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Guest Editorial

Regenerative Medicine, Stem Cells, and Low-Level Laser Therapy: Future Directives

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The idea of being able to replace, restore, or regenerate damaged or diseased tissues and organs in order to establish normal function in the human body has never been so prominent and possible than with the development of the field of regenerative medicine. Using material from the body or activating the body's own repair mechanisms to prepare and grow or heal irreparable tissues or organs is now a real possibility, as demonstrated by research and clinical studies published over the last 10 years. Born from the collaboration of several biomedical disciplines and clinical approaches, regenerative medicine promises the real possibility of not only replacing pharmaceutical solutions to disease but also paves the road to a more autologous and holistic approach in clinical treatment of disease and disease control.[1] Historically, the foundation of regenerative medicine was cemented with the successful transplantation of corneas, soft tissue, and bone in the early twentieth century. The first kidney transplantation in 1954 was followed by pancreas, liver, and heart transplants in the 1960s and success continued in the 1980s with heart–lung and living donor liver and lung transplants. Progressively, an increase in demand for tissues and organs and subsequent decrease in organ availability has left a need for new technology to meet the demand for suitable organs and organ donors as well as leading to an increase in the disgraceful enterprise of black market organs. Currently, tissue-engineered skin used for burn survivors and diabetic ulcers, products derived from tissue engineering to induce bone growth and regeneration, as well as the autologous reintroduction of *ex-vivo* engineered bladder are a reality, once again establishing a firm foothold for the development of further and more advanced applications for regenerative medicine.[2]

The discovery of stem cells by the Russian histologist Alexander Maksimov in 1908, as part of his theory of hematopoiesis followed by Joseph Altman and Gopal Das in the 1960s presenting evidence of constant stem cell activity in the brain and the demonstration of self-renewing cells found in the bone marrow of mice by James E. Till and Ernest A. McCulloch in 1963, established stem cell research and the development of stem cell therapy as a new and very promising and exciting discipline for regenerative medicine. Embryonic and adult stem cells are available from a variety of sources and hold variable differentiation potential, not to mention the myriad potential therapeutic applications, albeit associated with some ethical and political concerns. Mammalian stem cells can be sourced from either the embryo or the adult organism.[3] Embryonic stem cells originate from the inner cell mass of blastocysts, whereas adult stem and progenitor cells can be found in various tissues repairing or replenishing adult tissue. Of specific interest and application in regenerative medicine are autologous adult stem cells accessible from bone marrow, adipose tissue, or blood. Contemporary stem cell therapy includes bone marrow transplants for the treatment of leukemia, whereas extensive current research is undertaken for the implementation of stem cell therapy for the treatment of cancer, spinal cord injuries, and Parkinson's disease, as well as multiple sclerosis and muscle conditions including heart disease. The use of vascular grafts for heart bypass surgery and cardiovascular disease treatment have been researched extensively and are at the pre-clinical trial stage.[4] Advances in therapeutic applications do not come without much debate and controversy surrounding risks associated with it. The risk that transplanted stem cells could form tumors and metastasize uncontrollably is but one of the concerns of stem cell therapy. Inducing forced expression of specific genes in order to derive pluripotent stem cells from non-pluripotent cells generate the so-called induced pluripotent stem cell (iPSC). However, significant risk is associated with reprogramming of adult cells to obtain iPSCs. Potentially, this risk could limit their use in patients. The use of viruses to genomically alter the cells may lead to the expression of cancer-causing oncogenes.[5,6]

Low-level laser therapy (LLLT) has been scientifically proven as a beneficial therapeutic modality for numerous diseases and diseased conditions. Using very specific laser and light-emitting diode irradiation parameters, specific cellular activities can be induced, namely, cellular proliferation and viability while stimulating mitochondrial activity, thereby increasing adenosine triphosphate (ATP) production, synthesis of DNA and RNA, and activating cell-signaling cascades including the production of reactive oxygen species (ROS), nitric oxide (NO) release, activating cytochrome c oxidase, and modifying intracellular organelle membrane activity, calcium flux, and expression of stress proteins.[7–10] The molecular mechanism underlying these cellular activities is less well understood, and several research groups are conducting intensive research studies in an effort to elucidate the relation between these biological

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