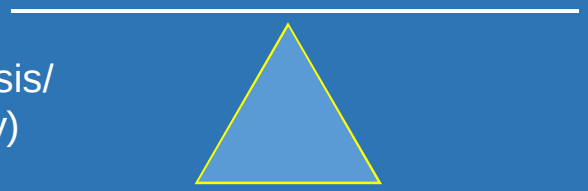
Alcohol-Induced Osteopenia

Martin Ronis, PhD

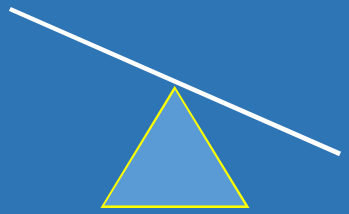
Professor, School of Medicine,
LSUHSC-New Orleans
Department of Pharmacology &
Experimental Therapeutics

Role of Bone Turnover in Normal Physiology and Bone Pathology

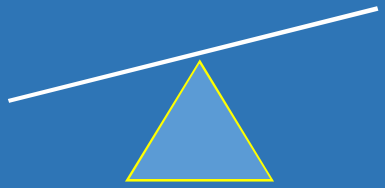
Bone Formation (Osteoblastogenesis/ Osteoblast Activity)



Bone Resorption (Osteoclastogenesis/ Osteoclast Activity)



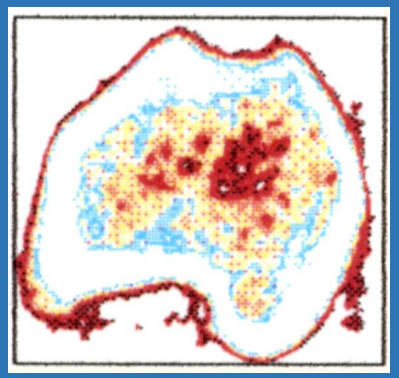
Skeletal growth during early development, puberty, attainment of peak bone mass (~age 25), bone rebuilding post-lactation. Pathology: Osteopetrosis.



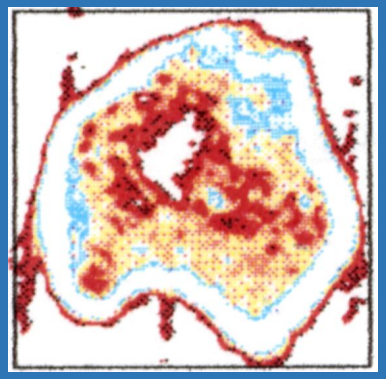
Aging, post-menopausal bone loss, bone loss during late pregnancy, lactation. Alcoholism. Pathology: Osteoporosis.

pQCT Analysis of Bone

Proximal Tibia

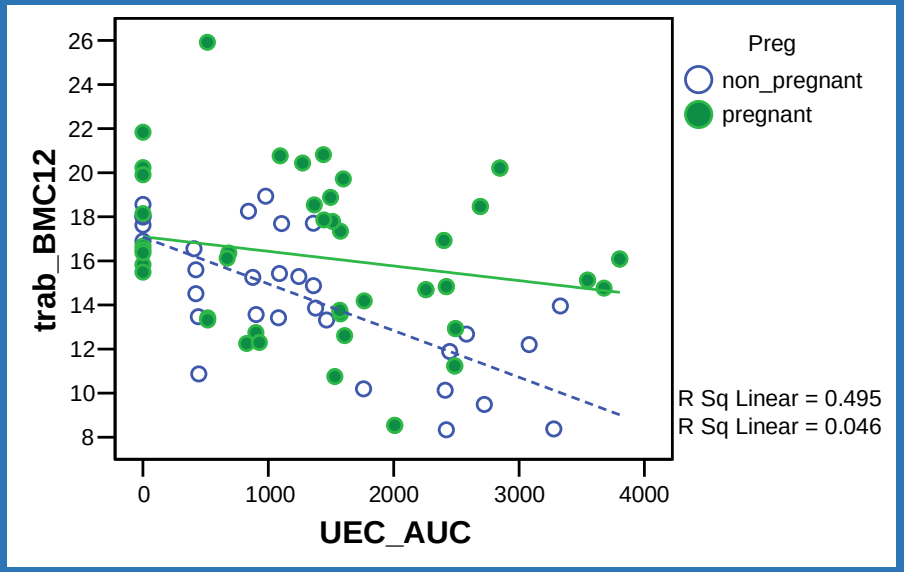


Control



High EtOH

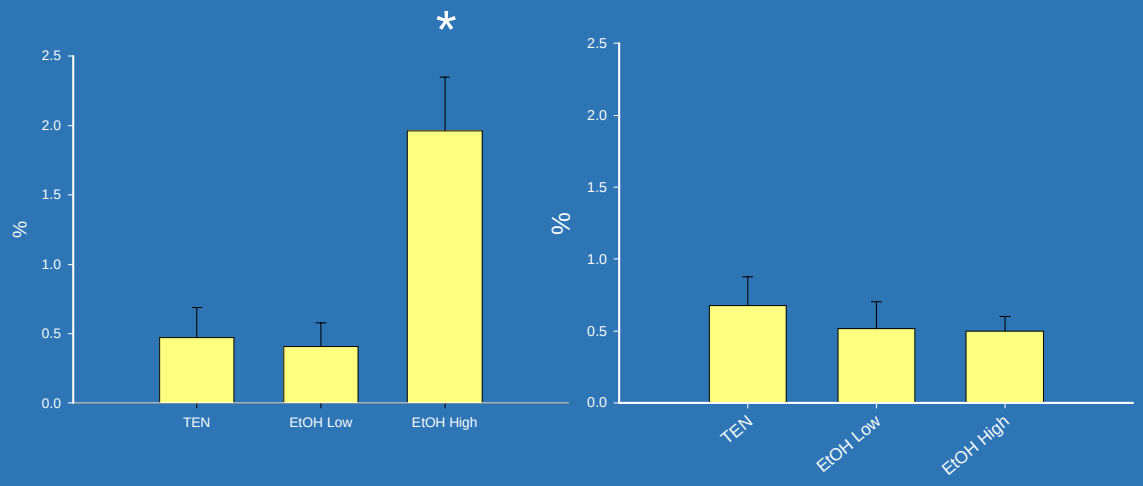
Dose-Responsive Decreases in Trabecular Bone Mineral Content (BMC) in Cycling and Pregnant Female Rats Exposed to Alcohol



UEC – urine ethanol concentration
AUC – area under dose-time curve

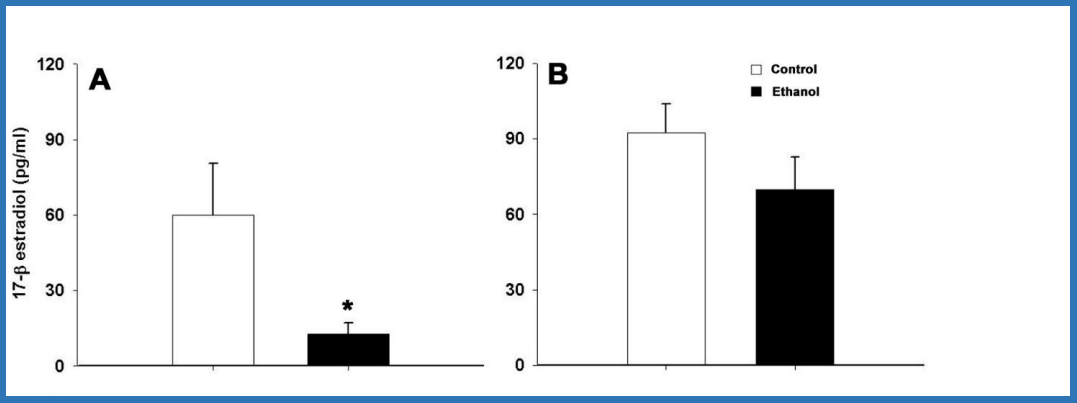
Shankar et al Endocrinology 147: 166-178, 2006

Osteoclast surface/Bone surface

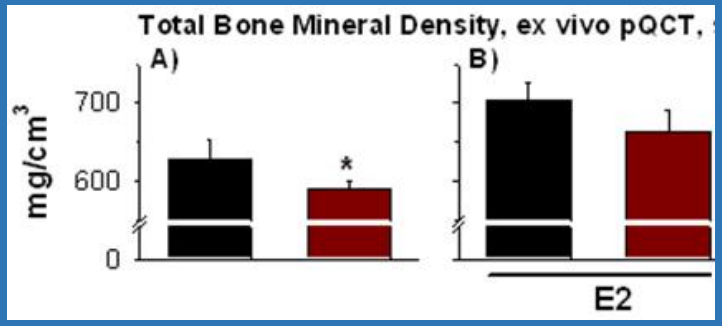


Cycling Rat

Pregnant Rat



Estradiol Protects Against EtOH-Induced Bone Loss in Cycling Female Rats



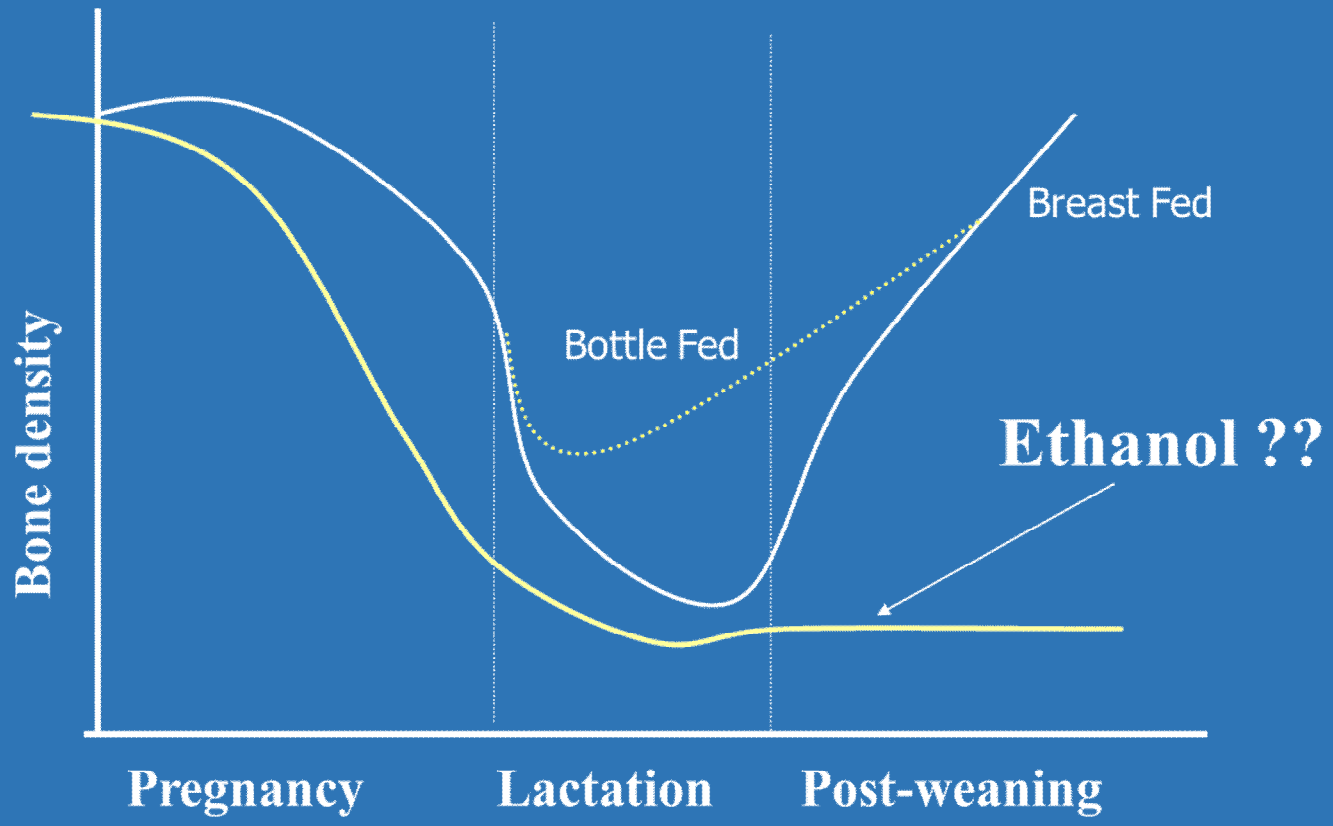
Control
Ethanol

E2 = Estradiol

Chen et al. J. Pharmacol. Exp. Ther. 319: 1182-1190, 2006.

Shankar et al Endocrinology 147: 166-178, 2006

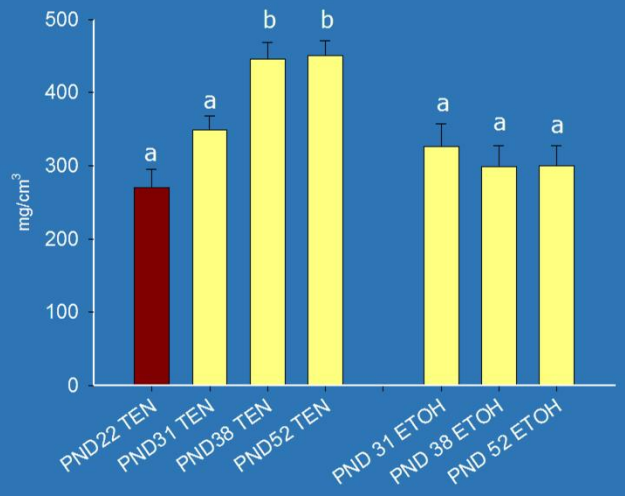
Bone density during pregnancy and lactation



Anabolic Bone Rebuilding Post Lactation is Inhibited by Alcohol Consumption in Female Rats

pQCT

Trabecular Bone Mineral Density (Slice 3+4)

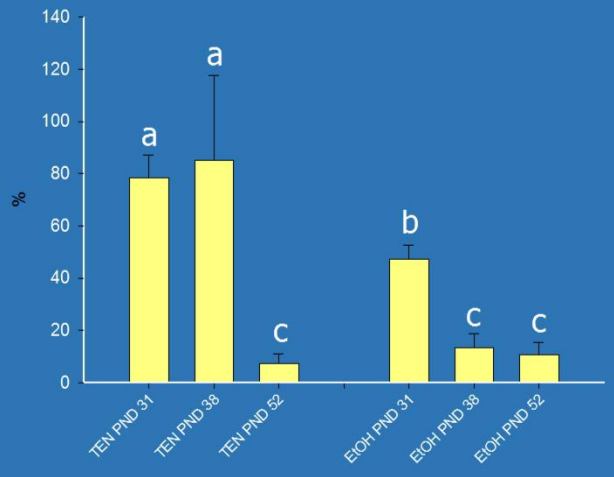


a<b

P<0.001

Dynamic Histomorphometry

Bone Formation/Trabecular Volume

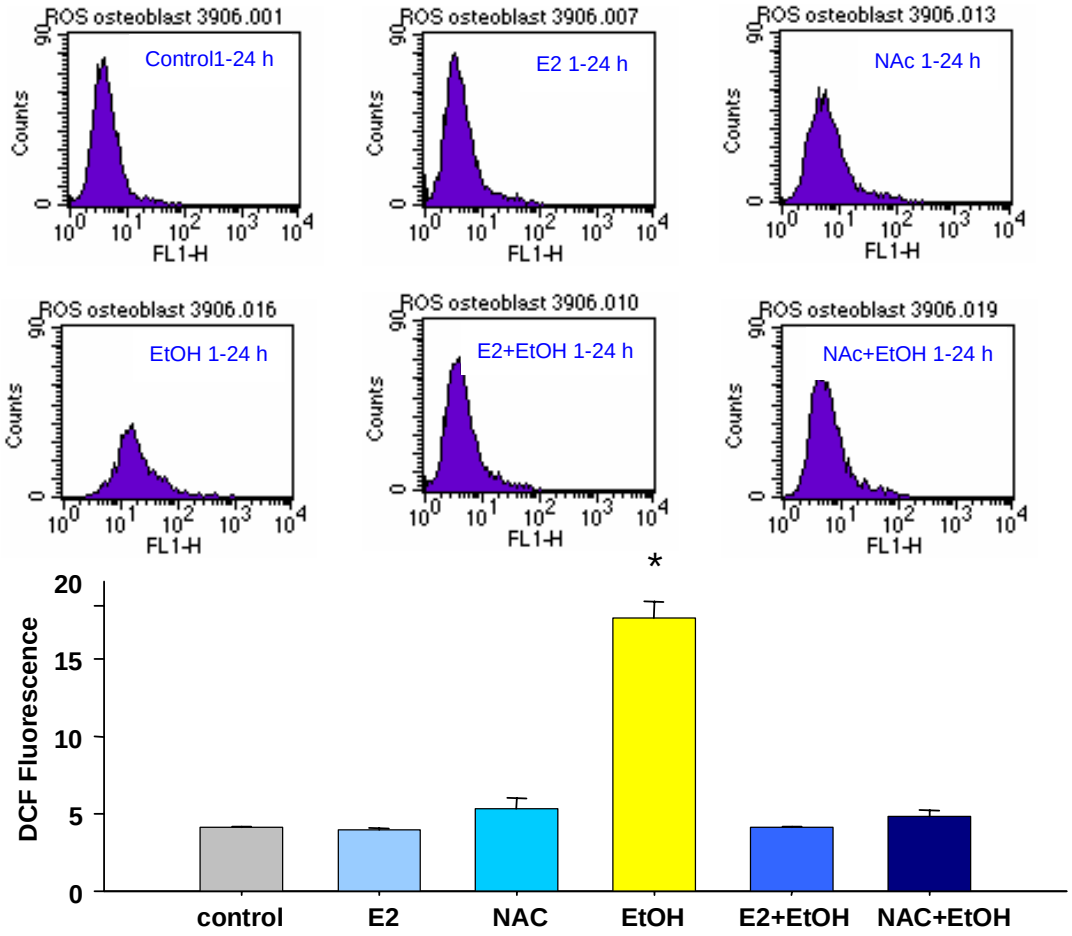


a>b>c

P<0.05

Shankar et al. J. Bone Min. Res. 23: 338-349, 2008.

NAC and E2 Both Block EtOH Induced ROS Formation in Differentiated Primary Osteoblast Cultures



NAC – Dietary antioxidant N-acetylcysteine

E2 – Estradiol

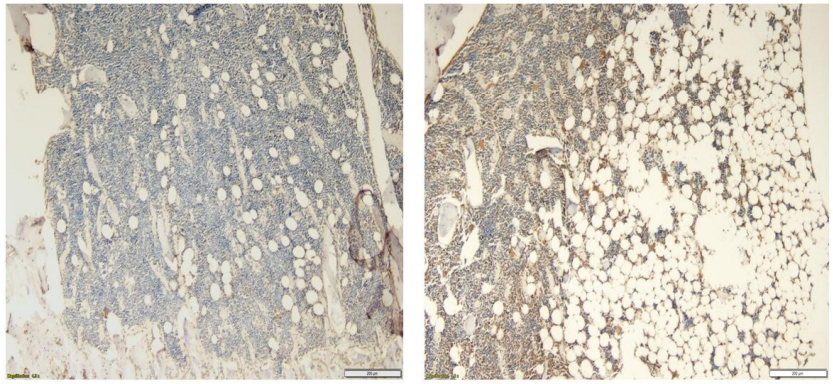
ROS – Reactive oxygen species

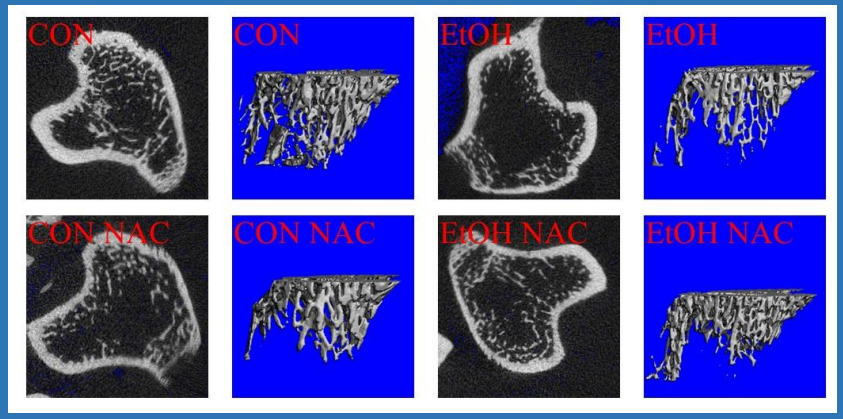
Molecular Mechanisms Underlying Alcoholic Osteopenia

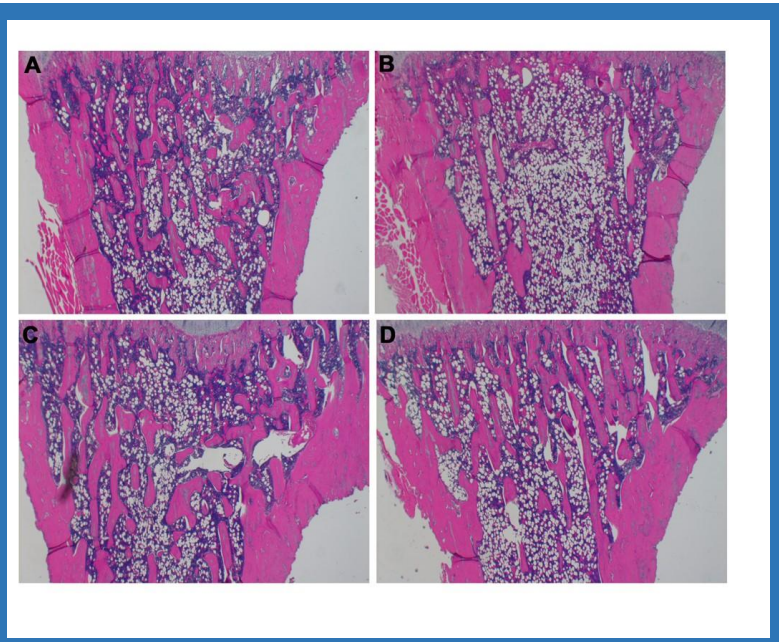
Chen et al. J. Pharmacol. Exp. Ther. 324: 50-59, 2008.

Dietary Antioxidants Block Alcohol-Induced ROS and Transdifferentiation of Mesenchymal Stem Cells into Adipocytes in Bone Marrow

EtOH induces ROS in mouse tibia
Nitrotyrosine Staining (10x)

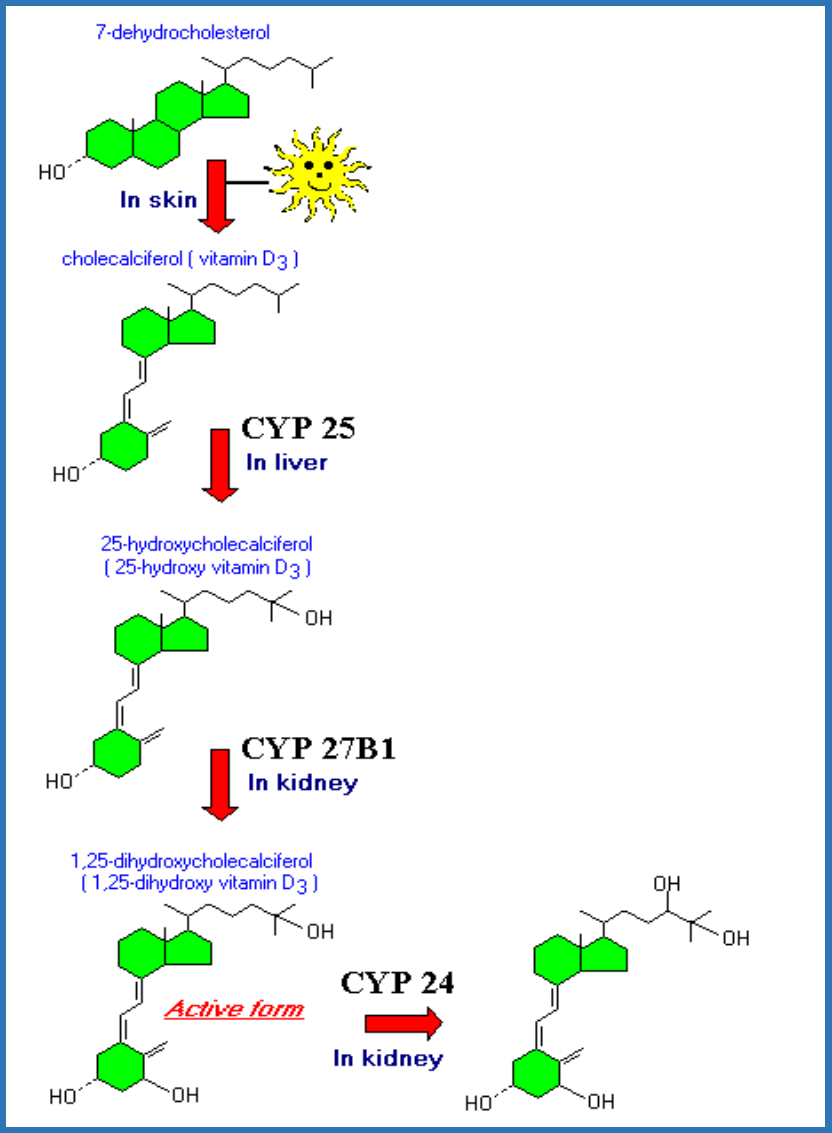




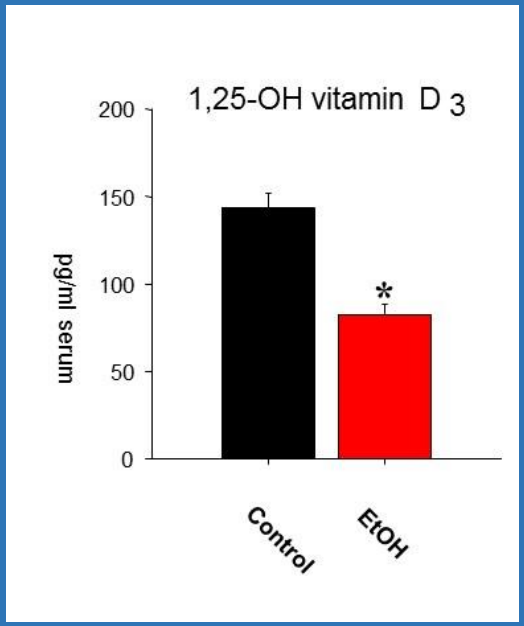


A: Control, B: EtOH, C: NAC, D: EtOH + NAC

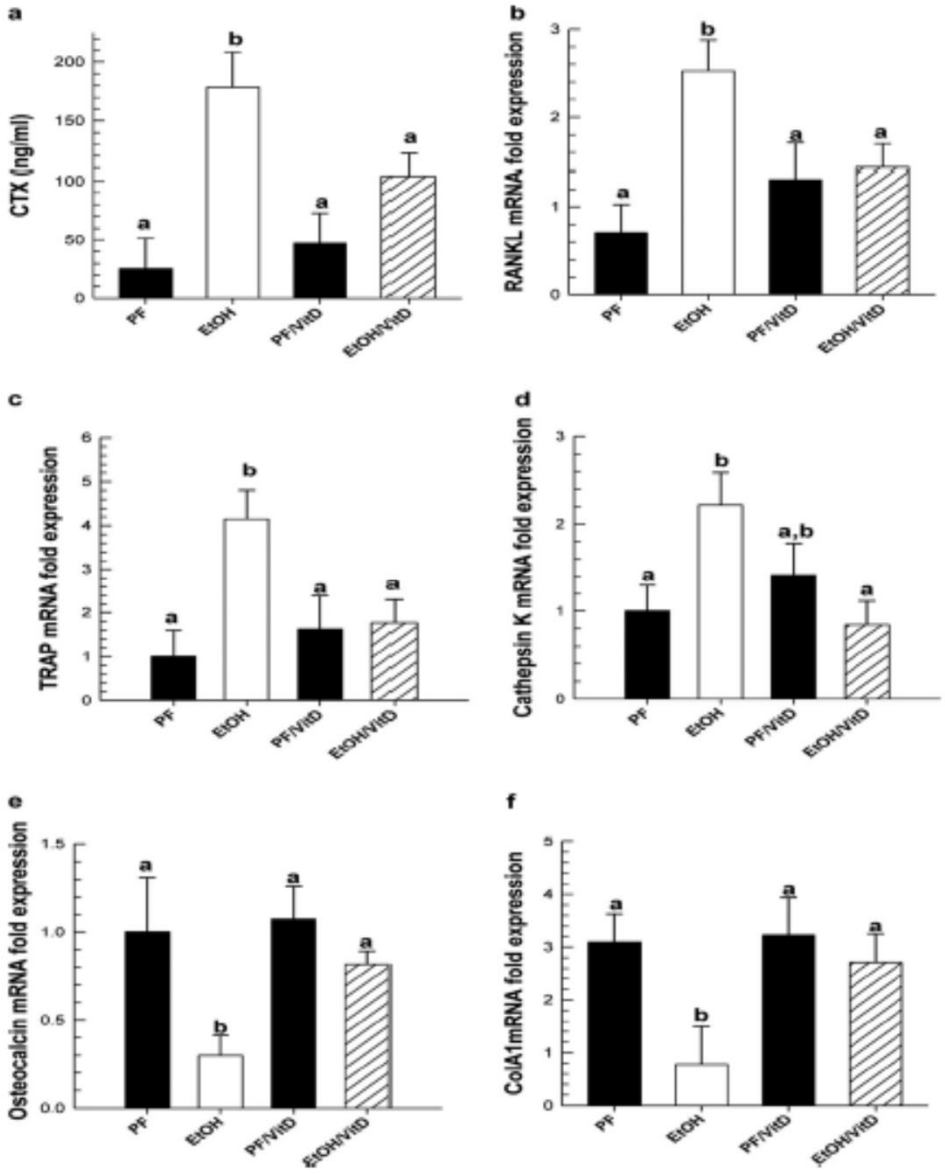
Shankar et al. J. Bone Min. Res. 23: 338-349, 2008.
Chen et al. J. Bone Min. Res. 25: 1117-1127, 2010.
Alund et al. Alc. Clin. Exp. Res. (In Press).



Alcohol also Acts as an Endocrine Disruptor of the Vitamin D3/Calcium Axis



Shankar et al. Endocrinology 149: 1748-1756, 2008.



Dietary Vitamin D3 Supplementation Reverses Alcoholic Osteopenia in Female Mice

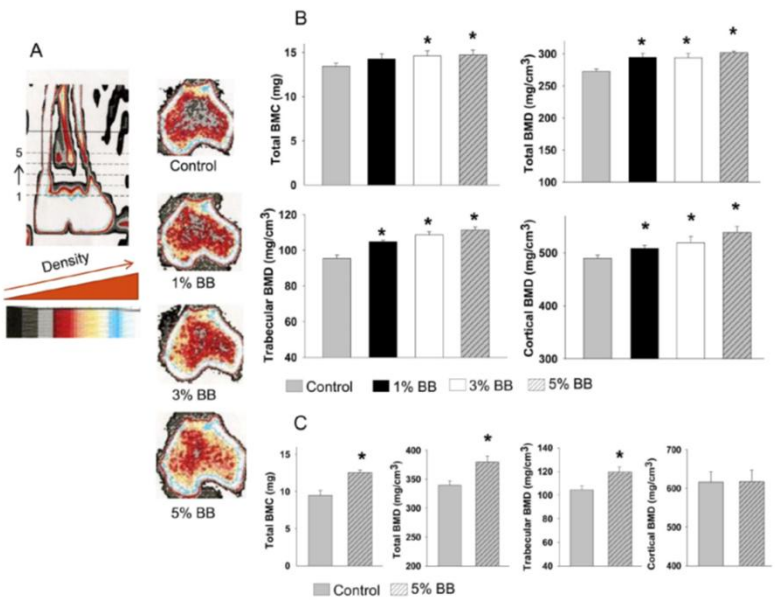
PF – pair fed EtOH – alcohol treated VitD – vitamin D

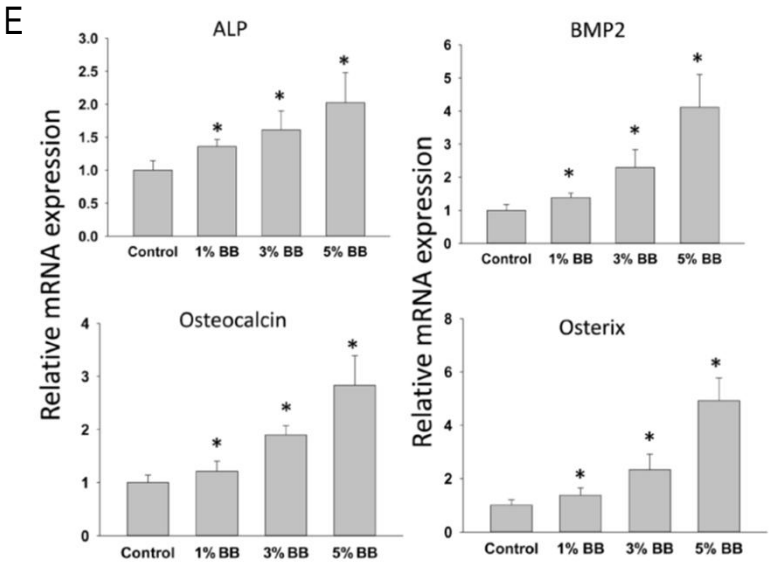
CTX – collagen cross links – bone resorption marker
TRAP – tartarate resistant acid phosphatase – bone resorption marker.
RANKL – TNF family member regulator of osteoclastogenesis
Cathepsin K – marker of osteoclast function

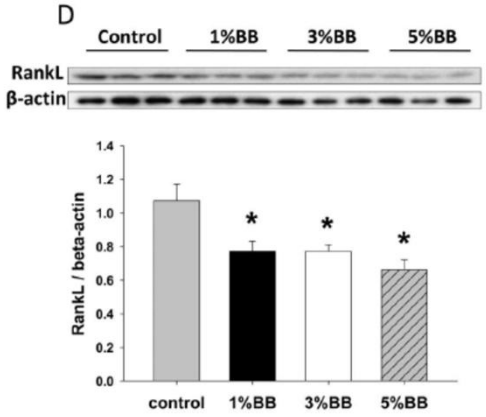
Osteocalcin – bone formation marker
Col1A1 – collagen – marker of osteoblast function

Mercer et al. J. Pharmacol. Exp. Ther. 343:401-412, 2012.

Dietary Feeding of Blueberries (BB) Dose-Dependently Increase Bone Mass Via Phenolic Acid Activation of GPR109A







Zhang et al. Plos One 8(8) e70438, 2013.

Chen et al. J. Bone Min. Res. 29: 1043-53, 2014.

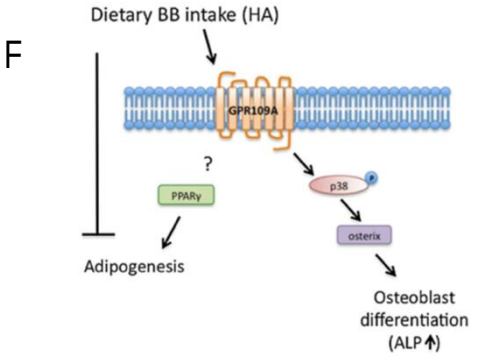


Fig. 2. Schematic model for HA actions on osteoblast differentiation and adipogenesis in bone marrow. HA = hippuric acid; BB = blueberry; ALP = alkaline phosphatase; PPAR = peroxisome proliferator-activated receptor; GPR = G protein.