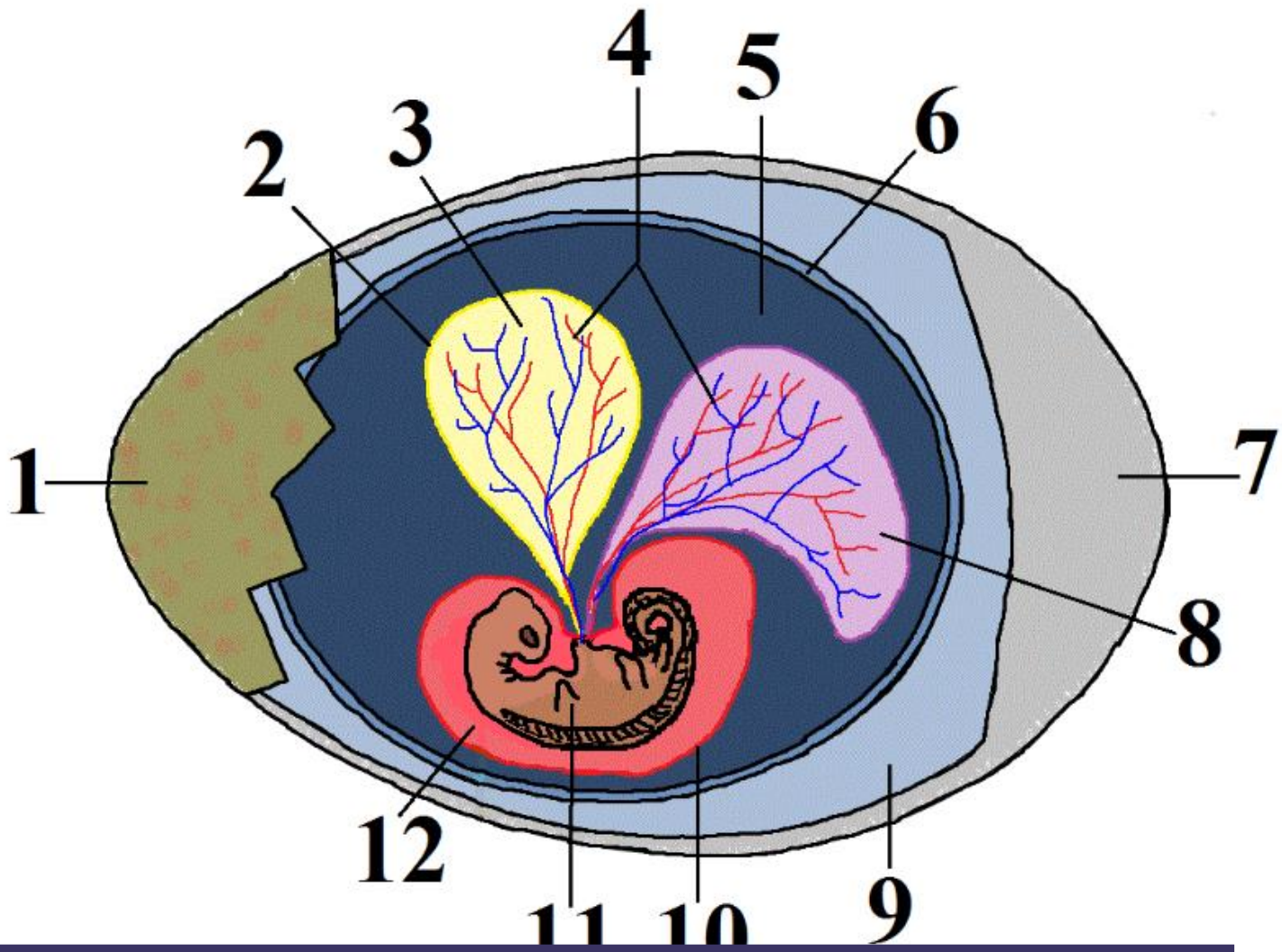

AFSC & AFMSC REPORT 2018

Physicians Products Inc. By: Douglas Ginter

info@prpkits.com

https://amniotictreatment.com

Tel: 866-704-8572

16165 Monterey Rd, 201A

Morgan Hill, CA 95037

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INTRODUCTION

History

In the last eight decades, doctors have used amniotic fluid (AF) in prenatal diagnoses for screening a variety of developmental and genetic disorders. Healthcare professionals consider it a safe, simple and reliable tool when it comes to screening pregnant women. (1) Research in regenerative medicine and stem cell therapies lead to the discovery of AF's potential role as a therapy for various pediatric and adult disorders. Initially, a subset of cells were identified in AF, capable of maintaining their undifferentiated status for long period of time while retaining their ability to differentiate into several diverse tissue types covering all three germ layers:

1. *"**THE ECTODERM** makes the central and peripheral nervous systems; the sensory epithelia of the eye, ear, and nose; the epidermis, nails and hair; the mammary glands; the subcutaneous glands; and the enamel of the teeth.*
2. ***THE MESODERM** produces connective tissue, cartilage, and bone; muscles; the heart walls, blood and lymph vessels and cells; the kidneys; the gonads (ovaries and testes) and genital ducts; the serous membranes lining the body cavities; the spleen; and the adrenal cortices.*
3. ***THE ENTODERM** gives rise to the epithelial lining of the gastrointestinal and respiratory tracts; the parenchyma of the tonsils, the liver, the thymus, the thyroid, the parathyroids, and the pancreas; the epithelial lining of the urinary bladder and urethra; and the epithelial lining of the tympanic cavity, tympanic antrum, and auditory tube."* (2)

Amniocentasis

First performed in 1930, this diagnostic procedure has evolved into a reliable, safe and authentic tool primarily used to collect amniotic fluid from which certain cells can be isolated to either diagnose potential disorders or used as powerful therapies for a variety of disorders. Usually, a very small amount of AF is collected (less than 1 ounce). AF contains diverse cell populations exhibiting a wide range of morphologies and characteristics.

Progenitor Cells

A progenitor cell is a stem cell with more specific tendency to differentiate into a certain cell/tissue type. Multiple types of progenitor cells can be isolated from AF. Approximately 0.8 to 1.4% cells in AF are progenitors.

The progenitor cells derived from amniotic fluid show a high self-renewal capacity with >300 population doublings, far exceeding Hayflick's limit (the number of times a normal human cell population will divide before cell division stops. (3)

This shows that the AF can be a great source for powerful potential therapies owing the high self-renewal capacity of its stem/progenitor cells.

Key Differences between AFSCs & Embryonic SCs

The five most prominent differences are:

1. AF derived stem/progenitor cells are not as primitive as embryonic stem cells yet they maintain a far greater potential for therapies than any other type of adult stem cells. **(4)**
2. After division from single cell, AF derived stem/progenitor cells maintain similar properties in growth and potential as the original cells.
3. Unlike embryonic stem cells, AF derived SCs, MSCs and progenitors do not cause teratomas (tumors that can contain fully developed tissues and organs, including hair, teeth, muscle, and bone).
4. AF progenitors don't need feeder layers for their growth and hence can easily differentiate into target cell lineage.
5. AF stem/progenitor cells don not require the termination of human embryos and therefore, do not involve any ethical and controversial issues.

THERAPEUTIC POTENTIAL OF AMNIOTIC PROGENITOR CELLS

AF derived progenitor cells possess great potential to differentiate into various cell type mentioned below:

- Osteocytes
- Adipocytes
- Myocytes
- Neural Cells
- Endothelial Cells
- Hepatocytes.

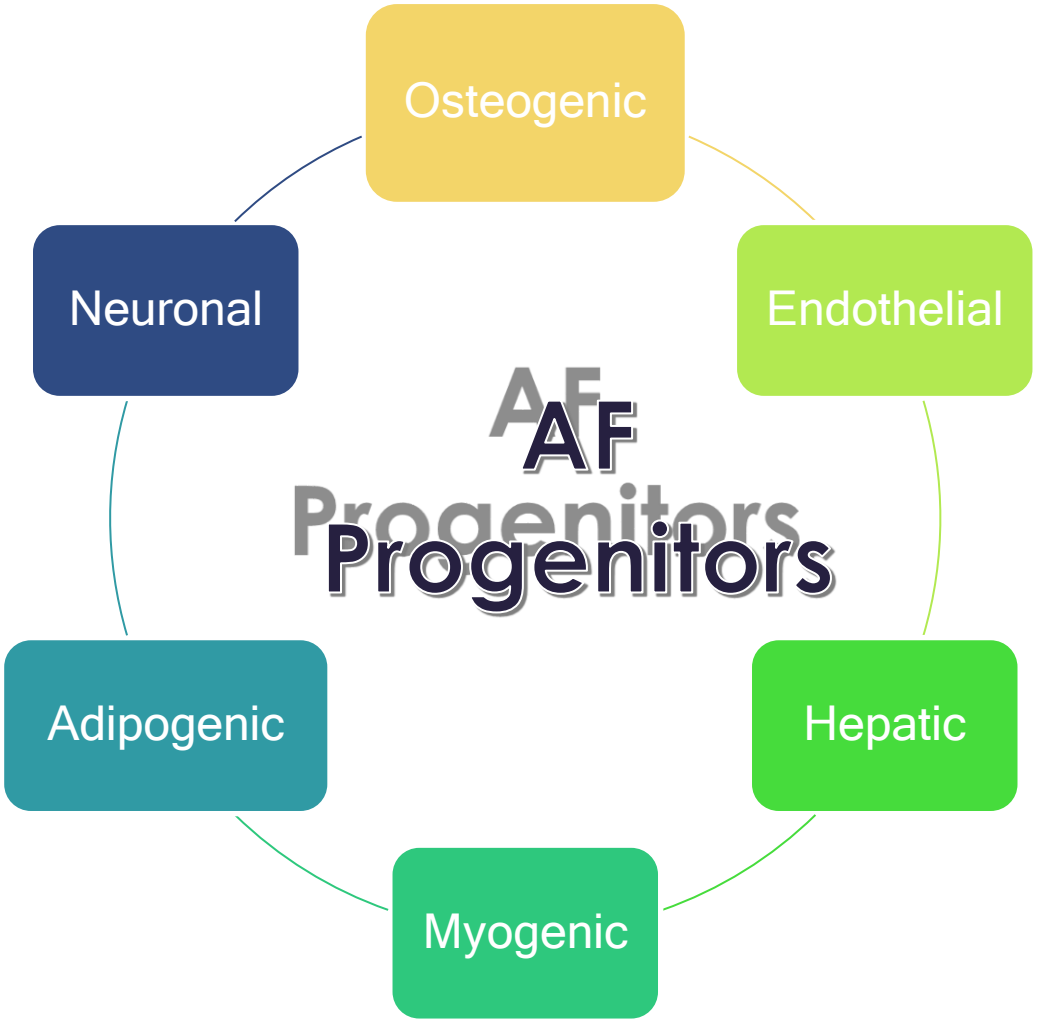
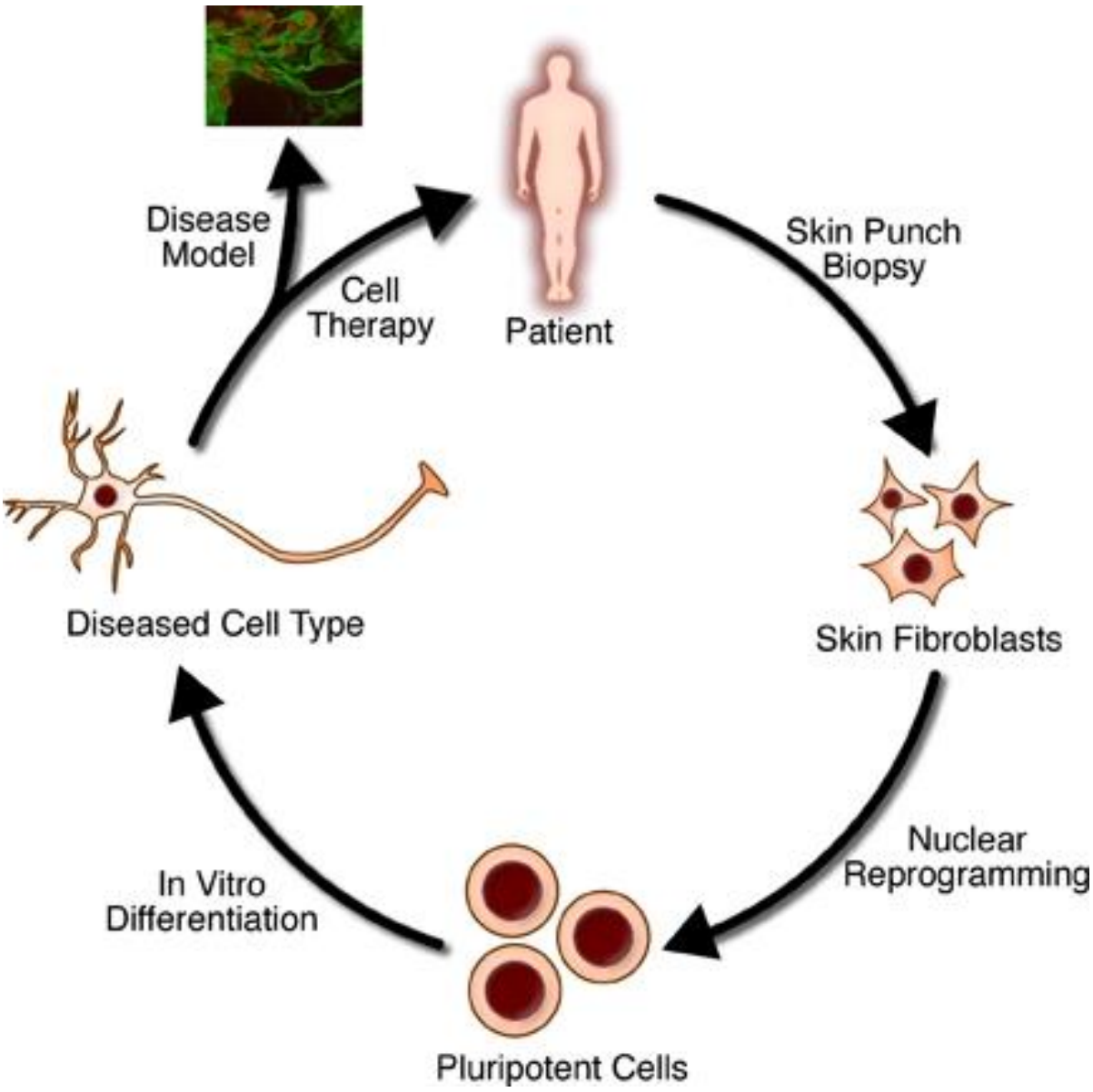


Figure Above: The isolated progenitor cells were capable of differentiation into multiple cell types, including muscle, liver, endothelial cells, adipocytes, osteoblasts, and neurons.



Tissue Engineering

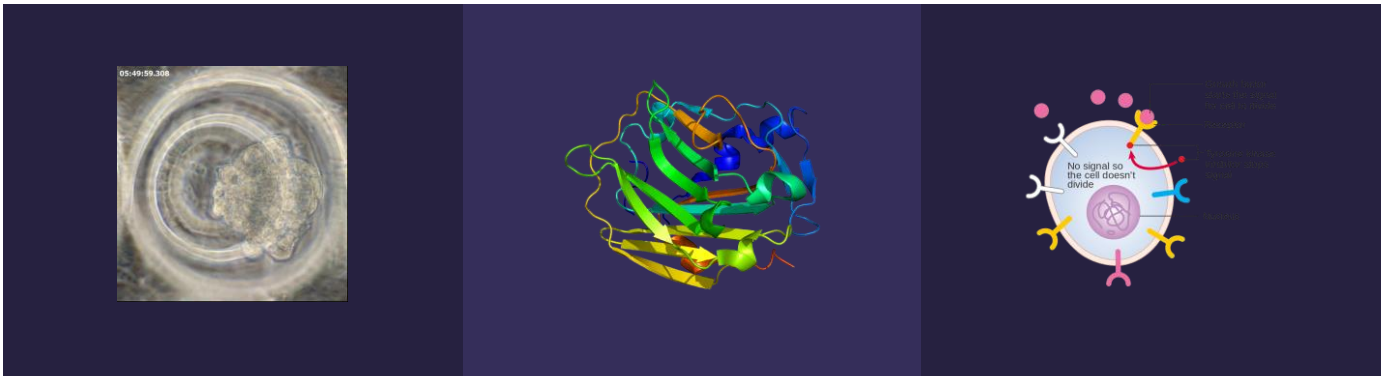
AMNIOTIC FLUID STEM CELLS AND TISSUE ENGINEERING

Definition

- "Tissue engineering is a multidisciplinary field focused in creating biological substitutes that mimic tissues. These substitutes are used in research, diagnostics and mainly in regeneration of injured or diseased tissues." **(5)**

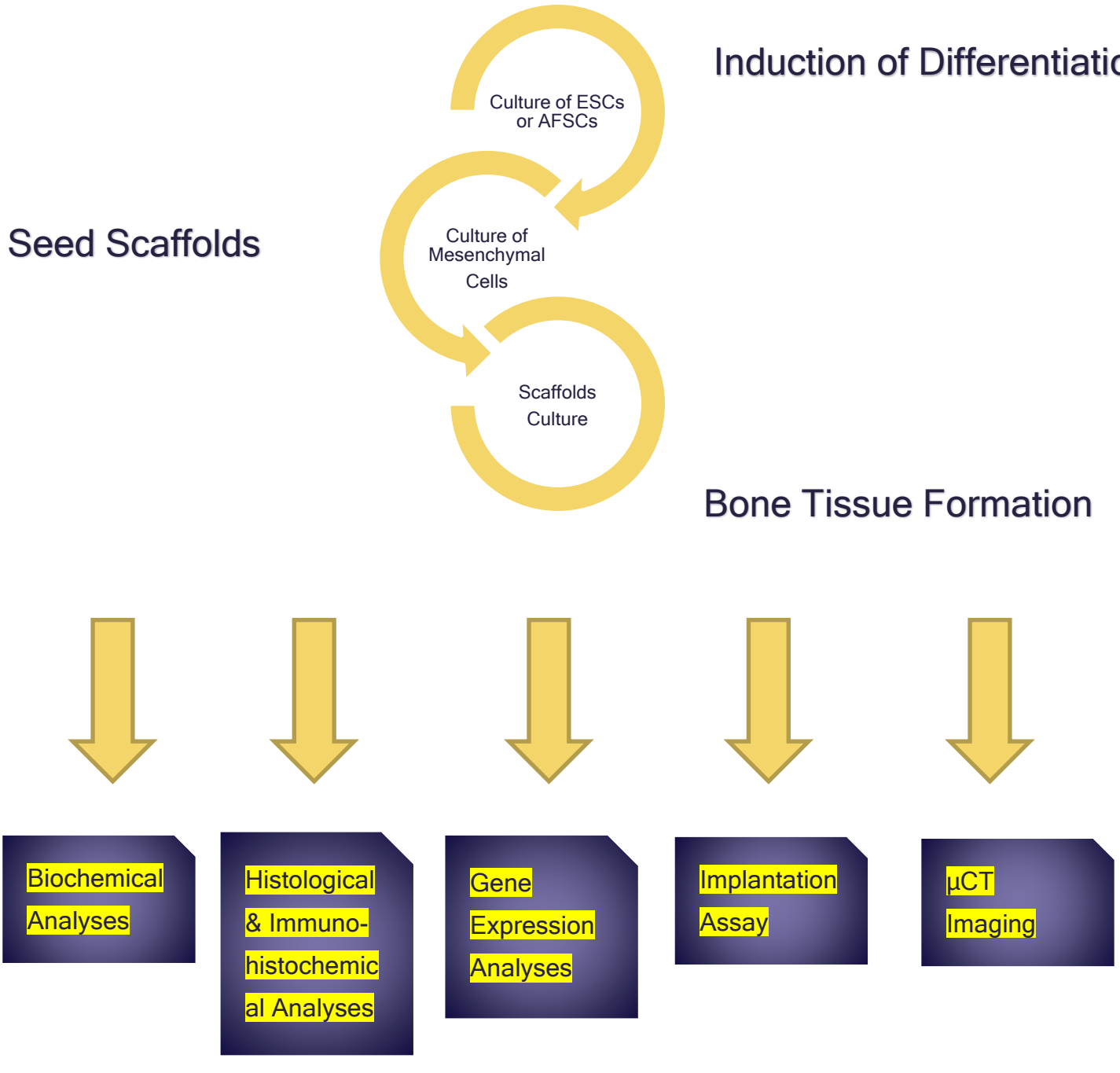
Tissue Engineering Tools

- Stem/Progenitor Cells
- Extracellular Matrix
- Growth Factors
- Bioreactors



AFSCs Proposed Role in Tissue Engineering

Unlike adult stem cells (ASC) who can differentiate to limited cell/tissue types **(6)**, AFSC are capable of differentiating into almost all cell lineages. Therefore, it is easy to use AFSCs in regenerative medicine approaches. As we already know that AFSCs are, similar to ESC when it comes to morphology and molecular signature so they can be induced to differentiate into a cell line of interest for tissue engineering purpose like ESCs. **(6)** Several protocols have been developed in the last decade to control the ESC/AFSC differentiation for tissue engineering. **(7)** Here is an example of an experimental design to prepare ESCs/AFSCs for bone tissue engineering developed by De Peppo and fellow scientists & tissue engineers.



Experimental steps to transform an AFSC or ESCs into bone cells and confirm the success of the methodology. (7)

Despite their very recent identification, several reports have investigated AFSCs potential applications in different settings.

Preclinical Studies

- **Bone**
  - Promising alternatives to bone grafting
  - An effective cell source for large bone defects.
- **Cartilage**
  - Enhancing the regeneration potential of hyaline cartilage.
- **Skeletal Muscle**
  - Effective in muscular degenerative diseases.
- **Heart**
  - Potential for replacing endogenous cardio-myocytes lost by myocardial infarction.
- **Hematopoietic System**
  - AFSCs have true hematopoietic potential both in vitro and in vivo.
- **Kidney**
  - AFS cells can differentiate towards the renal lineage
  - Can develop primordial kidney structures.
  - Can participate in all steps of nephrogenesis.
  - Can restore renal function in damaged kidneys.
- **Lung**
  - In injured lung, AFSCs not only exhibit a strong tissue engraftment but also express specific alveolar and bronchiolar epithelial markers.
  - No tumor formation in animal models warrants human clinical trials.
- **Intestine**
  - Intraperitoneal injection of AFSCs in newborn rates demonstrated 90% diffusion within hours.
  - Engraftment in different organs of gastrointestinal tract.
  - Colonizing the gut in 60% of the animals.

AMNIOTIC FLUID MESENCHYMAL STEM CELLS

In 2003, it was first demonstrated that AF contains mesenchymal stem cells that are multipotent in nature and are capable of multi-lineage differentiation potential. Their genetic analysis showed that:

1. AFMSCs' gene expression profile, as well as that of other MSC populations, remains stable between passages in culture, enduring cryopreservation and therefore can be preserved for use in later years of life.
2. AFMSCs share with MSCs derived from other sources a core set of genes involved in extracellular matrix remodeling, cytoskeletal organization, chemokine regulation, plasmin activation, TGF-β and Wnt signaling pathways.
3. They modulate the interactions between the fetus and the uterus during pregnancy.

Summary of Preclinical Studies

- Suitable for tissue engineering of congenital malformations.
- Repair of the muscle deficit in diaphragmatic hernia.
- Repair of tracheal defects in fetal lambs.
- Complete bone repair in two months' time in a leporine model of sternal defect.
- AFMSCs can harbor trophic and protective effects in the central and peripheral nervous systems.
- They have an immunosuppressive effect similar to that of bone-marrow-derived MSCs.

Conclusion

The new discoveries of easily procurable stem, progenitor and mesenchymal stem cells in AF have opened up new possibilities in the regenerative medicine approaches. Although we need to see the results of large clinical trials before it can be decided which cell sources are better, it seems that AF will take lead in many therapies due to its easy accessibility and no ethical burdens. Both AFSCs and AFMSCs can be used as primary cells in various therapies. In a future clinical scenario, AF cells collected during a amniocentesis could be banked and, in case of need, use later. (9)

DISCLAIMER

Author's Report

Despite the presented research breakthroughs and promising results, much work is still needed before the new treatment strategies are available for use in a large number of patients in a secure and effective way. **(8) Therefore, we do not take any responsibility for any injury or side effect arising from any of the treatments mentioned in this article.**

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