Cell-Biomaterial Interaction

Joachim Rychly
University of Rostock, Medical Faculty,
Cell Biology Laboratory
Schillingallee 69, 18057 Rostock

www.zellbiologie.uni-rostock.de

joachim.rychly@med.uni-rostock.de

Cell Biology Laboratory

Center for Medical Research

Outline

- Biomaterials in General
- Cell-Extracellular Matrix Interaction
- Designing Bioactive Biomaterials for Medicine
- Cellular Responses to Biomaterial Surfaces
- Stem Cells and Biomaterials

Therapies for a missing organ

- Transplantation (e. g. kidney, heart, liver, lung)
- Autografting (e. g. heart bypass, skin grafting)
- Permanent implants (hip prosthesis, pacemaker, breast implant)
- In vitro synthesis (e. g. epidermis)
- In vivo synthesis or regeneration (e. g. skin, nerves, bones)

Biomaterials

Definition by the National Institute of Health Biomaterials Consensus Conference (1998):

„Any material, natural, man made, or device that comprises hole or part of a living organism, which performs or replaces a natural function within a living organism“

“Any material of natural or of synthetic origin that comes in contact with tissue, blood or biological fluids, and intended for use in prosthetic, diagnostic, therapeutic or storage applications without adversely affecting the living organism and its components”

History of Biomaterials

The first biomaterials were used over 2000 years ago by the Chinese and Romans

They used gold in dental restoration.

Tomb of an Egyptian chief dentist 5th dynasty, 2200 BC

One of the major discoveries was made in Second World War II when shards of poly-methyl-metacrylate (PMMA) was tolerated in the eyes of pilots after a crash.

Most of the biomaterials were adopted from other areas of science and technologies.

Biomaterials

- Metals
- Ceramics
- Polymers
- Composites
- Natural Materials

Material	Advantages	Disadvantages
POLYMERS: Nylon, silicones, PTFE, UHMWPE	Resilient, easy to fabricate 	Not strong, deform with time, may degrade
METALS: Titanium, stainless steels, CoCr alloys, gold	Strong, tough, ductile 	May corrode, high density
CERAMICS: Aluminum oxide, carbon, hydroxyapatite 	Highly biocompatible, inert, high modulus and compressive strength, good esthetic properties	Brittle, difficult to make, poor fatigue resistance
COMPOSITES: Various combinations **Natural Materials:** Extracellular matrix proteins	Strong, tailor-made	Difficult to make

Principal Application of Biomaterials

Permanent implants

hip joint
tooth

Transient implants

tissue engineering
organ regeneration

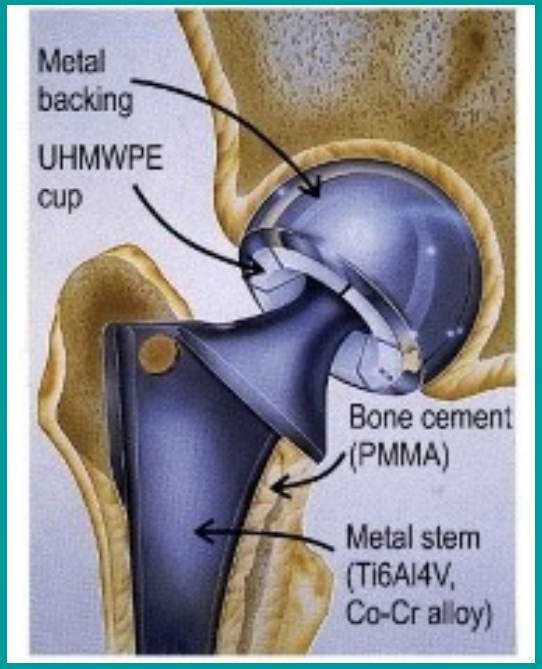
Ex-vivo biomaterials

dialysis
microchips

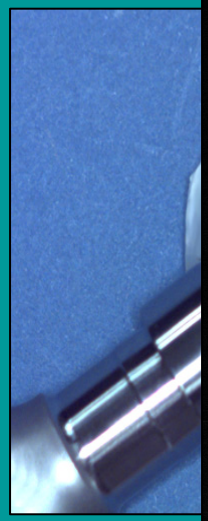
Bone Implants

Artificial hip implant

The surface of the titanium implant interacts with bone tissue



Developments of Materials

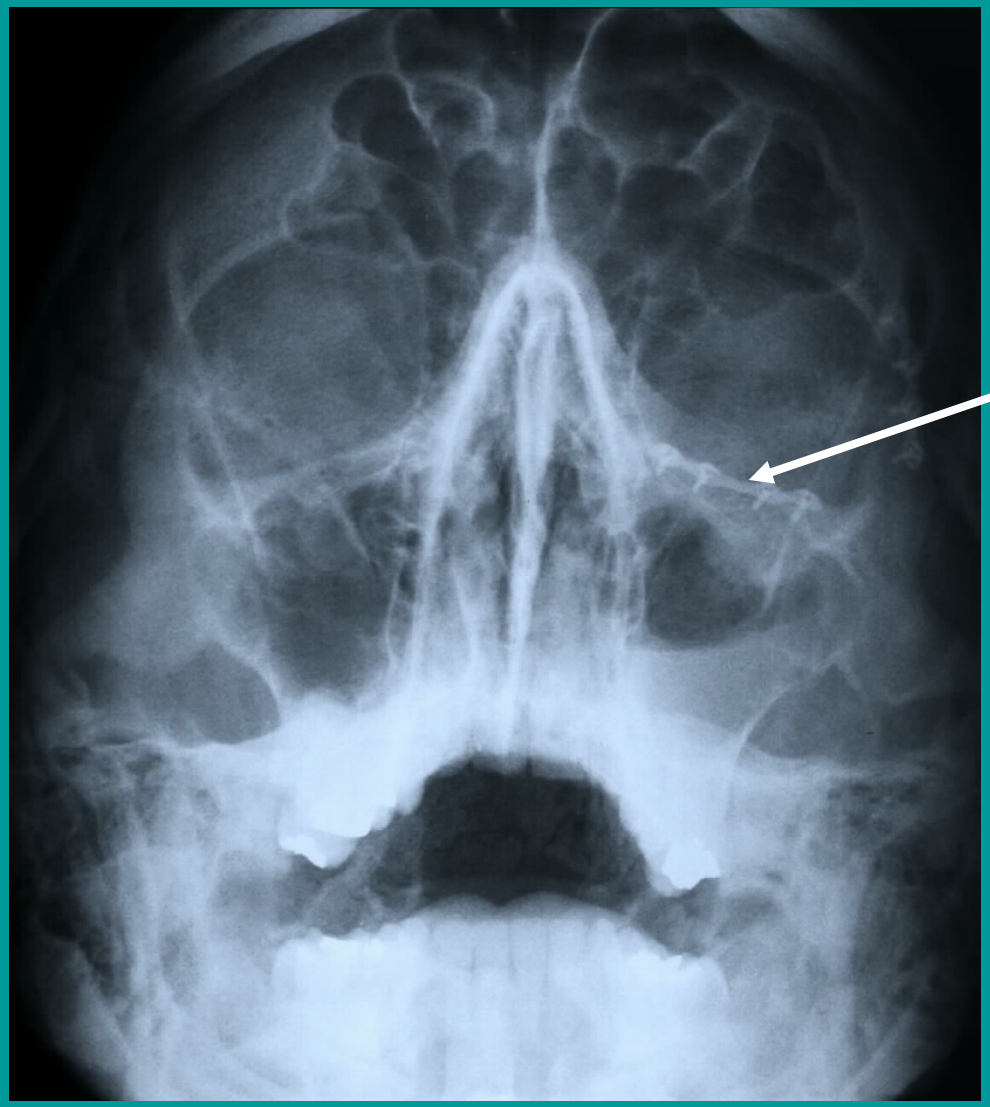


M
/

a-Ti-Leg.
tal
Delta-Keramik

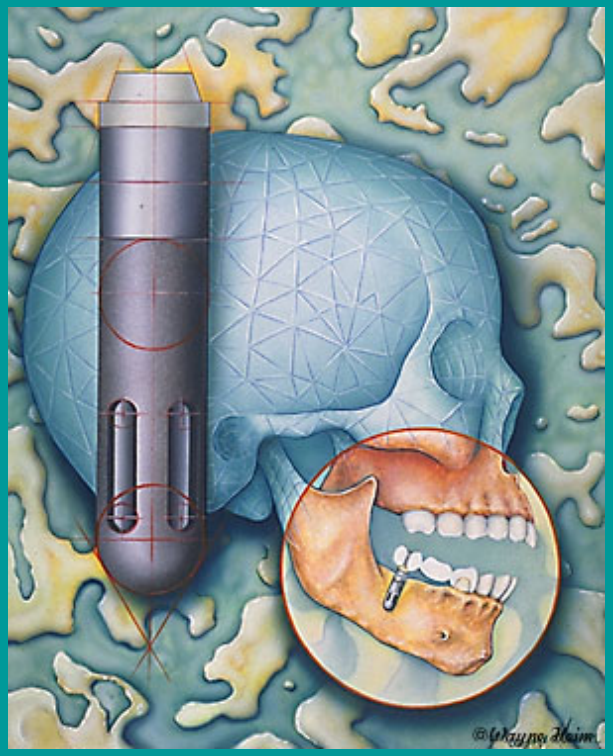
Implant Materials Produced by DOT GmbH

Implants to stabilize bone fractures

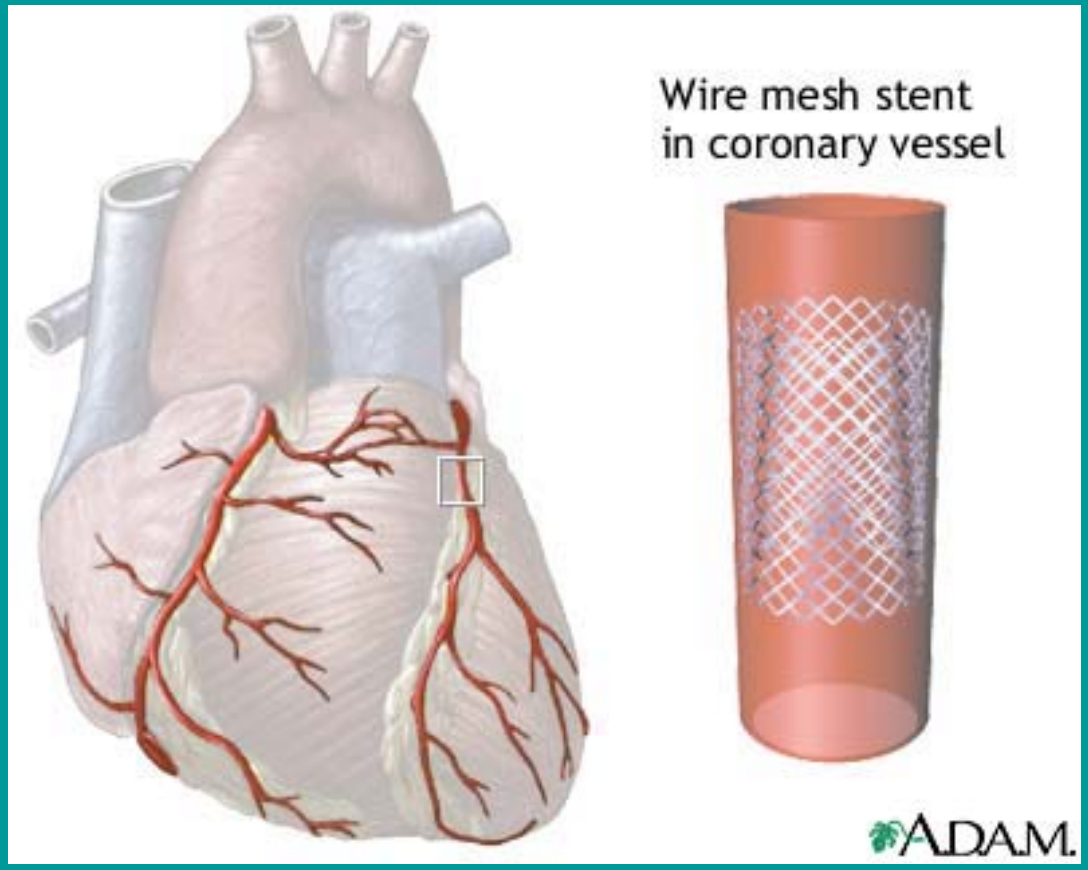


Titanium implant to stabilize zygomatic bone fracture

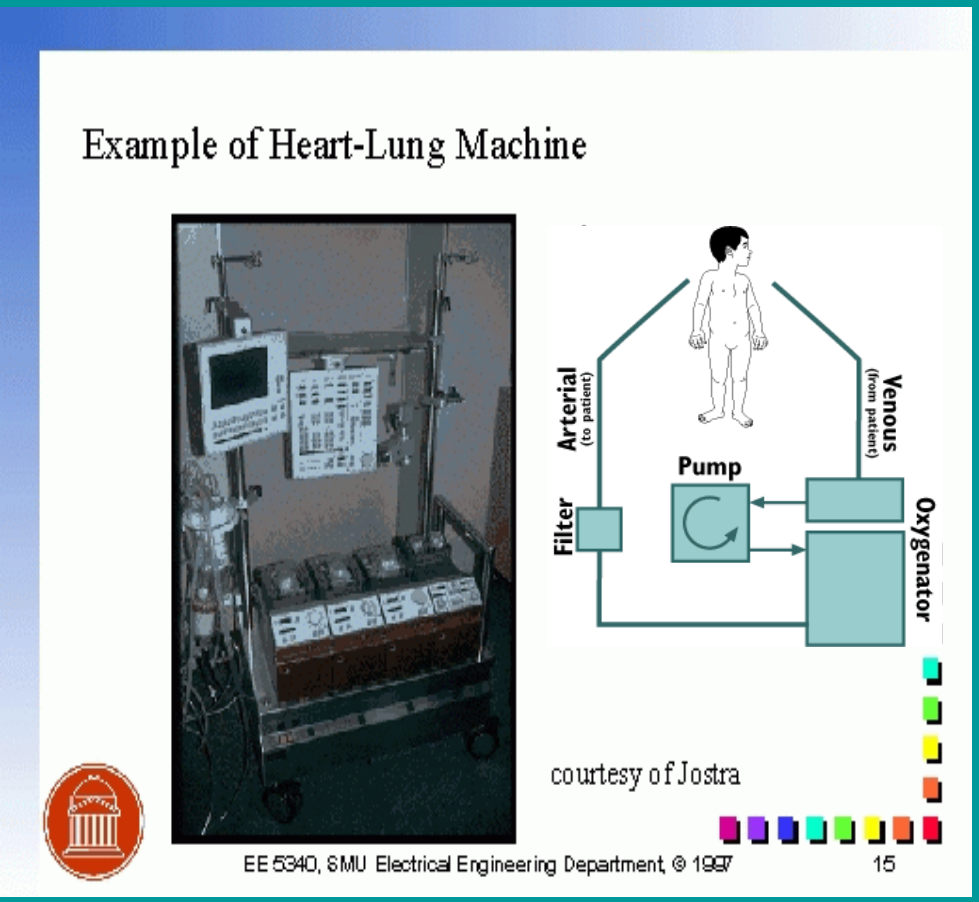
Implants in Dentistry



Stent for Opening the Vessel



Blood Cell Interaction in Extracorporal Systems



HLM during open heart surgery

Hemodialysis

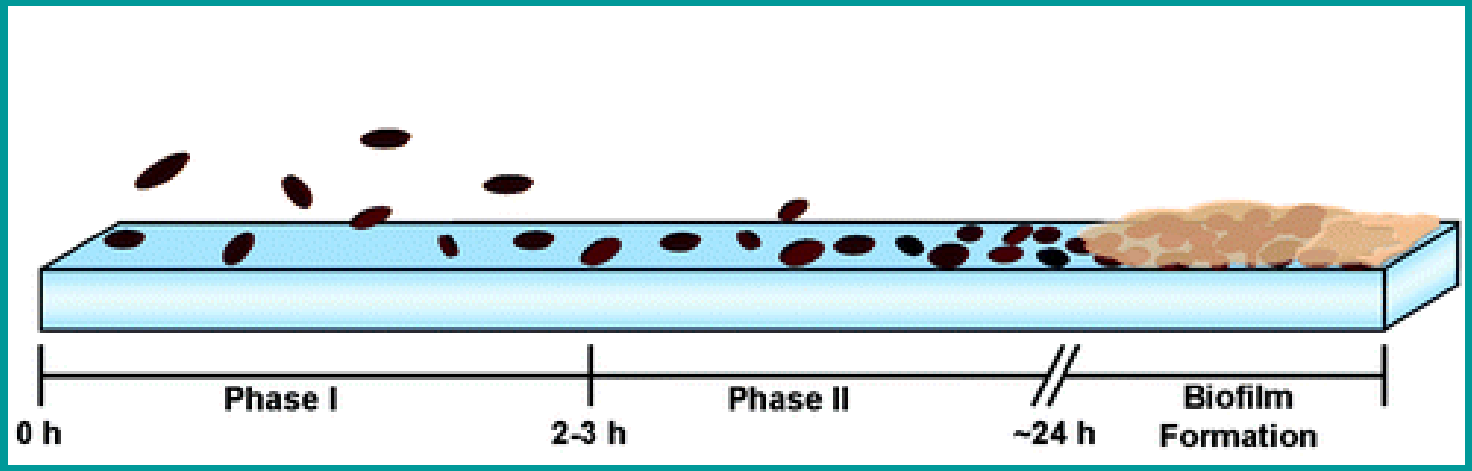
The design of the implant surface to interact with the tissue depends on the purpose of the implant:

Inside must have blood-compatible surface, i. e. schould not cause adhesion or clotting

Outside must firmly atttach to surrounding fibrous tissue but must not cause fibrous hyperplexia.

Vascular Prosthesis

Bacteria Interaction with Implants



Phase I: Reversible adhesion to the material

Phase II: Irreversible molecular bridging through surface adhesin compounds

Phase III: Biofilm secretion (Exopolysaccharide matrix)

Hetrick et al., 2006

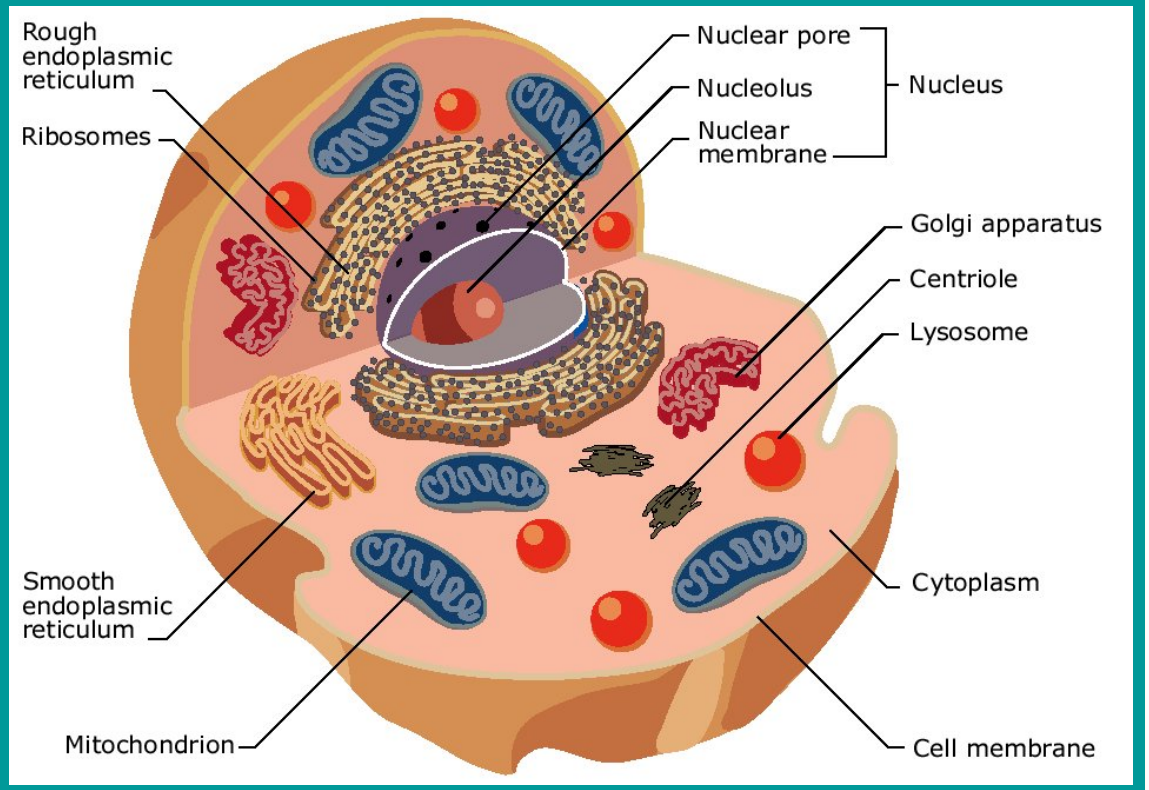
Biomaterial ?

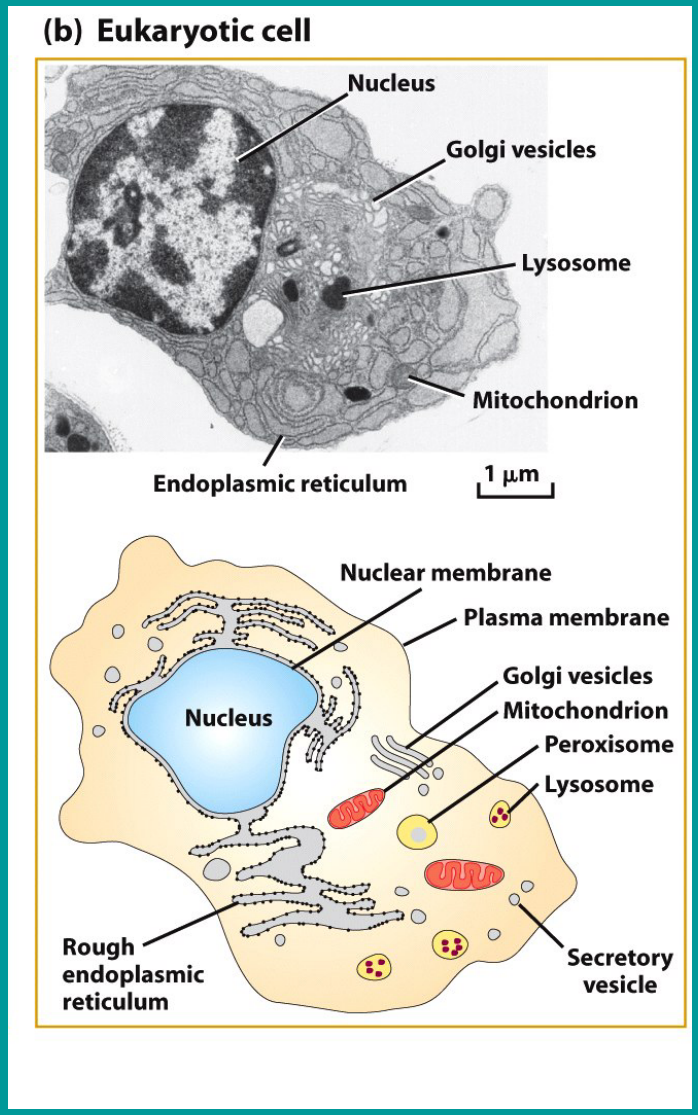
Biomaterials

Biocompatibility

Specific Bioactive Control of Cells and Tissues

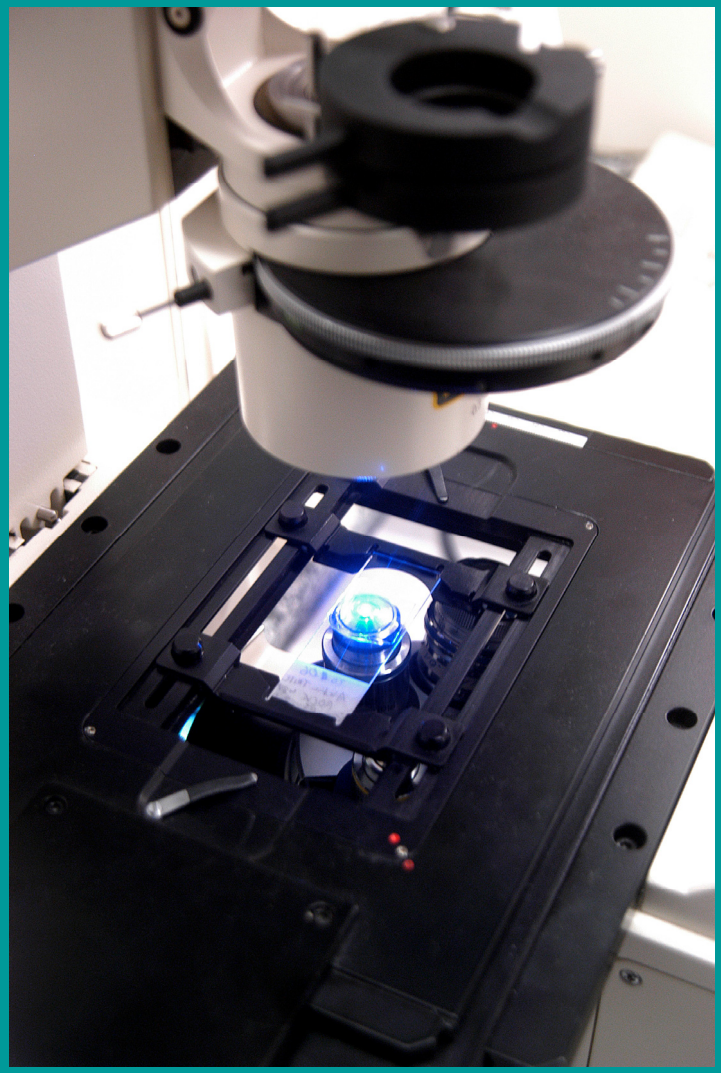
Aufbau der Zelle



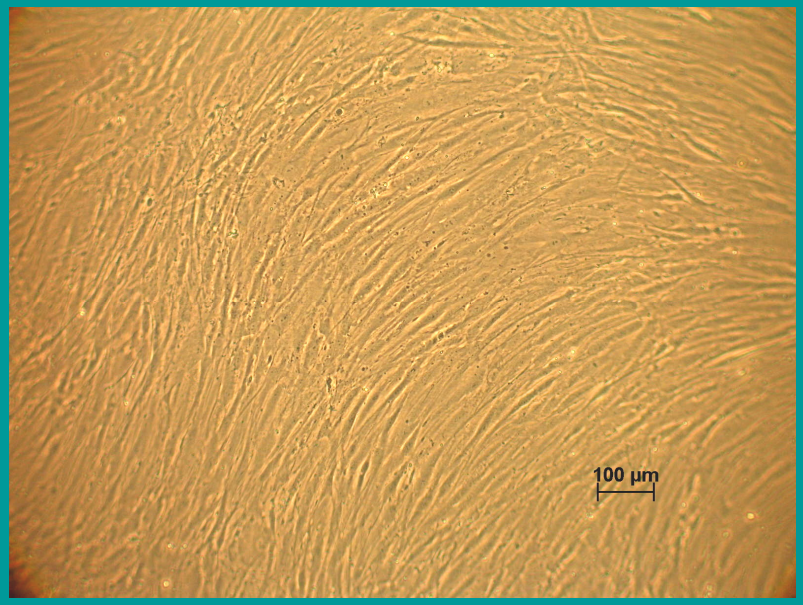


Arbeiten unter sterilen Bedingungen

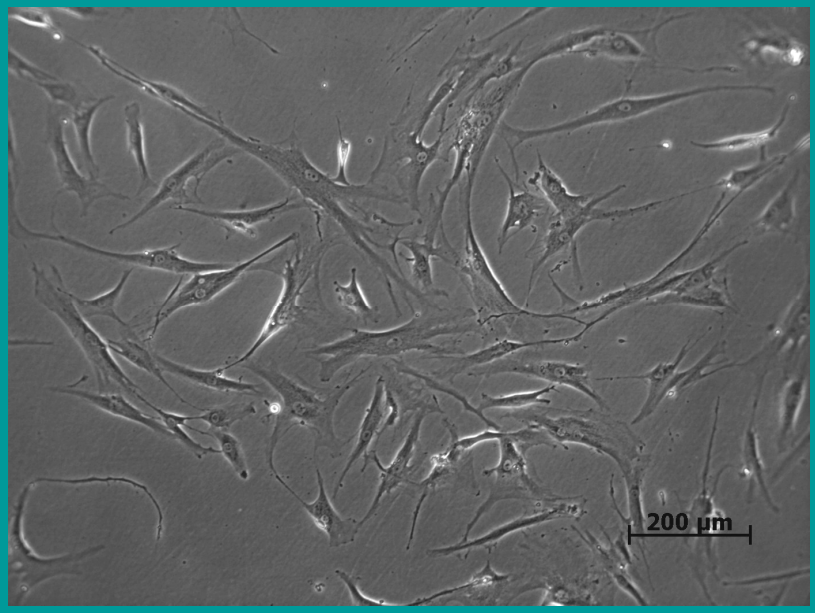
Mikroskopische Beobachtung der Zellkultur



Kultur von mesenchymalen Stammzellen

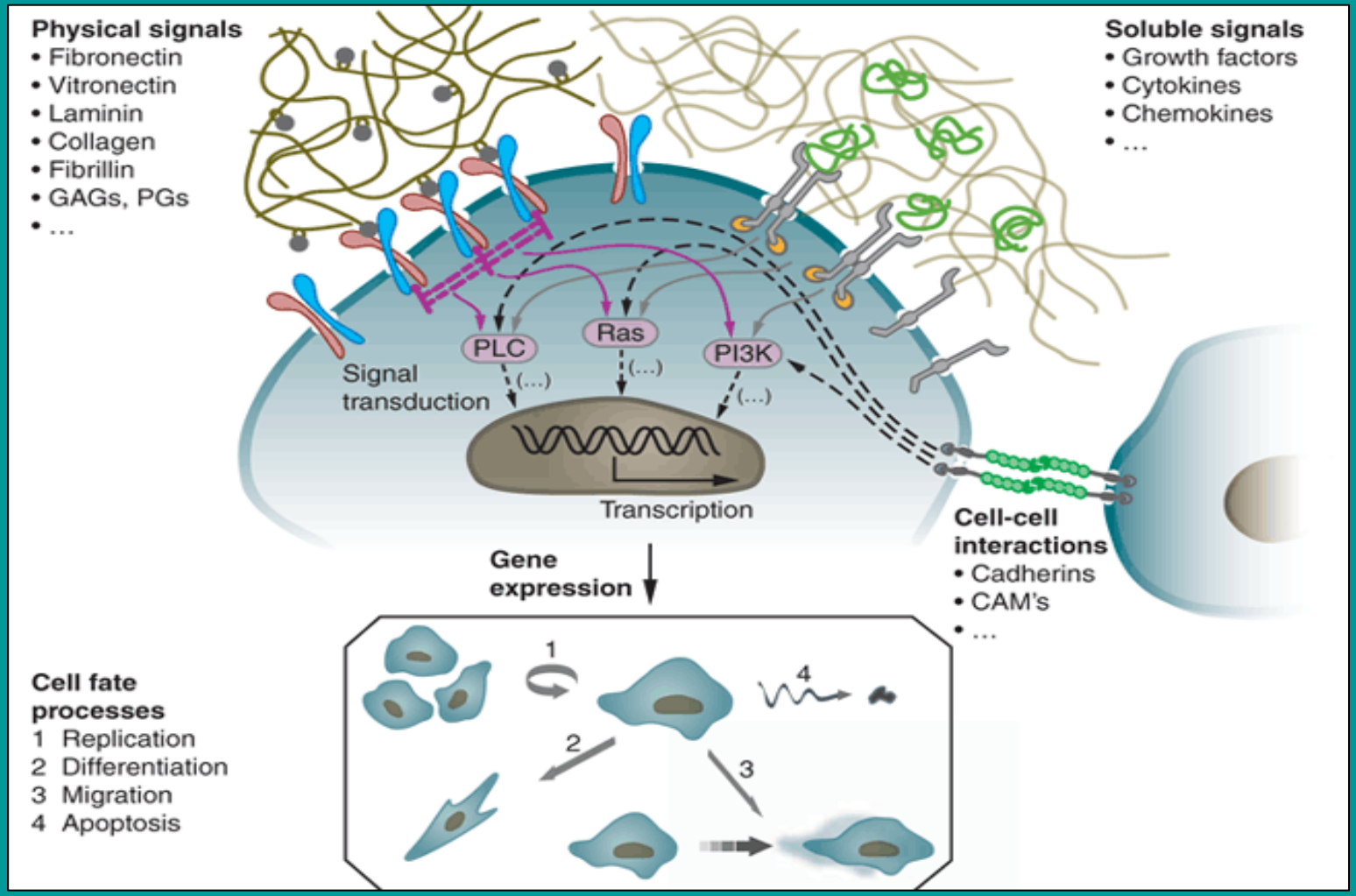


konfluent

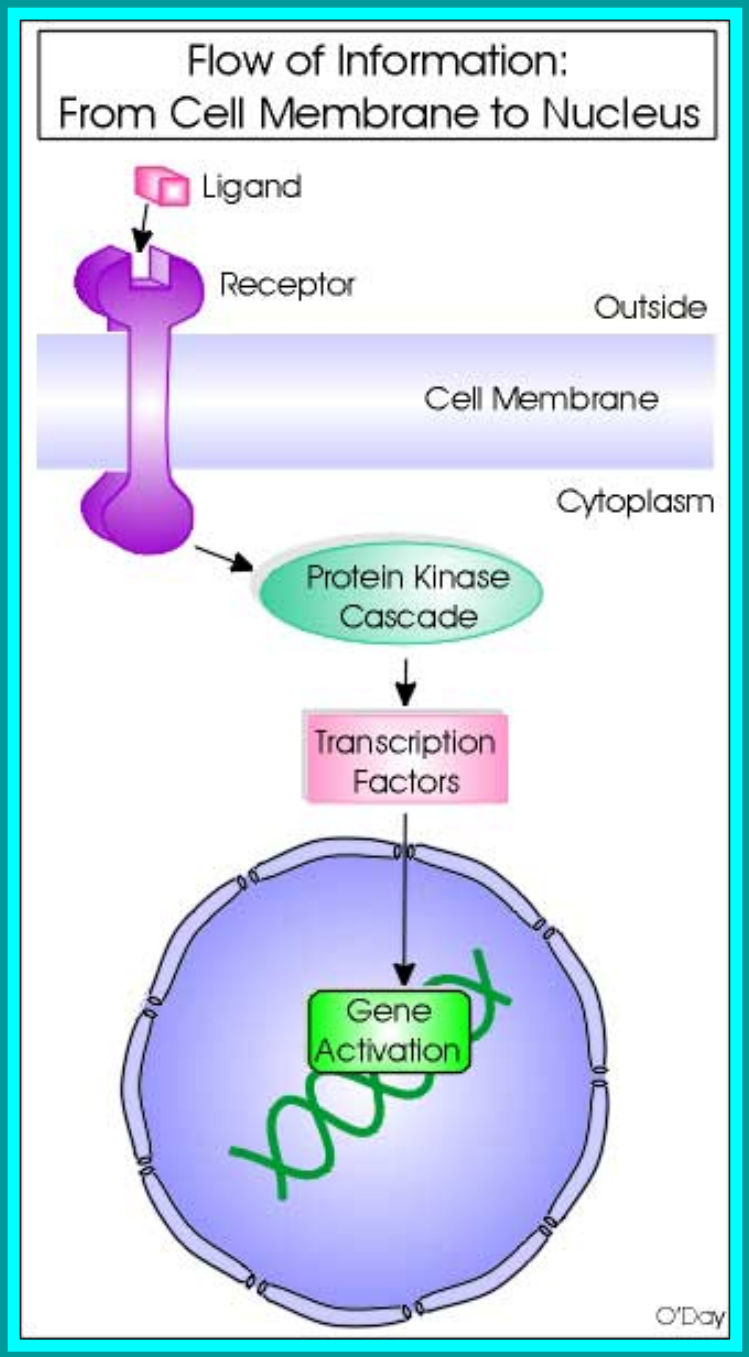


subkonfluent

Cell physiology is regulated by reciprocal molecular interactions between cells and their surroundings



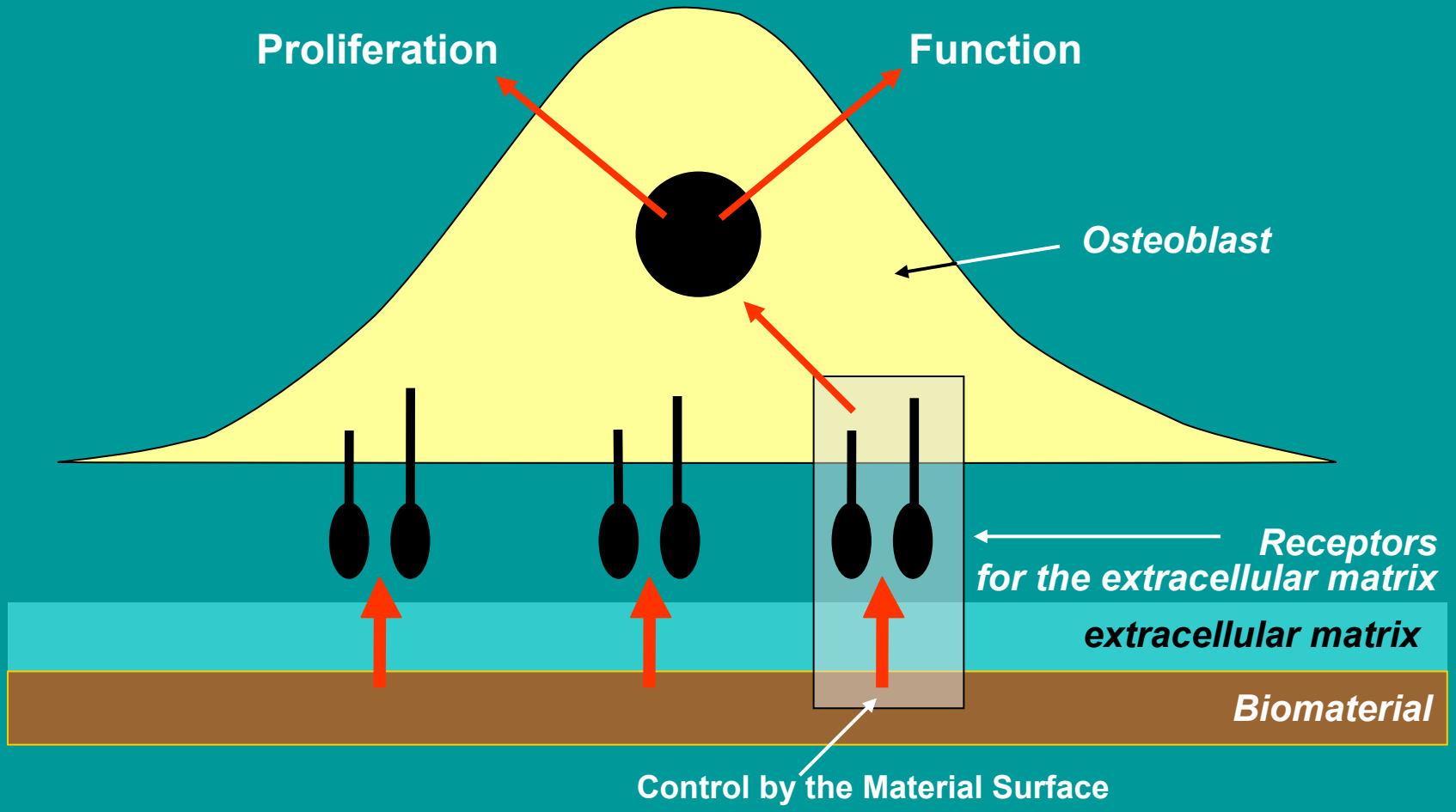
Lutolf & Hubbell, Nature Biotechn., 23, 2005


Flow of Information:
From Cell Membrane to Nucleus
Ligand
Receptor
Outside
Cell Membrane
Cytoplasm
Protein Kinase Cascade
Transcription Factors
Gene Activation
O'Day

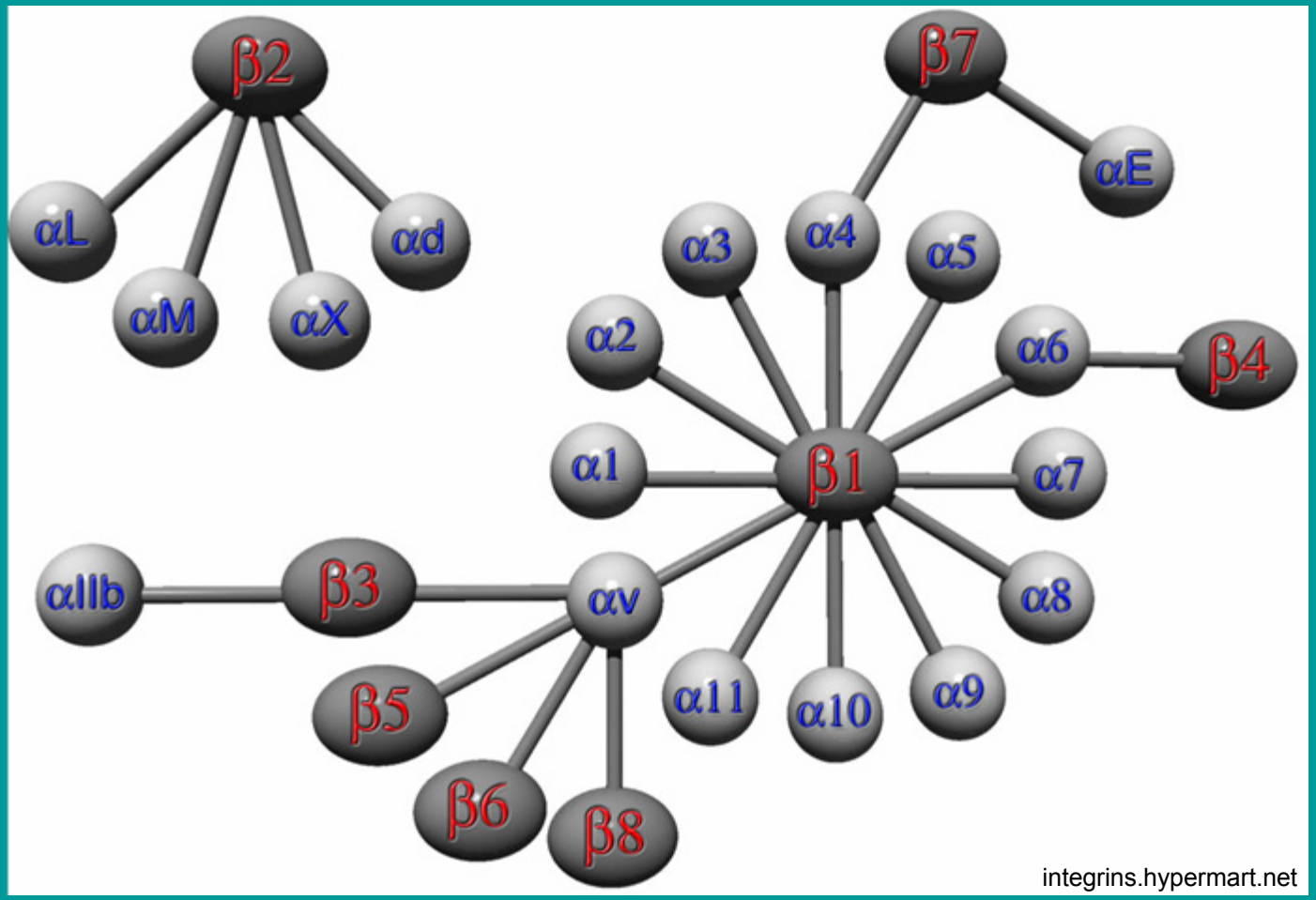
The Extracellular Matrix

- Extracellular Matrix - an insoluble network of polysaccharides, fibrous proteins,and adhesive proteins that are secreted by animal cells.
- It provides structural support in tissues and can affect the development and biochemical functions of cells.
- The composition of the ECM varies with specific tissues.
- The ECM is dynamic.

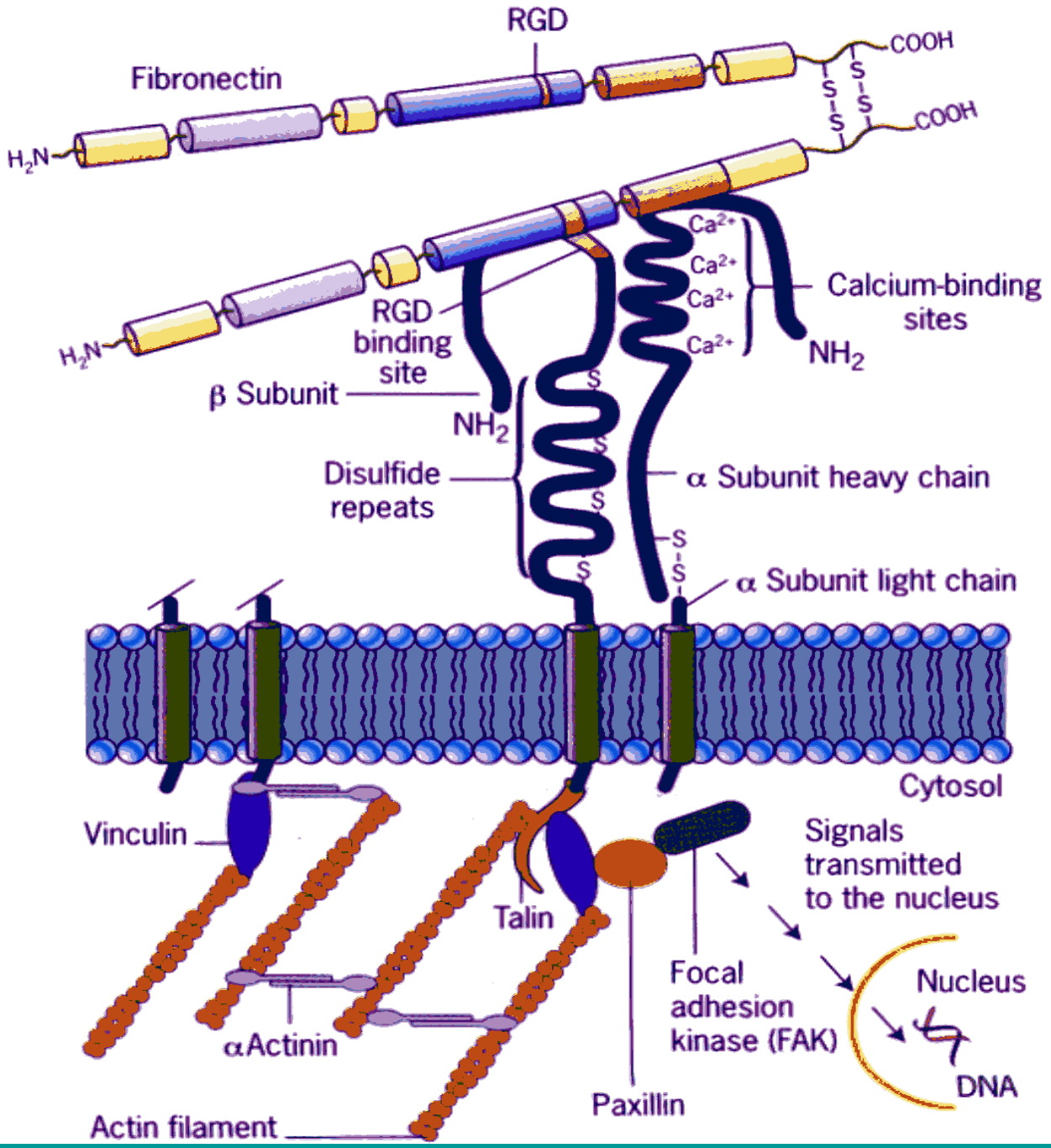
Signals from the Extracellular Matrix Regulate the Biological Response of the Cell



Integrins are heterodimeric receptors with specifities to extracellular matrix proteins or other receptors



e.g.
α2β1- collagen
α5β1- fibronectin



Integrin signaling regulates:

proliferation

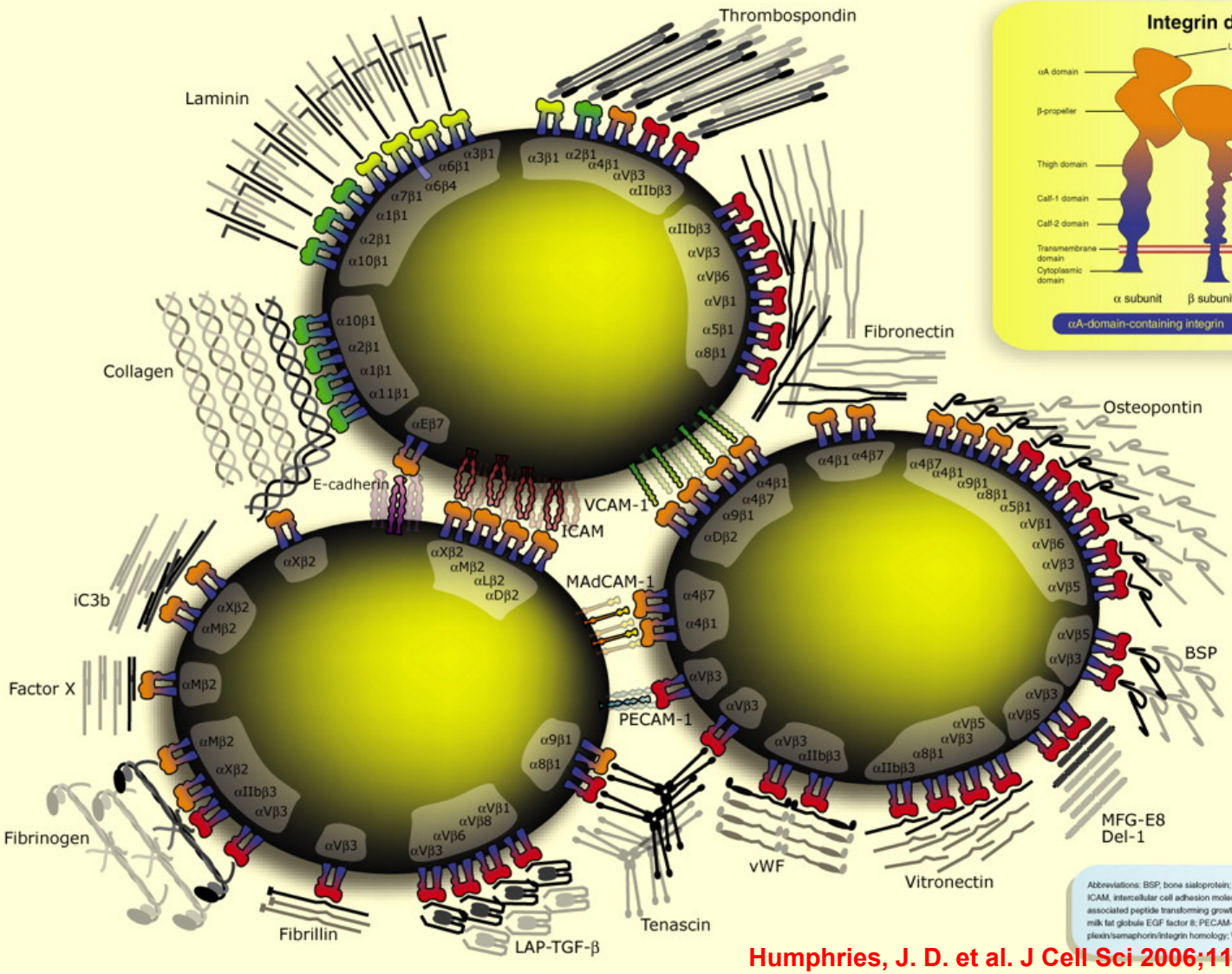
differentiation

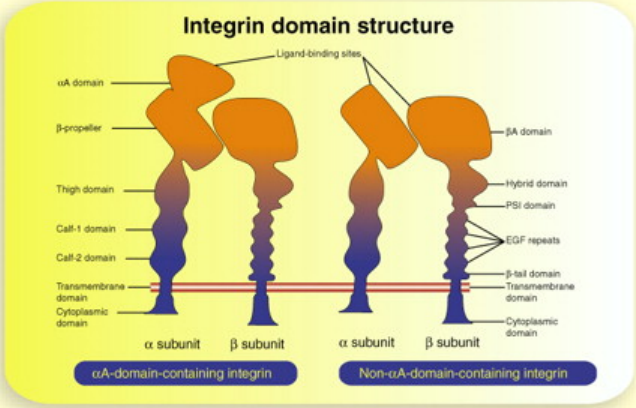
Motility

Survival

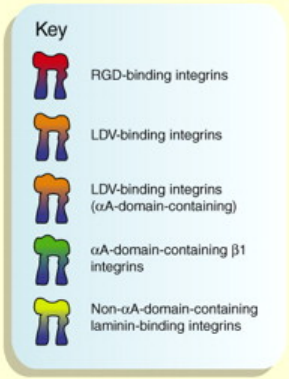
Integrin Ligands at a Glance

Jonathan D. Humphries, Adam Byron and Martin J. Humphries





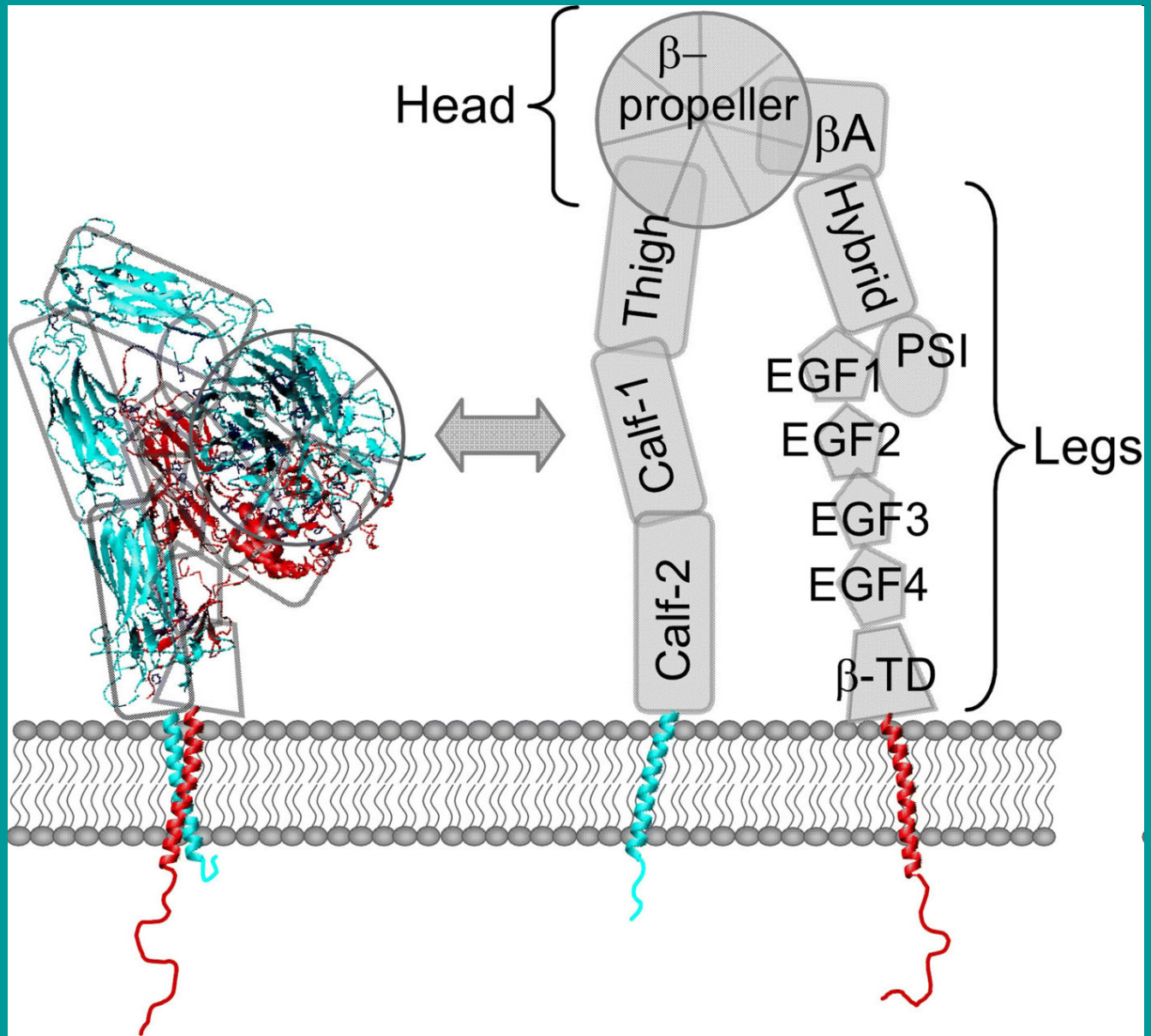
Journal of Cell Science
jcs.biologists.org



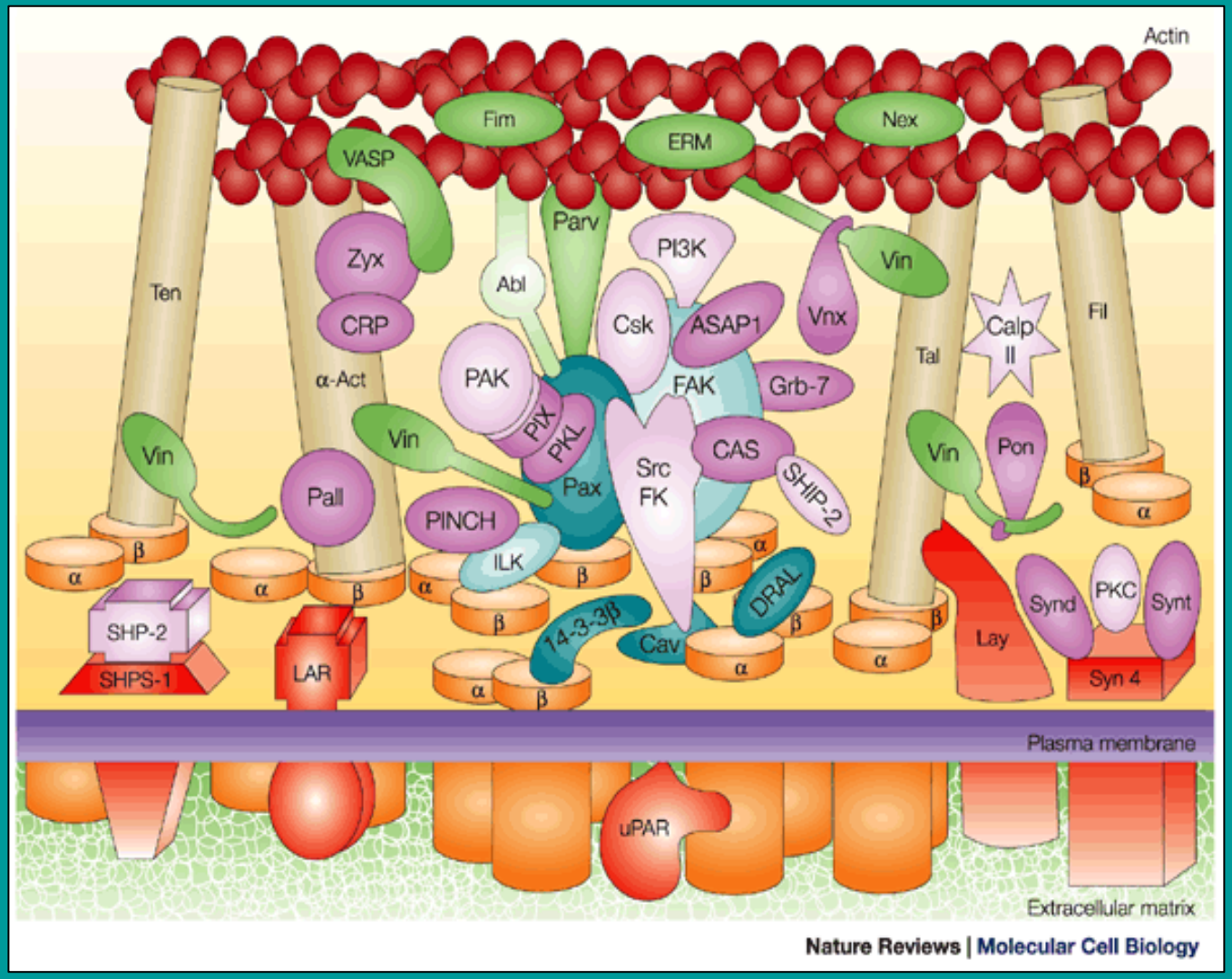
Abbreviations: BSP, bone sialoprotein; Del-1, developmental endothelial locus-1; EGF, epidermal growth factor; ICAM, intercellular cell adhesion molecule; iC3b, inactivated complement component C3b; LAP-TGF-β, latency associated peptide transforming growth factor β; MAdCAM-1, mucosal addressin cell adhesion molecule 1; MFG-E8, milk fat globule EGF factor 8; PECAM-1, platelet endothelial cell adhesion molecule 1 (CD31); PSI, plexin/semaphorin/integrin homology; VCAM-1, vascular cell adhesion molecule 1; vWF, von Willebrand factor.

Humphries, J. D. et al. J Cell Sci 2006;119:3901-3903

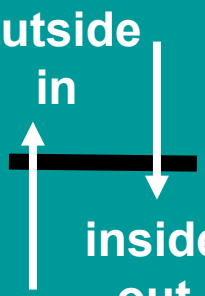
Schema der Aktivierung von Integrinen



A network of cytoskeletally associated proteins function as mediator of integrin mediated signal transduction

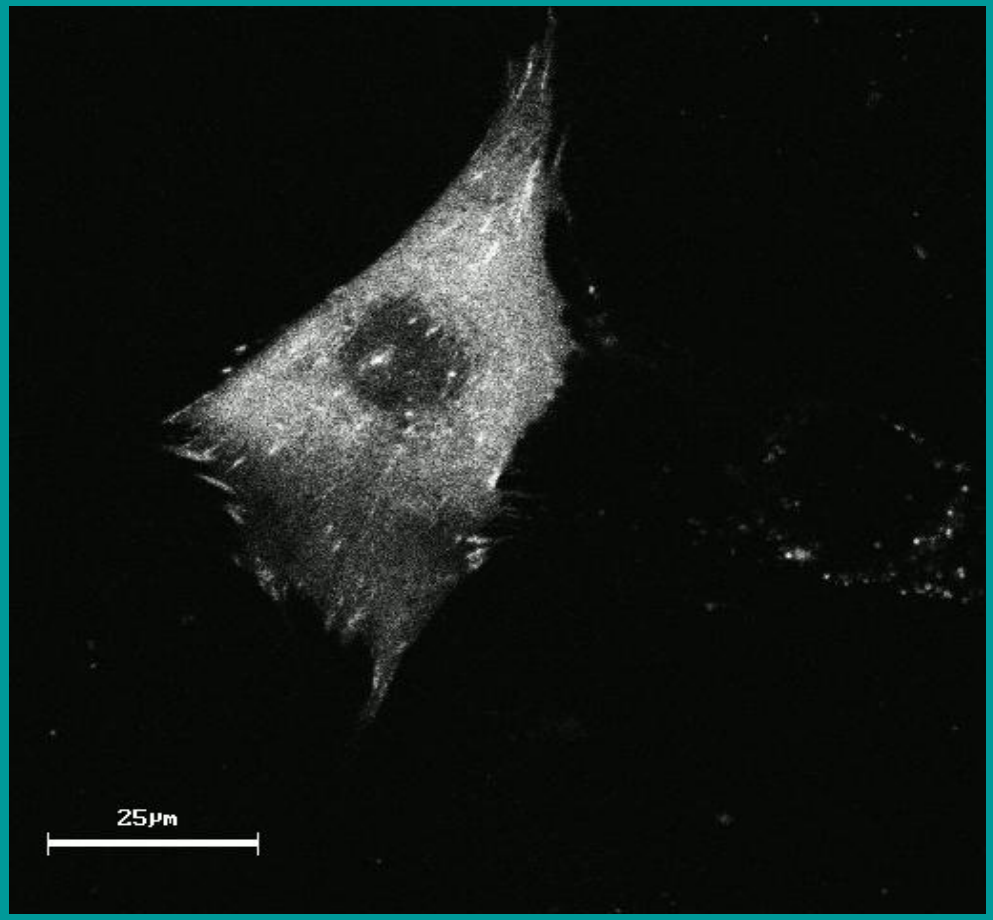


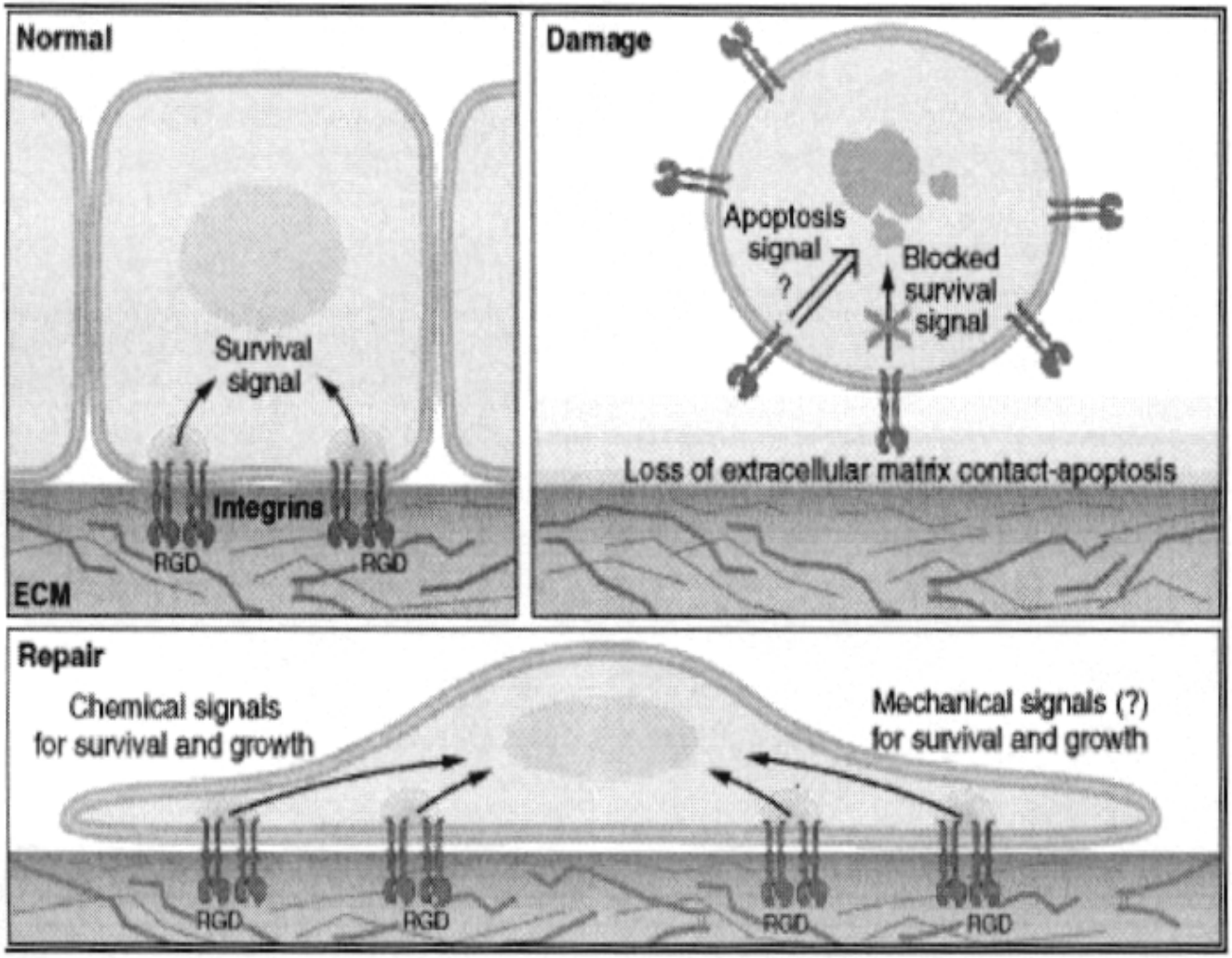
signalling



Focal adhesions play a key role in integrin mediated signal transduction

Fokalkontakte in einer lebenden Zelle





From: Ruoslahti, E. 1997. "Stretching is good for a cell" Science 276:1345

CYTOSKELETON

In the cytosol, arrays of protein filaments form networks that give the cell its shape and provide a basis for its movements. Three main kinds of cytoskeletal filaments are

1. microtubules

25-nm diameter

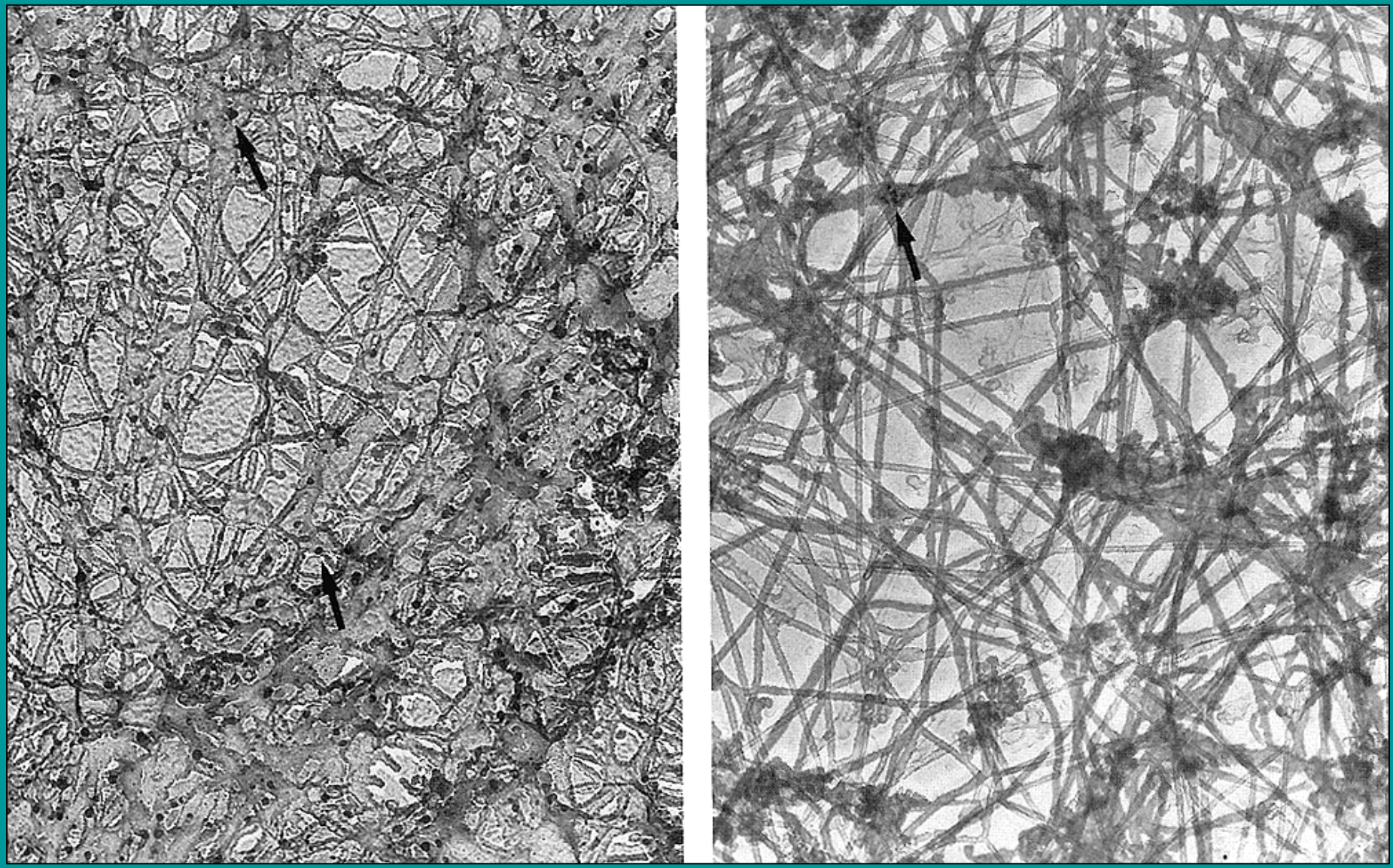
2. actin filaments

8-nm diameter

3. intermediate filaments

10-nm diameter

Actin cytoskeleton

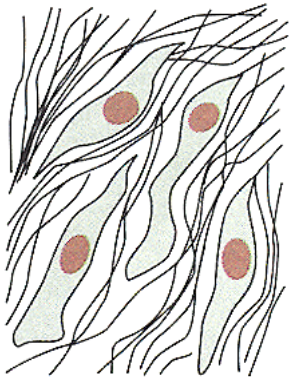


Bone

and Function of Bone Cells

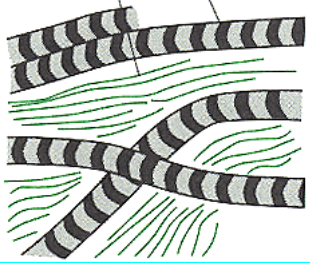
CONNECTIVE TISSUE

The spaces between organs and tissues in the body are filled with connective tissue made principally of a network of tough protein fibers embedded in a polysaccharide gel. This extracellular matrix is secreted mainly by fibroblasts.



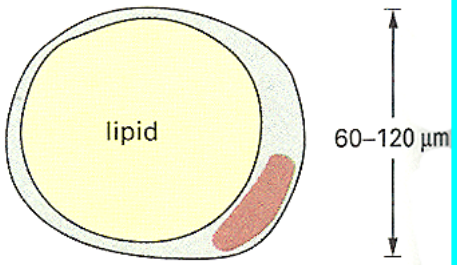
fibroblasts in loose connective tissue

Two main types of extracellular protein fiber are collagen and elastin.

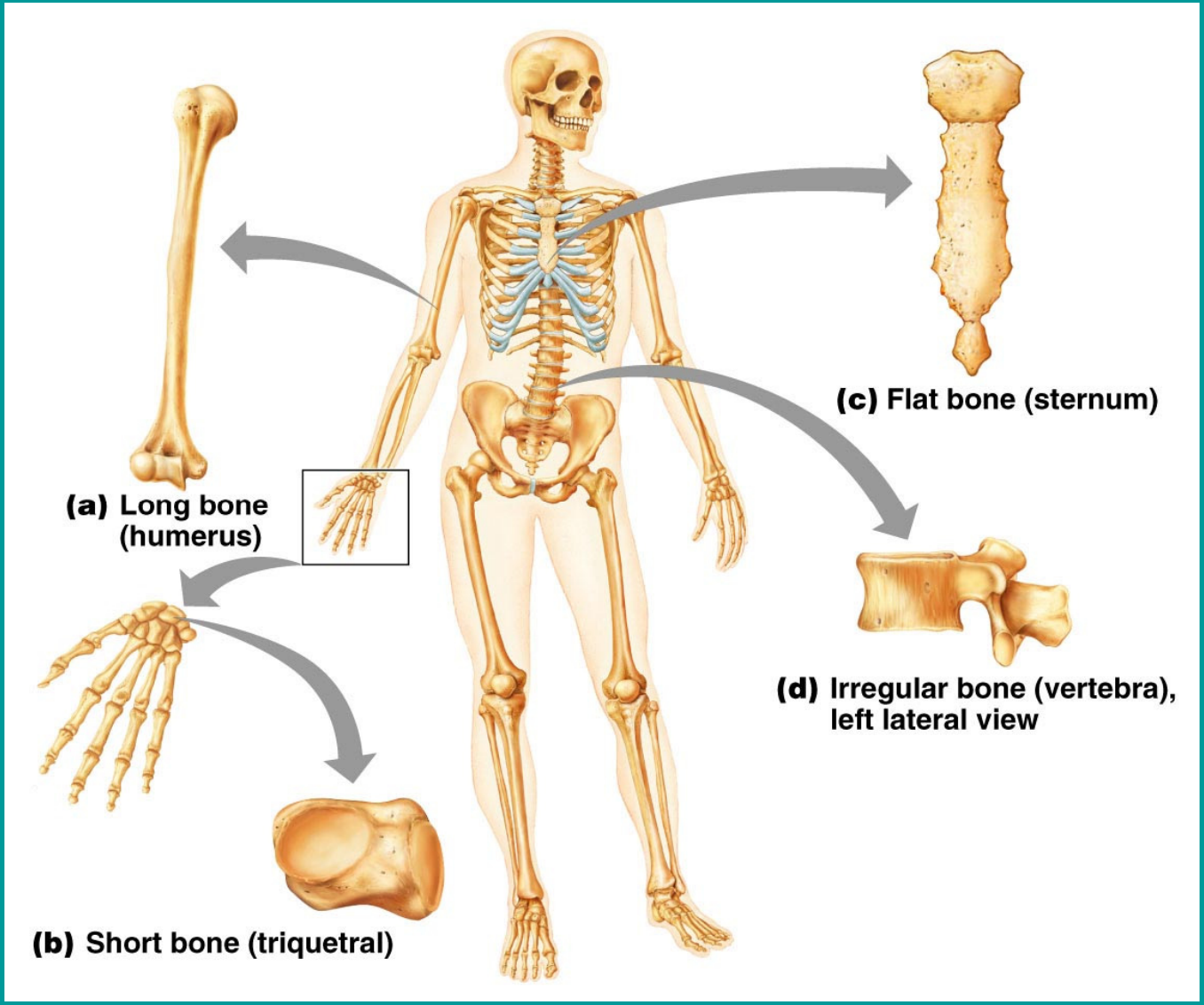


Bone is made by cells called osteoblasts. These secrete an extracellular matrix in which crystals of calcium phosphate are later deposited.

Adipose cells, among the largest cells in the body, are responsible for the production and storage of fat. The nucleus and cytoplasm are squeezed by a large lipid droplet.



Classification of Bones



Bone Composition

Organic Matrix:

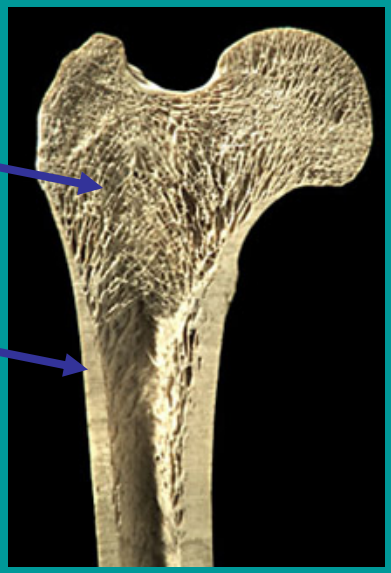
Collagen I etc.

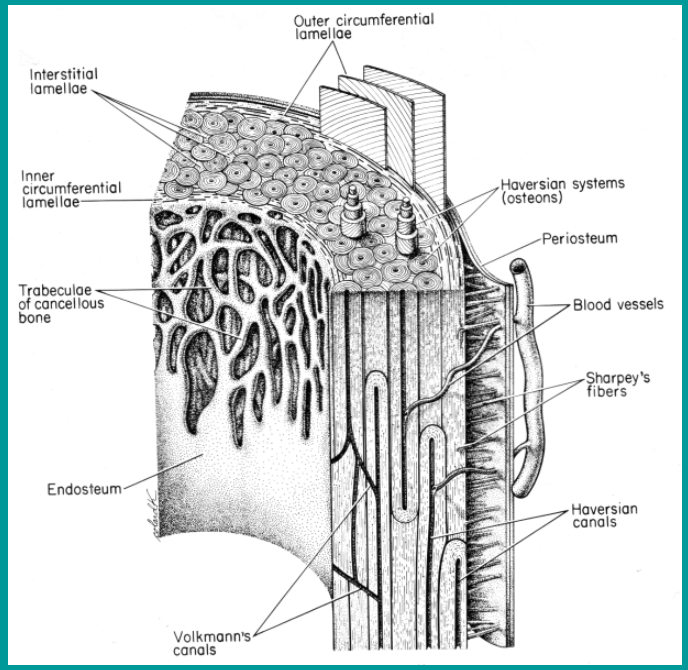
Inorganic Matrix:

Hydroxyapatite

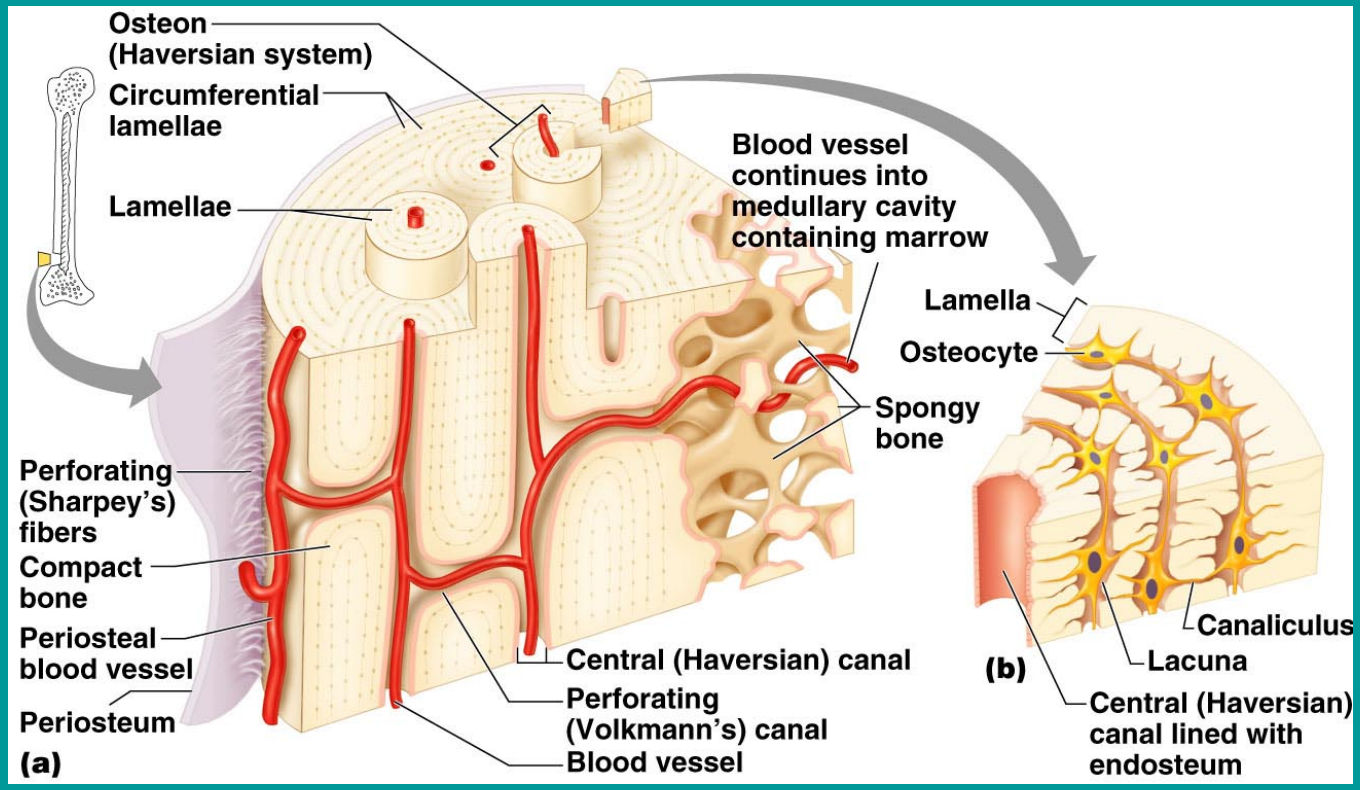
Trabecular Bone

Cortical Bone





Microscopic Structure of Compact Bones



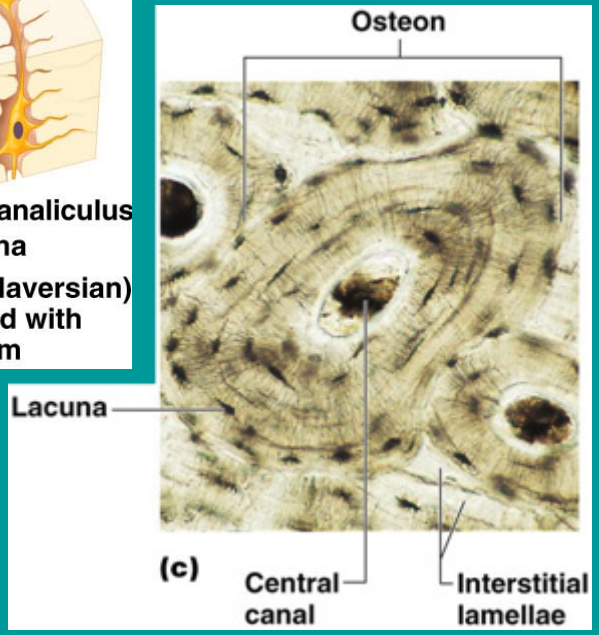
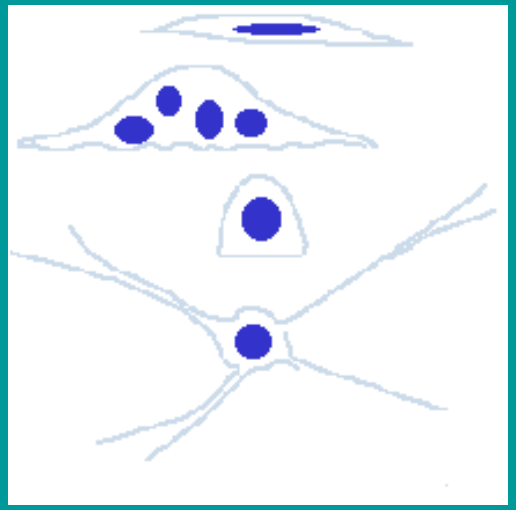


Figure 6.6

Bone Cells

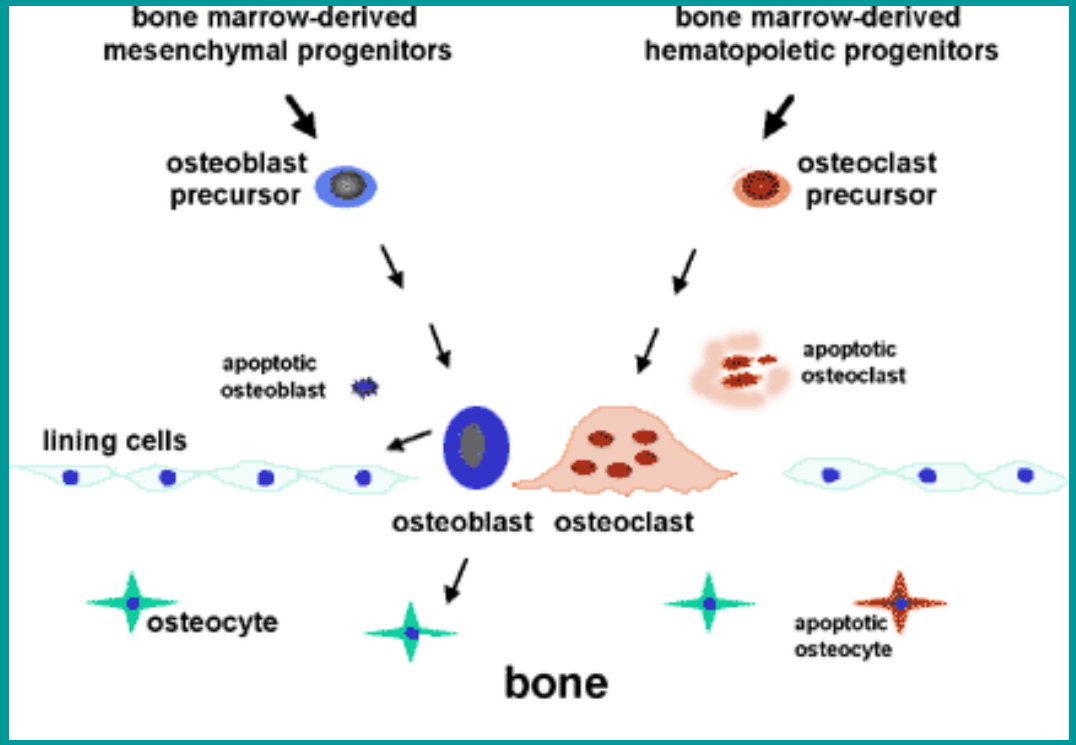
Osteoblasts → **Osteocytes**

Osteoclasts

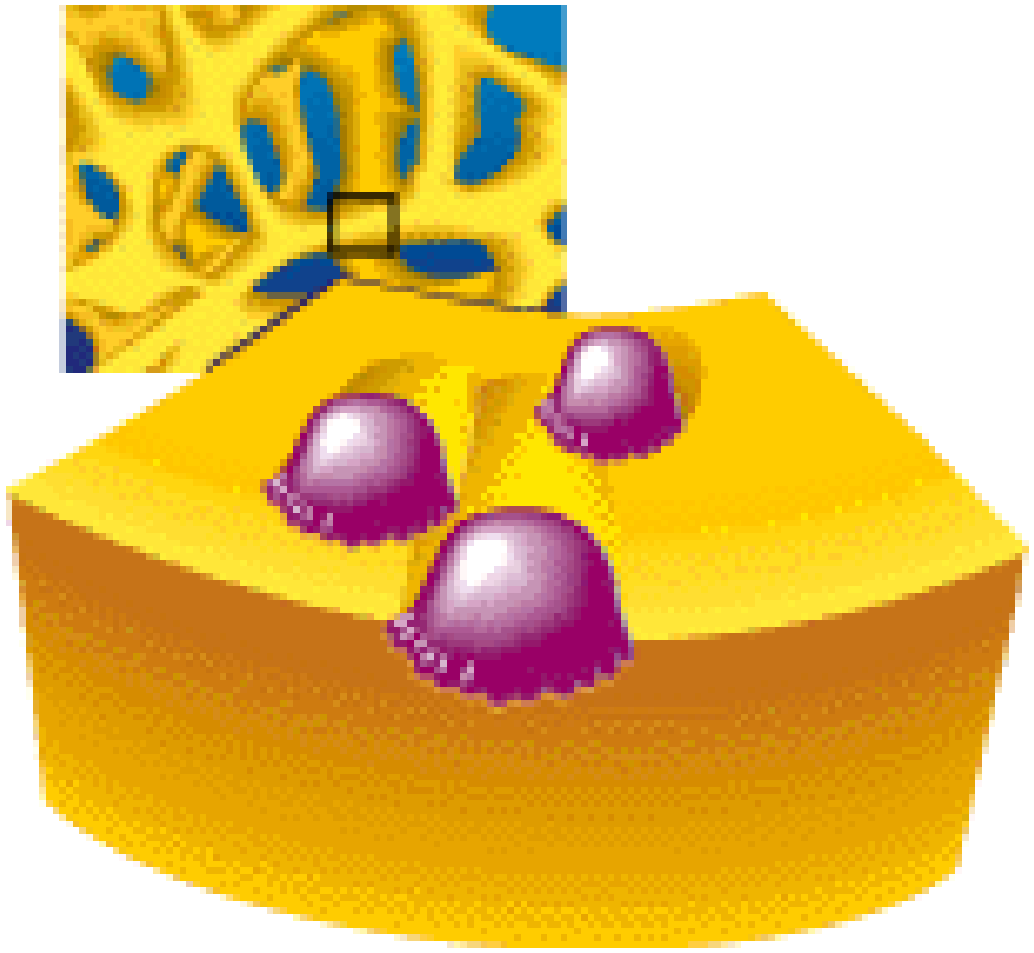


Osteoblasts are Mesenchymal Cells

Osteoclasts Derive from Blood Cells



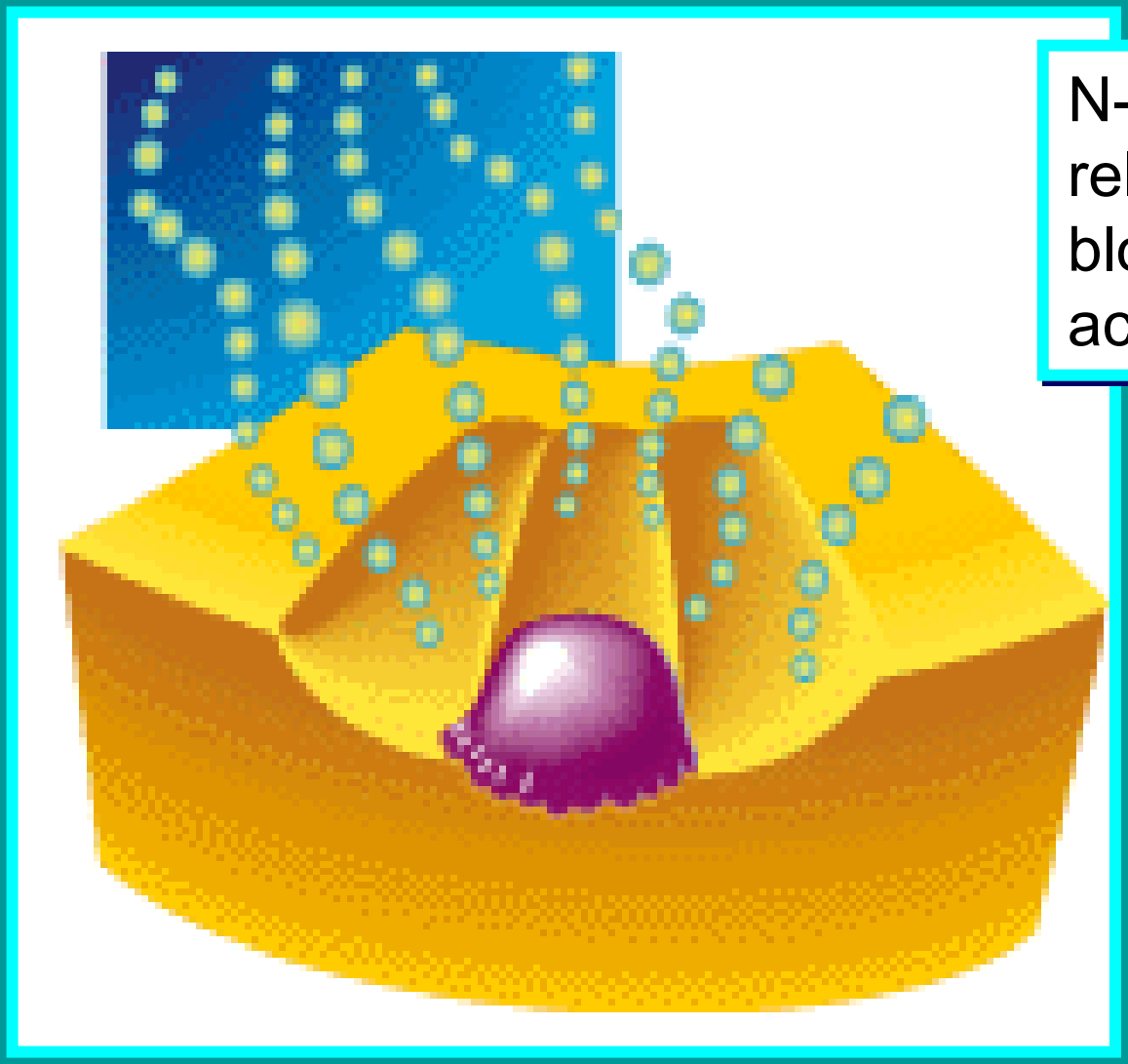
Bone remodeling



Bone resorption:

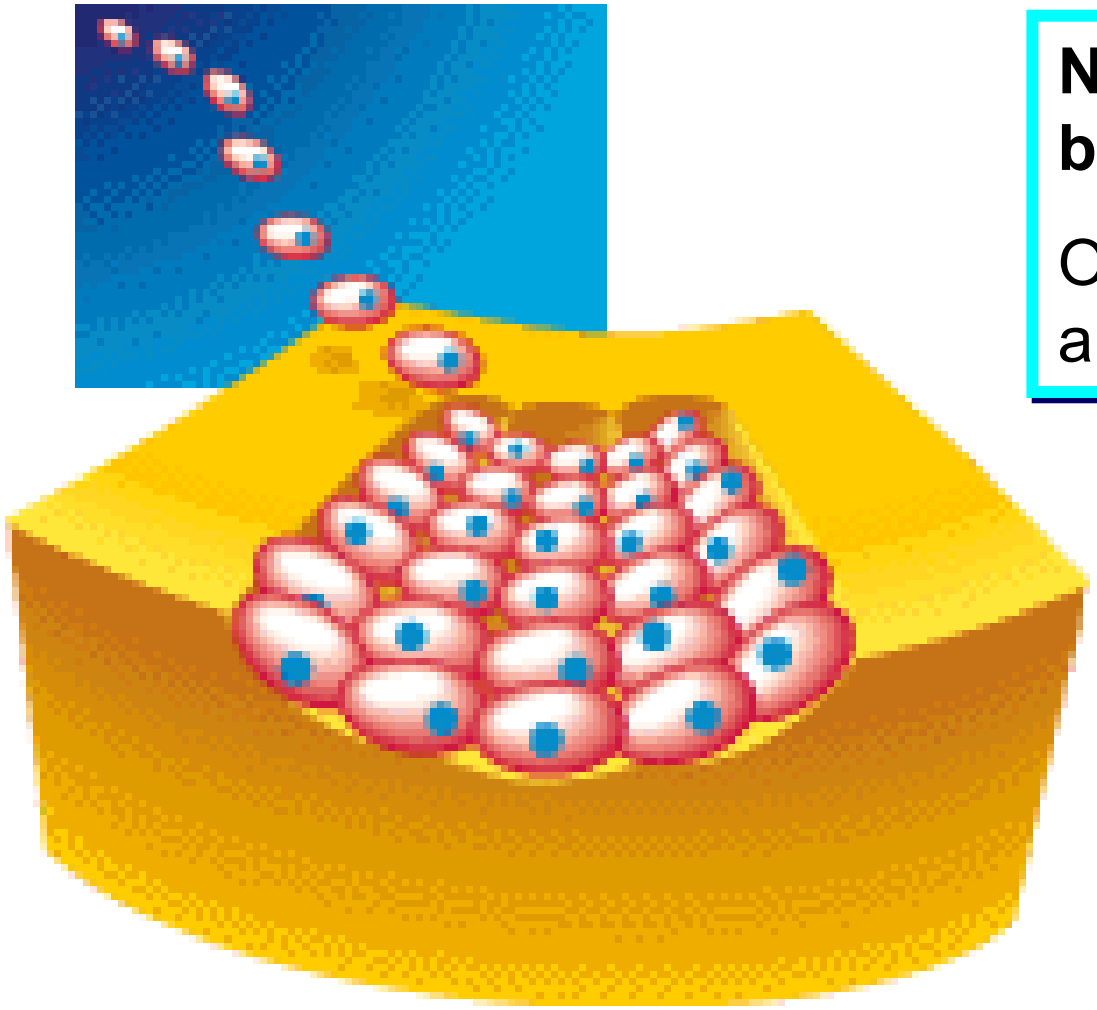
Osteoclasts bind to the matrix, dig holes and release collagen and minerals.

Bone remodeling



N-Telopeptids are released into the blood through the activity of osteoclasts.

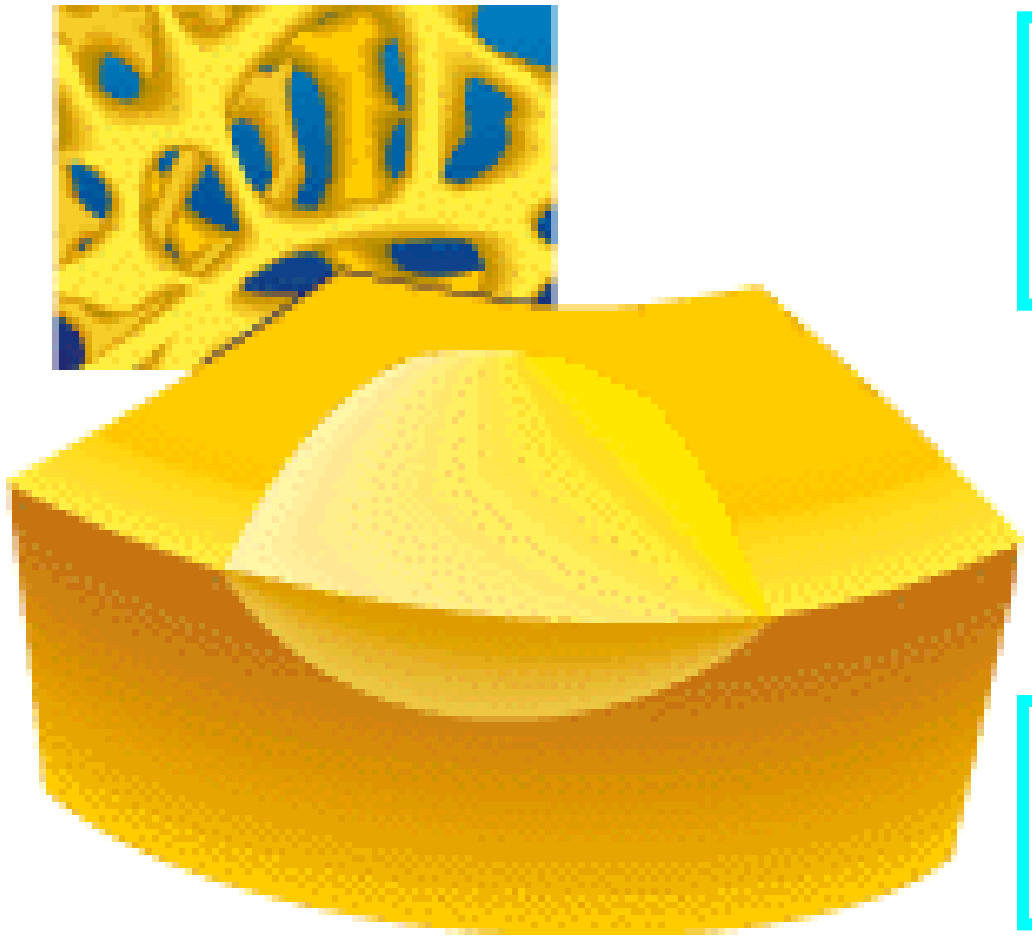
Bone remodeling



New formation of bone matrix:

Osteoblasts attach and secret collagen

Bone remodeling



New bone formation and resorption must be in balance to maintain bone mass.

Yearly this process replaces 20 % of the skeleton.

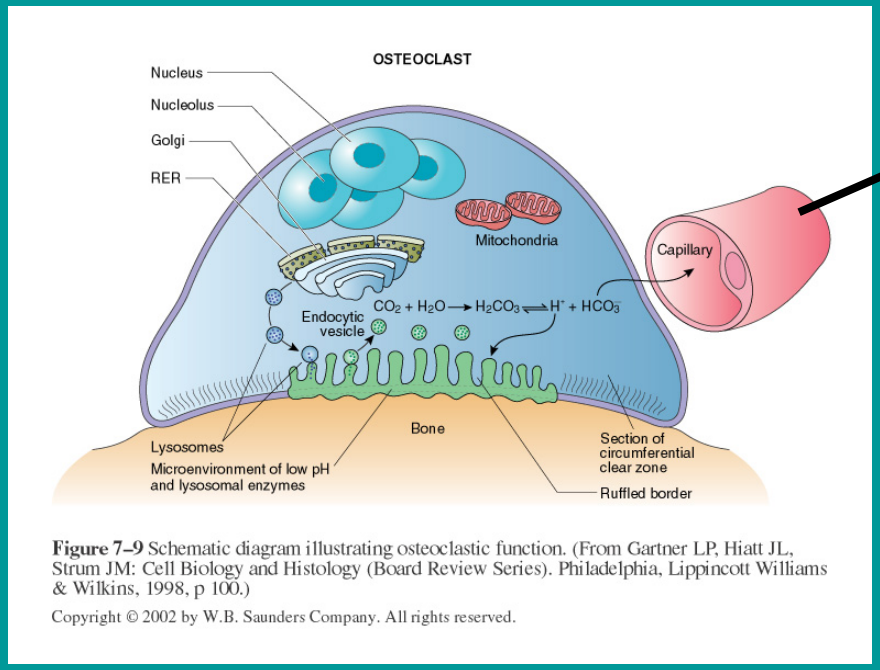
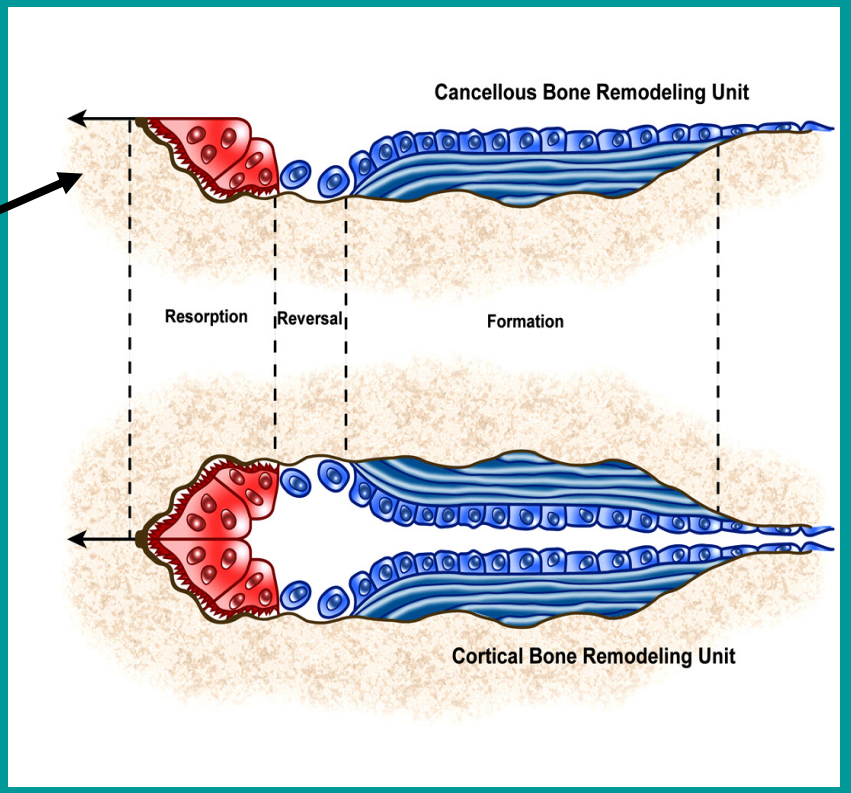


Figure 7–9 Schematic diagram illustrating osteoclastic function. (From Gartner LP, Hiatt JL, Strum JM: Cell Biology and Histology (Board Review Series). Philadelphia, Lippincott Williams & Wilkins, 1998, p 100.)



Knochenumbau in Knochenumbaukompartimenten (BRC)