An Introduction to Tissue Engineering

Lesley W. Chow

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October 30, 2015

The Brown and White
All the Lehigh news first since 1894

Bear sighted on Lehigh's Goodman Campus

0

BY DANIELLE DISTEFANO PUBLISHED JUNE 26, 2015, 3:09 PM

NEWS, TOP STORIES

disclosure:
not Lehigh bear

lehighvalleylive.com

Bear captured after surprising party near Lehigh campus

Steve Novak | For lehighvalleylive.com By **Steve Novak | For lehighvalleylive.com**
Email the author | Follow on Twitter
on June 27, 2015 at 1:35 PM, updated June 27, 2015 at 2:40 PM

An early morning party near **Lehigh University's** campus was startled by an unexpected guest wandering through South Side **Bethlehem**.

City police responded to a flood of 911 calls for a black bear roaming the city about 2 a.m. Saturday near Fifth and Pierce streets, Chief **Mark DiLuzio** said.

"I guess the bear must have gone to the party -- near the party -- and surprised a bunch of people," he said.

Tissue Engineering is...

*"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 or a whole organ**"*

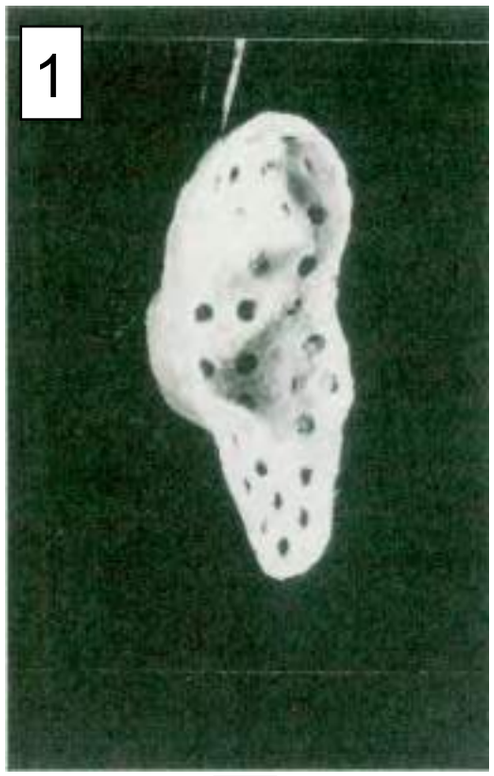
Langer and Vacanti, *Science* 1993

Classic Tissue Engineering: The Vacanti Mouse

landmark study from 1997 that helped launched the field

Cao, Vacanti, Paige, Upton, and Vacanti, *Plastic and Reconstructive Surgery* 100:297, 1997

Classic Tissue Engineering: The Vacanti Mouse



1

scaffold made from poly(glycolic acid) (PGA) and poly(lactic acid) (PLA) cast from plaster replica of an actual ear

Cao, Vacanti, Paige, Upton, and Vacanti, *Plastic and Reconstructive Surgery* 100:297, 1997

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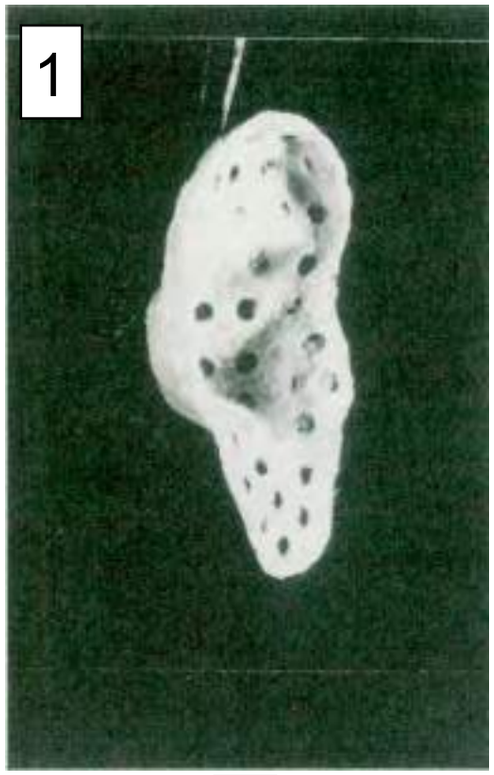

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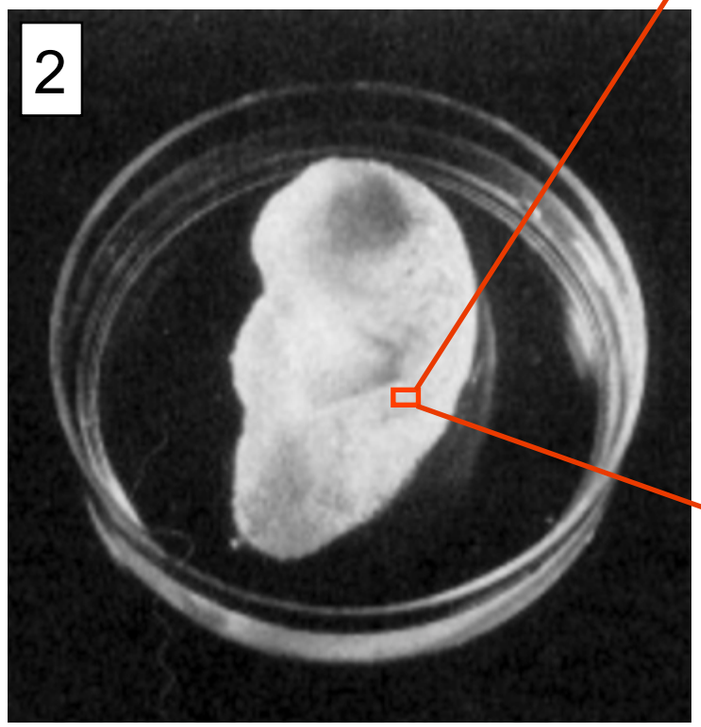
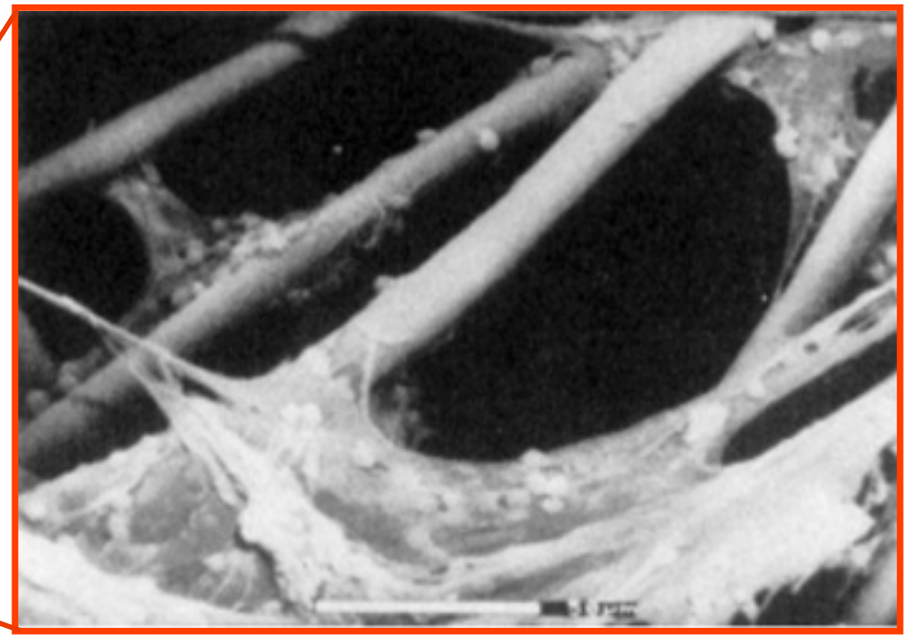


2

scaffold seeded with chondrocytes and cultured for 1 week



SEM micrograph showing cells and ECM on scaffold

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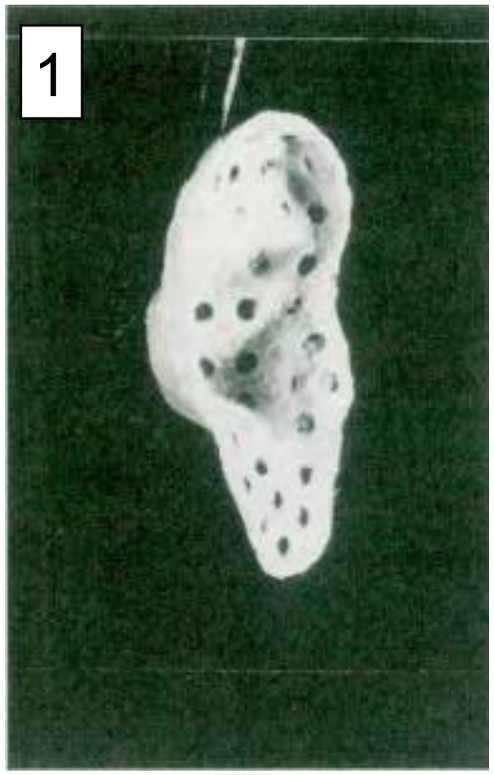

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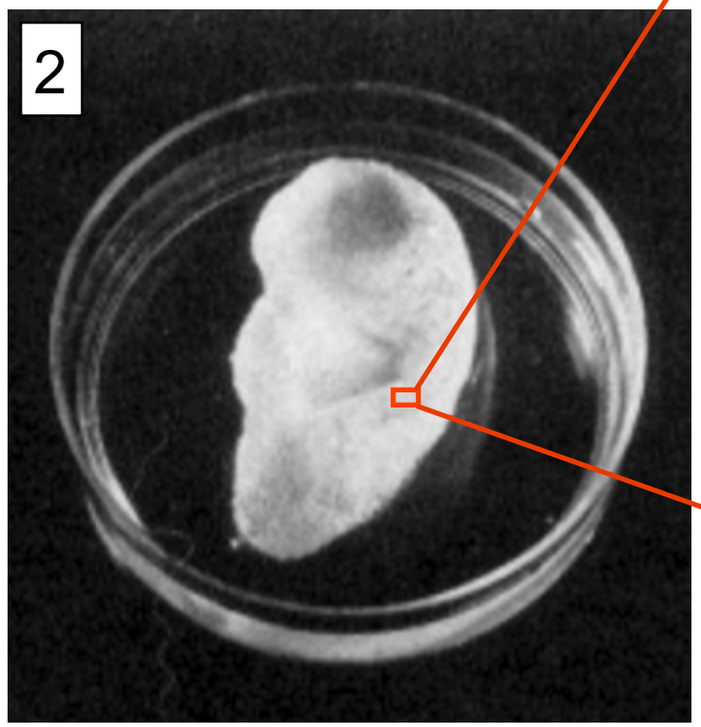
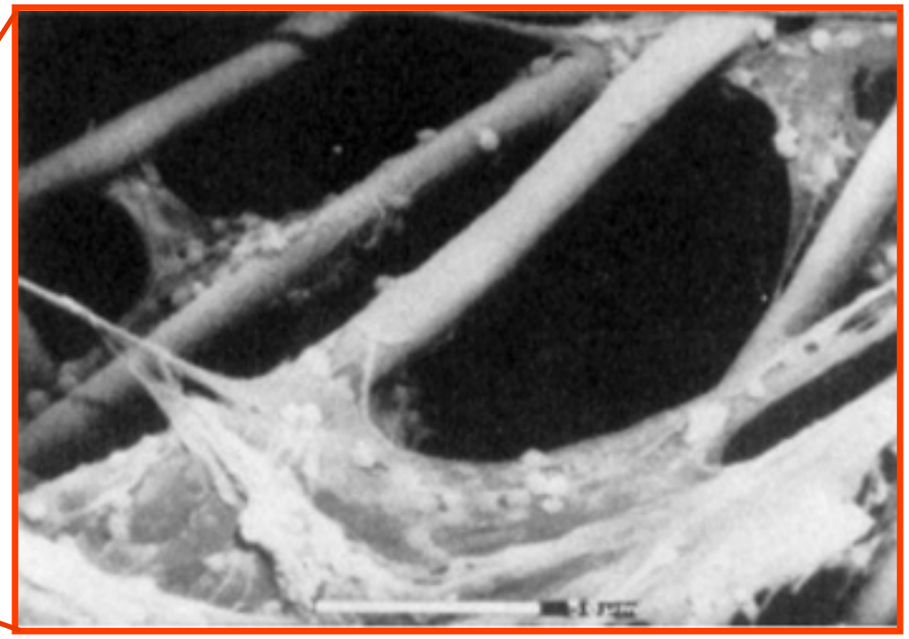


2

scaffold seeded with chondrocytes and cultured for 1 week

3

implanted subcutaneously on the back of a mouse



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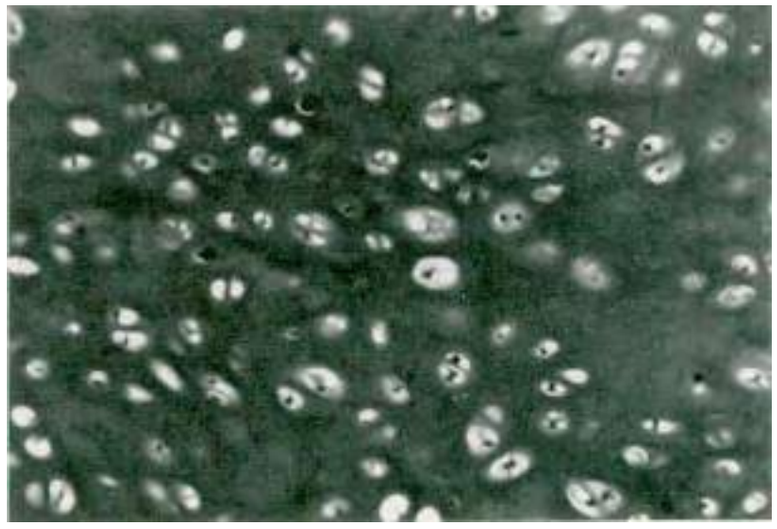
The Vacanti Mouse set the tone for TE field



histology of construct at 6 weeks

- Extensive cartilage formation
- Anatomical shape could be maintained (with external stenting)

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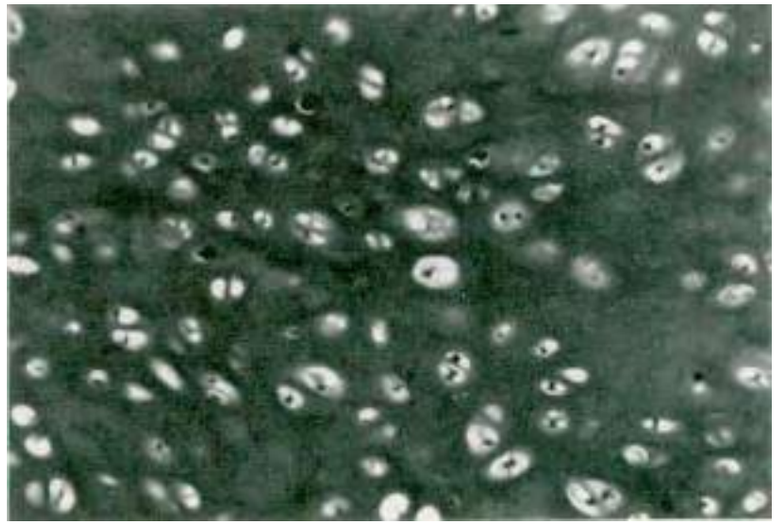

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- Extensive cartilage formation
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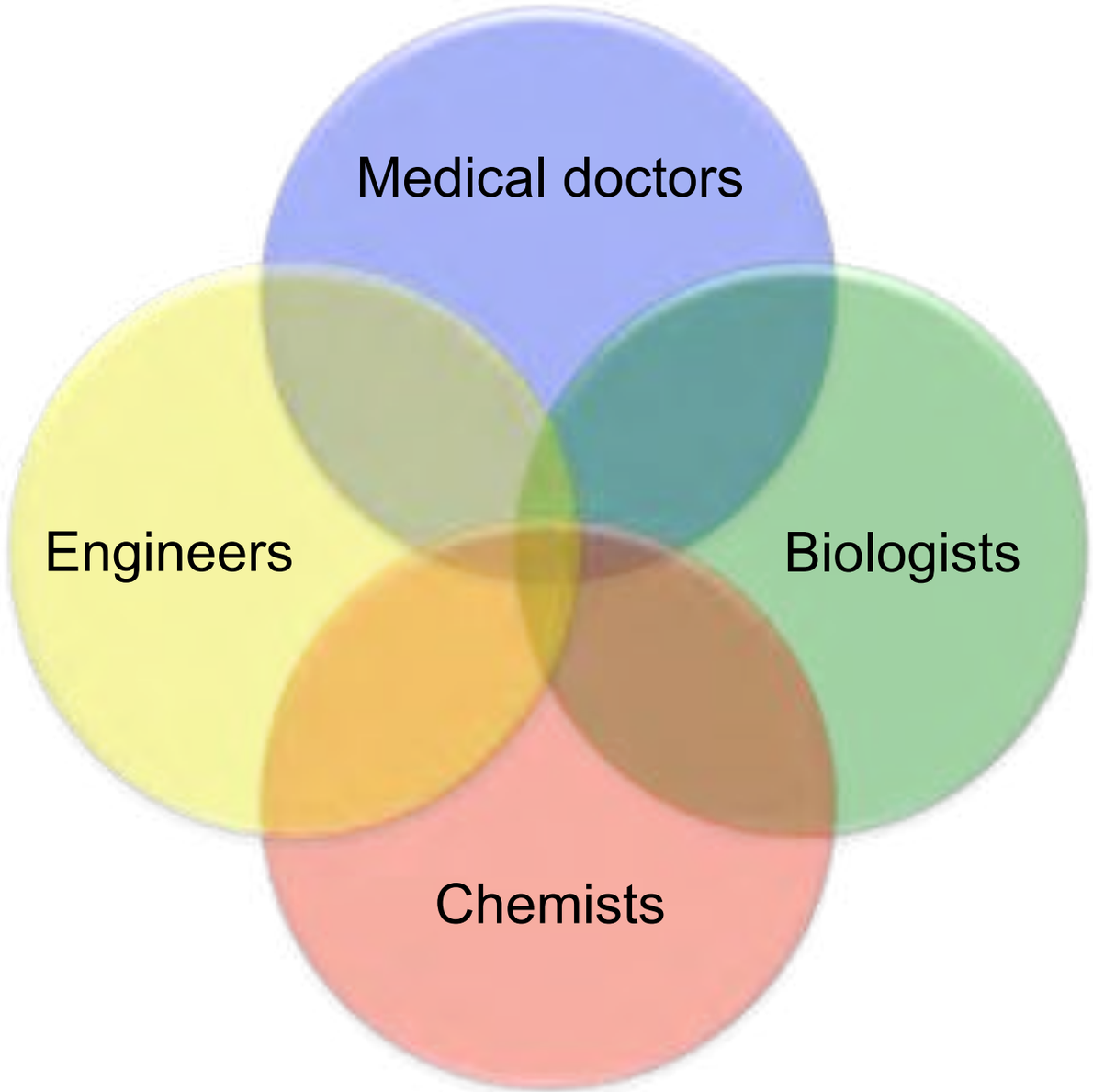
Interdisciplinary study involving materials science, chemistry, biology, and medicine

Cao, Vacanti, Paige, Upton, and Vacanti, *Plastic and Reconstructive Surgery* 100:297, 1997

Tissue engineering is multidisciplinary by necessity



*"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 or a whole organ**"*

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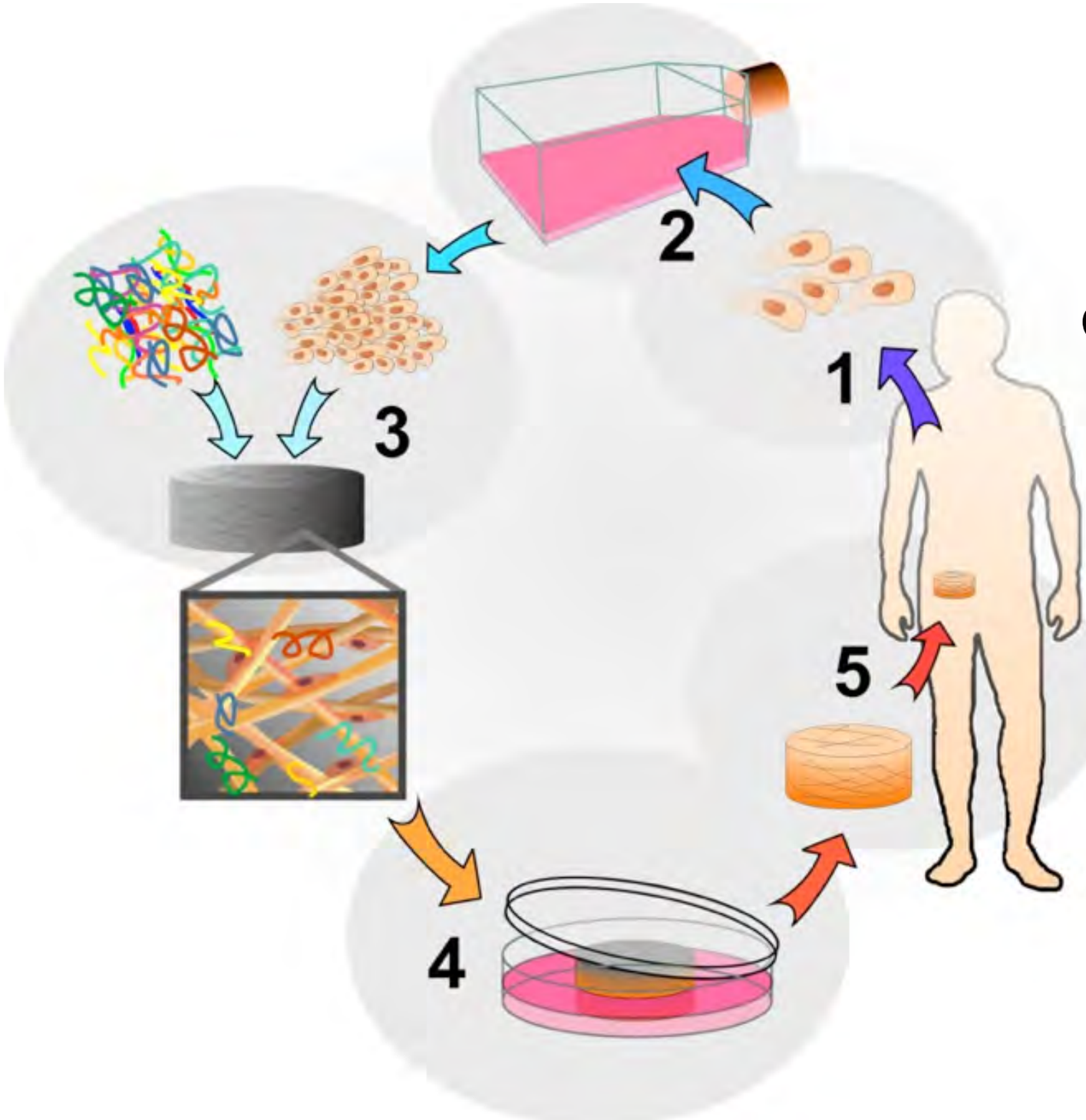
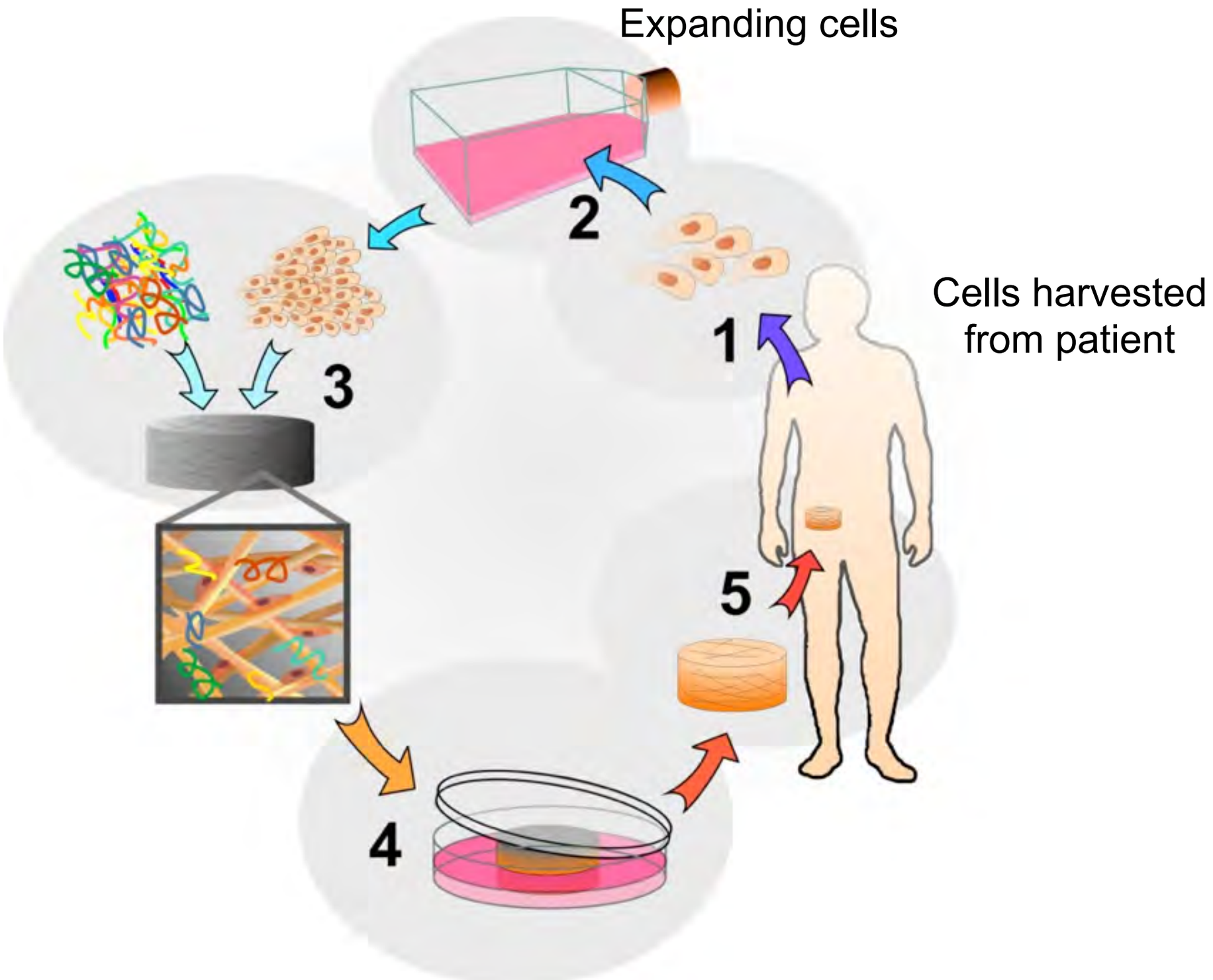
Paradigm of tissue engineering



Cells harvested from patient

image adapted from van Blitterswijk et al., *Tissue Engineering* 2008

Paradigm of tissue engineering



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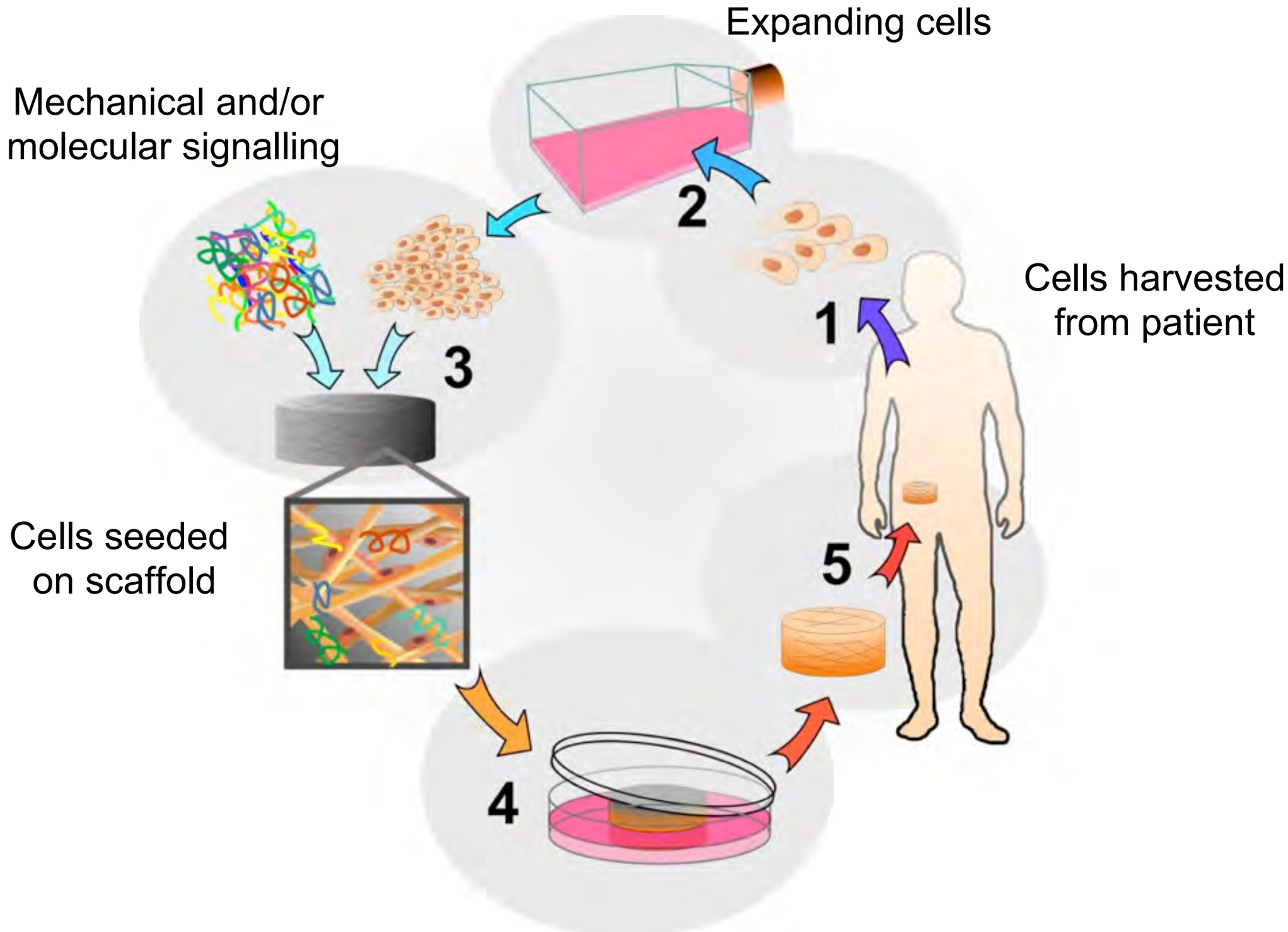

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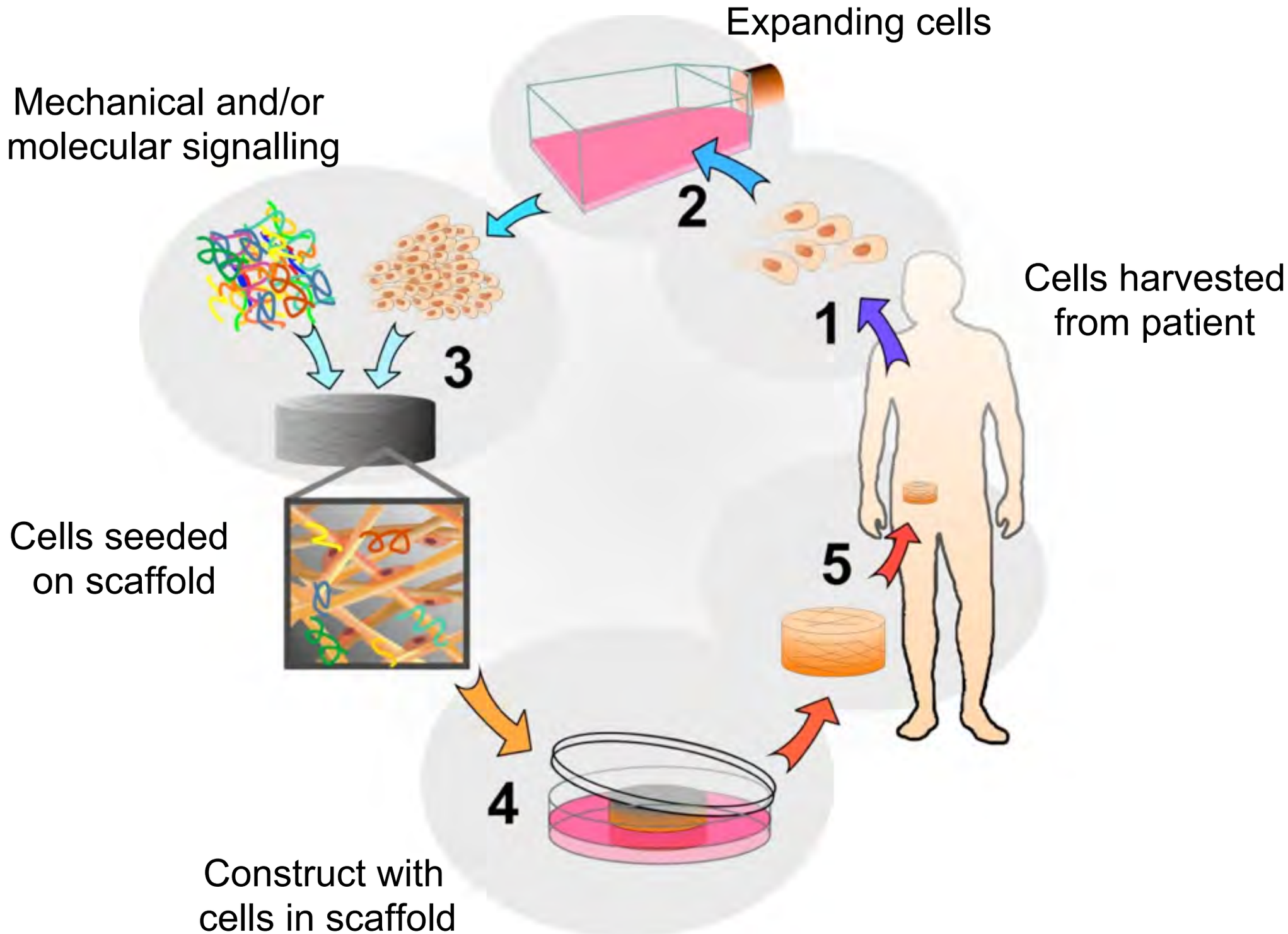

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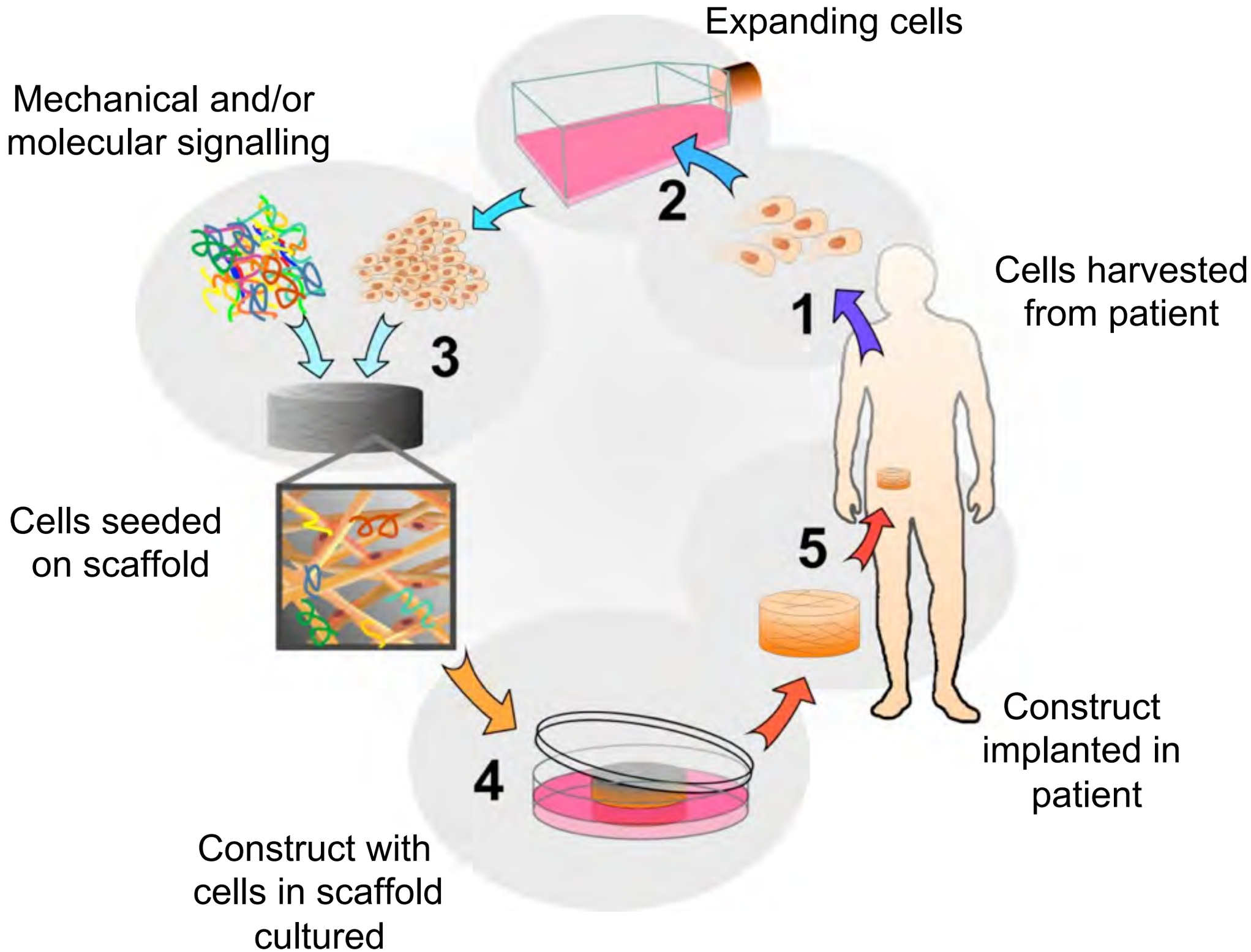

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Where do we get the cells?

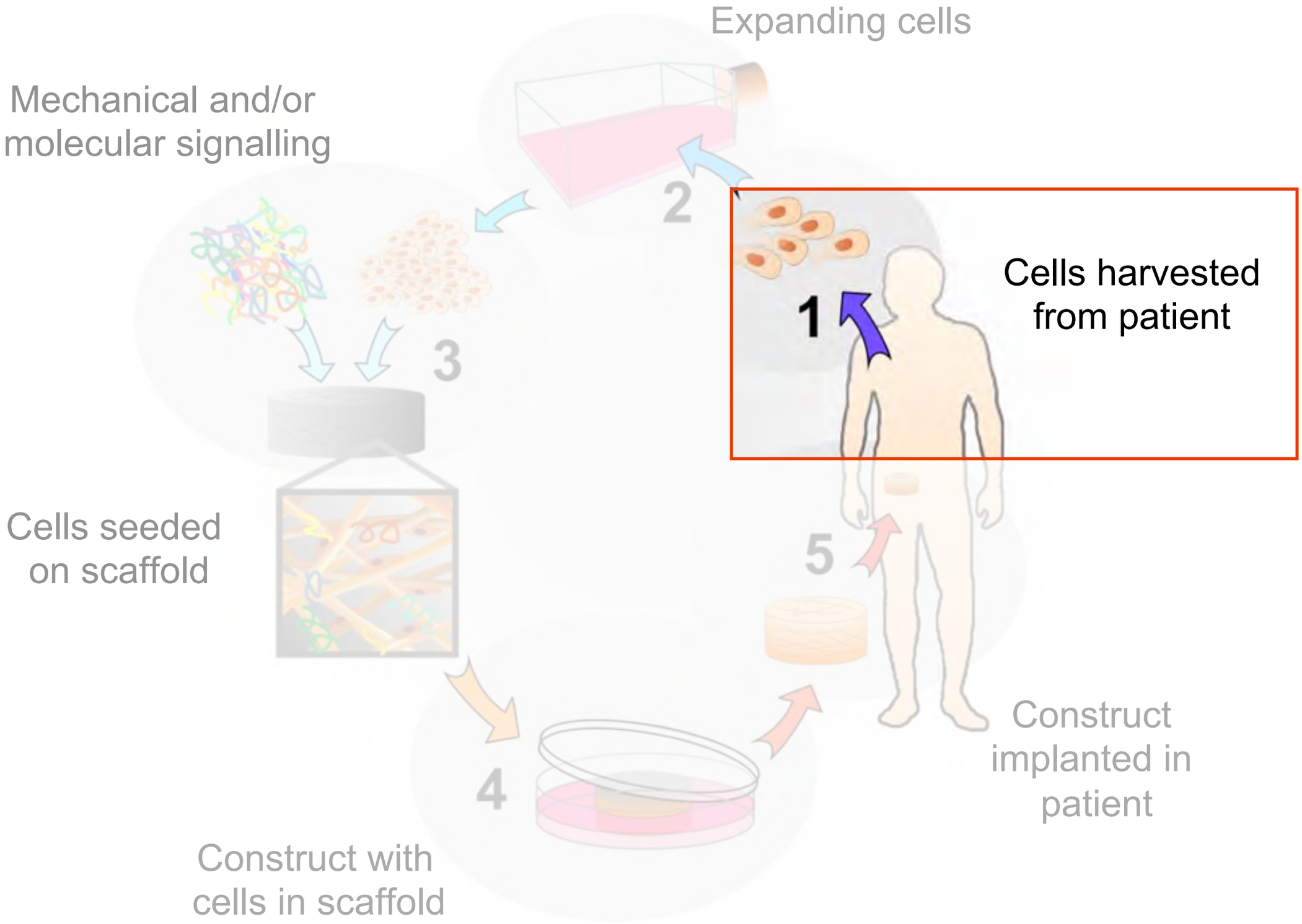

image adapted from van Blitterswijk et al., *Tissue Engineering* 2008

Cell source: autologous, allogenic, xenogenic?

Autologous cells:

- avoids rejection or pathogen transmission
- examples: blood, bone graft, skin graft, recellularizing a decellularized scaffold

but...

- pathology/disease may make cells unusable
- limited cell quantities
- time delay for expansion
- **COST**

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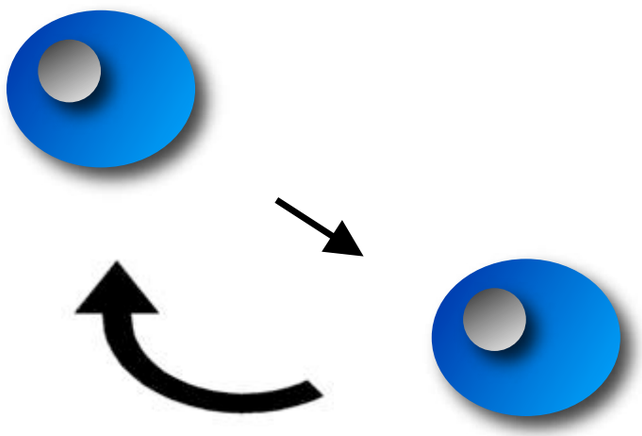
What about stem cells?

The potential of stem cells

capable of ***self-renewal***-- can divide and renew themselves for long periods

self renewal

stem cell



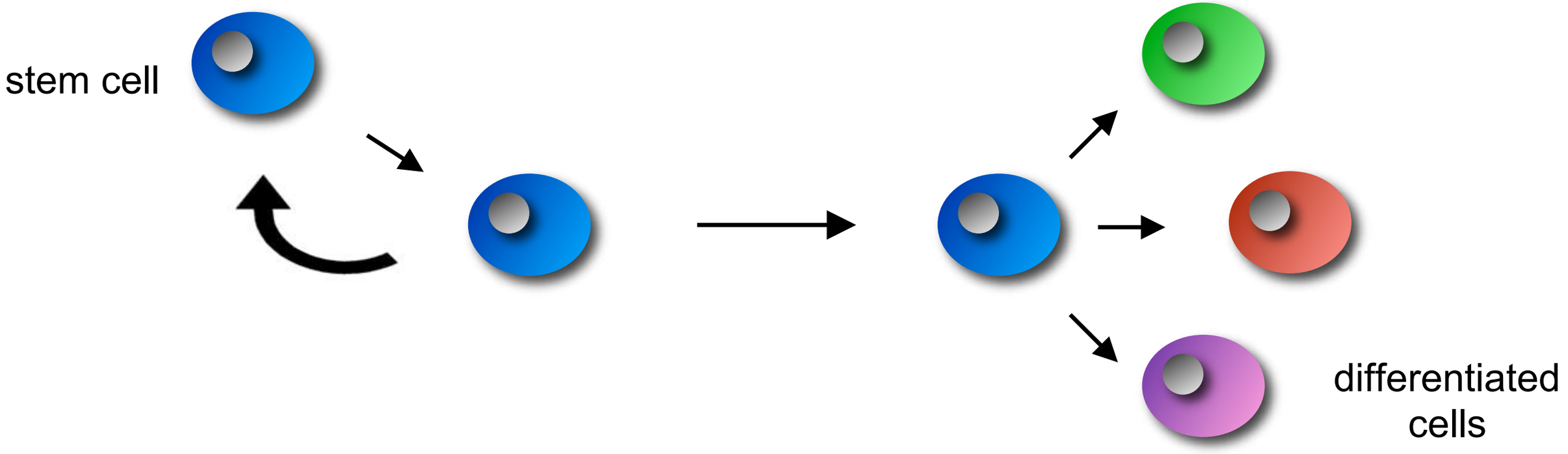
The potential of stem cells

capable of ***self-renewal***-- can divide and renew themselves for long periods

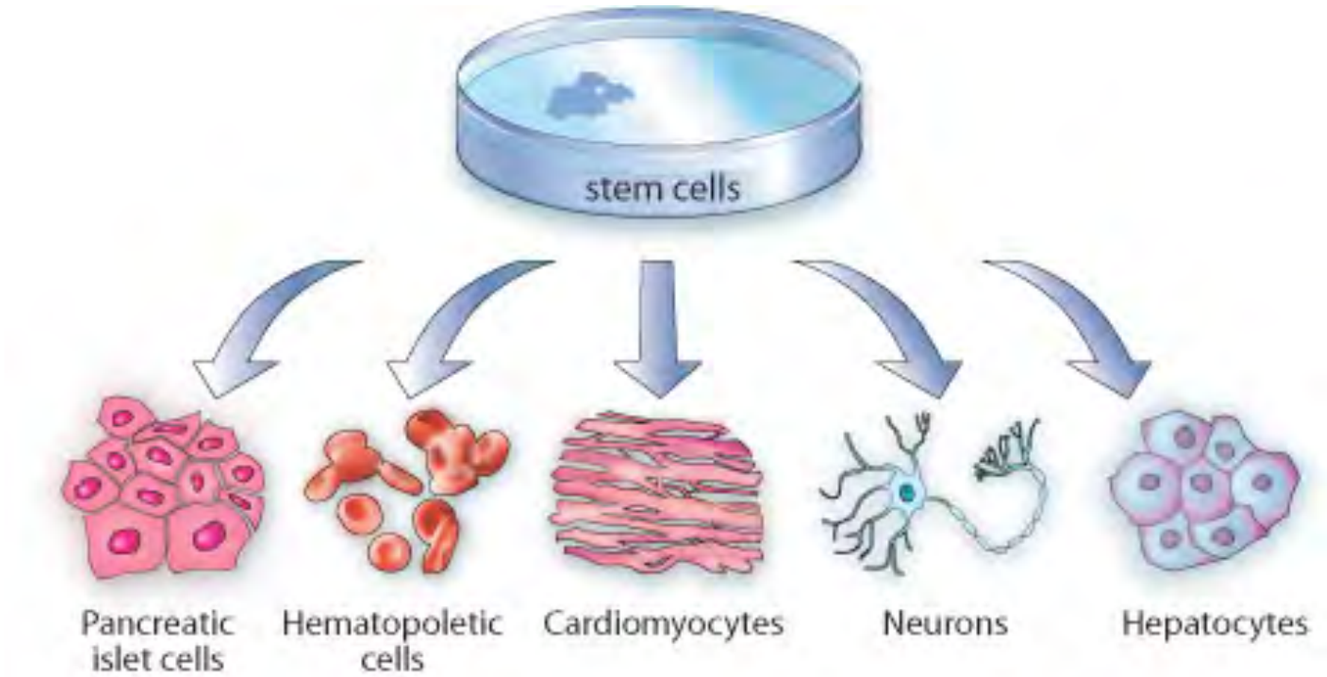
unspecialized cells that can ***differentiate*** into other types of cells

self renewal

differentiation



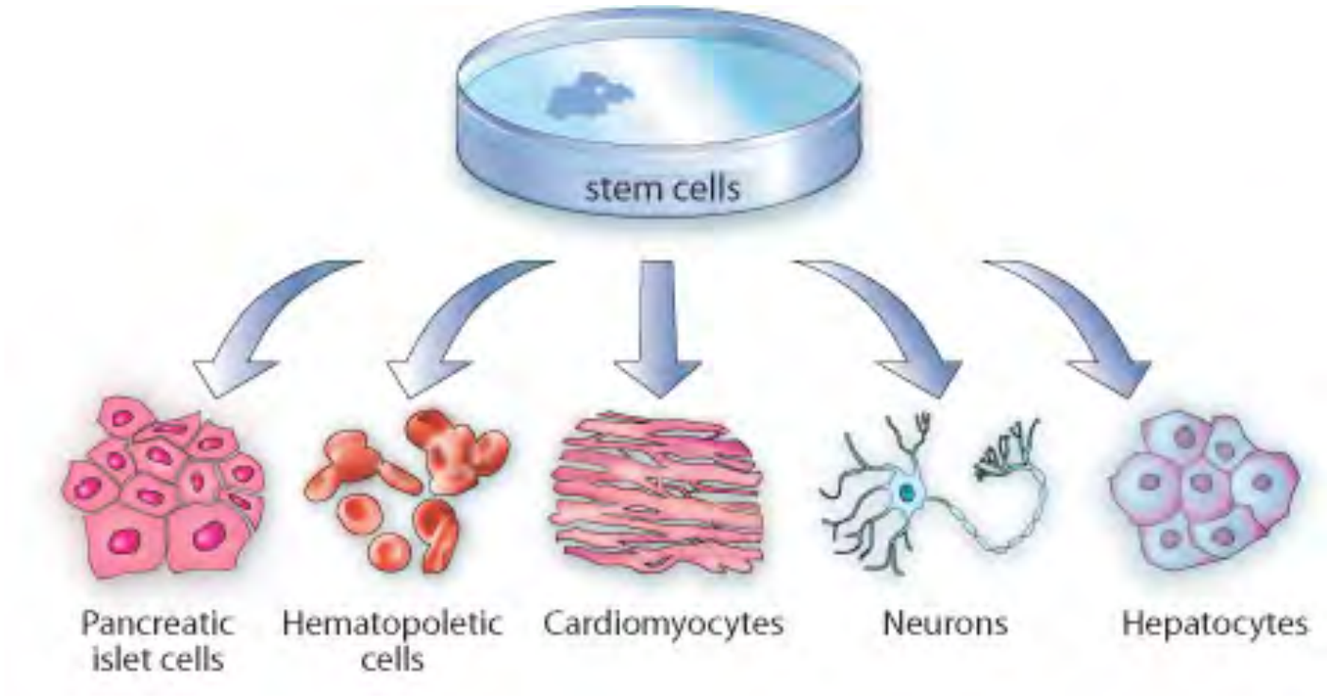
Stem cell potency = differentiation capacity



pluripotent	multipotent
can become any cell type in the body	can become multiple but limited number of cell types
examples: embryonic stem cells, induced pluripotent stem cells	examples: adult stem cells

Image: KUMC Center for Reproductive Sciences Cell Imaging Core

The pros and cons of stem cells



pluripotent
can become any cell type in the body

PROS:
- enormous potential
- self-renewal

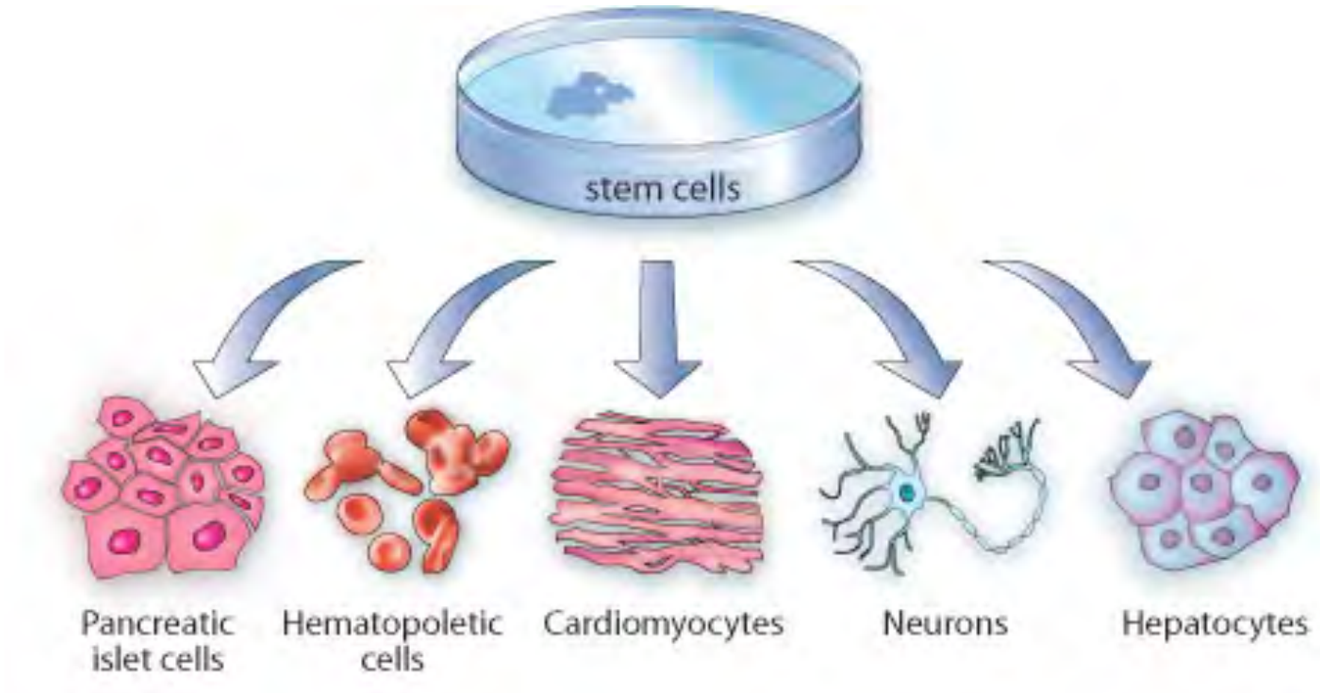
CONS
- controversial source
- immune rejection
- risk of tumor

multipotent
can become multiple but limited number of cell types

PROS:
- derived from patient
- reduced risk of immune rejection

CONS
- cannot differentiate into all cell types
- limited self-renewal
- rare in mature tissue

The potential of stem cells is vast

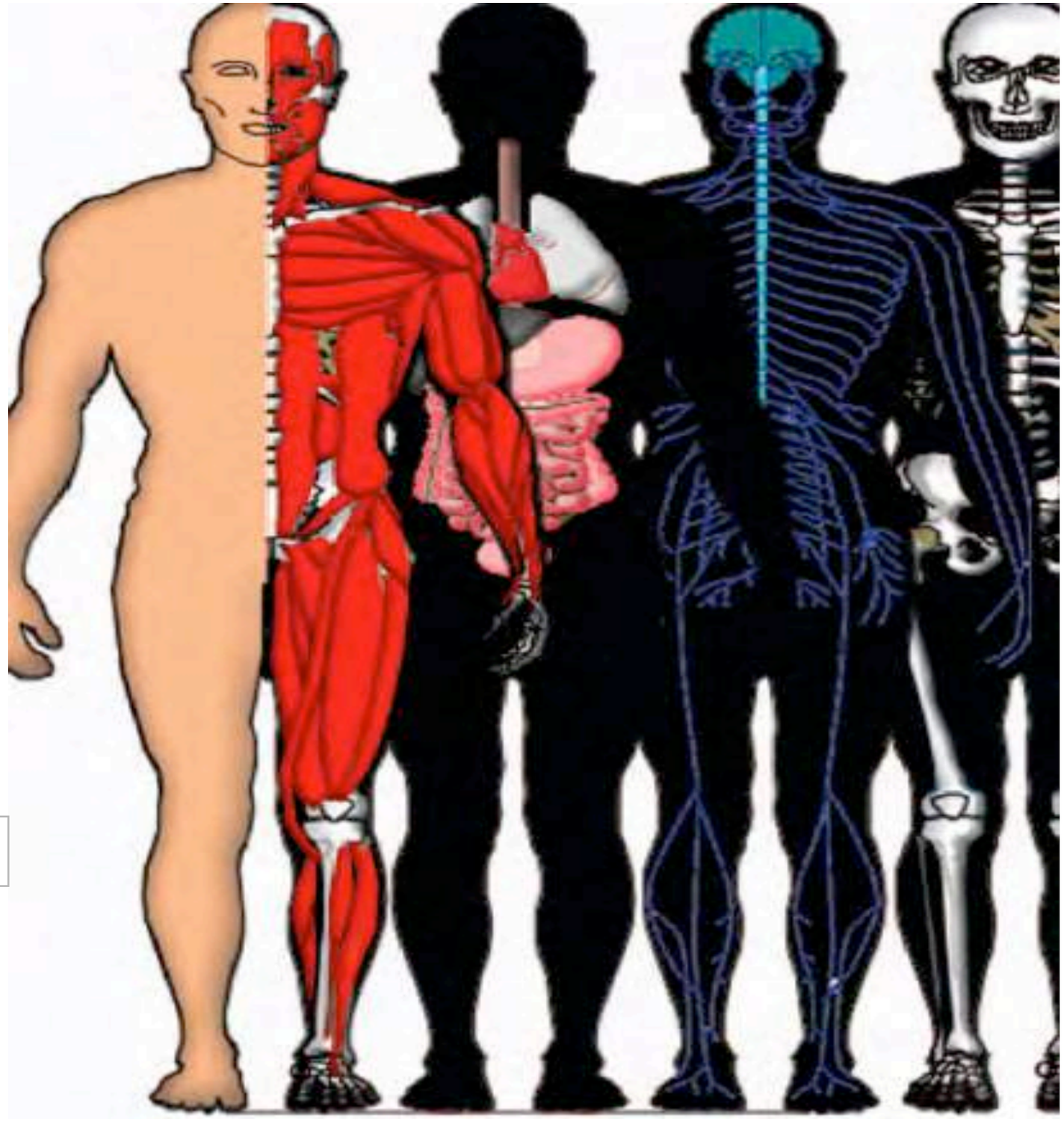


- renewable source of replacement cells and tissues to replace need for donors
- potential to treat diseases or injuries that affect tissues that cannot regenerate
- current research applications: cardiovascular disease, diabetes, osteoarthritis, spinal cord injury, Alzheimer's, strokes, burns, drug discovery,...

…especially for the salamander

Human body has capacity to repair and regenerate

skin



bone

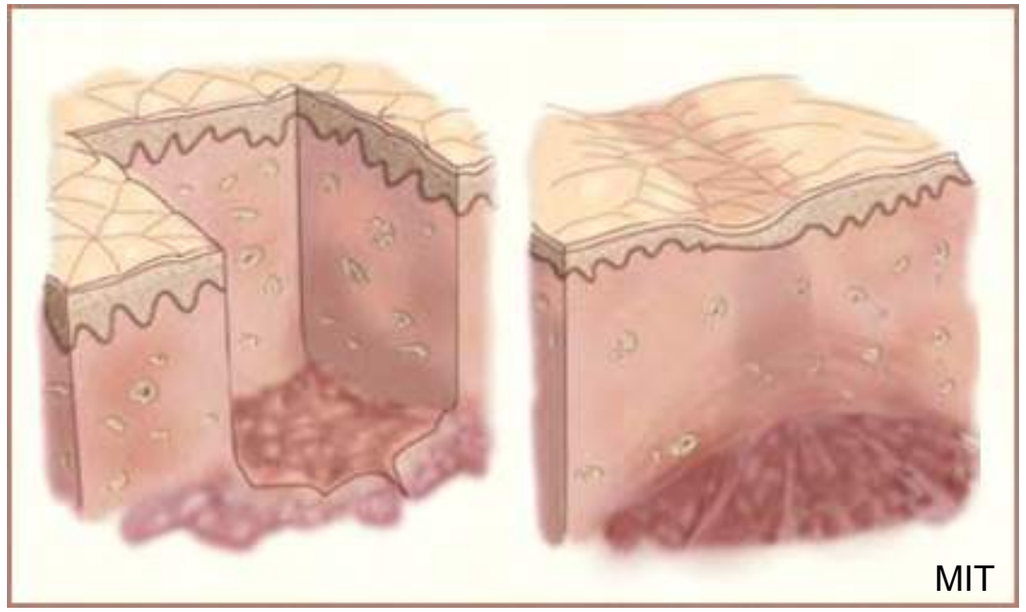
intestine

liver

image adapted from Stupp, *MRS Bulletin* 2005

Repair vs regeneration

<u>Repair</u> = reestablishing lost or damaged tissue to ***retain continuity***



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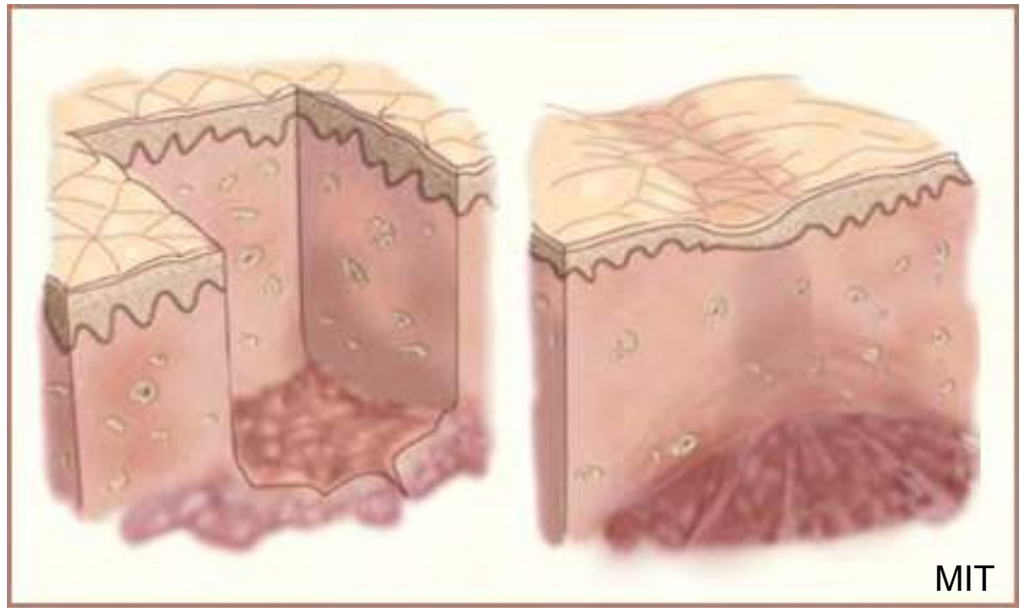
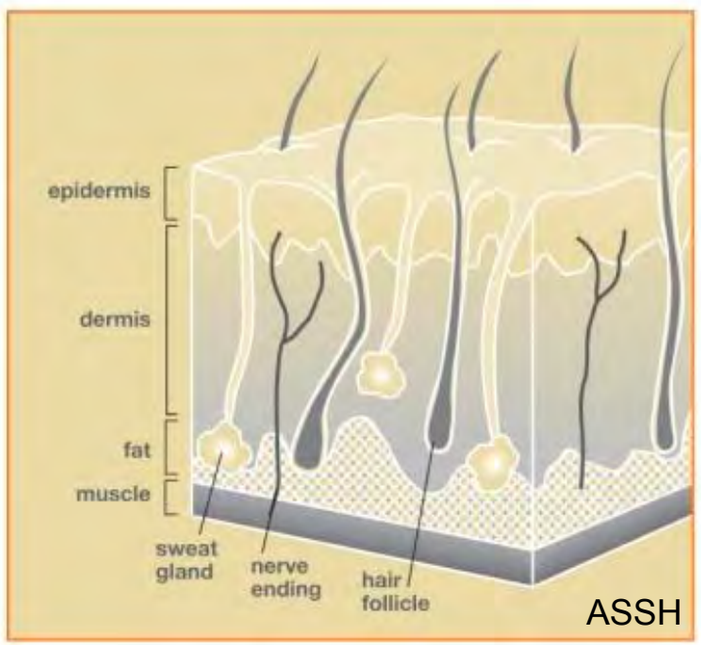


<u>Regeneration</u> = replacement of lost or damaged tissue with an exact copy so that ***morphology and function are restored***



Repair vs regeneration

Repair = reestablishing lost or damaged tissue to ***retain continuity***

Regenerative medicine aims to replace, engineer, or regenerate human cells, tissues, or organs to restore or establish normal function

R

exact copy so that ***morphology and function are restored***

Can we create biomaterials to stimulate regeneration?

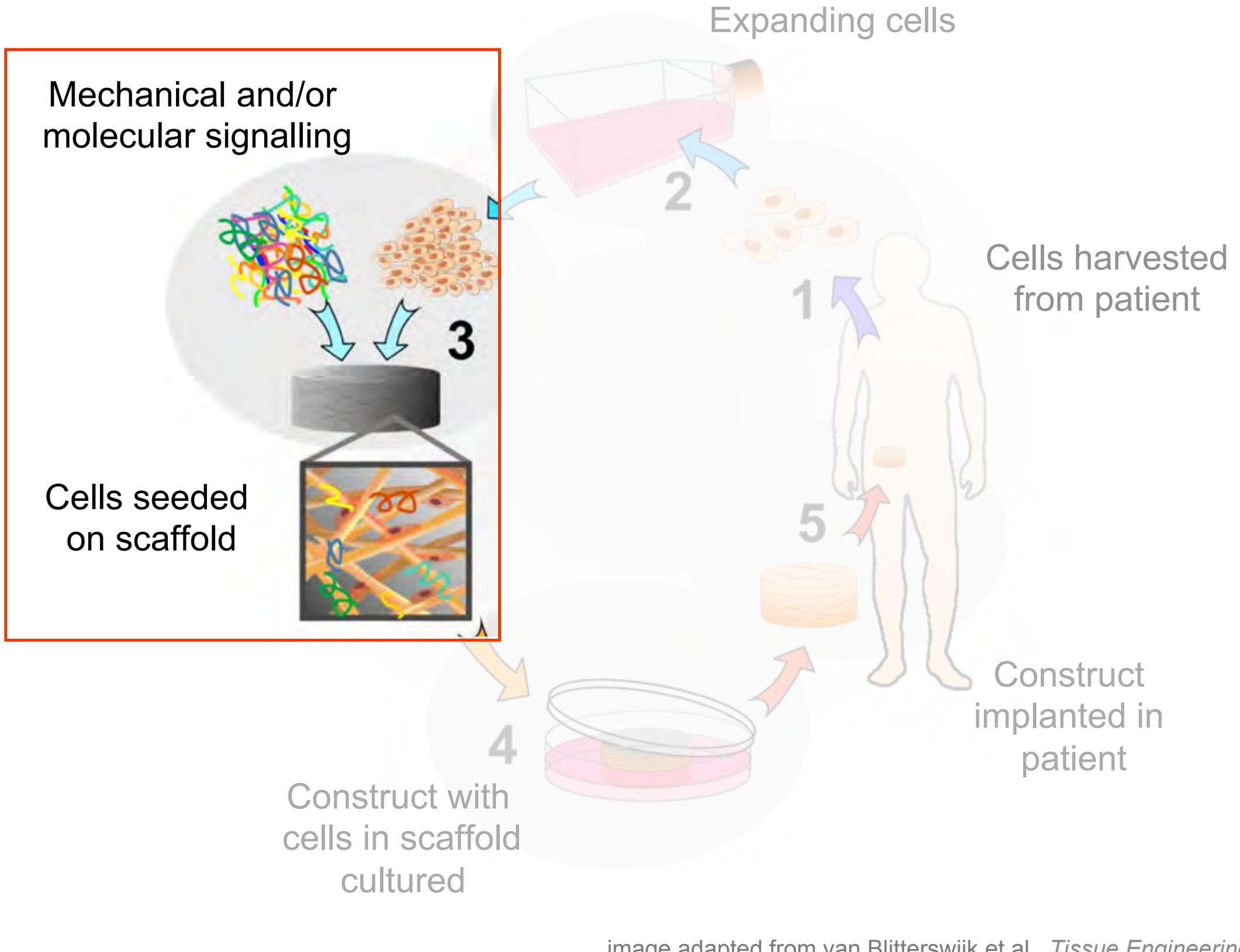
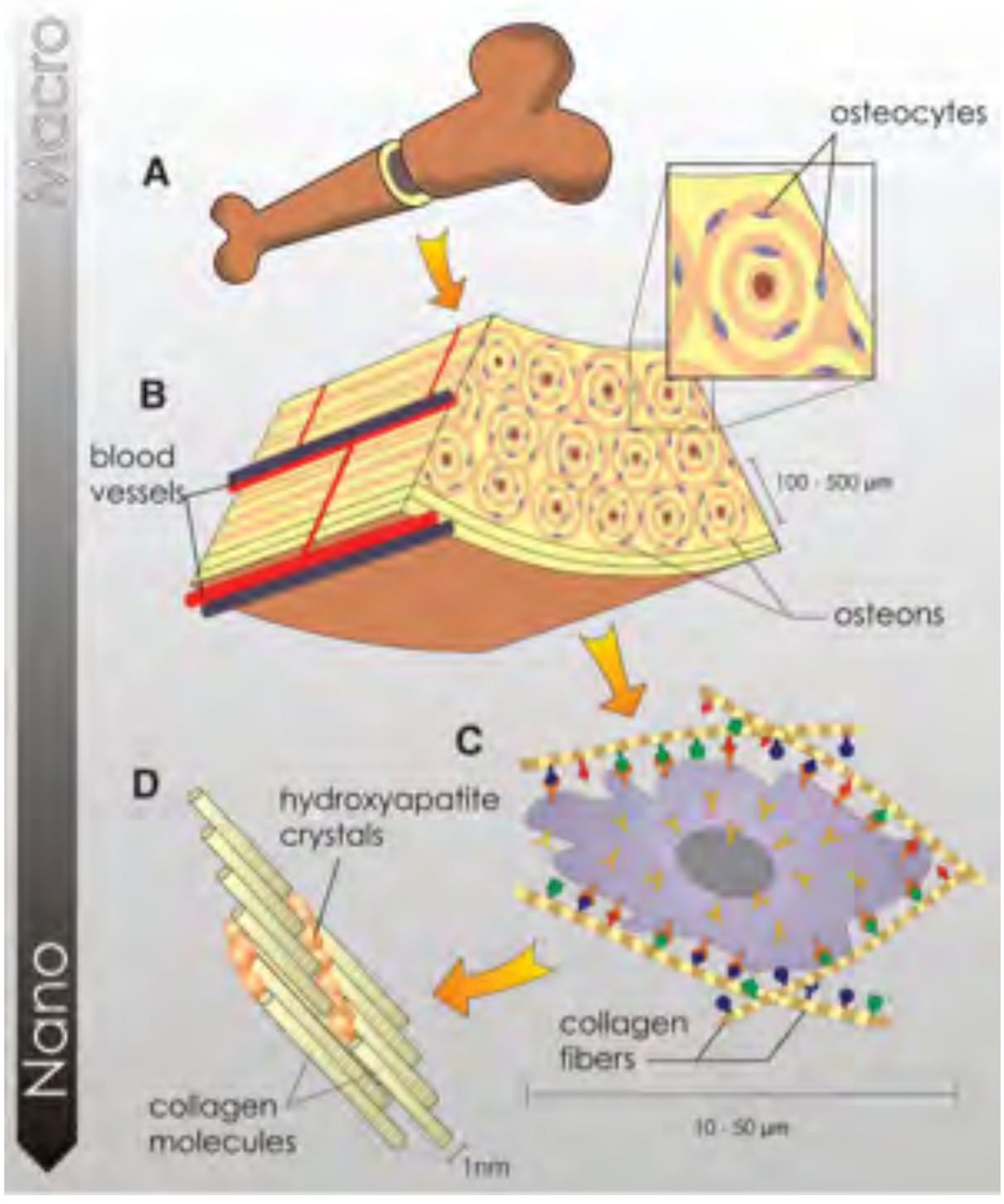
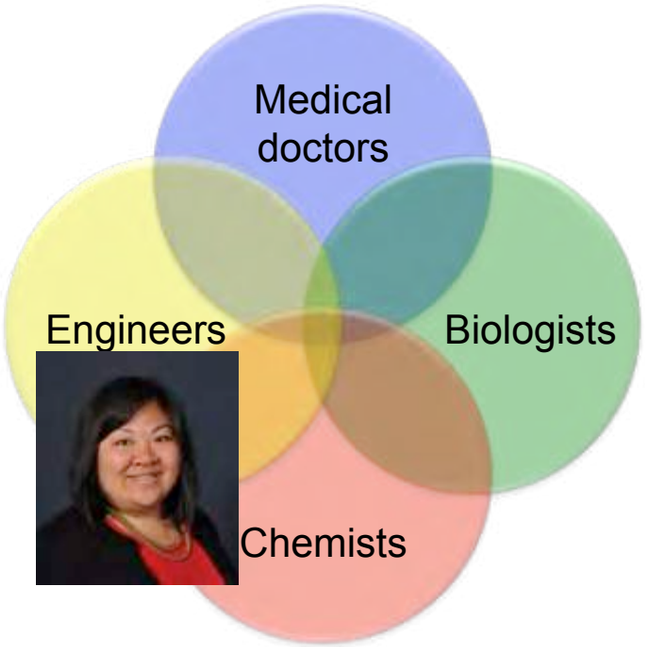


image adapted from van Blitterswijk et al., *Tissue Engineering* 2008

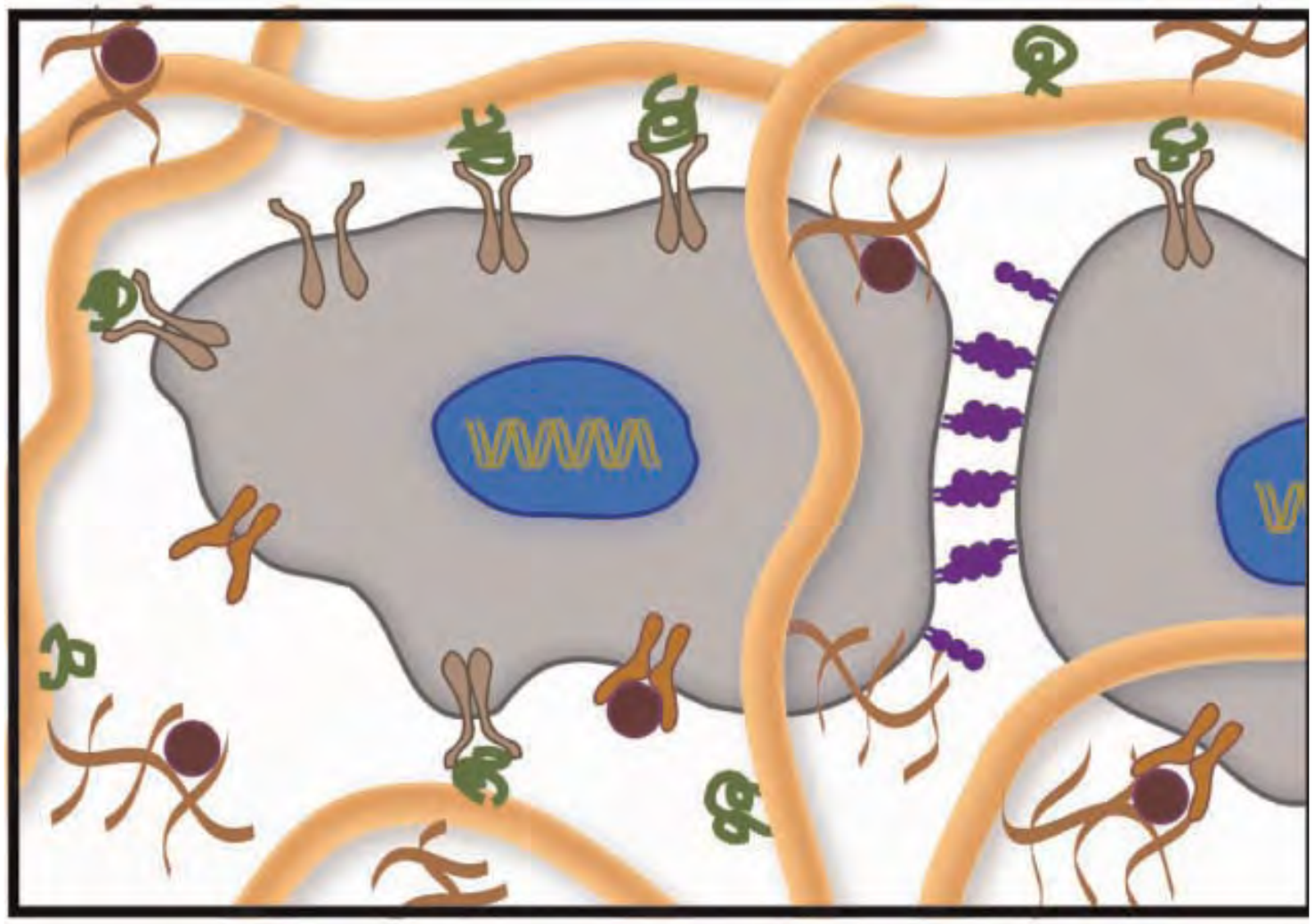
Perspective from a materials scientist





look at biological tissues as materials

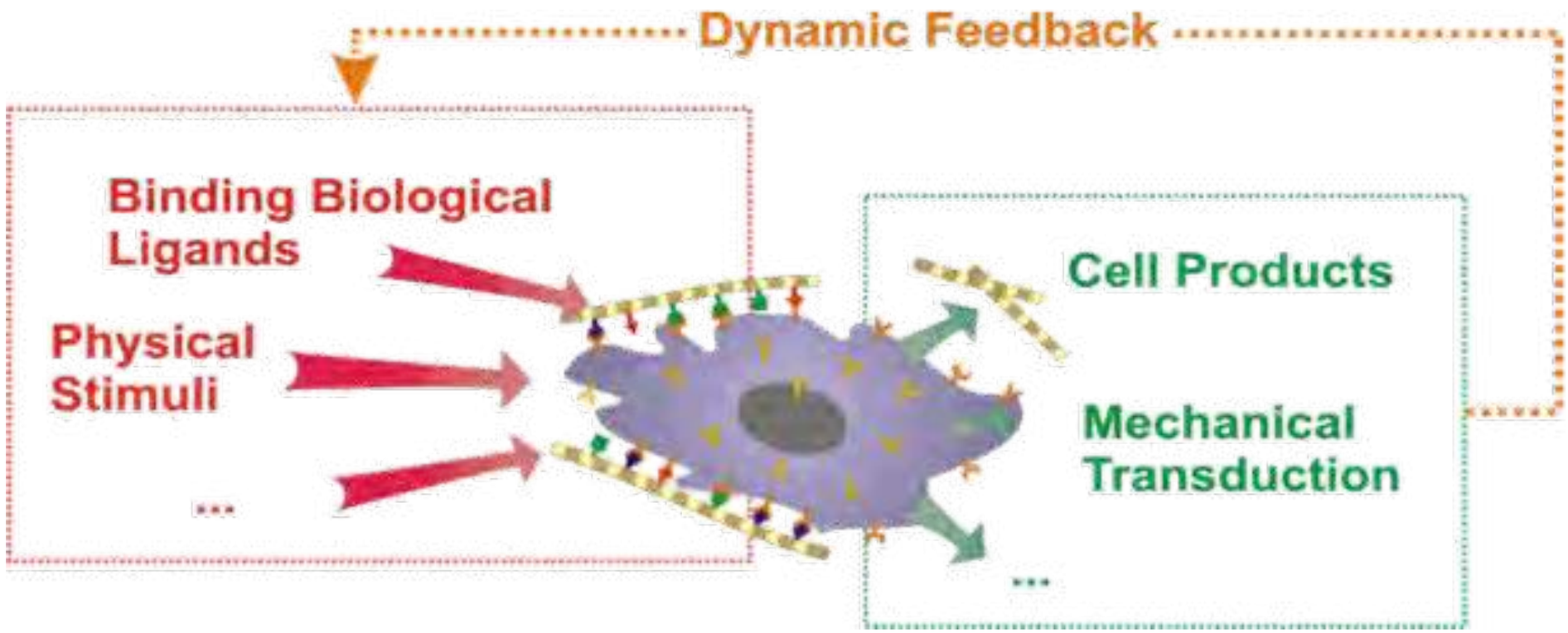
Extracellular matrix (ECM): home for cells



Tibbitt & Anseth, *Biotech & Bioeng* 2009

- composed of many cross-linked proteins and biopolymers
- provides mechanical support
- regulates biological functions such as cell adhesion, proliferation, migration, differentiation, etc.

Designing materials to mimic ECM to regenerate tissues

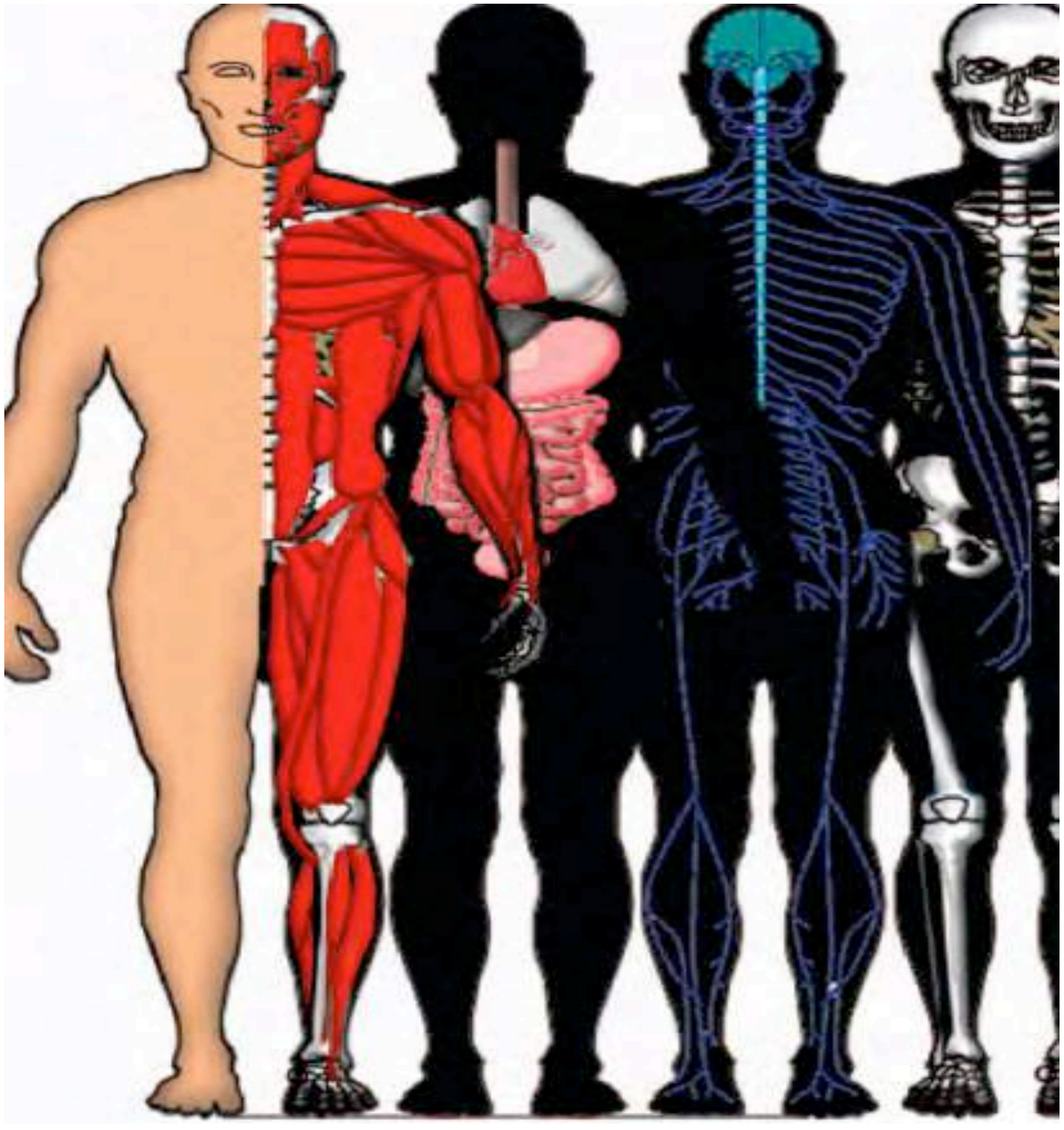


- apply principles and techniques from ***materials science and engineering*** to help understand biological processes and design systems

- take what we learn from nature to create ***biomimetic materials*** that can "jumpstart" regeneration

Can we mimic the ECM of biological tissues to ***direct the body to heal itself***?

Tailoring biomaterials to the specific tissue



- tissue type
- biochemical and mechanical functions
- size and scale of defect
- age of the patient
- disease conditions
- etc...

image adapted from Stupp, *MRS Bulletin* 2005

Decellularized heart maintains tissue architecture

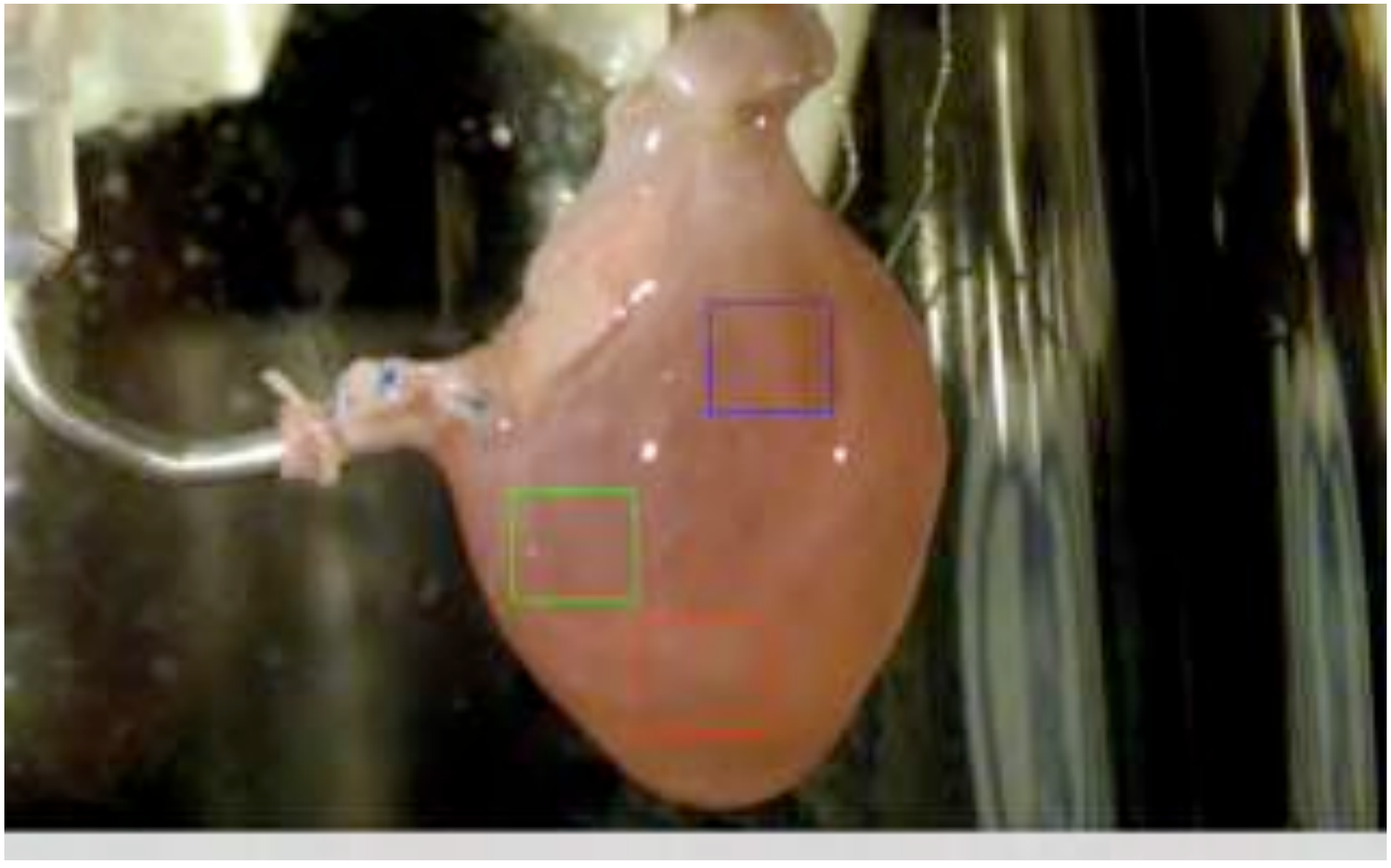
- composed of ***native ECM molecules***
- ***biodegradable*** and ***biocompatible*** after decellularization

Ott et al, *Nature Medicine* 2008.

Decellularized heart can be recellularized

Ott et al, *Nature Medicine* 2008.

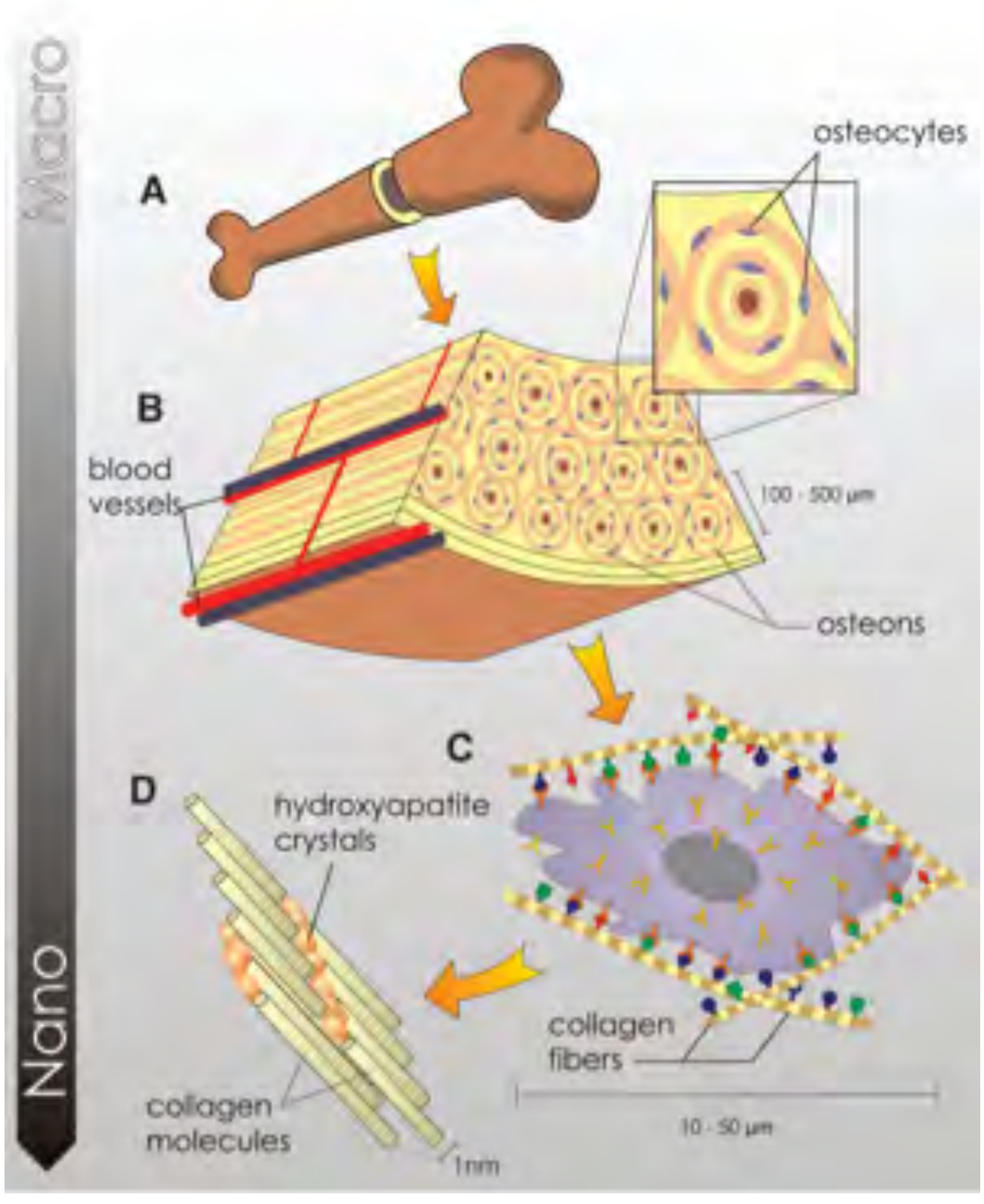
Recellularized heart beats again!



- composed of ***native ECM molecules***
- ***biodegradable*** and ***biocompatible*** after decellularization
- **requires donor…**

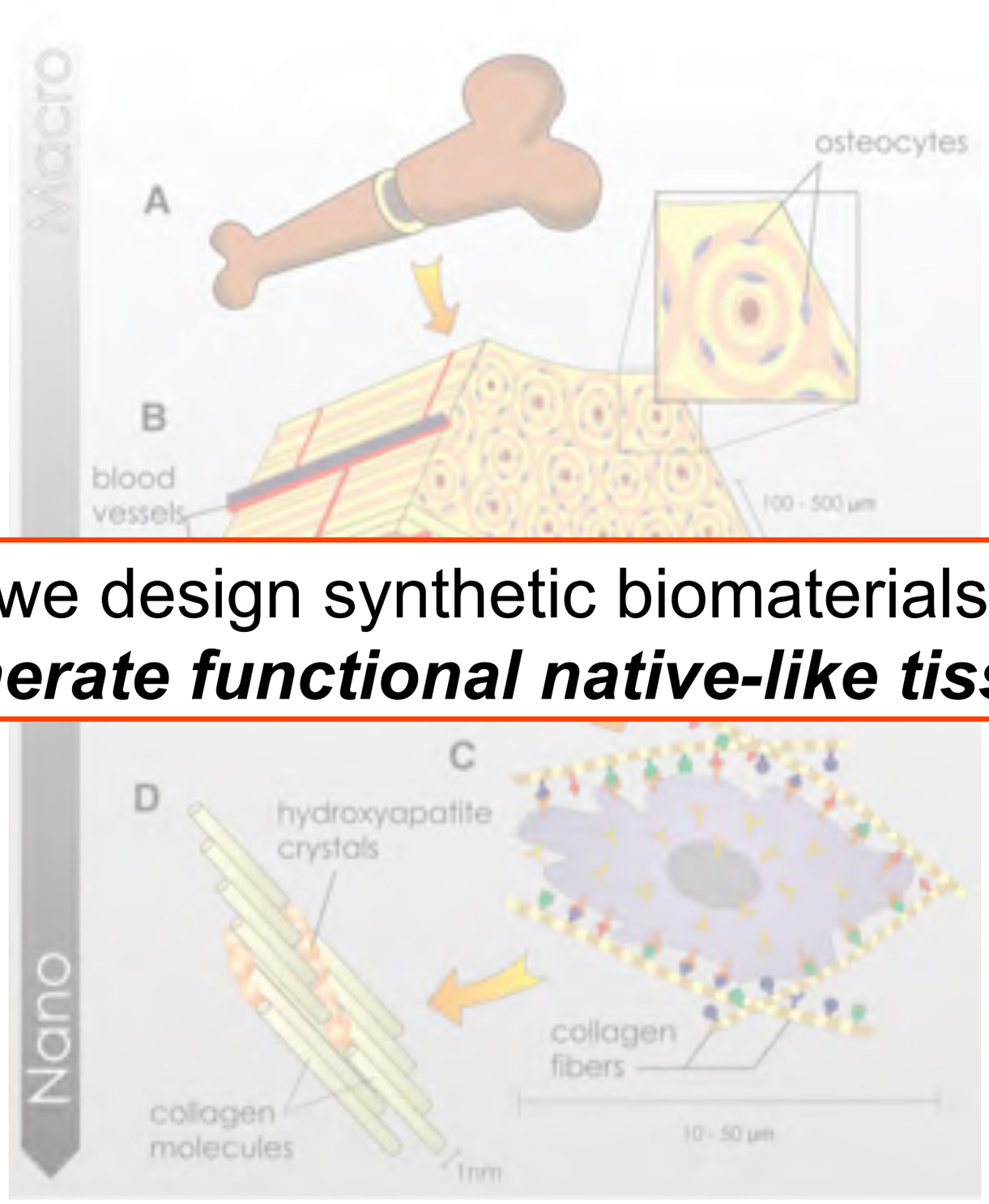
Ott et al, *Nature Medicine* 2008.

Biological tissues are complex



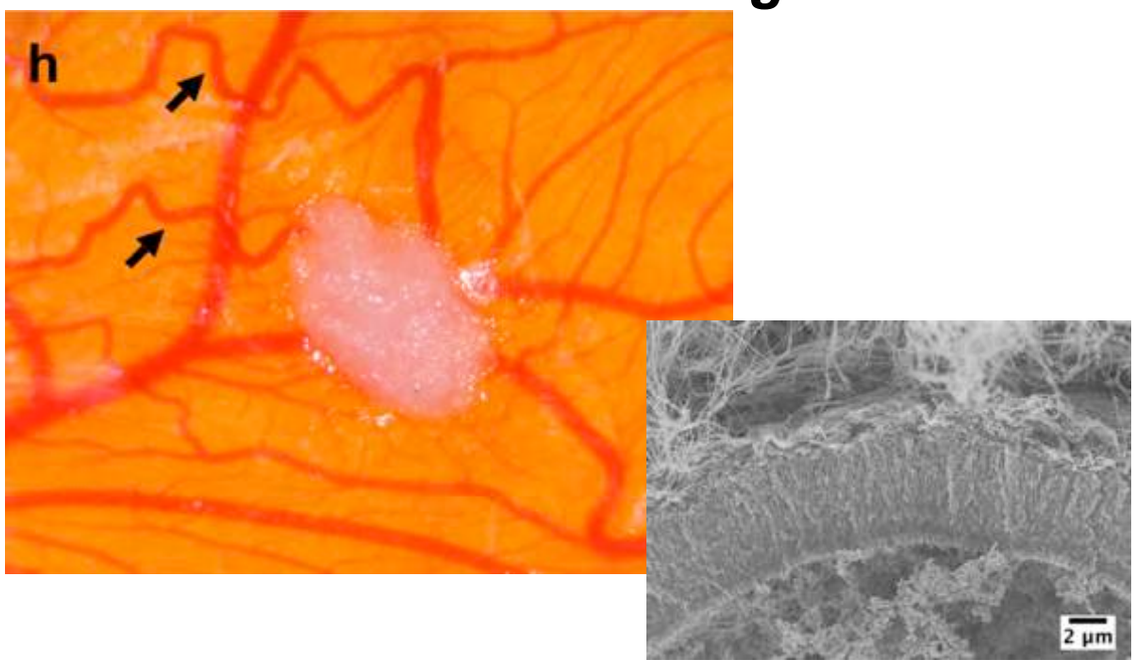
tissue composition and organization leads to biological function

Biological tissues are complex



Can we design synthetic biomaterials that ***regenerate functional native-like tissues***?

Injectable hydrogels for wound healing



Chow LW, et al. *Biomaterials* **31(24)**: 6154-6161, 2010.
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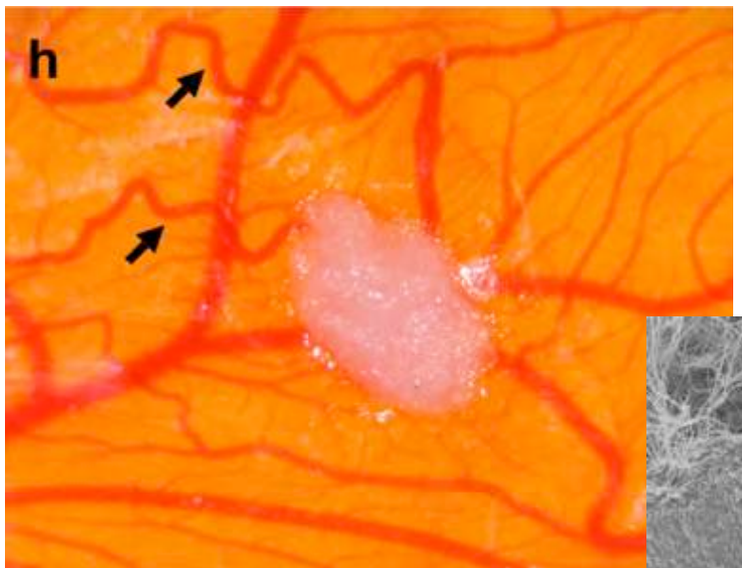

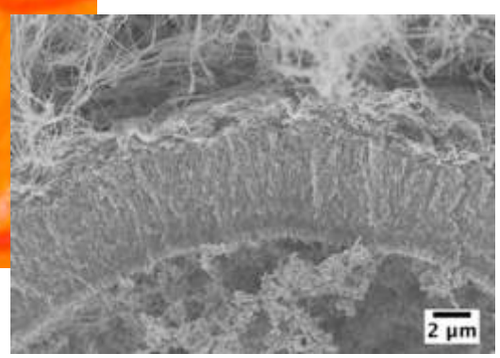

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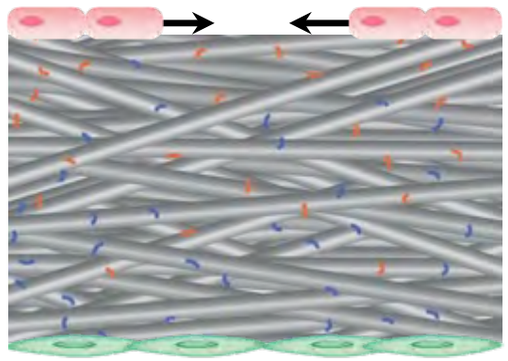
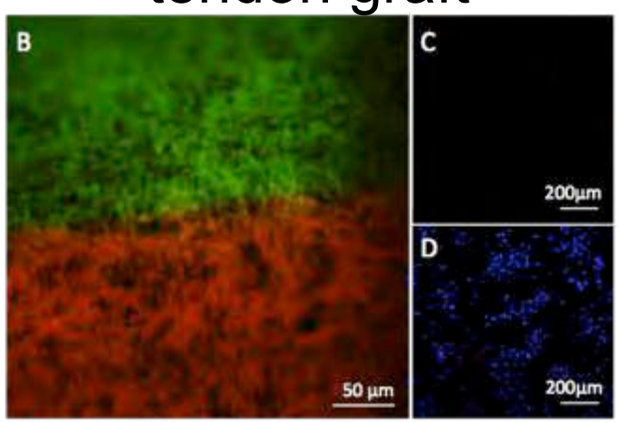
Biodegradable scaffolds for tissue engineering



vascular graft

tendon graft



Campagnolo P, Chow LW, et al. 2015 *(in prep)*.
Harrison RH, et al. *Adv Funct Mat* 2015 *(in press)*.

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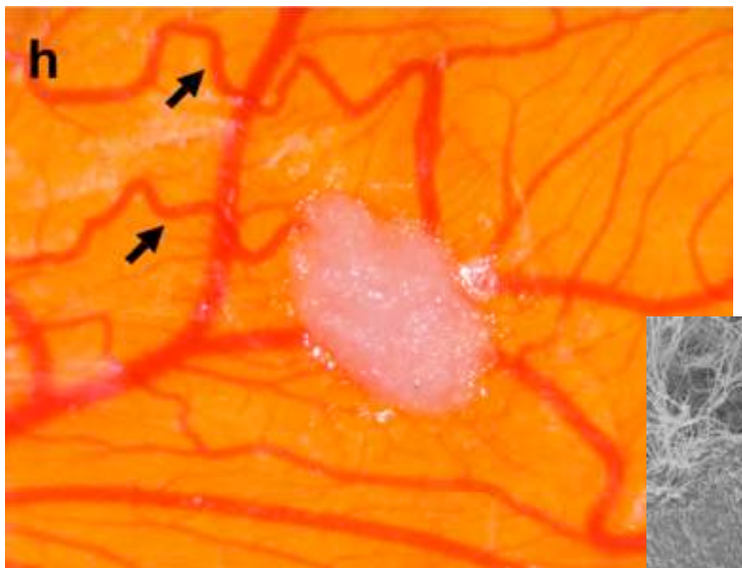

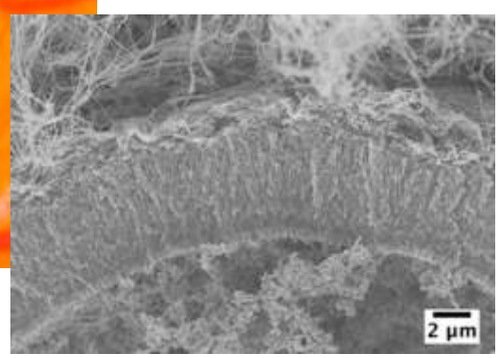

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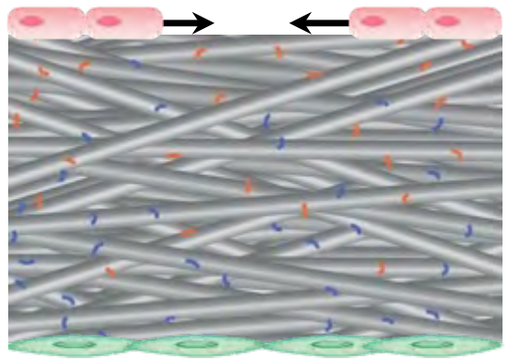

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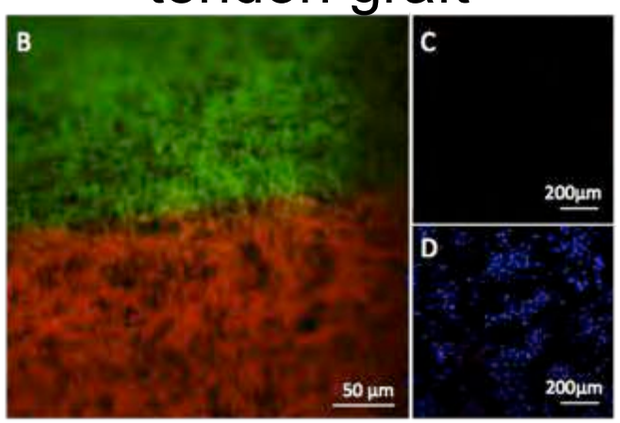
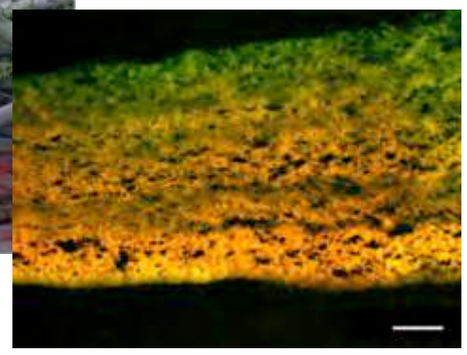
tendon graft

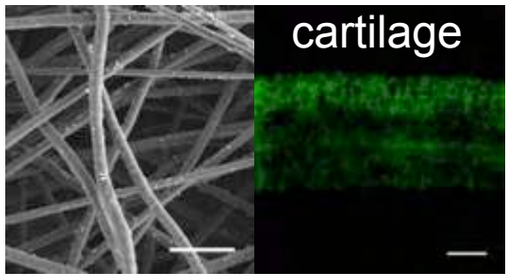


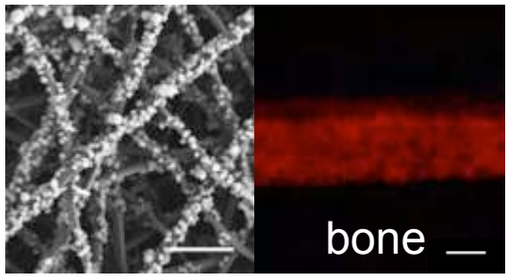
Campagnolo P, Chow LW, et al. 2015 *(in prep)*.
Harrison RH, et al. *Adv Funct Mat* 2015 *(in press)*.

Biodegradable scaffolds for regenerative medicine

biomimetic gradients

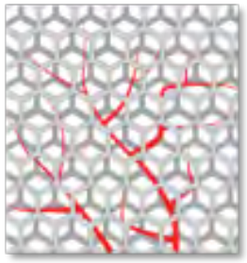






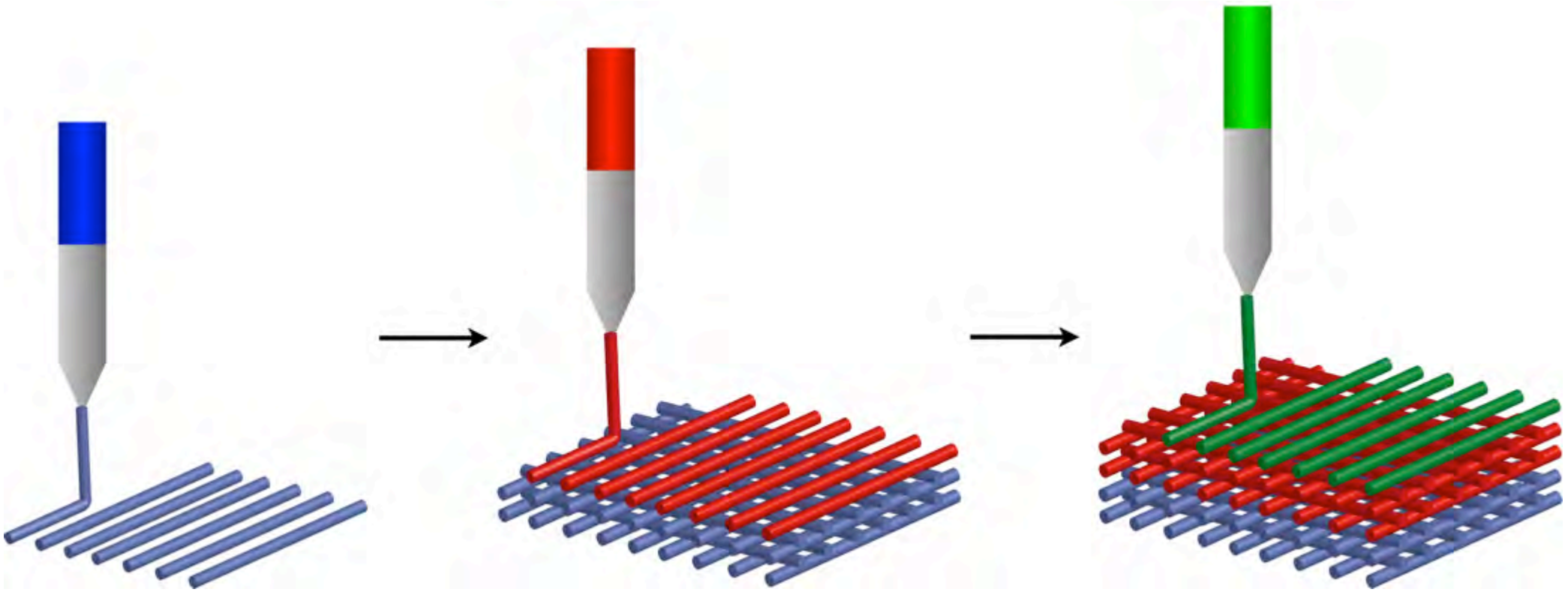
3D bioprinting

native architectures



Chow LW, et al. *Adv Healthc Mater* **3(9)**: 1381-1386, 2014.
Chow LW, et al. 2015 *(in prep).*

Designer “bioinks” to print tissue-specific scaffolds



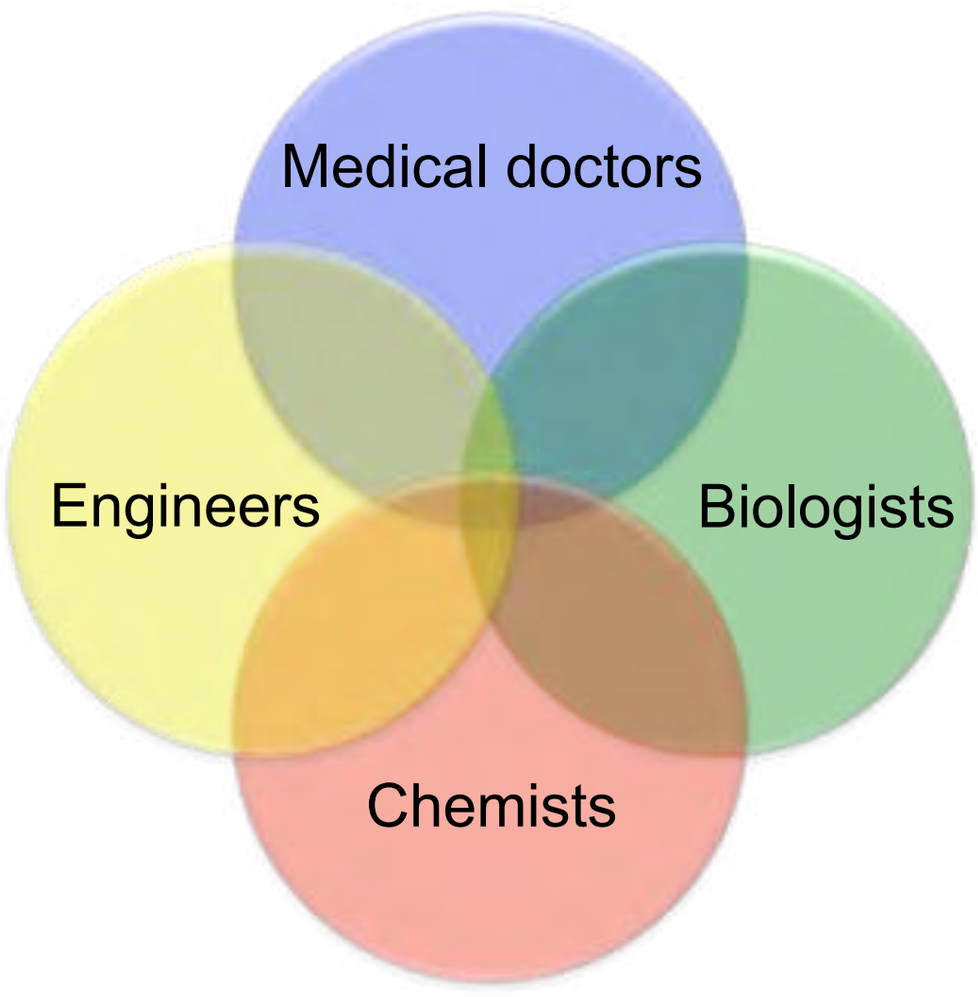
Combination of physical and biochemical cues influence cell behavior and tissue function

- polymers (e.g. biodegradable, co-polymers,…)
- bioactive groups (e.g., peptides, sugars, nucleic acids,…)
- functional groups (e.g., orthogonal chemistries, polymerization initiators,…)

Tissue Engineering is...

*"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 or a whole organ**"*

Langer and Vacanti, *Science* 1993



Regenerative medicine aims to replace, engineer, or regenerate human cells, tissues, or organs to restore or establish normal function

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