



Editorial

Redefining stem cells through their use in musculoskeletal tissue preservation, regeneration, and cancer metastases to bone



Stem cells have been initially associated with developmental processes. However, the hope of using stem cells and derivatives as therapeutic products has transitioned from concept to reality. Thus, fields of stem cell research grew out of a traditional basic research to explore the utility of stem cell in disease diagnosis, prevention, regenerative medicine and even tissue preservation. Here we feature a set of review manuscripts that illustrate the multipotential of stem/progenitor cells using musculoskeletal tissue and cancer as examples.

By gaining better insight into the fundamental biology of stemless and self-renewal, we have made tremendous progress in understanding disease onset, progression and even resistance to treatments in some cases. Thus, within the cancer field, light has been shed on how cancer stem cells can participate in drug resistance or control of the metastatic process. Within this Special Issue, the authors have addressed two specific utilities of stem/progenitor cells, including cells derived from iPSCs as well as EV expressed by the stromal cells in musculoskeletal tissue maintenance and repair as well as in cancer propagation (Ollodart et al., 2022; Bertolini and Roato, 2022). These articles highlight the antagonistic aspects of stem cell roles in medicine and specifically in musculoskeletal-associated health and disease.

For the musculoskeletal system, one chapter focuses on the example of osteoarthritis, in which affected people can experience debilitating pain leading to inactivity or at least reduced function. Overview of clinical data available on how progenitor cells have emerged as a putative therapy for OA to delay surgical interventions are provided (Pasculli et al., 2022). Concomitantly, the variety of cell products that are currently being used underscores the need for rigorous comparison of their efficiency (Kodama et al., 2022). This need is also reflected in the limited availability of these “medicinal” cells and the subsequent importance of implementing reproducible patient grade manufacturing strategies beyond the typical quality control methodologies (Bowles-Welch et al., 2023). Additionally, the need arises to monitor/adapt efficacy of products based on the tissue of origin, the donor factors, biomarkers and potency assay and the potential ensuing immune-related sequelae to only cite a few important directions that the scientific community is actively addressing.

Another one of the major directions that is addressed in this issue is whether actual cells or cell derivatives are most useful and how we can adapt to important regulatory restrictions that arise from their use (Frazier et al., 2022). In this regard, meeting the required safety and efficacy expectations inherent in human use is at the epicenter of potential expansion or reservations about cell and cell-product-based therapies and it has become clear that a strategy in which a strong partnership is built early between the manufacturers of cell- or cell-

product-based therapeutics and regulatory entities is an important way forward. These latter issues are touched upon in this Special Issue with specific examples that are relevant to musculoskeletal tissue.

In conclusion, understanding disease onset and progression in any pathological condition is crucial to optimizing therapeutic approaches. This Special Issue highlights this need with chapters on cancer stem cells and stem cells for cancer therapy. For example, how stem cell self-renewal can be both beneficial and detrimental and how to leverage dormancy versus self-renewal to repopulate drug-targeted disease tissue and avoid drug resistance, provide lessons that are informative beyond cancer itself. Similarly, until recently, it was counterintuitive to think of stem cells as therapeutic tools to target tumors and or metastases, another important discussion within this Special Issue.

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Hicham Drissi^{a,b,*}, Hanna Taipaleenmäki^{c,d}, Christian Jorgensen^e

^a Department of Orthopaedics, Center for Musculoskeletal Research, Emory University School of Medicine, Atlanta, GA, USA

^b Atlanta Veterans Affairs Medical Center, Decatur, GA, USA

^c Institute of Musculoskeletal Medicine, University Hospital, LMU Munich, Munich, Germany

^d Musculoskeletal University Center Munich, University Hospital, LMU Munich, Munich, Germany

^e University Hospital Montpellier, Institute for Regenerative Medicine, France

<https://doi.org/10.1016/j.bonr.2023.101678>

Available online 6 April 2023

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* Corresponding author at: Department of Orthopaedics, Center for Musculoskeletal Research, Emory University School of Medicine, Atlanta, GA, USA.

E-mail address: Hicham.drissi@emory.edu (H. Drissi).