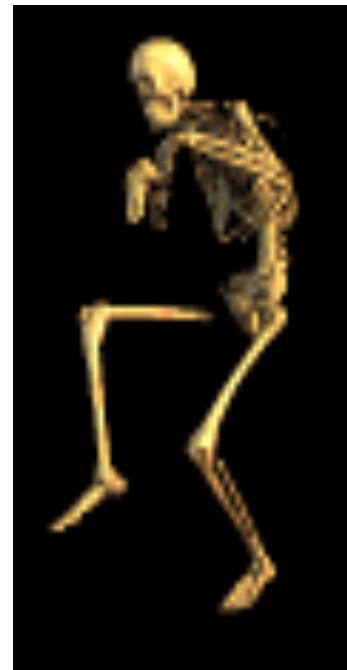


FISIOPATOLOGIA DEL METABOLISMO OSSEO

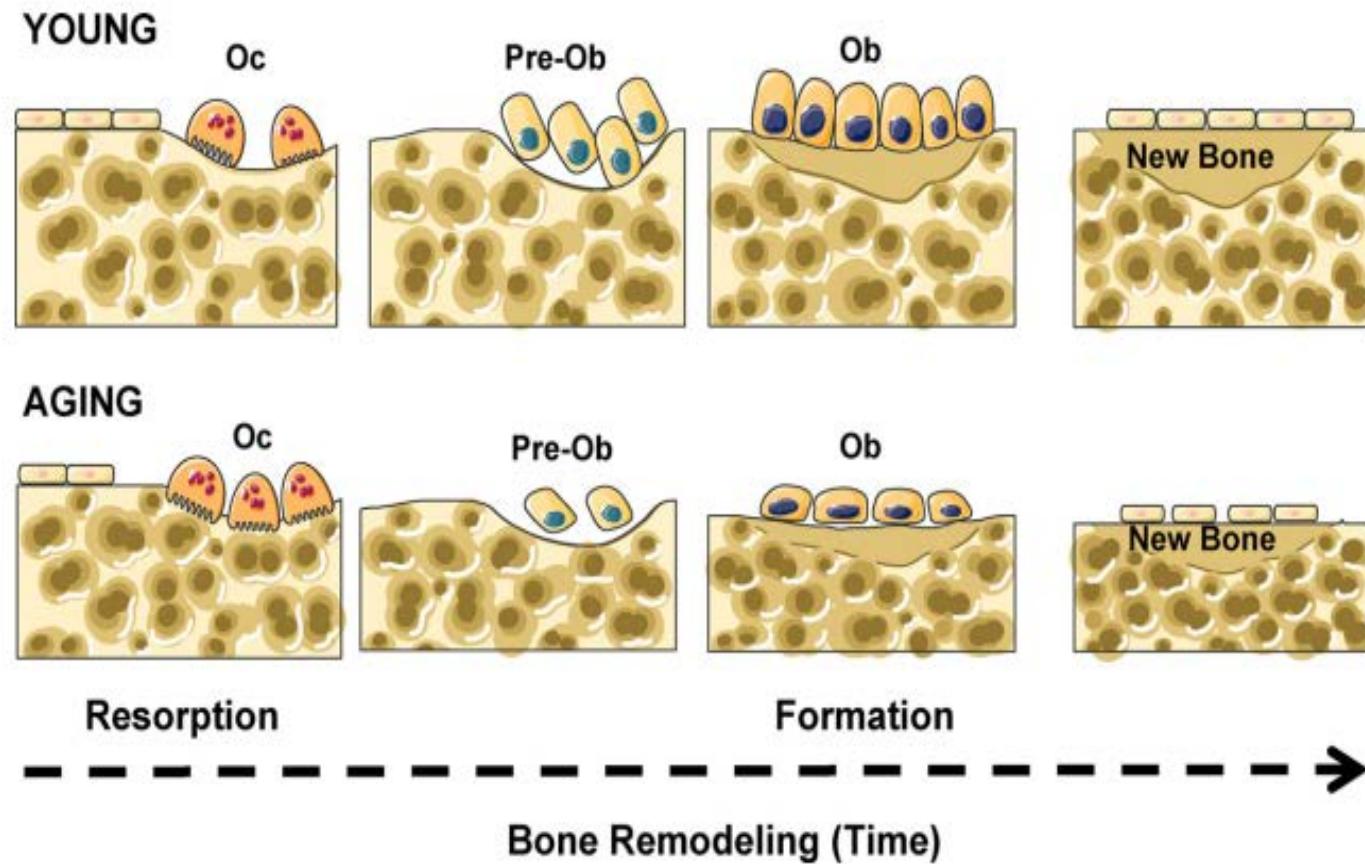
P. D'Amelio MD, PhD
patrizia.damelio@unito.it

AGENDA

- Turnover e cellule ossee
- Meccanismi estrinseci coinvolti nella regolazione del turnover
- Cellule scheletriche ed invecchiamento
- Osso ed altri sistemi
- Conclusioni

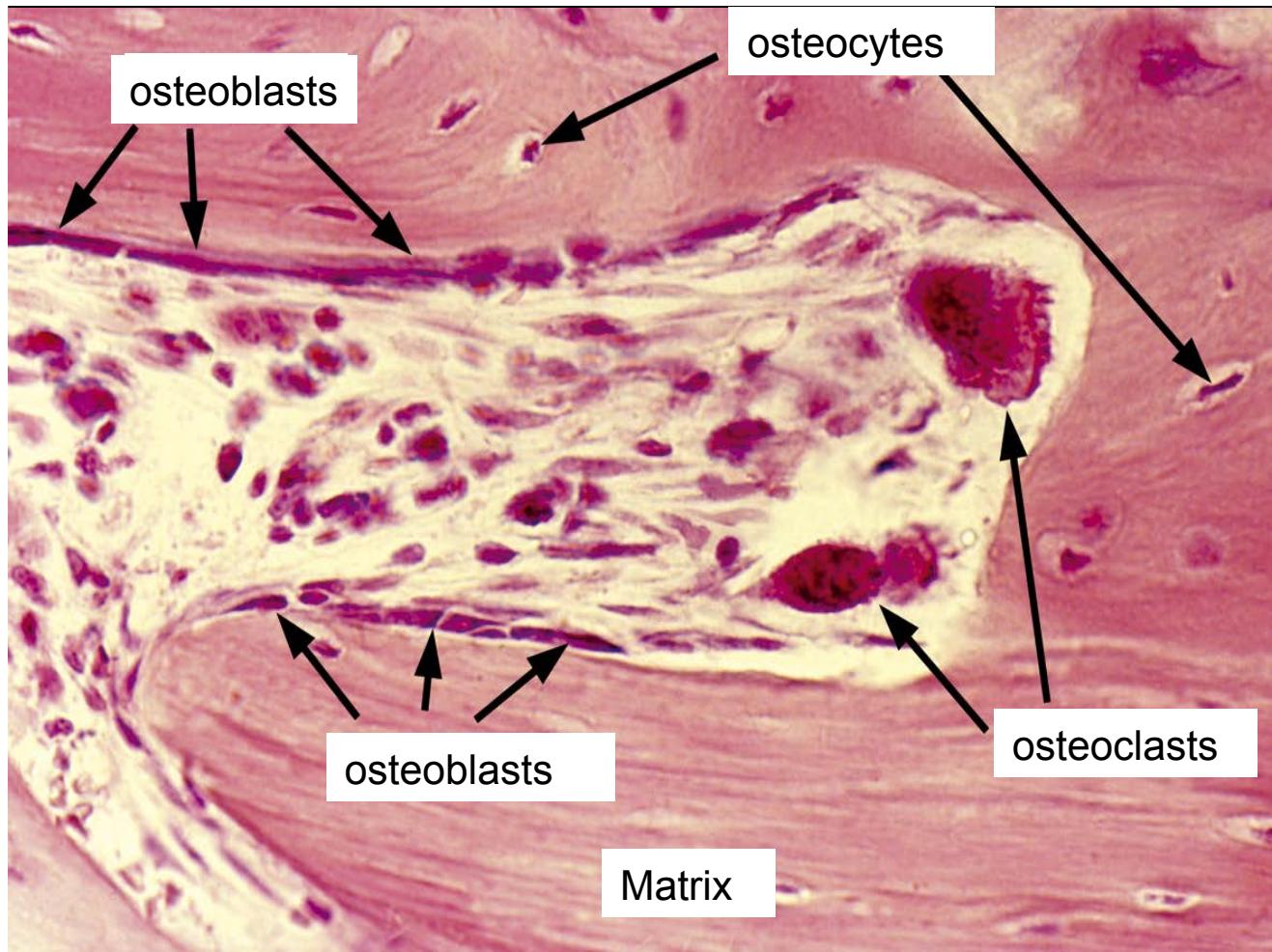


TURNOVER SCHELETTRICO

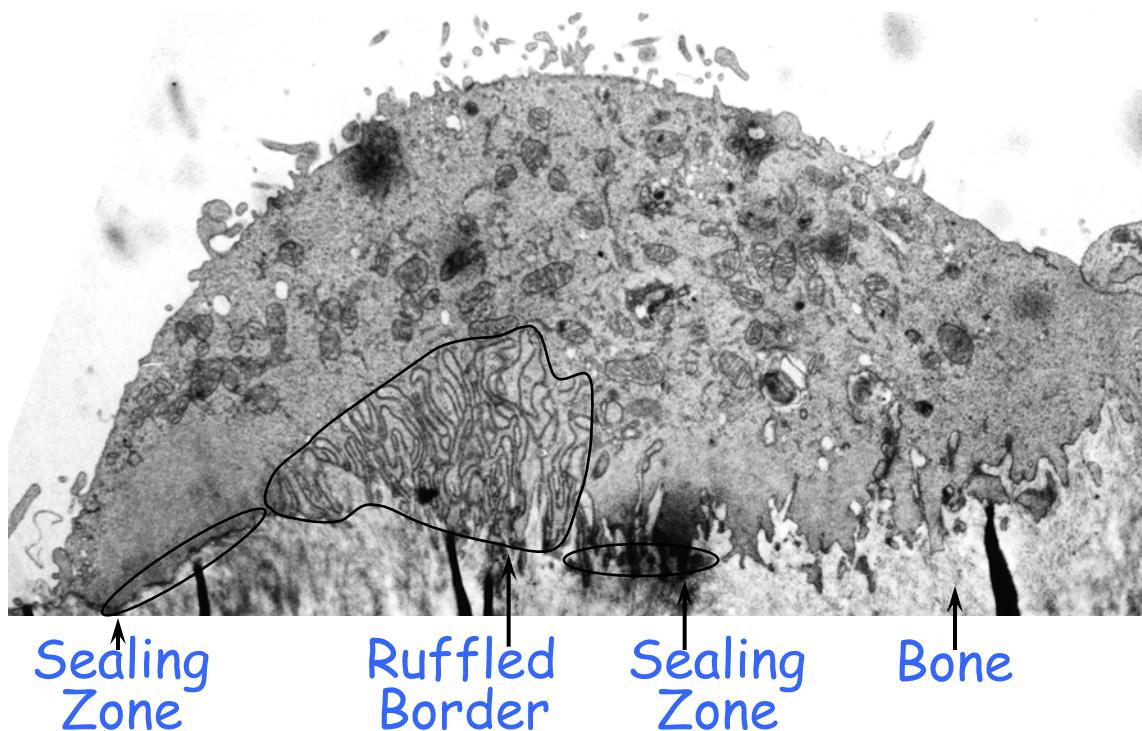


Marie PJ. and Kassem M, JCEM 2011

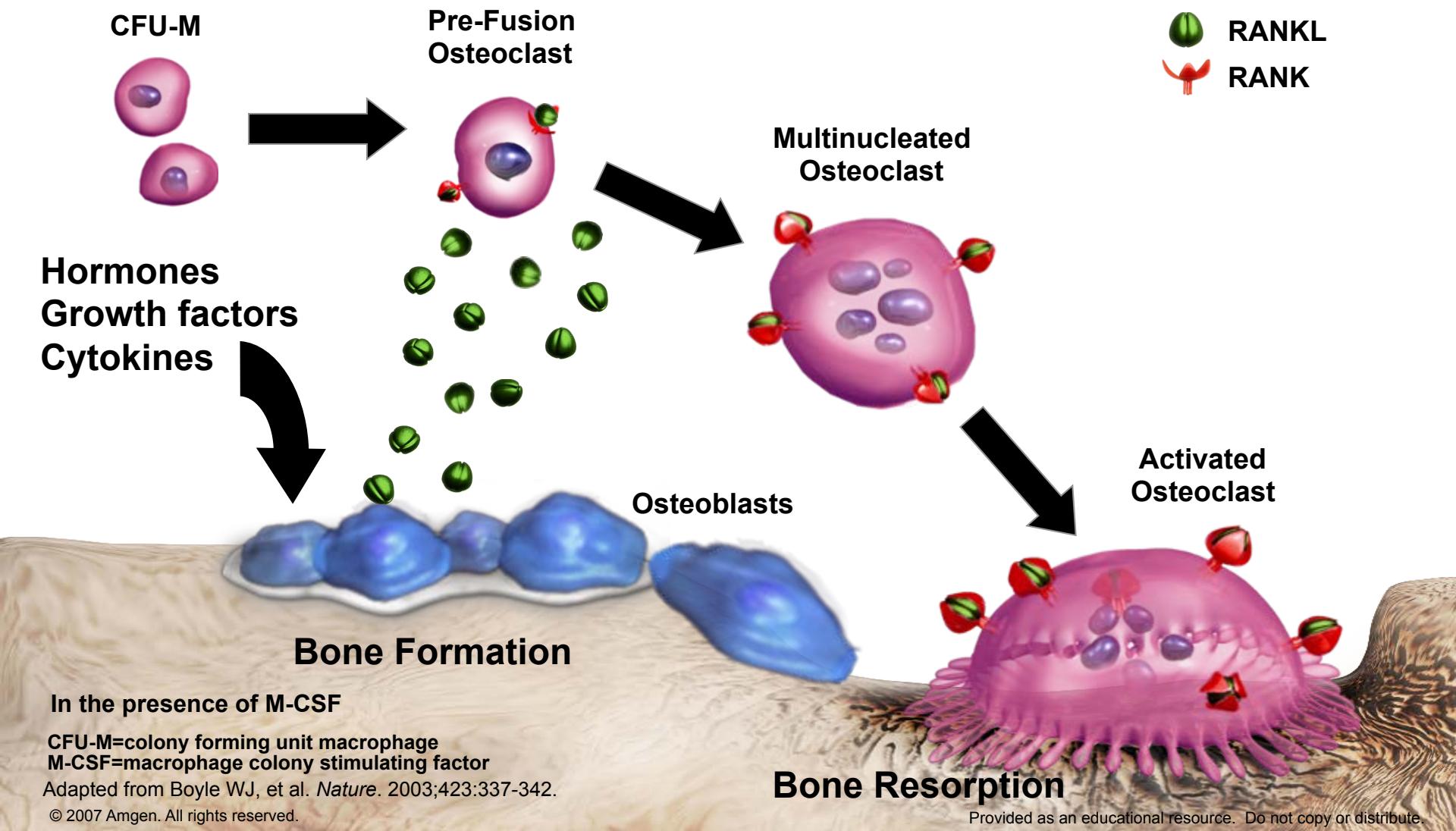
UNITA' MULTICELLULARE DI BASE



OSTEOCLASTI



RANKL è un mediatore essenziale dell'osteoclastogenesi



In the presence of M-CSF

CFU-M=colony forming unit macrophage
M-CSF=macrophage colony stimulating factor

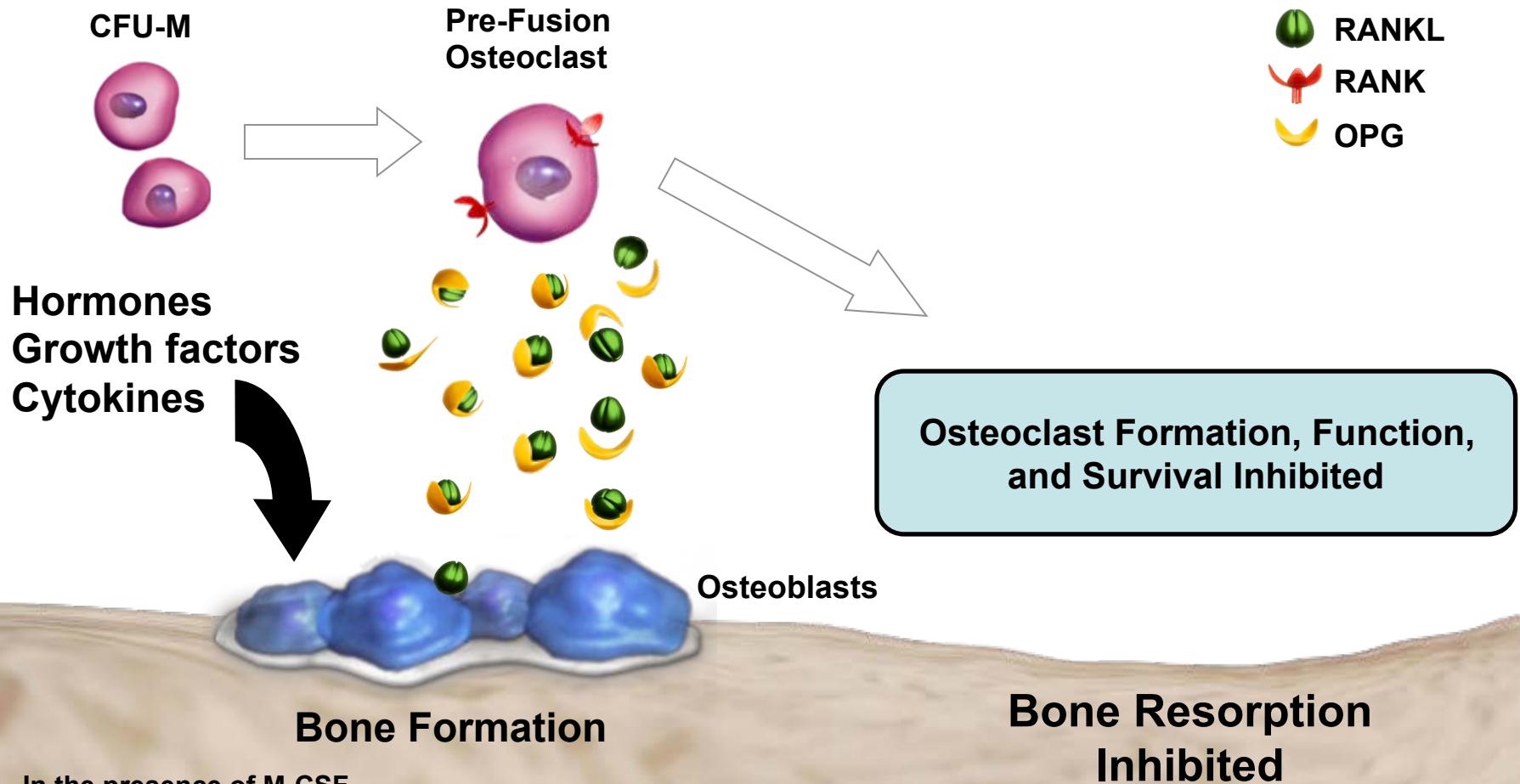
Adapted from Boyle WJ, et al. *Nature*. 2003;423:337-342.

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Bone Resorption

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Osteoprotegerin (OPG) è un recettore esca che impedisce a RANKL di legarsi al suo recettore RANK ed inibisce l'osteoclastogenesi



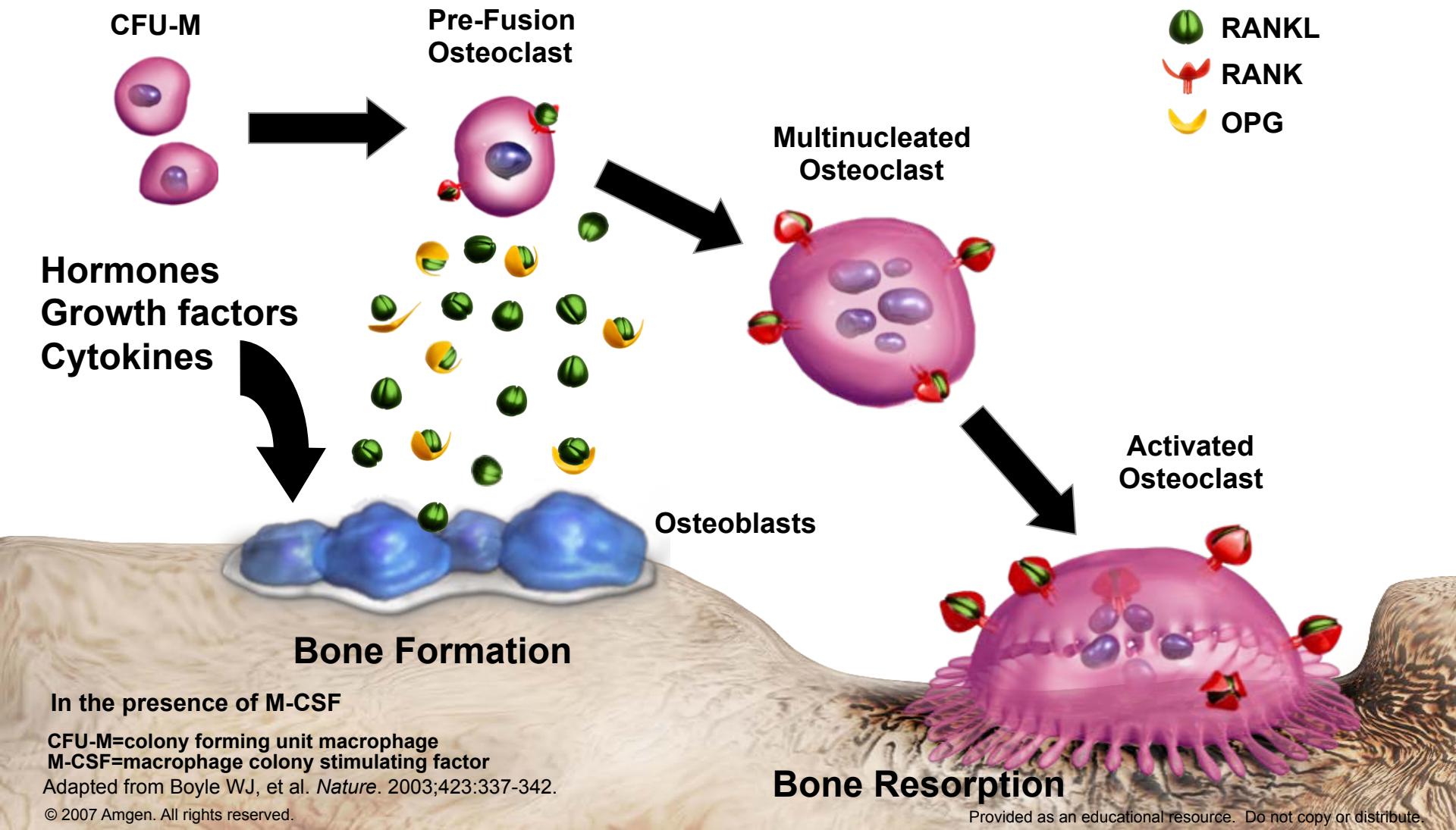
In the presence of M-CSF

CFU-M=colony forming unit macrophage

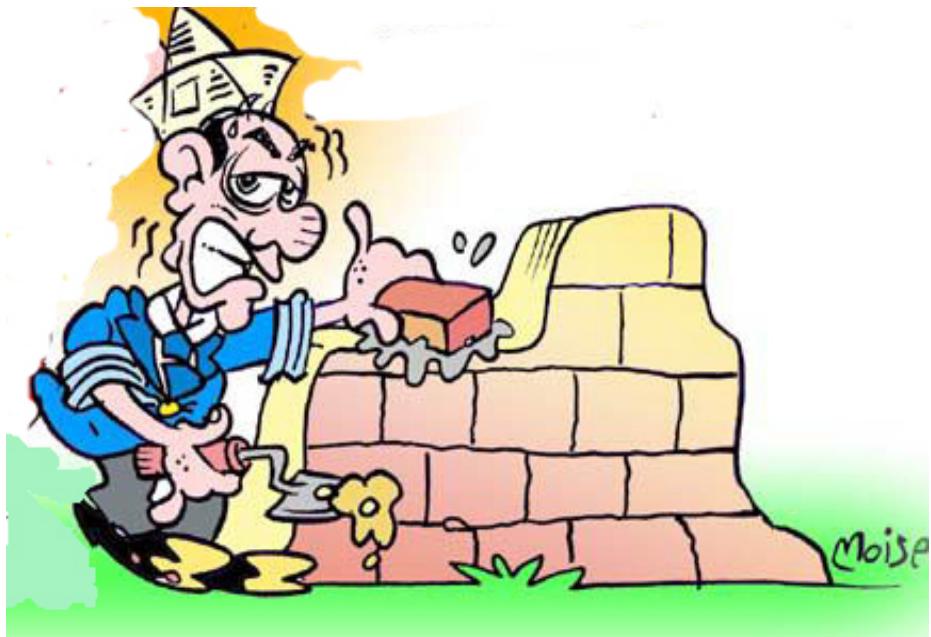
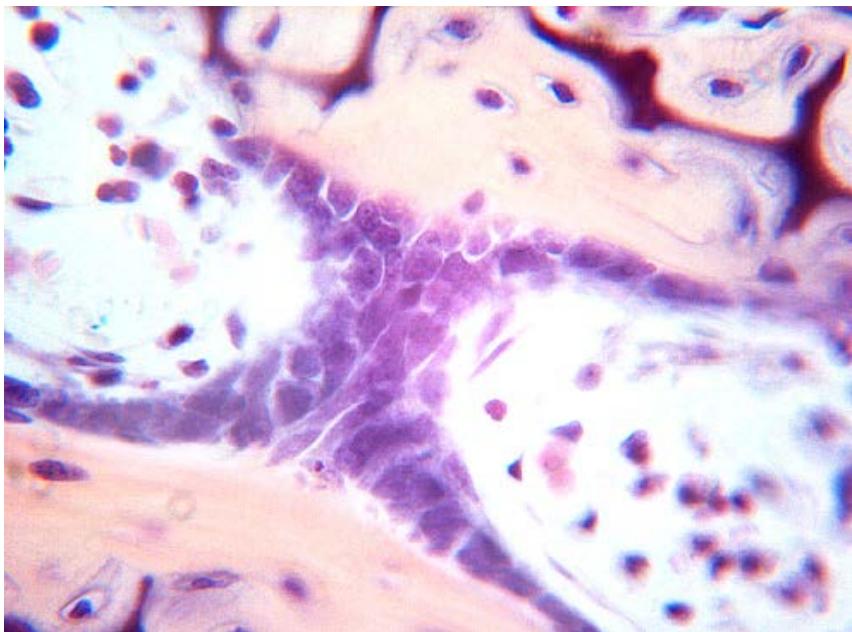
M-CSF=macrophage colony stimulating factor

Adapted from Boyle WJ, et al. *Nature*. 2003;423:337-342.

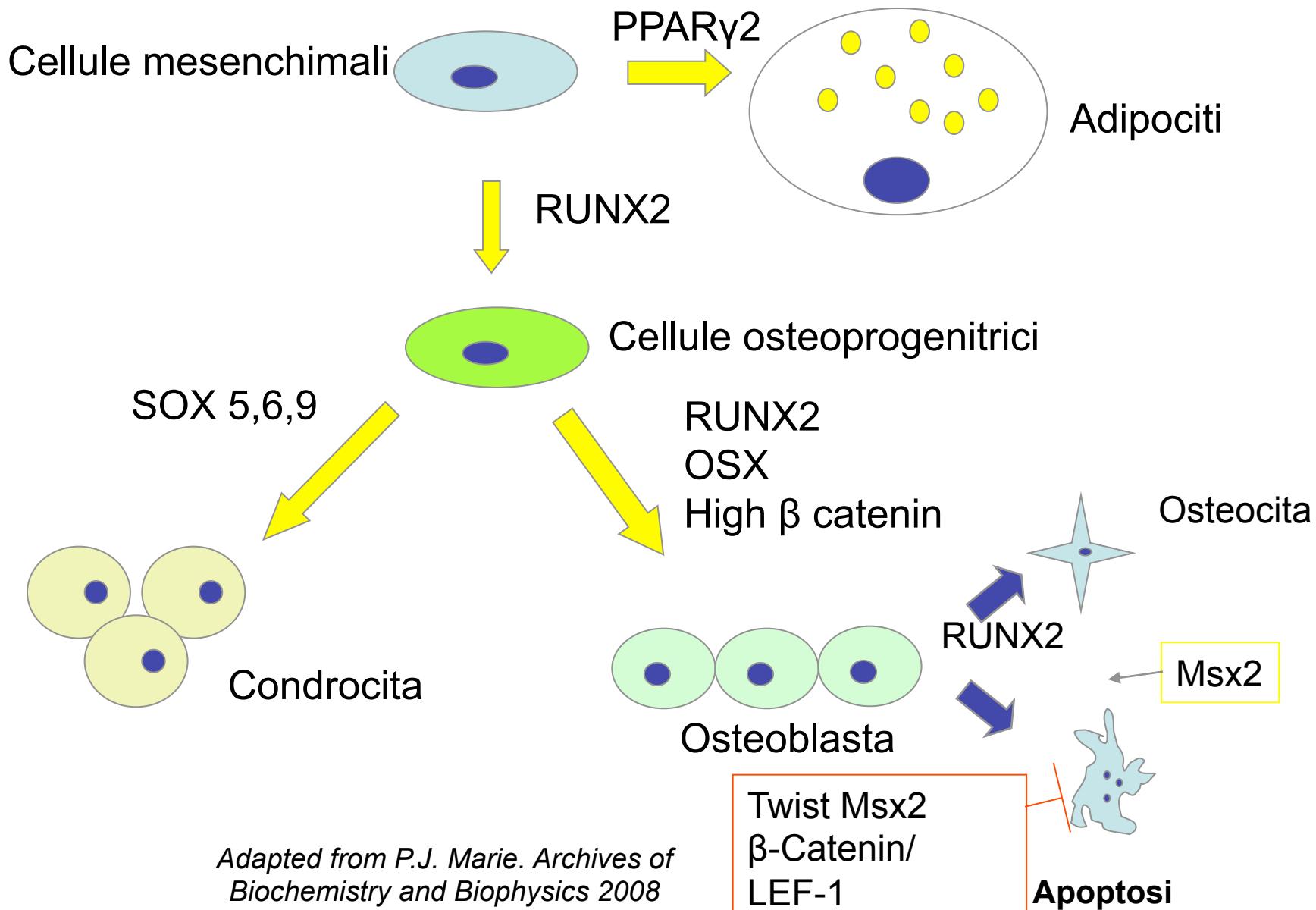
Quando RANKL è in eccesso rispetto ad OPG
si ha un incremento del riassorbimento osseo
che induce osteoporosi



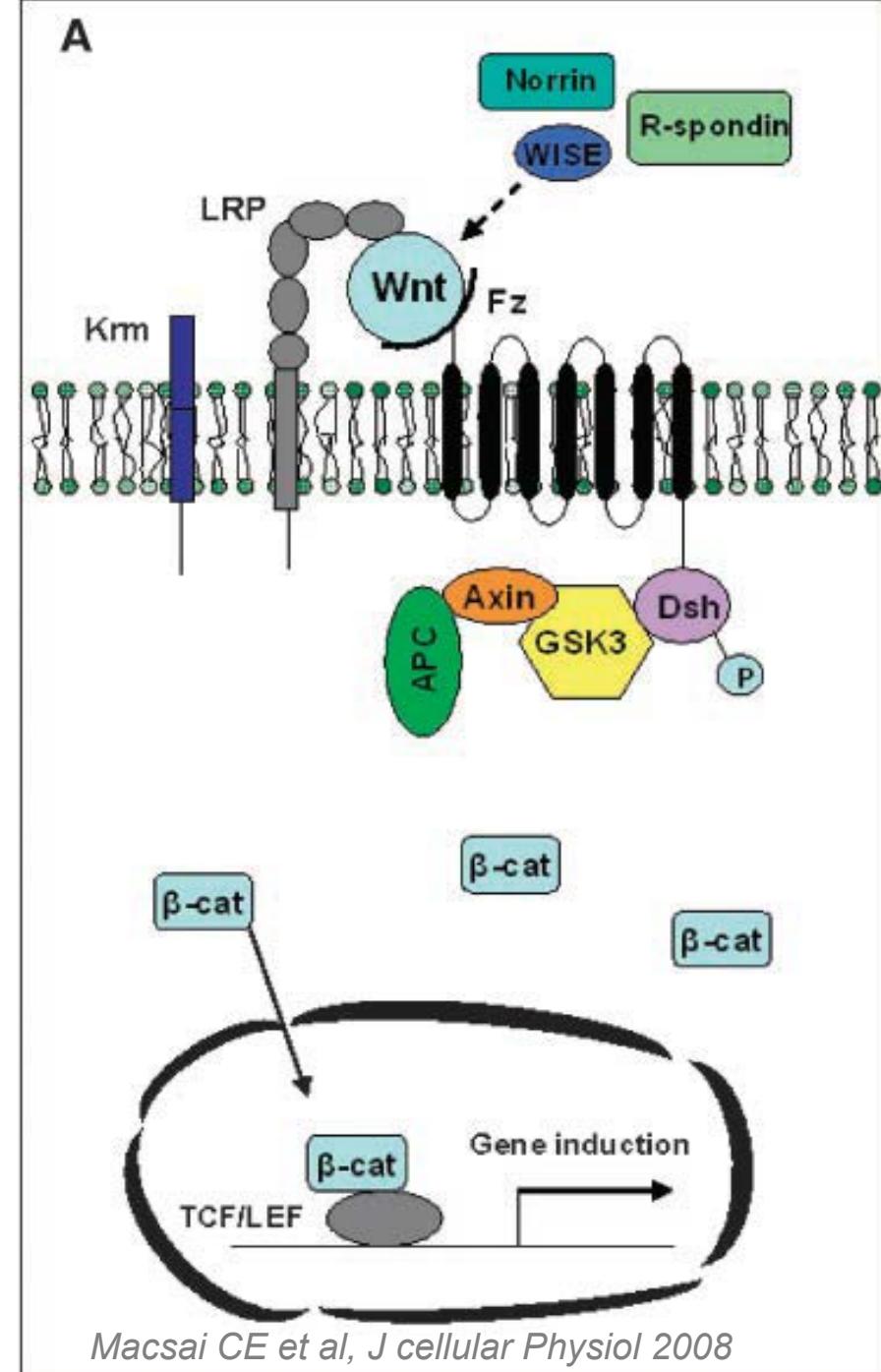
OSTEOBLASTI



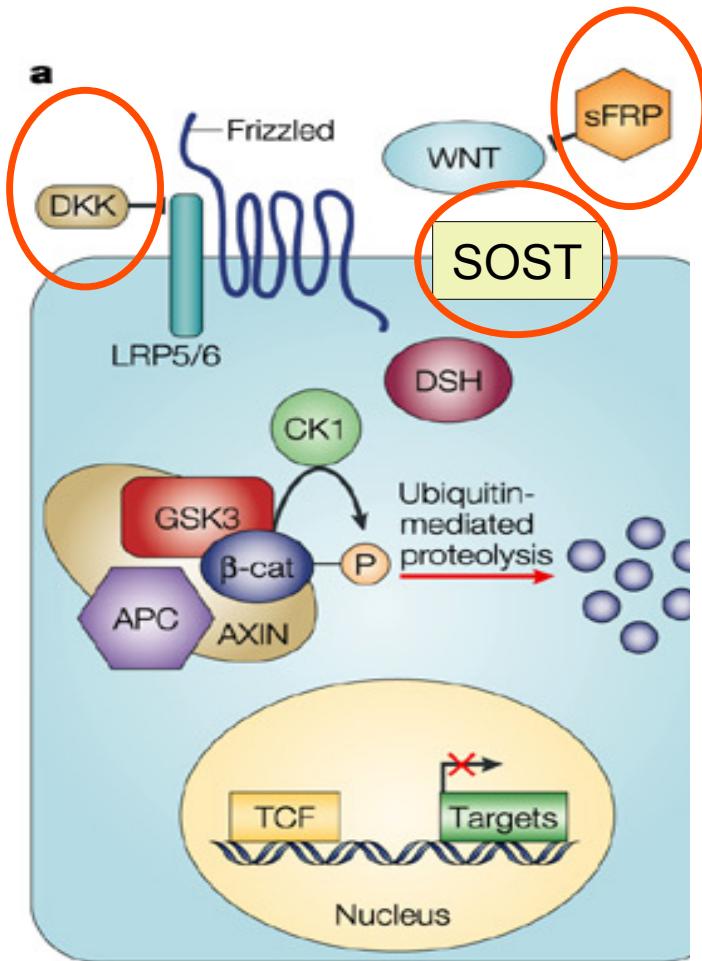
Fattori transcrizionali coinvolti nell'osteoblastogenesi



Via di segnale canonica di WNT/ β catenina



Inibitori della via di segnale di Wnt/β-Catenina

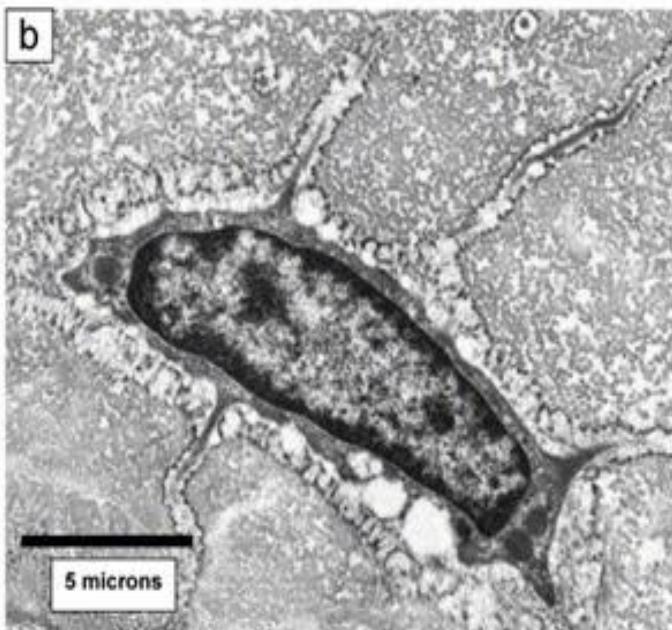
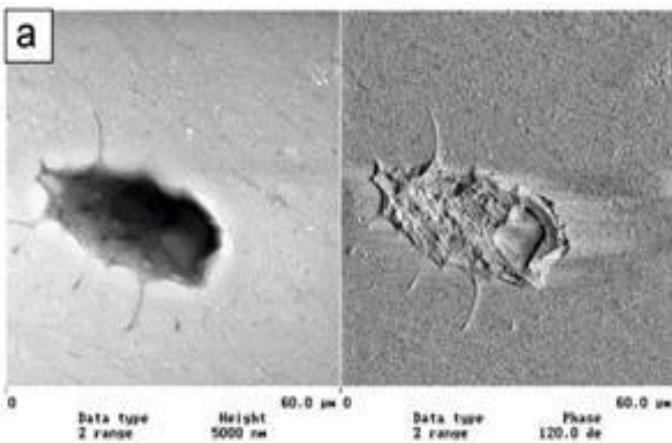


Perdita di funzione di LRP-5:
da origine ad una patologia
autosomica recessiva (OPPG)
caratterizzata da una massa
ossea molto bassa e con fratture
e deformazioni scheletriche

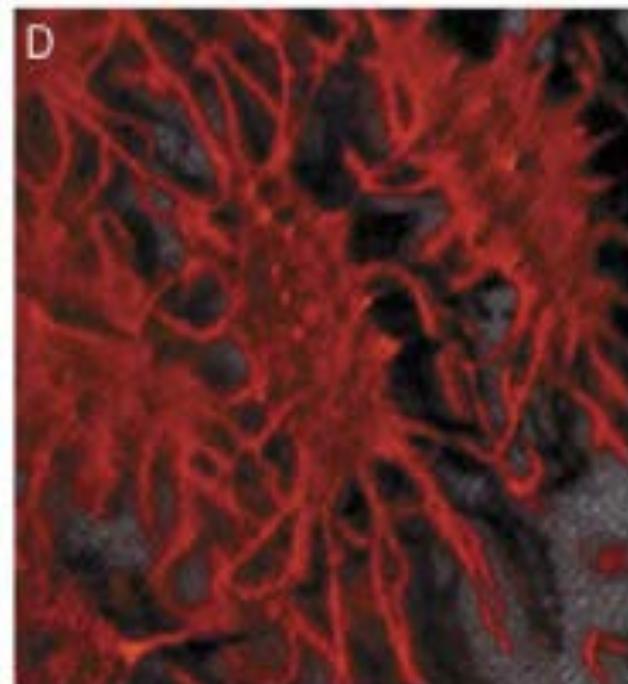
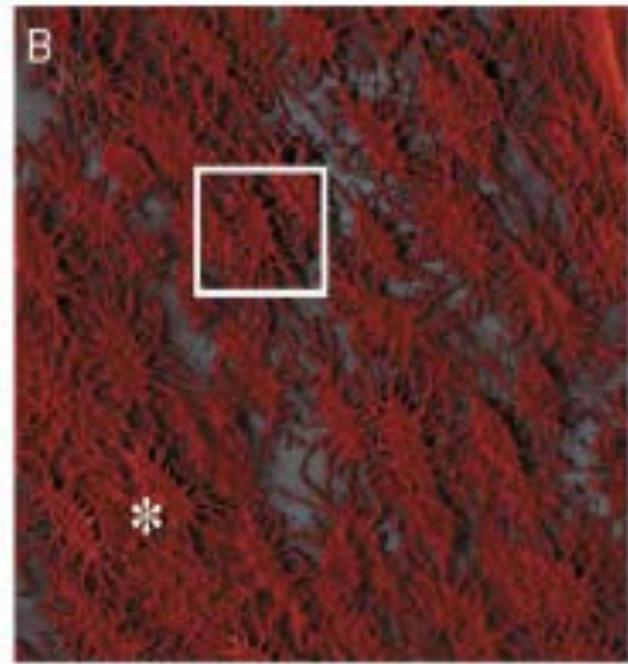
Aumento di funzione di LRP-5:
da origine ad una patologia
autosomica di elevata massa
ossea (HBM)

Perdita di funzione di SOST:
da origine alla malattia di Van
Buchem ed alla sclerostosi per
un aumento di funzione di Wnt

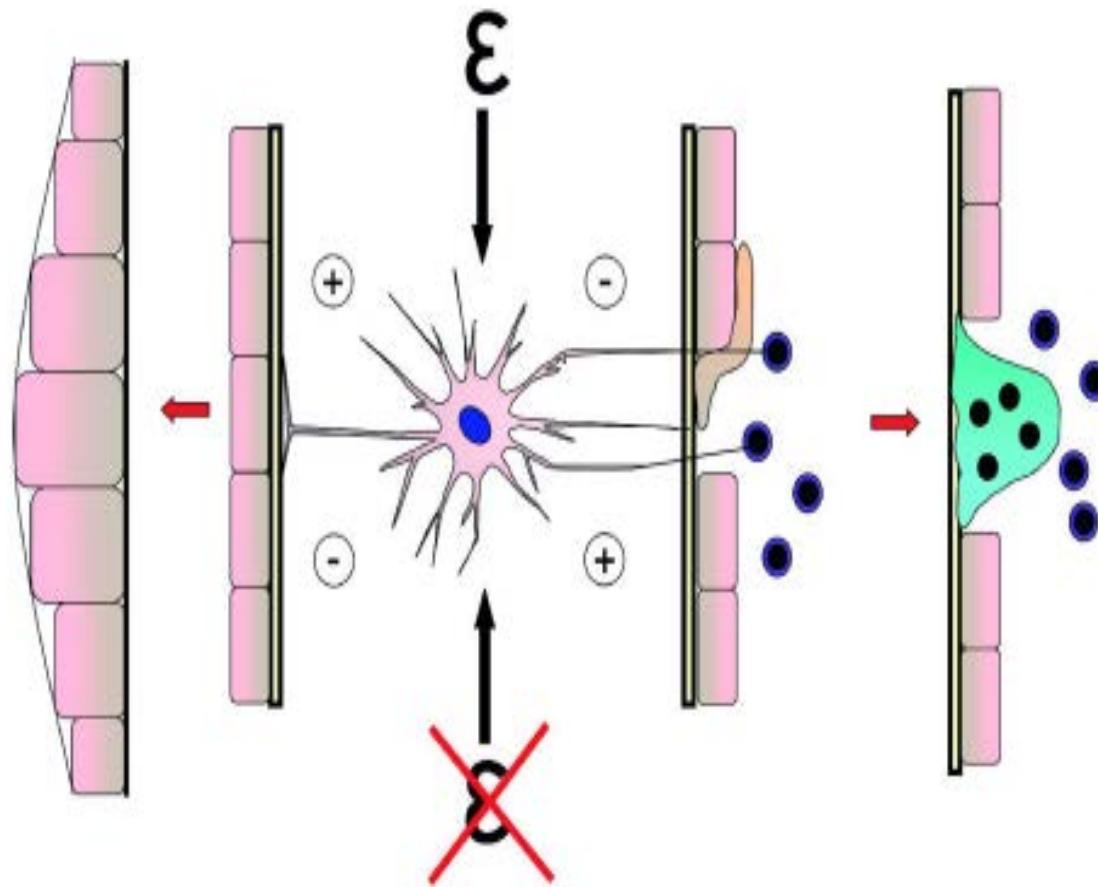
OSTEOCITI



Canaliculari

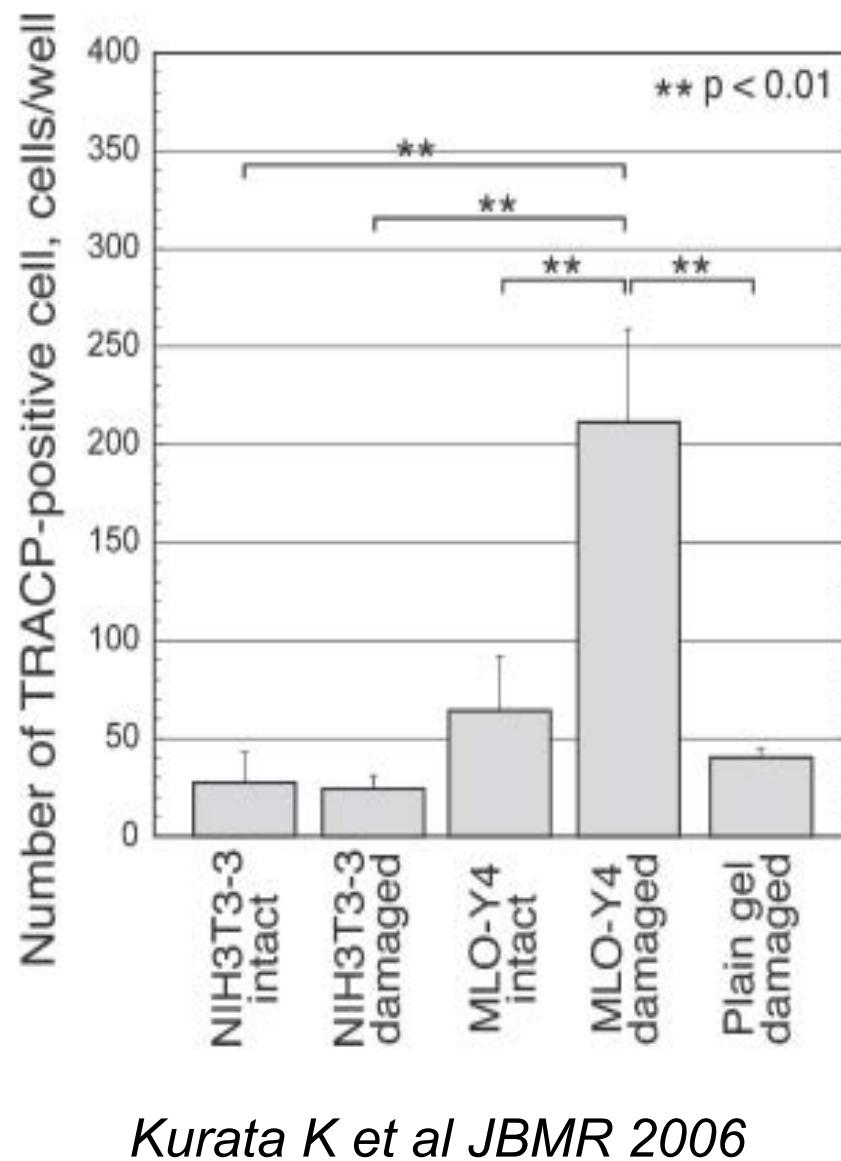
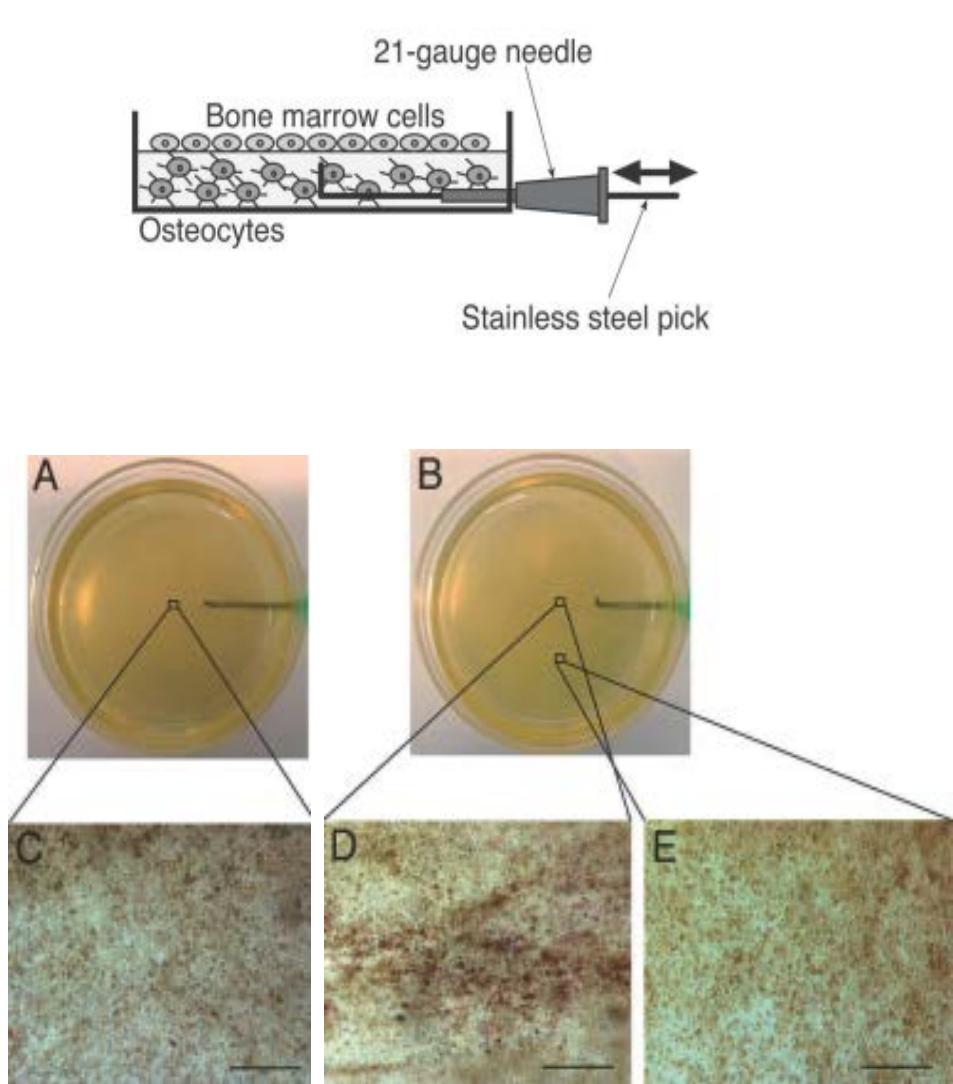


OSTEOCITI COME MECCANO SENSORI?

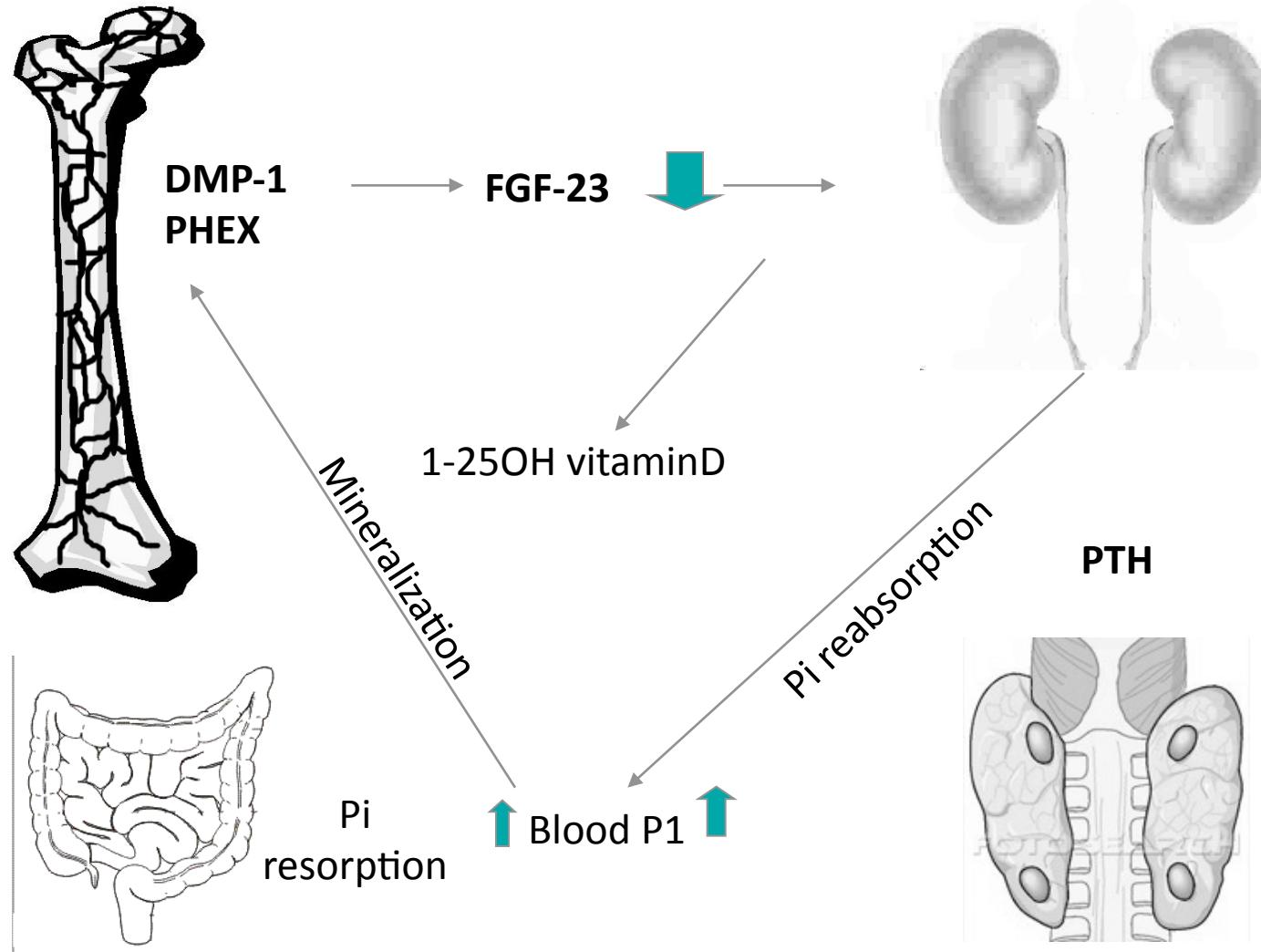


Bonewald L. Ann New Acc Science 2008

OSTEOCITI E CONTROLLO DEL RIASSORBIMENTO OSSEO



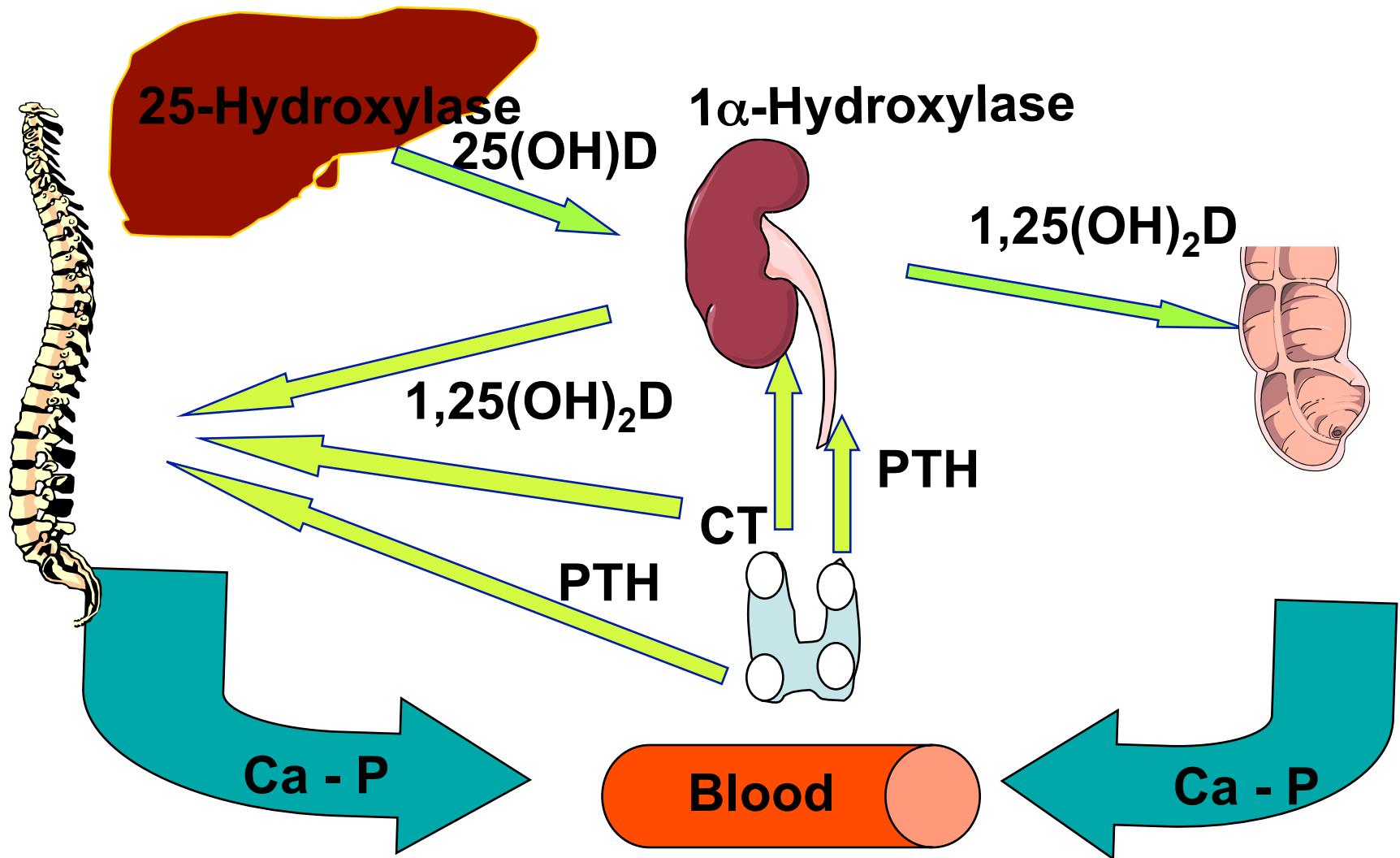
OSTEOCITI E CONTROLLO DEL TURNOVER OSSEO

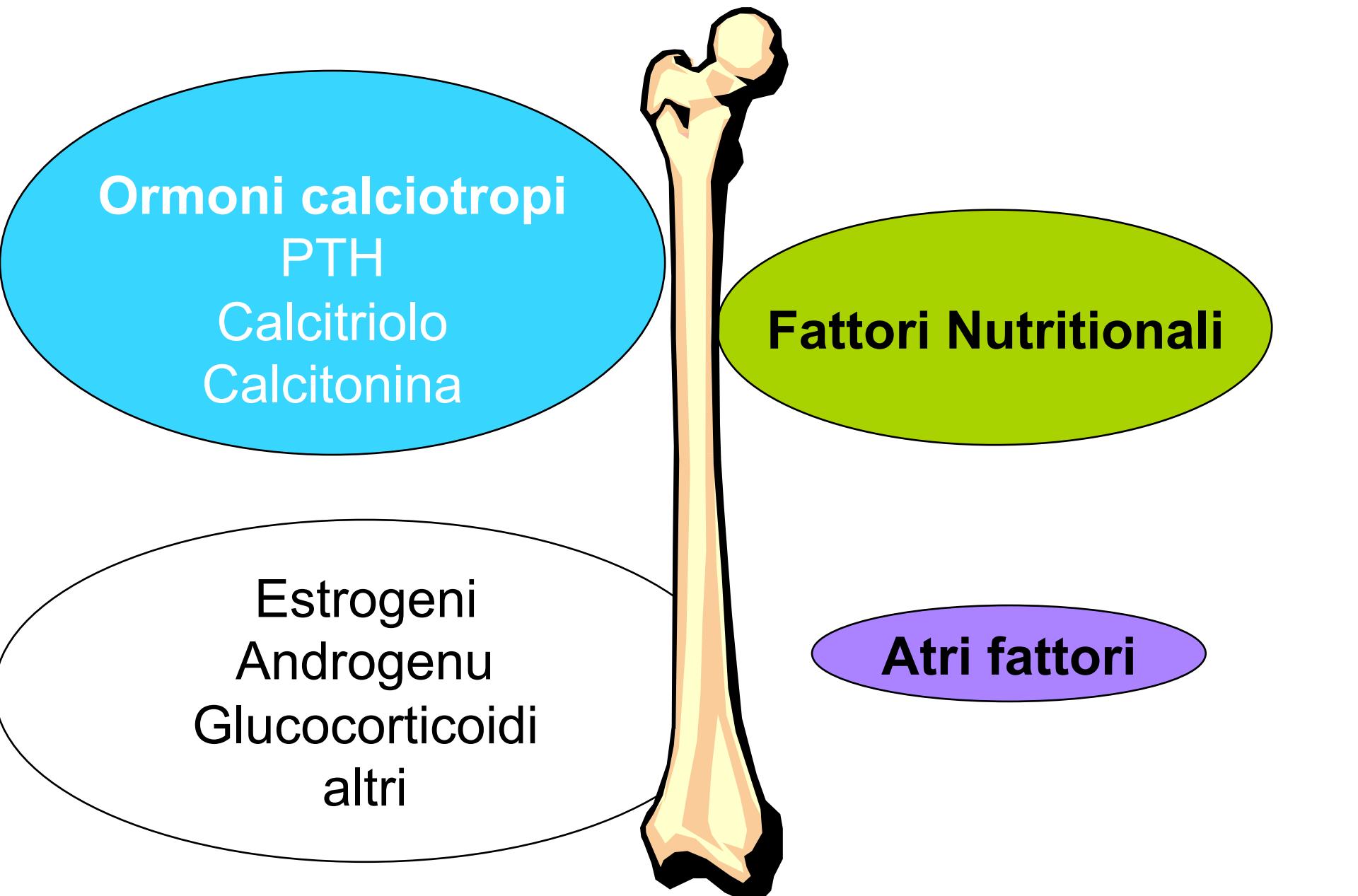


AGENDA

- Turnover e cellule ossee
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- Conclusioni

Metabolismo minerale





Ormoni calciotropi

PTH

Calcitriolo

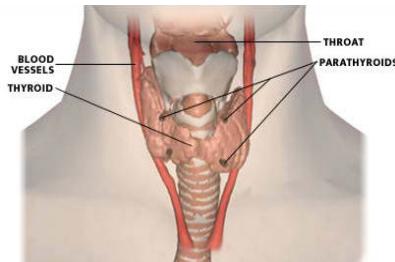
Calcitonina

Estrogeni
Androgeni
Glucocorticoidi
altri

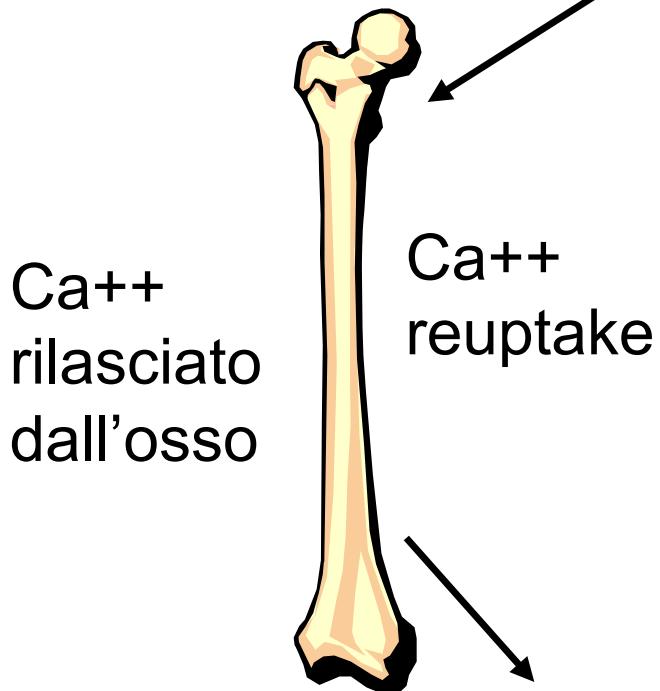
Fattori Nutritionali

Atri fattori

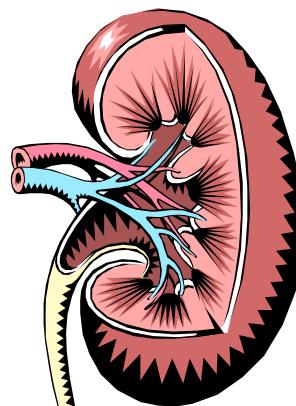
PTH



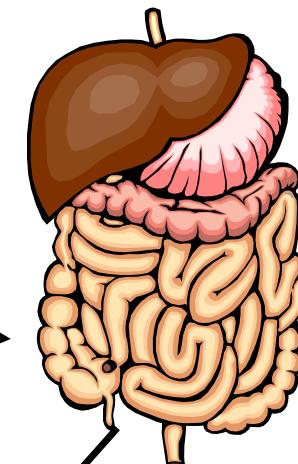
PTH



PTH



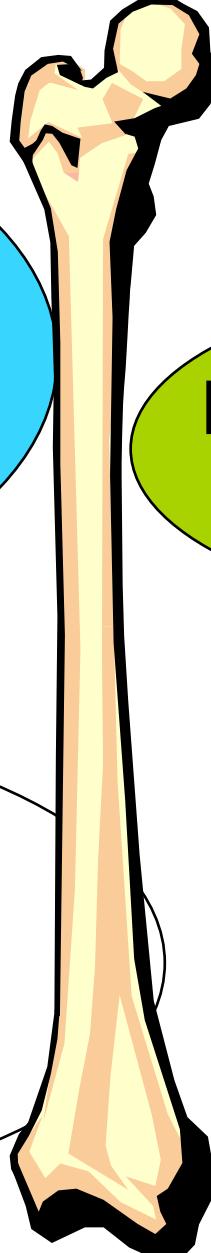
$1,25(OH)_2 D_3$ sintesi



Ca^{++} and PO_4^{--}

Assorbimento
intestinale

**Omeostasi sierica di
calcio e fosfato**



Ormoni calciotropi

PTH

Calcitriolo

Calcitonina

Fattori Nutritionali

Estrogeni
Androgeni
Glucocorticoidi
altri

Atri fattori

ESTROGENI ED OSSO

**INIBIZIONE
DELL'OSTEOCLASTOGENESI**

**INIBIZIONE
DELLA ATTIVITA'
OSTEOCLASTOGENESI**

**INIBIZIONE DEL
RIASSORBIMENTO OSSEO**

**INDUCONO NUOVA
FORMAZIONE OSSEA**

INDIRETTAMENTE
• VITAMINA D
• PTH

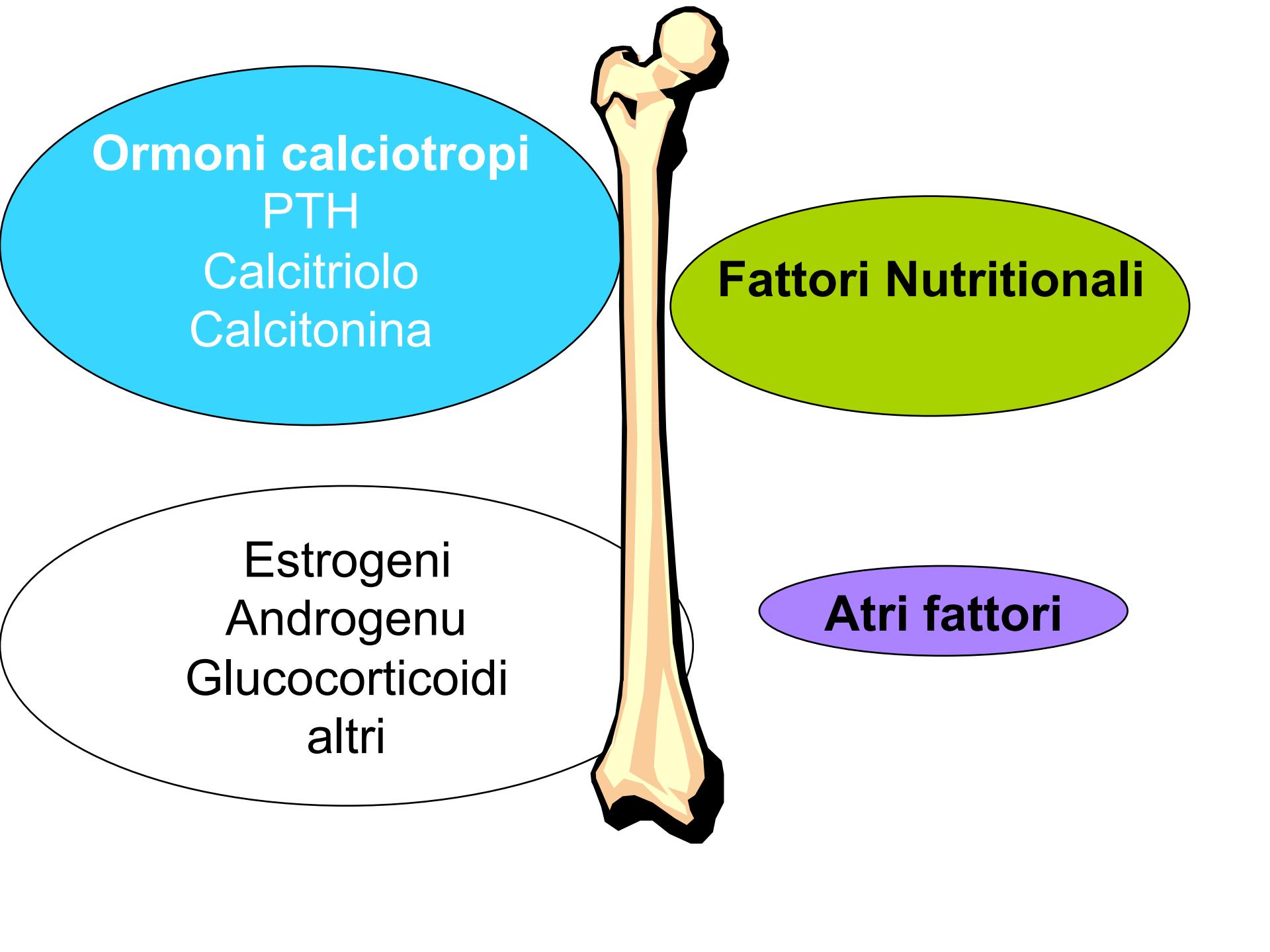
ANDROGENI E OSSO

**INIBIZIONE
DELLA ATTIVITA'
OSTEOCLASTOGENESI**

**INIBIZIONE DEL
RIASSORBIMENTO OSSEO**

**INCREMENTO
DELLA MASSA
MUSCOLARE**

**INDUCONO NUOVA
FORMAZIONE OSSEA**



A central diagram shows a human bone, likely a femur, oriented vertically. The upper portion of the bone is yellow, representing trabecular bone, while the lower portion is black, representing cortical bone. Four colored ovals are positioned around the bone, each containing a list of factors:

- Ormoni calciotropi** (Calcium-regulating hormones) in a blue oval: PTH, Calcitriolo, Calcitonina.
- Fattori Nutritionali** (Nutritional factors) in a green oval.
- Atri fattori** (Other factors) in a purple oval.
- Estrogeni, Androgeni, Glucocorticoidi, altri** (Estrogens, Androgens, Glucocorticoids, others) in a white oval.

PTH

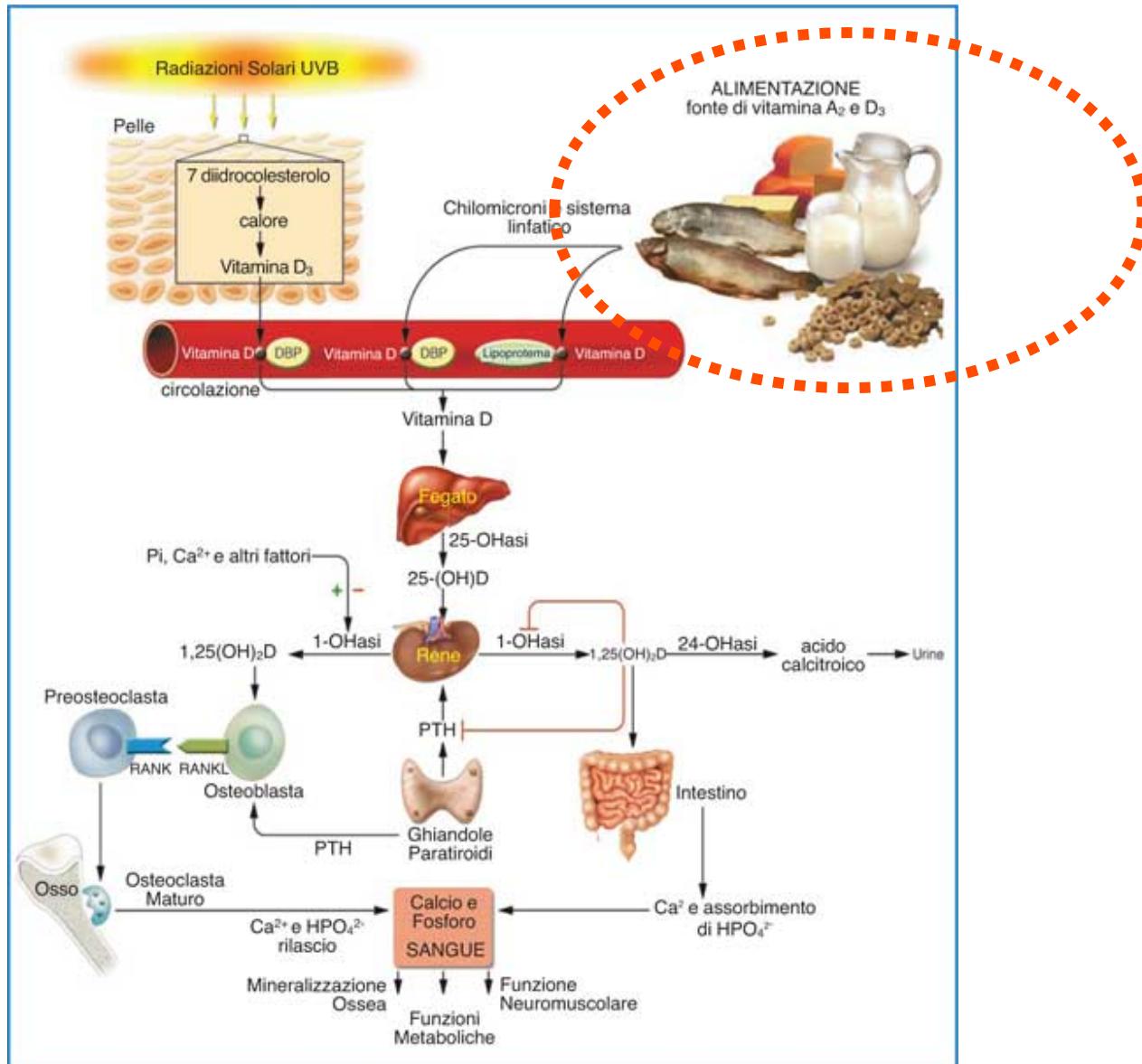
Calcitriolo
Calcitonina

Fattori Nutritionali

Atri fattori

Estrogeni
Androgeni
Glucocorticoidi
altri

METABOLISMO DELLA VITAMINA D



Alimento	Contenuto di vitamina D in UI
Latte	3-40/L
Burro	35/100 g
Yogurt	89/100 g
Formaggi	12-44/100 g
Funghi shiitake freschi	100/100 g
Funghi shiitake secchi	1660/100 g
Tuorlo d'uovo	20-25/tuorlo
Gamberetti	152/100 g
Fegato di manzo	15-50/100 g
Tonno, sardine, salmone, sgombro in scatola	224-332/100 g
Salmone rosa con lisca in scatola	624/100 g
Salmone, sgombro cotto	345-360/100 g
Sgombro dell'atlantico (crudo)	360/100 g
Aringa dell'atlantico (cruda)	1628/100 g
Aringa affumicata	120/100 g
Aringa sottoaceto	680/100 g
Merluzzo	44/100 g
Olio di fegato di merluzzo	175/g – 1360/cucchiaio

Fonte Misra M et al. Pediatrics 2008; 122: 398-417

I livelli sierici di vitamina D e la sua produzione diminuiscono con l'età^{1,2}

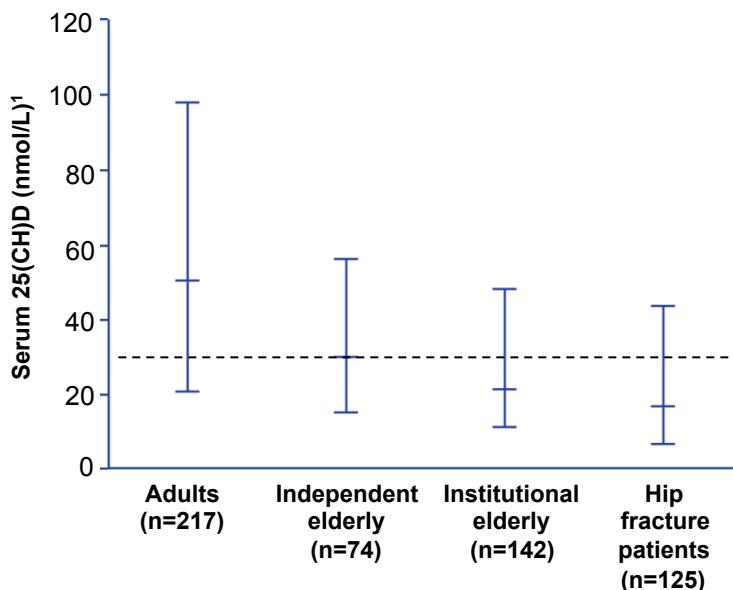


FIG. 4. Serum 25(OH)D (median, 5th-95th percentile) in 250 healthy adults (blood donors), 74 independent elderly subjects, 142 institutionalized elderly patients, and 125 patients with hip fracture. The samples in all groups were collected throughout the year. All measurements were performed by HPLC followed by competitive protein binding assay (data from Refs. 37,56,85). [Reproduced with permission from M. E. Ooms: Thesis. Vrije Universiteit Amsterdam, 1994 (105).]

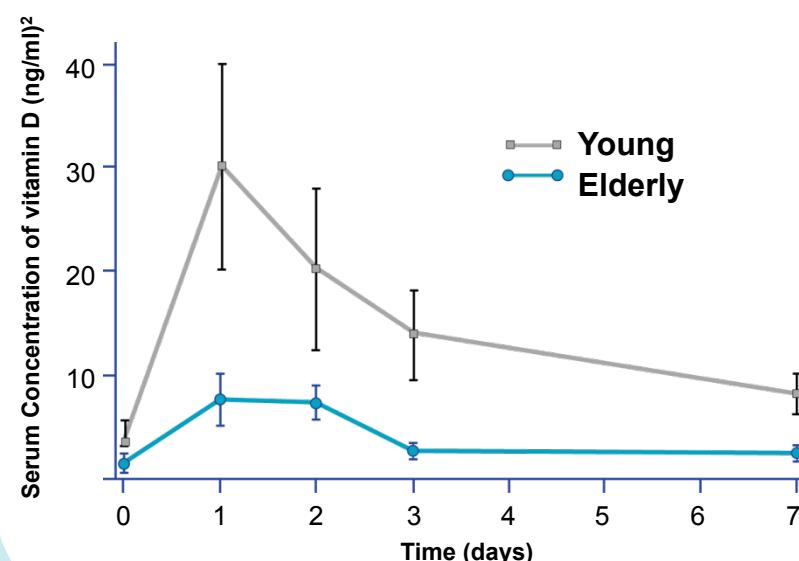
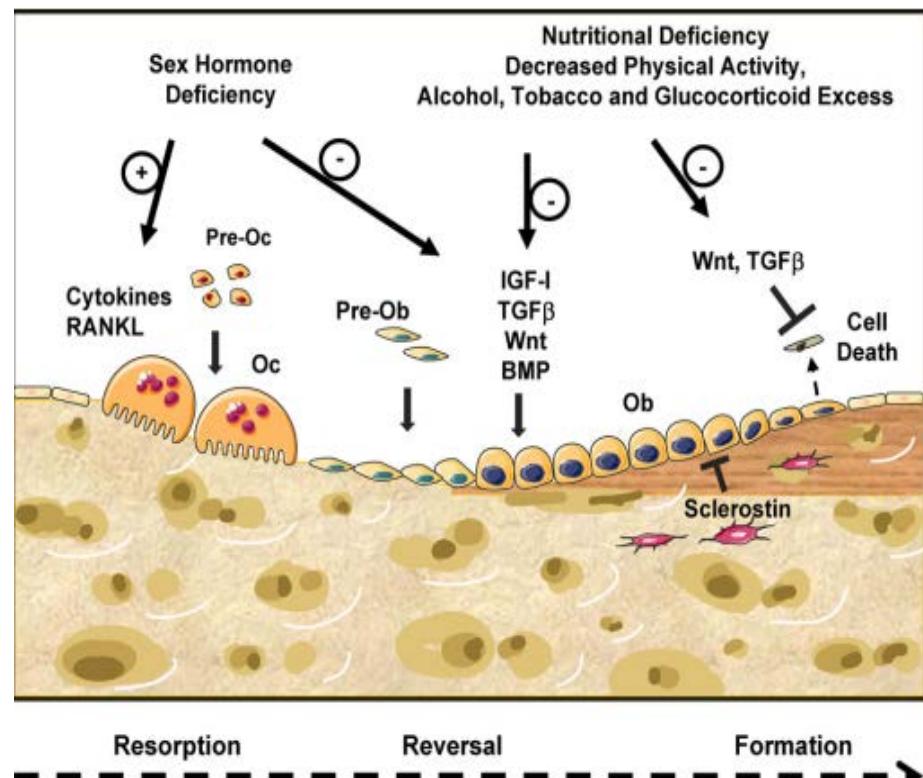
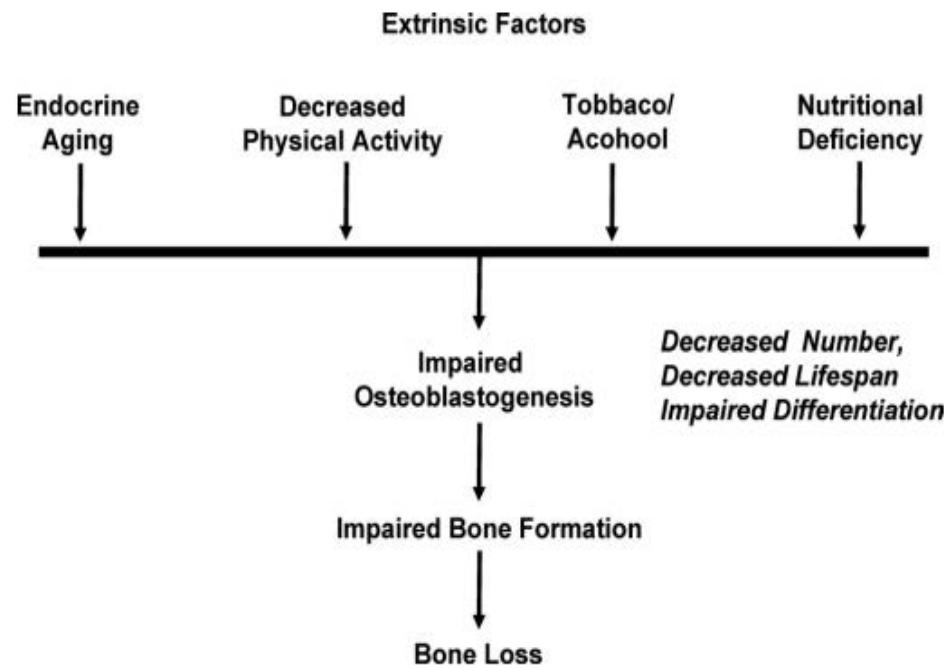


FIG. 2. Serum vitamin D₃ concentration after total body exposure to artificial sunlight (UV 260–360 nm) in six white young adults (20–30 yr) and six white elderly people (62–80 yr) with skin type III. Serum vitamin D₃ concentration was measured for 7 d. The area under the curve for serum vitamin D₃ suggests that the production of vitamin D₃ in the skin in the elderly is about 25% of that in young adults. [Reproduced with permission from M. F. Holick *et al.*: Lancet 2:1104–1105, 1989 (35). © The Lancet Ltd.]

Scheletro ed invecchiamento: fattori estrinseci



Marie PJ. and Kassem M, JCEM 2011

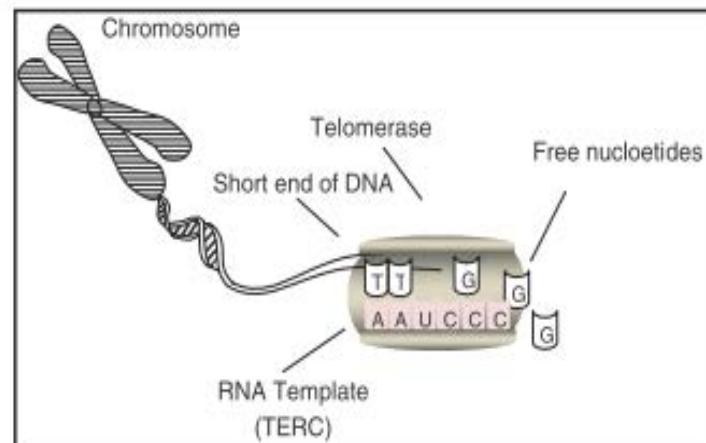
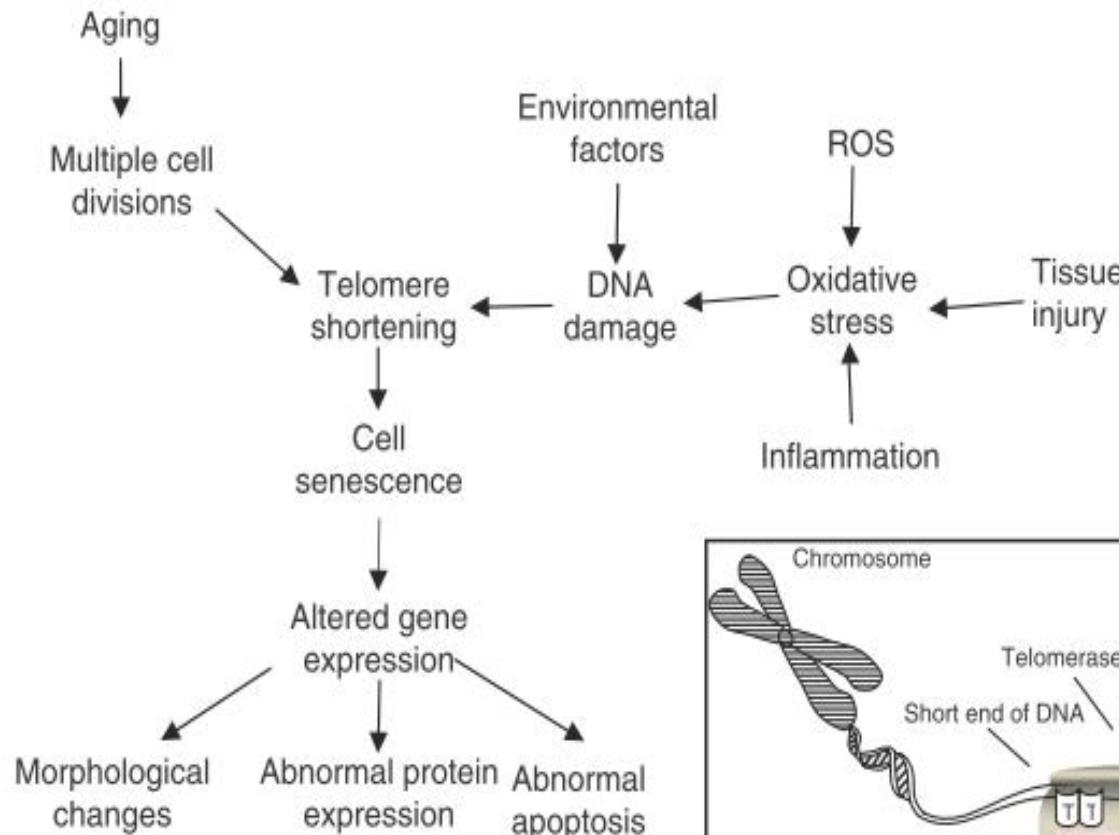
AGENDA

- Turnover e cellule ossee
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- Cellule scheletriche ed invecchiamento
- Osso ed altri sistemi
- Conclusioni

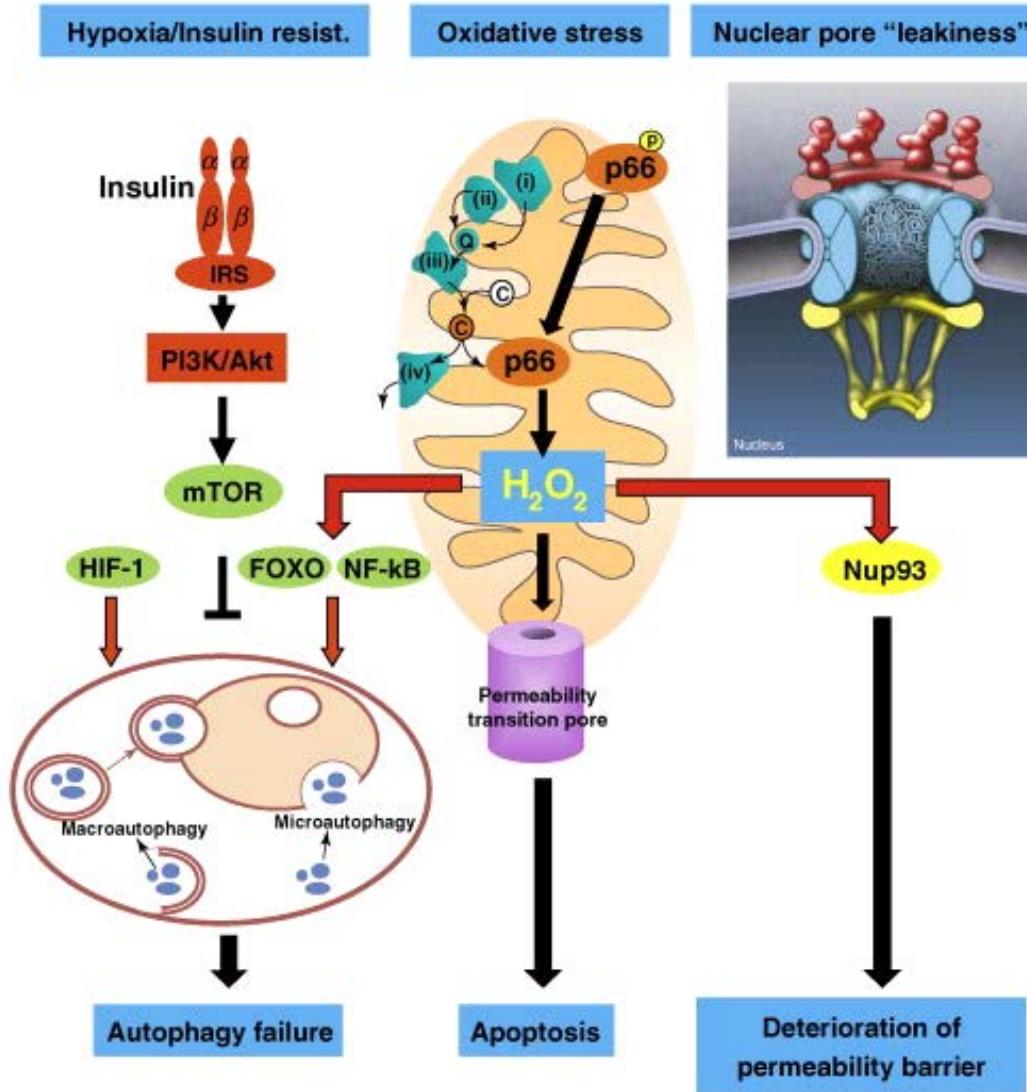
LIFESPAN DELLE CELLULE OSSEE

Cell type	Lifespan
Osteoclasts	1-25 days
Osteoblasts	1-200 days
Lining cells	1-10 years
Osteocytes	1-50 years

Invecchiamento e cellule ossee

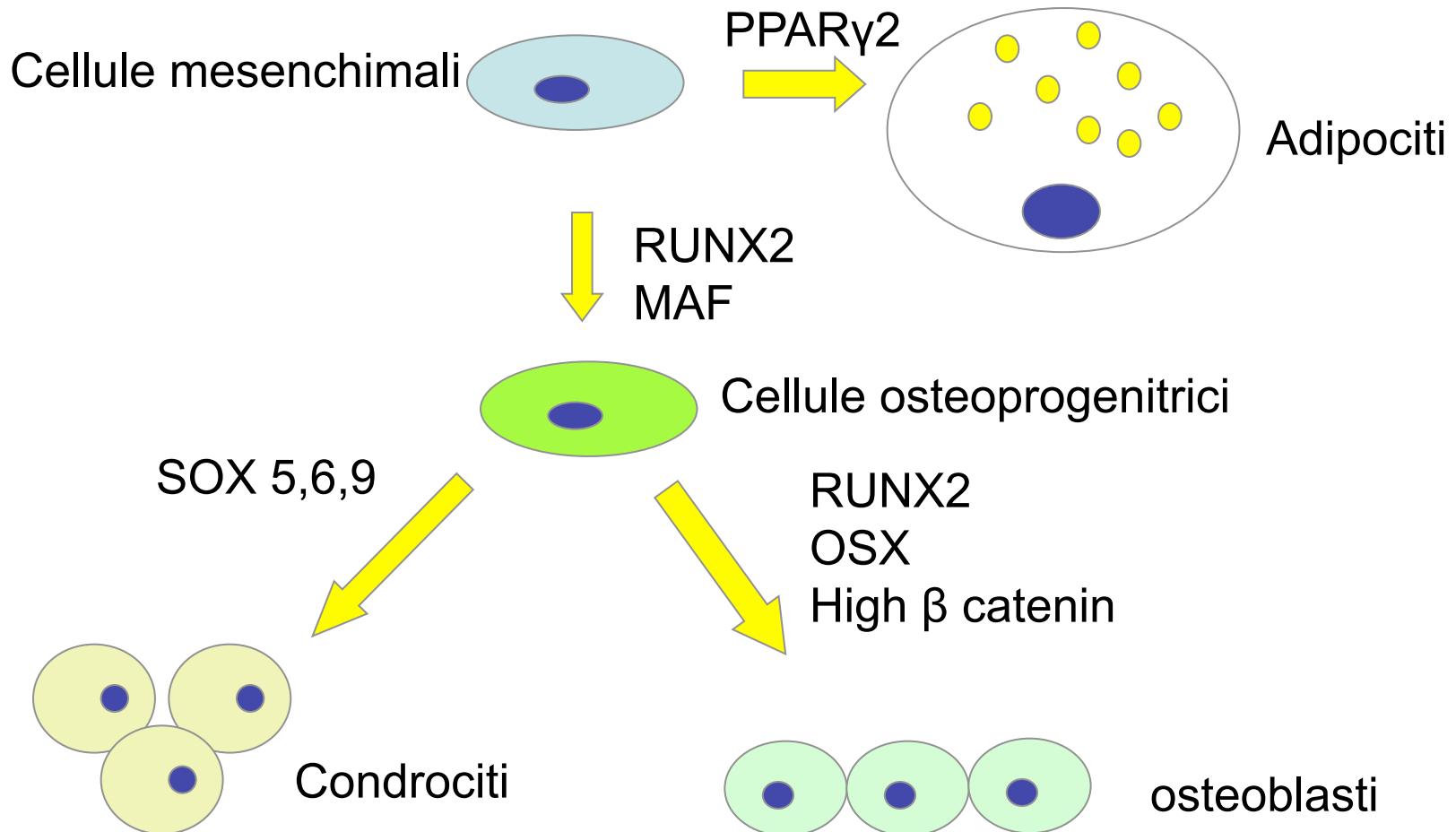


Invecchiamento e morte degli osteociti



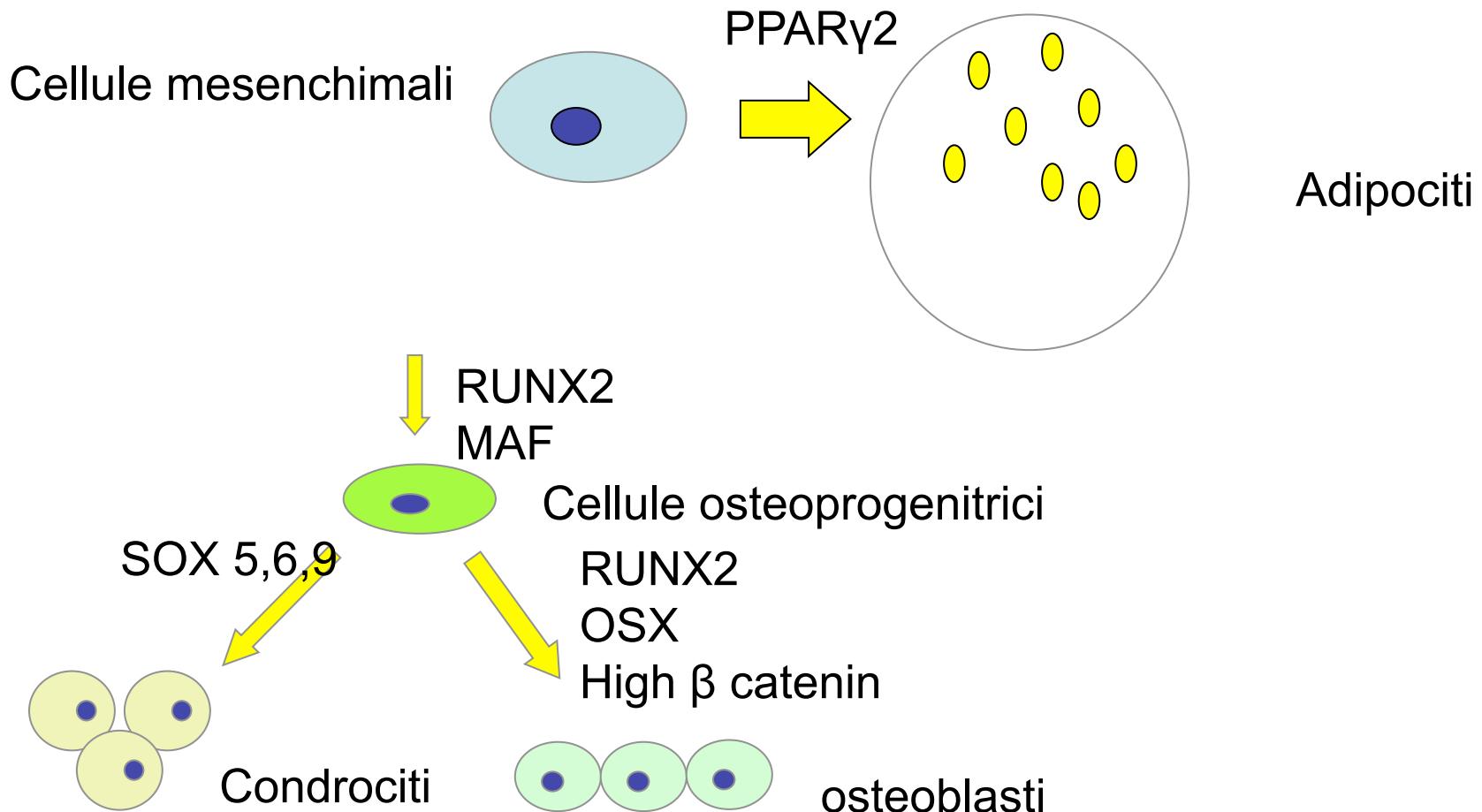
TRENDS in Endocrinology & Metabolism

Fattori transcrizionali coinvolti nell'osteoblastogenesi



Adapted from P.J. Marie. Archives of Biochemistry and Biophysics 2008

Fattori transcrizionali coinvolti nell'osteoblastogenesi

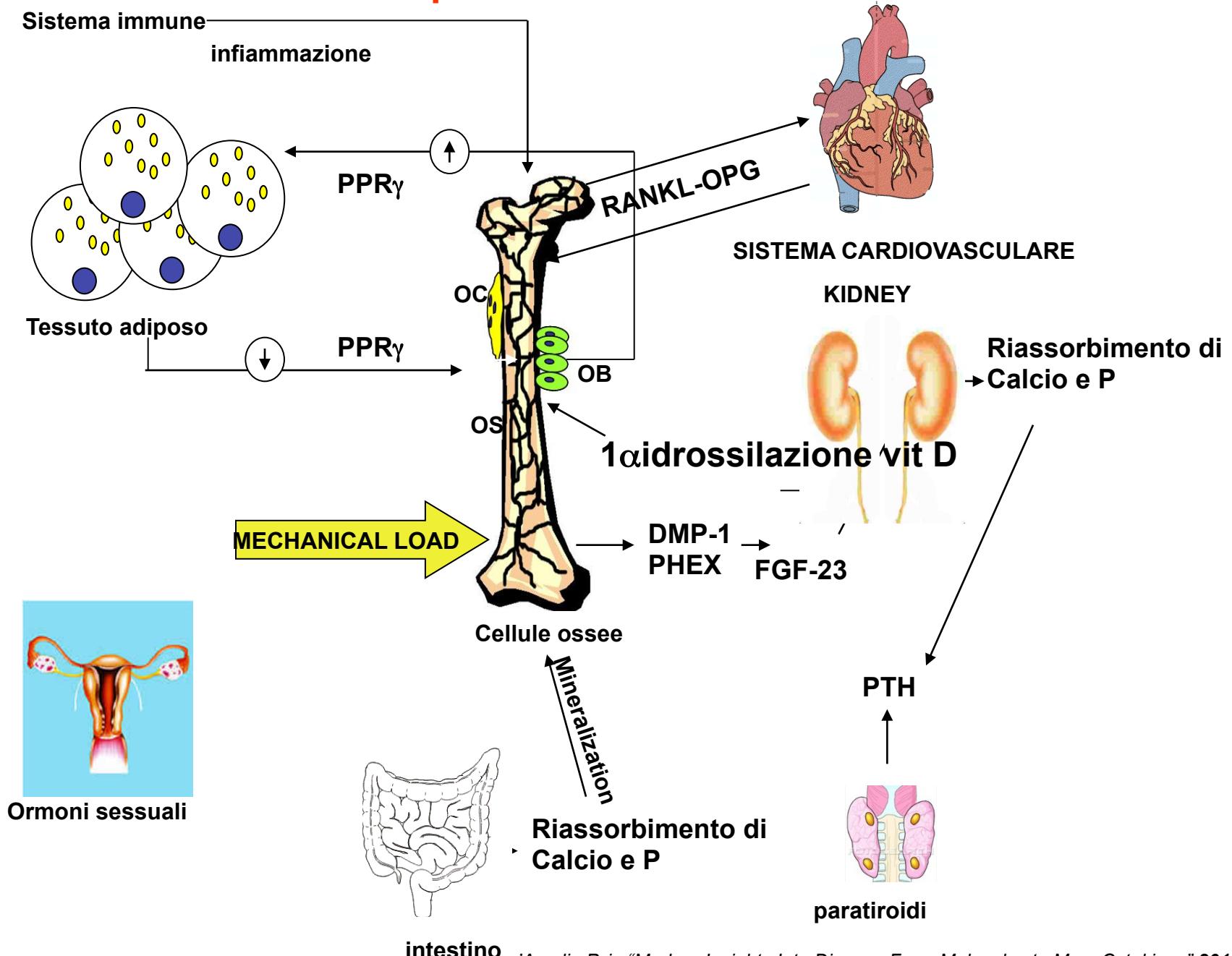


Adapted from P.J. Marie. Archives of Biochemistry and Biophysics 2008

AGENDA

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Influenze multiple sullo scheletro



AGENDA

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- Conclusioni

CONCLUSIONI

- L'osso è un tessuto vivo ed attivo in continuo rinnovamento
- Lo scheletro è il bersaglio di diversi ormoni
- Patologie di organi diversi possono alterare lo scheletro
- I processi di invecchiamento coinvolgono lo scheletro agendo sia su fattori estrinseci che intrinseci allo stesso

