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Pharma Europe 2020: Regenerative Medicine for the treatment of diabetes and cardiovascular diseases - Ahmad Ghorbani - Mashhad University, Iran

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Historically, small molecule (i.e., compounds of <500–800 mol. wt.) pharmaceutical research and development has focused on compounds with increasingly selective mechanisms of action. This makes sense from a symptom-based approach to the treatment of disease, wherein one wishes to focus on the primary mechanism of action required for drug efficacy while simultaneously limiting off-target effects and minimizing adverse events/side effects. The development requirements for regenerative pharmacology will be much more demanding. In fact, the challenges associated with regenerative pharmacology, that is, curative therapeutics, will in many instances require complex mixtures of compounds [i.e., growth factors such as fibroblast growth factor (FGF), epidermal growth factor (EGF), platelet-derived growth factor, nerve growth factor (NGF), vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF), bone morphogenic proteins (BMPs), etc.] for restoration of tissue/organ function. These latter compounds have significantly higher molecular weights (generally ≈10,000 to >100,000 mol. wt.) than those traditionally developed by the pharmaceutical industry. Regenerative medicine technologies cross the boundaries of various scientific fields, including cell and biology , chemical and material sciences (i.e., nanotechnology), engineering, genetics , physiology and pharmacology. As such, regenerative medicine truly represents an integrative and logical (r)evolution of life science . This groundbreaking field of research has the potential to radically alter the treatment of diseases or disorders characterized by the shortage of viable cells or tissues. The goal of this report is to review the present challenges and opportunities within the emerging field of regenerative medicine and to explain the role of the pharmacological sciences within the acceleration, optimization, and evaluation of engineered tissue function within the service of regenerative medicine technologies. This review focuses on the present status of research that utilizes the appliance of pharmacological sciences to accelerate, optimize and characterize the event , maturation and performance of bioengineered and regenerating tissues. These regenerative pharmacologic approaches are applied to diseases of the urogenital tract, the heart, the brain, the system and diabetes. Approaches have included the utilization of growth factors (such as VEGF and chemokines (stromal-derived factor - CXCL12) to mobilize cell to the sights of tissue loss or damage. The promise of this approach is to bypass the lengthy and expensive processes of cell isolation and implant fabrication to stimulate the body to heal itself with its own tissue regenerative pathways.

Regenerative medicine may be a rapidly evolving multidisciplinary, translational research enterprise whose explicit purpose is to advance technologies for the repair and replacement of damaged cells, tissues, and organs. Scientific progress within the field has been steady and expectations for its robust clinical application still rise. The major thesis of this review is that the pharmacological sciences will contribute critically to the accelerated translational progress and clinical utility of regenerative medicine technologies. In 2007, we coined the phrase “regenerative pharmacology” to explain the big possibilities that would occur at the interface between pharmacology, regenerative medicine, and tissue engineering. The operational definition of regenerative pharmacology is “the application of pharmacological sciences to accelerate, optimize, and characterize (either in vitro or in vivo) the event , maturation, and performance of bioengineered and regenerating tissues.” intrinsically , regenerative pharmacology seeks to cure disease through restoration of tissue/organ function. This strategy is distinct from standard pharmacotherapy, which is usually limited to the amelioration of symptoms. Our goal here is to get pharmacologists more involved in this field of research by exposing them to the tools, opportunities, challenges, and interdisciplinary expertise that will be required to ensure awareness and galvanize involvement. To this end, we illustrate ways during which the pharmacological sciences can drive future innovations in regenerative medicine and tissue engineering and thus help to revolutionize the invention of curative therapeutics. Hopefully, the broad foundational knowledge provided herein will spark sustained conversations among experts in diverse fields of scientific research to the benefit of all.

The increased incidence of chronic metabolic disorders, including diabetes and cardiovascular diseases, has become one of the worldwide health challenges of the 21st century.

Despite extensive effort in the past years to develop new therapeutics, currently available drugs failed to cure these diseases. For example, many diabetic patients in the advanced stage may need organ transplantation because of developing life-threatening complications such as nephropathy and heart failure. However, transplantation therapy is restricted by organ availability and immune reactions, indicating the importance of need for stem cells therapy and tissue regenerative approaches.

Nowadays, substantial progress has been made in cell therapy technologies. In spite of this, several challenges remain to be resolved to achieve more effective therapy. Some of these challenges include: insufficient amount of stem cells that can be

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obtained from tissues; inadequate migration and homing of exogenous stem cells; limited differentiation potential of stem cells under in vivo situation; and decease of stem cells in damaged tissue.

A growing body of evidence suggests that pharmacological manipulation can help to overcoming these challenges and improve the preclinical and clinical utility of regenerative medicine technologies. This review focuses on studies performed by our research group and others to enhance proliferation, survival, migration, homing, and differentiation potential of stem cells by application of pharmacological sciences.

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