Editorial

Developing Stem Cell-Based Therapeutic Strategies in Orthopaedic Surgery

Kivanc Atesok,1 Mitsuo Ochi,2 Nicola Baldini,3 Emil Schemitsch,4 and Meir Liebergall5

1Department of Orthopaedic Surgery, University of Alabama at Birmingham, Birmingham, AL, USA
2Department of Orthopaedic Surgery, Hiroshima University, Hiroshima, Japan
3Department of Biomedical and Neuromotor Sciences, The Rizzoli Institute, University of Bologna, Bologna, Italy
4Department of Surgery, Western University, London, ON, Canada
5Department of Orthopaedic Surgery, The Hadassah-Hebrew University Medical Center, Jerusalem, Israel

Correspondence should be addressed to Kivanc Atesok; Katesok@uabmc.edu
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The term “stem cell” first appeared in scientific literature in 1868, when the German scientist Ernst Haeckel merged the concepts of phylogeny and ontogeny to describe the “stammzelle” (stem cell), an evolutionary concept of a primordial cell that evolves into all cells and multicellular organisms [1]. Although Haeckel’s argument and use of the term “stem cell” nearly 150 years ago were impressive, they were based on his observations of embryo development and the distinction between fertilized and nonfertilized eggs. The first definitive evidence for the existence of stem cells came in the early 1960s, after the Canadian scientists Ernest McCulloch and James Till performed experiments on the bone marrow of mice and observed that different blood cells come from a special class of cells [2]. Stem cell research has progressed rapidly since 1981, when the British scientist Martin Evans and the American scientist Gail Martin succeeded in isolating and culturing mice embryonic stem cells (ESCs). In the late 1990s, American scientist James Thomson first isolated human ESCs, revealing the potential for a pluripotent stem cell that would be a source of various germ layers and new organs [3]. Arguably, this recognition of the pluripotency of human stem cells triggered the exponential developments in stem cell research seen over the last two decades. Regenerative medicine has emerged as a new discipline, and its principles have been extended to surgical and nonsurgical specialties in medicine.

As a surgical specialty covering the pathologies of tissues and organs derived from two different germ layers, including the mesoderm (bone, cartilage, muscle, and ligaments) and the ectoderm (spinal cord and nerves), orthopaedic surgery is arguably one of the disciplines in which stem cell-based therapeutic strategies can be applied the most diversely. This special issue is aimed at presenting and discussing the current concepts and groundbreaking developments in stem cell-based treatment strategies in the field of orthopaedic surgery. Since adipose tissue is easier to retrieve and can often be harvested in ample quantities, K. Kjaergaard et al. studied the in vivo osteogenic potential of adipose-derived culture-expanded stem cells in an animal model. The authors showed that adipose-derived cells were capable of forming new bone, although their potential was significantly lower than that of stem cells derived from bone marrow. C. L. Roberts et al. aimed to answer the question of whether human osteoblasts can be reverted to the pluripotent embryonic state. Their results demonstrated that pluripotent stem cells that are reverse induced from osteoblasts are capable of generating osteogenic and chondrogenic cells, but lack the ability to form adipocytes.
N. Kamei et al. reviewed endothelial progenitor cells (EPCs) as a promising source of cell-based therapies to regenerate musculoskeletal and neural tissues. B. D. Bates et al. demonstrated the potential of EPCs to enhance the radiographic and morphometric parameters of bone healing when applied three weeks after bony injury in a rat model of delayed fracture healing.

Stem cell-based therapeutic applications have become the focus of intensive research in the treatment of degenerative joint pathologies, including osteoarthritis and degenerative disc disease (DDD) [4]. H. Madry et al. contributed a review article to this special issue that summarizes the technical, clinical, and biological aspects of using bone marrow aspirate concentrate with mesenchymal stem cells (MSCs) to repair and regenerate osteochondral defects. Furthermore, to enhance structure-specific regeneration of hyaline cartilage in a rabbit model, W. Guo et al. loaded MSCs onto a composite scaffold that mimicked the aligned configuration of native cartilage tissue. In another interesting study from Japan, E. E. Mahmoud et al. investigated the therapeutic potential of human multilineage differentiation to enhance bone healing in patients with diaphyseal and/or metaphyseal fractures (femur, tibia, and humerus) that had statuses of atrophic or oligotrophic nonunion.

We hope that this special issue, “Developing Stem Cell-based Therapeutic Strategies in Orthopaedic Surgery,” will help the scientific community find answers to some of its questions and will make a few strides toward benefitting our patients.

**Acknowledgments**

This special issue is dedicated to Zeki Atesok, the best brother one can have.

Kivanc Atesok
Mitsu Ochi
Nicola Baldini
George Muschler
Emil Schemitsch
Meir Liebergall

**References**


