in effectively averting ventricular remodeling. To overcome this problem small molecules have been employed to modulate signaling pathways and gene expression in various cellular processes. Among them, 1,4-dihydropyridine compound, ITD, has high potency in inducing degradation of the TGF- $\beta$  type II receptor. Another small molecule, KY02111 promote cardiomyocyte differentiation in stem cells by inhibiting Wnt signaling.

**Objectives:** Innovating a synergistic strategy by implanting induced cardiac progenitors into ischemic reperfusion injury model could enhance cardiac function.

**Methodology:** MSCs were isolated from cord tissue, expanded, and characterized, treated with LiCl to activate Wnt pathway following the treatment with KY02111 and ITD to induce differentiation into CPCs. An MI model was established, and CPCs were transplanted into the infarcted myocardium.

**Results:** Cardiac function was assessed via echocardiography, and tissue histology. Echocardiography demonstrated significant improvement in heart function ( $P < 0.001$ ), while histological analysis confirmed cell survival, engraftment, reduced infarct size, and increased angiogenesis. This innovative synergistic approach of preconditioning MSCs and implantation into MI model considerably increased cardiac function, reduced scar formation and improved neo-vascularization with reduced cardiomyocyte apoptosis.

**Conclusion:** These findings will lead to alternative treatment options for cell-based regenerative therapies for heart disease.

**Keywords:** Myocardial Infarction, ITD-1, KY02111, Cardiomyocyte, Wnt Signalling.

## REFERENCES

1. Shafique, S, *et al.* Cardiac Transcription Regulators Differentiate Human Umbilical Cord Mesenchymal Stem Cells into Cardiac Cells. *Alternatives to Laboratory Animals* 51.1 (2023): 12-29.
2. Ali, SR, *et al.* Xenogeneic Stem Cell Induced Cardiac Progenitor Cells Regenerated Infarcted Myocardium in Rat Model Short. *Regenerative Engineering and Translational Medicine* 10 (2023): 110-125.