Stem Cells in Tissue Engineering

Assist. Prof. Görke Gürel Peközer

Introduction to Biomedical Engineering

22.12.2022, YTU

Tissue and Organ Losses

- Tissue and organ losses can be as a result of trauma, cancer, infection and diseases.
- They can be lethal or decrease the quality of life of patients affecting them mechanically, aesthetically or psychologically.
- The golden standard in the treatment of tissue and organ losses is to transplant their biological equivalents which is done by tissue grafting and organ transplantation.

Transplantation-Organ Donor Statistics (USA)

109,000+

Number of men, women, and children on the national transplant waiting list as of September 2020.

39,718
transplants were performed in 2019.

17
people die each day waiting for an organ transplant.

We All Need to Register. Here's Why:

90%
of U.S. adults support organ donation

but only

60%
are actually signed up as donors.

every 9 minutes
another person is added to the transplant waiting list.

only 3 in 1,000
people die in a way that allows for organ donation.

One Donor Can Save Eight Lives.

One person can donate up to 8 lifesaving organs.

Heart · 2 Lungs · Liver · Pancreas · 2 Kidneys · Intestines

Transplantation-Organ Donor Statistics (Türkiye)

Lungs	Kidney	Kidney Pancreas	Right Leg	Right Arm	Left Leg	Left Arm	Intestine	Heart	Heart Valve	Liver	Pancreas	Face and Hairy Skin	Grand Total
55	21.932	10	8	30	6	30	2	962	4	2.111	282	1	25.263

	2017	2017	Total
	Live Donors	Cadaver	
Lungs		42	42
Kidney	2.649	693	3.342
İntestine		2	2
Heart		76	76
Liver	1.087	359	1.446
Grand Total	3.736	1.172	4.908

To expand the organ donor pool

E-nabız (enabiz.gov.tr)

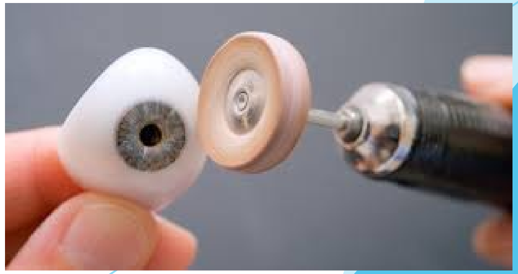
TÜRKÖK (http://www.kanver.org/sayfa/kan-hizmetleri/kok-hucre-bagisi/5)

Prosthesis

- When tissue and organ transplantation is not an option prosthesis are used to partially compensate the organ losses.
- Prosthesis is an artificial body part to replace or augment a missing or impaired part of the body
  - made of biomaterials such as metals, ceramics or polymers
  - generally permanent but have an expiration date
  - integrates poorly with the tissue at the defect site
  - can fail due to infection or fatigue






A Better Solution?

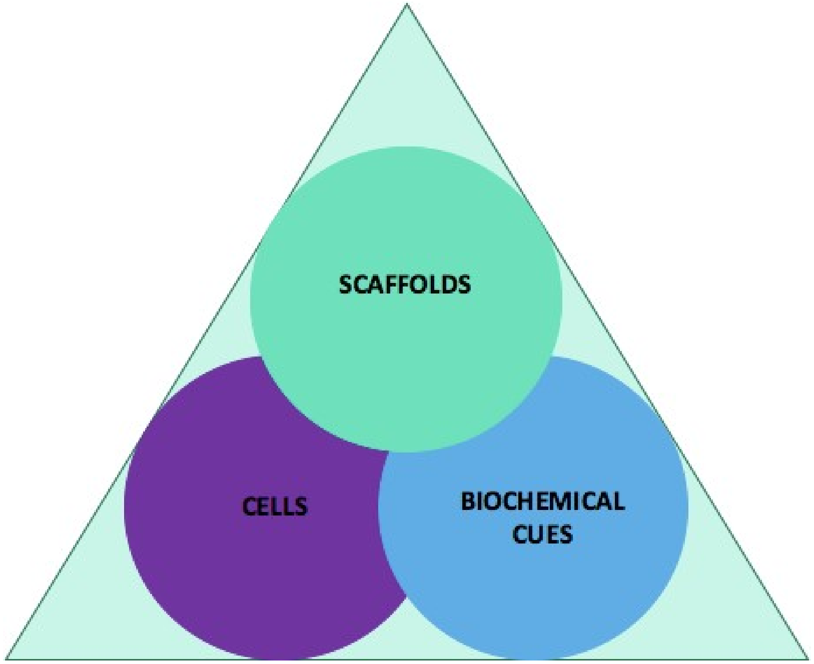
- Waiting lists for the organ transplantation, donor shortage and inefficiency of prosthesis in terms of satisfying the patients mechanical, physiological and aesthetic needs drive the scientists to search for a superiror solution.
- Tissue engineering can be a potential solution addressing the drawbacks of those conventional methods.

Tissue Engineering

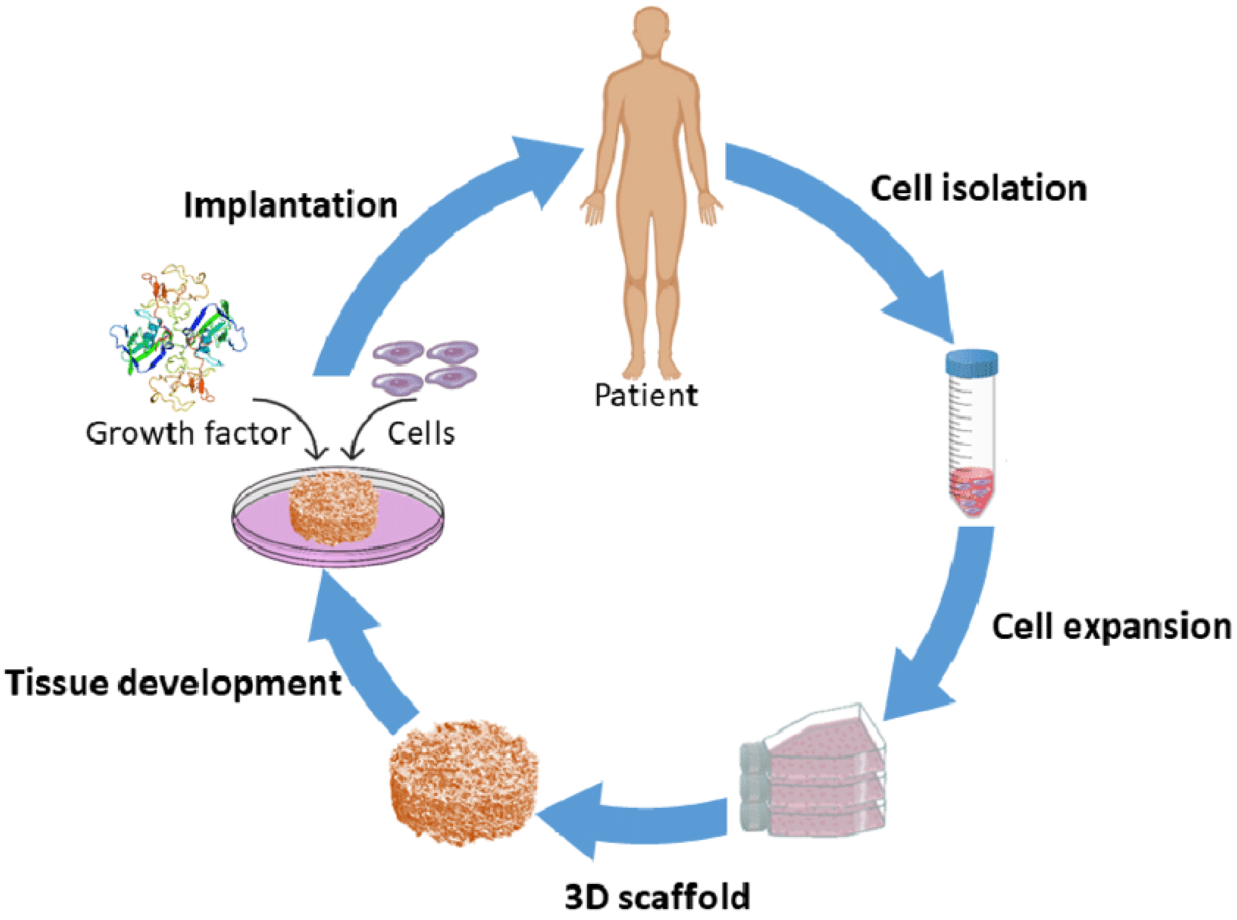
- *An **interdisciplinary field** that applies the principles of engineering and life sciences towards the **development of biological substitutes** that restore, maintain, or improve tissue function.*
- **Tissue engineering** evolved from the field of biomaterials development and refers to the practice of combining scaffolds, cells, and biologically active molecules into functional tissues.
- Tissue engineering research began as a response to the growing need for tissues and organs for transplantation.
- It offers a life-long solution and a better quality of patients' life reducing the need for repeated hospitalization and health care costs associated with pharmaceutical therapy

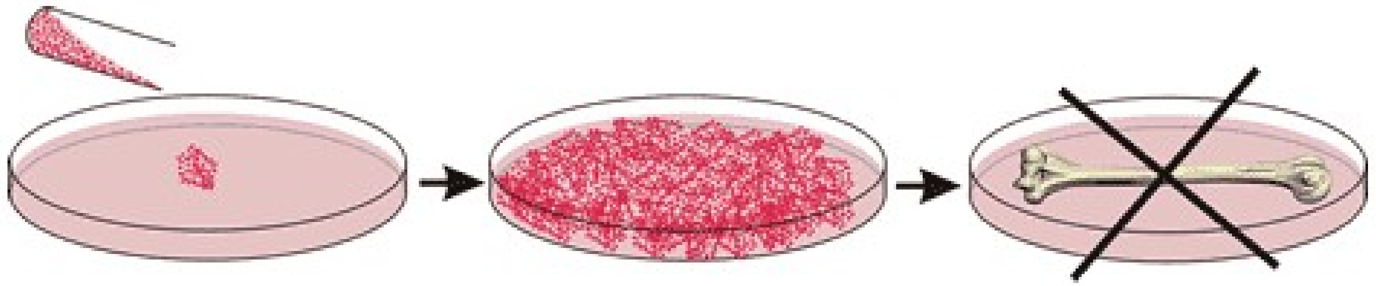
TISSUE ENGINEERING ESSENTIALS

- Tissue Engineering has 3 main components: Cells, Scaffolds, Biochemical Cues



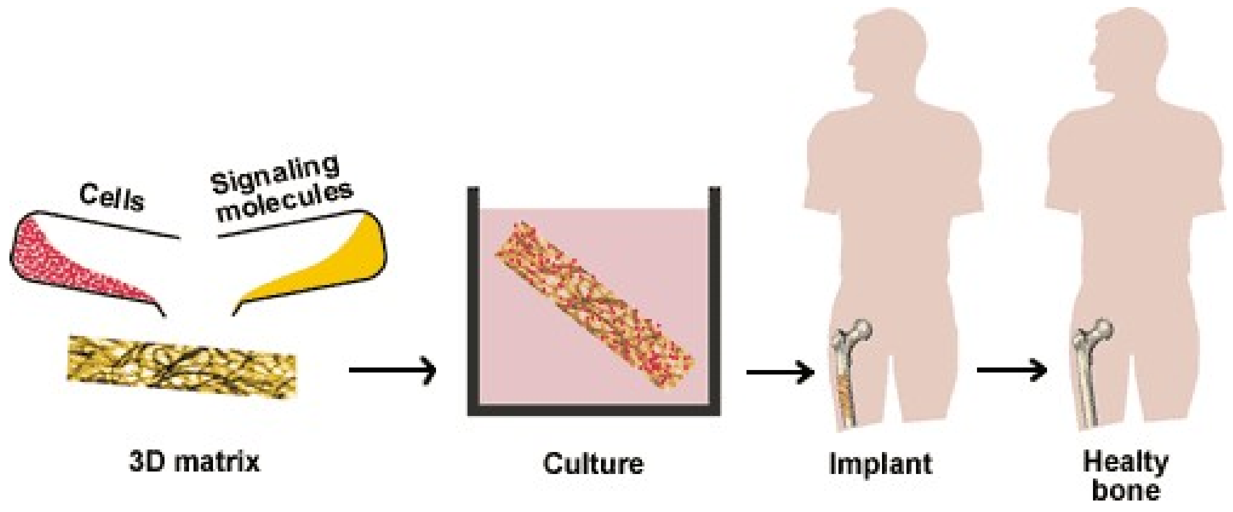
Tissue Engineering Methodology





Simple culture techniques can't be used to grow organized tissue. Why?

Cells require mechanical, electrical, structural, and chemical cues



Scaffold-guided tissue regeneration

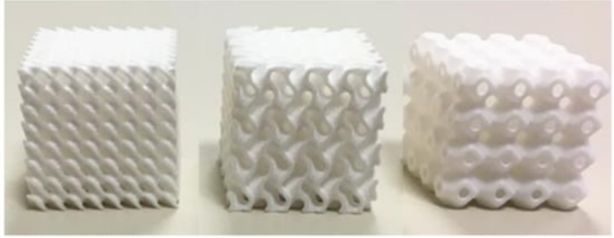
Scaffolds

- a platform which is designed for the cells to grow on and to guide them for the ultimate three dimensional (3D) architecture of the tissue
- serves as a substitute for damaged tissues by providing the necessary mechanical support until healthy tissue regenerates
- acts as a template for the guided organization of cells by providing specific signals to guide the cells and regulate the cellular function
- serves as a barrier to prevent the infiltration of surrounding tissue that may impede the process of regeneration
- serves as a delivery vehicle for exogenous cells, growth factors, and genes

An ideal scaffold:

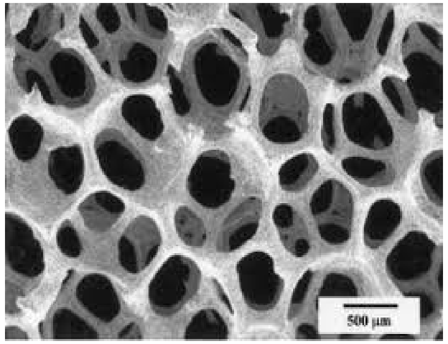
- Should be biocompatible
- Should match tissue or organ's mechanical needs
- Should promote tissue regeneration
- Should be biodegradable

metals

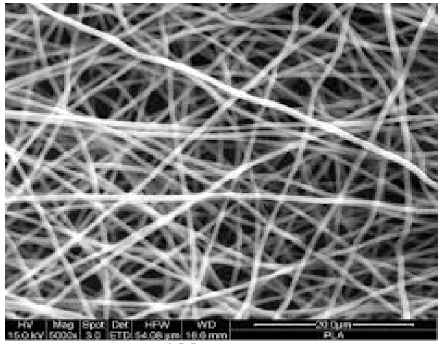


polymers

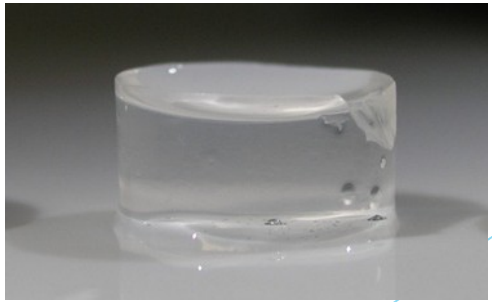
ceramics



porous



fibrous



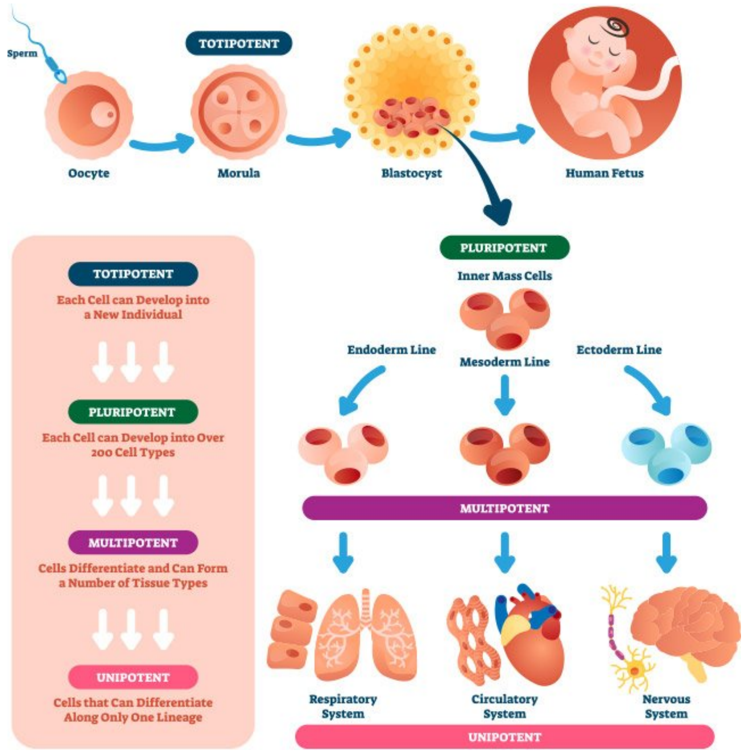
hydrogel

Primary Cells

- Chosen according to intended tissue/organ
- Autologous, allogenic, xenogenic
- Donor site morbidity, donor shortage, immune risk, pathogen transmission
- Hard to obtain high cell number
- Limited proliferation capacity

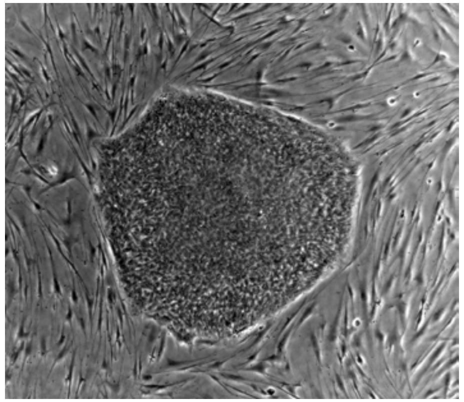
Stem Cells

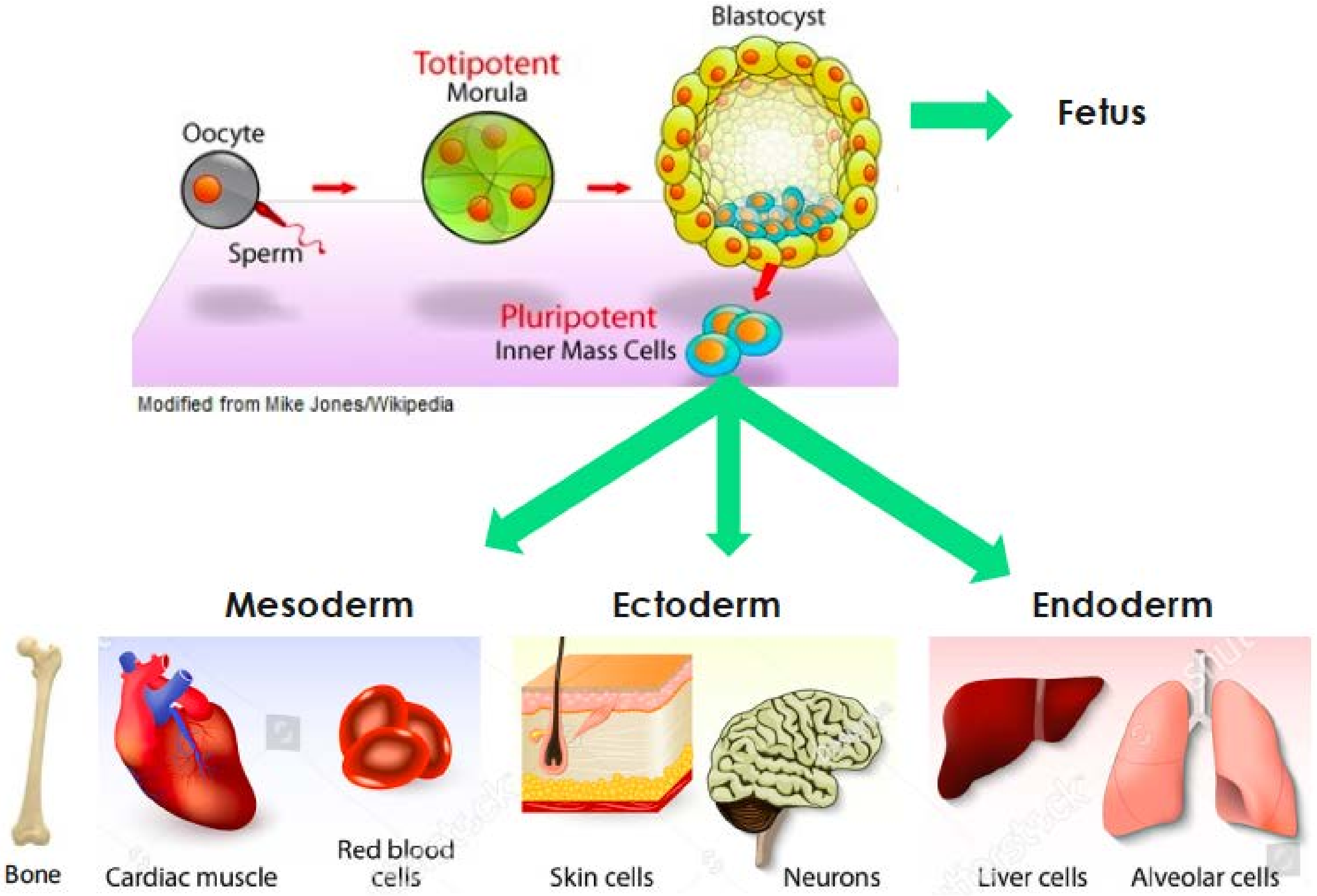
- Stem cells are undifferentiated cells that have 2 different properties: **self-renewal** and **potency.**



Embryonic Stem Cells (Pluripotent)

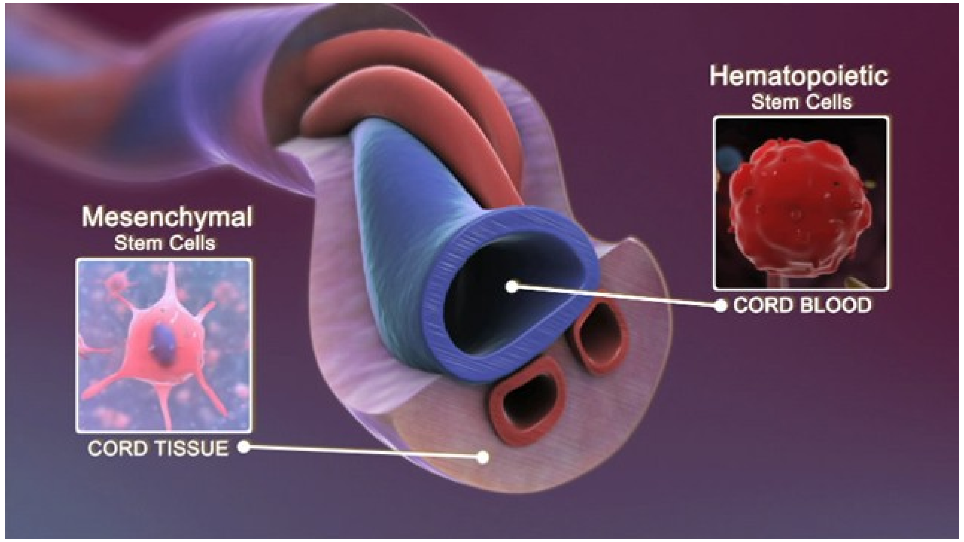
- ESCs can be isolated from ICM of blastocyst stage embryos and grown under culture conditions.
- They have the ability to self-renew with an endless capacity under appropriate conditions.
- When appropriate conditions are supplied they can differentiate all cell types from the 3 lineages body: ectoderm, mesoderm, endoderm.
- They form teratomas when implanted in body.
- There are ethical issues involved with their usage.




Blastocyst
Totipotent
Morula
Oocyte
Sperm
Fetus
Pluripotent
Inner Mass Cells
Modified from Mike Jones/Wikipedia
Mesoderm
Ectoderm
Endoderm
Bone
Cardiac muscle
Red blood cells
Skin cells
Neurons
Liver cells
Alveolar cells

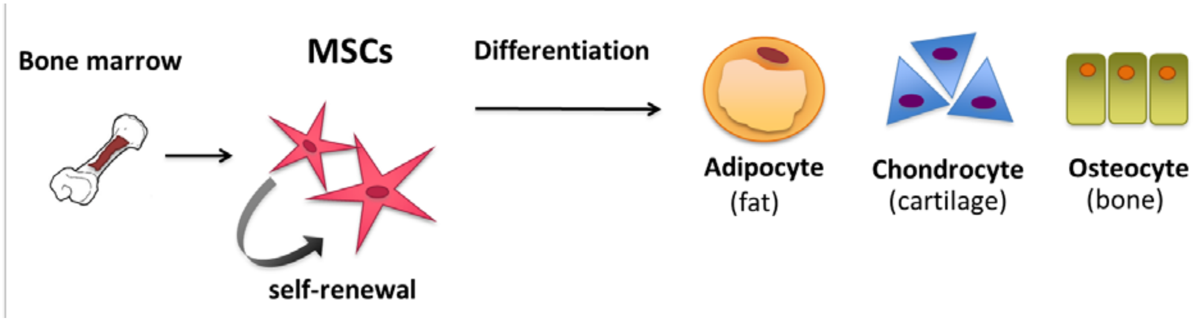
Fetal Stem Cells

- The developing organs and tissues in a fetus contain a relatively large supply of stem cells because they are needed for growth and maturation.
- The difference between embryonic stem cells and fetal stem cells is the fetal stem cells have gone through part of the way to mature cells.
- Stem cells that are isolated from umbilical cord blood as soon as the baby is born are one type of fetal stem cells.



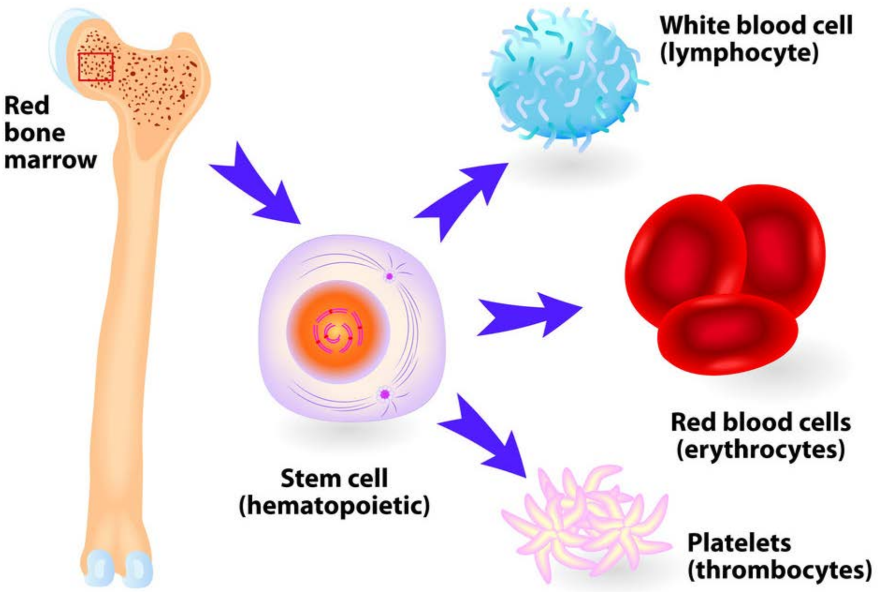
Adult Stem Cells:
Mesenchymal Stem Cells (Multipotent)

- Mesenchymal stem cells (MSCs) are a type of adult stem cells that are able to self-renew and multipotent.
- They are present in adult tissues like **bone marrow, adipose tissue and dental tissues** serving as a cell source for regeneration of various mesenchymal tissues.
- MSCs come from mesodermal lineage thus thay can differentiate into multiple tissues such as bone, cartilage and adipose under defined culture conditions.



Adult Stem Cells: Hematopoietic Stem Cells (Multipotent)

- Hematopoietic stem cells (HSCs) are stem cells that are able to self-renew and multipotent.
- They give rise to blood cells through the process of haematopoiesis.
- They are isolated from bone marrow.



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Microvascular Research

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Influence of co-culture on osteogenesis and angiogenesis of bone marrow mesenchymal stem cells and aortic endothelial cells

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Research Article

Bone Formation from Porcine Dental Germ Stem Cells on Surface Modified Polybutylene Succinate Scaffolds

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ORIGINAL ARTICLE

Osteo/odontogenic differentiation analysis of dental stem cells from tooth germ, apical papilla, and dental follicle

Pinar Ercal[1] | Fatma Cayir[2] | Gorke Gurel Pekozer[3] | Gamze Torun Kose[2]

TÜBİTAK

Turkish Journal of Biology

http://journals.tubitak.gov.tr/biology/

Research Article

Turk J Biol
(2019) 43: 235-245
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doi:10.3906/biy-1904-63

Fibrous bone tissue engineering scaffolds prepared by wet spinning of PLGA

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Role of STRO-1 sorting of porcine dental germ stem cells in dental stem cell-mediated bone tissue engineering

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Carbohydrate Polymers

journal homepage: www.elsevier.com/locate/carbpol

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Evaluation of natural gum-based cryogels for soft tissue engineering☆

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A Current Overview of Scaffold-Based Bone Regeneration Strategies with Dental Stem Cells

Pınar Ercal and Gorke Gurel Pekozer

Adv Exp Med Biol – Cell Biology and Translational Medicine
DOI 10.1007/5584_2018_171

Dental Stem Cells in Bone Tissue Engineering: Current Overview and Challenges

Pinar Ercal, Gorke Gurel Pekozer, and Gamze Torun Kose

Clinical Oral Investigations
https://doi.org/10.1007/s00784-020-03625-6

ORIGINAL ARTICLE

The effect of polyethylenglycol gel on the delivery and osteogenic differentiation of homologous tooth germ–derived stem cells in a porcine model

Mustafa Ramazanoglu[1] • Tobias Moest[2] • Pınar Ercal[3] • Zacharias Polyviou[2] • Katharina Herrmann[2] • Gorke Gurel Pekozer[4] • Aart Molenberg[5] • Rainer Lutz[2] • Gamze Torun Kose[6] • Friedrich Wilhelm Neukam[2] • Karl Andreas Schlegel[2]

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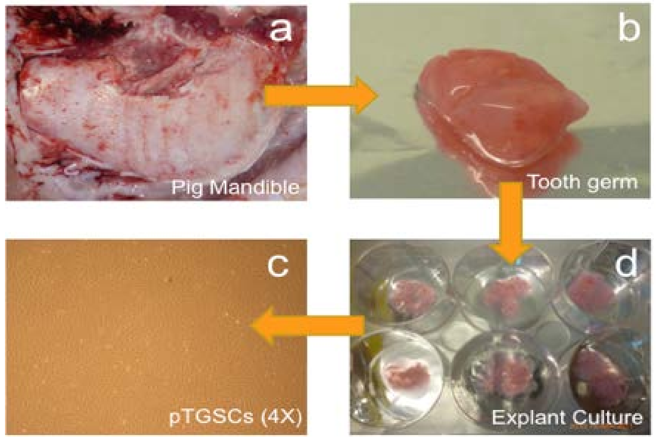
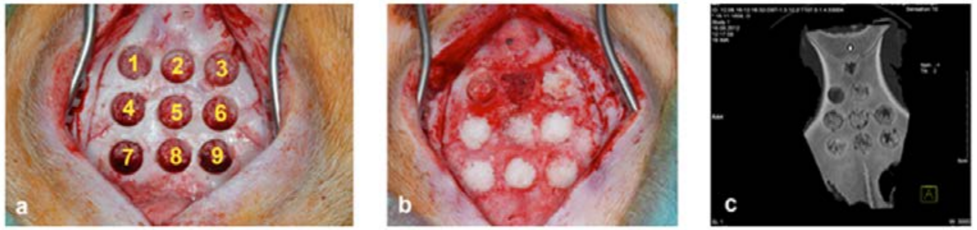
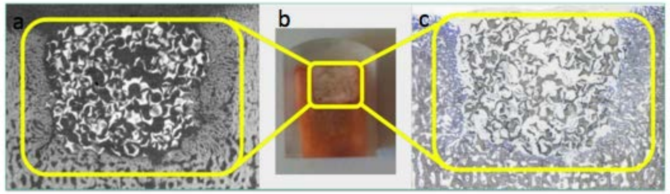
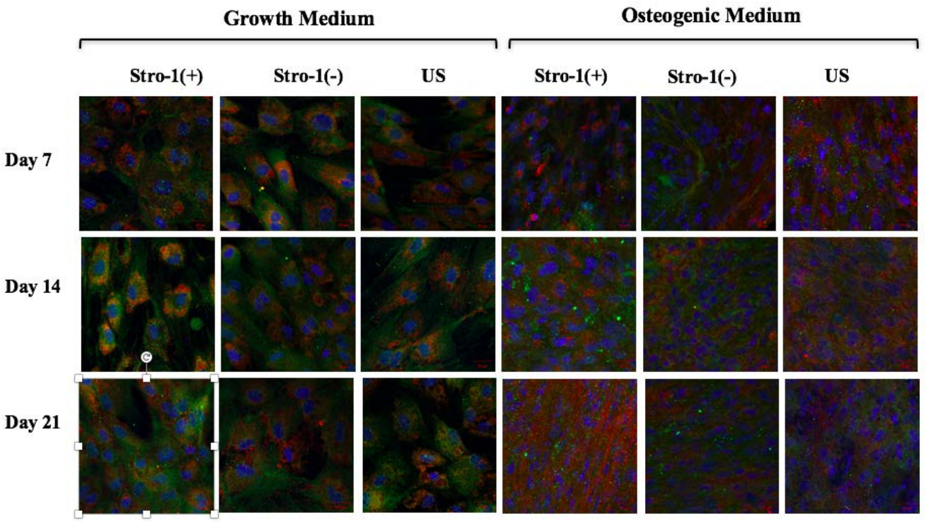
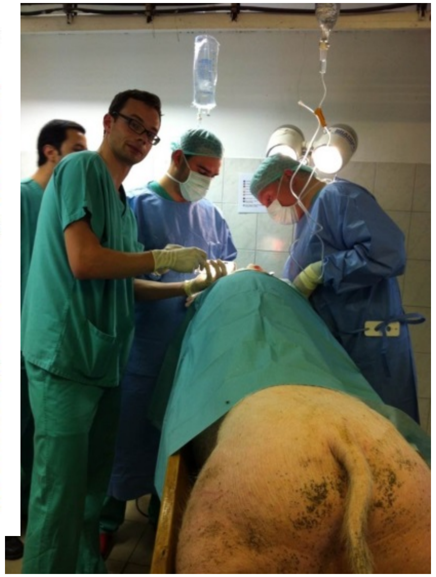
Bone Tissue Engineering with dental germ stem cells on pig model

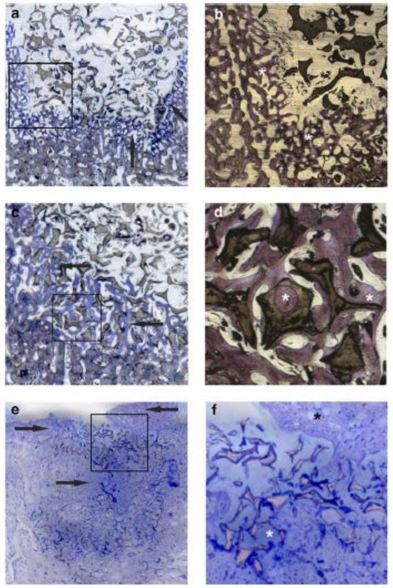












ACS Biomaterials SCIENCE & ENGINEERING

pubs.acs.org/journal/abseba Article

Investigation of Vasculogenesis Inducing Biphasic Scaffolds for Bone Tissue Engineering

Gorke Gurel Pekozer, Nergis Abay Akar, Alev Cumbul, Tahsin Beyzadeoglu, and Gamze Torun Kose*

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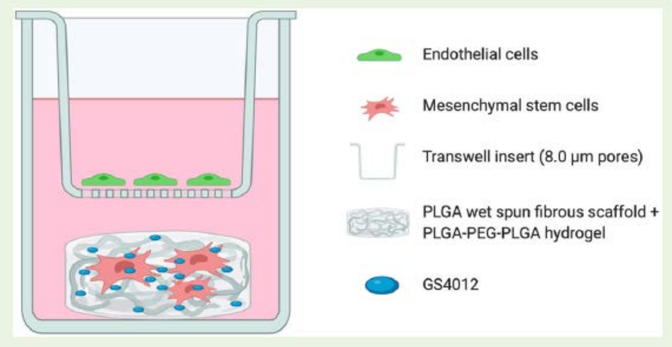

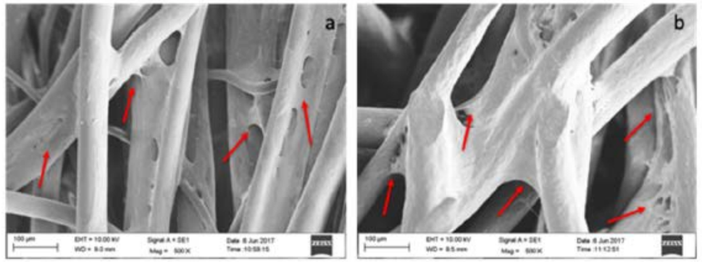

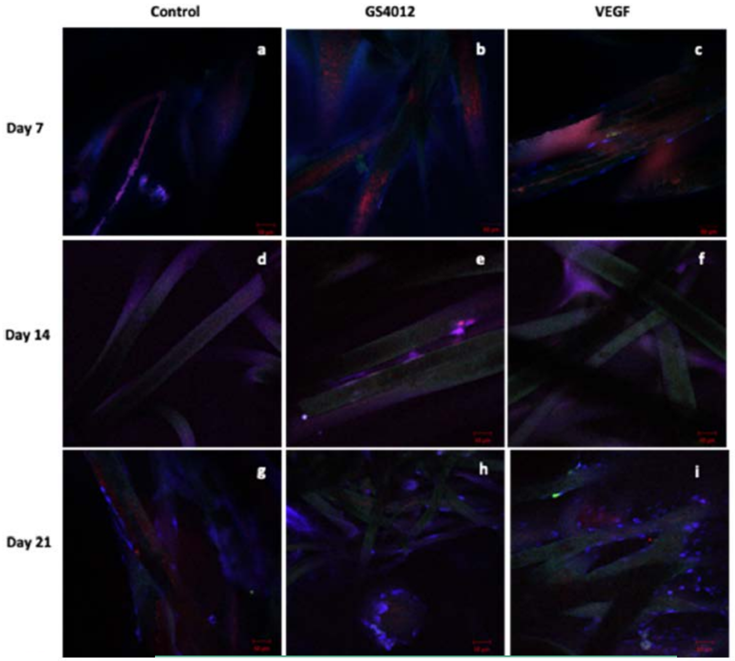

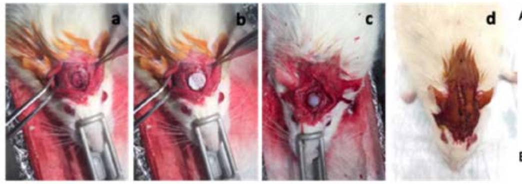

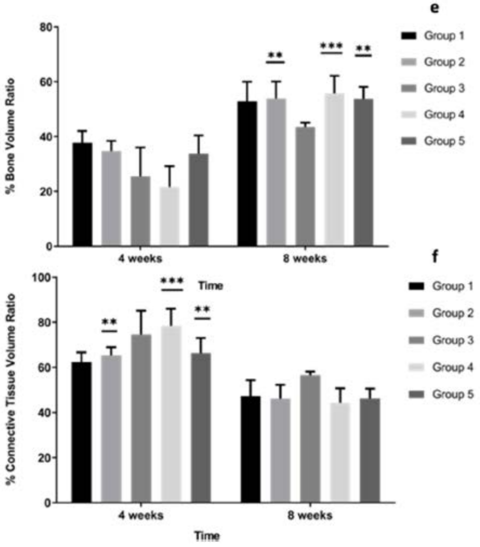

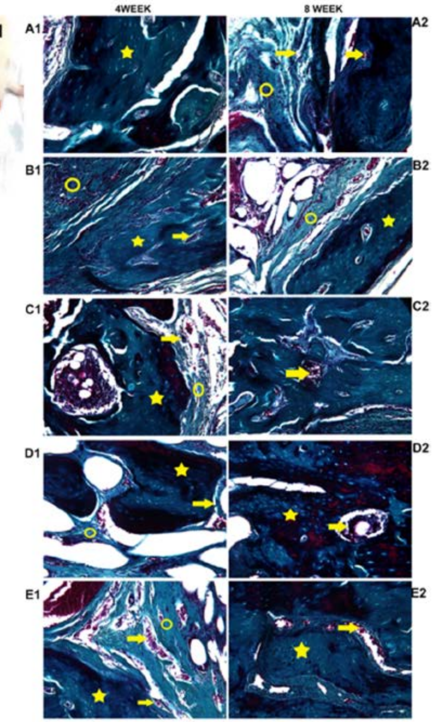

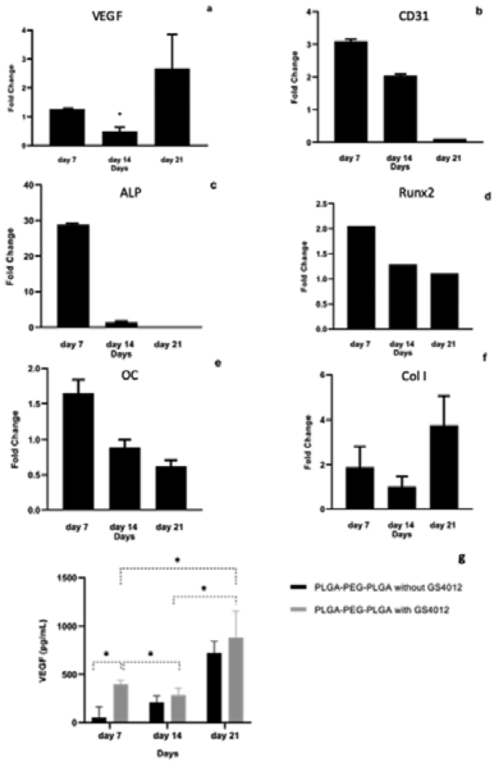

Induction of Vasculogenesis by GS4012 VEGF inducer from biphasic scaffolds on rat model