Cellular and Molecular Biology 2018- Trends and limitation in hydrogel-based therapies for myocardial regeneration

Ali Mohammad Hasan Joshaghani1, Maryam Eslami1, 2, Atefe Soluk1, 3, Karim Nayernia2, 4 and Dariush Farhood

Islamic Azad University, Iran Farhud-Nayernia Center for Genomics Medicine, Iran Amirkabir University of Technology, Iran International Center for Personalized Medicine, Germany Tehran University of Medical Sciences, Iran

C truggling to expand man's life expectancy, scien-Jtists have always come across a rather remarkable obstacle damage done to cardiac tissue by myocardial infarction. Incapability of self-regeneration in myocardium causes major problems in the treatment of cardiovascular diseases. Myocardial infarction cannot be tackled effectively by existing approaches such as pharmaceutical therapy, organ transplant or implantation of medical devices; Said methods lack the efficiency expected of the modern technology, since they exert matters such as shortage of donor organs, long periods of hospitalization, rejection of the immune system, heavy operations often including high invasiveness and a high risk of degeneration. In order to regenerate damaged heart muscle, cell-based regenerative therapies and tissue engineering products have gained popularity these days. Injectable hydrogels are one of the tissue engineering products with great potential in treating heart diseases. Different kinds of hydrogels including cell-free hydrogels or those loaded with cardiac stem cells or bioactive agents are available, and previous treatments of heart diseases are now becoming less popular. Hydrogels can be injected intracoronary, epicardial or endocardial. These gels have satisfactory stiffness and viscoelasticity, most of them are biocompatible, and some are biodegradable and conductive as well; such traits encounter myocardial patches' downsides such as hypoxia, electro-provocation, patch rejection and many more. In what follows we are going to shed some light on hydrogels loaded with or carrying angiogenesis drugs or cardiac stem cells and their advantages against the aforementioned methods.

Biography: Ali Mohammad Hasan Joshaghani has

completed his BS in Biomedical Engineering from Islamic Azad University and is currently an MS student in Biomedical Engineering in Islamic Azad University. He has won awards at 10th and 12th Royan International Congress on Stem Cell Biology and Technology in 2014 and 2016.

Keywords: hydrogels, myocardial infarction, tissue engineering, regenerative medicine, cardiac repair, stem cell.

Conclusion: Injectable hydrogels offer huge potential for application in repair and regeneration of infarcted heart after MI. They can be used as carriers to deliver therapeutic drugs, biomolecules or cells to invoke a specific response in the infarcted heart tissues, or to form functional cardiac tissue constructs for replacement of infarcted cardiac tissues. In recent years, numerous hydrogels have been investigated for their application in cardiac repair and regeneration. Several of these hydrogels have shown great promises toward achieving cardiac tissue repair. To date, no hydrogel composition has shown both the necessary biological and mechanical properties for sufficient transition to clinical cardiac tissue repair. While naturally derived hydrogels from collagen, hyaluronic acid, chitosan, and ECM hydrogels have shown promise in the left ventricle modeling of the myocardium, synthetic hydrogels have been shown to offer better control over their properties such as degradation time, gelation time, and most importantly the mechanical stiffness of the hydrogel.

One school of thought is that hydrogels can induce stem cell homing. However, not much is known about the exchange of signals that take part in the movement of stem cells to an injured myocardium posthydrogel treatment. The importance of hydrogels also manifests itself in their ability to deliver drugs and chemical signals throughout the body to the heart. In such cases, targeted delivery and long-term controlled sustained release are the advantages. Cytokines, such as the stem-cell factor (SCF), granulocyte SCF, or stromal-cell-derived factor (SDF), may enhance cell transplantation and infiltration.130 When SCF was combined with G-SCF, a 250-fold increase in the number of circulating cells was made apparent in a model version. Cell microenvironments regulate and repair cellular fate and function. The ECM is a crucial element of the cell microenvironment that includes different chemical and physical cues.131 Encapsulating cells in a suitable hydrogel before transplanting or injection also increases the chances for their survival, as it increases the cell-ECM interactions. This is why much attention has now been focused on hydrogels obtained from ECM molecules. These biomaterials are now made to replicate ECM interactions, thus providing the best way to ensure the sustainability, survival and full function of the transplanted cells.132

Besides, the hydrogels can be specifically designed to help in myogenic differentiation. Despite a considerable amount of research having been done on repair of infarcted heart tissue using injectable hydrogels in small animals such as rats, mice, and rabbits, research on application of hydrogel therapies on large primates and humans is still lacking. Thus, more investigations are required before the injectable hydrogel therapies with cells or biomolecules for cardiac repair are implemented in humans. Challenges in this endeavor include ensuring the survival and integration of the delivered cells in the cardiac environment and their differentiation into the required myogenic phenotypes so that they can start performing like beating cardiac cells in minimal time from the time of injection. Another challenge is the use of chemical cross-linking which can often be harmful for the cells. Photocrosslinking, ionic cross-linking, or temperature or pH-based crosslinking might be alternate options; however, application of these methods in situ is often difficult. Deficiency of needed cells, the lack of full integration with the host tissue, and the absence of electrical communication through gap junctions are also among challenges that can compromise the success of the injectable hydrogel-based stem cell therapy or cardiac repair and require further research. Research has shown improvements in wall thickness, LV repair, and vascularization of the ischemic region with the use of injectable hydrogel based therapies. Studies performed so far in rodents and pigs give hope to the potential of hydrogel based therapies for cardiac repair in primates and humans.