
Editorial Letter

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Introduction

Stem cell biology is an exciting and rapidly evolving field in the life sciences. Every year, there is more interest from scientific researchers, international congresses and clinical doctors in discussing key questions about what stem cells are, how they are regulated, which possible sources of stem cells could be more functional, safer and which applications would be the most promising in human therapy. Clearly, there is a multitude of differences in the laws in force in different countries that condition research or even the application of stem cells for clinical use in humans. Even so, it is imperative to state that there is already a lot of evidence in the application of techniques using stem cells for the regeneration of cartilage and associated tissues in cases of orthopaedics or medical aesthetics, support for neuroplasticity in cases of neurodegenerative diseases and, above all, in recent years, immunotherapies as a revolutionary cell therapy to support treatment for cancer and autoimmune diseases.

Cell Therapy and Regenerative Medicine

The process of activating, replacing, engineering or regenerating human cells, tissues or organs to restore or establish normal function refers to regenerative medicine. Cell therapy is the use of various cells and their derivatives to reverse or repair the disease state of tissues or organs. Cell therapy can be administered locally or systemically and is almost always minimally invasive. In this century we have entered the era of ultra-personalized and precision medicine, biohacking and the incessant search for longevity. It is on this path that cell therapy and stem cell applications have their greatest influence. Cell therapy has always been used in some form over the centuries, but today, with the technologies available, there is an unimaginable range of possibilities. There are two classic lineages of stem cell research and

applications: embryonic or adult. Both have the ability to regenerate and the potential to differentiate. The advantage of embryonic stem cells is that they are totipotent, while adult stem cells, despite their inherent limitations, have a more specific ability to take on a morphology and function characteristic of a particular tissue. In clinical practice, there are three most common forms of stem cell application: autologous (in the case of own stem cells; e.g. umbilical cord, bone marrow, dental pulp, bone, skin or fat); allogeneic (from a donor to a recipient; e.g. bone marrow and umbilical cord) or xenogeneic (animal stem cells for clinical use in humans). In addition, there are also other studies and encouraging results in the use of iPSC-induced stem cells, where a pluripotent stem cell can be, in vitro, induced to differentiate into a specific functional tissue. This is the case for promising applications in neurodegenerative diseases.

Sources of stem cells and their main characteristics.

Briefly, we can mention below the groups most studied as sources of stem cells:

1. **Embryonic Cells:** Apart from the ethical issues surrounding the use of stem cells derived from human embryos for clinical application, this option would probably provide a great regenerative totipotency with an unparalleled capacity for self-preservation, renewal, differentiation and proliferation. Even so, there are numerous disadvantages to this modality, starting with the legislation and bioethical status limiting scientific research and ending with the development of a molecular network that would allow us to control the fate of these cells so that they develop perfectly into the desired tissues. The ethical complexity and biomolecular tangle that this network represents, despite the constant breakthroughs, is still far from being unraveled.
2. **Mesenchymal Stem Cells:** The use of mesenchymal cells, although more limited in relation to the totipotency of embryonic cells, offers an excellent and more common regenerative option. There are various protocols for extracting mesenchymal stem cells derived from the umbilical cord, fat, bone marrow, dental pulp, skin, etc. In research centers and hospitals accredited in regenerative therapy in Central America, for example, it is possible to purify mesenchymal cells from the umbilical cord so that they can be applied not only autologously, as is more usual in hematopoietic cell transplants, but also allogeneically. This last option ensures an inexhaustible source of young regenerative stem cell factors that can be applied in medical practice for a variety of pathologies, regardless of the age limit; which is a disadvantage when we mention autologous therapy.
3. **Fetal Precursor Cells or Xenotransplants:** Cells derived from controlled animal fetuses and certified for clinical use in humans is probably the most researched, exciting and studied field today, stemming from more than a century of publications, experiments and clinical applications, mainly in renowned regenerative medicine centers in Switzerland, Germany and Asia. Yet it is still little discussed. Fetal precursor stem cells have the vast quality of an extremely young stem cell coupled with the specificity that allows them to determine the type of tissues to be regenerated, since animal fetuses are already more embryologically advanced and their receptors and differentiation networks are in progress. Fetal precursor cells have high therapeutic power, differentiate and divide more quickly than embryonic cells, are better adapted to the immune system and the molecular environment, with practically zero immunogenicity. In addition, they

offer a large source of available cells with a higher survival ratio compared to embryonic cells. With enzymatic digestion and cryopreservation technology, it is possible to purify and maintain animal cell factors that are similar and can be recognized by the human histocompatibility system as "self", maintaining regenerative capacity without causing rejections or allergic events.

4. **Exosomes:** Transcription messenger vesicles from one cell to another called exosomes are the newest trend and novelty in regenerative medicine and in the studies and clinical application of stem cell biology. Exosomes contain countless regenerative and immunogenic factors that can be transferred to cells in order to maintain their regenerative and immune-modulating tissue identity. Exosomes can be purified from plant stem cells and all human tissues. The wide-ranging use of exosomes extends from applications in aesthetic medicine and orthopedics to immunotherapies and vaccine development and in the support of tumor diseases, immunosenescence and autoimmunity.
5. **Immunotherapies:** Last but not least, immunotherapy is also a form of cell therapy in regenerative medicine. Autologous specific active immunotherapy (ASI), for example, with targeted cells taken from the patient themselves, replaces, remodels or regenerates the immune system to fight disease and provide longevity. In fact, it is the most widely used and marketed form of regenerative medicine. Regenerative immunotherapy takes advantage of the intrinsic capacity of hematopoietic stem cells or more mature cells to attack and eliminate cancer cells, viruses or modulate autoimmune diseases. These cells serve as biological material for subsequent selection, manipulation and/or sensitization to increase their anti-aging potential. Among the different types of cell therapies that are receiving the most attention are stem cells, chimeric antigen receptor (CAR) T cells, natural killer (NK) cells, autologous specific active immunotherapy (ASI), thymotherapy, exosomes and GcMAF (Group-specific component Macrophage-Activating Factor). While immunotherapy has proven to be very effective in the treatment of cancers, both academia and industry around the world are now demonstrating the vast potential of these therapies also in autoimmune diseases or for longevity, in the case of immunosenescence. This brings new hope to all those seeking longevity and health.

Future of Cell Therapy and Stem Cell Applications

Where are cell therapy and stem cell applications heading? With the speed of knowledge acquired, the future is already the present and the introduction of 3D printing is already gaining greater relevance in the engineering of autologous cells and promises great advances in the regeneration of cornea, skin and fibromuscular tissues. The presence of nanotechnology, artificial intelligence and virtual reality means that potentially regenerative cells can increasingly be developed and monitored in the laboratory, regardless of the limitations of their natural sources and with much safer and more effective differentiation. The fact is that the scientific field of regenerative medicine, cell therapy and stem cell biology is growing exponentially and all eyes are on this specialty, which promises to break down the pillars of the limits of longevity and degenerative diseases.

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