Novel, Versatile System for Progenitor Cell Recruitment in Tissue Repair/Regeneration (Case 1594)

Published date: June 11, 2012

Technology description

Brief Description:
Within the last decade, there is growing significant data on the therapeutic potential of endothelial progenitor cells (EPCs). EPCs present in bone marrow can be recruitedin vivoin adult animals and humans for direct, effective targetedin situtreatment, and/or harvested for autologous re-implantation or transplantation anew in another patient. As examples, EPC infusion has improved angiogenesis in ischemic limbs, can endothelialize exclusively implanted Dacron grafts, and colonize left ventricular assist devices (LVADs), shown after 6 months to have presence of CD34+ and VEGFR2+ endothelial and hematopoietic cells – both markers for early progenitor cells. In addition, autologous bone marrow EPC [cell] transplantation has improved patient peripheral vascular disease. Hence, the vasculogenic potential of bone marrow by either whole transplants or selected EPC [cell] populations, via intravenous/intramuscular administration, is of great interest as a treatment that can significantly improve patient outcomes for those suffering from pathophysiological cardiovascular conditions, among many other diseases and defects. Moreover, the enormous economic and societal burden of caring for existing chronic conditions/diseases could be lessened significantly from the benefits – alleviation, control, cure – derived from tissue repair and regeneration.

Three main approaches have been explored to acquire or recruit endothelial progenitor cells in an adult animal. However, each method is limited in human clinical applications. Cells can be selected using fluorescence-activated cell sorting with markers specific to progenitor cells from the bone marrow, isolated using the same technique from the bloodstream after exposure to systemic recruiting factors, or recruited to a peripheral site after sequential administration of exogenous cytokines. The first two methods may involve cellular transplant with the co-administration of immunosuppressive agents; the third approach would require at least daily administration of the appropriate cytokine to achieve desired therapeutic effect due to very short cytokine half-lives in the blood. Therefore, a new improved EPC recruitment and isolation method is needed that could negate current limitations and add further advantages in terms of simplicity, reproducibility, safety, cost and effectiveness. The compelling technology offered below indeed addresses limitations and surpasses current state-of-the-art.

The invention is a novel method and [drug] delivery system – implant – that uses one or more growth

factors and/or cytokines to mobilize and recruit bone marrow progenitor cells to particular regions in the body for direct affect and/or isolation, harvesting and removal. Growth factors/cytokines such as angiogenic/vasculogenic factors and a bone marrow recruiting factor, among many others, are used to recruit the EPCs or other progenitor cells. The flexible implant delivery system can be comprised simply of bioactive molecules, i.e., proteins, or any number of more complex materials such as polymers depending upon application. This versatile method and system can be used in a wide variety of tissue repair and/or regeneration scenarios to treat a plethora of diseases, disorders, conditions and defects such as, but not limited to, genetic abnormalities, heart or neurdegenerative disease, infection, necrosis, trauma or external stress from wounds/surgery.

Furthermore, this innovative method/system facilitates isolation of progenitor cells prior to lineage commitment or differentiation for harvesting from specific regions in the body. Isolation and harvesting may be accomplished via a porous implant housing (e.g., mesh/sieve, etc.) for usein vitroor culturingex vivofor therapeutic re-implantation in the same host or transplantation to a different individual. EPCs or other progenitor cells, i.e., endothelial, hematopoietic, hemangioblasts, neural, or epithelial, etc., migrate over time to the ectopic porous mesh implant for removal from the individual, due to the controlled release of intact, bioactive molecules/growth factors in this system. The unique ability to recruit particular cells specifically to a removable implant substantially reduces the need to further purify the cellsex vivoand eliminates dependence on embryonic stem cells as a source of progenitor cells for tissue repair and regenerationin vivo, since it uses only adult progenitor cells. Also, there is no repeated administration of growth factors, as the invention provides a sustained, controlled (steady) release of factors for increased efficacy.
A wide variety of implant conformations can be employed including, but are not limited to: encapsulations, microspheres/particles, nanospheres/particles, macrospheres/particles, matrices, beads, films, rods, coatings or hydrogels. Depending upon application and/or if isolating and harvesting is desired, implant materials may be biodegradable (fully, partially or non-) and of a variety of polymers or bioactive molecules such as proteins. Additionally, this novel implant can be introduced by any number of routes into the body: intravascularly, subcutaneously, gastrointestinally, intra-spinal, etc., among others, and can be localized in myocardium, vasculature, skin, muscle, liver, lung, mouth, spine, and cranium, among many other sites. Overall, in this way, the most appropriate and effective system – medically and financially – can be created for a given application/treatment.

Applications are for use as a medical treatment/therapeutic through tissue repair and regeneration in a plethora of diseases, disorders/conditions, and defects/abnormalities. Examples include, but are not limited to, repairing and/or replacing damaged or absent tissues in: neurodegenerative diseases such as Alzheimer’ s and Parkinson’ s; heart disease post myocardial infarction; genetic diseases/ abnormalities of the blood or in congenital heart defects; damaged lung, vasculature or liver tissue due to COPD, stroke or cirrhosis, respectively; and various cancers. Further applications include use as a research tool in biomedical/scientific R&D to advance the fields of medicine, stem cell and regenerative

research, drug delivery devices, biomedical engineering, among others. Markets include: pharmaceutical – therapeutics; medical devices – drug delivery; biomedical R&D tools.

Institution

Brown University

Inventors

Diana James (formerly Ferris)
Edith Mathiowitz
Professor of Medical Science
Bio Med Molecular Pharmacology, Physiology & Biotechnology