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Regenerative Health Care an Advantage for Creating Organoids and Brief Description of Cardiovascular Disease and Regeneration of Heart Organs

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Abstract

Regenerative medicine has promise for normalizing congenital abnormalities and healing or replacing tissues and organs damaged by illness, aging, or trauma. It can prevent illnesses in a variety of organ systems and situations, as well as treat acute insults and chronic disorders. Using materials and de novo produced cells to restore missing tissue, promoting tissue recovery, or utilizing the body's natural healing ability are some ways employed in regenerative medicine. Globally, cardiovascular disease is a serious problem due to the projected 46% rise in cases by 2030. The foundation for reconsidering therapeutic strategies and creating novel bioengineering treatments has been laid by developments in tissue engineering, stem cell engineering, functional biomaterials, and biofabrication technologies. Organoid technology is being used in regenerative medicine to produce miniature tissue models that can simulate human physiopathology and compete with widely used platforms for medication safety.

Keywords: Transplantation; Regeneration; Heart transplant; Gene therapy; Obstacles

Abbreviations: NCDs: No Communicable Diseases; TE: Tissue Engineering; RM: Regenerative Medicine; IPSCs: Induced Pluripotent Stem Cells.

Introduction

Regenerative medicine has promise for normalizing congenital abnormalities and healing or replacing tissues and organs damaged by illness, trauma, or aging. Regenerative medicine has the potential to treat a wide range of organ systems and contexts, including wounds on the skin, traumas and cardiovascular diseases, some forms of cancer, and more. So far, promising preclinical and clinical data support this potential for treating both acute insults and chronic diseases. Although there is a limited supply of donors and frequently serious immunological difficulties associated with the existing approach of transplanting intact organs and tissues to cure organ and tissue failures and loss, these challenges may be overcome with the application of regenerative medicine techniques . Regenerative medicine is a multidisciplinary field that uses a variety of techniques, such as materials and de novo generated cells, in different combinations, to replace missing tissue in a structurally and functionally sound manner or to aid in tissue healing. Although mature humans have a reduced ability for regeneration than other vertebrates, the body's natural healing response can also be used to encourage regeneration [1].

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The term "regeneration" refers to the process in humans wherein damaged specialized structures proliferate to replace lost specialized tissue. With the exception of the regular replacement of individual cells in tissues like the intestinal mucosa and epidermis, the process is distinct in humans for only a few tissues like the liver [2].

Gene therapy, which involves introducing exogenous genes into cells for biological and therapeutic goals *in vitro* or *in vivo*, is a very interesting and promising technology. The first and most important step in experimental biology and gene therapy is to make it feasible for the gene to internalize into the cell as effectively as possible and to facilitate its expression for a prolonged or brief duration, regardless of the ultimate goal. Gene therapy technologies have been applied to many forms of genetic material delivery to cells and tissues using physical technologies, non-viral vectors, and viral vectors. The multidisciplinary discipline of regenerative medicine blends engineering and biological sciences to create methods for the preservation, improvement, and repair of living tissues and organs on biomaterials. Creating natural tissue that can replace lost organs or tissue functions that the organism has not been able to recover under physiological settings is its main goal [3].

A Succinct Overview of Cardiovascular Disease

17.9 million Lives are lost annually due to cardiovascular disease, which is the leading cause of death and accounts for around 32% of deaths worldwide. Compared to civilians, military personnel have a much higher likelihood of reporting work-related stress, which can lead to the acute onset of heart failure and the long-term development of cardiovascular disorders. Over 10% of military pilot groundings are attributed to cardiovascular illness. Veterans admitted to hospitals have a heart failure rate of up to 0.5%. The significance of cardiovascular research in military medicine is demonstrated by these studies. Heart failure still has significant rates of death and morbidity despite enormous efforts and advancements in cardiovascular research and treatments. Based on factors such as increased life expectancy, elevated rates of obesity and diabetes, and contemporary lifestyle choices, epidemiologic studies projected a 46% rise in the number of heart failure patients by 2030. Although pharmacological treatment can now halt the course of heart failure, a breakthrough is still needed [4].

Non-communicable diseases (NCDs) are acknowledged as a serious global health concern. Despite fifty years of progress in preventive medicine and cardiovascular research, NCDs still have high rates of morbidity and mortality around the globe. Even if they are not acknowledged as a permanent cure, pharmaceutical therapy or revascularization procedures can frequently save the heart and avoid transplantation. Regenerative medicine treatments have given new hope for the repair or replacement of damaged hearts because the adult human heart has a limited capacity for regeneration. Cell-based and cell-free techniques have demonstrated minor advantages, although these have been strongly linked to incorrect administration and retention, as well as inadequate therapeutic efficacy. Tissue engineering (TE) has come a long way in the last few decades, particularly in the areas of stem cell engineering, the creation of functional biomaterials and biomimetic scaffolds, and the use of biofabrication techniques to create intricate biological structures with high resolution. This advancement has created a strong foundation for reconsidering present therapy modalities and developing novel bioengineering treatments. However, the process of growing fully developed and functioning heart tissue in vitro remains difficult. In spite of this, it is now feasible to effectively design miniature tissue versions that can rival, if not completely replace, widely utilized platforms for evaluating drug safety and simulating human physiopathology to direct effective drug discovery [5].

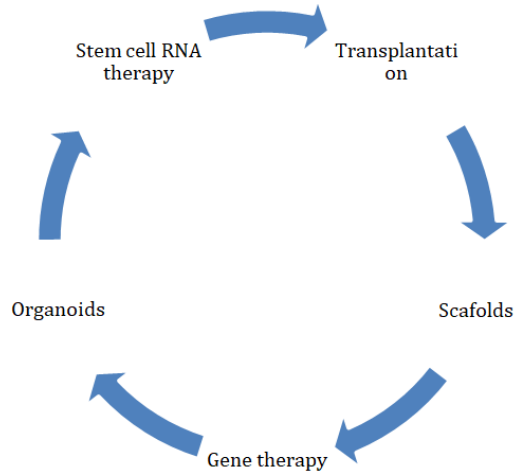

Figure 1: Techonologies used in RM at Present [6].

Application of Organoid Technology in RM [6]

- Intestinal organoids
- Hepatic organoids
- Pancreas organoids
- Kidney organoids
- Heart Organoids
- Lung and Airway organoids
- Brain organoid
- Retinal organoids
- Organoids of female reproductive tract

Technologies from Regenerative Medicine used in Transplant Medicine

Transplant medicine is evolving as a field thanks to the

advances made in regenerative medicine (RM). The goal of regenerative medicine is to create and apply techniques that allow diseased or damaged tissues or organs to regenerate, repair, or replace them. Regenerative medicine looked at creating successful patient-specific treatments employing tools including extracellular vesicles, novel technologies or procedures, cell-based therapies, and tissue-engineered constructions [7].

A New Direction in Cardiac Regenerative Medicine: Gene Therapy during Ex Situ Heart Perfusion?

Ex situ organ preservation via machine perfusion can enhance organ preservation for transplantation. Additionally, machine perfusion provides opportunities for the correction of a pathogenic genetic flaw, the development of resistance to ischemia reperfusion damage, and selective immunomodulation. Given the difficulties with vector administration experienced in in vivo cardiac gene therapy clinical trials, the use of gene altering therapies to treat heart ailments resulting from pathogenic mutations during ex situ heart perfusion appears promise. It is possible to actively regulate factors that increase the success rate of cardiac gene therapy by keeping the heart isolated in a metabolically and immunologically favorable environment, avoiding off target effects, and preventing dilution. In order to find all pertinent research on gene therapy during ex situ heart perfusion, a literature search of the PubMed and Embase databases was conducted. The goal was to examine the intriguing approach's future clinical prospects and to highlight significant lessons gained [8].

The Most Important Prerequisite for Regenerative Medicine

Replacing lost or impaired tissue components is the most obvious prerequisite for regenerative therapies. Although stimulating endogenous stem cells is a desirable approach, cell treatments have shown the most promise thus far. Regenerative therapies based on adult stem cells have demonstrated clinical benefits in the treatment of burn injuries, retinal degeneration, and hematological malignancies. Gene editing is another useful tool for correcting monogenic aberrations in these therapeutic approaches. An autologous skin transplant, for example, was utilized to cure a young boy with junctional epidermolysis bullosa, a fatal skin disease brought on by mutations in the laminin-332 gene (2). After obtaining a millimeter-sized sample of the boy's skin, the tissue was enlarged ex vivo and grafted to restore 80% of the body surface area. The skin sample was transduced using a retroviral vector expressing the wild-type laminin 332 cDNA [9].

Limitations of the Regenerative Medicine

Not with standing these initial signs of promise, numerous biological and technological obstacles still face cell treatments. Immune aggravation is prevented by autologous hPSC-based therapies produced from induced pluripotent stem cells (IPSCs); nonetheless, this labor- and money-intensive approach need safety testing for every usage. Nonautologous cell treatment raises a significant risk of immunological rejection of the transplant. Hence, in order to prevent rejection, "off-the-shelf" allogeneic therapies need to be combined with protective measures such systemic immunosuppression in T1D hPSC therapy (NCT04786262) [9].

Conclusion

Regenerative medicine has promise for normalizing congenital abnormalities and healing or replacing tissues and organs damaged by illness, aging, or trauma. It can prevent illnesses in a variety of organ systems and situations, as well as treat acute insults and chronic disorders. Materials and de novo produced cells are among the tools used in regenerative medicine to replace lost tissue, aid in tissue regeneration, and stimulate the body's natural healing process. Globally, cardiovascular disease is a serious problem due to the projected 46% rise in cases by 2030. Technological developments in tissue engineering, stem cell engineering, biofabrication tools, biomimetic scaffolds, and functional biomaterials have paved the way for re-evaluating therapeutic strategies and creating novel bioengineering treatments. Organoid technology is being used in regenerative medicine to produce miniature tissue versions that can mimic human physiopathology and compete with widely established platforms for medication safety. Through the development of techniques to regenerate, restore, or replace damaged tissues or organs, regenerative medicine is changing transplant medicine. Novel technologies, extracellular vesicles, cell-based therapeutics, and tissue-engineered constructions are some of the advances in this sector. In addition to offering the possibility of selective immunomodulation and genetic flaw correction, machine perfusion can enhance organ preservation. Regenerative therapies—especially cell therapies—are essential for restoring tissues that have been lost or damaged by illness. Allogeneic therapies must be incorporated into these treatments due to obstacles including immunological rejection and safety assessment.

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