

Bone Tissue Engineering

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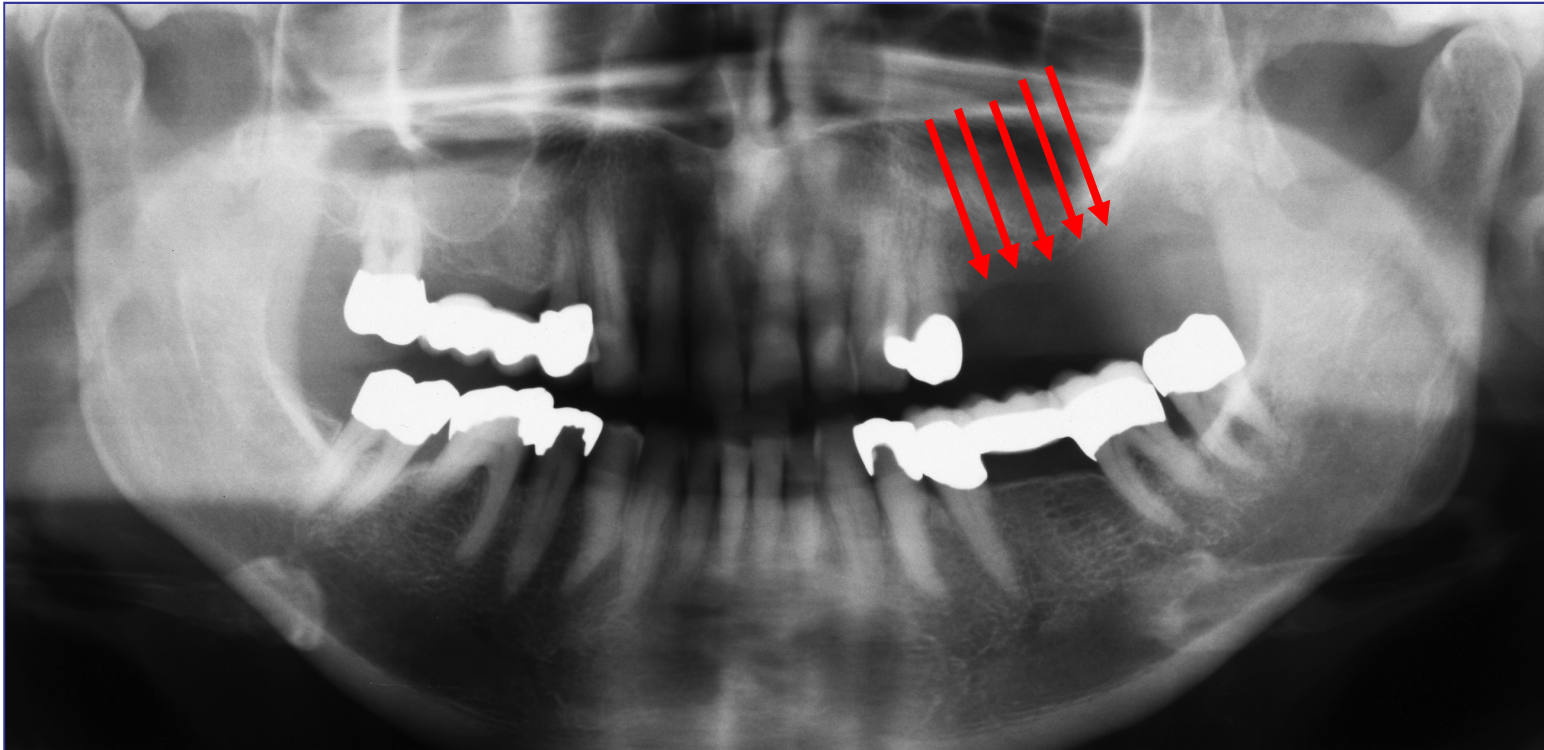


Indication I



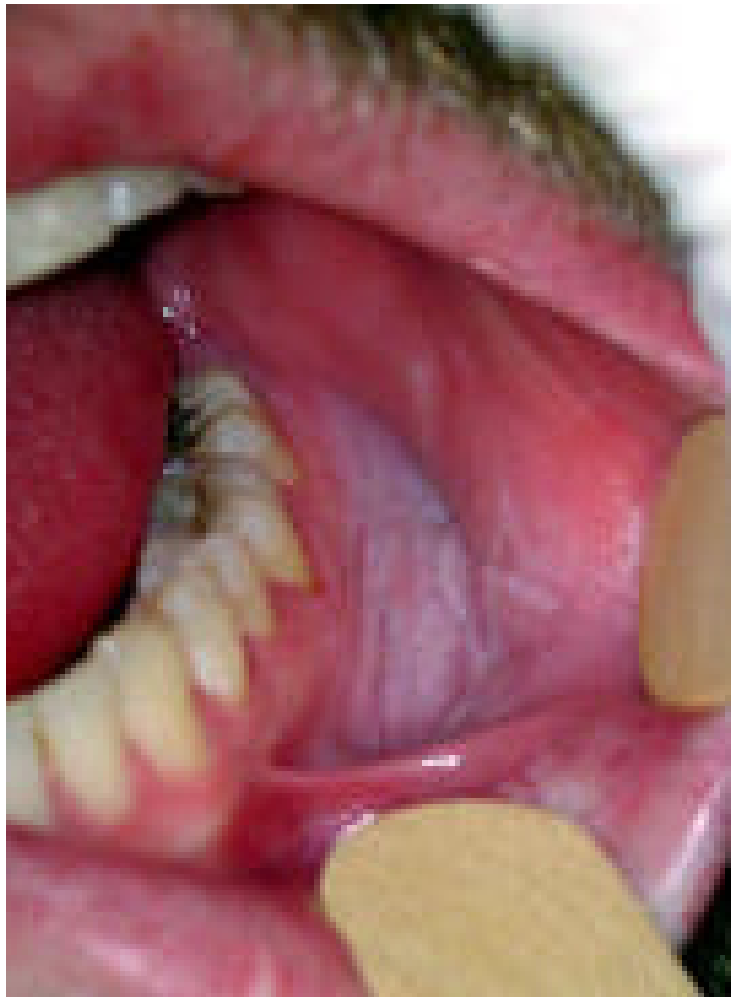
Toothless jaws – edentulism

Indication I



Jaw bone atrophies

Indication II



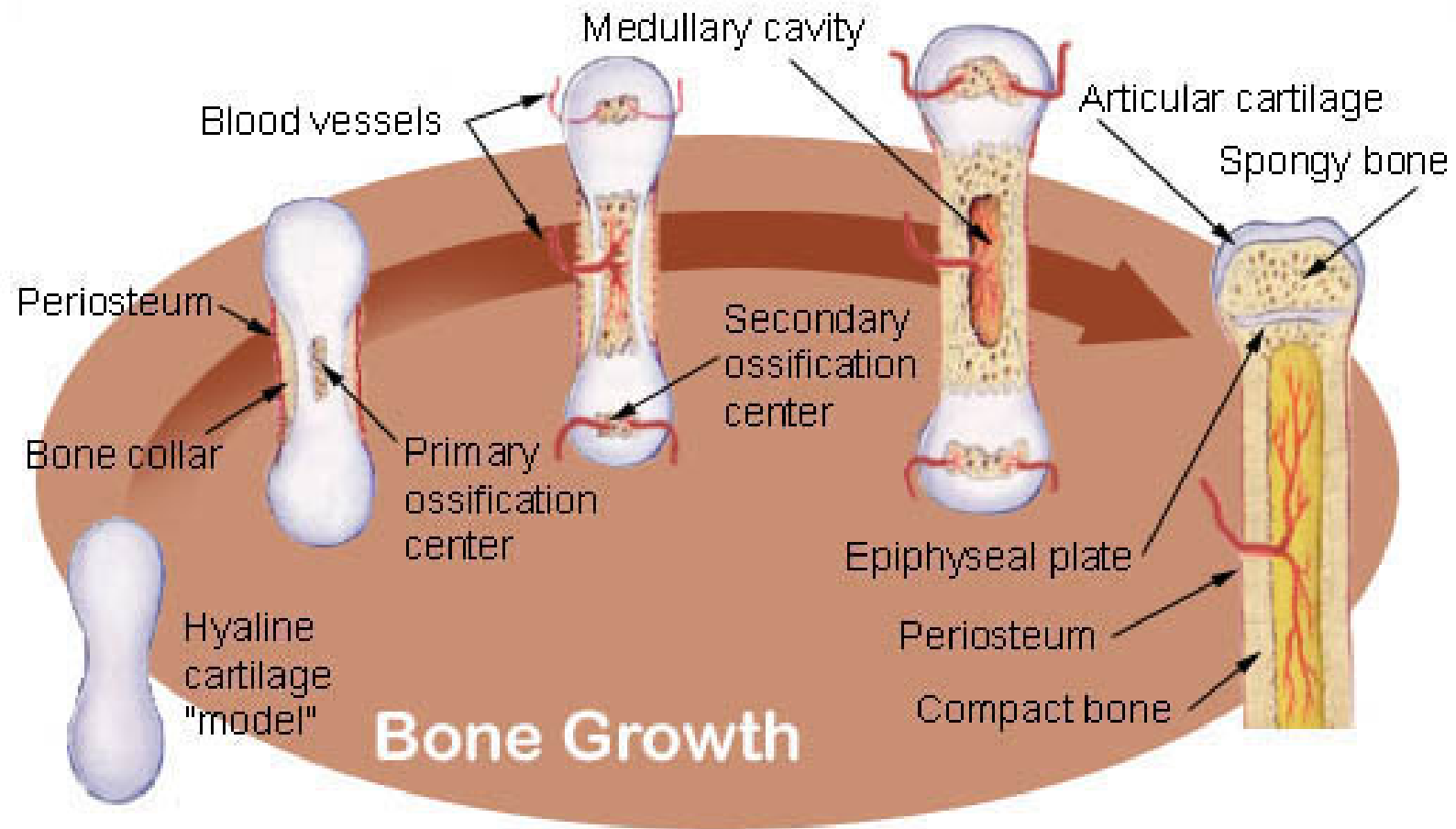
Carcinoma of the oral cavity

Indication III



Cleft lip and/or palate

Bone growth



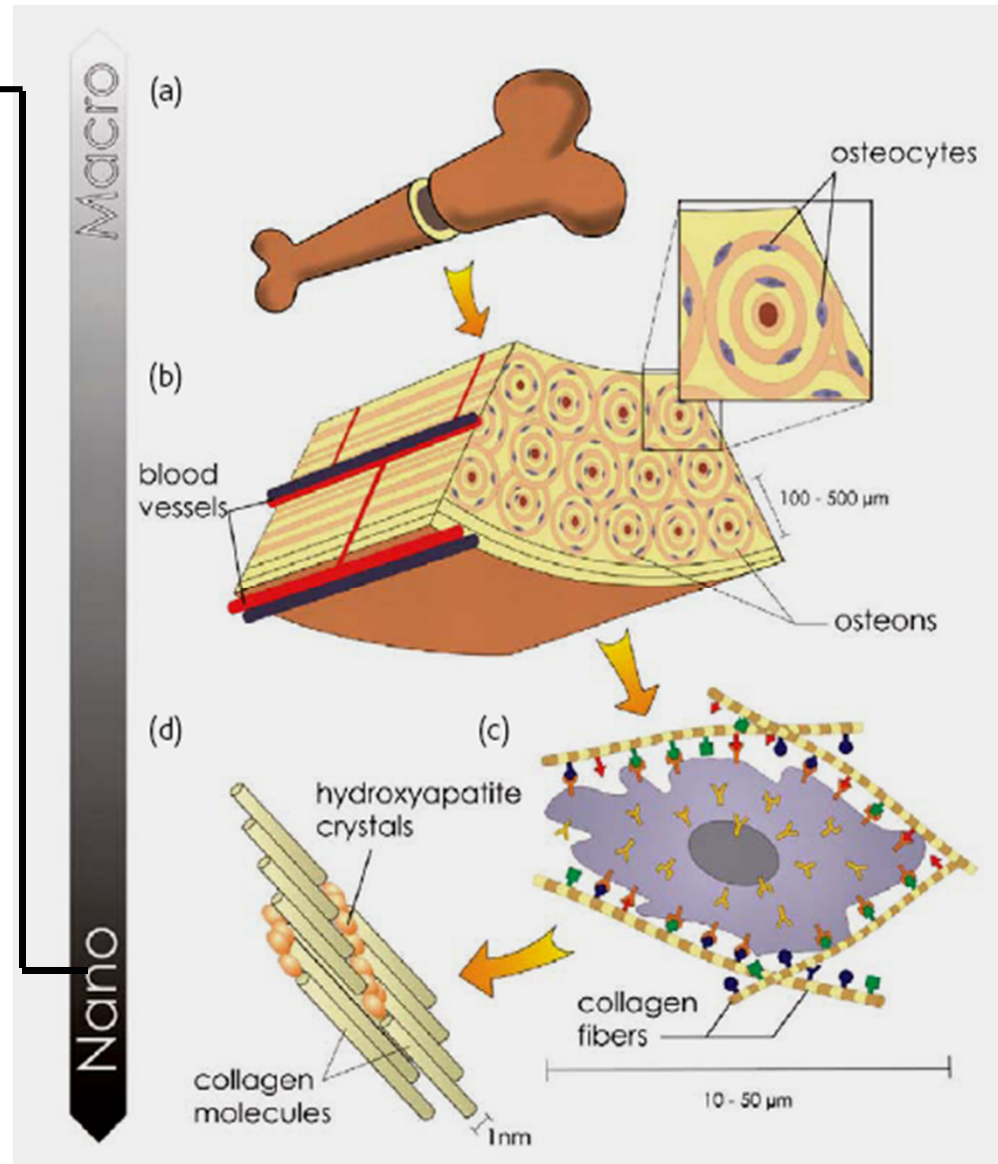
Hierarchical organization of bone

Bone ECM

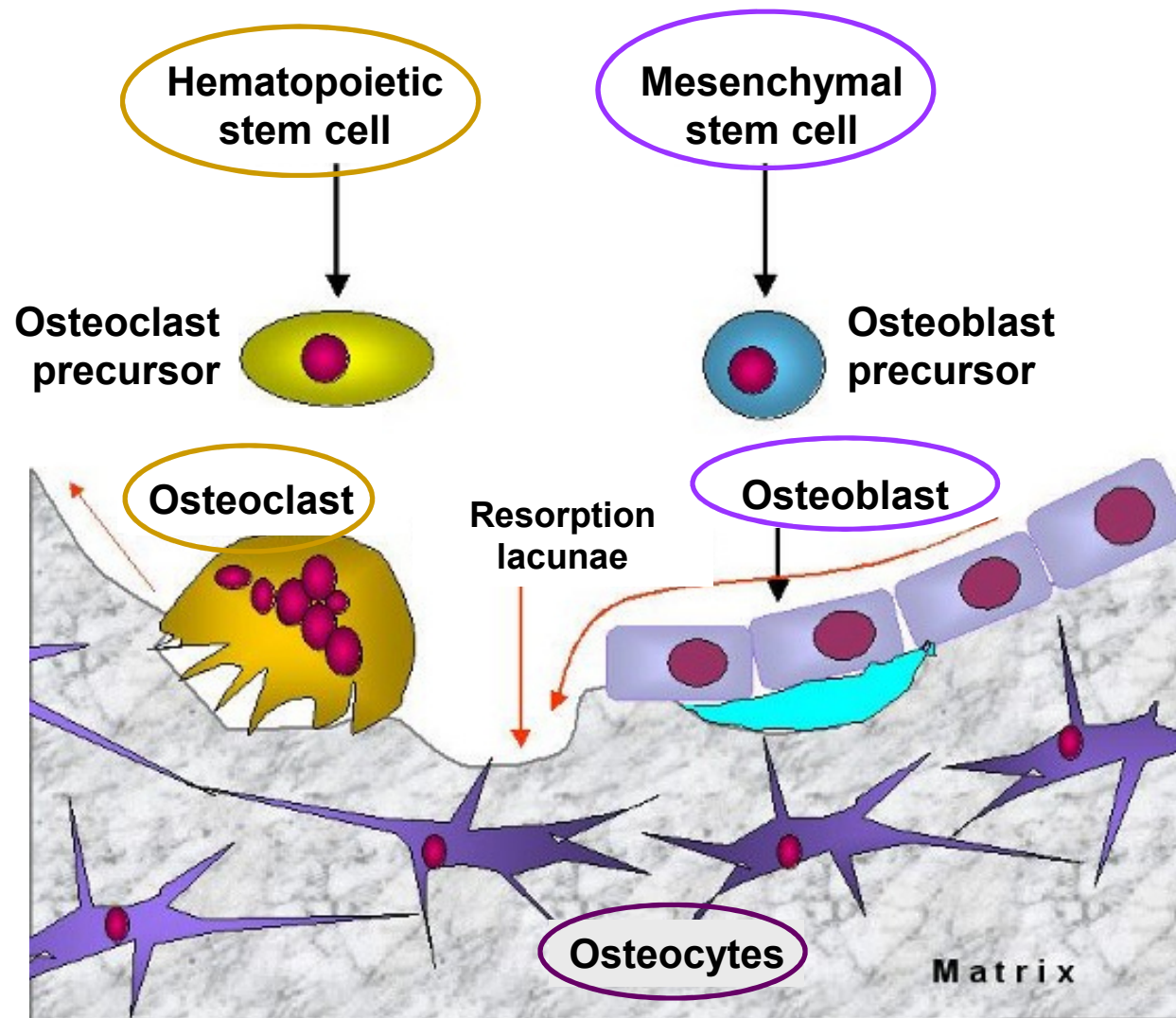
- mineralized inorganic components (hydroxyapatite)
– 60-70%

- non-mineralized organic components (collagen type I)
 - non-collagenous matrix proteins (glycoproteins, proteoglycans, bone sialoproteins)
- 20-30% + water

**MM Stevens et al.,
Science 2005**

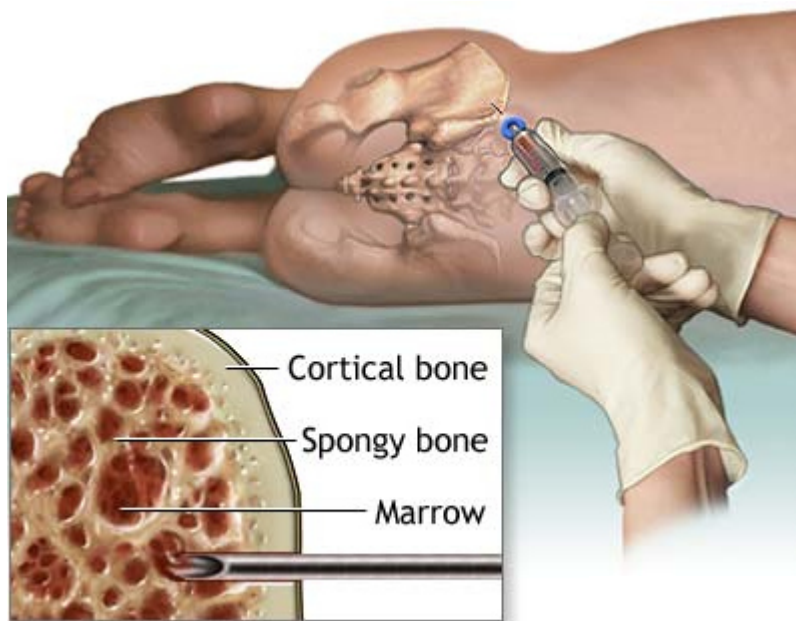


Cells of bone tissue: Osteoclasts / osteoblasts / osteocytes

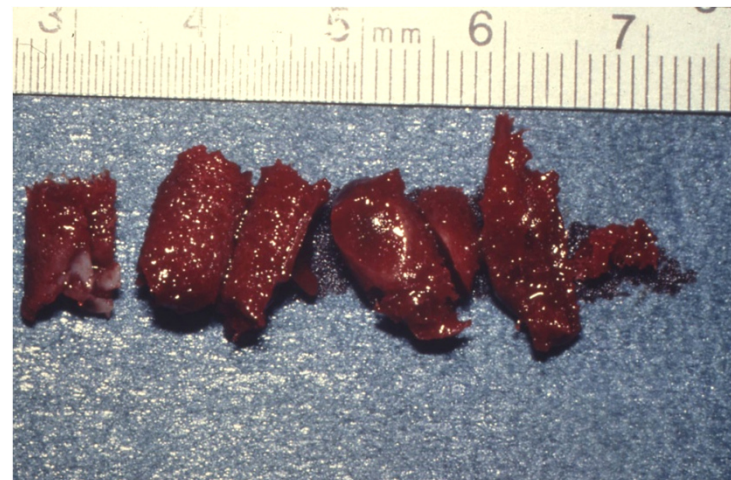
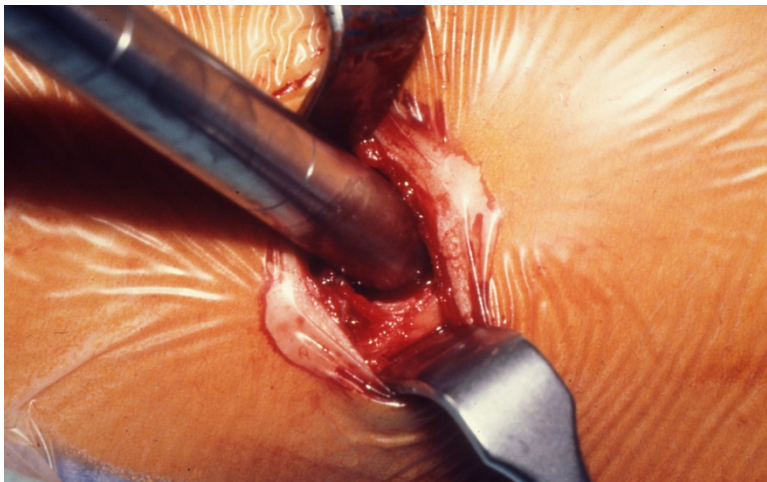


<http://www.andreas-unterberger.at/2012/07/chronische-entzuendungen-sind-ausloeser-von-knochenschwund/>

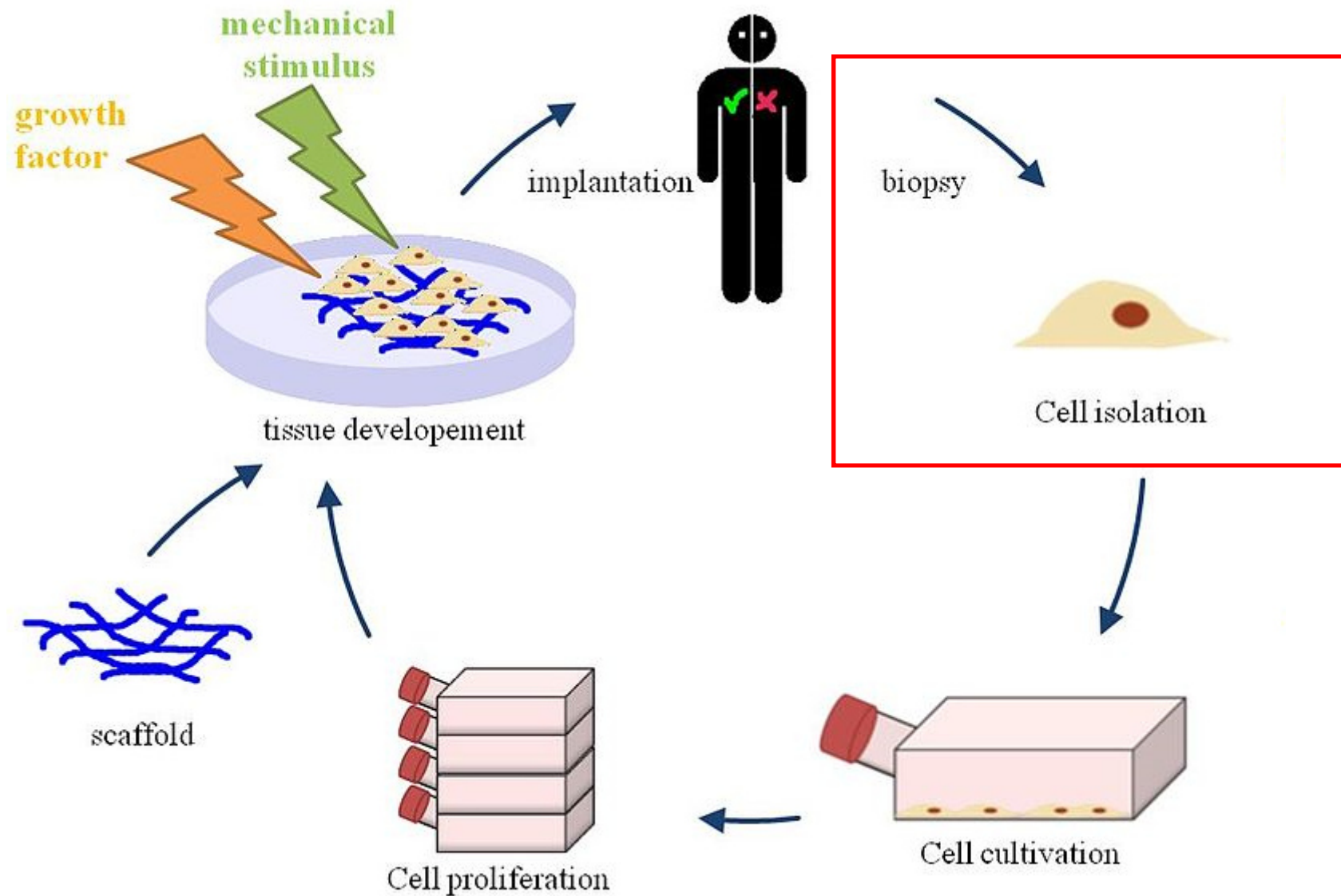
Gold standard for autologous bone regeneration



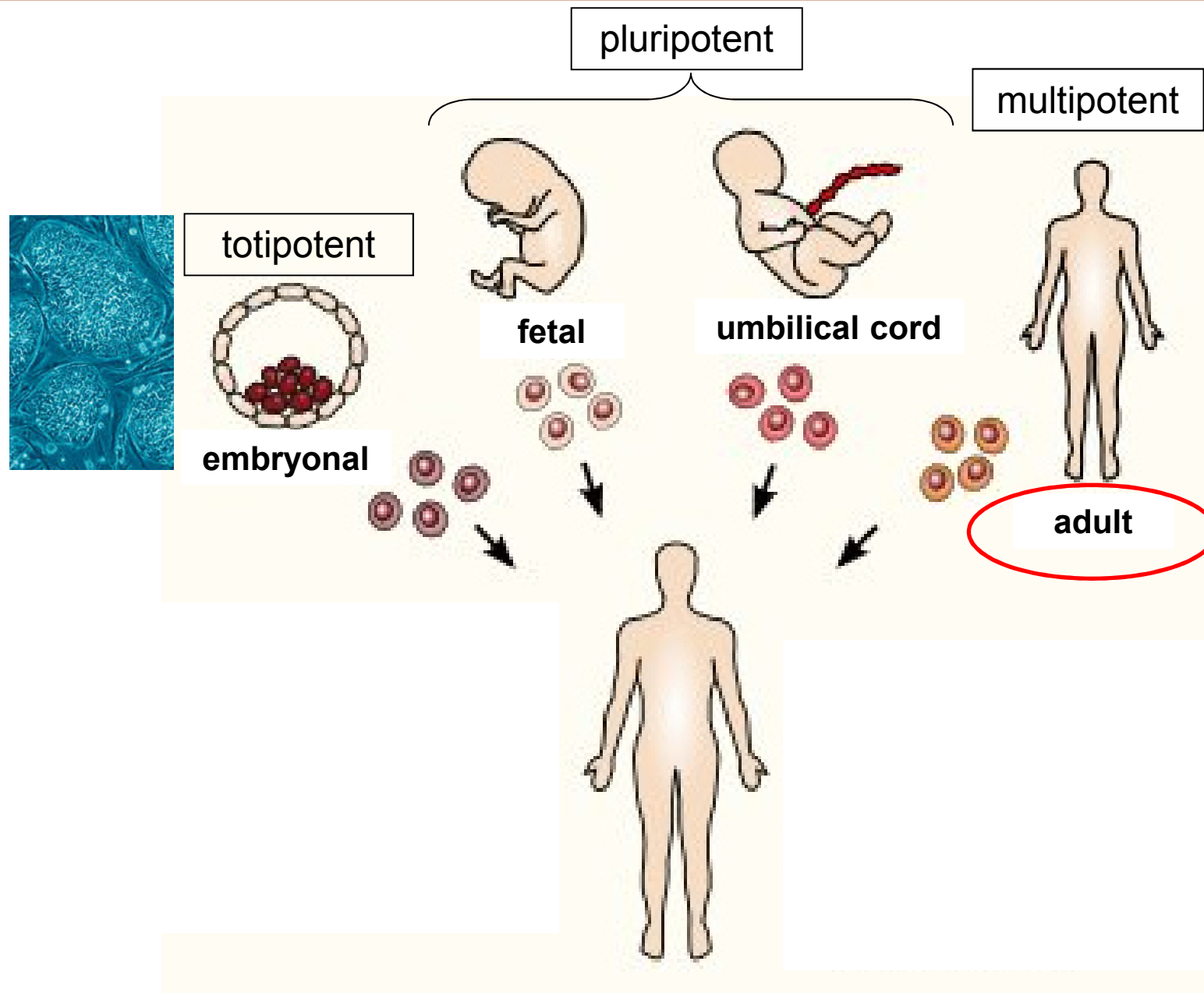
- spongy bone/marrow biopsies
- sufficient bone material is required
- morbidity of the donor site



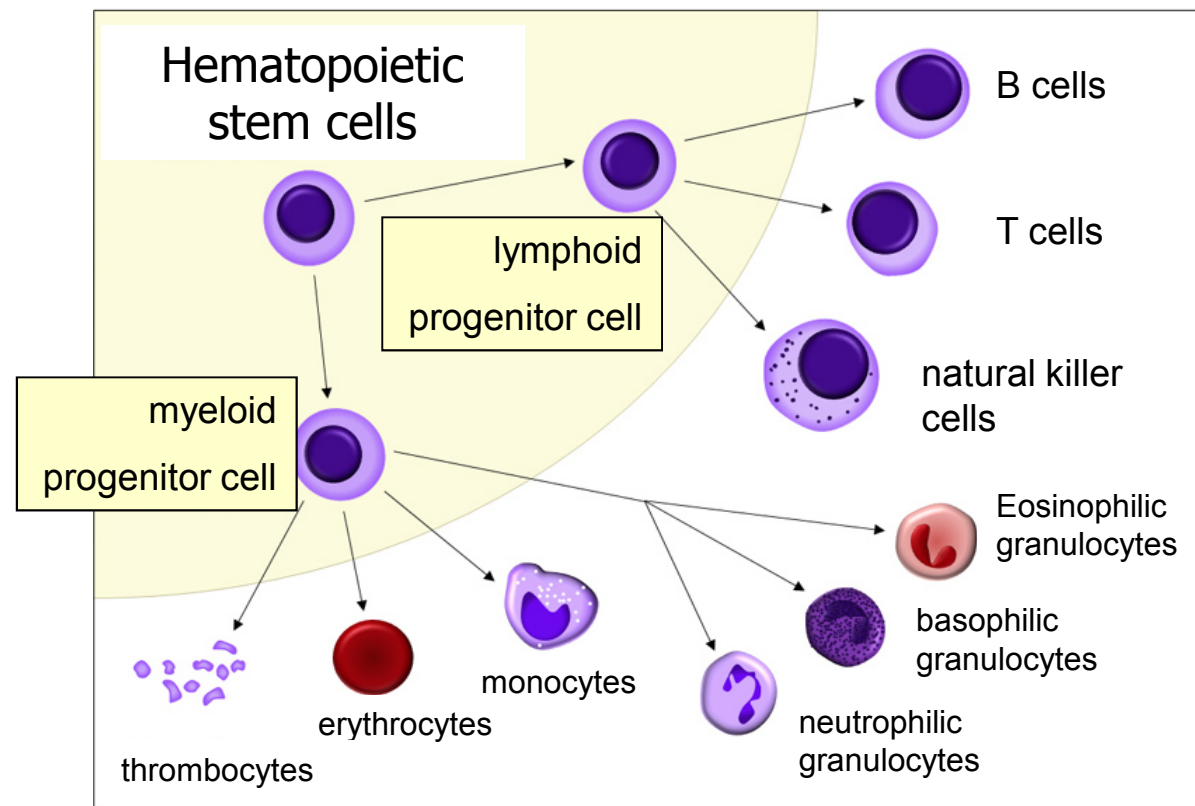
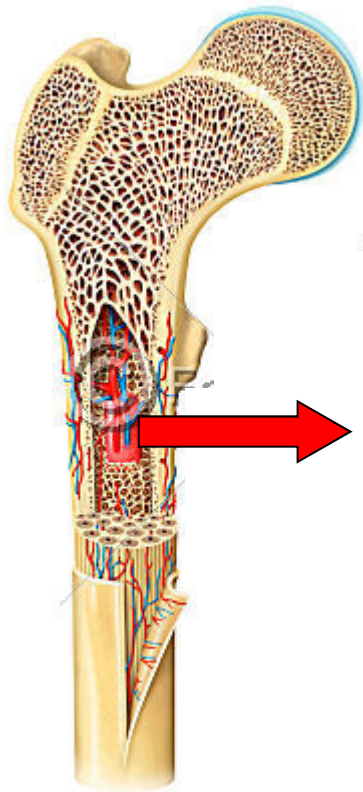
Tissue Engineering approach



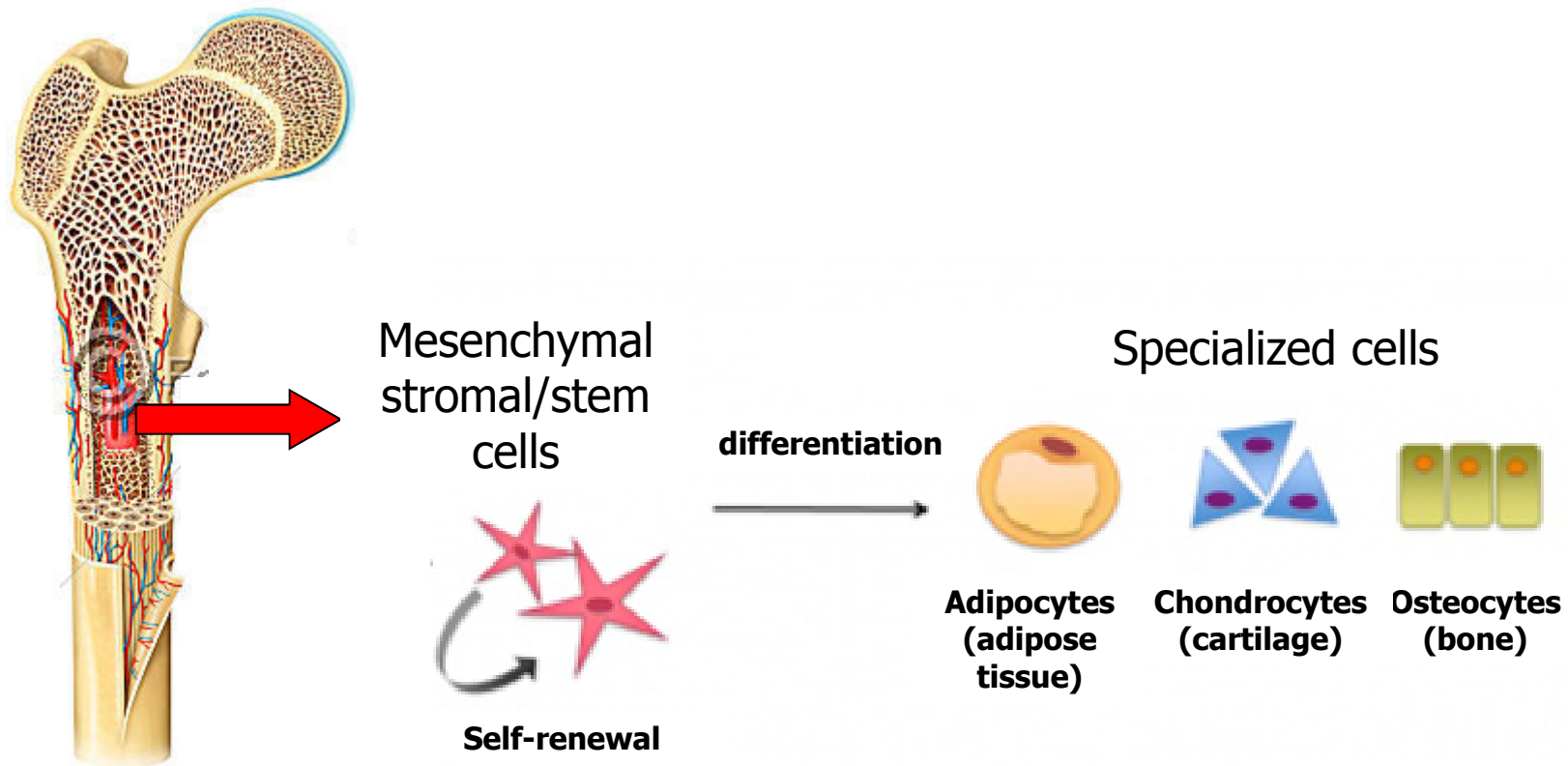
Stem cells



Bone marrow



Bone marrow

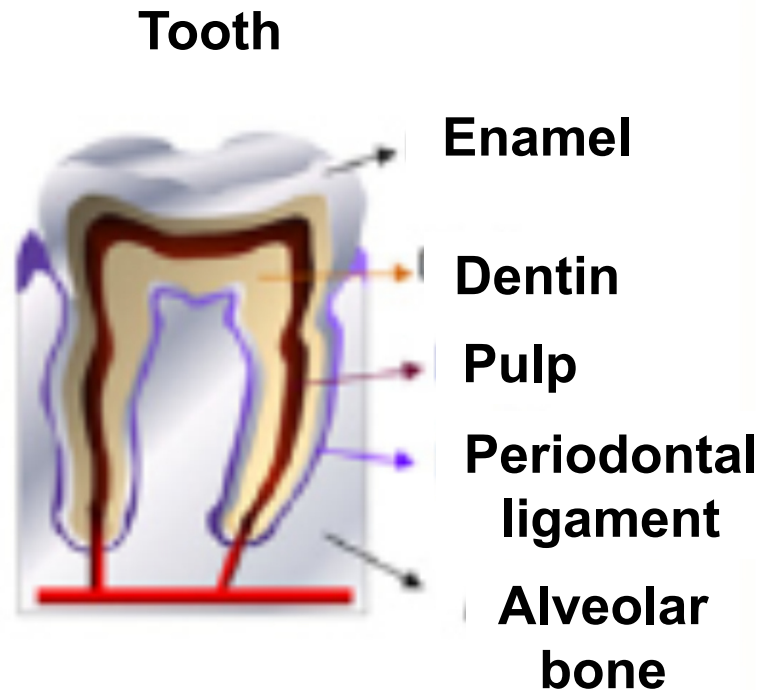


Mesenchymal stem cells (MSCs)

- **adherent** mesenchymal stem cells
 - Dominici criteria (*Cytotherapy 2006*):

1. adherence to plastic in standard culture conditions		
2. phenotype	positive ($\geq 95\%$)	negative ($\leq 2\%$)
	CD105	CD45
	CD90	CD34
	CD73	CD14 or CD11b
		CD79 α or CD19
		HLA-DR (MHC class II)

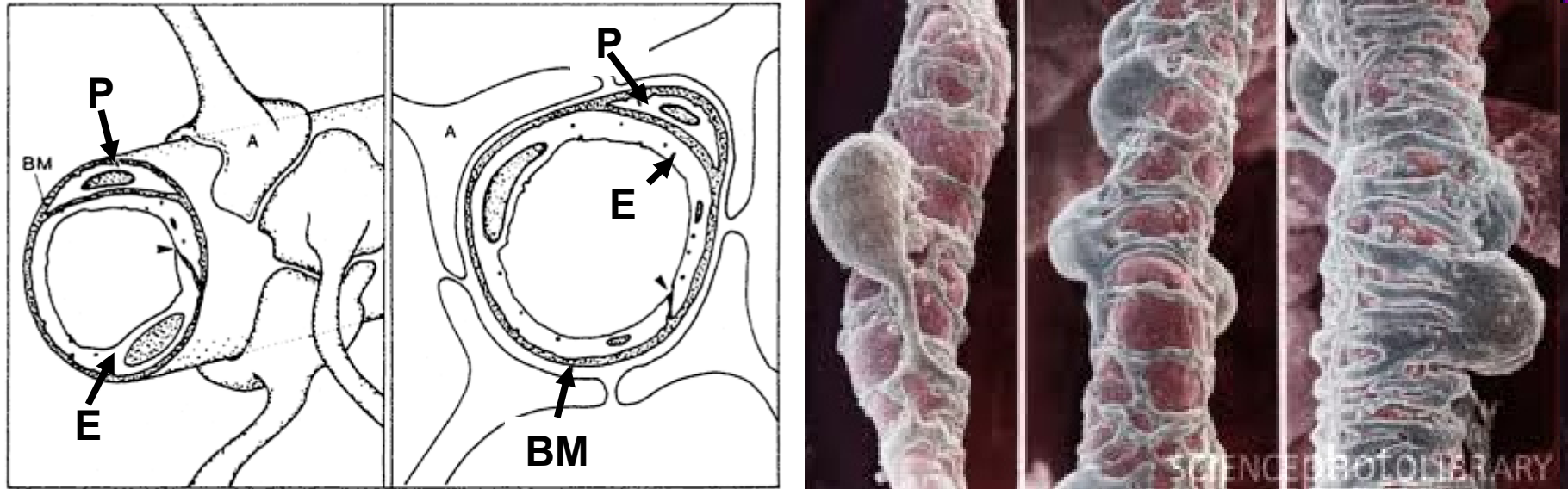
MSCs from other tissues



Dental Pulp Stem Cells

- dental pulp
- cord blood
- cord Wharton's jelly
- adipose tissue
- amniotic fluid
- compact bone
- periosteum
- synovial membrane
- articular cartilage
- fetal tissues

Are mesenchymal stem cells pericytes?

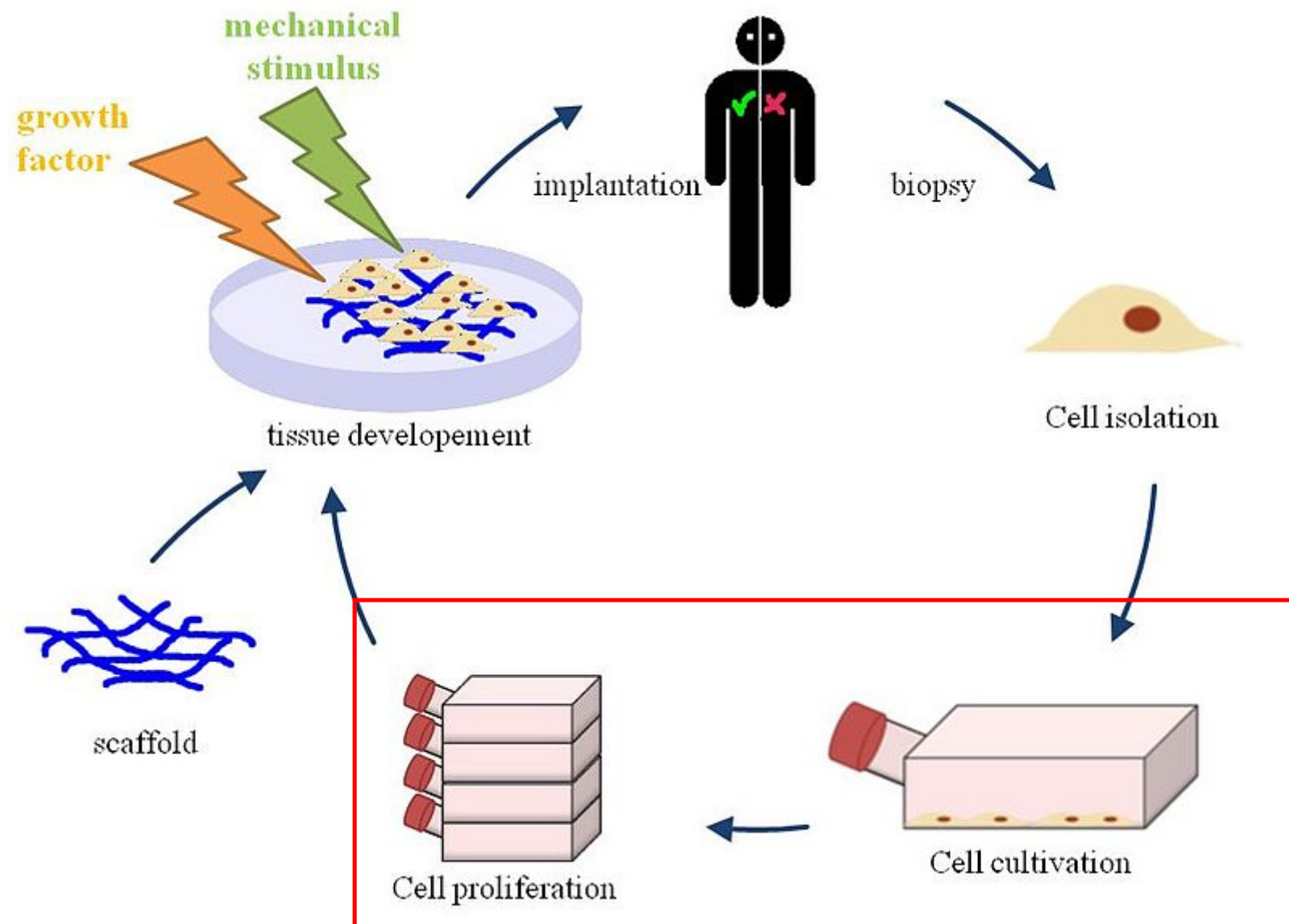


Pericytes (P) also known as mural or Rouget cells are closely associated with capillary endothelial cells (E) with which they share a common basal lamina (BM). Pericytes are able to differentiate into adipocytes, osteoblasts, fibroblasts, smooth muscle cells and macrophages.

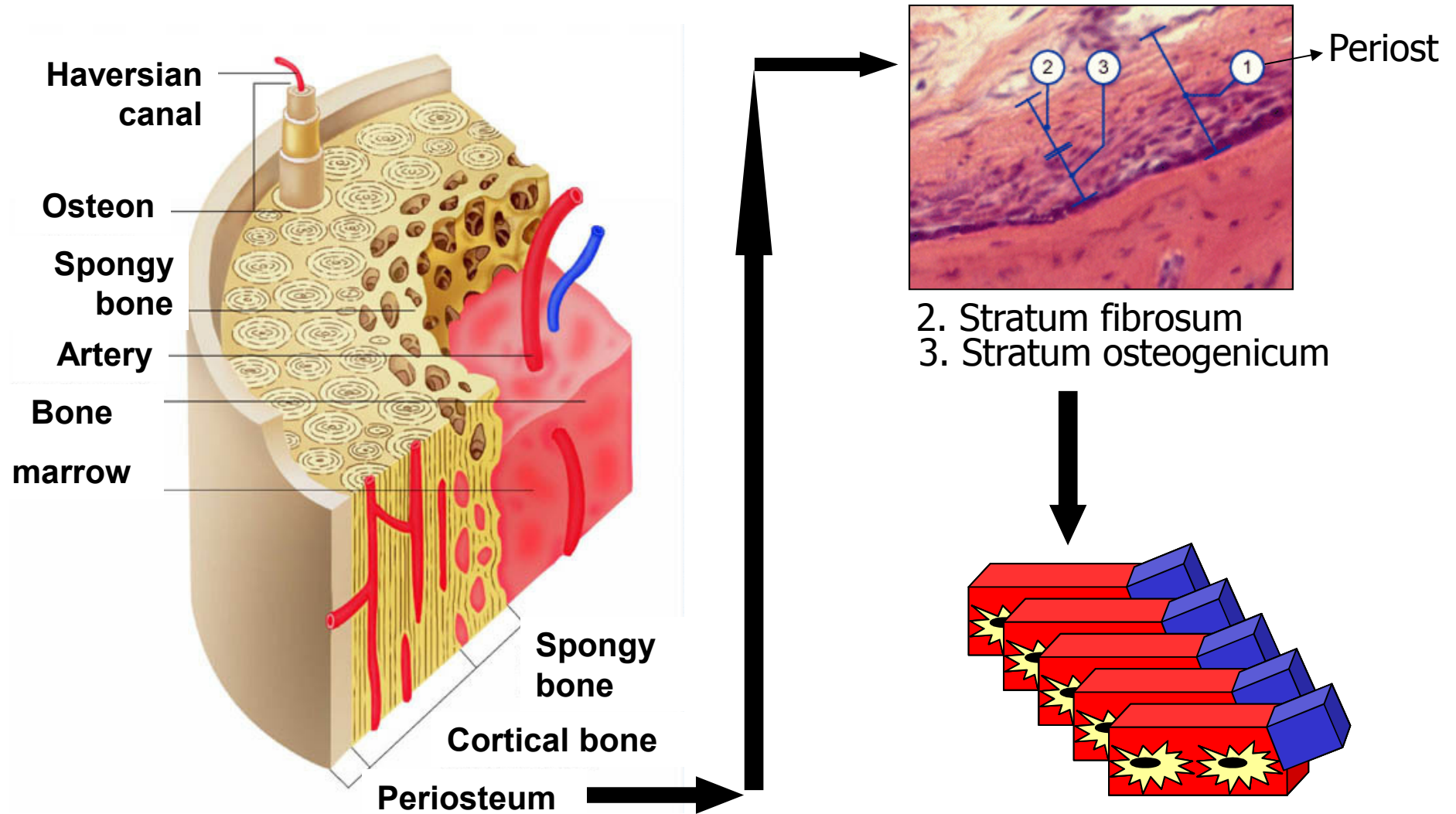
Pericytes were demonstrated to be CD105+, CD146+ and CD31-, CD34-

G Allta and J.G. Lawrensona, Cell Tissues Organs 2001

Tissue Engineering approach

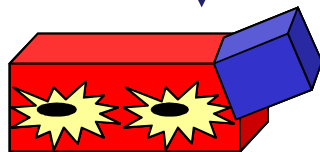
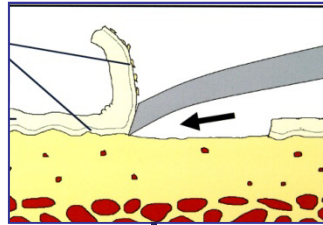


Periosteal tissue

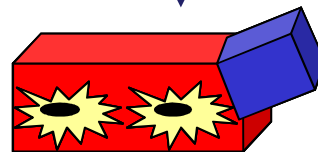


In vitro cultivation of stem cells

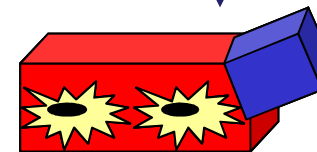
**Isolation and
expansion of
periosteal cells**



untreated



**osteogenic
supplement 1**



**osteogenic
supplement 2**

**proliferation
analysis**

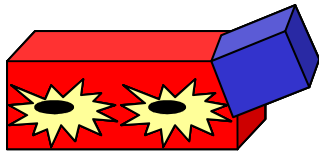
**Quantification of
calcium
precipitates**

gene expression analysis

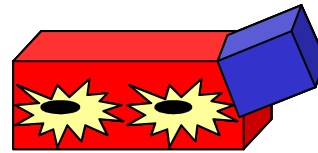
**protein-
expression
analysis**

stainings

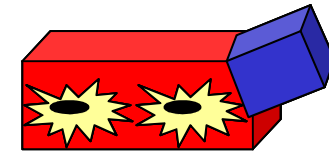
Gene expression analysis of differentiating cells



untreated



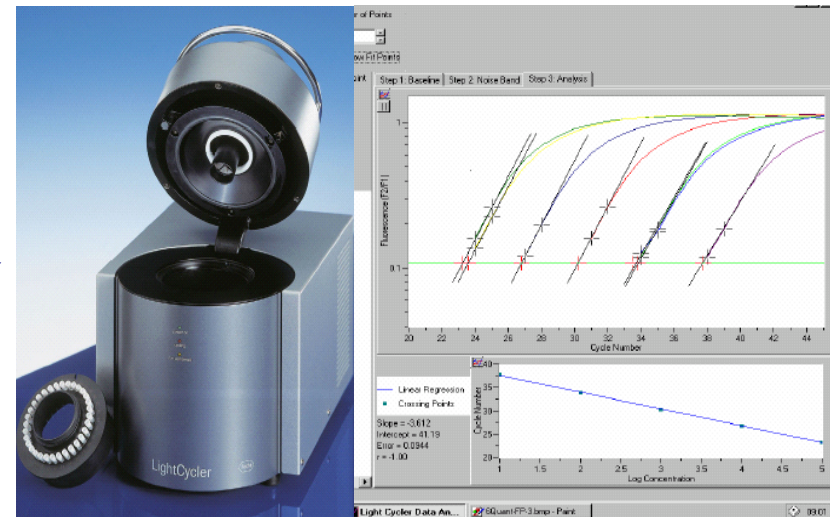
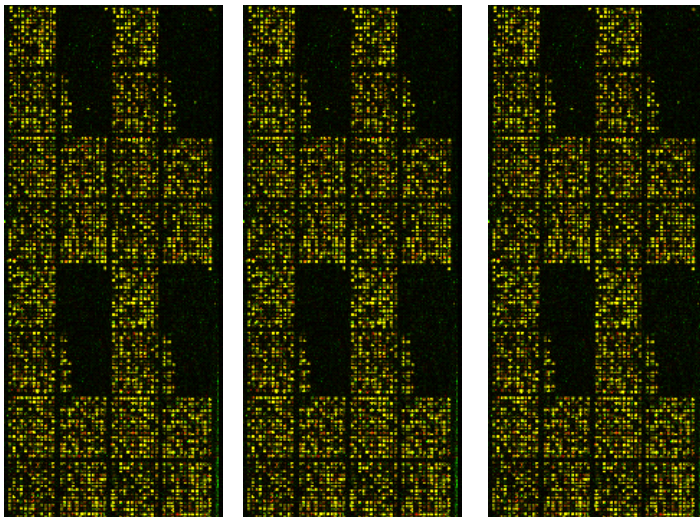
osteogenic
supplement 1



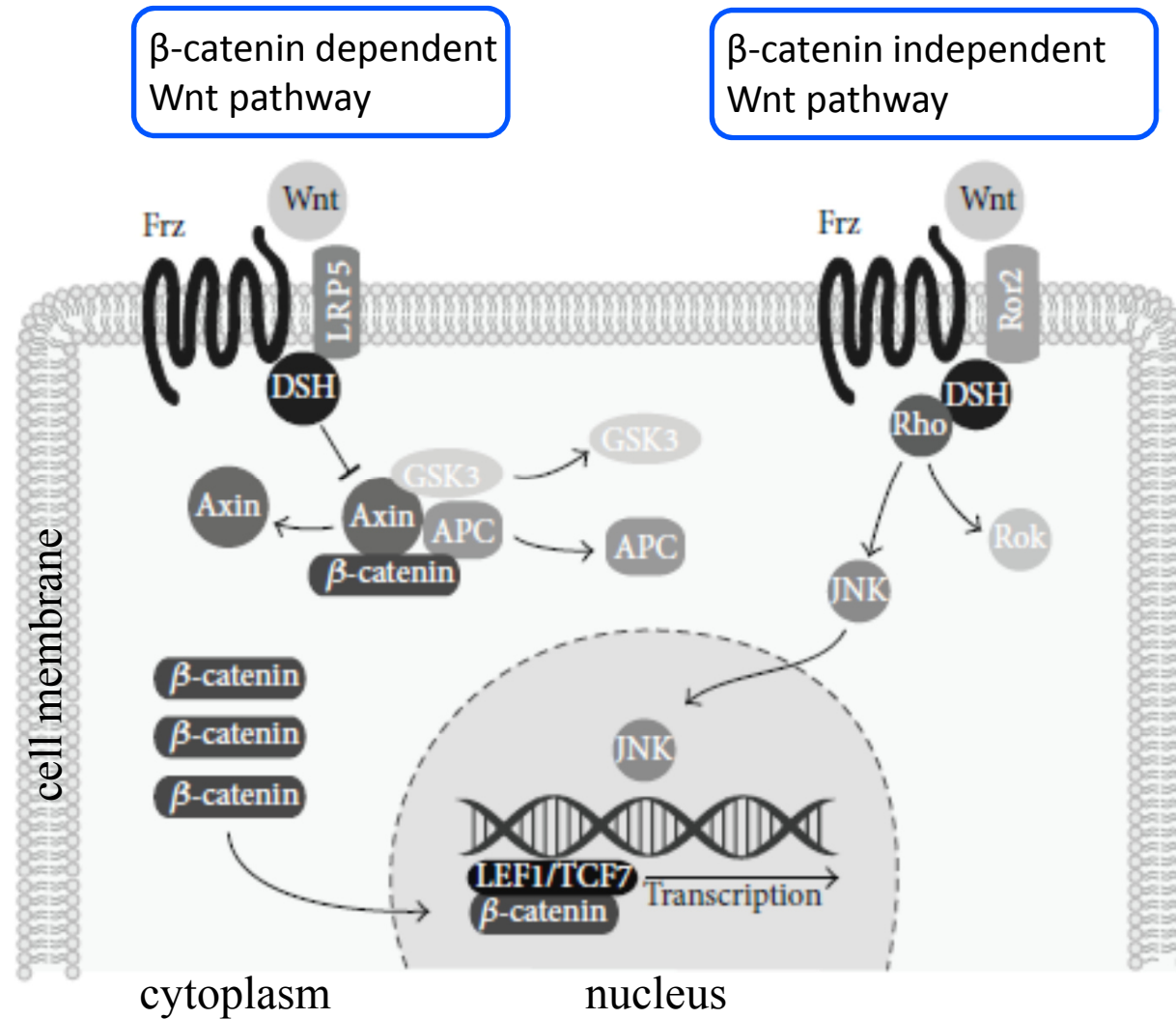
osteogenic
supplement 2

Microarrays

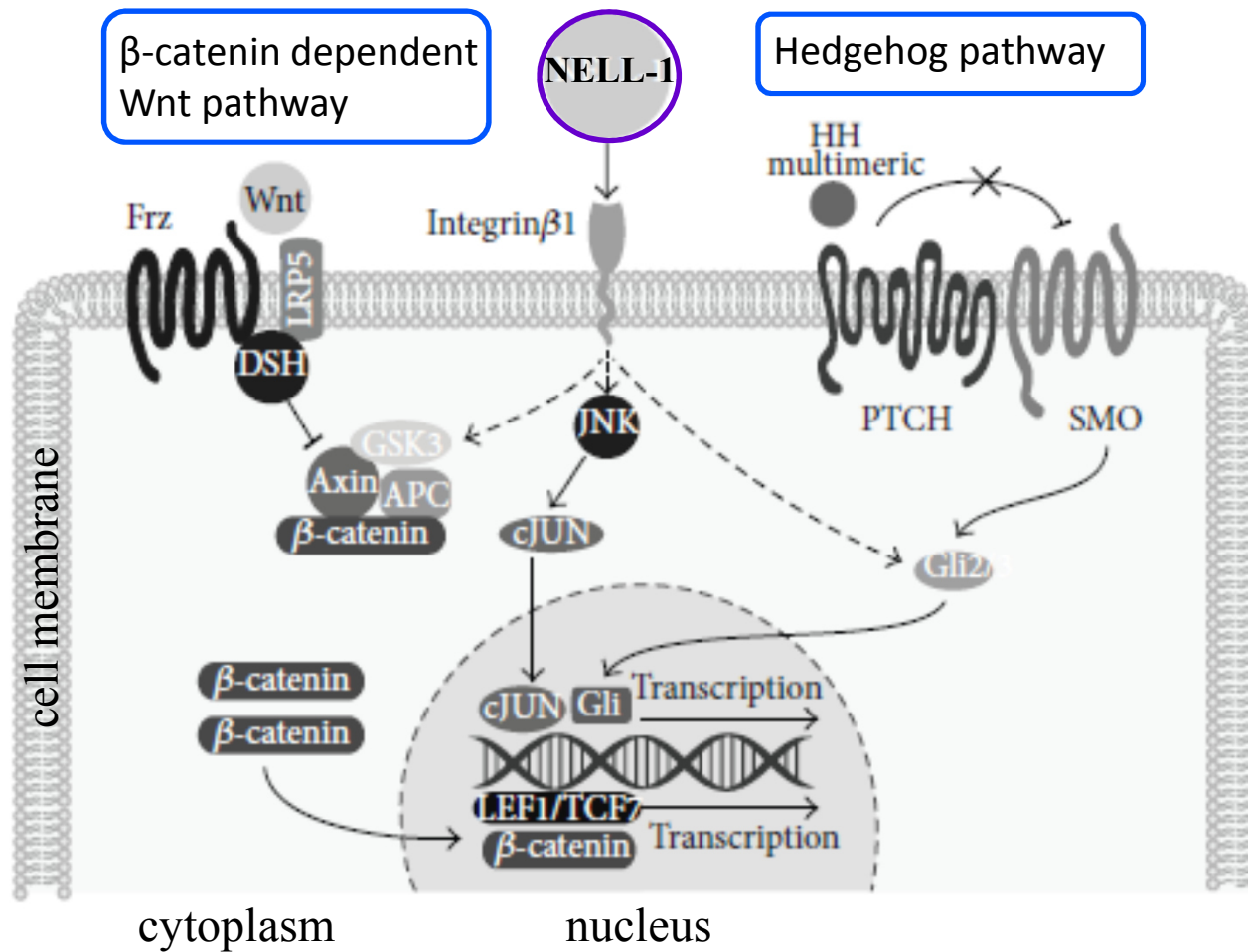
quantitative PCR



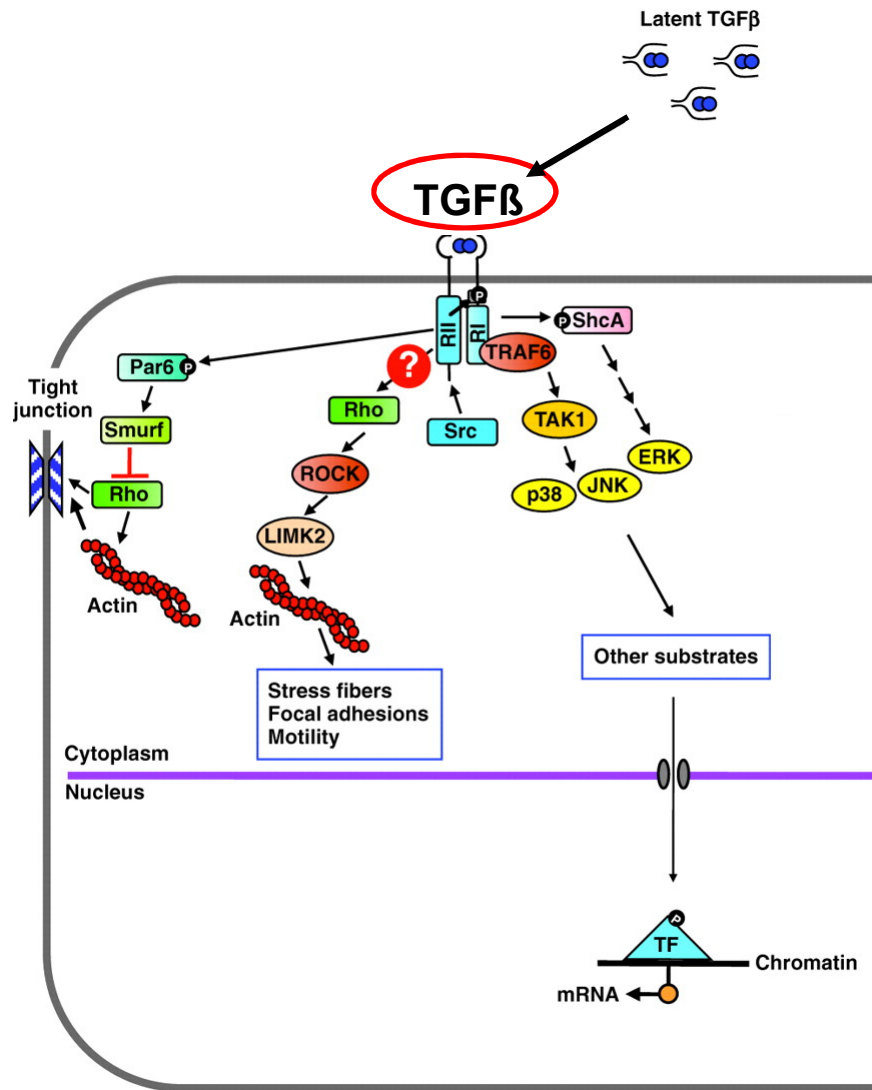
Signaling pathways for osteogenesis



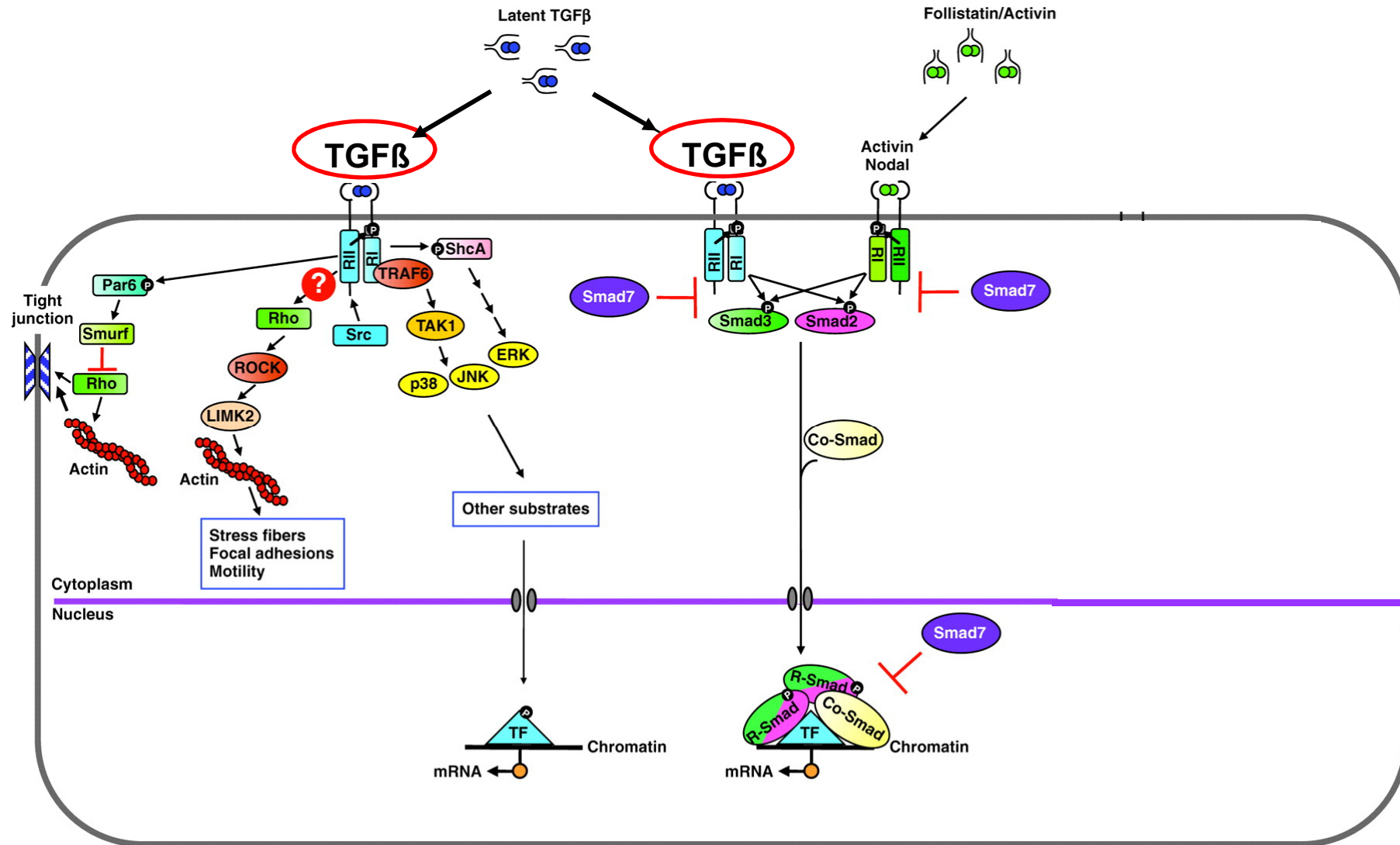
Signaling pathways for osteogenesis



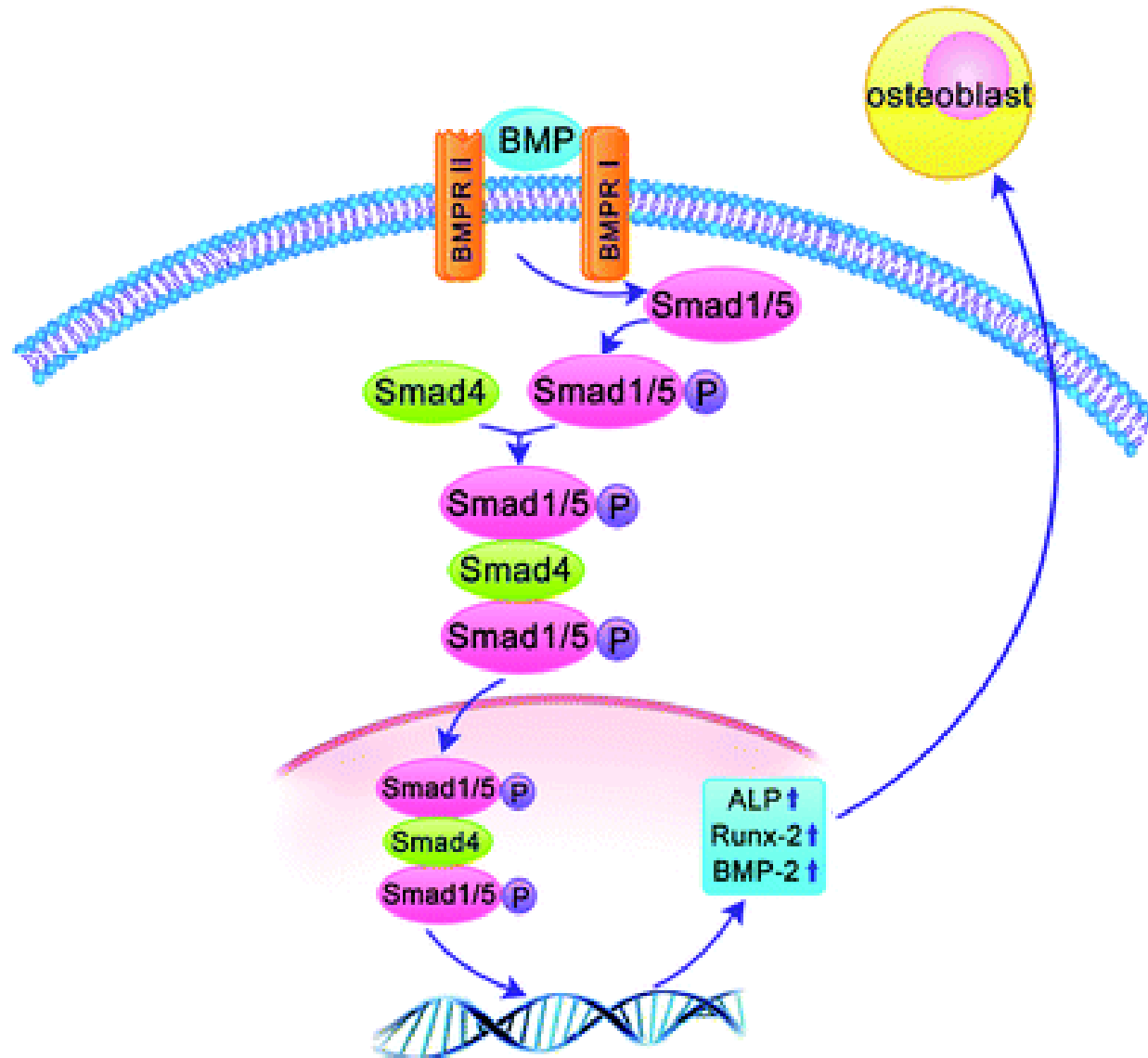
Signaling pathways for osteogenesis



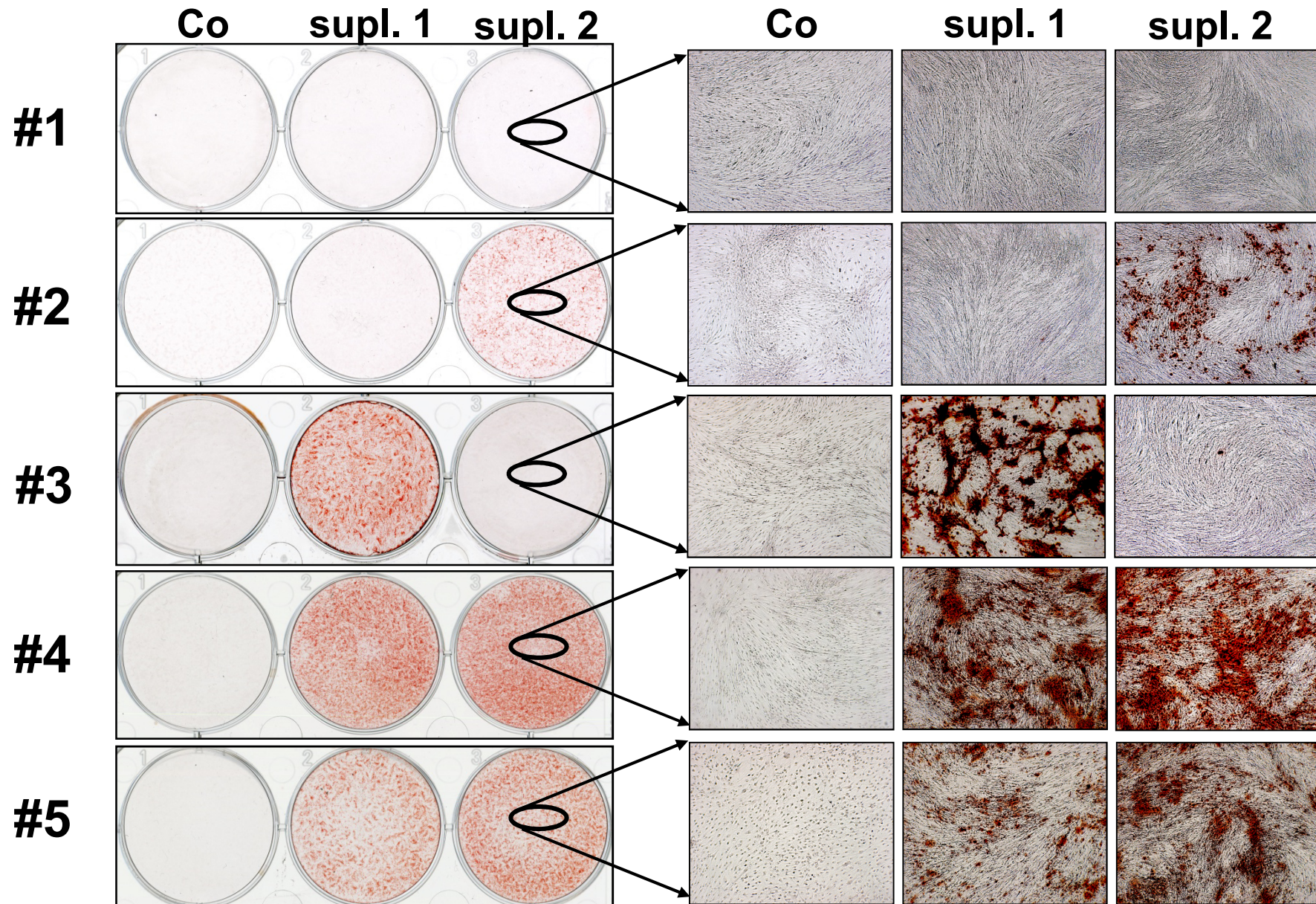
Signaling pathways for osteogenesis



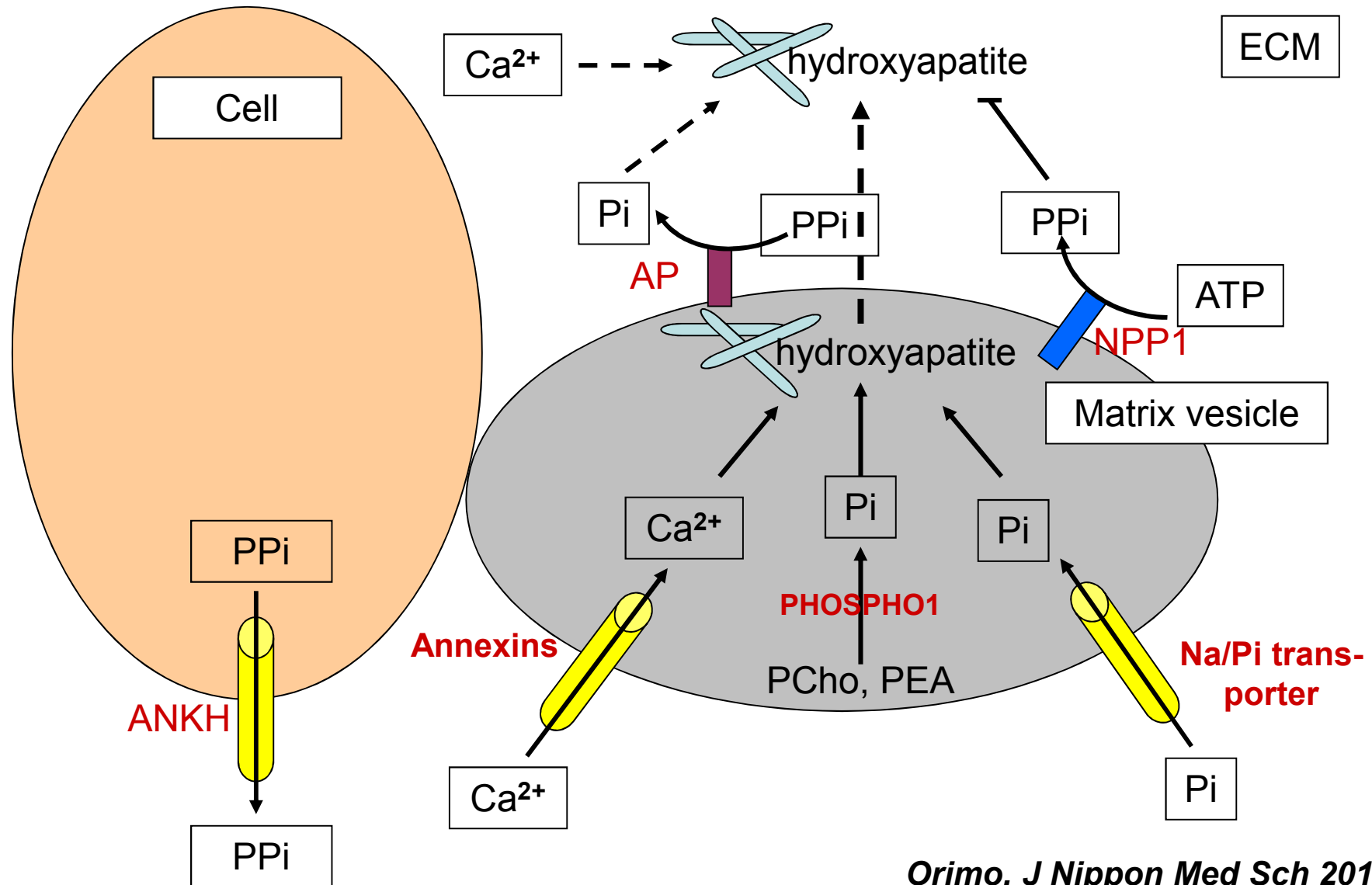
Bone morphogenetic protein (BMP) signaling pathways



Different osteogenic potential of periosteal cells

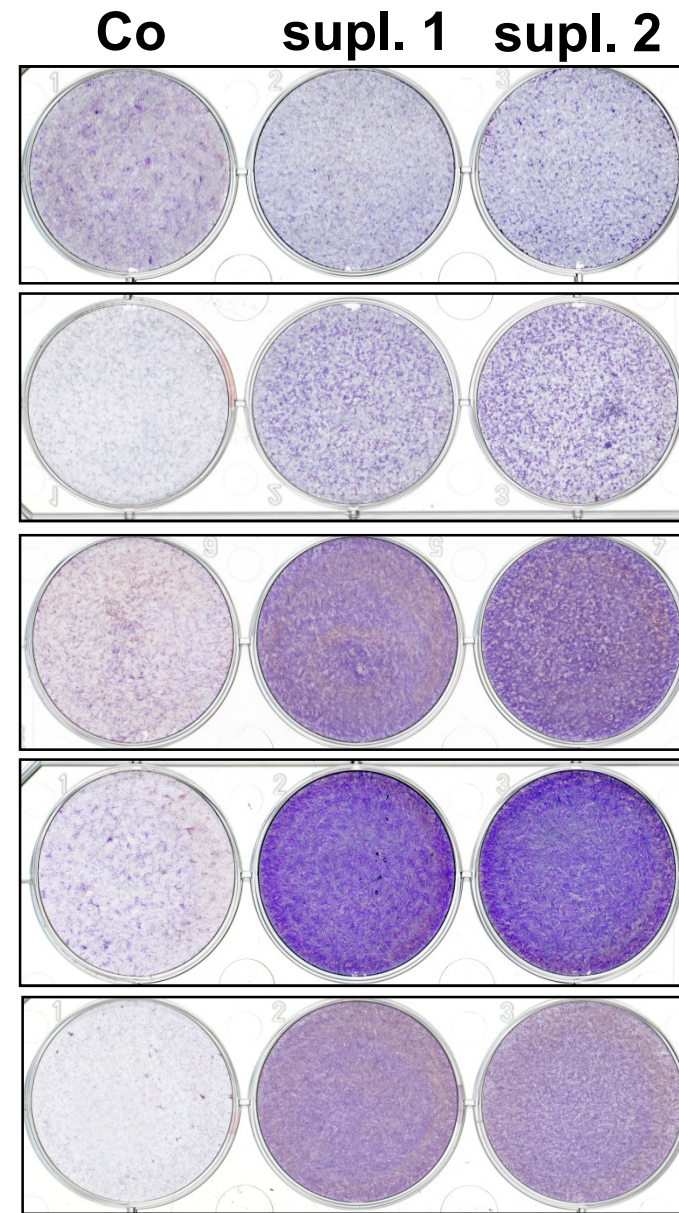
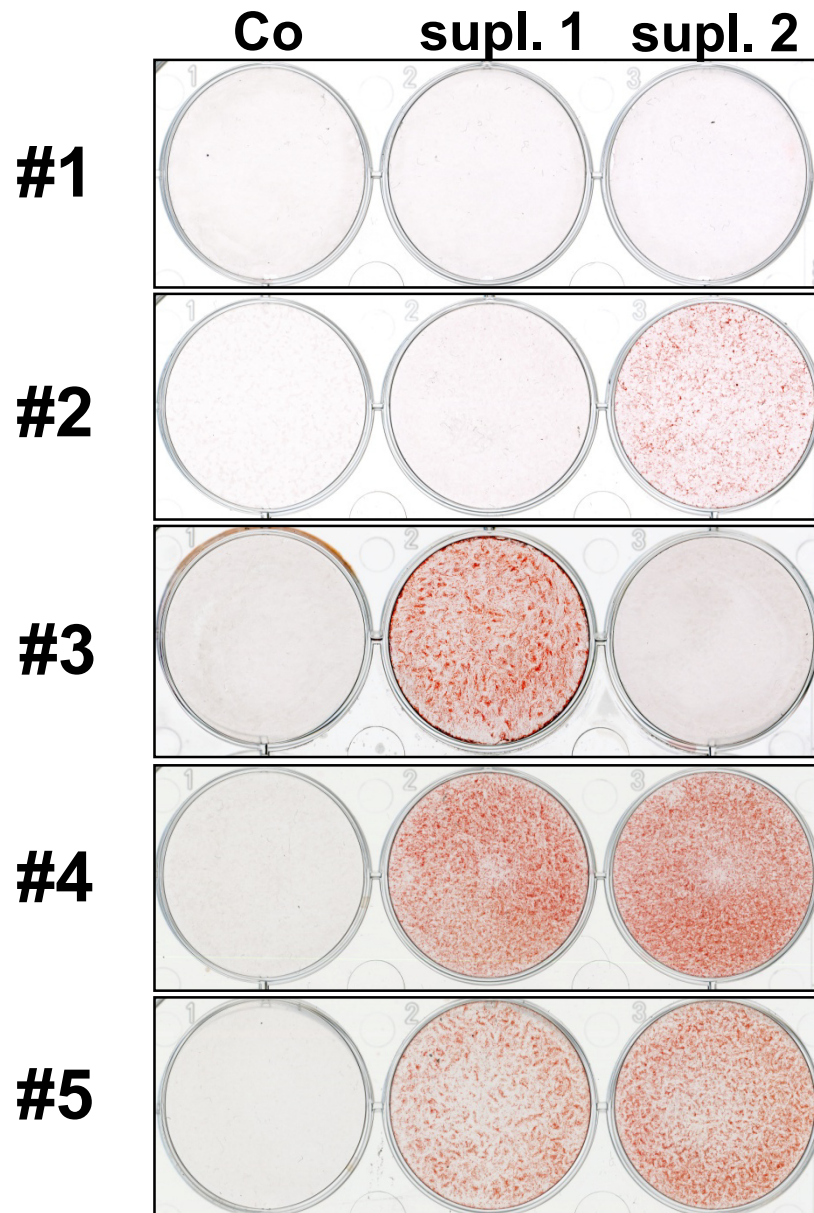


Schematic diagram of the mineralization process

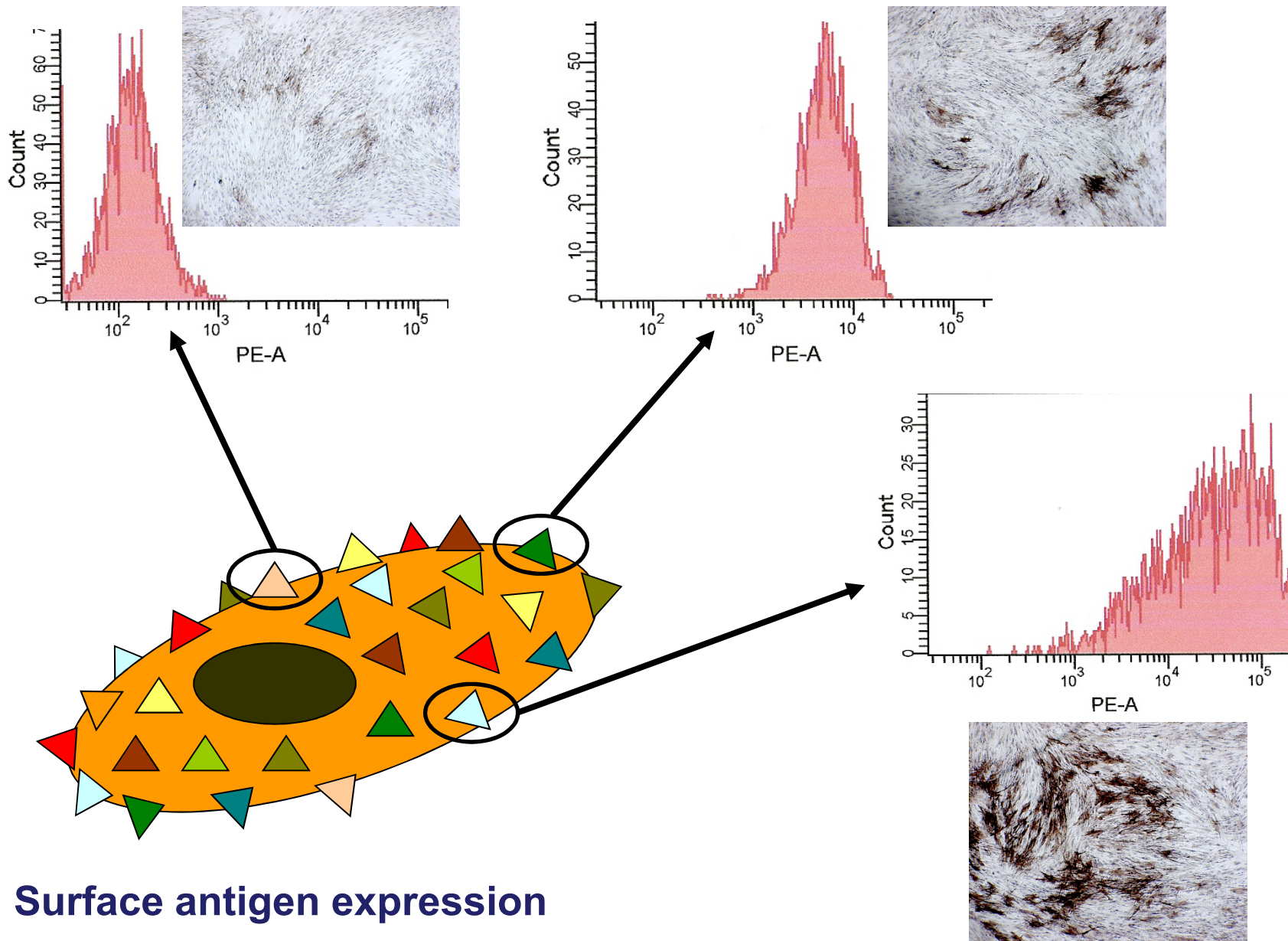


Orimo, J Nippon Med Sch 2010

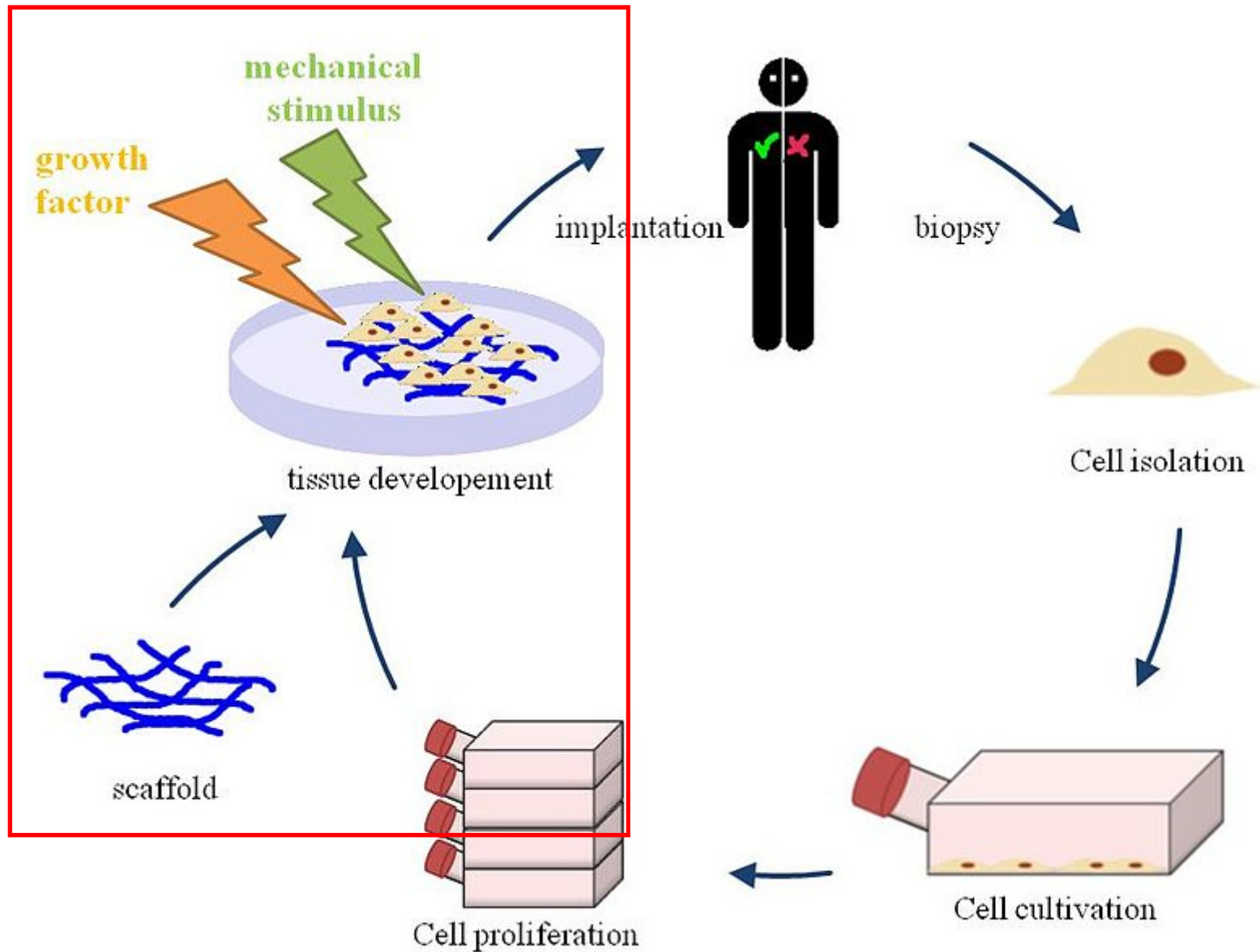
Correlation with the alkaline phosphatase activity



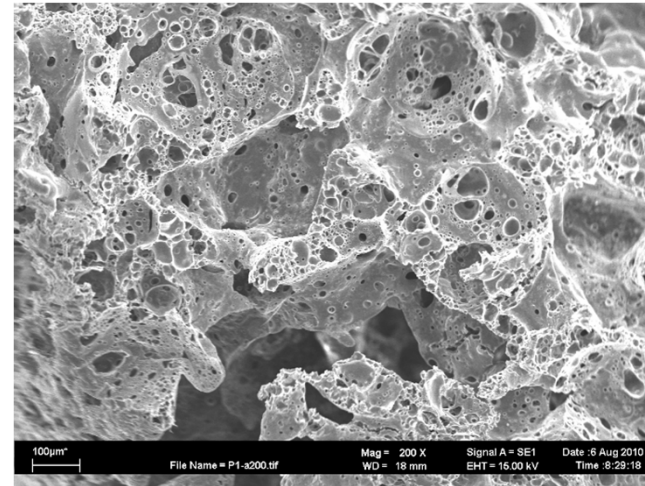
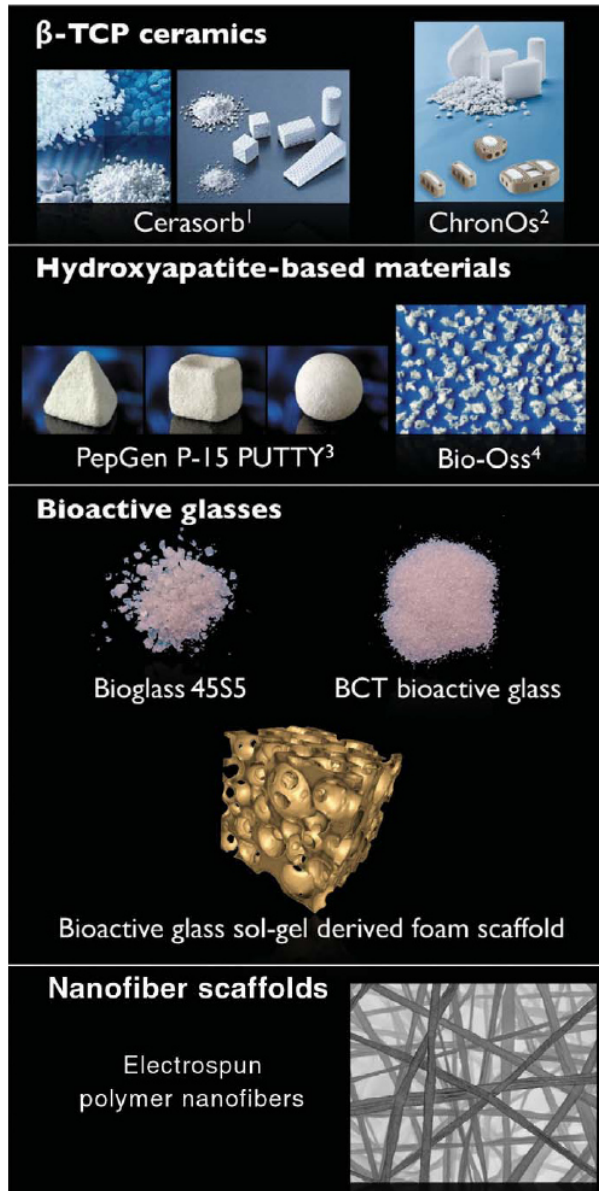
FACS (fluorescence activated cell sorting)



Tissue Engineering approach

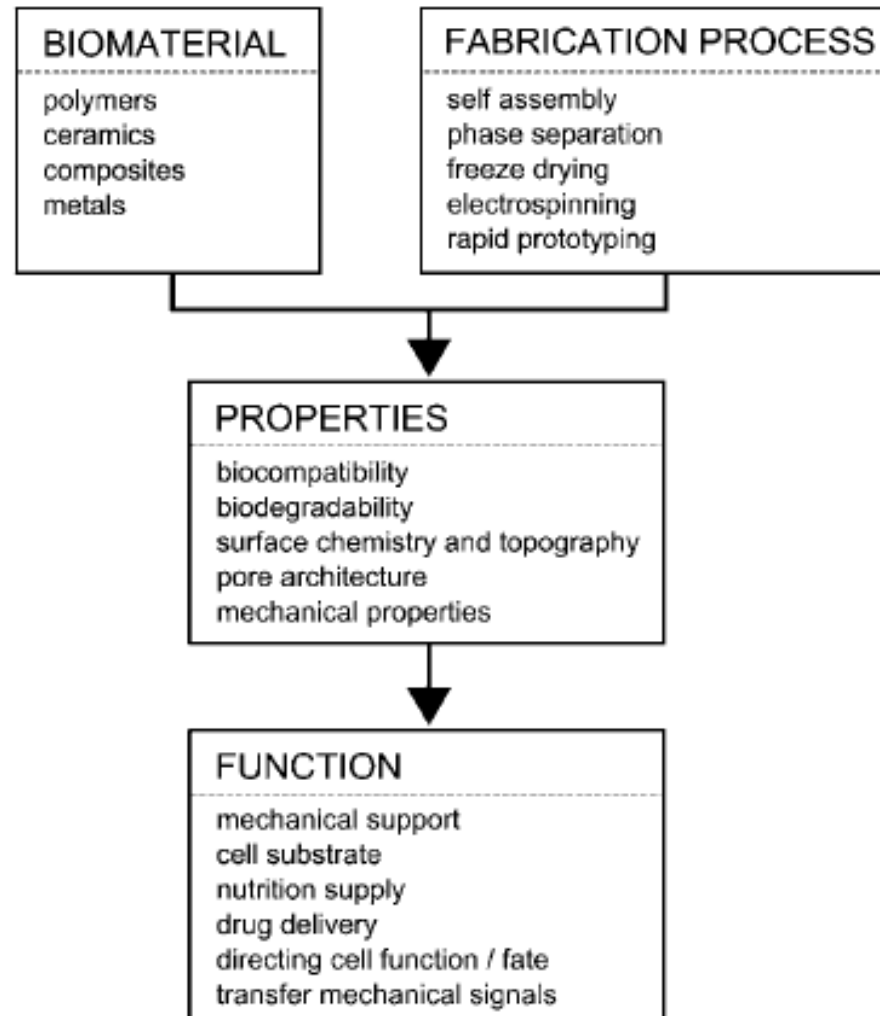


Biomaterials for bone TE



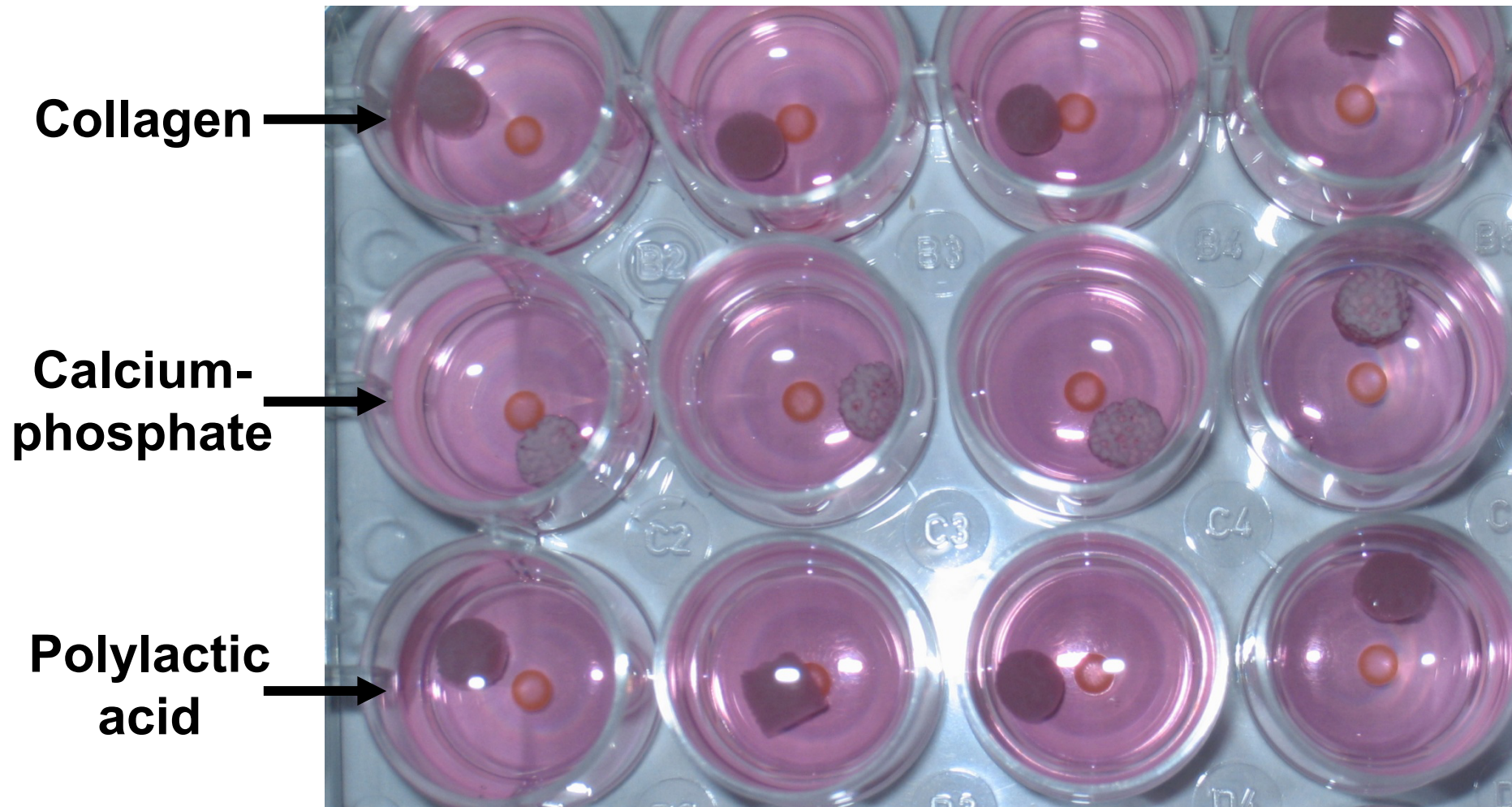
- bioactive inorganic materials
- biological polymers
- composite materials

Fundamental features of biomaterials for bone regeneration

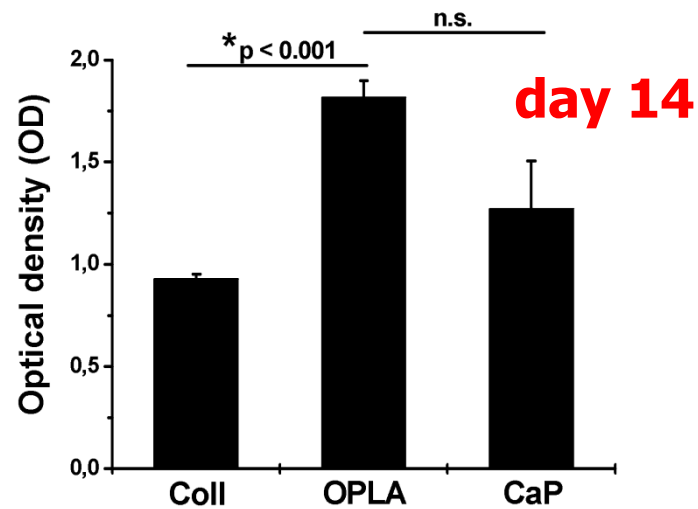
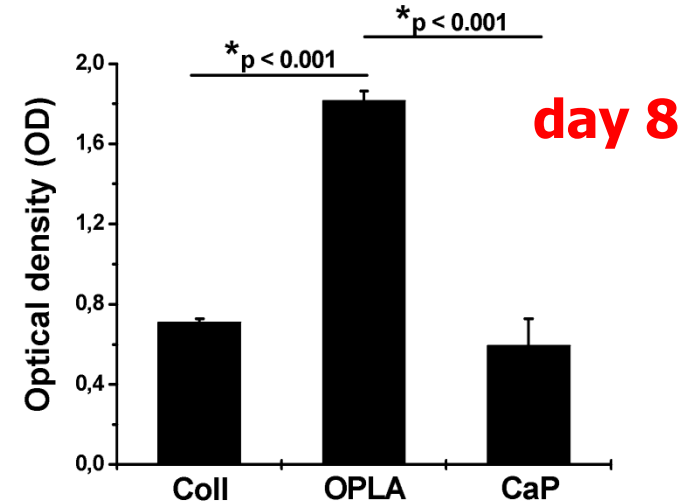
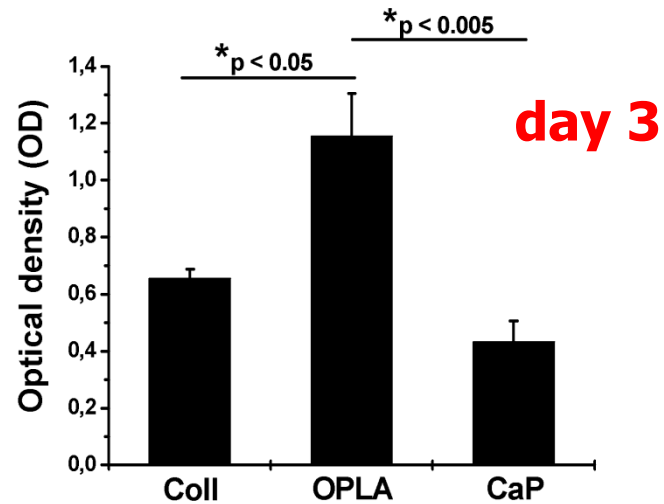


3D biomaterials for different stem cell types

Periosteal cell-seeded biomaterials

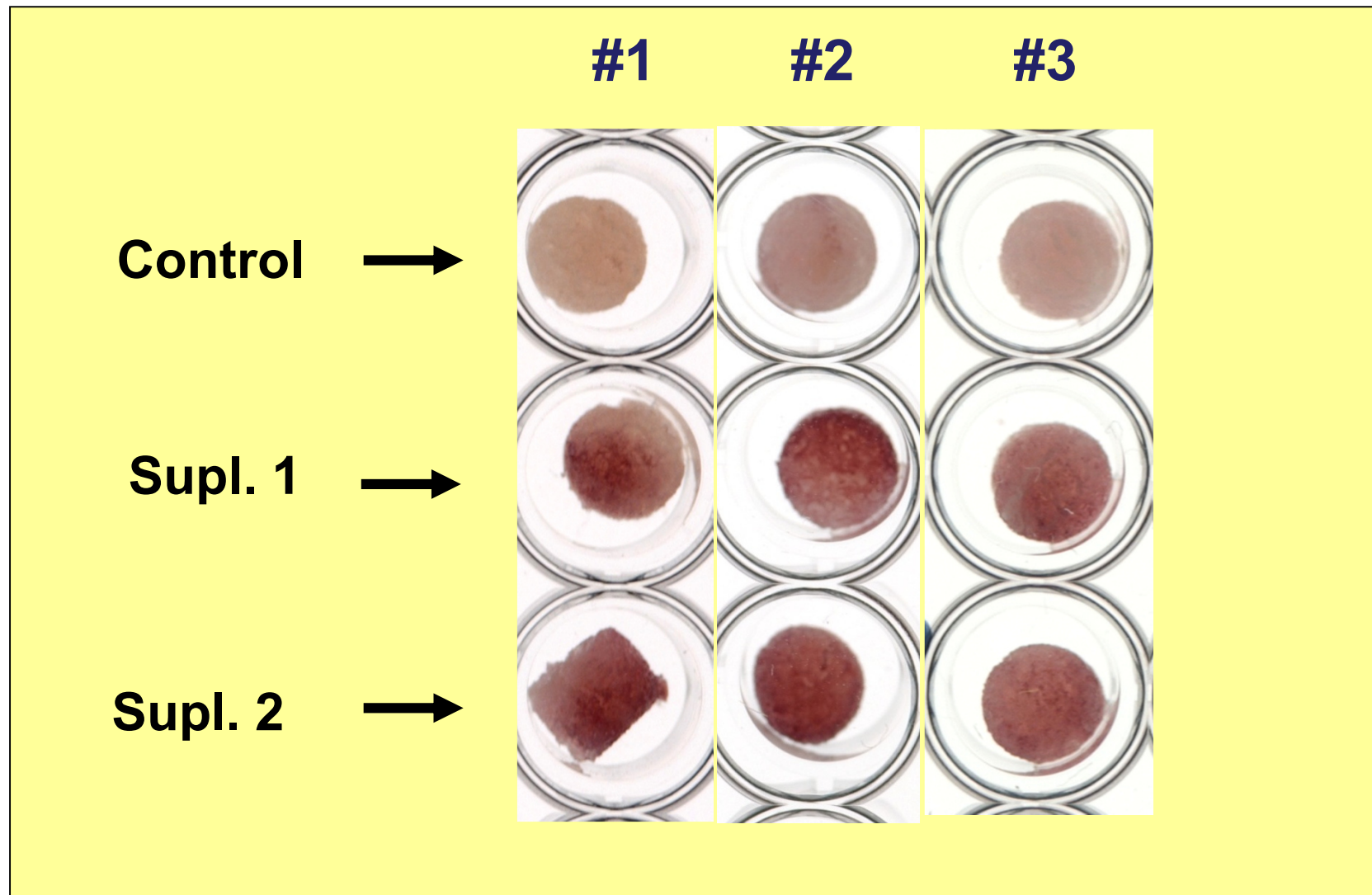


Proliferative behaviour of periosteal cells within different biomaterials



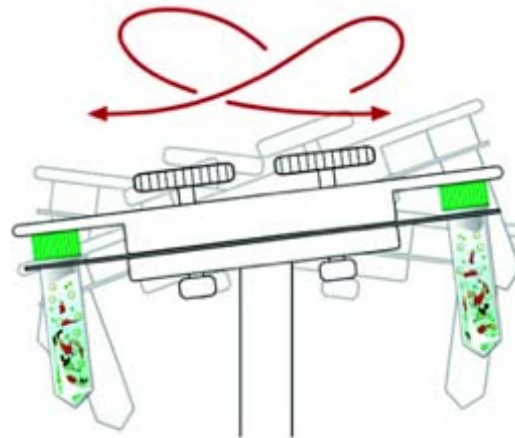
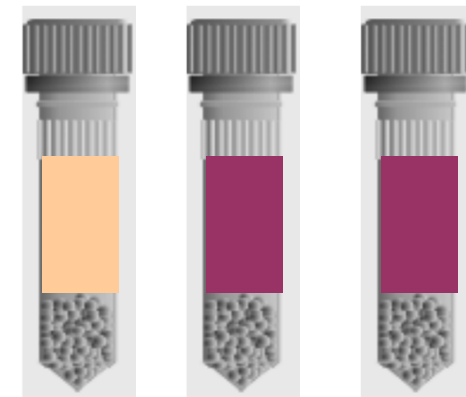
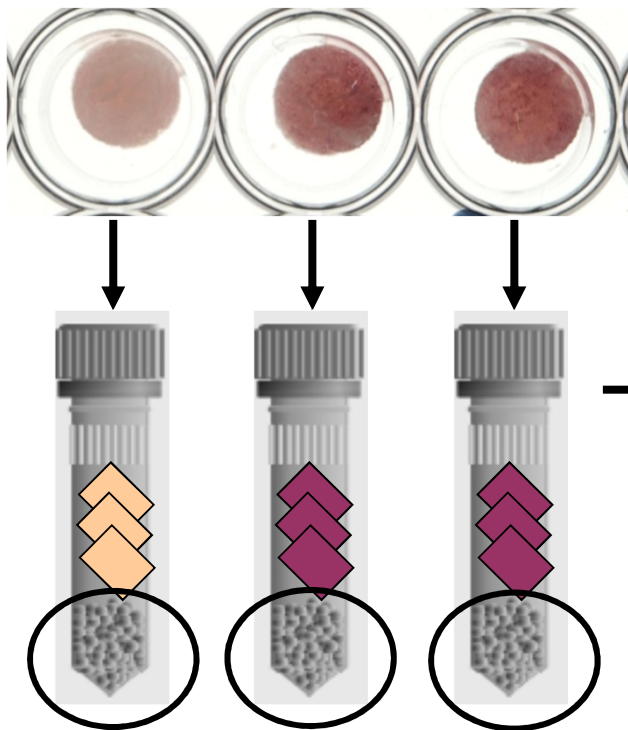
Osteogenic differentiation of cell-seeded polylactic acid 3D constructs

Detection of alkaline phosphatase



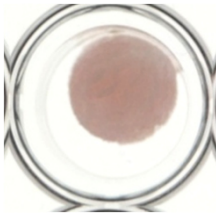
RNA extraction from cell-seeded 3D constructs

MagNA Lyser

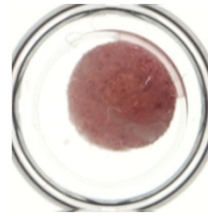


RNA extraction

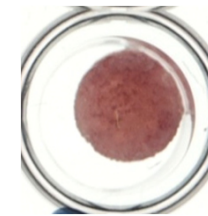
Gene expression analysis in cells growing within 3D scaffolds



untreated

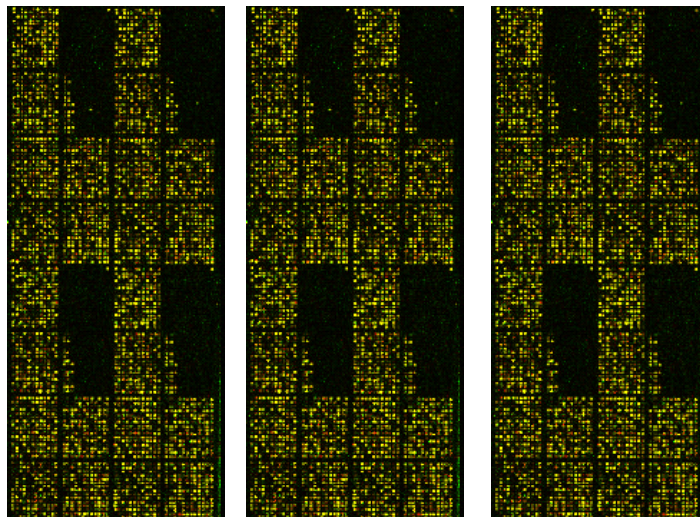


osteogenic
supplement 1

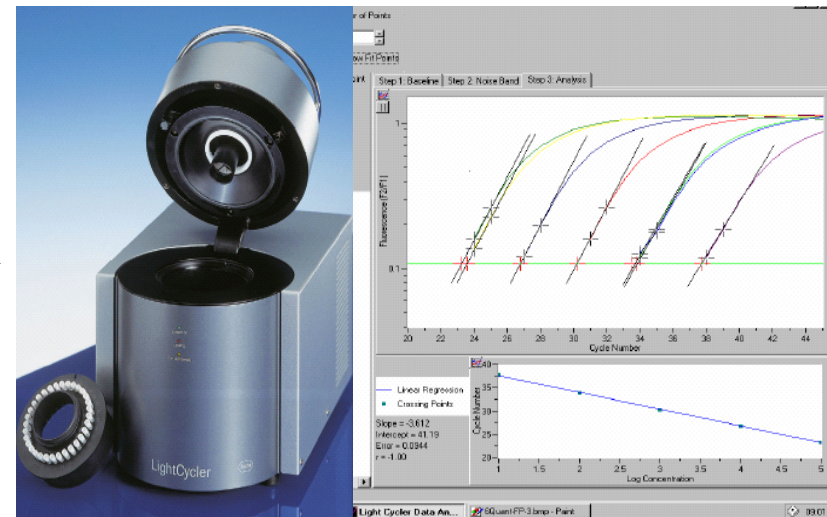


osteogenic
supplement 2

Microarrays

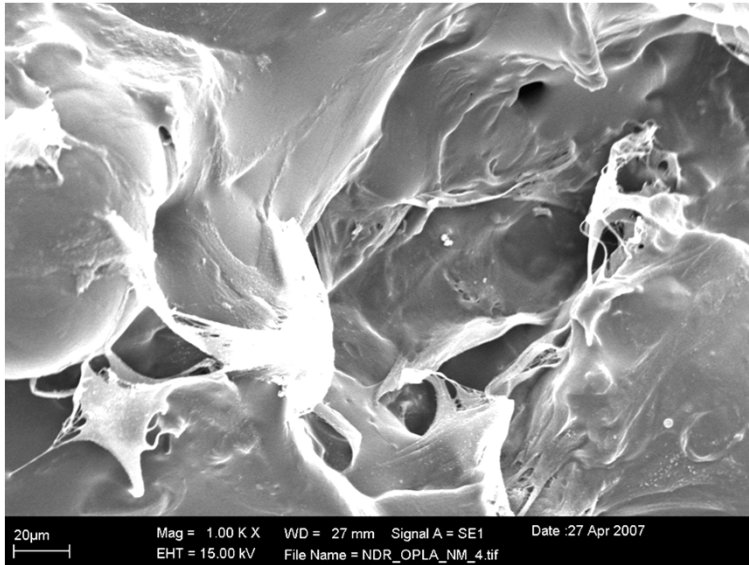


quantitative PCR



Electron microscopy of cell-seeded scaffolds

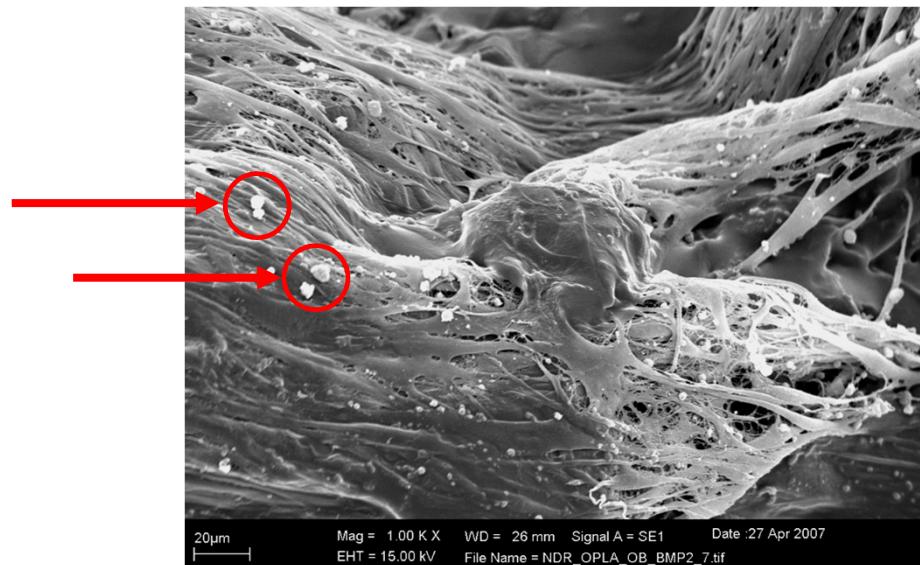
untreated control



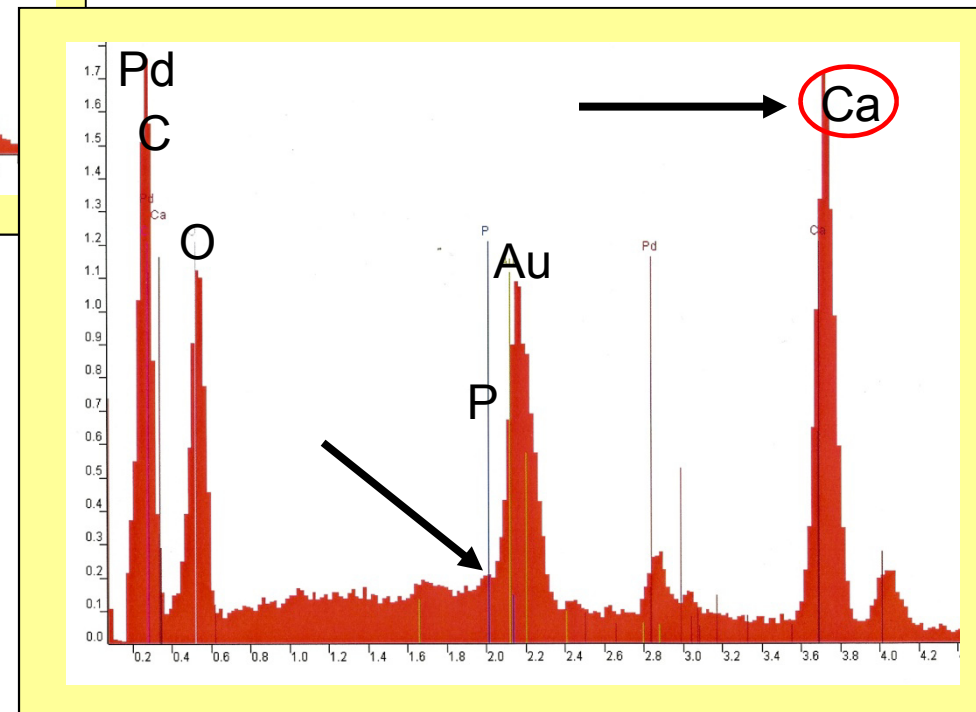
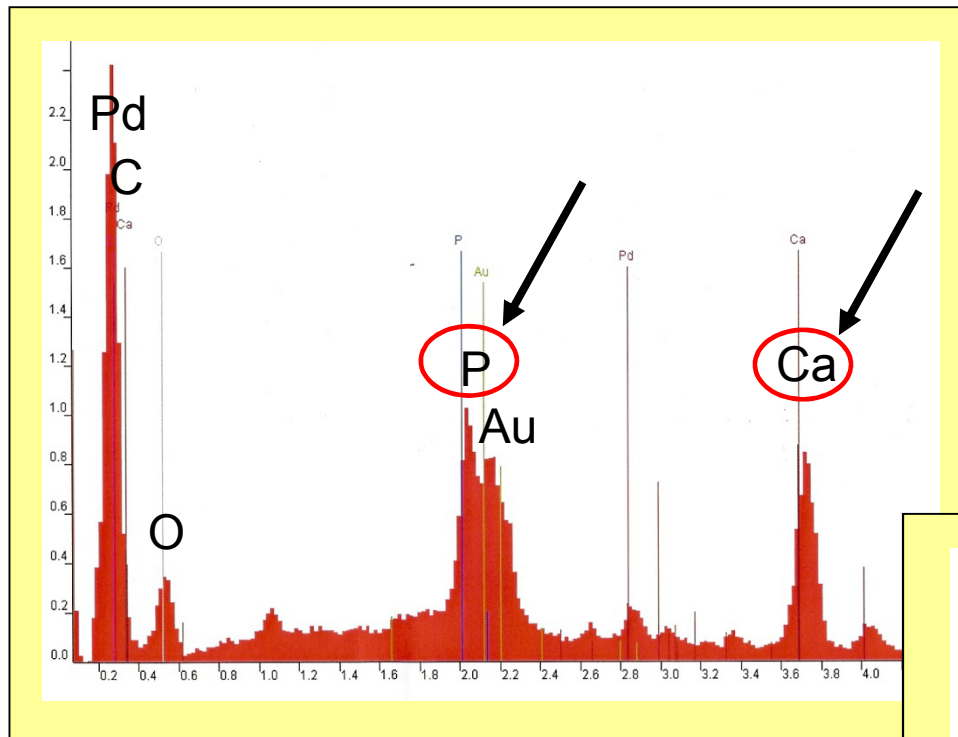
ost. suppl. 1



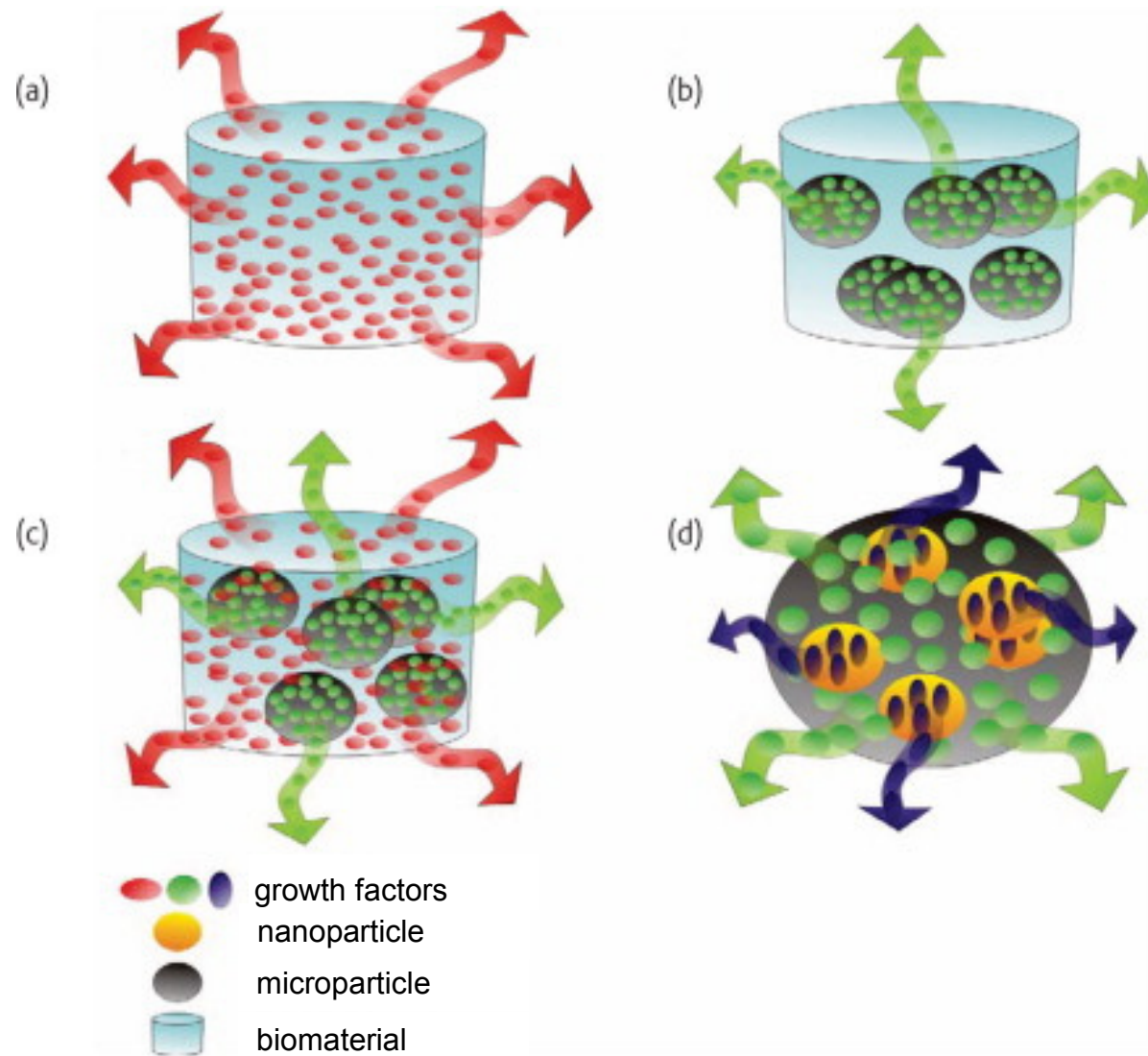
ost. suppl. 2



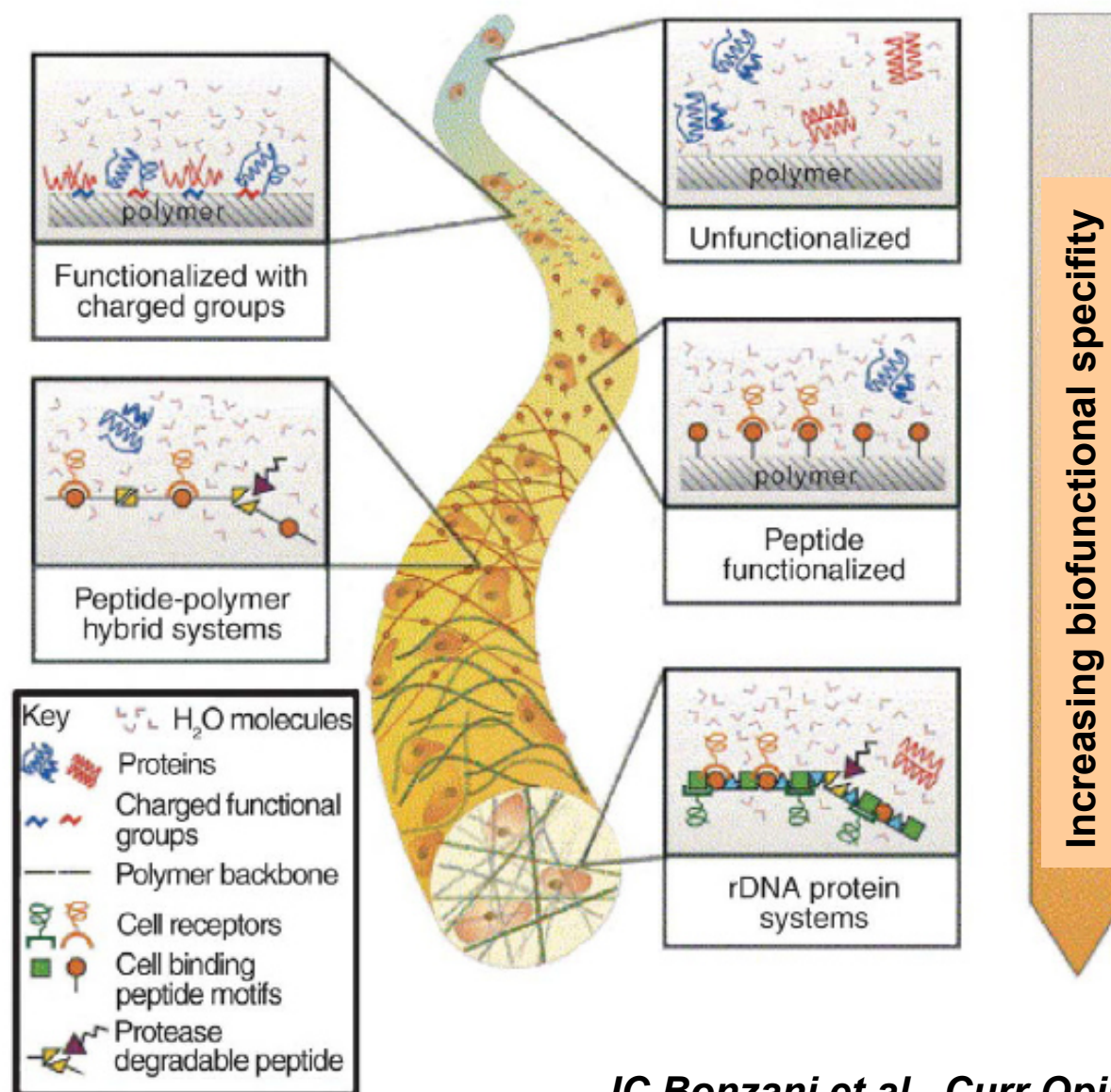
Element analysis by EDX spectrometry



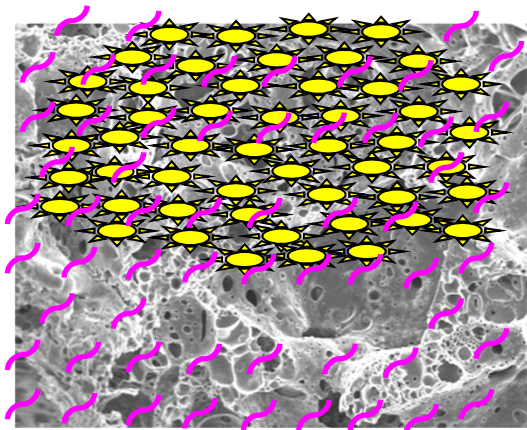
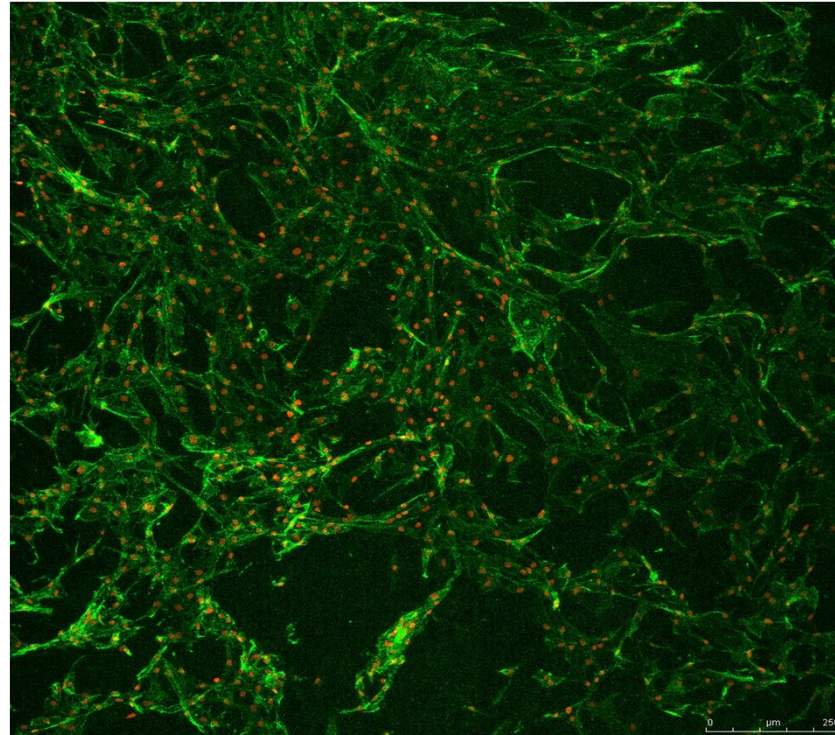
Potential biofunctionalization approaches



Enhancing material biofunctionality

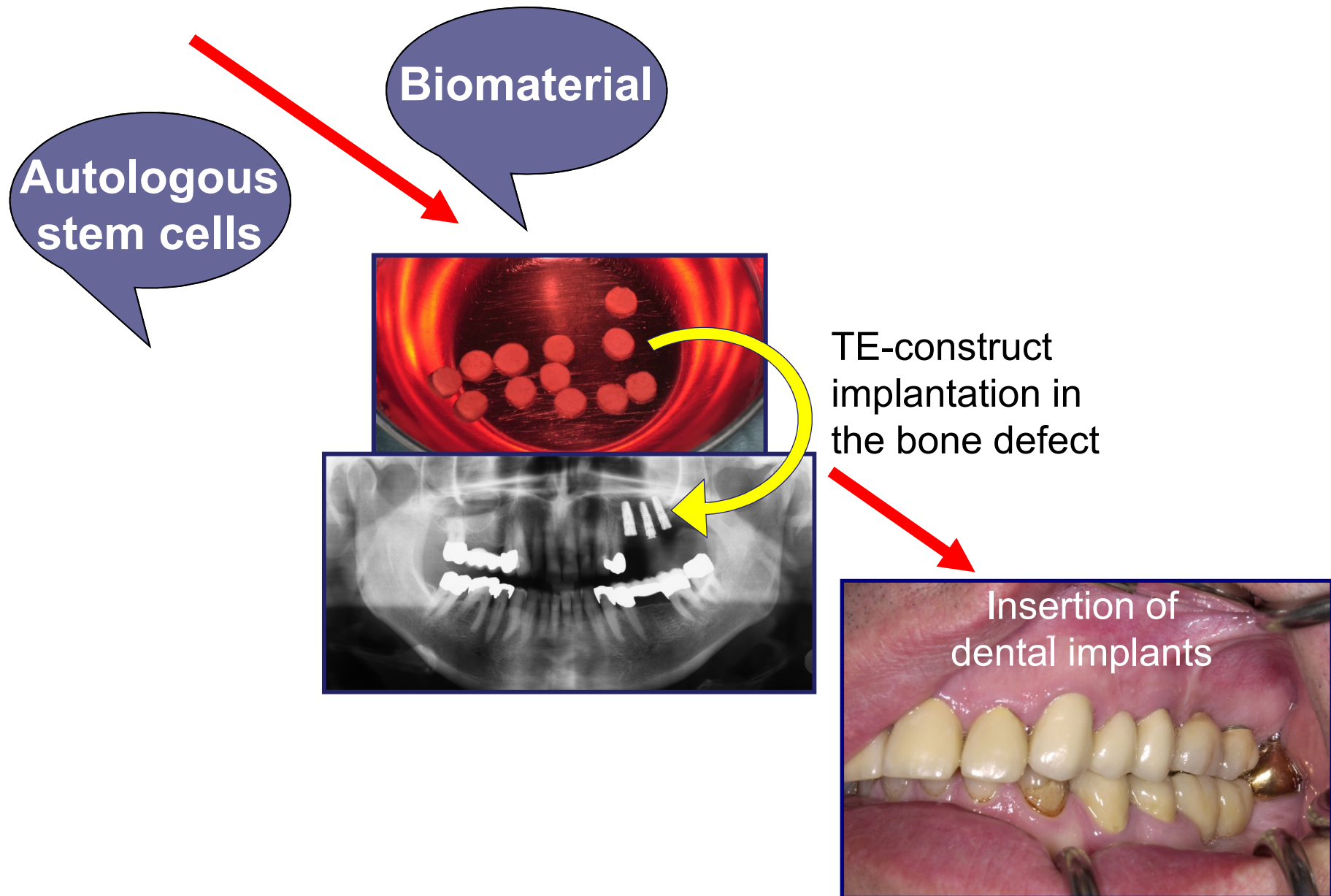


Enhancing material biofunctionality



 activating molecules
 MSCs

TE approach in the oral and maxillofacial surgery



**Learning goals of the “Implantology module”
Bone Tissue Engineering
(Master - Medical Technology)**

1. The students should be able to reproduce/describe/define **contents of the lecture** concerning:

- the process of osteogenesis, detection methods of osteogenesis
- stem cells sources for bone tissue engineering
- bone composition including the most important cell types
- biochemical processes of cell mineralization
- signaling pathways for osteogenic differentiation
- standard technique for the reconstruction of bone defects in the oral and maxillofacial surgery
- biomaterials for bone tissue engineering and possible biofunctionalization approaches

Relevant questions for the exam are referred to learning contents of the lecture!

2. **In the practical part** of the learning module the students should carry out experiments and they should be able to summarize, discuss/reflect and present the data in a professional way.

The practical contents of the learning module have to be documented (in form of a protocol)!