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Letter to the Editor

Photobiomodulation Therapy: Communicating with Stem Cells for Regeneration?

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To the Editor:

NEVER HAS THERE been a more exciting time in the human race when the quest for knowledge has been expanded outward to the farthest universe, as well as inward to subatomic scales. It is likely not a mere coincidence that the ultimate frontier extending across all these vast scales happens to be light—a still mysterious but omnipresent form of physical energy whose impact on biological systems is still being uncovered.[1] The use of photonics in medicine has already changed our healthcare system dramatically from electronic access to data to better illumination fields, digital cytology and pathology, endoscopy, and precision surgery with lasers.[2] As in the clinical realm, biophotonics applications are leading research studies with innovations in optical imaging, optogenetics, molecular analyses, as well as surgical and nonsurgical applications.[3]

In other fields, the tremendous progress in our understanding of the human genome has paved the way for precision-medicine initiatives to harness this information for diagnoses and therapy.[4] Many of these breakthroughs have been made possible by the use of induced pluripotent stem cell technologies. These studies have demonstrated differentiated (lineage committed) cells, either morphologically or functionally, are in a stable but potentially reversible state.[5] There have been major concerns on the promiscuity of the process of lineage reversibility (epigenetic memory) and this remains an area of intense investigation.[6] Nonetheless, the ability of a few genes or small molecules to strikingly manipulate these stem-like states has prompted exploration of clinical applicability of these technologies for regenerative medicine.

A Biophysical Approach to Directing Differentiation: A Question of Communication?

The major premise of directed differentiation is based on the essential fact that every cell in our body is equipped with the complete genetic information that is essentially fully manipulatable. A stem cell or, a little less so, a progenitor cell offers the most primed state in a cell's potential for regenerative applications. It is, essentially, a blank permissive state receptive to signals that could direct its behavior and functions (Fig. 1). Regulatory cues such as small molecules (drugs), biological (miRNA, shRNA, and transcription factors), or biophysical agents (light, ionizing radiation, ultrasound, and radiofrequency) would all be potential regulatory modalities mediating biological communication. In this context, the use of low dose biophotonics therapy termed photobiomodulation (PBM) therapy, previously called low level light/laser therapy, would represent such a biophysical cell communication cue capable of modulating stem cell behavior.[7] The PBM-induced biological changes could affect stem cell bioenergetics, metabolism, signal transduction pathways, epigenetic modulators, or gene expression to evoke therapeutic benefits.

Sadly, since the inception of the PBM field, there has been persistent skepticism on the biological efficacy of this treatment modality. The inherent disbelief that such low doses (approximating routine ambient light irradiant energy) can evoke any substantive (nonthermal) biological response appears to be rather misplaced. It is indeed normal light irradiances that enable vitamin-D metabolism in skin or modulate the vision-enabling retinal pigment, rhodopsin.[8] It is also prudent to point out that biological reactions are predominantly either biochemical or biophysical (conformational) changes. Therefore, the use of PBM treatments not only offers a reasonable biophysical modality to modulate biological molecules therapeutically, but it may also be inherently harnessing naturally occurring photoreceptive biomolecules playing key roles in physiological homeostasis processes.

Evidence for the Use of PBM Therapy with Stem Cells

The major purpose of this special issue is to provide a collated overview of the progress and increasing excitement for the use of PBM therapy with stem cells for regenerative applications. The ethical controversies surrounding embryonic stem cells aside, a key fact remains that most tissues in the adult human have a potent pool of resident stem and progenitor cells. These cells play a pivotal role in routine physiological turnover during tissue–organ maintenance as well as contribute to repair after injury. This special issue including comprehensive, state-of-the-art reviews as well as primary research articles highlights the role of stem cells in various niches that have been noted to be responsiveness to PBM treatments. Three articles in this issue focus on fibroses in heart and kidney or damage to knee joint in animal models, where PBM therapy in combination with stem cells

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