ETH zürich

Tissue Engineering I + II

Materials and Mechanics in Medicine HS 2019

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Learning Goals TE I

- 4 tissue types
- 3 ways cell receive information and how TE can provide these signals
- Different cell sources for TE and their pros and cons
- Pros and cons of scaffolds vs hydrogels

Quick Review

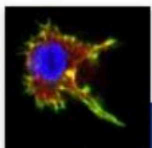
Polymers:

- PE, PP, PVC, PMMA, PTFE, PDMS → non degradable
- PLGA → degradable
- Pluronic → drug delivery
- PEG, PVA → hydrophilic, synthetic
- Collagen, fibrin, hyaluronic acid, alginate → hydrophilic, natural

→ relevant for Tissue Engineering !

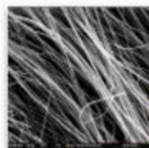
Three pillars of Tissue Engineering

GOAL: construction of living, functional components to regenerate malfunctioning tissues



Cells

- Stem cells
- Differentiated cells
- Source



Scaffold

- Biocompatible
- Porous
- Mechanical stability

Cell Signals

- Cell-Cell Adhesion
- Cell-Matrix Adhesion
- Growth Factor Signaling

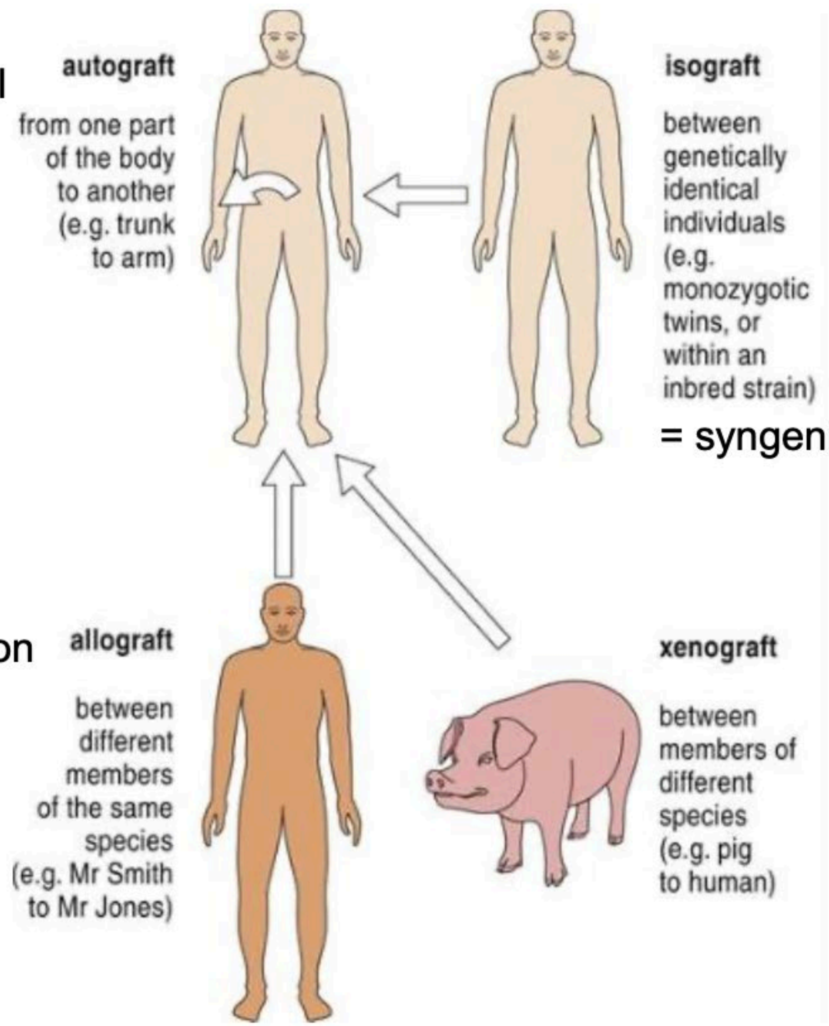
Tissue Types

- **Connective** – bone, cartilage, fat, fibrous tissue (SUPPORTING)
  - → consists of collegen fibers, polysaccharide gel
- **Epithelium** – lines the inner and outer surfaces of the body (COVERING)
  - → types: cuboidal, simple columnar, pseudostratified, columnar, stratified squamous, simple squamous
- **Nervous tissue** – conducts electrical signals (COMMUNICATING)
- **Muscle tissue** – produces mechanical force by contraction (MOVING)

Cell Sources for Tissue Engineering

No immunological response

No rejection



= syngenic

Chance of rejection

High chance of rejection

Scaffold fabrication methods

- **Porogen Leaching Method** (pore size > 13 µm)

→ macroporous scaffold

- **Reverse Opal Method** (pore size ~ 300 µm)

→ template fusion (gelatin in methanol) → PLGA scaffold

- **Cryogelation** (pore size 50-200 µm)

→ freezing of mixture (polymer solution) at subzero temperature

→ produces compressible sponges

- **Electrospinning**

→ fibrous like structure which resembles the natural collagen matrix

→ PLGA

How cells interact with their environment

- **Cell-Cell Adhesions:** Cadherins

→ TE approach: cadherin mimic peptide

- **Cell-Matrix Adhesions:** Integrins

→ TE approach: collagen mimic protein GFOGER

→ cells are allowed to spread and proliferate if GFOGER is present

How cells interact with their environment

- **Soluble Growth Factor Signalling**

→ autocrine factors

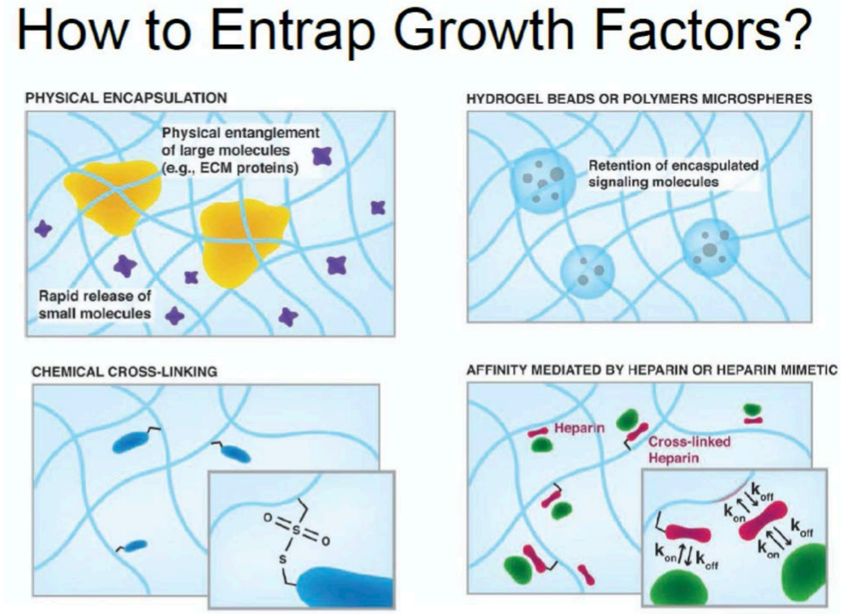
→ paracrine factors

- **Examples of GF in TE**

→ VEGF (vascularization)

→ BMP (bone)

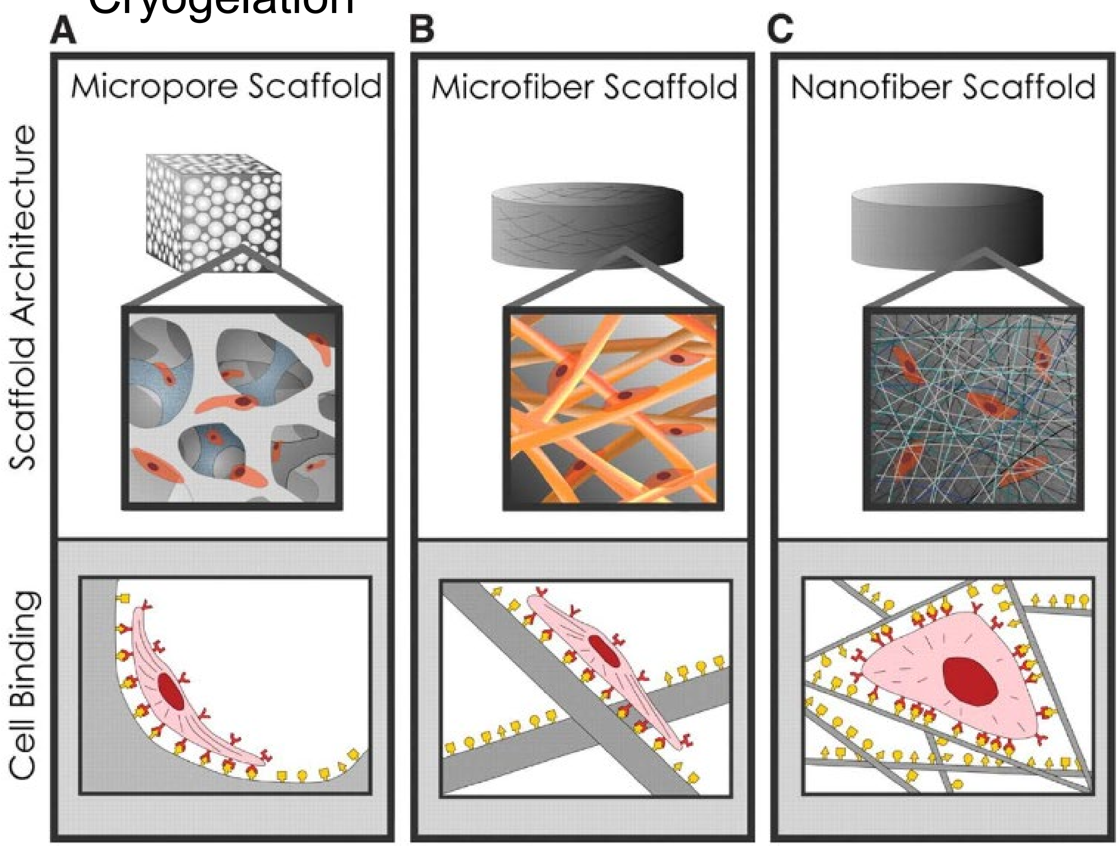
→ ...



How cells interact with their environment

Porogen Leaching,
Reverse Opal,
Cryogelation

Electrospinning



- cell motility
- diffusion of nutrients
- angiogenesis

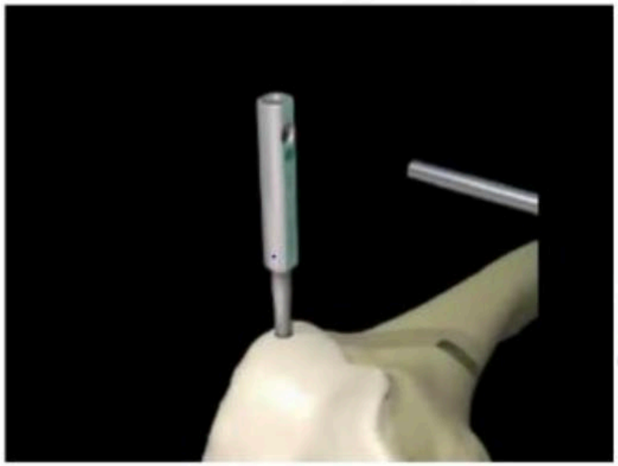
- Mechanical stability
- Biocompatibility
- Degradability
- Connectivity

Learning Goals TE II

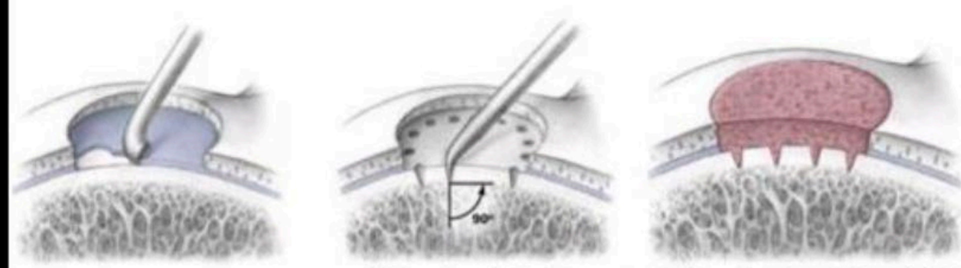
- Understand cartilage engineering (flat)
- Know how to make autologous skin grafts (flat)
- Know the important properties of a material for encapsulating cells (artificial pancreas)

Cartilage Engineering

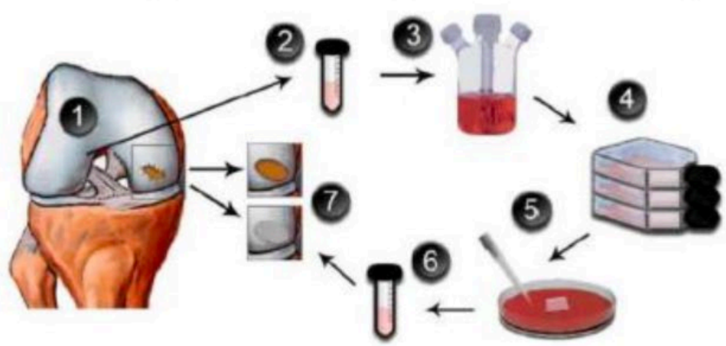
1. Mosaicplasty



2. Microfracture:
Poor man's cell therapy



3. Autologous Chondrocyte Implantation (ACI)



4. Novocart 3D, Aesculap

- Cell isolation (chondrocytes)

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- Expansion
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→ fabrication of Novocart 3D

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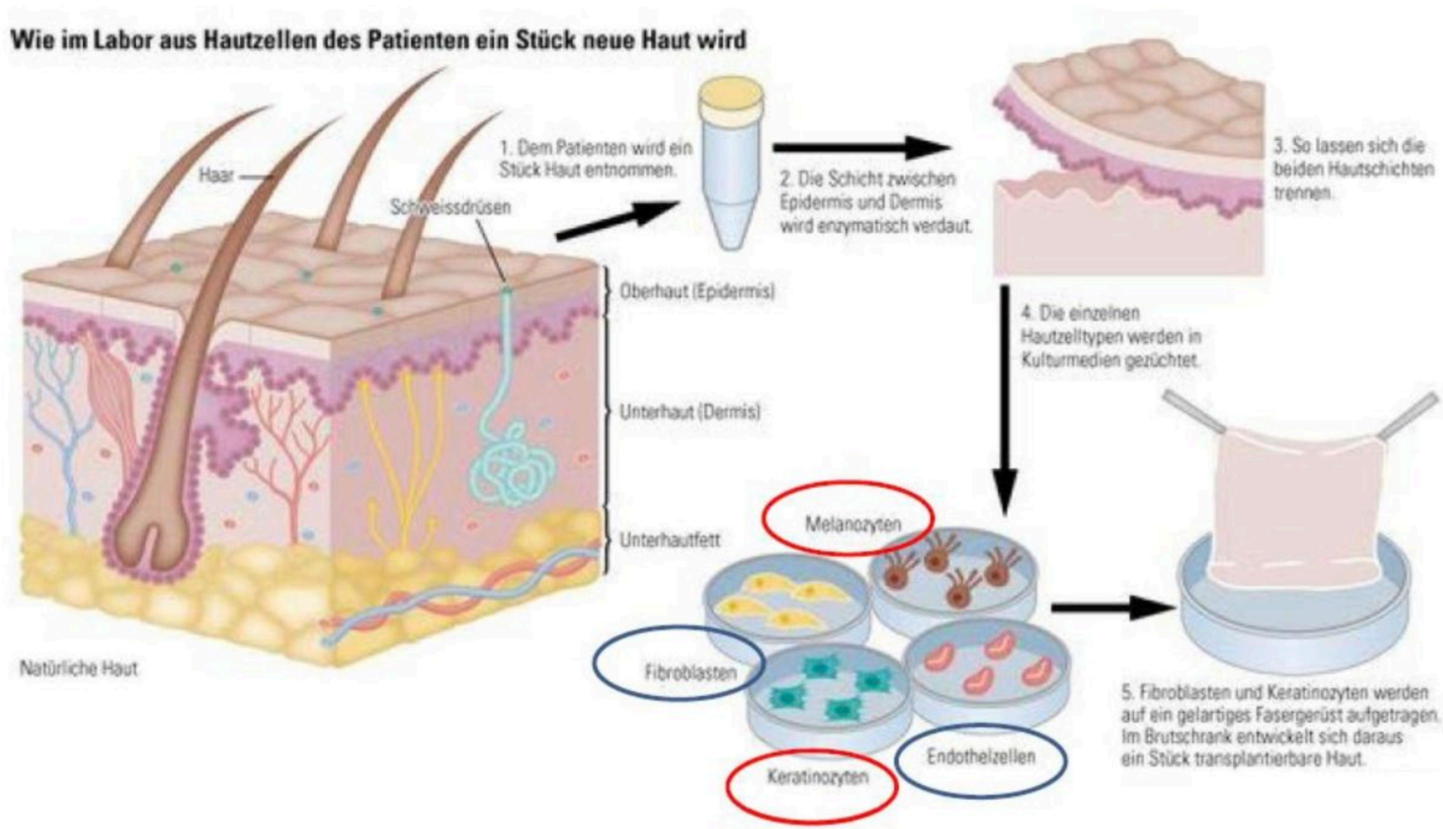
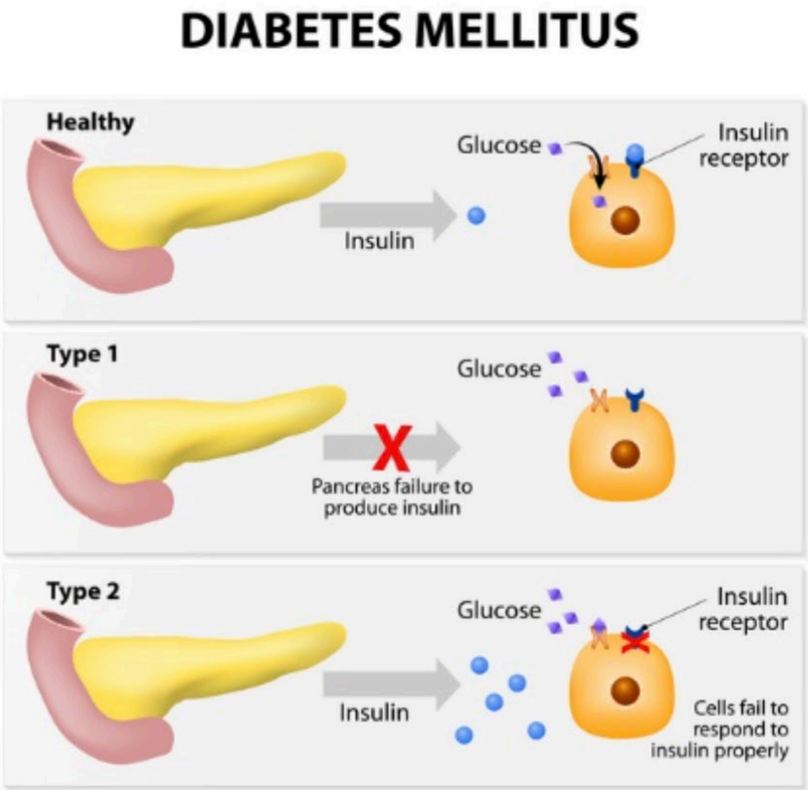
- Implantation (minimal invasive)

Skin Engineering



- Skin graft assumes pigment of donor
- BauxScore to predict mortality of burn patients

Pancreas Engineering



Pancreas Engineering

- Replacement of non-functional islets of Langerhans

- Sheet to protect the donor islets from host rejection
  → thin: O_2 can diffuse
  → Islets can sense glucose levels and secrete insulin
  → Alignate is used to protect islets
    - No enzymes to break down alginate
    - Biocompatible
    - Gelation methods:

    - $CaCl_2$ (fast, uncontrolled, anisotropy)
    - $CaCO_3$ – GDL (time controlled, homogenous structure)

Kidney Engineering (extracorporal)

Current situation:

- high blood pressure and diabetes → nephron damage
- low life expectancy on dialysis

TE Applications:

- Artificial Kidney – „Hemodialysis“
  → Hollow-fiber Design using counterflow current
- Bioartifical Kidney – The Renal Assist Device (RAD)
  → Renal epithelial cells line hollow fibers in device
- iRAD – Implantable Renal Assist Device

Q1: Novocart 3D Treatment

- from whom are the cells taken? (autologous vs allogenic)

- cells isolated from cartilage tissue

→ what kind of cells do you find in cartilage tissue?

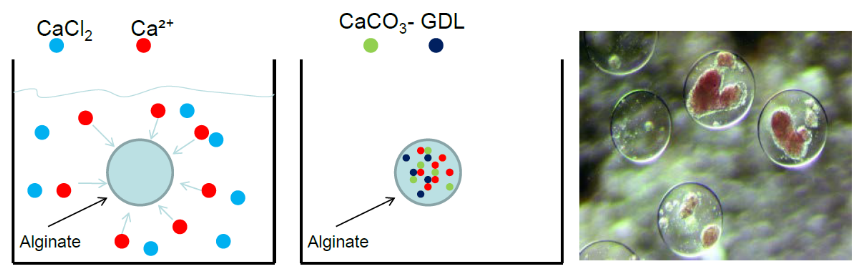
Q2: Biopolymer Alginate

a. Look at periodic table
b. In vivo vs in vitro
c. Think about differences in degradation mechanisms in marine seaweed and mammalian cells
d. Advantage for TE
e. two options

Alginate – Ion-Induced Gelation

2 Gelation Methods:

- $CaCl_2$: fast, uncontrolled, non-homogeneous, hard shell softer core
- $CaCO_3$-GDL (D-(+)-glucono-δ-lactone): time controlled, homogeneous structures



Q3: Key Features of Scaffolds

- Think about cell signals and cell interactions discussed during the lecture today

- The following points each match to one picture:

→ Tissue stiffness gradient
→ Recognition sites
→ Growth factors
→ Cell-cell interactions
→ Crosslinking density

Q4: Pore Size

- Pore size dependent on used material/ polymer/ particle?
- Cell-Cell interconnections?