

17-20
Dicembre
2025
Napoli

70^o C O N G R E S S O
N A Z I O N A L E
S I G G
LIBERI E LONGEVI

Università degli
Studi di Napoli
Federico II
Polo Didattico
di **SCAMPIA**



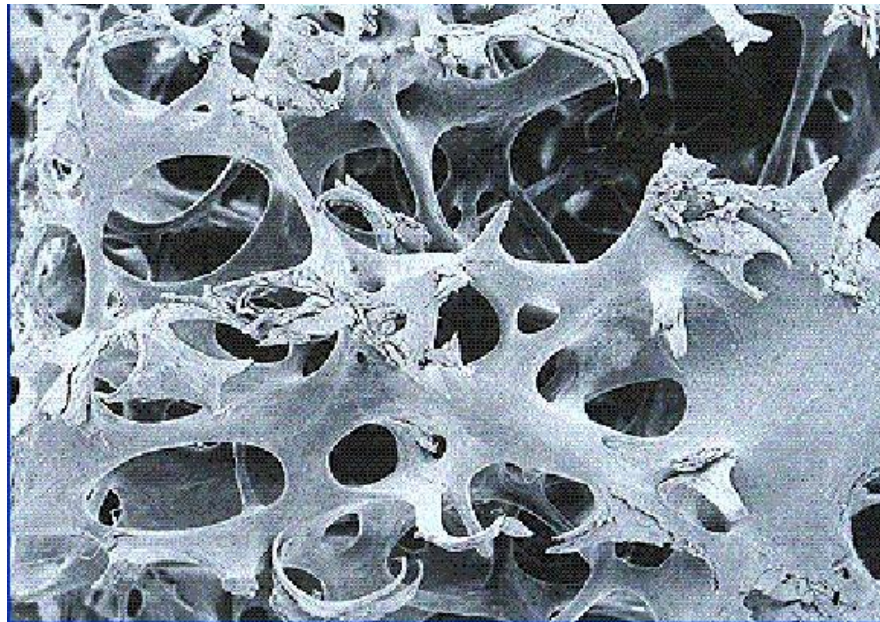
Focus su osteoporosi: meccanismi patogenetici e target terapeutici

Giuseppe Sergi

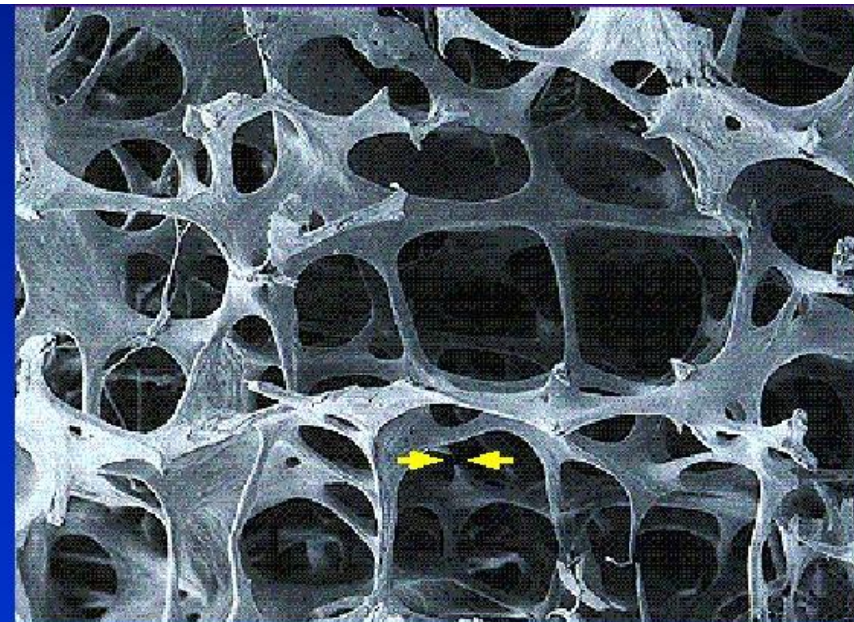
Dipartimento di Medicina - Clinica Geriatrica - Università di Padova

Osteoporosi

“...malattia scheletrica generalizzata..., caratterizzata da una riduzione della massa ossea e da un danno microarchitetturale del tessuto osseo, cui conseguono un **aumento della fragilità dello scheletro e una maggiore suscettibilità alle fratture**”

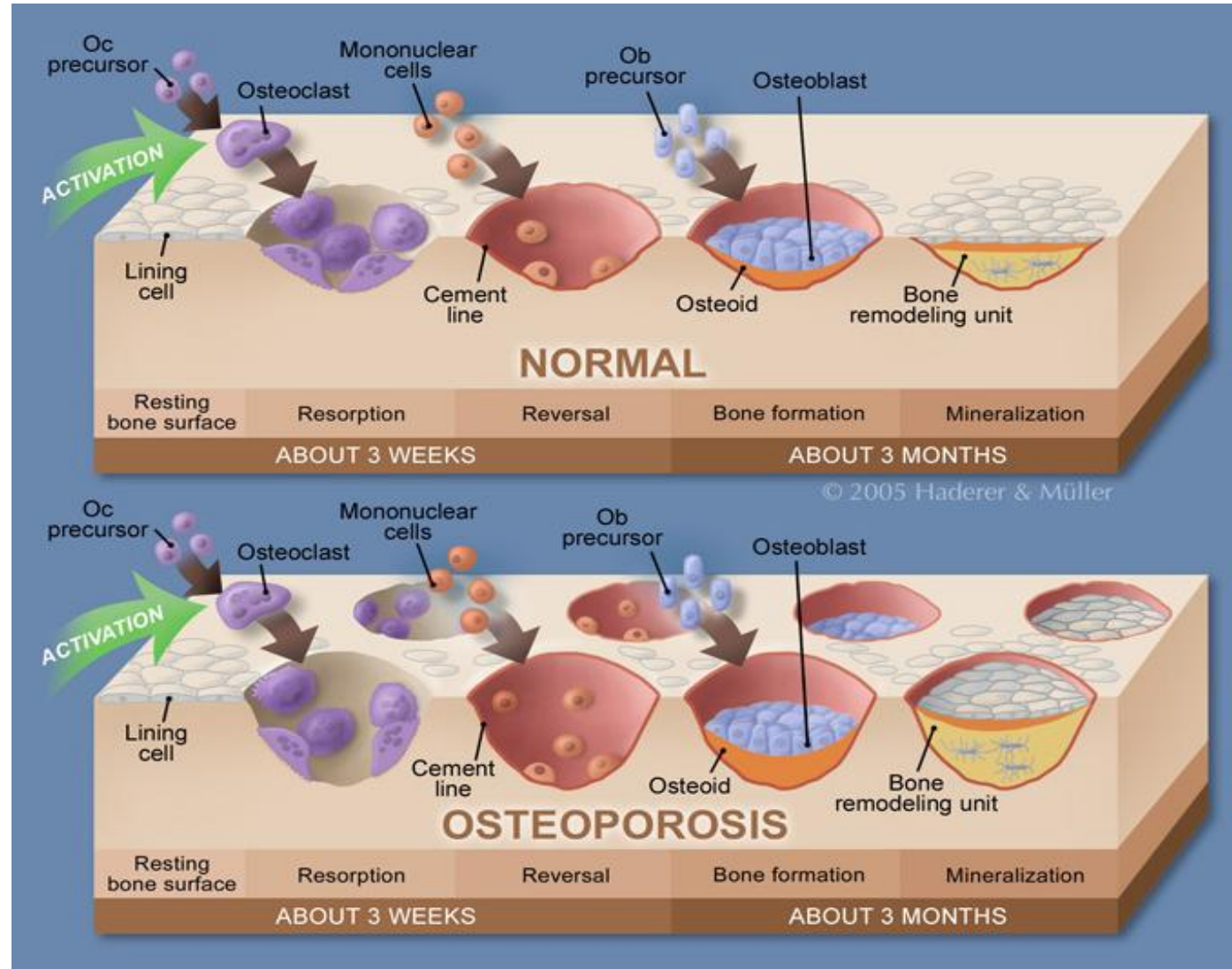


Normale²



Osteoporosi²

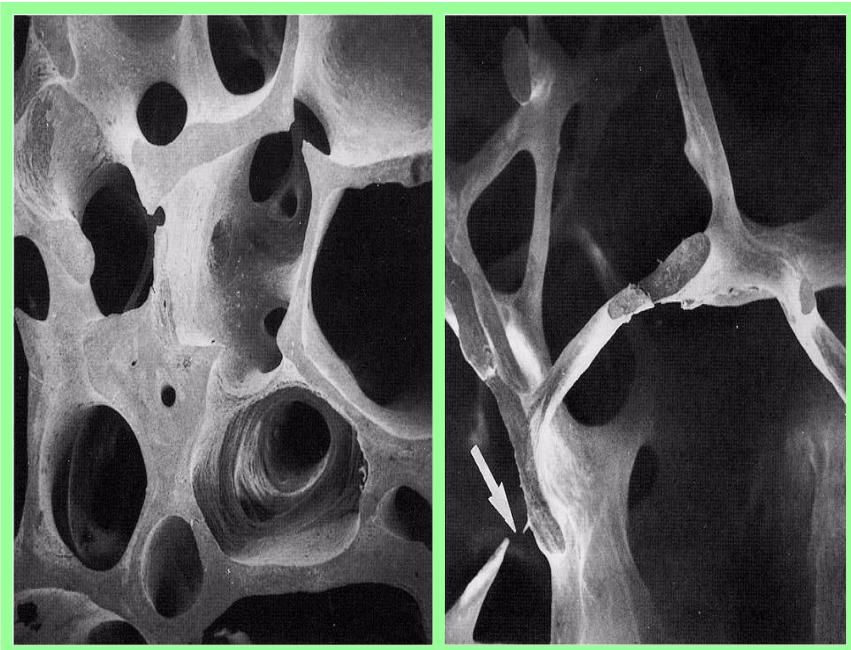
BMU: Bilancio e numero



Osso trabecolare e Corticale

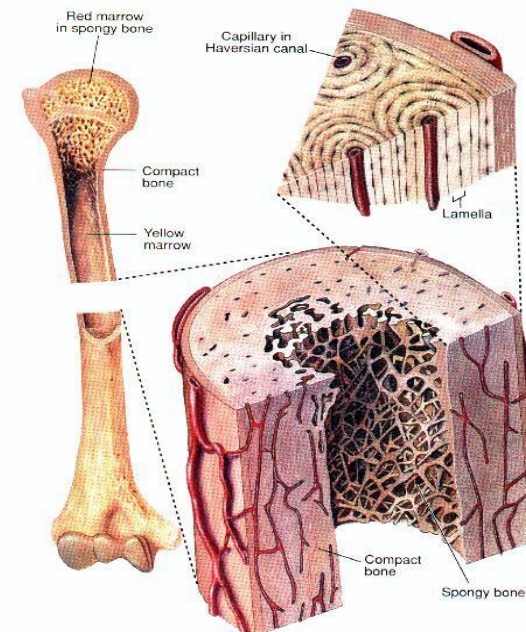
OSSO TRABECOLARE

- circa 12 BMU attive per minuto
- ricambio annuo medio del 25-30%

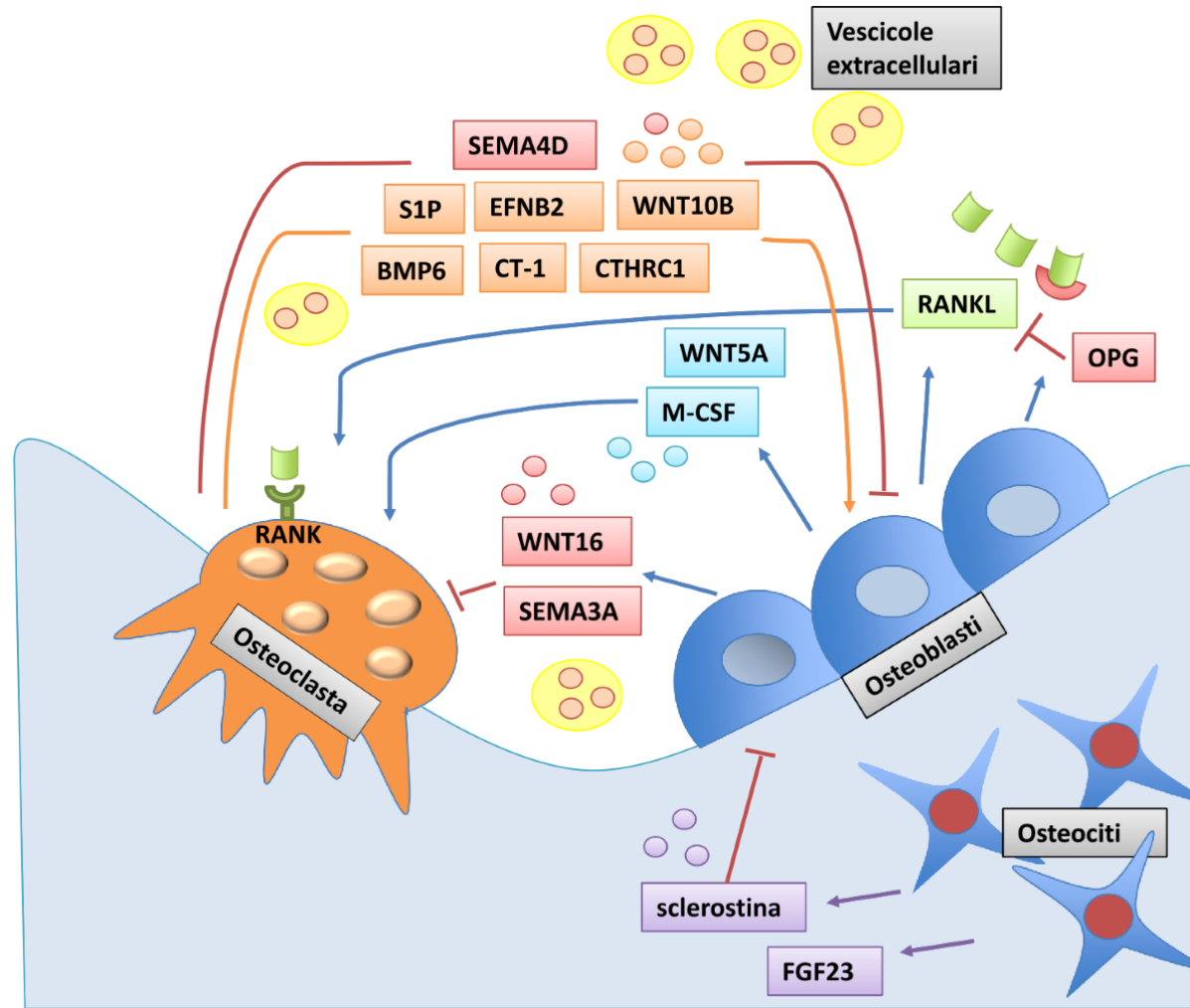


OSSO CORTICALE

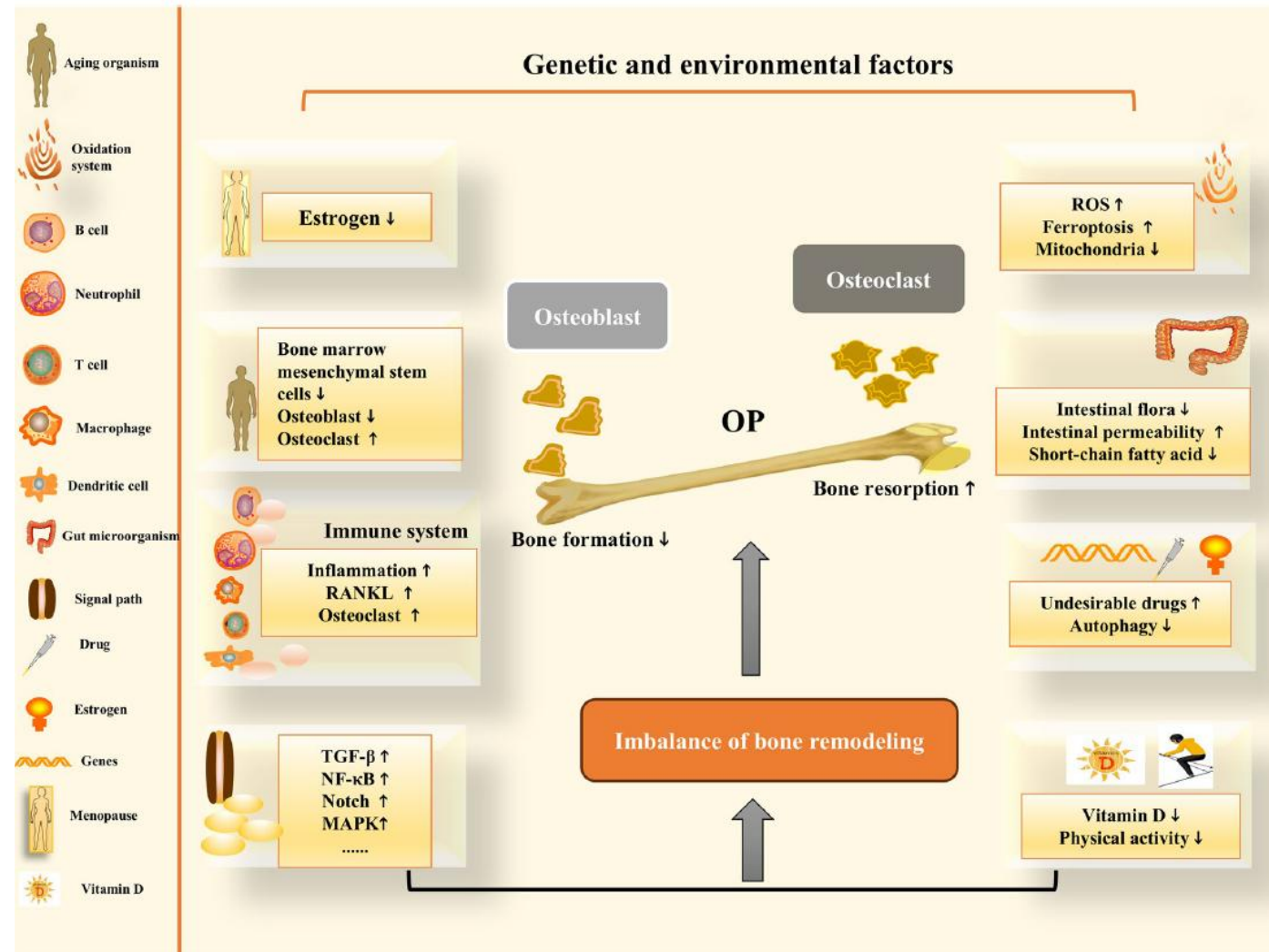
- circa 3 BMU attive per minuto
- ricambio annuo medio del 2-3%



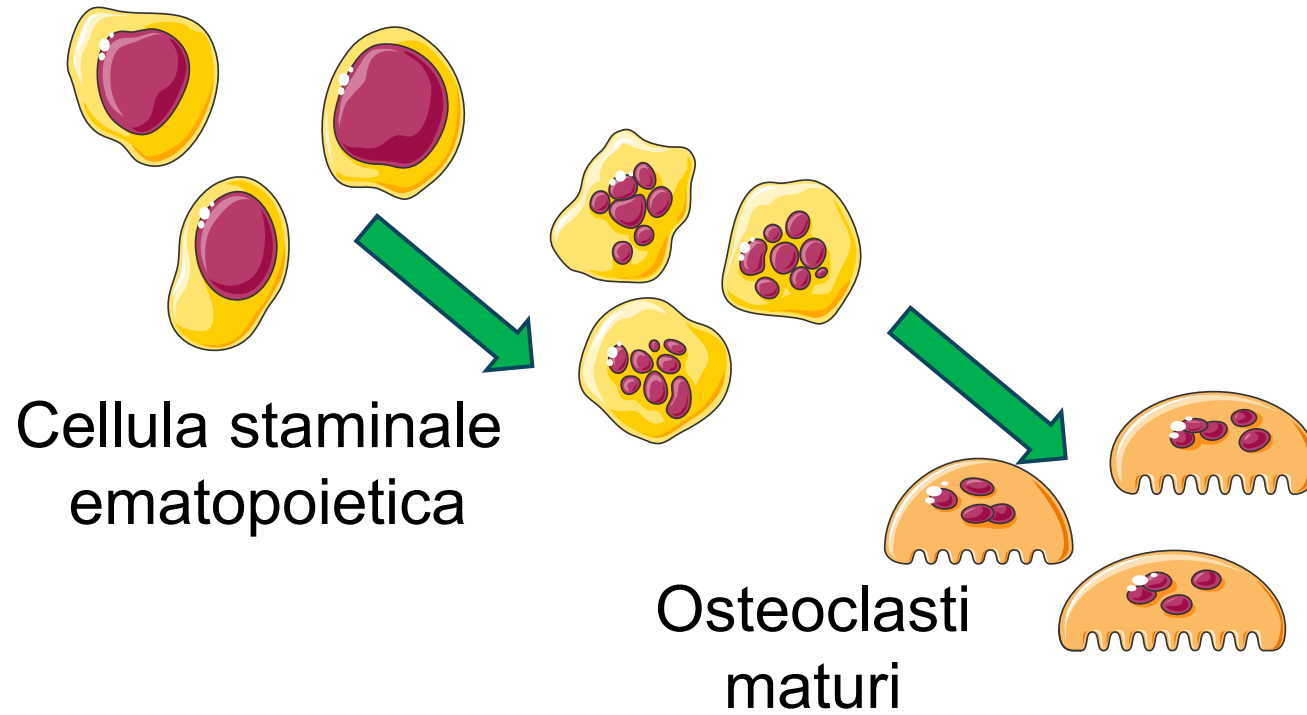
Rimodellamento osseo



Osteoporosi: fattori genetici e ambientali

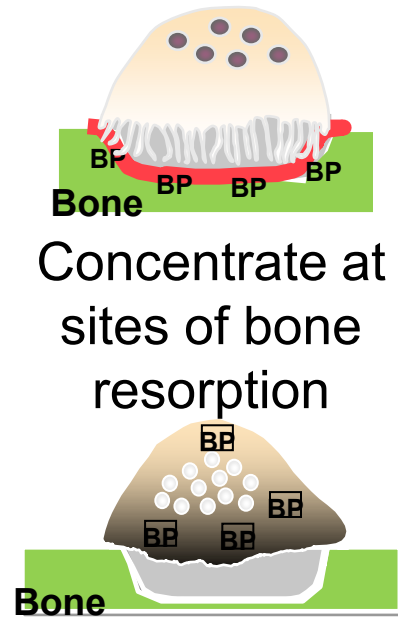


Osteoclasti

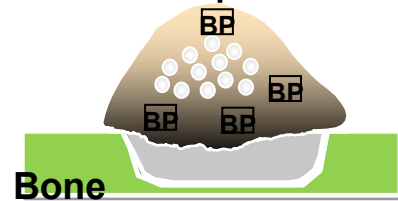


Azione dei bifosfonati sugli osteoclasti

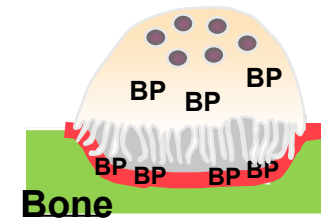
Bind to
bone mineral



Concentrate at
sites of bone
resorption

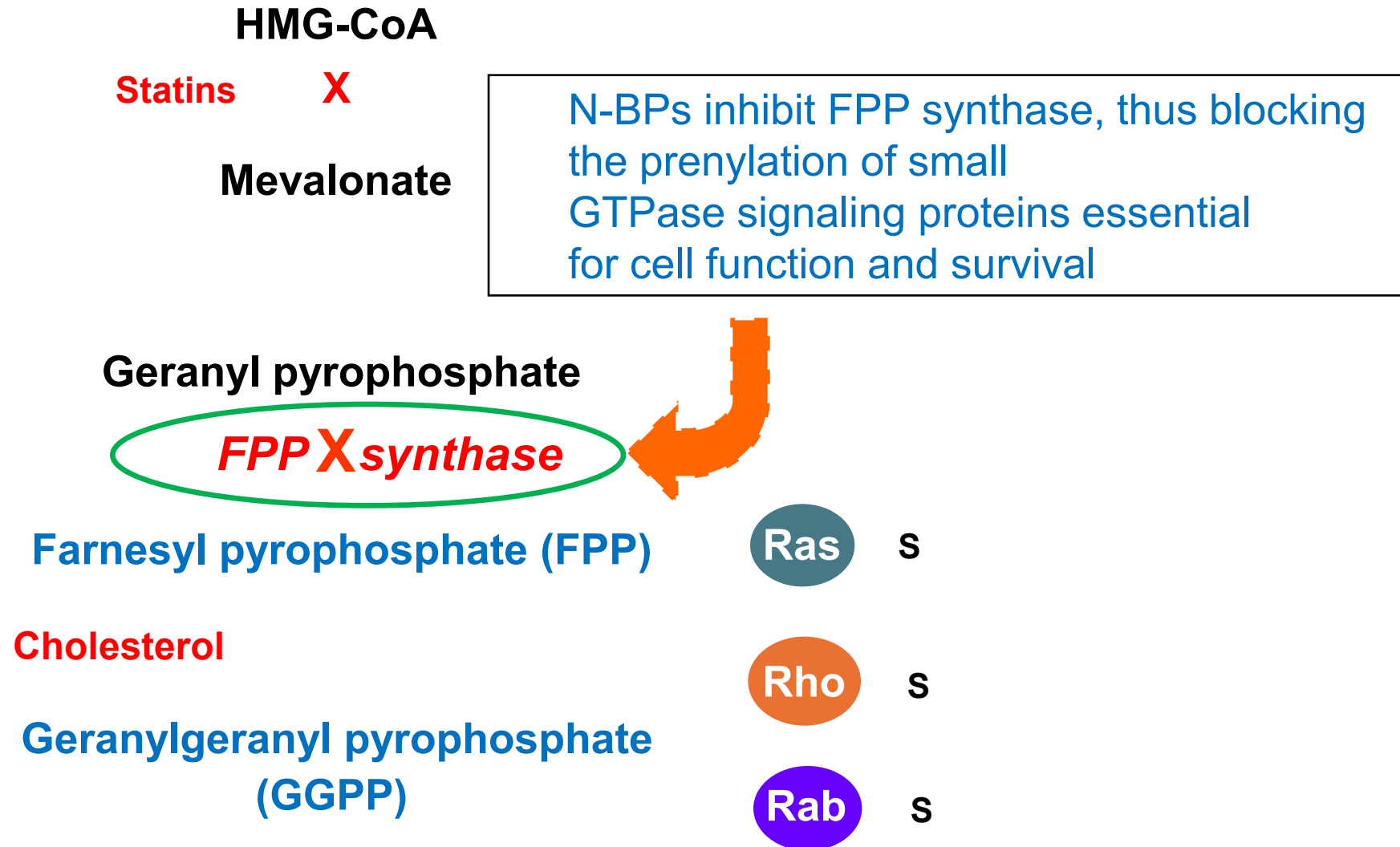


Loss of
resorptive
function

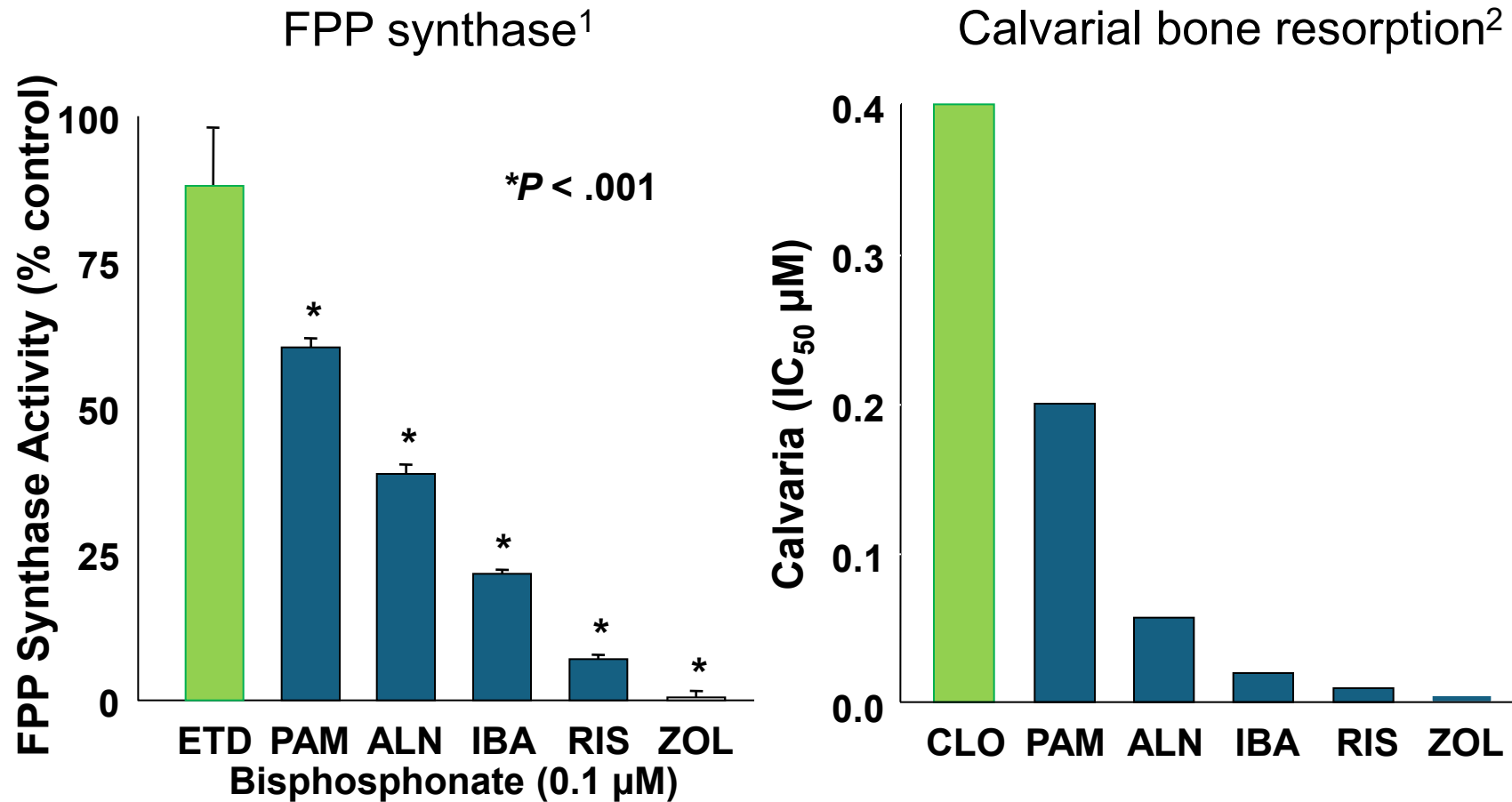


Release and
intracellular
uptake during
resorption

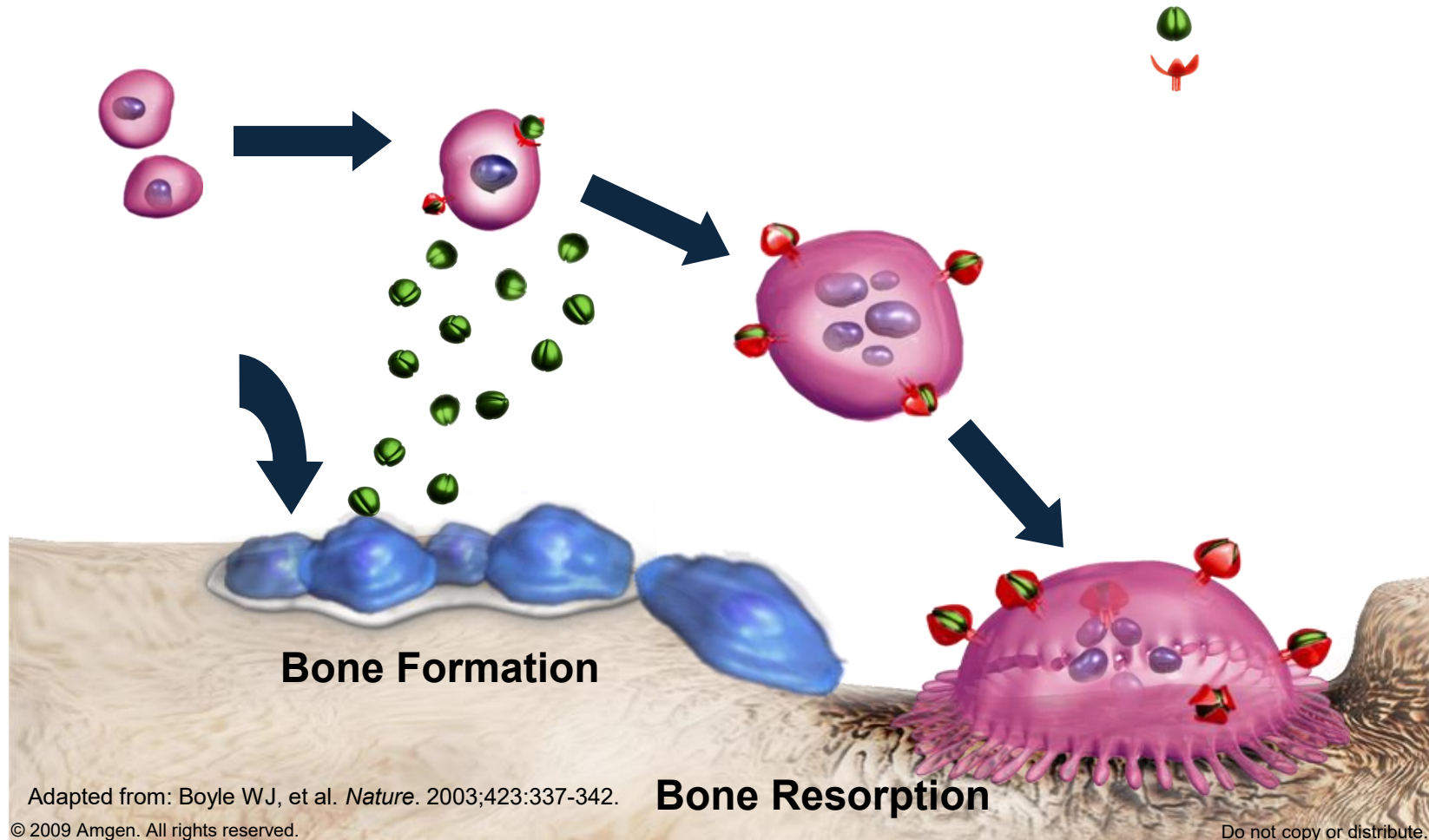
Meccanismo biochimico di azione degli amino-bisfosfonati



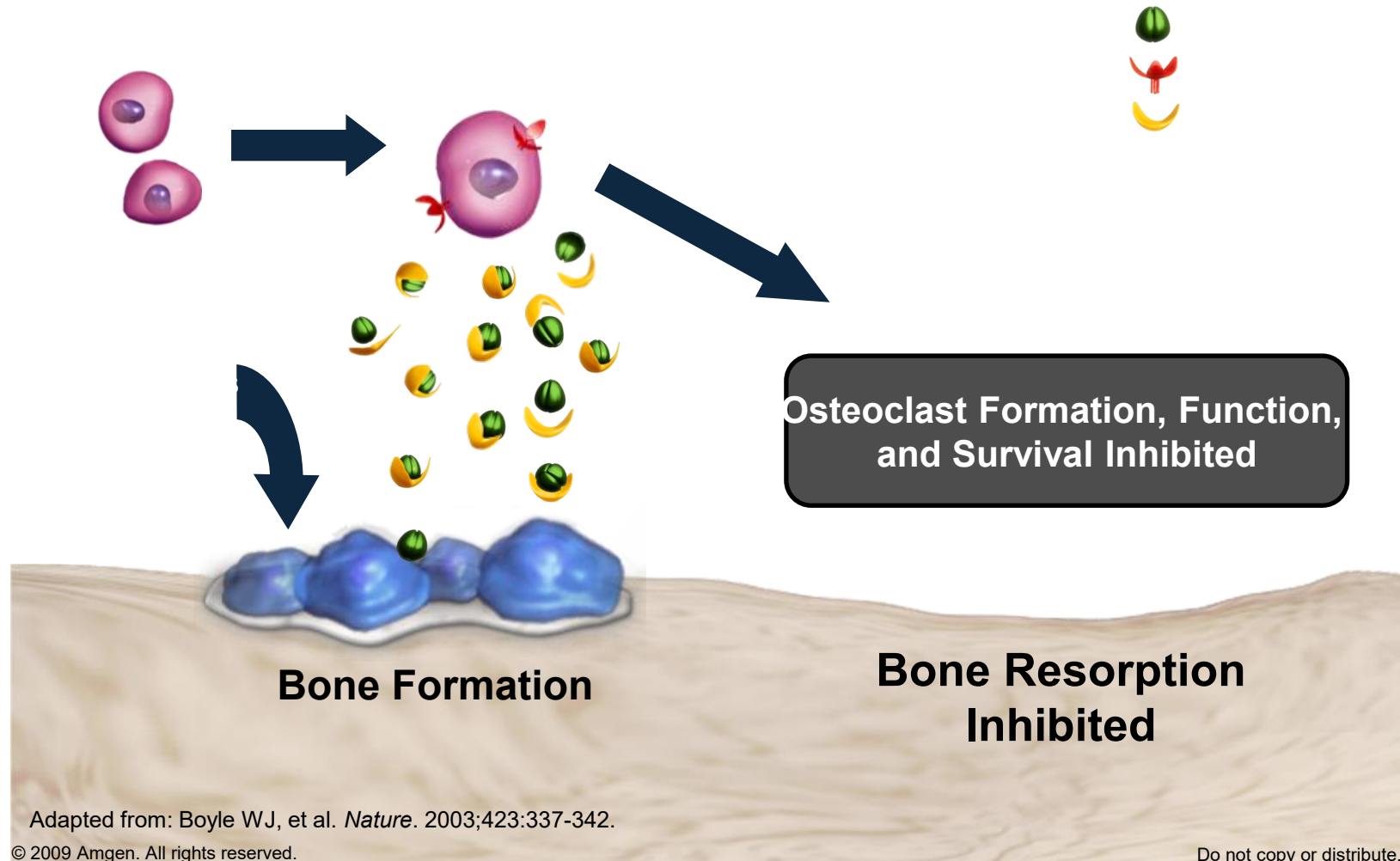
Relazione tra inibizione di FPP Synthase e inibizione del riassorbimento osseo



RANK Ligando è un mediatore essenziale di formazione, funzione e sopravvivenza degli osteoclasti



OPG previene il legame tra RANKL e RANK and inibisce la formazione, funzione e sopravvivenza degli osteoclasti



Role of OPG in the Regulation of Bone Mineral Density



No BMD Change

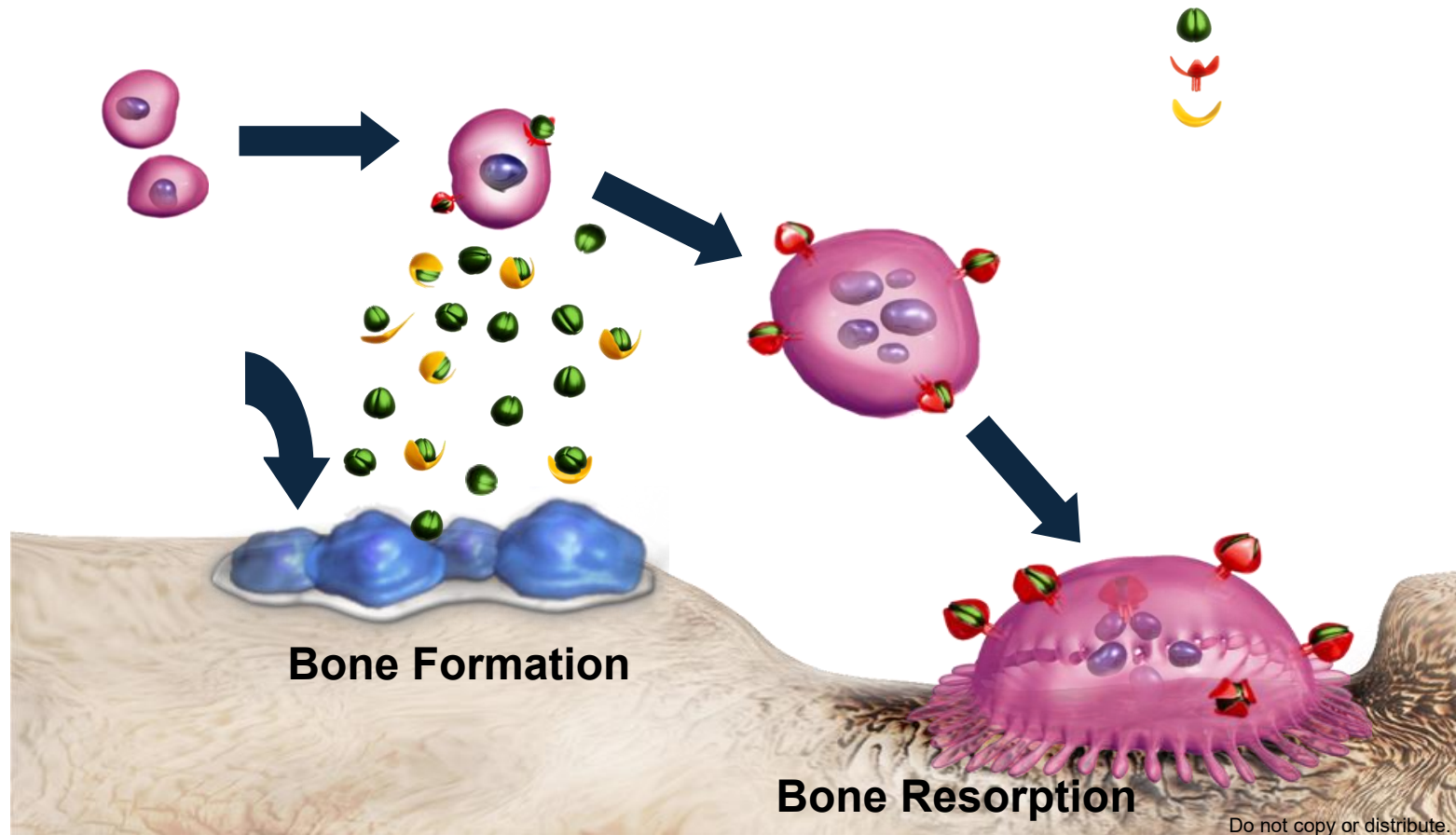
Decreased BMD ↓

Increased BMD ↑

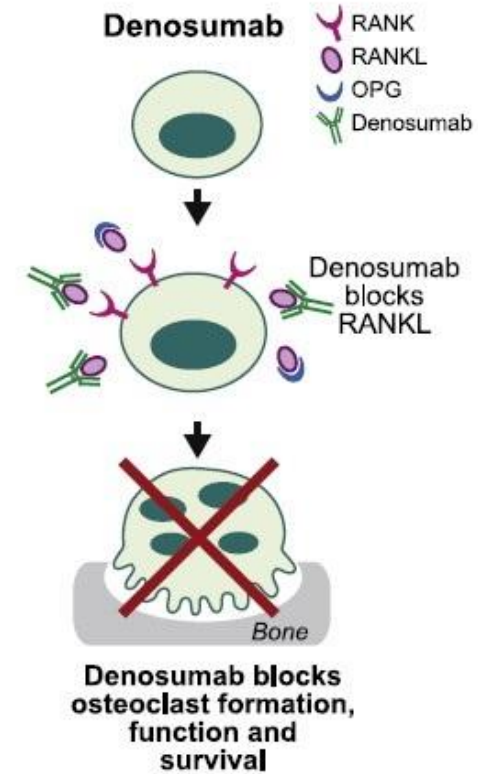
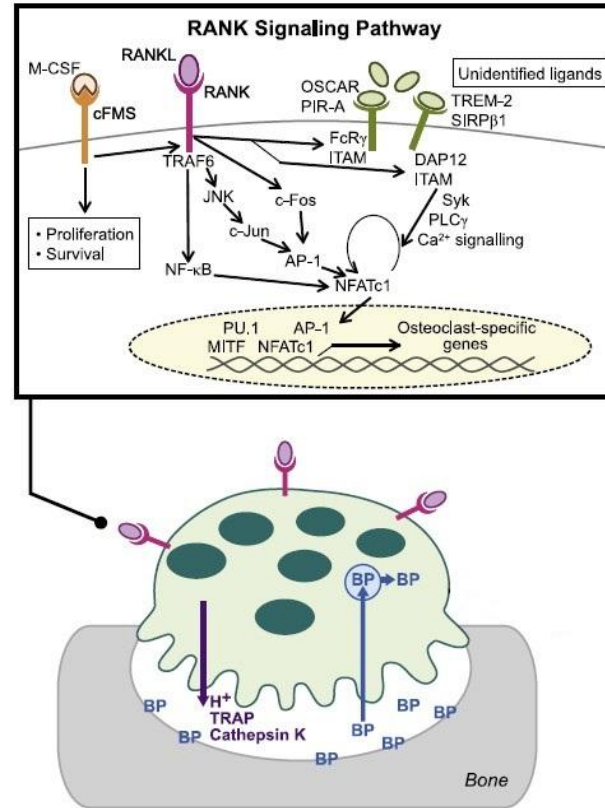
Bolon B, *et al. Arthritis Rheum.* 2002; 46: 3121-3135. Reprinted with permission of Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc.

Eccesso di RANKL aumenta il riassorbimento osseo

Menopausa
Terapia con corticosteroidi

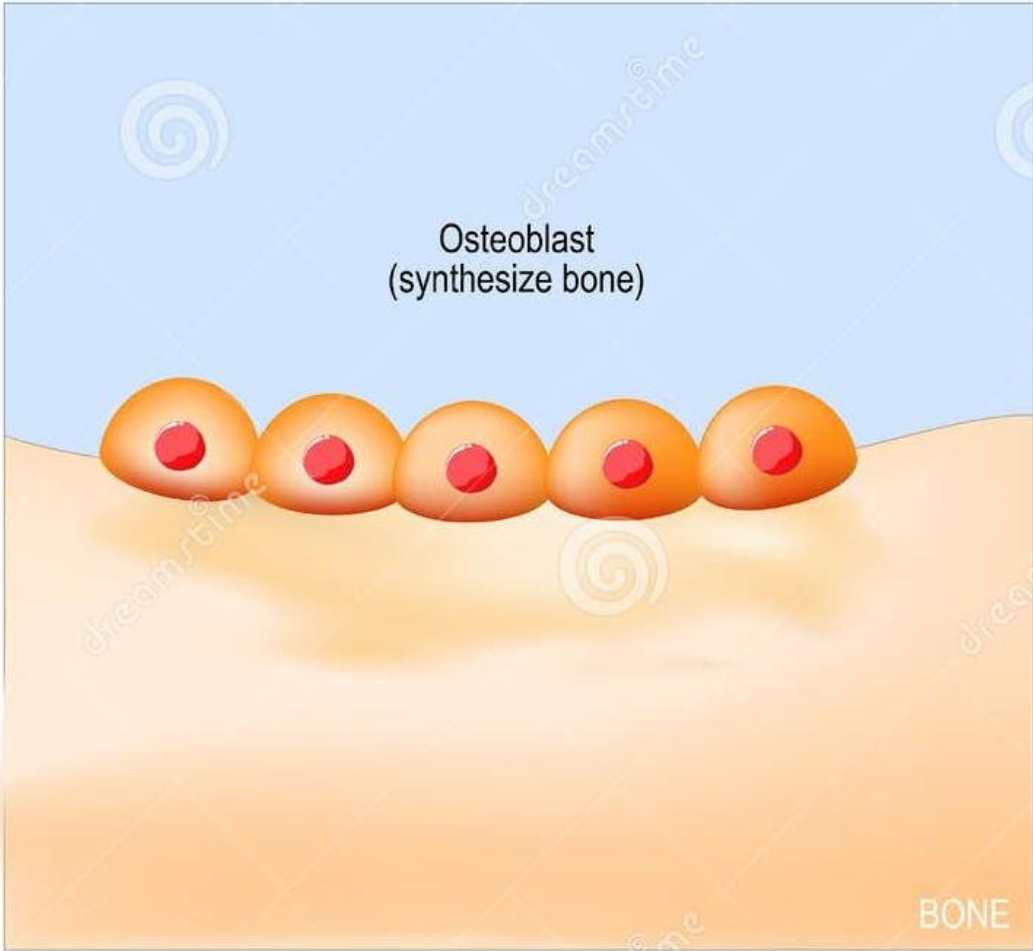


DENOSUMAB

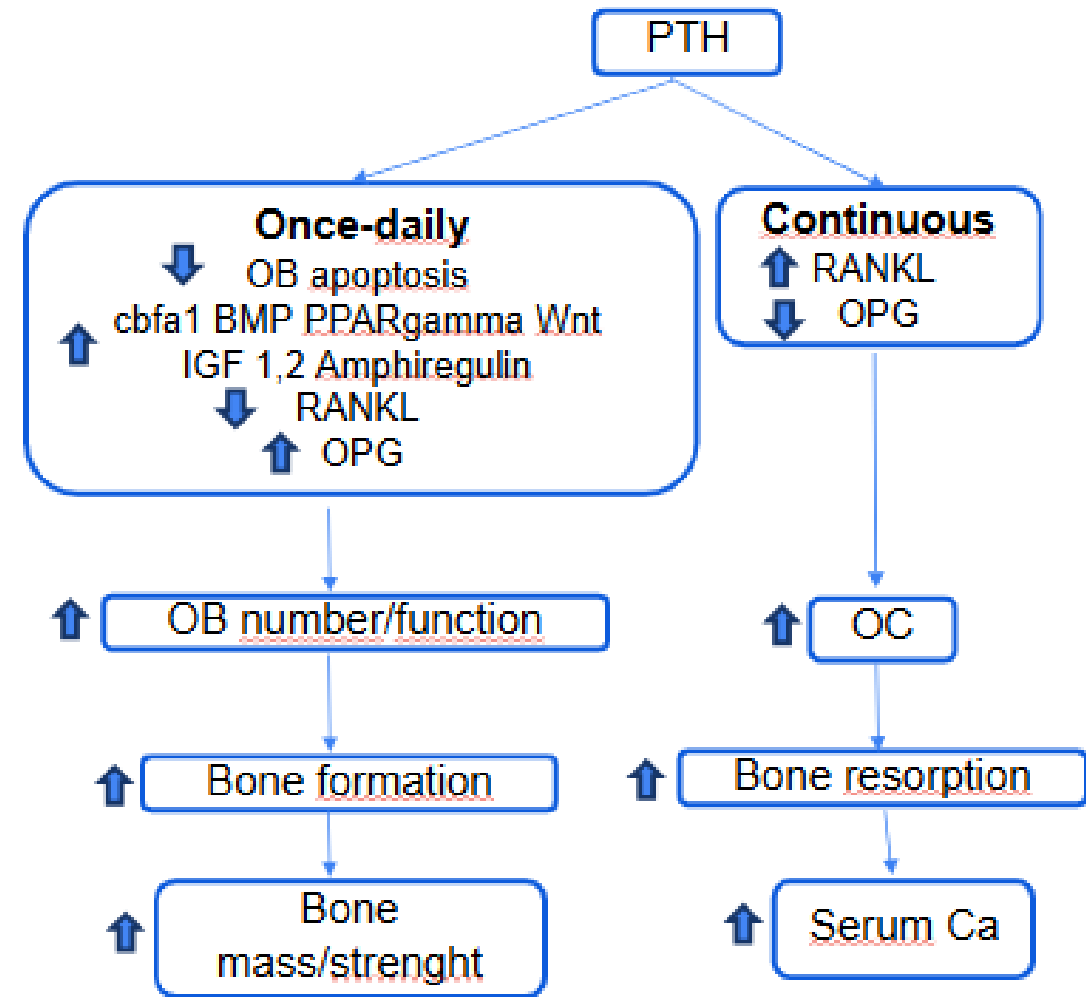
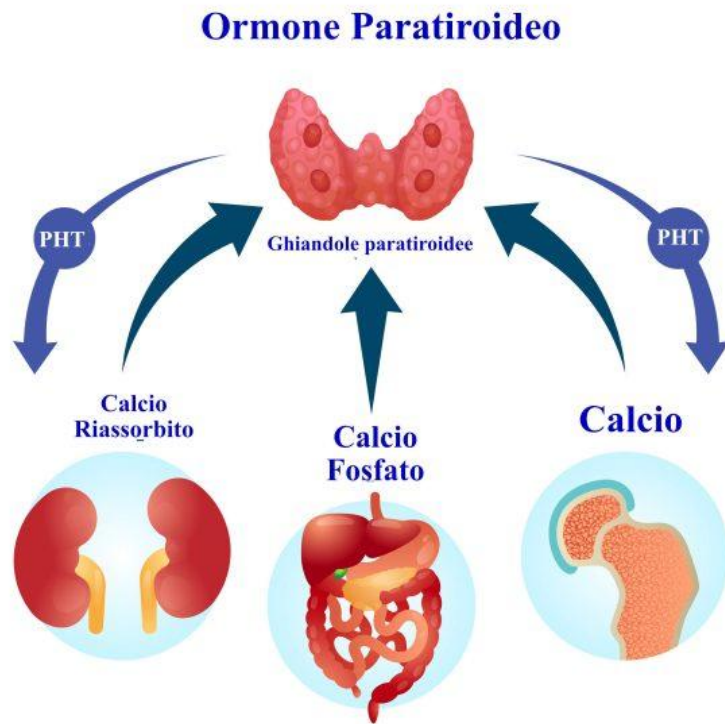


Dmab lega RANKL e previene il legame RANKL-RANK, con conseguente inibizione dello sviluppo, dell'attivazione e della sopravvivenza degli OC.

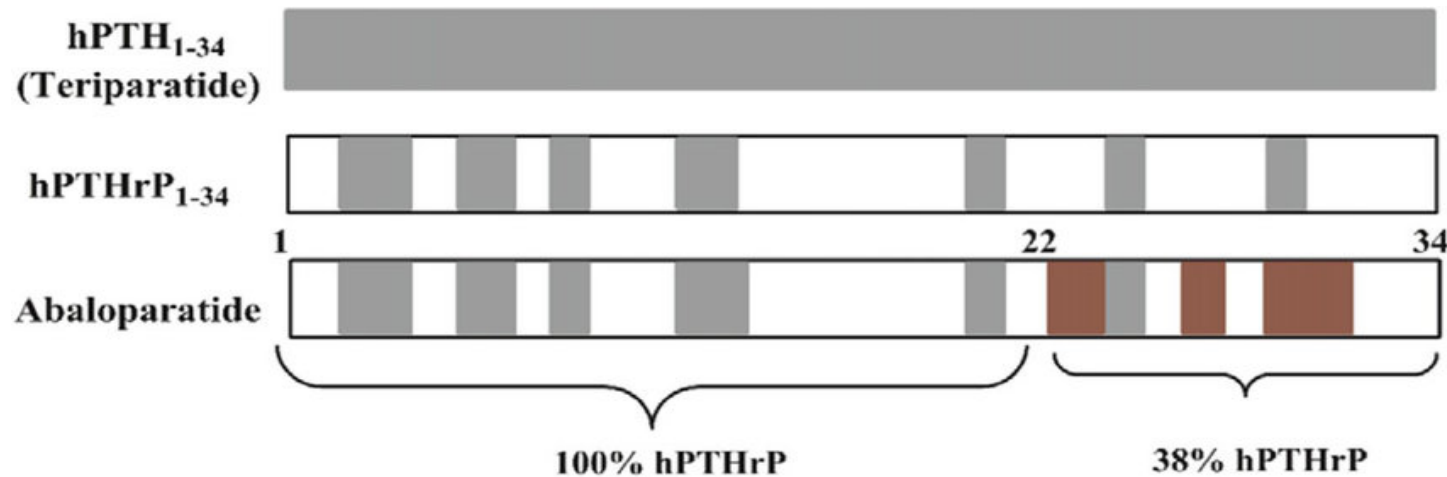
Osteoblasti



meccanismo di azione del PTH: continuo e pulsato



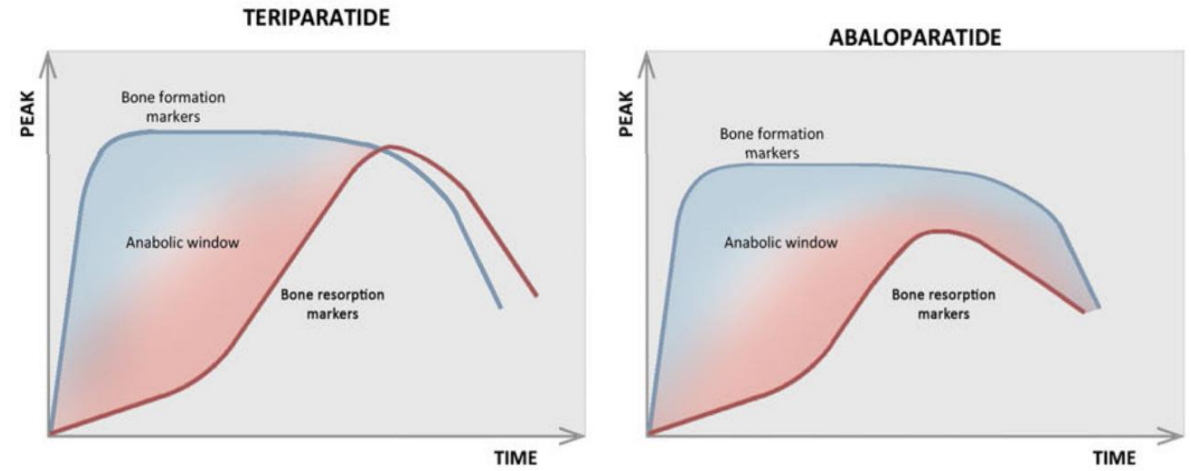
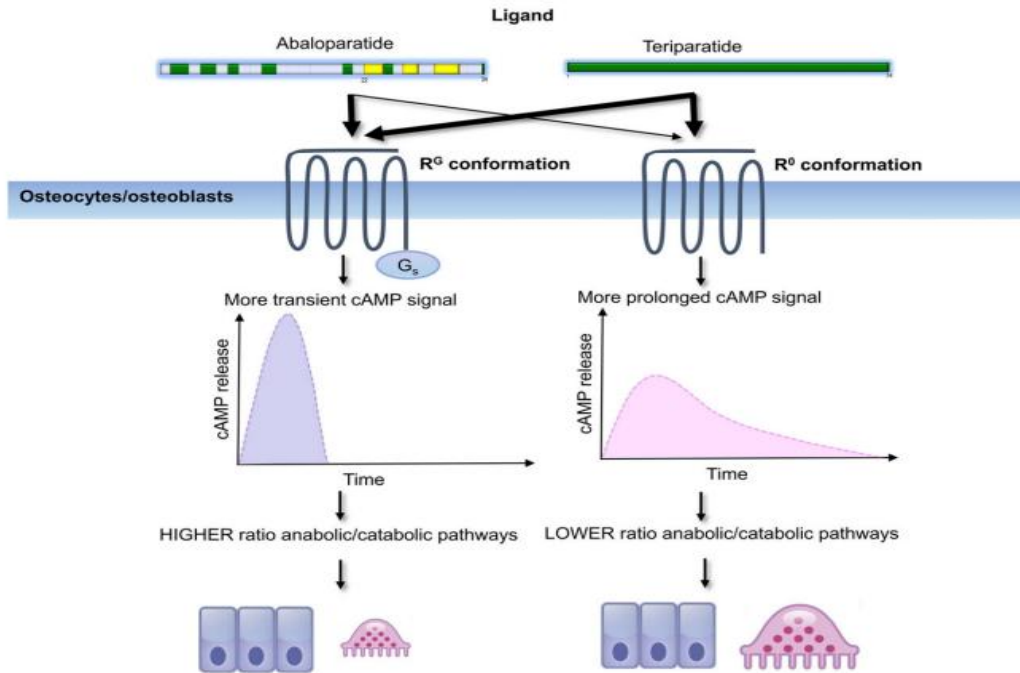
Teriparatide e Abaloparatide



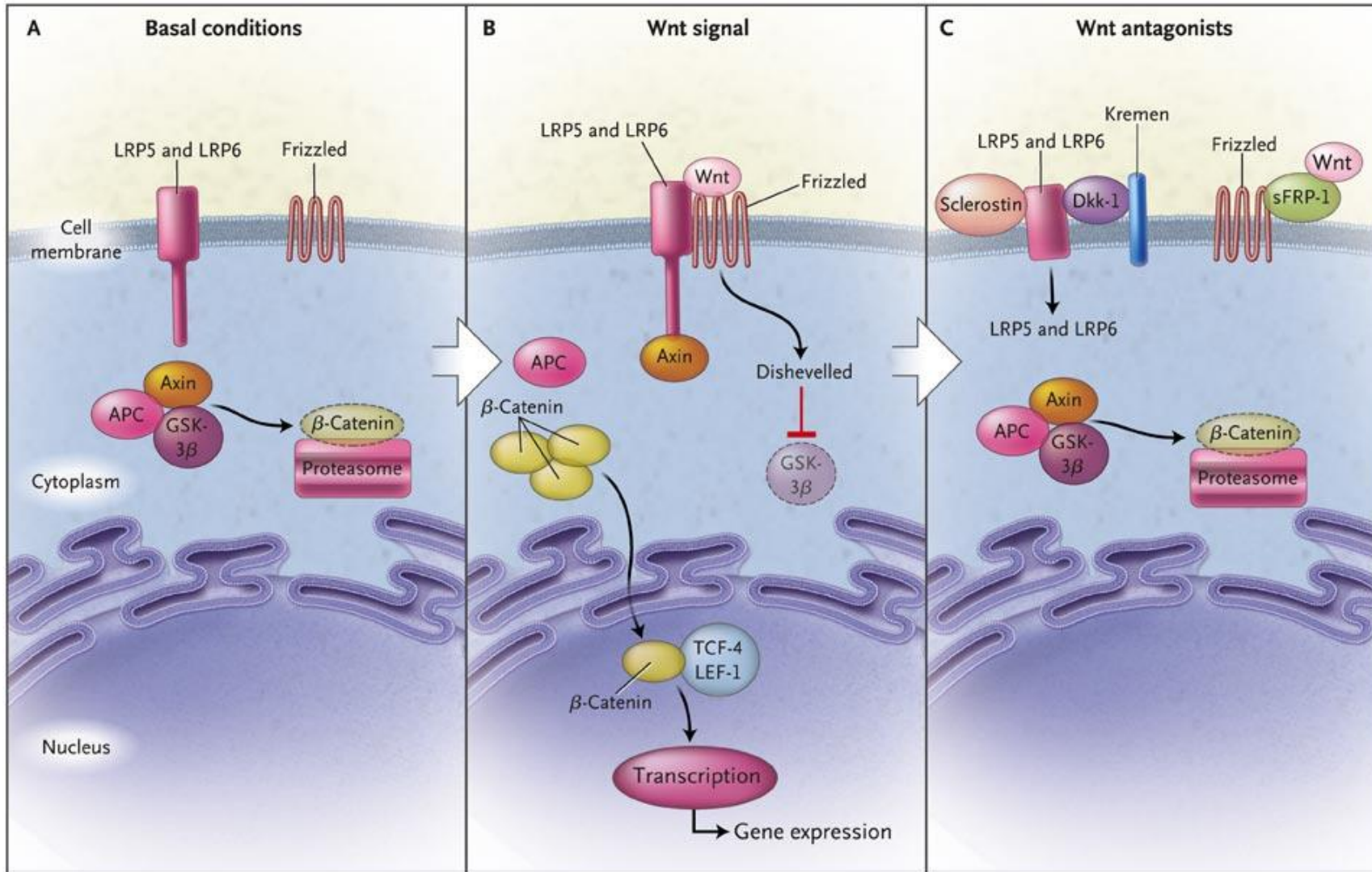
TPTD è un frammento di 34 amminoacidi che è identico nella sua sequenza primaria ai **34 amminoacidi dell'ormone paratiroideo umano completo** [hPTH(1-84)].

ABL è identico al peptide correlato all'ormone paratiroideo (PTHrP) nei **primi 22 residui**, con amminoacidi significativamente diversi inseriti successivamente, tra i residui 22 e 34.

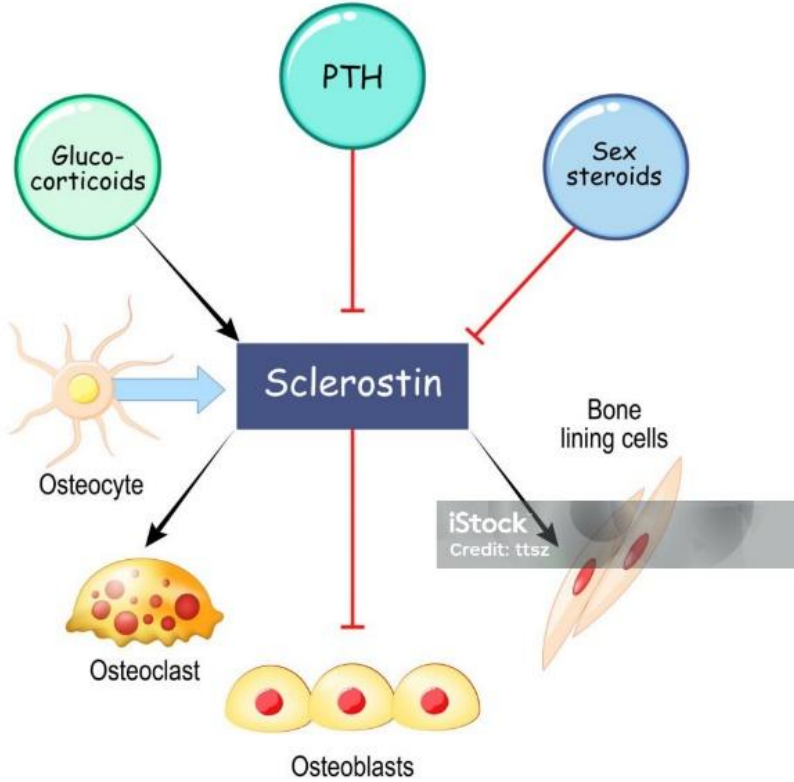
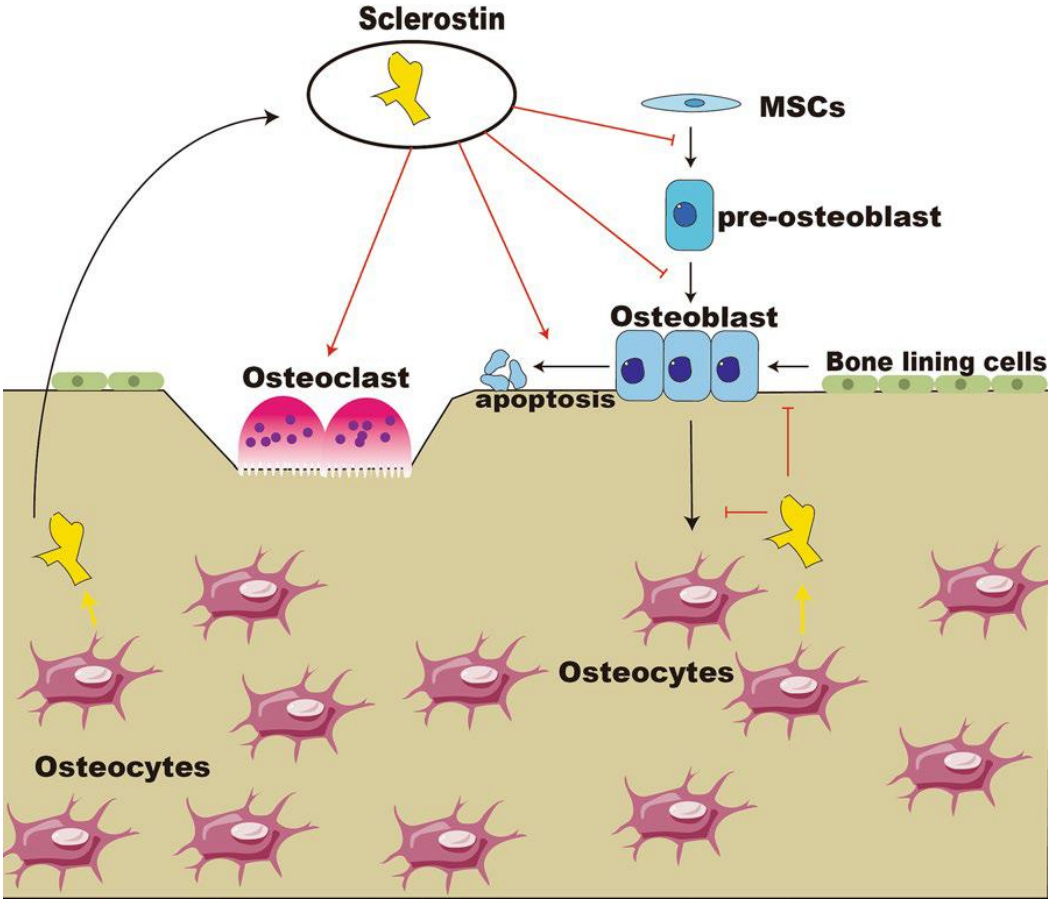
Teriparatide e Abaloparatide



segnale canonico Wnt-β-catenina



sclerostina

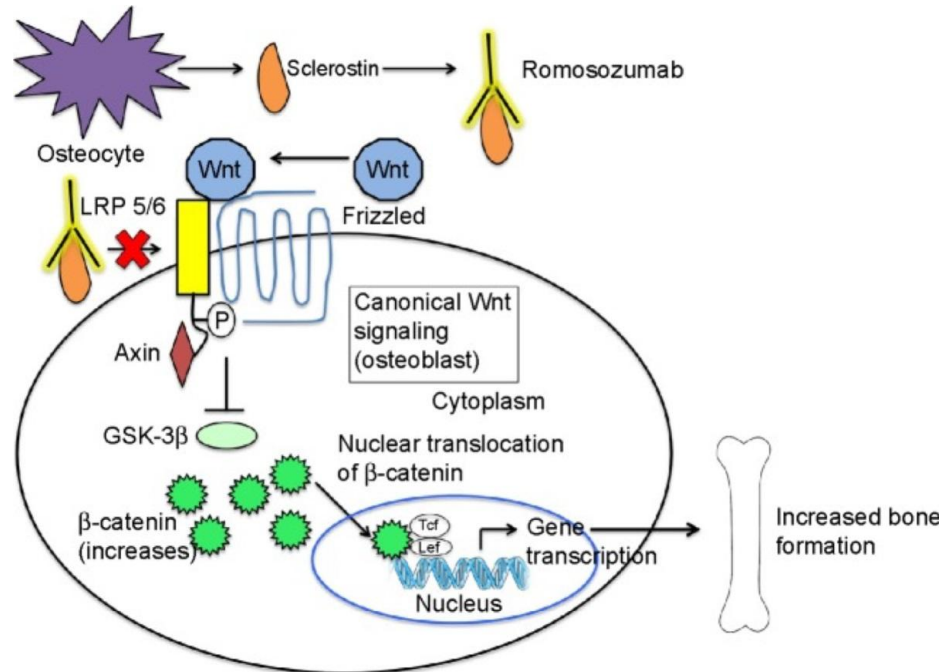


Mutazione del gene della sclerostina

Sclerosteosis: malattia autosomica recessiva causata da mutazione del gene che codifica per la sclerostina



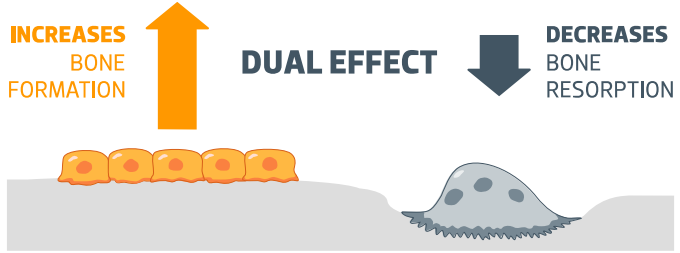
AC anti sclerostina: ROMOSUZUMAB



- **aumenta la formazione ossea** per l'attivazione delle cellule del rivestimento osseo
- aumenta la produzione di matrice ossea da parte degli osteoblasti
- aumenta il reclutamento di cellule osteoprogenitrici.

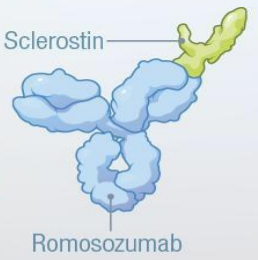
Altera l'espressione dei mediatori osteoclastici, **riducendo pertanto il riassorbimento osseo.**

Romosozumab: effetto duale



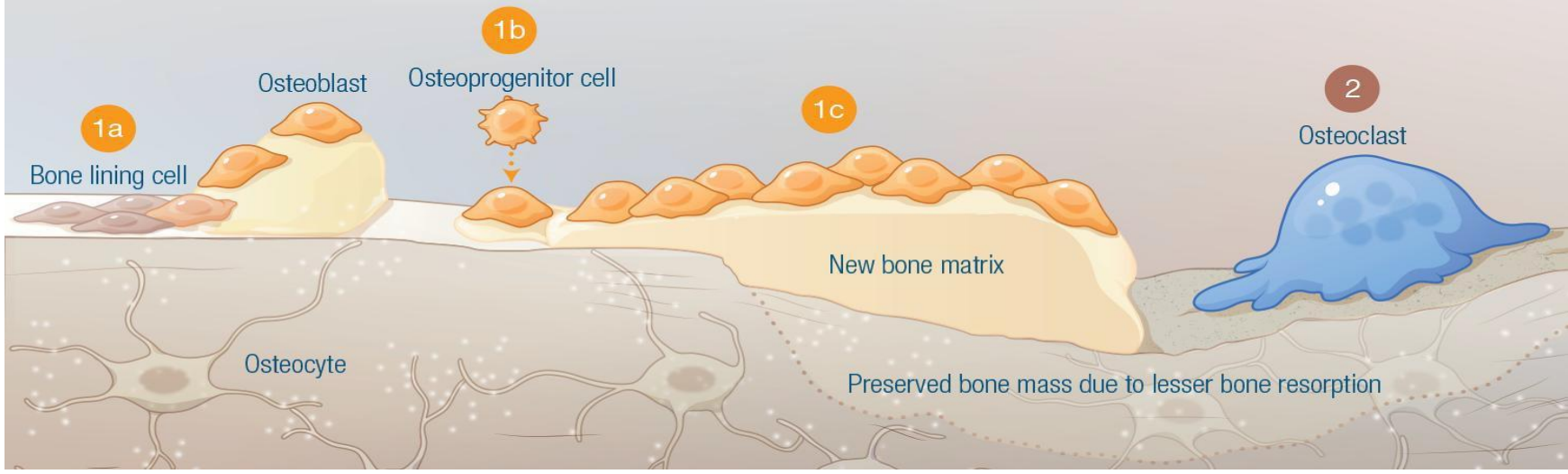
1 Romosozumab increases bone formation by promoting osteoblast differentiation and activity through:

- a. conversion of bone lining cells to osteoblasts,
- b. osteoblastic differentiation of osteoprogenitor cells, and
- c. increased bone matrix production by mature osteoblasts.

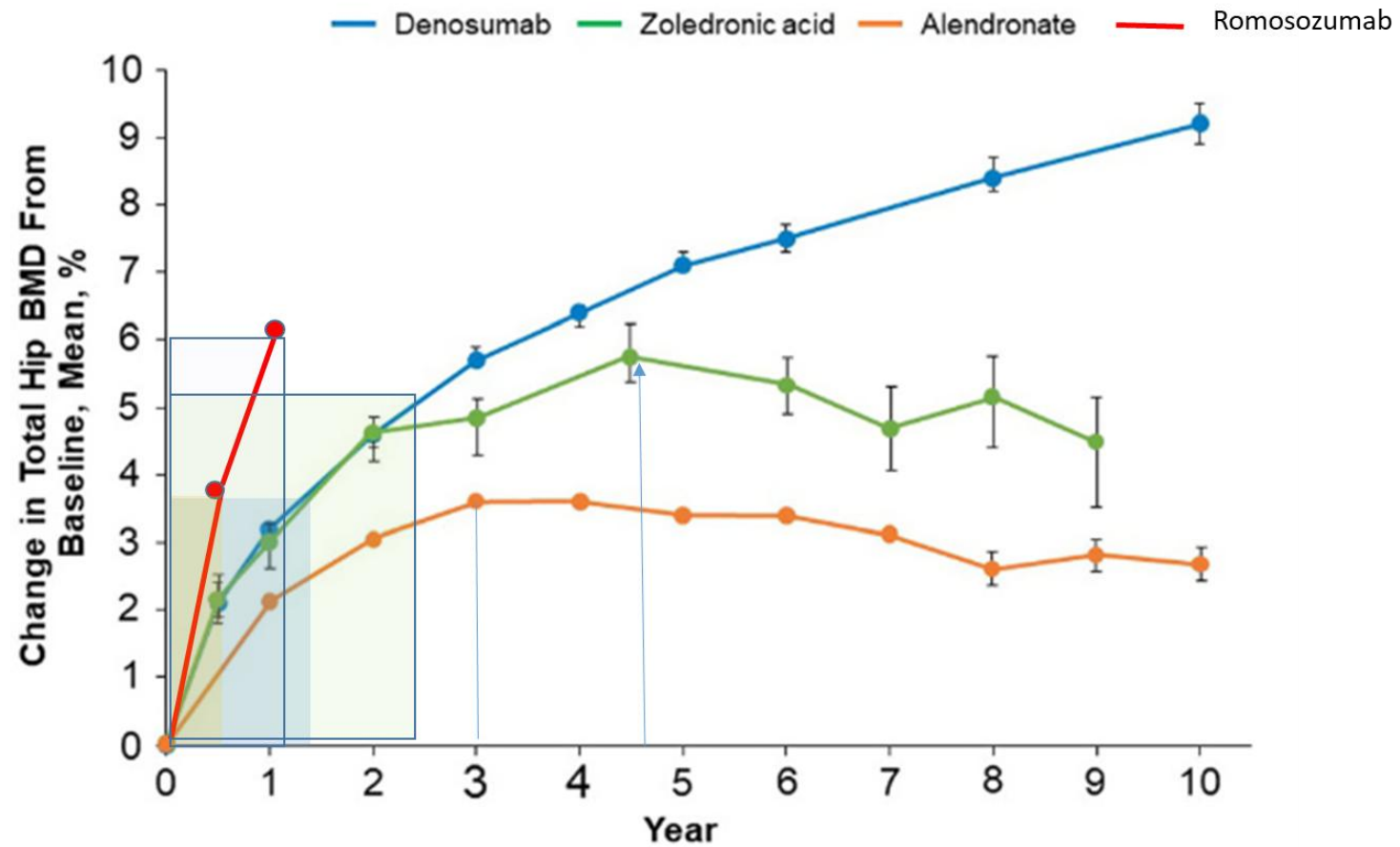


2 Romosozumab decreases bone resorption by altering expression of osteoclast regulators including:

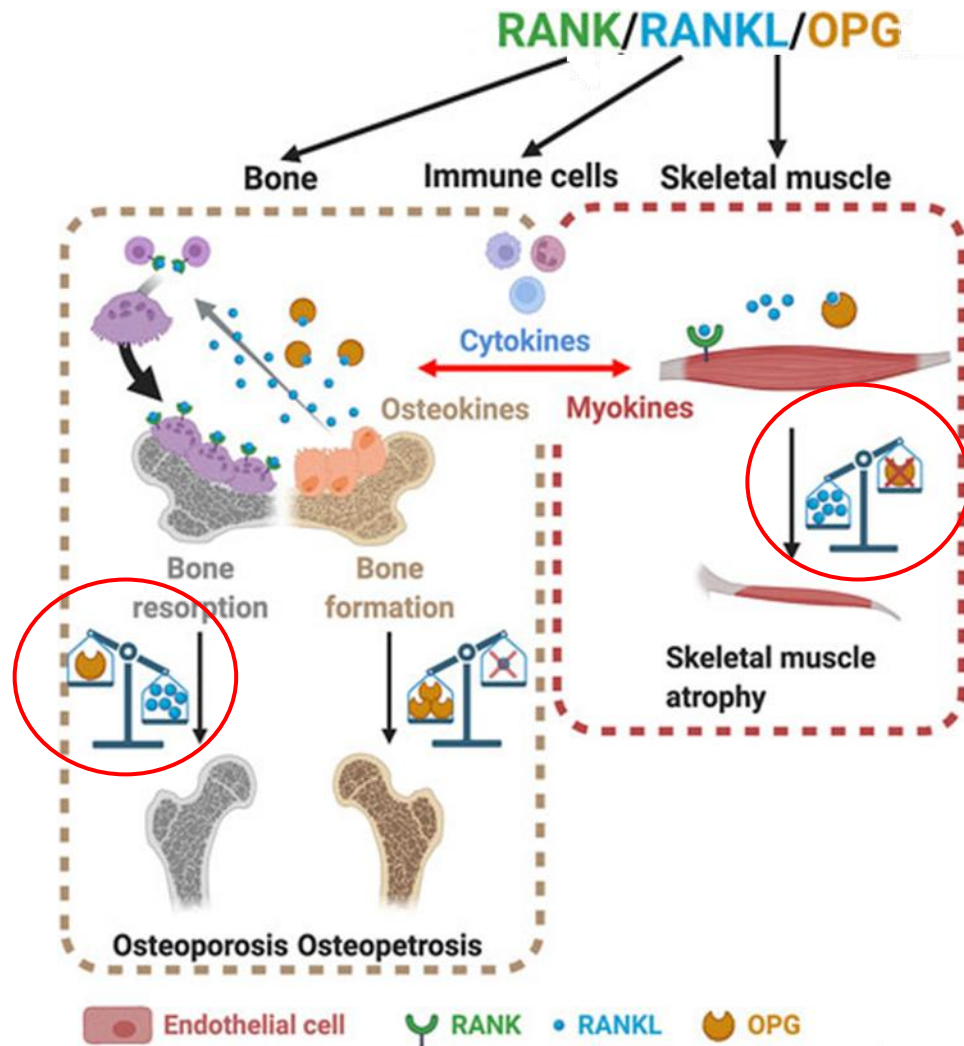
- decreasing osteoclast activators RANKL and CSF-1 and
- increasing osteoclast inhibitors OPG and Wisp-1.



Rapidità d'azione dei farmaci per l'osteoporosi



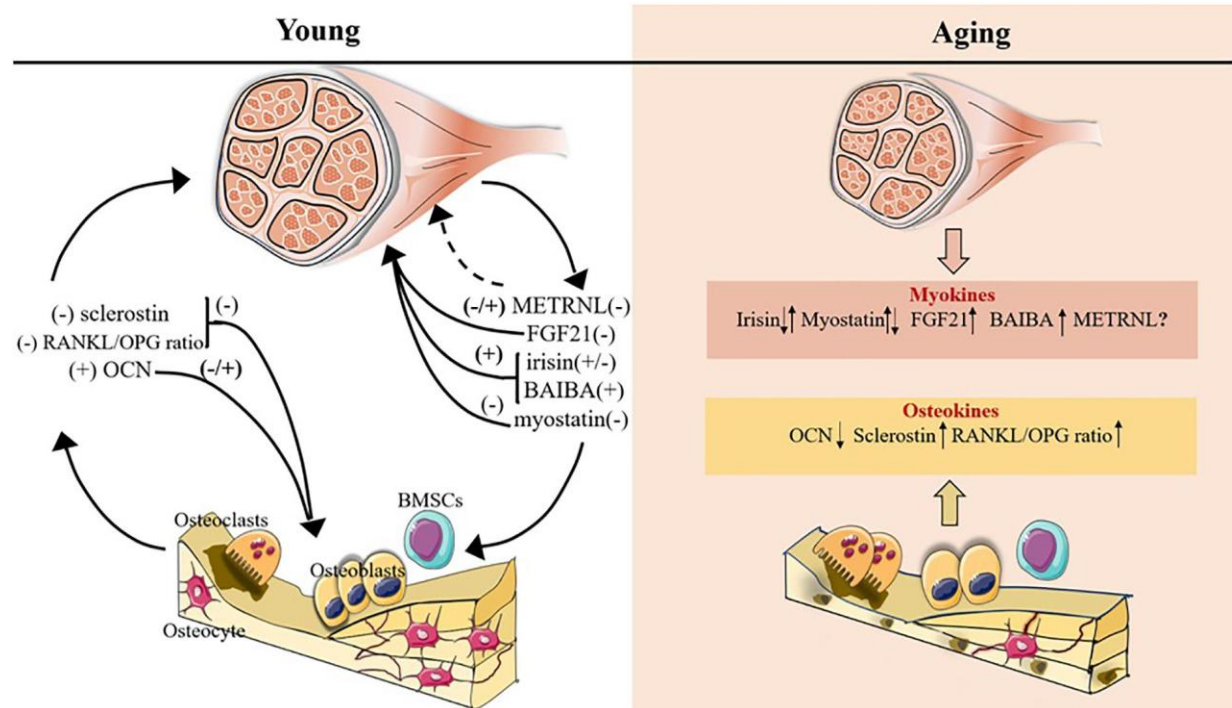
Cross-talk osso–muscolo via RANKL-OPG



RANKL/RANK altera tre processi che contribuiscono alla atrofia muscolare

1. Cytokine signaling
2. Atrophy signals
3. Regulation of intracellular Ca^{2+}

Cross-talk osso–muscolo via Wnt/ β -catenina



.Wnt/ β -catenina è un pathway condiviso da osso e muscolo

- La sua modulazione fornisce un razionale per effetti funzionali extrascheletrici

Take home messages

Dai farmaci tradizionali si è arrivati a farmaci di precisione

Farmaci che inibiscono gli osteocasti

Farmaci che stimolano gli osteoblasti

Farmaci duali