

**A tale of two antiresoptives:  
ABD56 versus Fosamax®**



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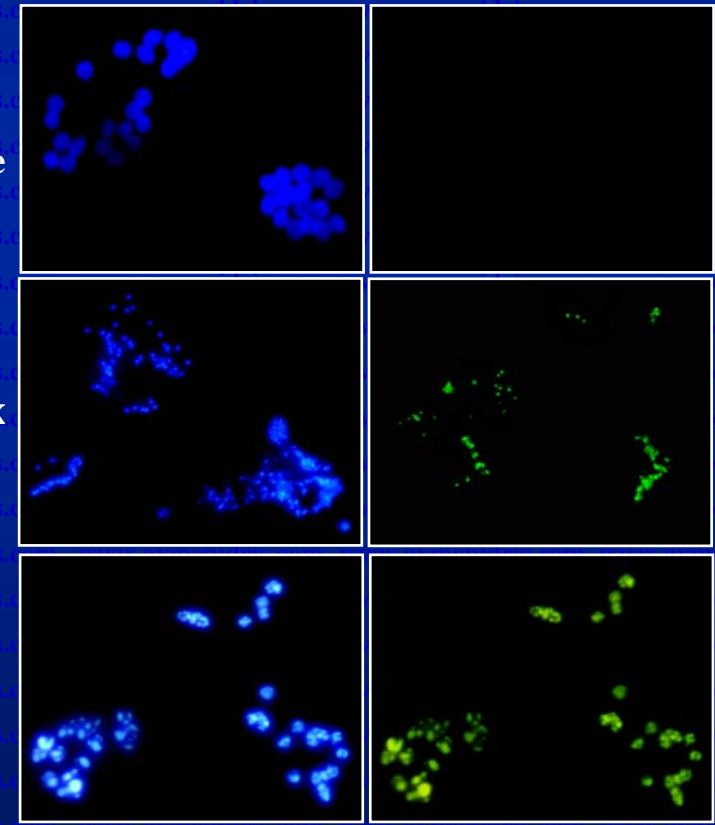
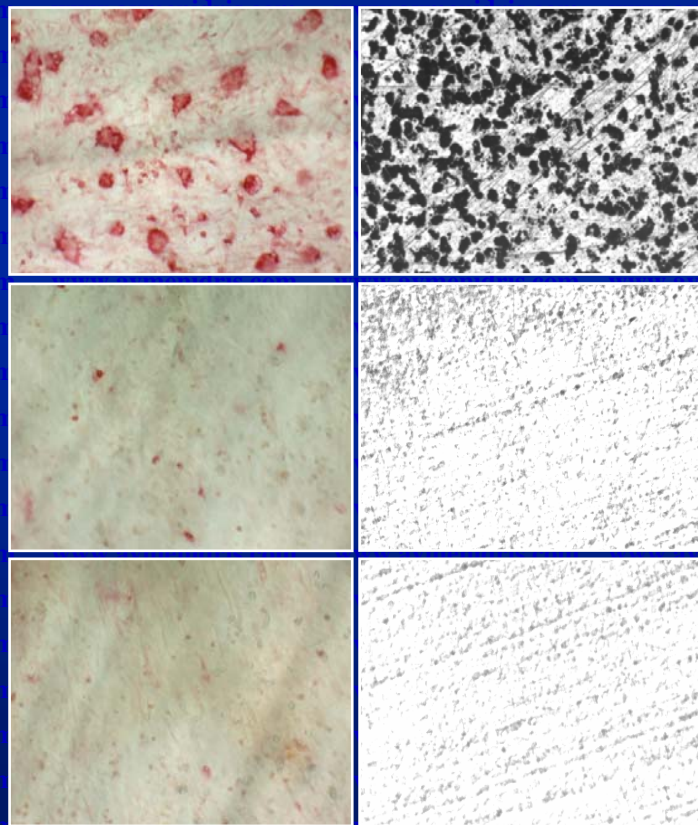
**Institute of Genetics and Molecular Medicine  
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# ABD56 and Fosamax® inhibit osteoclast formation and activity

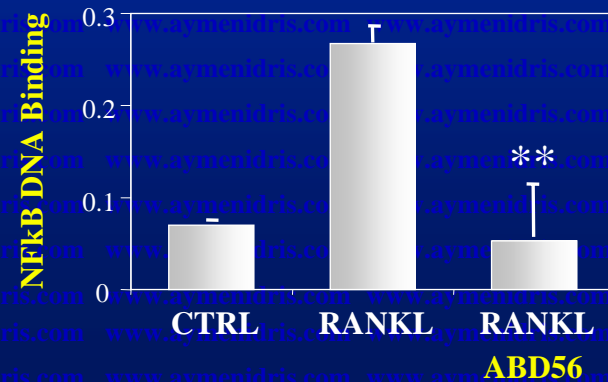
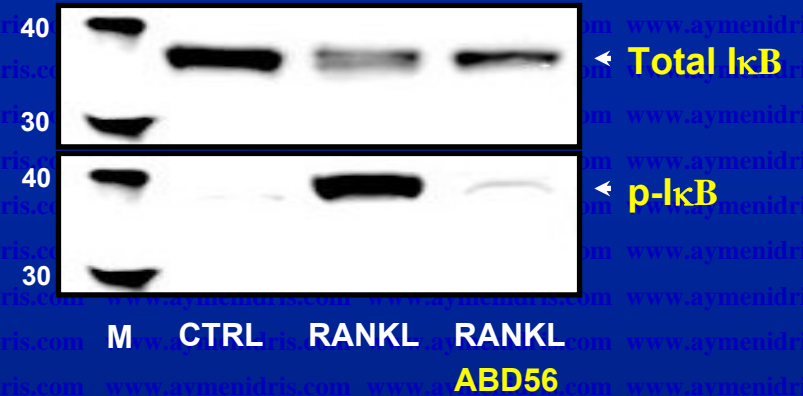
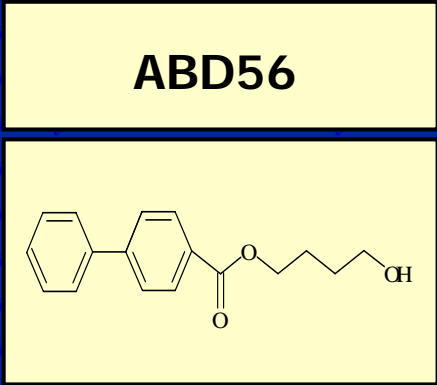
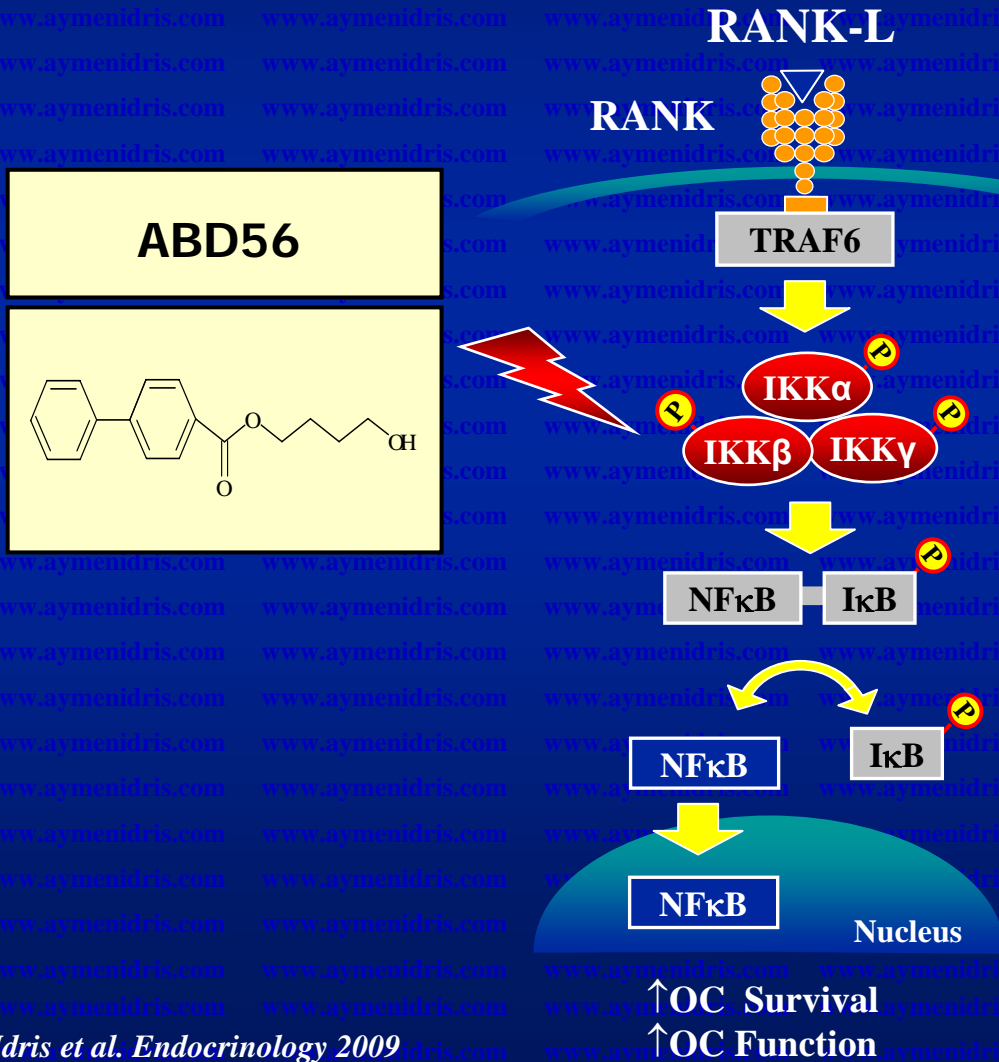
# ABD56 and Fosamax® induce mature osteoclast apoptosis

**TRAcP<sup>+</sup> Osteoclast**  
**Bone Resorption**

**DAPI<sup>+</sup> Osteoclast**  
**Tunnel<sup>+</sup> Osteoclast**

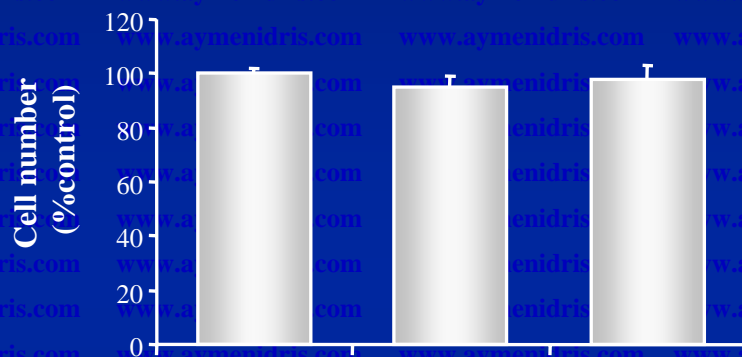


# ABD56 prevents RANK ligand induced NFκB activation in osteoclast



# ABD56 does not inhibit osteoblast growth, differentiation or bone nodule formation

## OB viability



Vehicle      Fosamax 0.5µM      ABD56 2µM



Vehicle

Fosamax 0.5µM

ABD56 2µM

## Osteoblast function



vehicle



Fosamax (0.5µM)



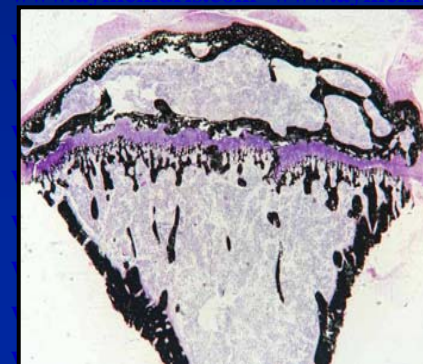
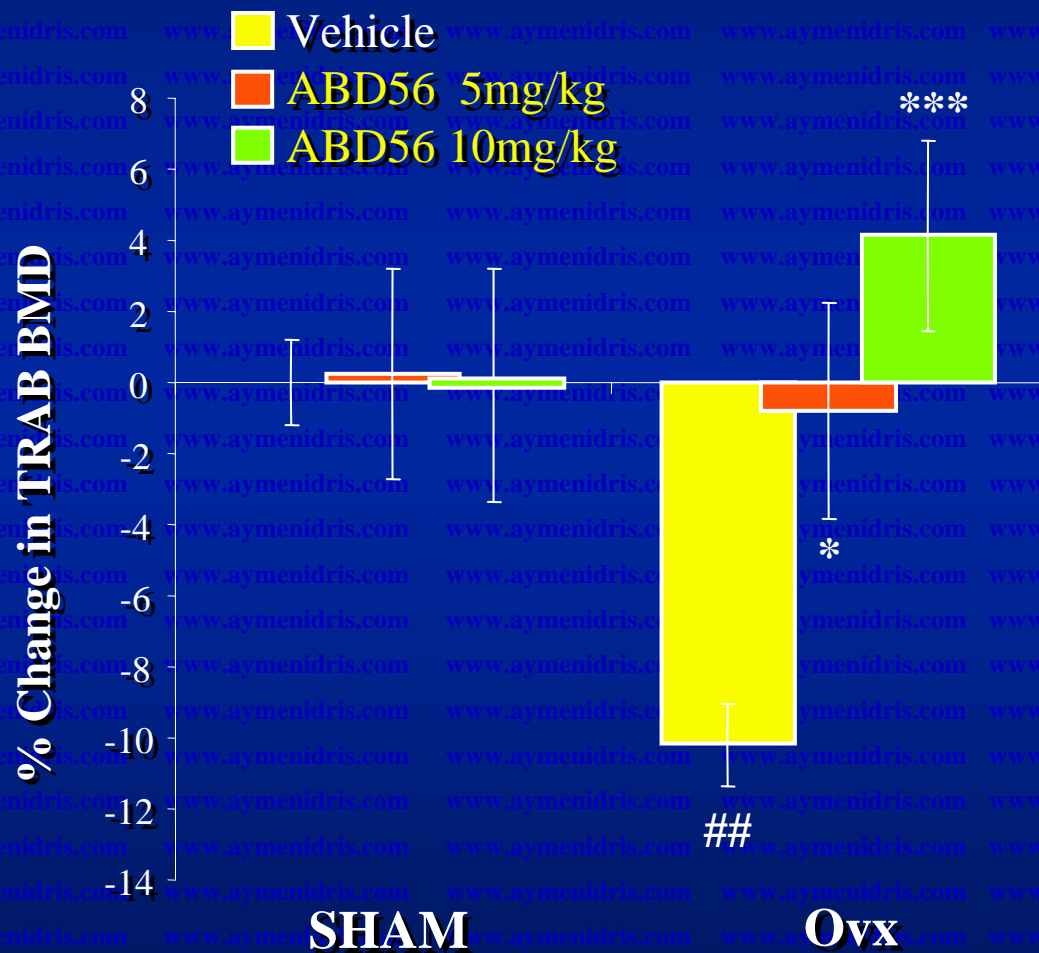
ABD56 (2µM)

*Idris et al. CTI 2008*

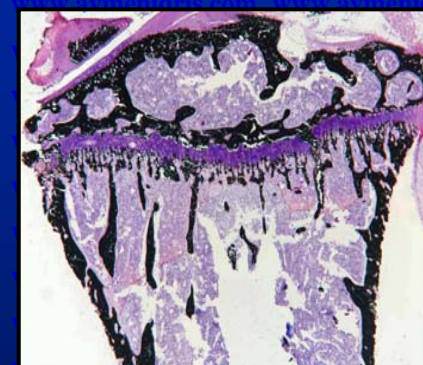
*Idris et al. Endocrinology 2009*



# ABD56 prevents bone loss due to oestrogen deficiency in mice

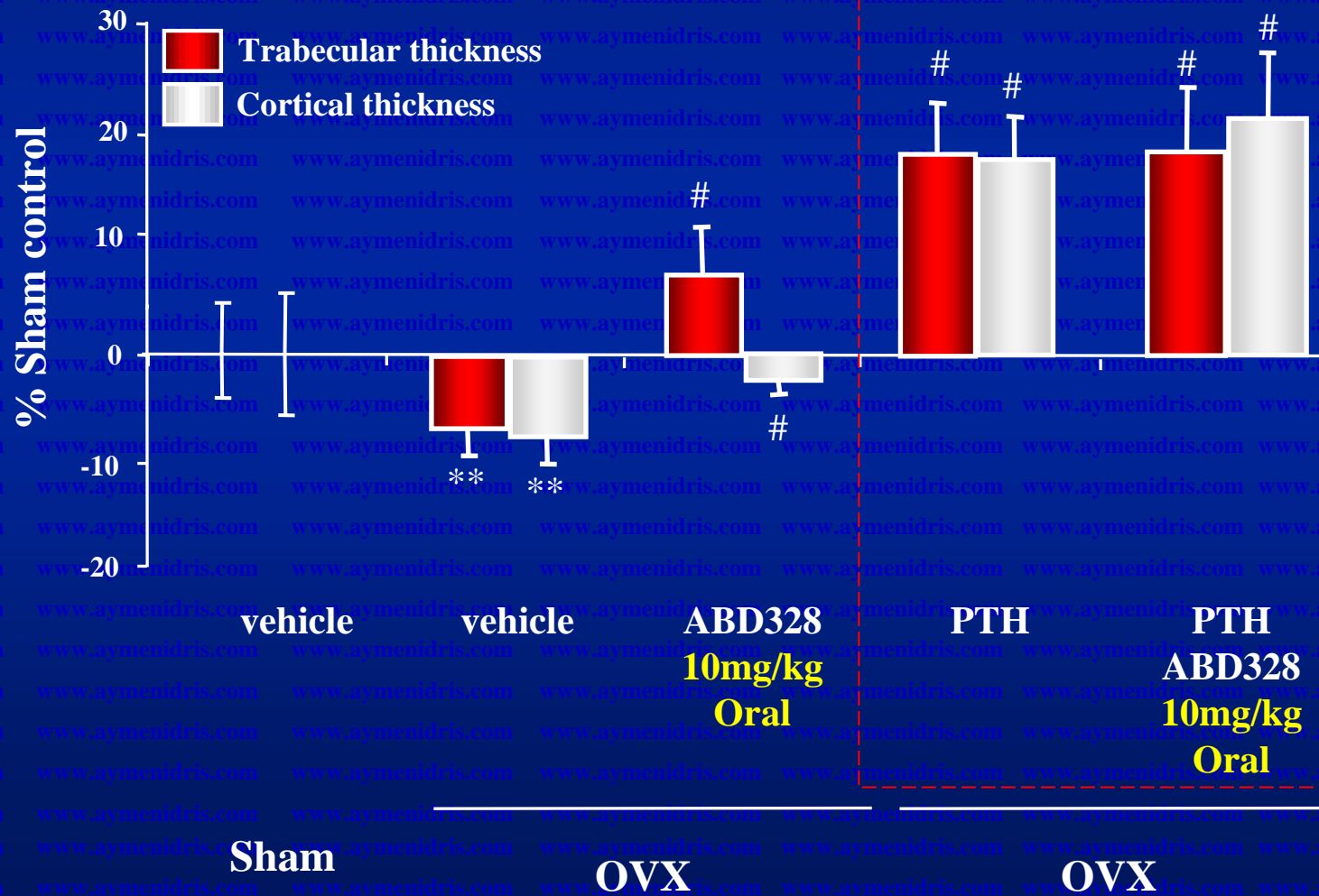


Ovx

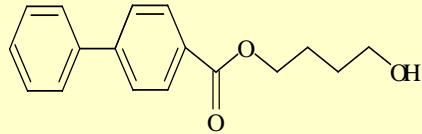


Ovx  
ABD56

# The non-hydrolysable derivative of ABD56 – ABD68 – does not impair parathyroid hormone (PTH) induced bone formation



**ABD56**



**ABD56 inhibits cytokines-induced NF $\kappa$ B activation**

**ABD56 prevents ovariectomy-induced bone loss**

**ABD56 does not inhibit osteoblast function**

**ABD56 does not blunt the effects of PTH in vivo**

**ABD56 derivatives represent a novel class of anti-resorptive drugs**