



Osteoblast : A cell under compression

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 **CNRS**
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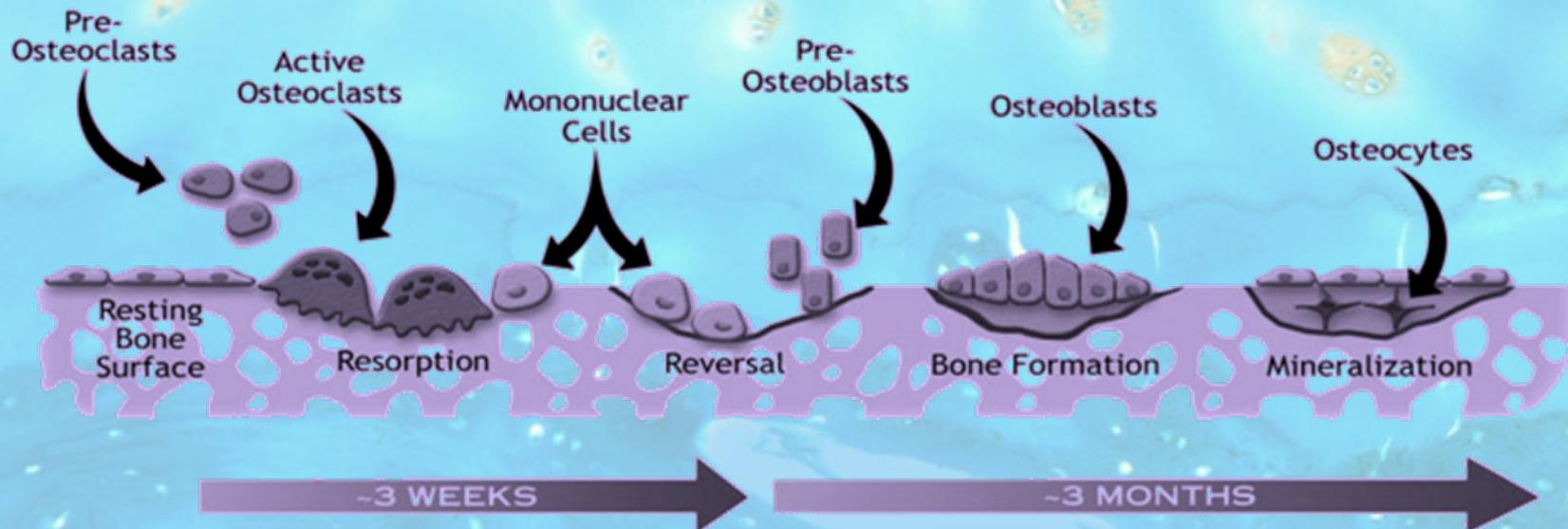
Prof Francis BERENBAUM

Université
de Liège

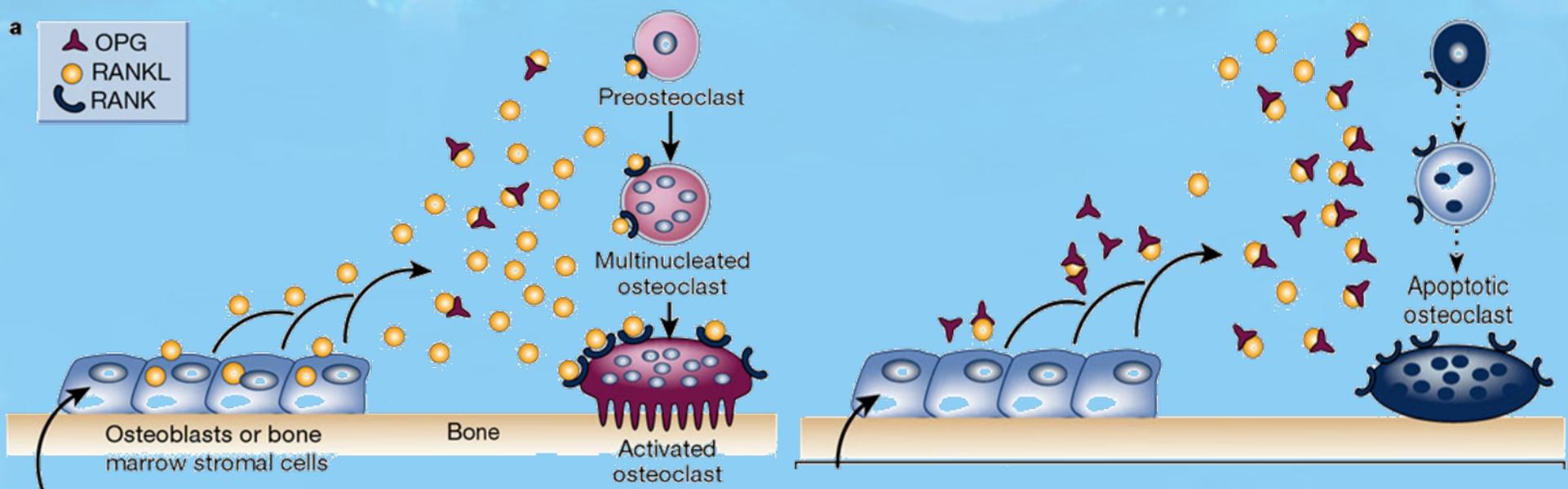


Bone and Cartilage Research Unit

Prof Yves HENROTIN



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Pro-resorptive and calcitropic factors	1,25(OH) ₂ vitamin D ₃ , PTH, PTHrP, PGE2, IL-1, IL-6, TNF, prolactin, corticosteroids, oncostatin M, LIF
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Anabolic or anti-resorptive factors	Oestrogens, calcitonin, BMP 2/4, TGF-β, TPO, IL-17, PDGF, calcium
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Osteoblast : a cell under compression

Different mechanical stimuli applied on bone

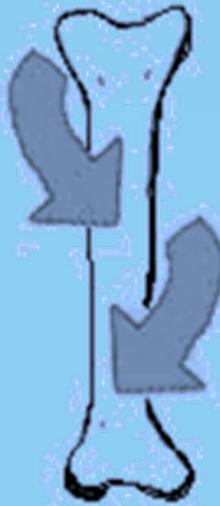
Compression



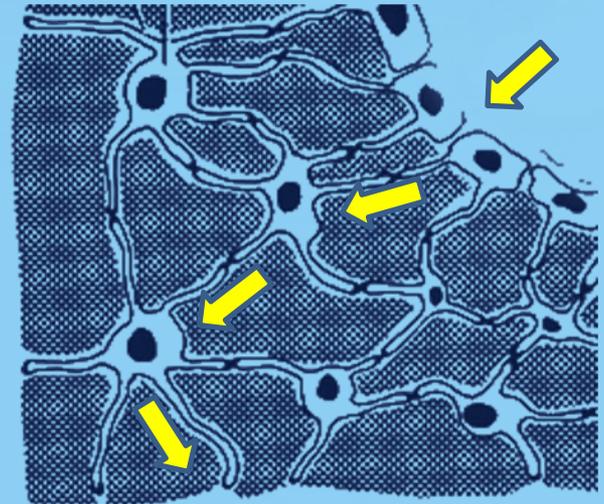
Tension



Shear (torsion)

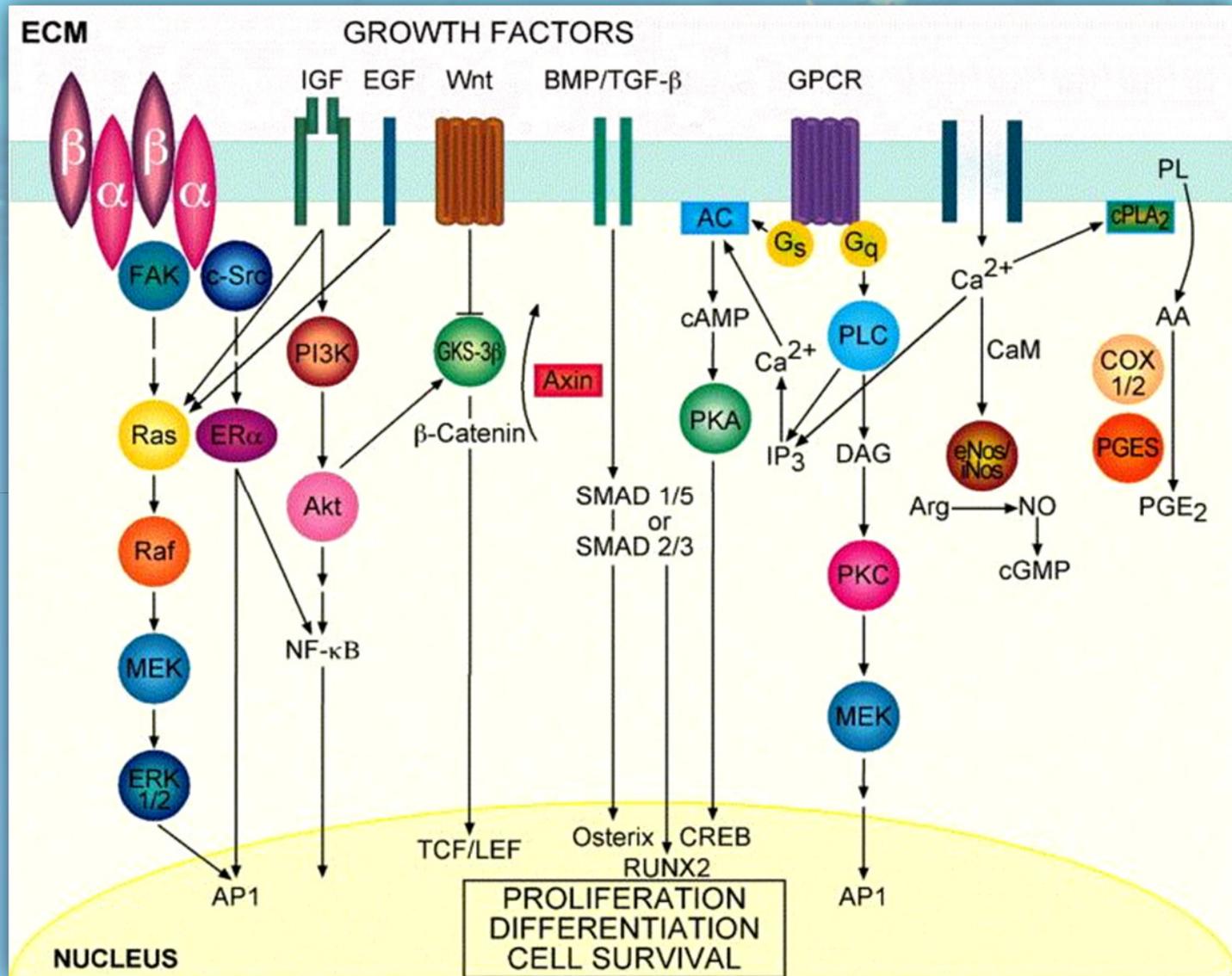


Fluid flow

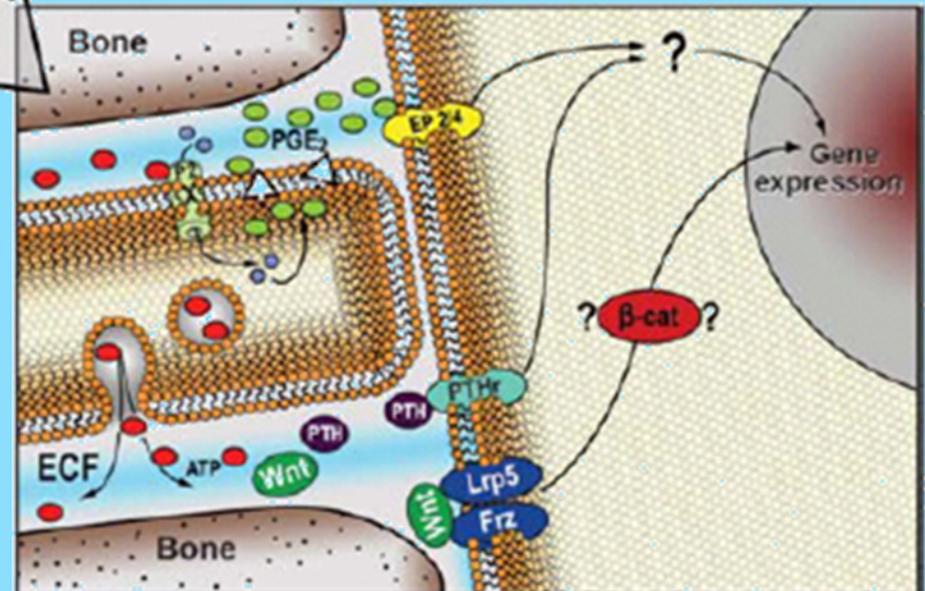
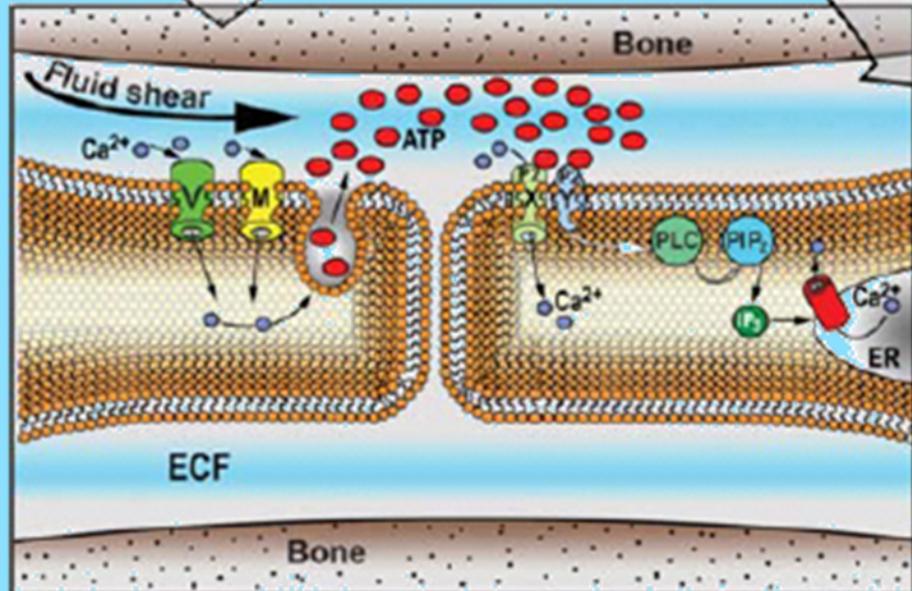
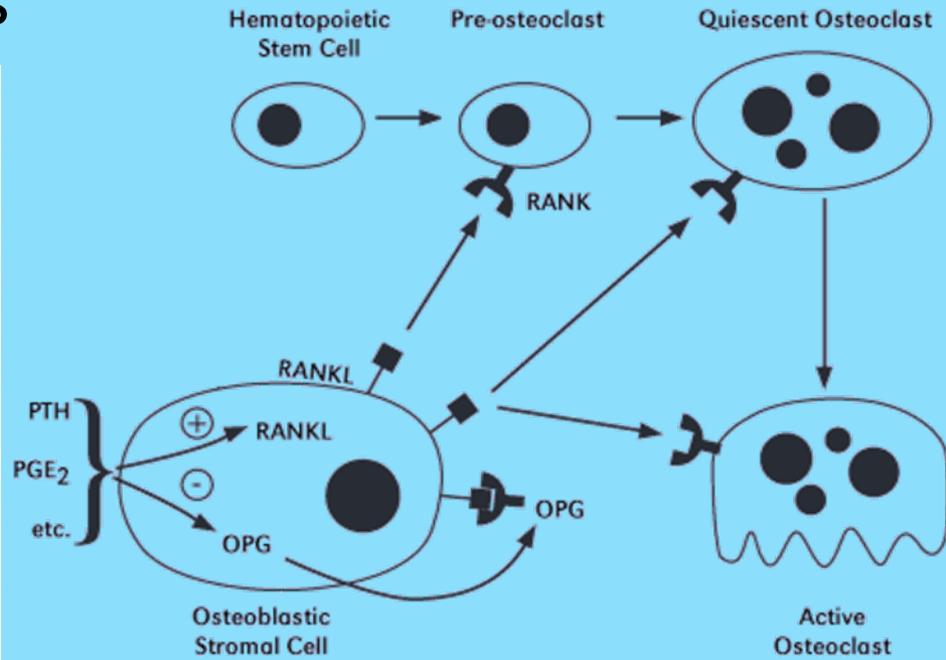
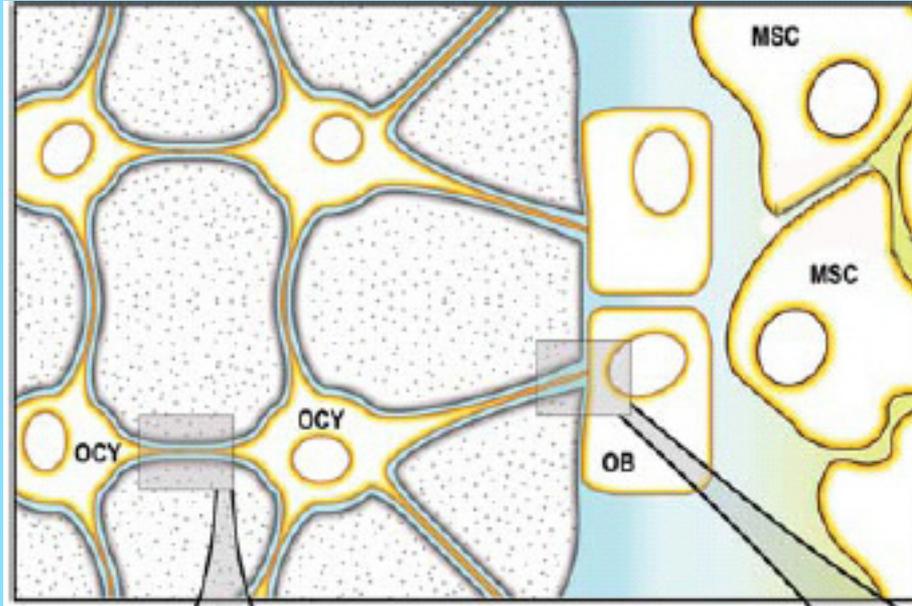


Mechanotransduction pathways in OB

Liedert A 2006

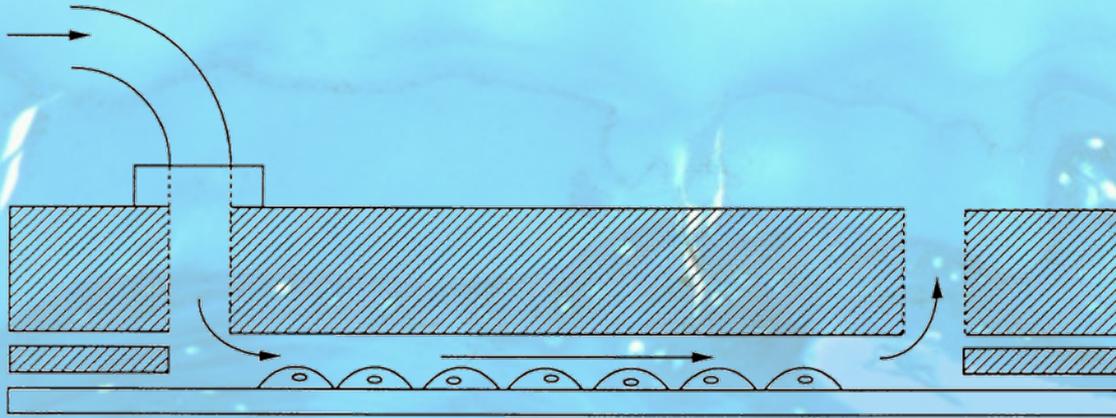


Cross talk between bone cells

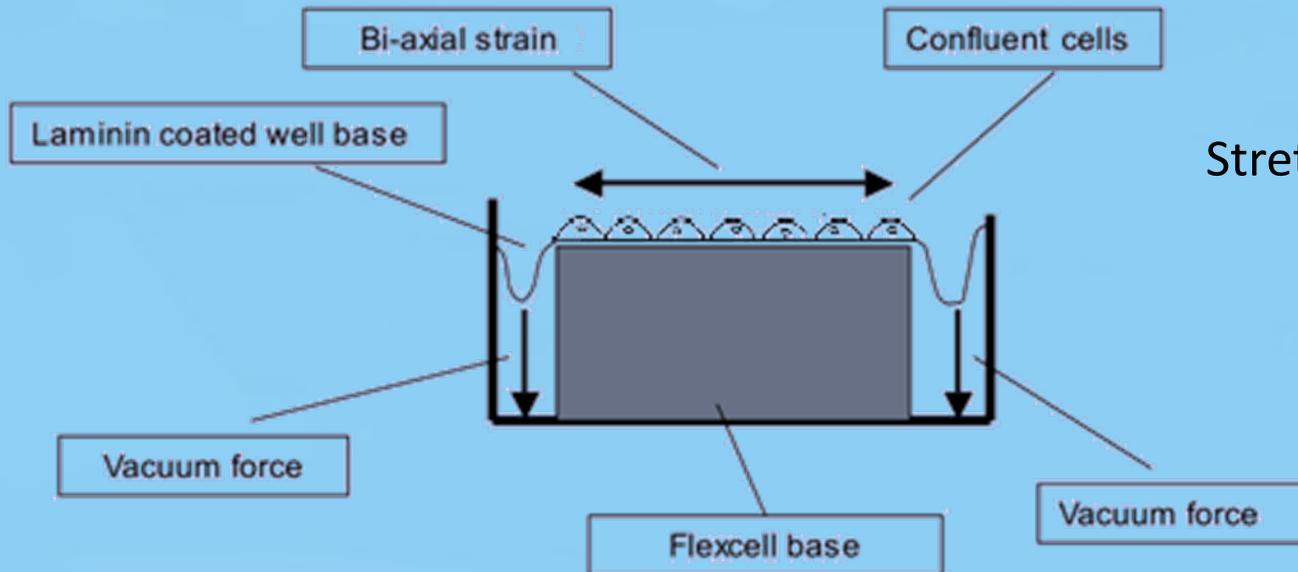


Classical *in vitro* models to study mechanical stress

inflow



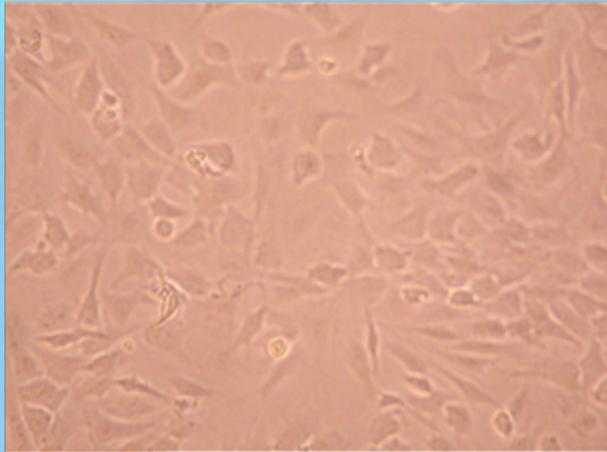
Fluid shear models



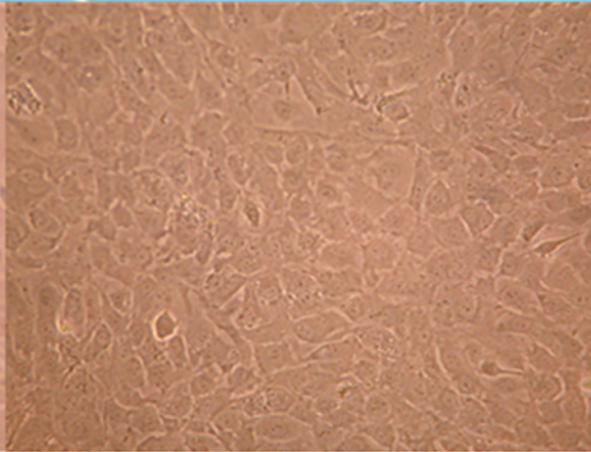
Stretching models

3D osteoblasts compression model

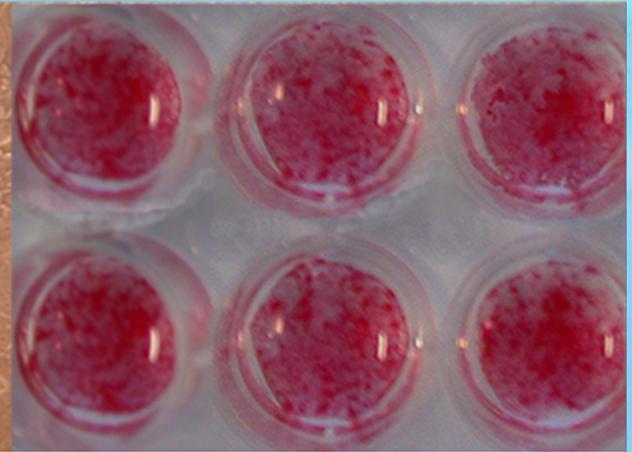
(a) Freshly isolated mouse calvaria osteoblasts



(b) 7 days of culture osteoblasts



(c) 28 days of culture : ALP activity of osteoblasts in their collagen matrix



(f) Plates disposition in Flexercell Compression Plus FX-4000C



(e) Sealing plate



(d) Membrane disposition in Biopress plate





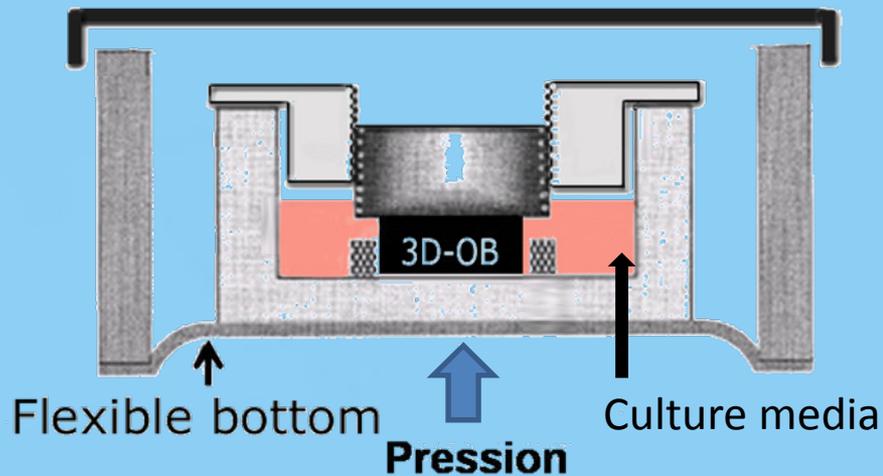
3D osteoblasts compression model

- Advantages
 - 3D connections between cells and extracellular matrix
 - Matrix neosynthesized by OB cells
 - Highly differentiated OB and also OCY
 - Compression of this 3D OB membrane submit many types of mechanical stimuli, including compression, tension and fluid shear
 - Easy to realize and manipulate, matrix resistant to large amplitude compression
 - Easy to recover cells and the matrix separately and to analyze gene expression and protein production

3D osteoblasts compression model

- Compressive stress submitted with flexercell
 - ▶ Dynamic sinusoidal at 1 Hz frequency
 - ▶ 6 - 10 % amplitude, corresponding to 1 - 1,7 MPa loading ($\sim 10 - 17 \text{ Kg/cm}^2$)
 - ▶ 1 – 16h

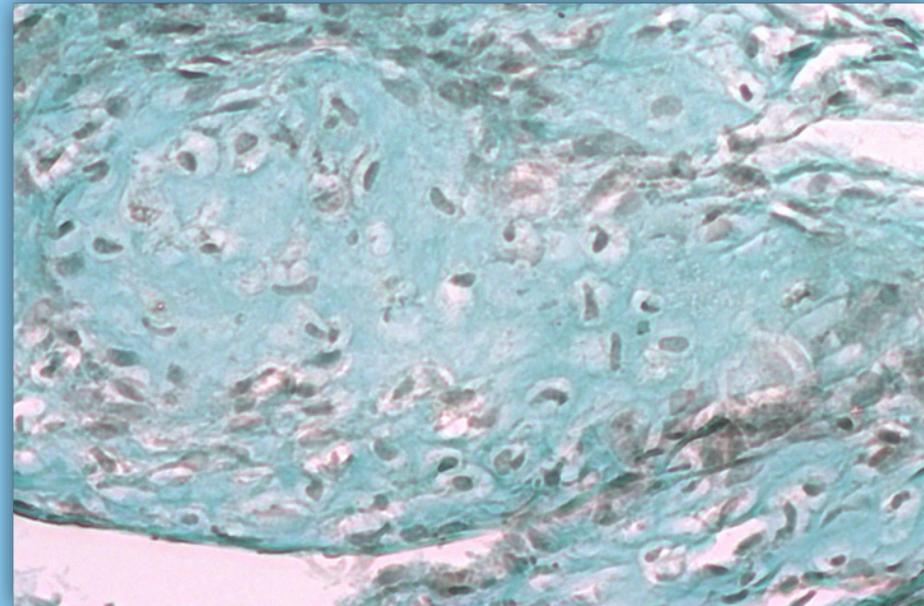
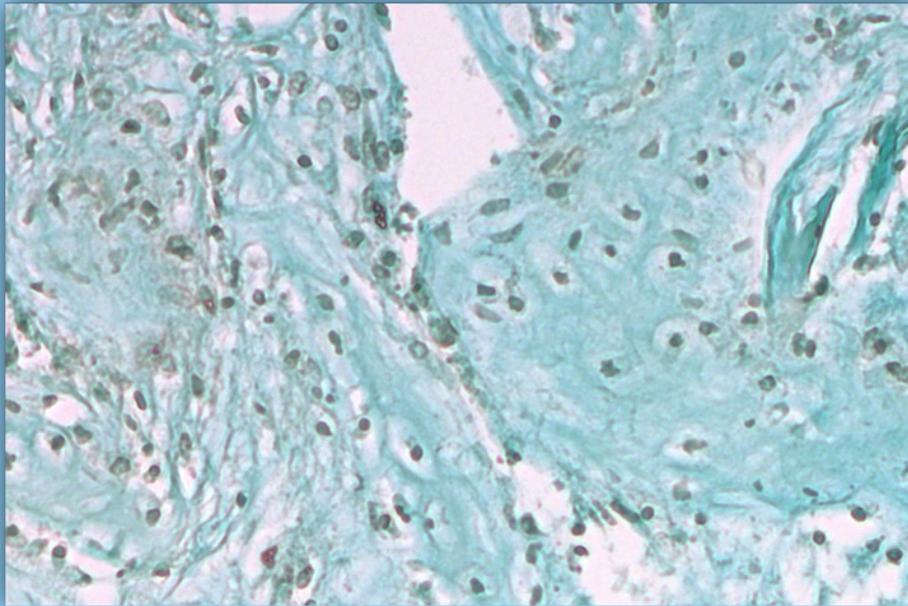
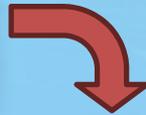
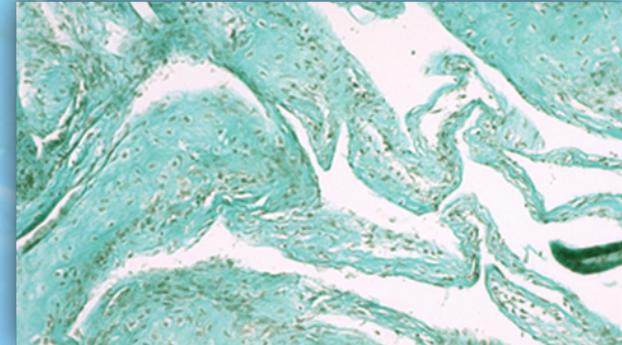
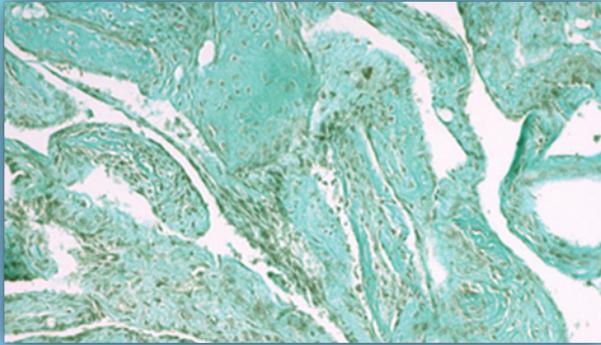
Schema of a well of a 6-wells compression plate



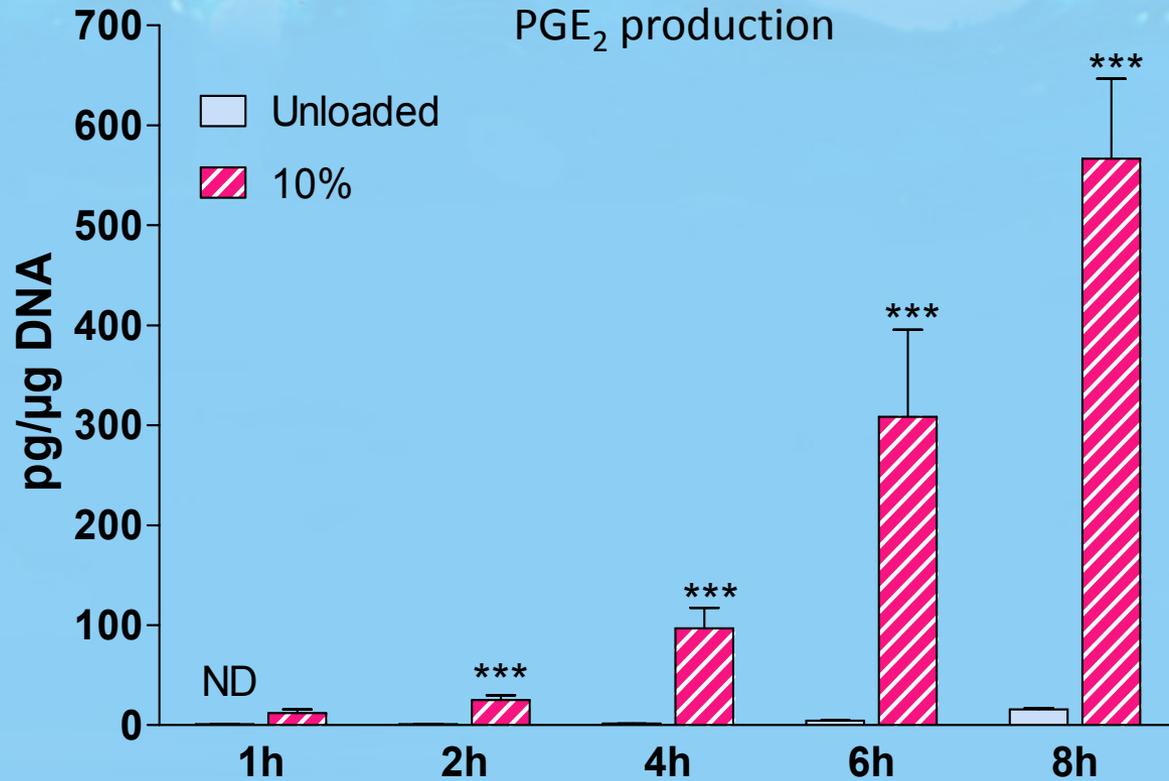
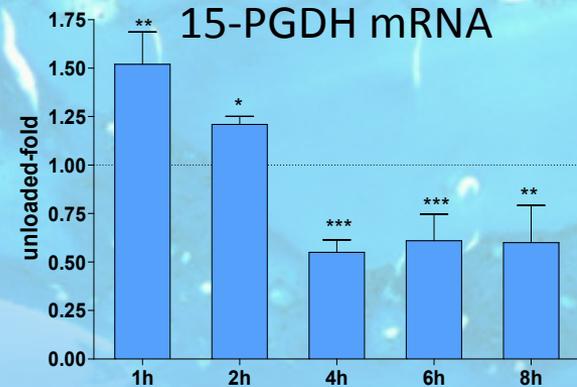
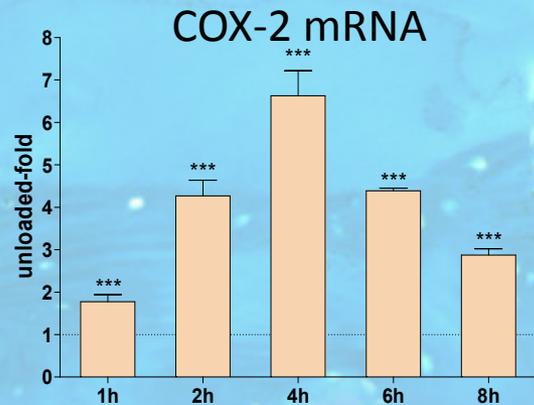
3D osteoblasts compression model

Unloaded control

16h of 10 % compression, 1 Hz

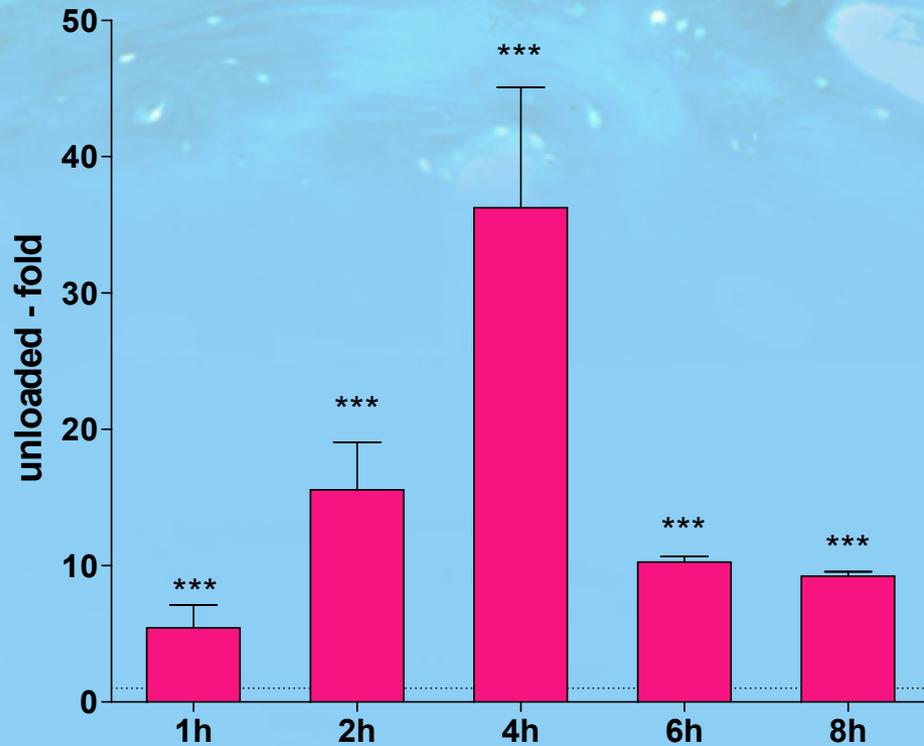


3D osteoblasts compression model

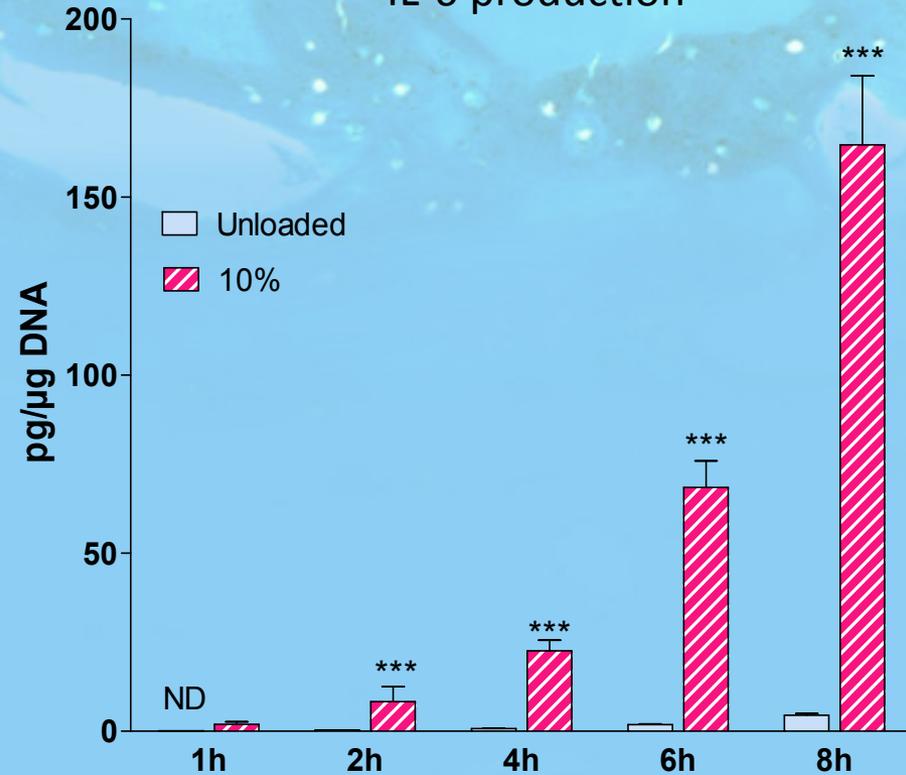


3D osteoblasts compression model

IL-6 mRNA

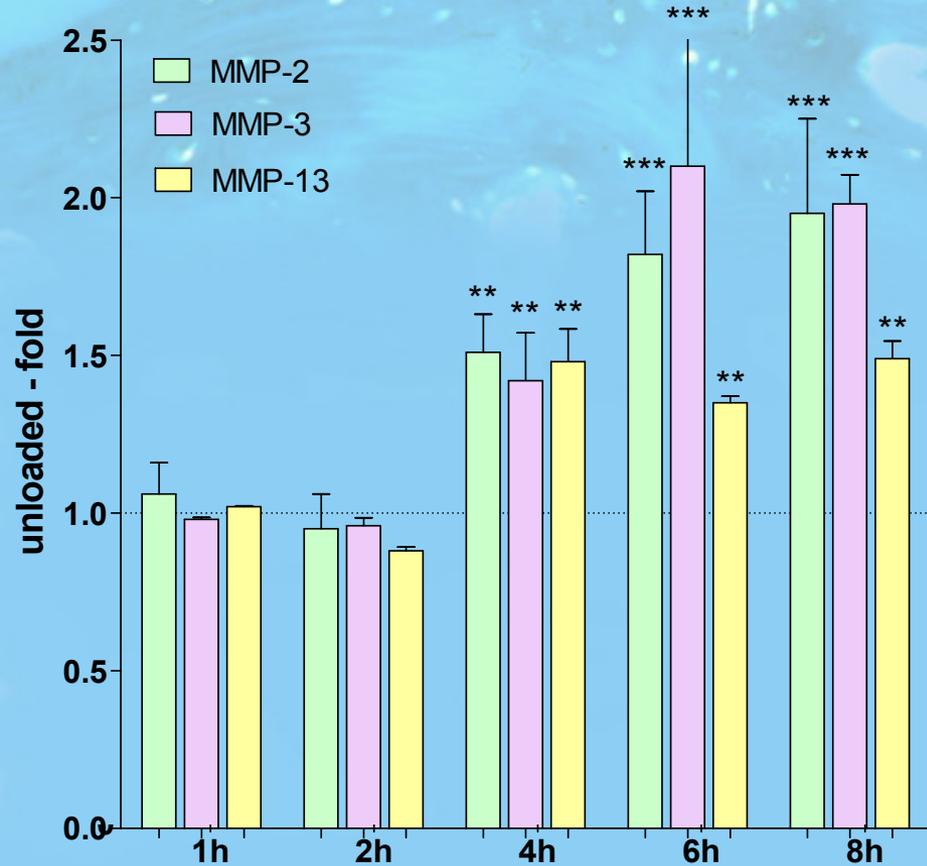


IL-6 production

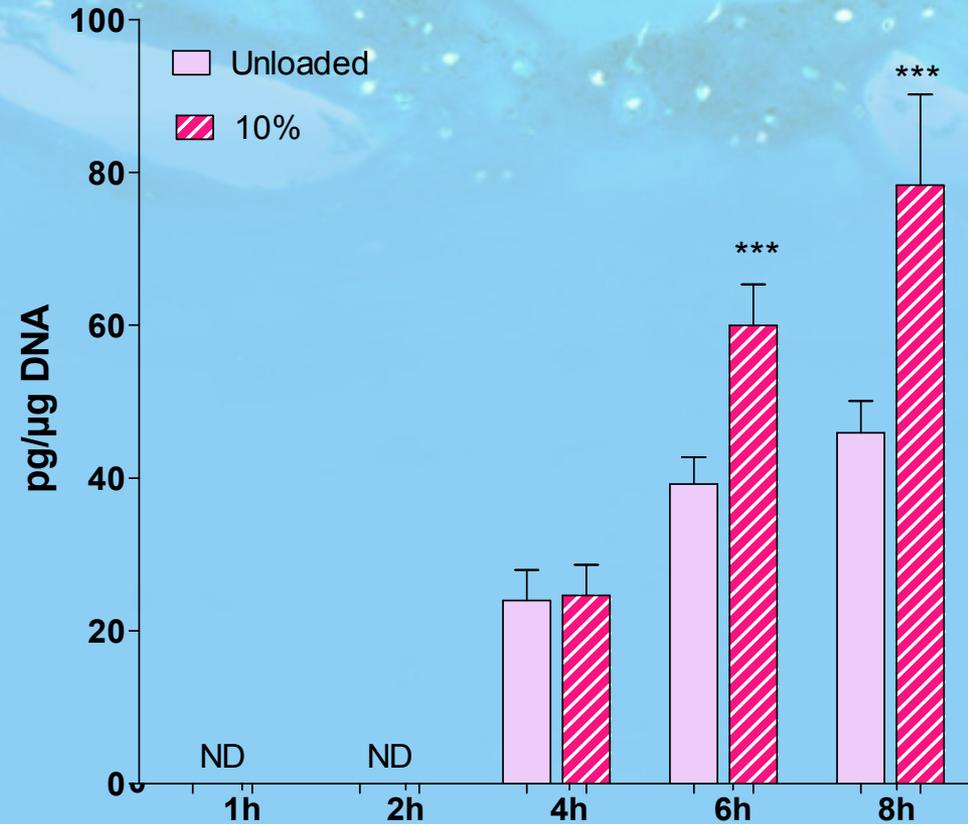


3D osteoblasts compression model

MMPs mRNA



MMP-3 production





3D osteoblasts compression model

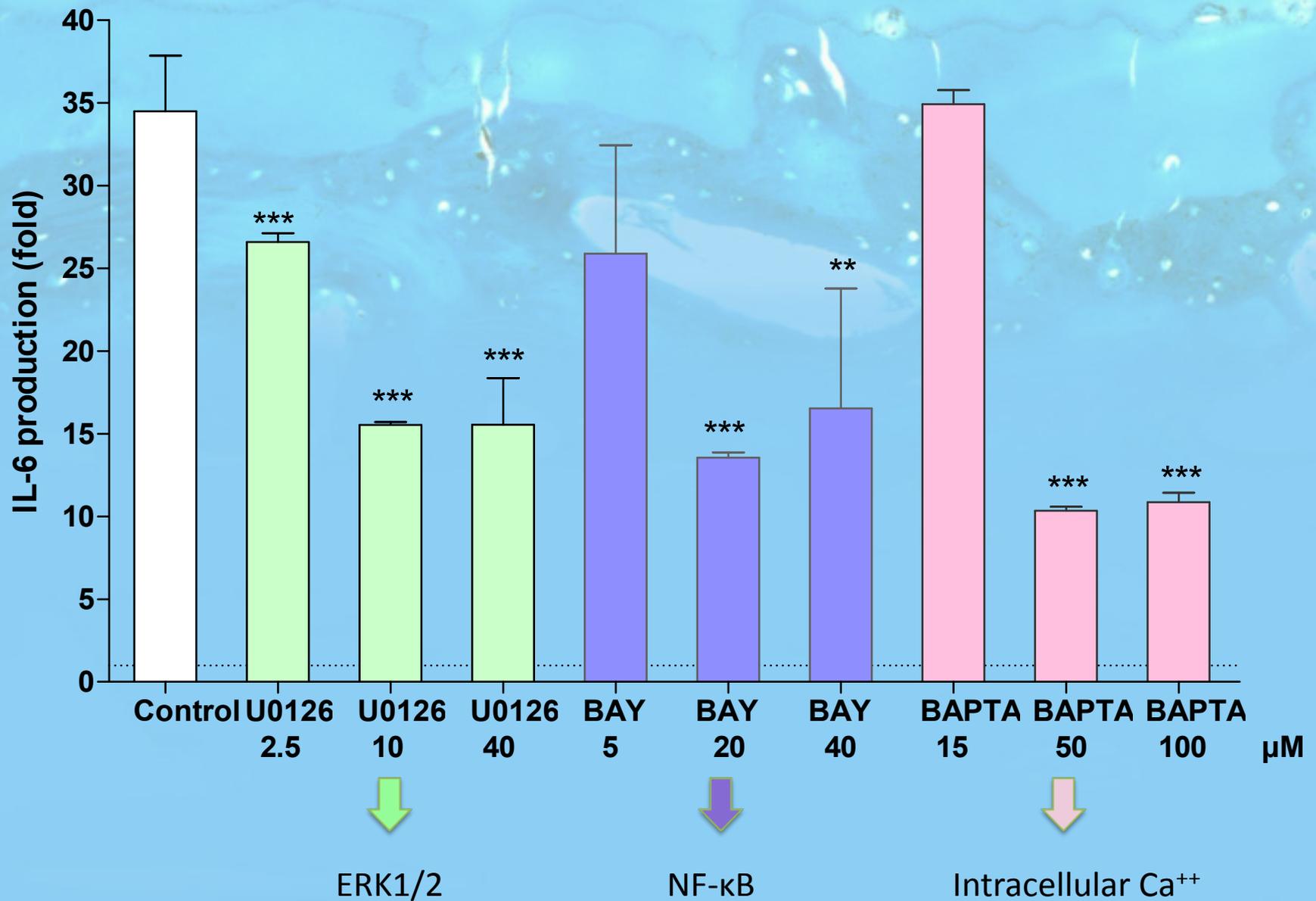
Other results:

Compression ↑ iNOS expression (4-fold)

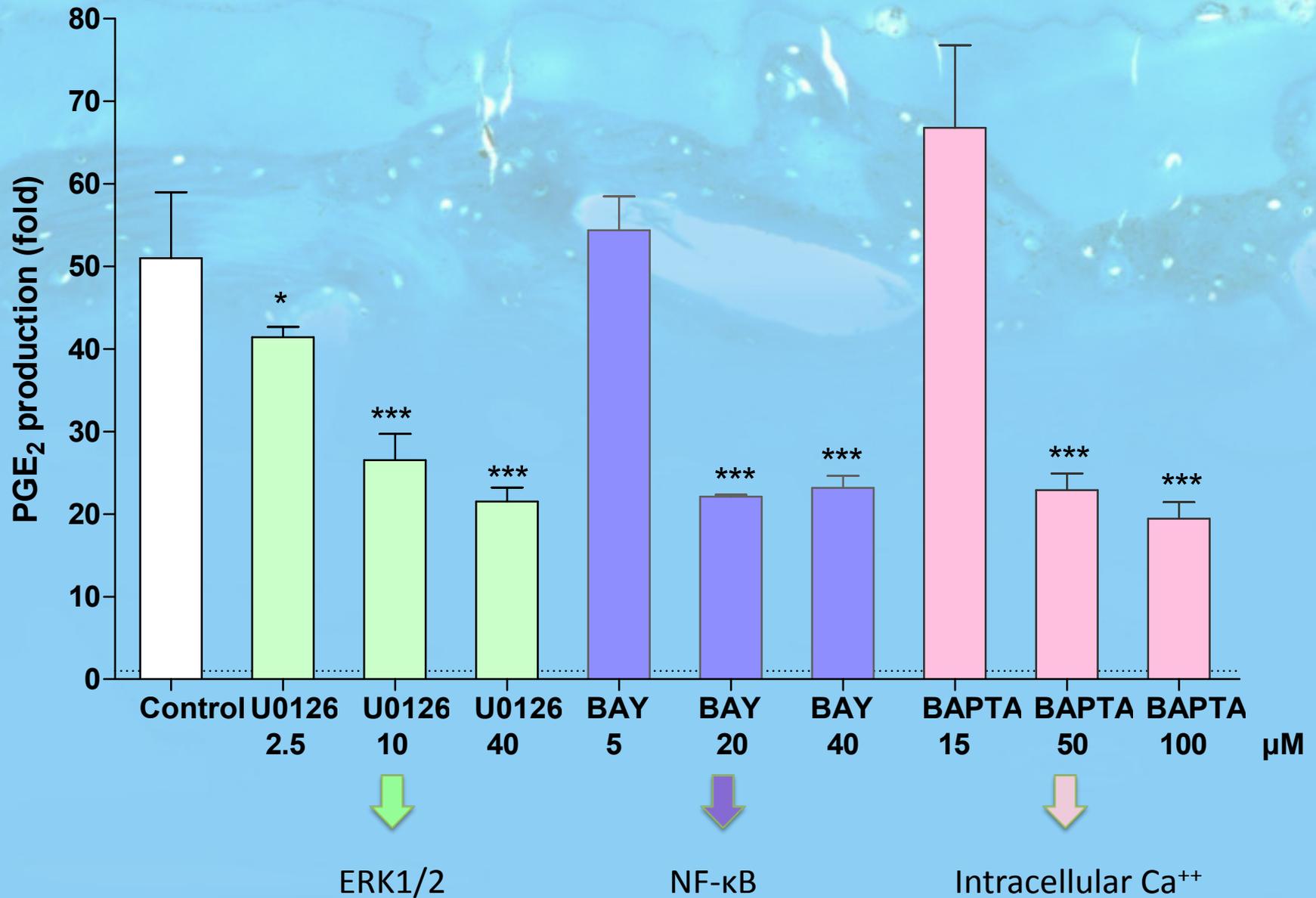
↑ VEGF expression (3-fold)

↓ OPG expression by half

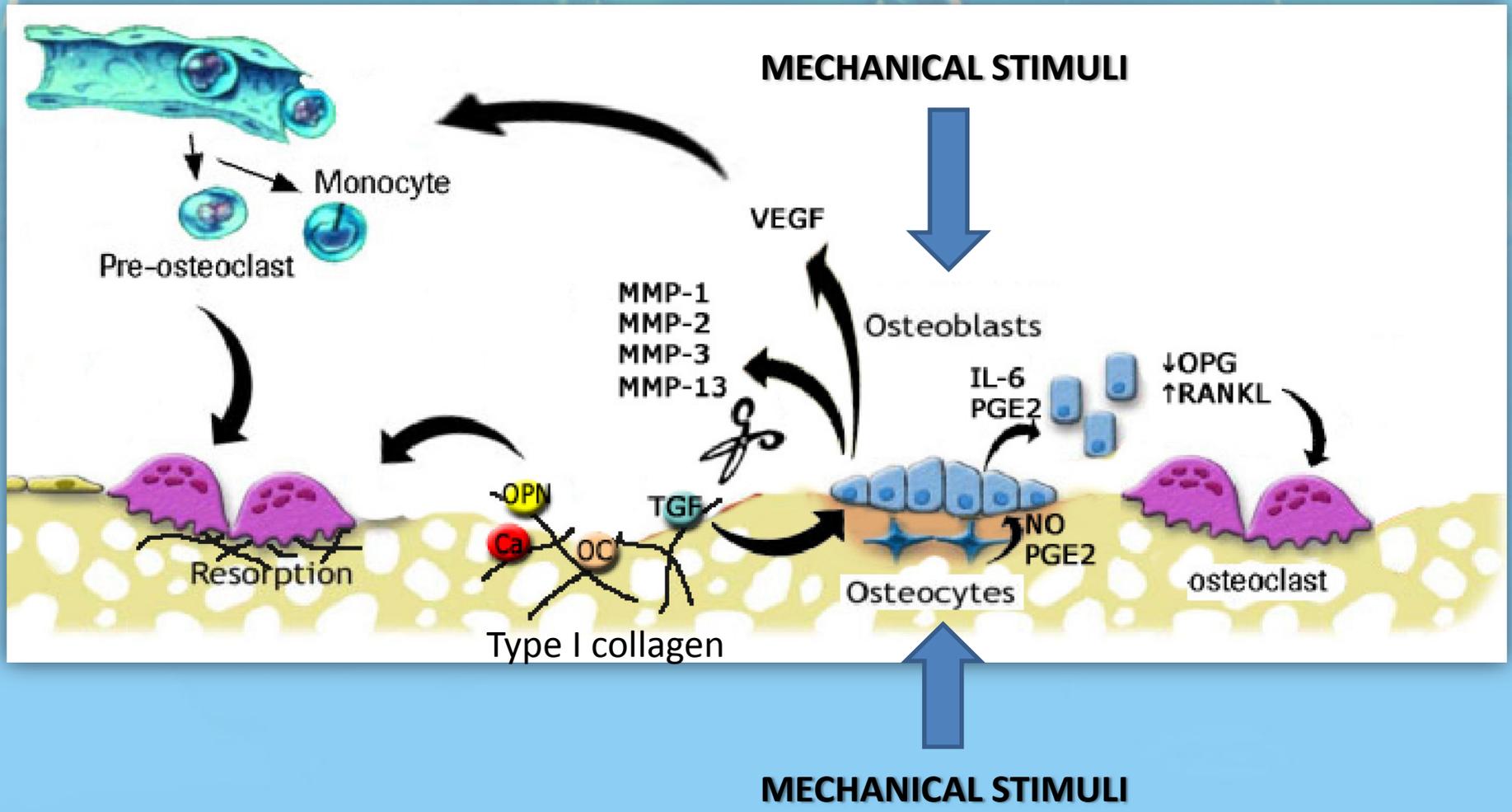
3D osteoblasts compression model



3D osteoblasts compression model



Hypothetical model for the biomechanical control of bone remodeling



Thanks to

- Professor Berenbaum team (UPMC Paris 6 / CNRS)

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- Jacques Claire
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and Bone and Cartilage Research Unit team



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