

# DENTAL STEM CELLS

Study Club

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# What are stem cells?

- ▣ Cells that have the potential to develop into multiple different types of cells.
  - i.e. The same stem cell could develop into a brain cell, a muscle cell or a nerve cell.

Theoretically, the cells can divide without limit, so one batch of stem cells could eventually replicate then differentiate into any type of cell that was needed for repair or healing.

# Stem cells can be harvested from many places ( but some cells are much more useful then others)

- ▣ Human embryos
- ▣ Amniotic fluid
- ▣ Brain
- ▣ Bone Marrow
- ▣ Blood vessels
- ▣ Skeletal muscle
- ▣ Skin
- ▣ Teeth
- ▣ Heart

# There are stem cells everywhere... Why teeth?

- ▣ While stem cells are in many different tissues it is sometimes hard to isolate and retrieve them.
- ▣ Teeth stem cells show promise at being more prone to replicate easily, and differentiate into different types of cells
- ▣ While some methods to extract stem cells are invasive and expensive, people lose primary teeth anyway, so harvesting is minimally invasive
- ▣ Opportunity for people to save cells from when they were young

# What classes of stem cells are there?

- ▣ Pluripotent – cells that can differentiate into any type of cell in the body
- ▣ Multipotent – cells that can only differentiate into a few different cell types.

# Multipotent cells

- ▣ Adult stem cell – Undifferentiated cell found among differentiated cells in the body
  - Also known as Somatic Stem Cell
  - Adult stem cells are thought to be limited to differentiating into different cell types of their tissue of origin.
    - ▣ However new studies suggest adult stem cells may be more adaptable than earlier thought.
  - The older the cells/persons are, the harder it is to grow and replicate them
  - These are the type of cells found in teeth and any many of the organs of the body

# Pluripotent Cells

- ▣ “True” Embryonic cells
  - These are taken from embryos
  - Usually donated by couples that have had their eggs fertilized in vitro
  - These cells more likely to be rejected by host.
  - Ethical considerations of harvesting cells from embryos.
  - Can divide without limits
  - Can differentiate into any cell of the primary 3 germ layers

# Pluripotent Cells

- Induced pluripotent cells (IPS)
  - These cells are derived from ordinary human cells. Several genes are added to convert the ordinary cell into a pluripotent cell
    - Advantages –
      - easy to obtain and process
      - Differentiate into any cells of the primary 3 germ layers
      - Patient specific, unlikely to be rejected
      - As they can be harvested from many places in the patient there is essentially an unlimited supply of cells
    - Disadvantage – The genes and viruses that are added to the cells currently cause cancer.

# Induced pluripotent cells (IPS) cont

- ▣ Disadvantages
  - The cells may have epigenetic memory of their original cell type, which limits differentiation potential.
  - Uncontrollable proliferation leads to teratomas
  - Early methods for creating IPS cells caused cancer in animals
  - Concerns over artificial nature of the cells
    - Viruses and gene modifiers used change cells from normal cells to pluripotent cells

# The primary 3 germ layers

- Ectoderm
  - Skin and nervous system
- Endoderm
  - gastrointestinal and respiratory tracts, endocrine glands, liver, and pancreas
- Mesoderm
  - bone, cartilage, most of the circulatory system, muscles, connective tissue

# **Board question – What germ layer are teeth derived from?**

- ▣ Ectoderm and Mesoderm

# Stem cell treatment that is currently being used

- ▣ Stem cell transplants also known as bone marrow transplants (most common)
- ▣ Currently used to treat leukemia, hodgkin lymphoma, non-hodgkin lymphoma, and multiple myeloma.
- ▣ Process
  - Find a matching donor, possibly take stem cells from umbilical cord from a new birth
  - Bone Marrow Killed by Chemo and radiation
  - Infusion of stem cells

# Future hopes for stem cells

- ▣ Regenerative therapy
  - Instead of using transplants for failing organs, may be able to kill some of the bad cells in the failing organs, inject the person with stem cells and then heal the organ.

# What actually can be done with dental stem cells currently

- ▣ Stem cells can be taken from a primary tooth pulp and implanted in a necrotic permanent tooth and the nerve and blood supply can be regenerated.
- ▣ Study completed in China, Clinical trial
  - Aug 2018 – Journal of science and translational medicine.
- ▣ 40 patients, all had traumatized permanent teeth that necrosed and still had primary teeth present in their mouth to harvest stem cells from (essentially children 12 and younger)

# Clinical trial cont.

- ▣ 10 patients underwent traditional apexification.
- ▣ 30 patients underwent stem cell treatment (26 returned for follow up)
  - Primary tooth extracted
  - Stem cells extracted and replicated in vitro
  - Permanent tooth pulp chamber cleaned
  - Stem cells inserted
  - 12 months after treatment- Dental pulp tissue was present with nerves and blood vessels, the length of the tooth increased and the apex decreased in size
  - After 24 months no adverse effects were found
  - Apexification allowed the tooth to be kept but did not create vital pulp tissue or increase the length of the tooth.

# Complications

- Currently, stem cell technology has not advanced enough to do much with cells harvested from adult teeth.
- Once a person no longer has baby teeth, currently unable to complete stem cell treatment to attempt to regenerate pulp.

# Hopes for regenerative therapy in dentistry

- ▣ Use stem cells in vitro to make a tooth germ that could then be placed in the jaw and grow into a tooth
- ▣ Use stem cells to fabricate a “biotooth” in vitro then transplant into the jaw
- ▣ Use stem cells to propagate cementum, PDL, and alveolar bone formation
- ▣ Use stem cells to regenerate a necrotic nerve

# Tooth Banking

- ▣ Websites are promoting tooth banking their promotions state:
- ▣ Regenerative therapies on the rise, banking teeth ensures that stem cells will be available if your child needs them
- ▣ Personal stem cells are a perfect match, no rejections
- ▣ Younger cells are better cells

# Tooth banking

- Dentists extract tooth and place into solution immediately
- Dentists Send to tooth bank company
- Company processes and tests stem cells
  - In culture cells are replicated, this insures cells can grow, creates enough cells to freeze, and creates enough cells to test that stem cells are actually present.
  - This step can be skipped, the pulp can just be extracted and frozen, decreases cost but you never really know if stem cells are saved or not
- Cryogenically frozen for future use

# Best teeth to teeth bank

- ▣ Younger cells are better at dividing, also younger teeth generally have larger pulp chambers thus more potential cells to harvest. As a result the best teeth to bank are:
  - ▣ 1<sup>st</sup> – Baby teeth
  - ▣ 2<sup>nd</sup> – Wisdom teeth
  - ▣ 3<sup>rd</sup> – Healthy adult molars

# Tooth banking cost

- ▣ Processing \$475 -1500
- ▣ Yearly fee \$115 -150
- ▣ First year total \$590 - 1650
- ▣ \$115 -150 a year after that

# What does the dentist need

- ▣ Must have a preservation kit before teeth are extracted
- ▣ Extract the perspective tooth with minimal trauma to pulp chamber
- ▣ Place tooth in preservation solution and send to tooth bank of dentists/ patients choosing.

# Tooth banking benefits

- Currently they are mostly theoretical.
- The hope is stem cell technology will advance enough in the future that harvested stem cells could be used for:
  - Tooth regeneration
  - fight cancer
  - organ replacement
  - disease recovery
- Potentially these cells could be used for pulp regeneration as earlier mentioned study used them, but again this has never been attempted.

# Places to tooth bank

- ▣ [Stemsave.com](http://Stemsave.com)
- ▣ [Store-a-tooth.com](http://Store-a-tooth.com)
- ▣ [Toothbank.com](http://Toothbank.com)