

Perinatal Stem Cells

Biology, Manufacturing and Translational Medicine

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This book focuses on a new category of stem cells derived from perinatal tissue, including amniotic fluid, fetal membranes, umbilical cord, and placental tissue. Thirteen chapters overview the biology, production, and the use of perinatal stem cells in translational medicine. They are a particular type of stem cells similar to embryonic and adult stem cells and endowed with multipotent phenotypes.

As well known, the significantly high differentiative potential of embryonic stem cells, tied to the ethical concerns they raise with the risk of teratoma formation, limits their use in pre-clinical and clinical studies. On the other hand, both somatic stem cells and induced pluripotent stem cells have limitations and disadvantages. Induced pluripotent stem cells may be at risk for epigenetic abnormalities and integration of viral genomes. Somatic stem cells (*i.e.*, the most used cells in regenerative medicine) can be difficult to isolate (and this sometimes becomes a limiting factor) and may have a limited proliferative capacity. Fortunately, new shreds of evidence show that related perinatal tissues (umbilical cord, placenta, and both membrane and amniotic fluid) are new sources of stem cells, known as perinatal stem cells. The latter are classified according to their anatomical origin and divide into three groups: stem cells of the amniotic fluid, placenta, and umbilical cord; moreover, the stem cells of the placenta can be divided into three further main subgroups based on distinct anatomical districts from which they can be isolated (amnion, villi, and blood) while the umbilical cord stem cells are known as cord blood and Wharton's jelly's stem cells.

Two main biological features make these cells attractive in regenerative medicine.

1. Their differentiation potential lies between embryonic and somatic stem cells according to the stages of development they derive: the umbilical cord blood, amniotic fluid, placenta, post-gestational maternal peripheral blood.
2. Their remarkable immunomodulatory properties modulate various cells of the innate and adaptive immune systems, which can expand the applications of stem cells derived from perinatal tissues, thus opening up new therapeutic strategies.

These biological features make perinatal tissue-derived stem cells the promise El Dorado for future cellular therapies since they are free of any ethical or biological constraints usually bundled to

the other categories (*i.e.*, embryonic and induced pluripotent stem cells).

Studying the genetic stability and stemness of perinatal stem cells will undoubtedly advance our understanding of the molecular basis of stem cell pluripotency and plasticity. As I scrolled through the chapters, I discovered the fascinating world of new reagents provided by the perinatal stem cells: the secretomes they produce. It is well known that another look into the future of stem cell therapies comes from the use of stem cell derivatives such as stem cell extracts and exosomes. These soluble factors (proteins) exert paracrine activity in various biological processes such as wound healing, inflammatory response, angiogenesis, and cell proliferation, to name a few.

Secretomes produced in conditioned media can be manufactured and then used as protein drugs to treat various diseases in the near future. The exosomes (nanovesicles containing proteins, RNA and DNA) present in the secretomes produced by mesenchymal stem cells (from perinatal tissues) have already been active in regenerative processes and modulating angiogenic effects.

Several colored figures, tables, and a very rich bibliography enrich each chapter that composes this book. The reader draws essential information from this reading: mesenchymal stem cells derived from perinatal tissues are already effective in treating the nervous system, cardiovascular, inflammatory, and liver diseases, diabetes mellitus, and kidney regeneration.

The book offers detailed insights into the sources of perinatal stem cells and how to derive, multiply and store them. It is intended for researchers in stem cell biology, tissue engineering, regenerative medicine, and students in developmental/stem cell biology. Usually discarded as medical waste, such a new and versatile source of stem cells will allow new technologies to meet unmet therapeutic needs. One of the essential needs will likely involve developing effective therapies for the treatment of severe COVID-19: mesenchymal stem cells can inhibit the onset of a cytokine storm and exercise pulmonary fibrosis. Therefore, perinatal tissue-derived mesenchymal stem cells are expected to play an important role, along with massive vaccination campaigns, in restoring human health in the coming years.

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