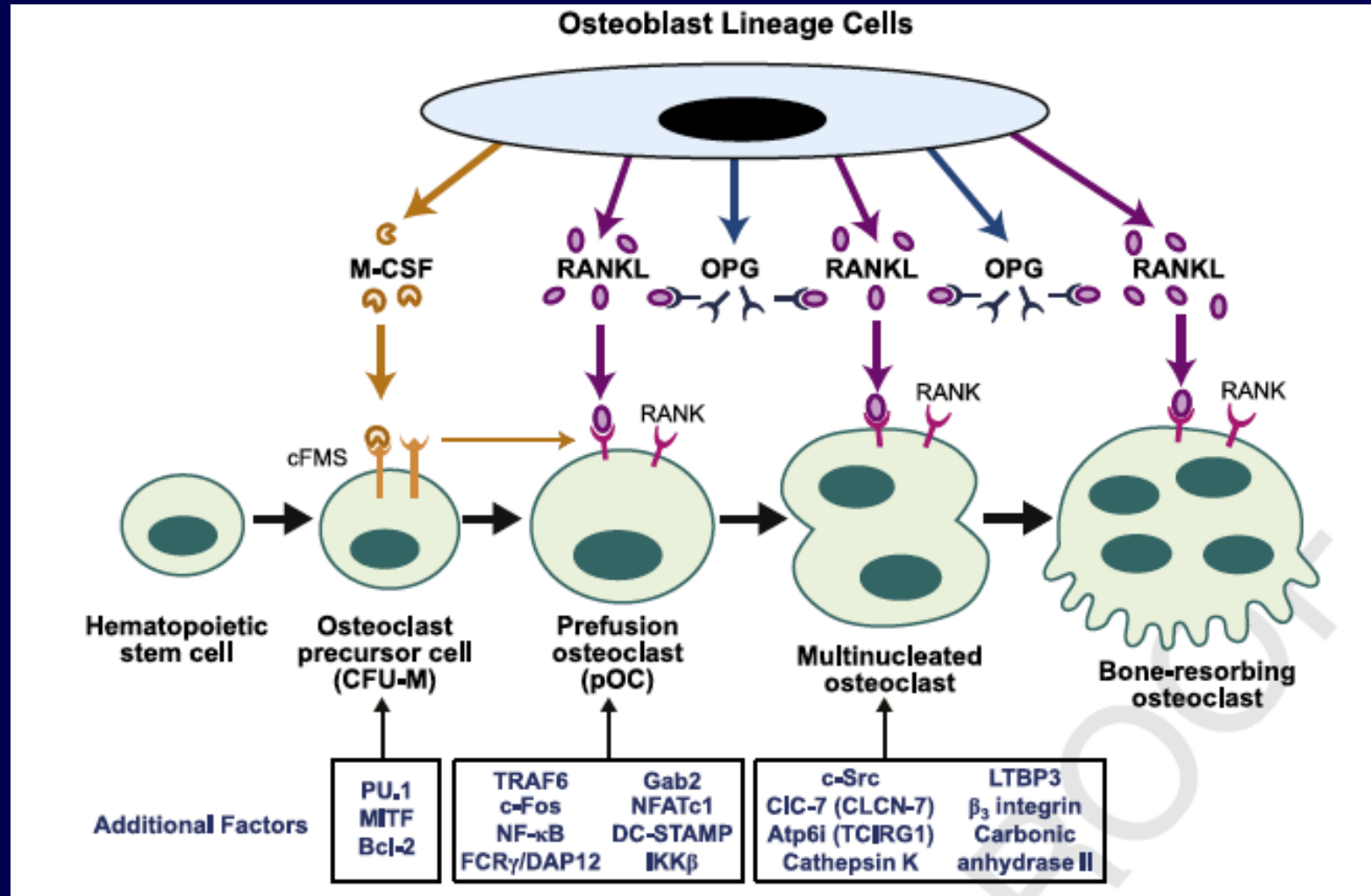


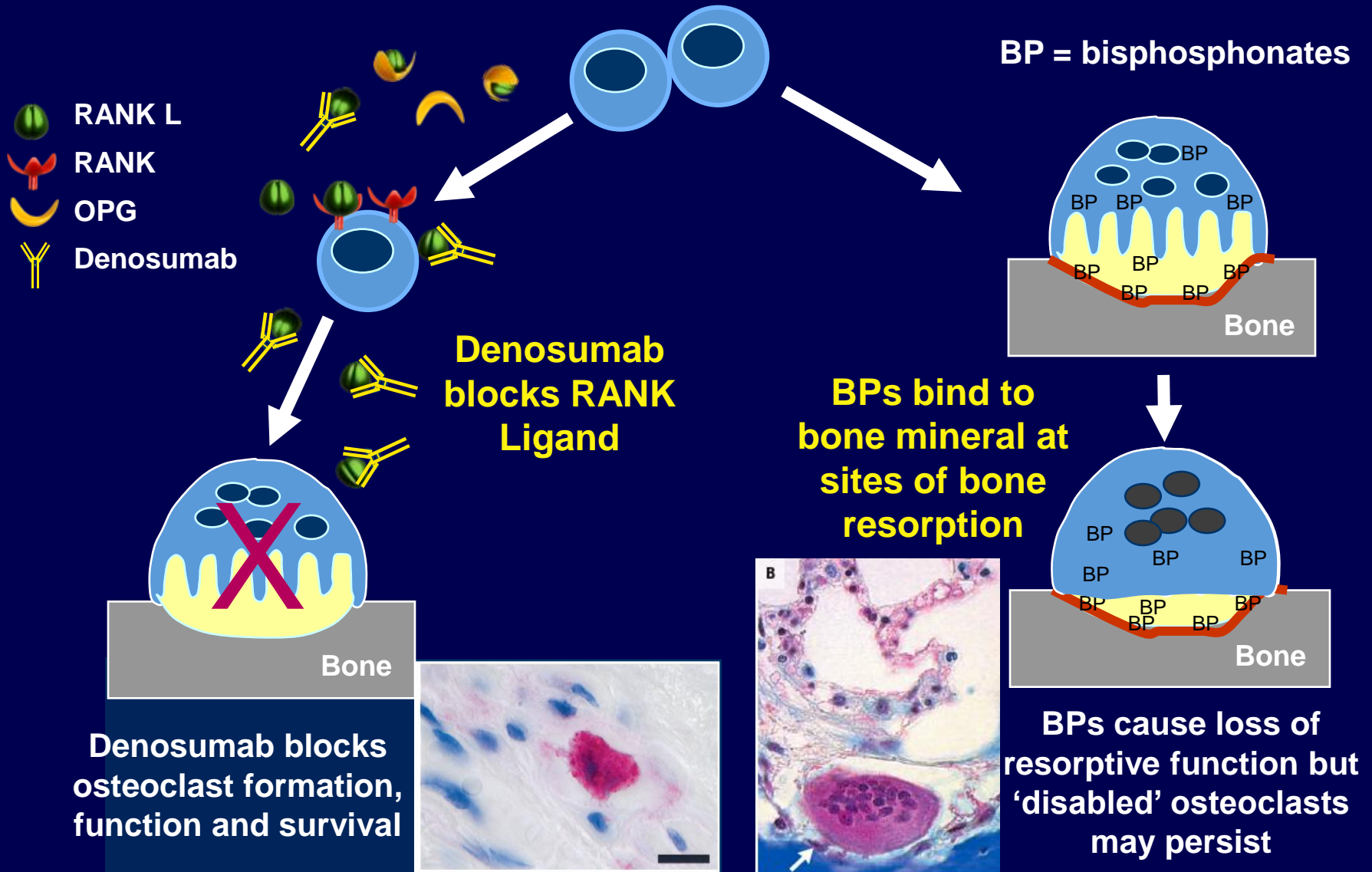
# Biological approaches for the development of novel therapeutic targets

- More complete and broader inhibition of osteoclasts and bone remodeling
- Selective inhibition of bone resorption (i.e. preserving bone formation)
- Selective activation of bone formation (i.e. without increasing overall bone turnover)

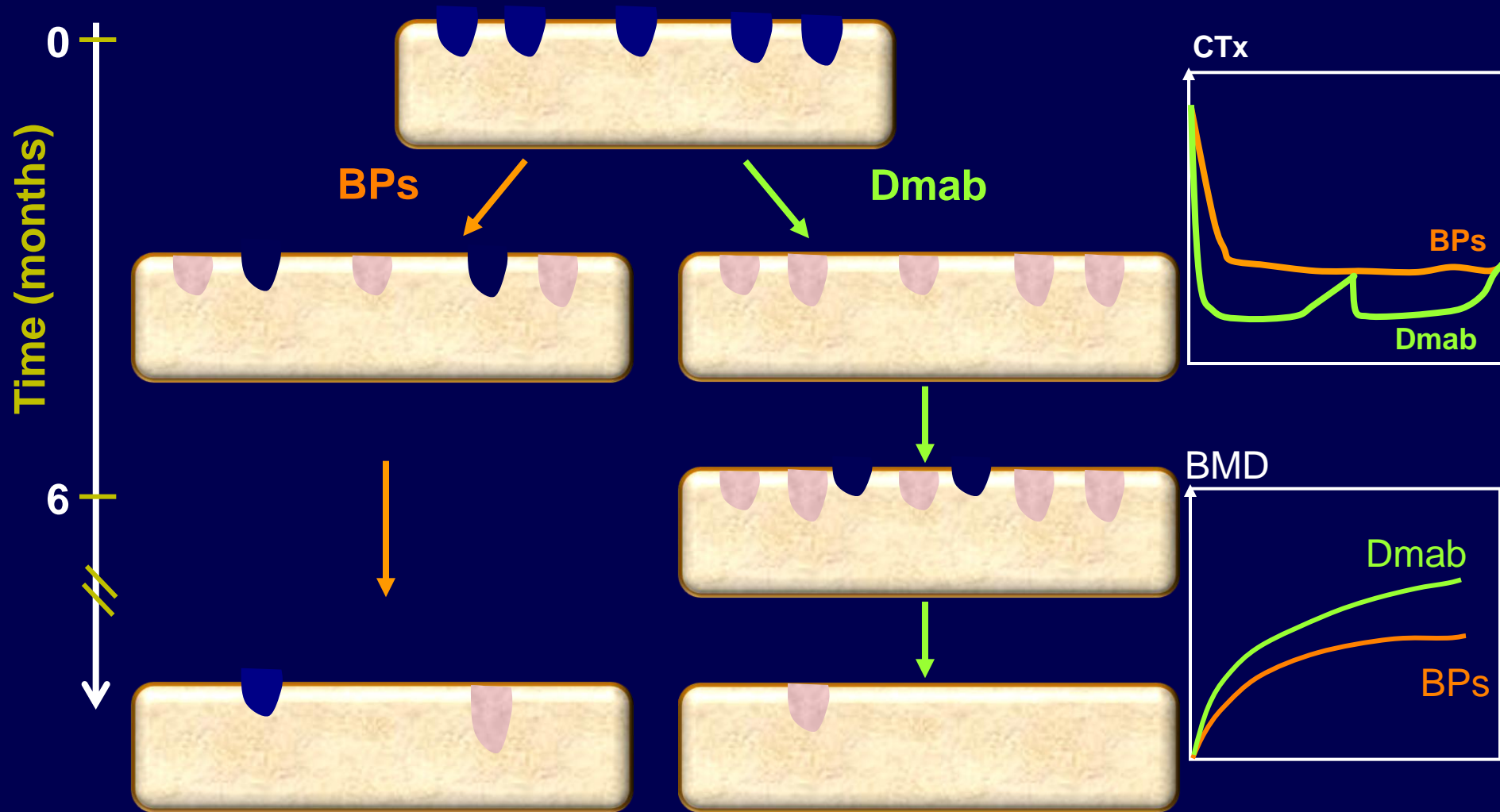
# RANKL-RANK drives differentiation and activation of osteoclasts



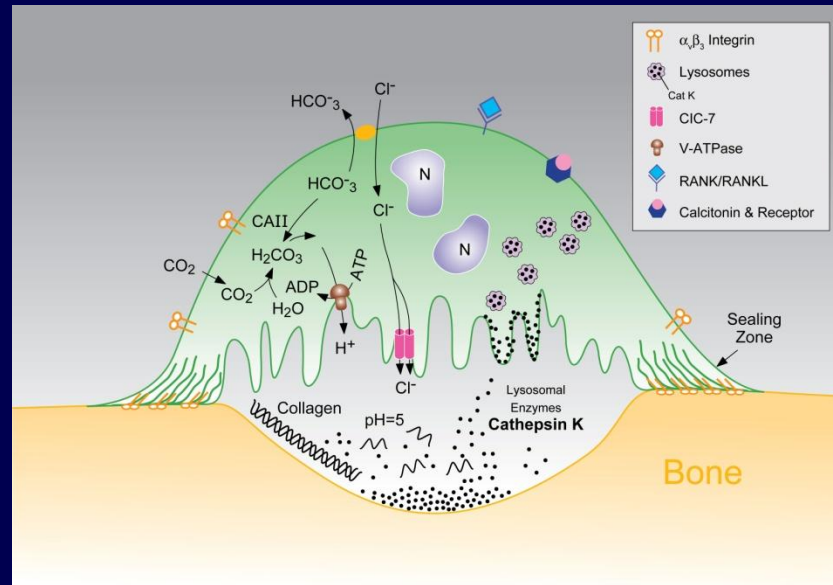
# Denosumab and bisphosphonates work differently



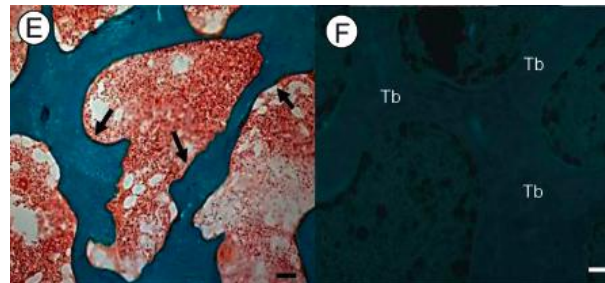
# Different effects of BPs and denosumab on bone remodeling



# CatK mutations : Pycnodysostosis



2D parameters (histomorphometry)	Baseline	Age- and sex-matched controls
Cancellous bone volume (%)	38	23.3 ± 4.1*
Trabecular thickness (μm)	158.8	146 ± 19 <sup>†</sup>
Tabecular number (/cm)	2.4	1.7 ± 0.4 <sup>†</sup>
Trabecular separation (μm)	258.7	505 ± 99 <sup>†</sup>
Eroded surfaces (%)	6.0	3.6 ± 1.1
Osteoclast number (/mm)	0.02	NA
Osteoid volume (%)	1.4	2.0 ± 1.2
Osteoid thickness (μm)	8.5	11.5 ± 1.7
Mineralizing surfaces (%)	0.83	8.1 ± 3.4 <sup>‡</sup>
Bone formation rate (μm <sup>3</sup> /μm <sup>2</sup> /d)	0.004	0.060 ± 0.022 <sup>‡</sup>



# PTH regulates Sost expression in osteocytes

