Stem cells in orthopaedics - retrospective analysis of 10 year translational research

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Abstract

More than 40 years have gone since Friedenstein described the so called colony forming unit fibroblasts. At least in the late 1990ties, a boom of stem cell research aiming for clinical application was trigger mainly but not only by publications of the groups of Pittenger, Caplan, Bruder and Prokop et al.. These publications include information of the last 20 years about the multipotency of mesenchymal progenitor cells and emphasize the significance of the human bone marrow as a cellular source for tissue regeneration. At those days “mesenchymal stem cells” (MSCs) seems to be a promising candidate to regenerate almost every local musculo-skeleteal defect. Getting more precise and detail data about the stem cell biology including differentiation potential, intracellular signaling, homing behavior and immunosuppression stem cell research was strongly promoted by industrial grants but also by public funding. There was great euphoria and hope to treat even systemic diseases such as osteoporosis, osteogenesis imperfecta and others diseases sufficiently by cell therapeutics.

In contrast to the rapid increase in knowledge and a spirit of optimism in MSC research, the regulatory authorities observe the clinical application of autologous progenitor cells more critically and sometimes with suspect. This skepticism seems to be based on the indistinct use of the word “stem cell” in many publications but also on a lack of clinical reliable data justifying a broad application besides healing attempts. In addition, the use of and research on embryonic stem cells was controversially discussed in public leading to new regulations and laws on the national and European level. Third, due to a lack of money in the health care systems insurance companies did not promote or reimburse new treatment concepts including tissue regeneration by MSCs.

Especially during the last few years controversy has arisen regarding the role and relevance of MSC in orthopaedic surgery. In contrast to the limited results in cartilage regeneration, bone regeneration was successful as shown in several clinical case series and is therefore one major focus for potential clinical application. Some investigators as the authors of this abstract suggested that the application of bone marrow aspiration concentrate (BMAC) is a valuable tool to stimulate local bone formation.

This hypothesis is based on recent data which demonstrate that a) MSCs are not the exclusive source of osteoblast, b) hematopoietic cells promote osteoblastic differentiation and c) both cell lineages are located next to each other in their physiological niches.

However, it is questionable if the relatively small number of living spongingous MSC is sufficient to induce relevant bone regeneration in vivo.

Therefore osteoconductive or osteoinductive bone substitutes are essential mimicking as a scaffold and osteopromoting microenvironment. In a review of the literature and the presentation of own in vitro but also in vivo data it is demonstrated that especially progenitors from the adult bone marrow are still promising for the treatment of defined musculoskeletal disorders. Compared to tissues with a complex three dimensional histoarchitecture such as cartilage or muscle, bone regeneration seems to be most effective. However, controlled and prospective clinical trials are strongly required to establish orthopaedic cell therapy as a standard procedure in the near future.

Key words:
osteoblast, mesenchymal stem cell, bone regeneration, bone marrow