Review

Advanced cell therapies with and without scaffolds

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Tissue engineering and regenerative medicine aim to produce tissue substitutes to restore lost functions of tissues and organs. This includes cell therapies, induction of tissue/organ regeneration by biologically active molecules, or transplantation of in vitro grown tissues. This review article discusses advanced cell therapies that make use of scaffolds and scaffold-free approaches. The first part of this article covers the basic characteristics of scaffolds, including characteristics of scaffold material, fabrication and surface functionalization, and their applications in the construction of hard (bone and cartilage) and soft (nerve, skin, blood vessel, heart muscle) tissue substitutes. In addition, cell sources as well as bioreactive agents, such as growth factors, that guide cell functions are presented. The second part in turn, examines scaffold-free applications, with a focus on the recently discovered cell sheet engineering. This article serves as a good reference for all applications of advanced cell therapies and as well as advantages and limitations of scaffold-based and scaffold-free strategies.

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1 Tissue engineering and regenerative medicine: Evolution of concepts

The rapidly emerging fields of tissue engineering and regenerative medicine have a great potential for the production of viable tissue substitutes. Tissue engineering is a promising multidisciplinary field aimed at improving health and life standards of people by recovering the lost functions of tissues and organs. The development of artificial tissues to augment, repair or substitute for the biological activity lost due to a variety of reasons is the major concern of regenerative medicine. Regenerative medicine refers to a group of biomedical approaches involving: (i) injection of stem or progenitor cells (cell therapies), (ii) induction of regeneration by biologically active molecules, or (iii) transplantation of in vitro grown organs and tissues (tissue engineering). Cell therapies involve introducing new cells into a tissue or organ to treat a disease or augment the function of an organ.

Tissue engineering and regenerative medicine use cells as the main tool to achieve healing. Cells from a variety of sources can be used, e.g., functional mature cells, modified cells producing a ther-

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Abbreviations: **EC**, endothelial cell; **ECM**, extracellular matrix; **ESC**, embryonic stem cell; **FGF**, fibroblast growth factor; **GAG**, glycoseaminoglycan; **HA**, hyaluronic acid; **HAp**, hydroxyapatite; **HSC**, hematopoietic stem cell; **IGF**, insulin-like growth factor; **MSC**, mesenchymal stem cell; **NSC**, neural stem cell; **ORS**, outer root sheath; **PCL**, poly(e-caprolactone); **PDGF**, platelet-derived growth factor; **PGA**, poly(glycolic acid); **PHBV**, poly(3-hydroxybutyrate-co-3-hydroxyvalerate); **PLA**, poly(lactic acid); **PLGA**, poly(lactic acid-co-glycolic acid); **PNIPAM**, poly(N-isopropylacrylamide); **PU**, polyurethane; **RP**, rapid prototyping; **SMC**, smooth muscle cell; **TGF-β**, transforming growth factor-β; **VEGF**, vascular endothelial growth factor

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