

Recent Advances in Genetics and Stem Cells that Suggest the Human Heart's Ability to Regenerate after an Acute Myocardial Infarction.

Sir,

Myocardial infarction (MI), as we know is increasingly seen among the elderly population worldwide. After an attack of MI, a part of the heart cells die and scarring occurs. The scar tissue however, does not function like a healthy heart tissue and so, the heart begins to get weakened and further complications can occur in such individuals. Now, recent advances in genetics and stem cells have proved that the human heart can regenerate even after fatal heart diseases like acute myocardial infarction.

A series of amputation experiments were performed on adult zebrafish, in which the cardiomyocytes had been genetically labeled 48 hrs after fertilization. About 20% of the ventricle was removed, and cardiac regeneration was subsequently assessed at 7, 14 and 30 days after the amputation. The results which were obtained, suggested that the regenerated cardiomyocytes arose from the pre-existing cardiomyocytes. [1]

The cardiomyocytes within the ventricular wall were found to activate the *gata4* (a transcription gene) regulatory sequences, proliferate, and contribute substantially to the local muscle regeneration [2].

It was found that both platelet-derived growth factor- α and - β were upregulated during the regeneration of the zebra fish hearts and that the inhibition of the PDGF signaling in vivo impaired the epicardial cell proliferation, the expression of the mesenchymal and the mural cell markers, and coronary blood vessel formation.

Further studies have shown that calcium levels have been specifically linked to the mechanical behaviour of the cardiomyocytes [4]. By using a calcium-sensitive fluorescent dye that could be measured, the researchers were able to discover that the human cardiac stem cells showed spontaneous oscillations in their internal calcium levels, with the higher values being found right before the cell division. So, it was suggested that the cardiac stem cells, if they were induced to increase their internal calcium oscillations, could be activated to regenerate the dead heart tissue after an acute attack of myocardial infarction.

Also, a "3 ingredient molecular cocktail" that could transform the fibroblasts directly into beating heart cells has been developed [3]. It

was found that the fibroblasts could be reprogrammed into cardiac muscle which just functioned like the muscle in a healthy beating heart.

The drug, 'Pravastatin' was found lately to mobilize the bone marrow progenitor cells and to thus improve the cardiac function in animals with diseased hearts in preclinical studies [5]. The number of cardiac myocytes increased in the hibernating hearts after Pravastatin administration, and this 'new' population of myocytes was remarkably smaller than the existing myocytes, thus suggesting that they arose from myocyte regeneration. It was noted that animals with normal hearts, who received Pravastatin, showed no increase in the number of the new myocytes, even though the drug was found to increase the number of circulating and cardiac progenitor cells.

This finding suggests that the new myocytes were formed directly in response to the need and to the presence of the heart's diseased state, thus preventing uncontrolled cardiac muscle growth and proliferation in otherwise normal hearts.

With the advances in science, one can hope to successfully treat various cardiovascular related problems in the near future and live a healthier life with a healthy Heart!

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