

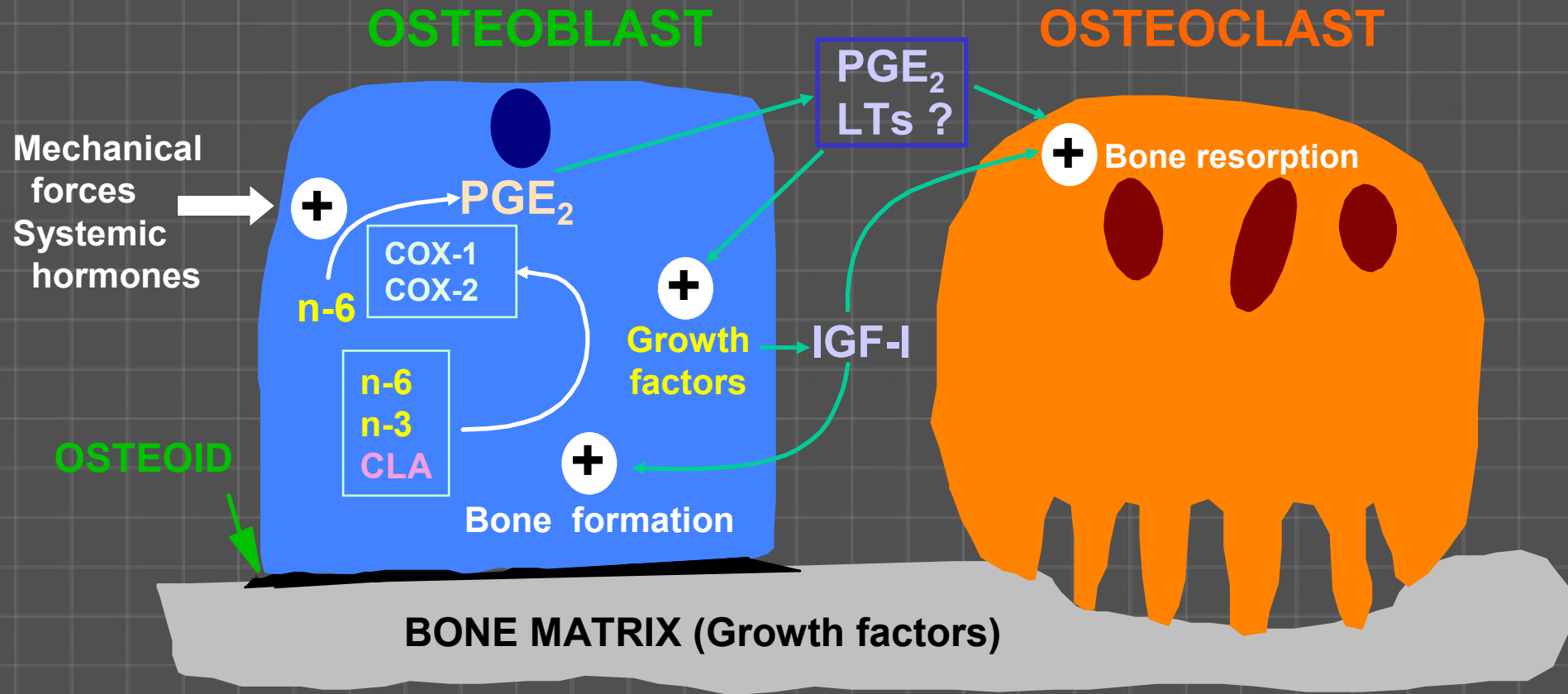
CLA and Bone Formation

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Cells of the Bone Microenvironment: Local Factors Regulating Osteoblast and Osteoclast Functions (PGE₂ orchestrates biochemical, physiological, molecular events)

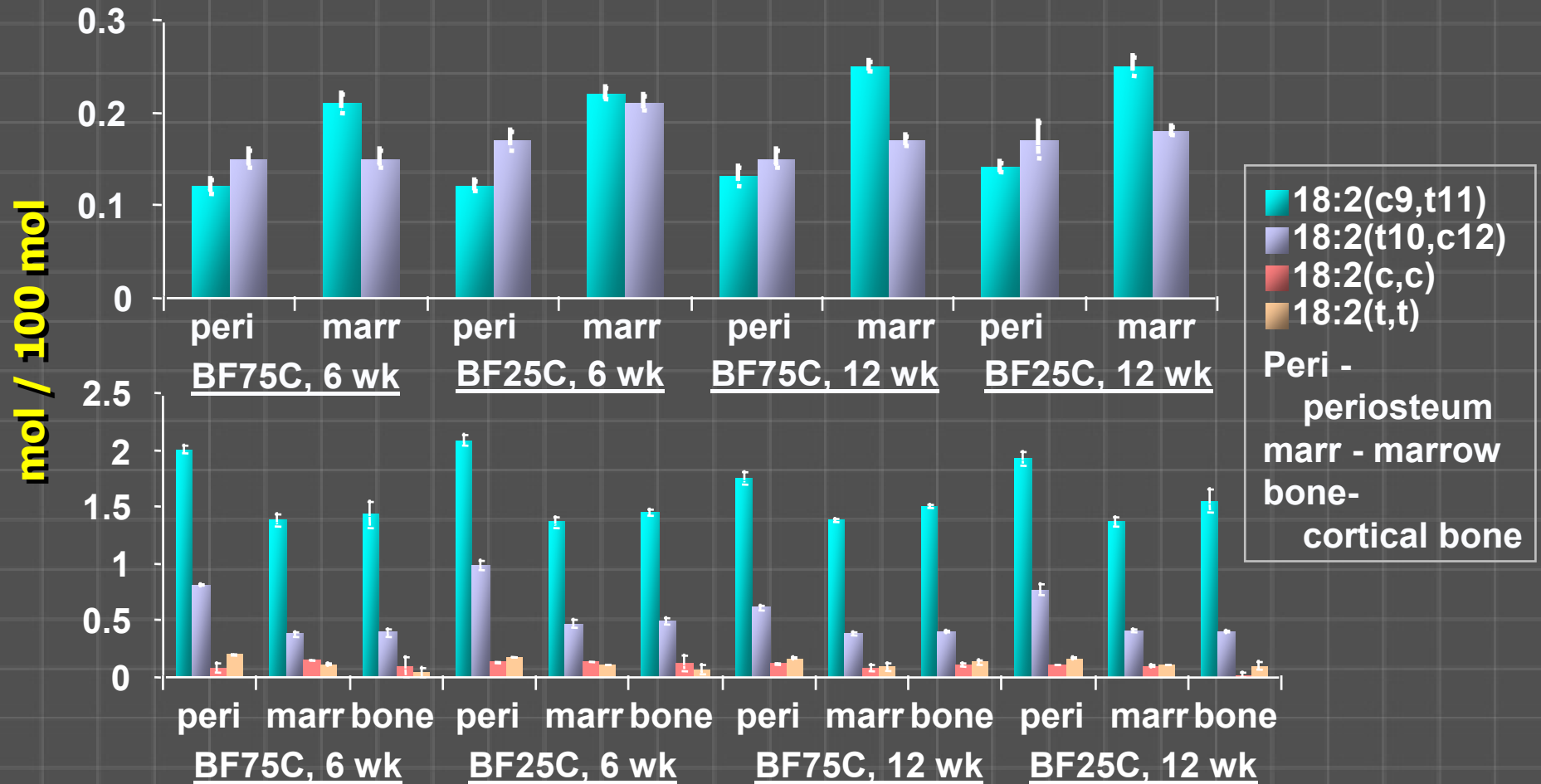


Studies on CLA and Bone Formation

Approach:

- **Characterization:** dietary fats alter the fatty acid composition of bone and cartilage compartments
- **Biochemical Factors:** prostaglandin E and insulin-like growth factors, osteocalcin, BALP
- **Functional Aspects:** bone formation rates, chondrocyte function, activity of osteoblast-like cells

Effect of Dietary CLA Isomers on Rat Tibia CLA Concentration



Dynamics of Bone Tissue

FUNCTIONS



BALANCE

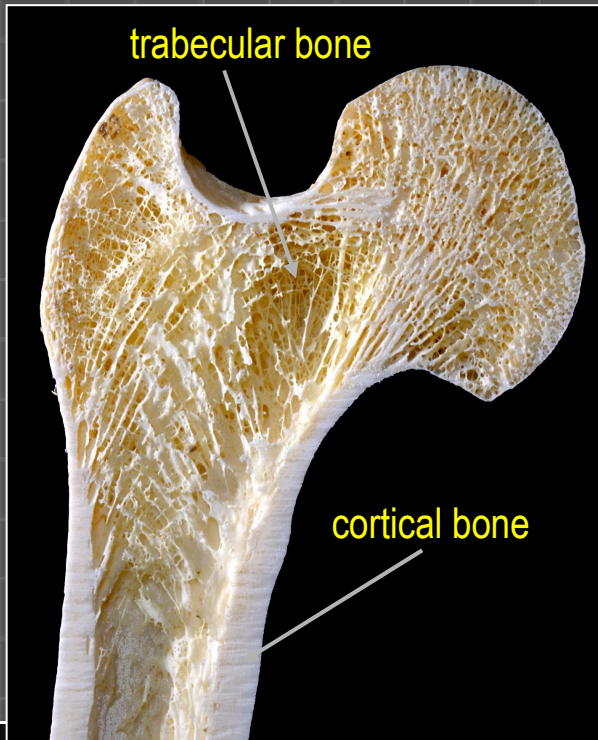


❖ Structural competency

- Support
- Locomotion
- Protection

❖ Metabolic efficiency

- Mineral reservoir
- Composite of cells



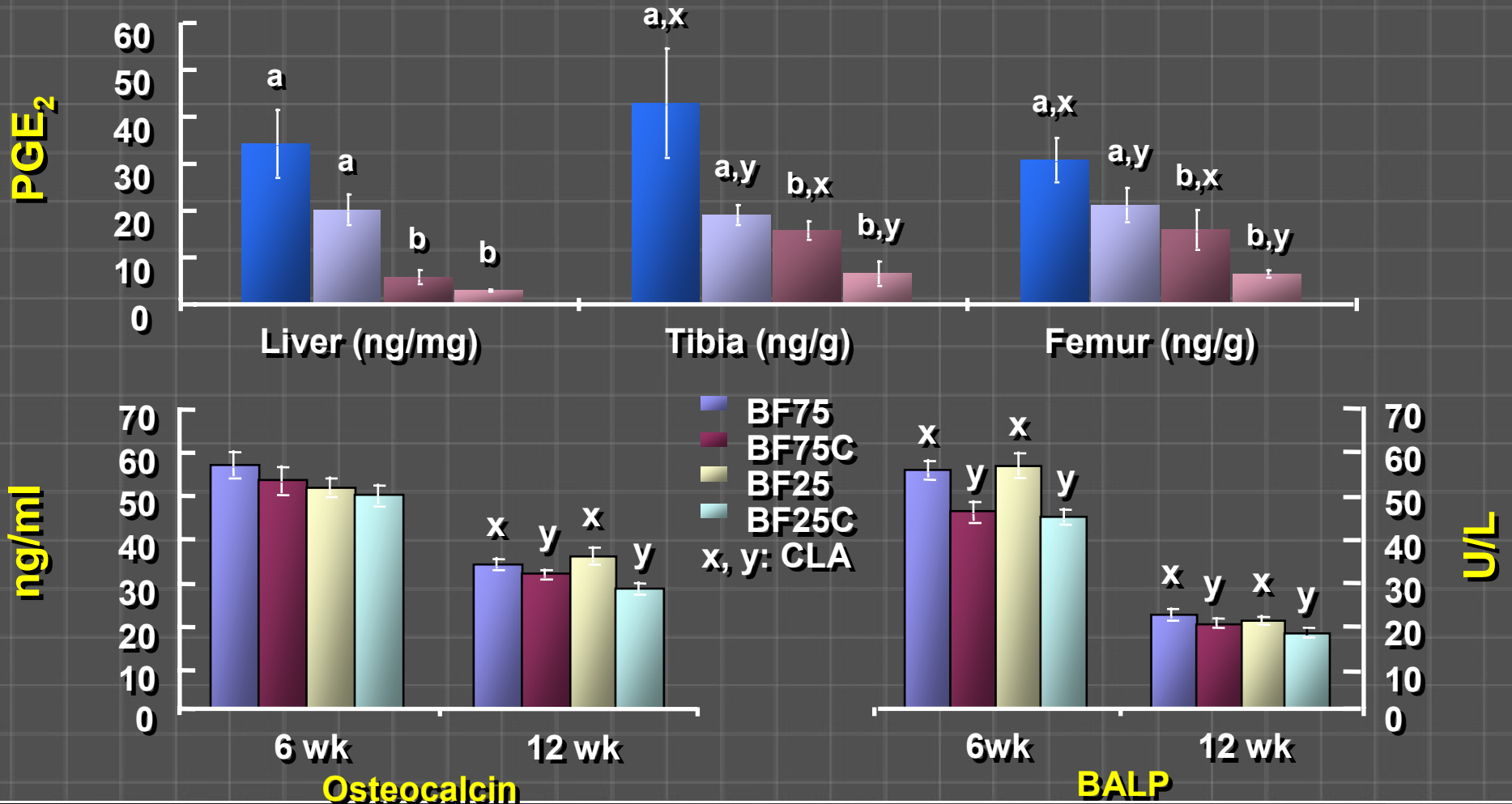
local **growth factors**
(e.g. IGF-I, IG-F-II, TGF- β)

resorptive regulatory
factors

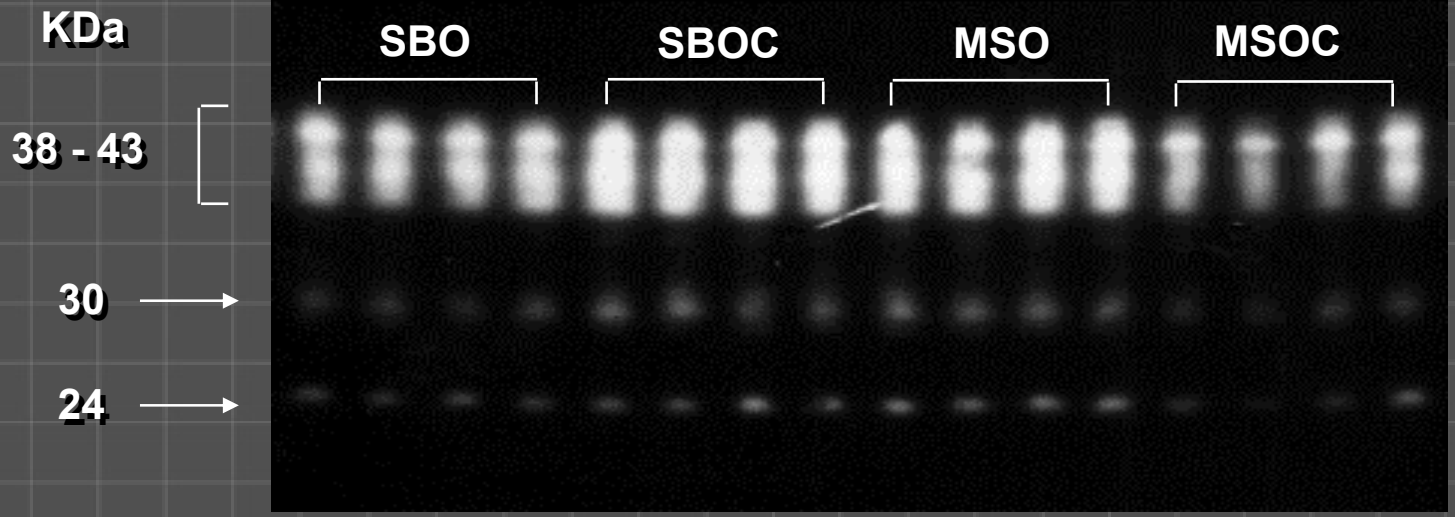
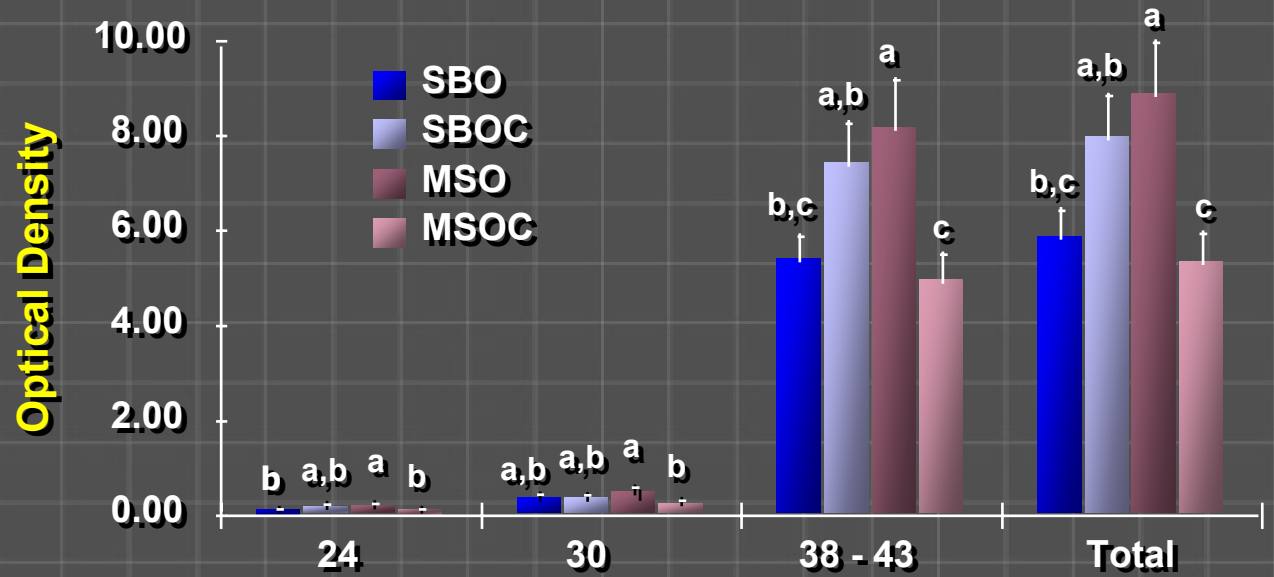
(e.g. IL-1, TNF, EGF, PDGF)

mediatory factors
(cytokines, eicosanoids)

Effects of CLA and PUFA on Ex Vivo Bone PGE₂ Production, Serum Osteocalcin and Bone Specific Alkaline Phosphatase (BALP) in Rats

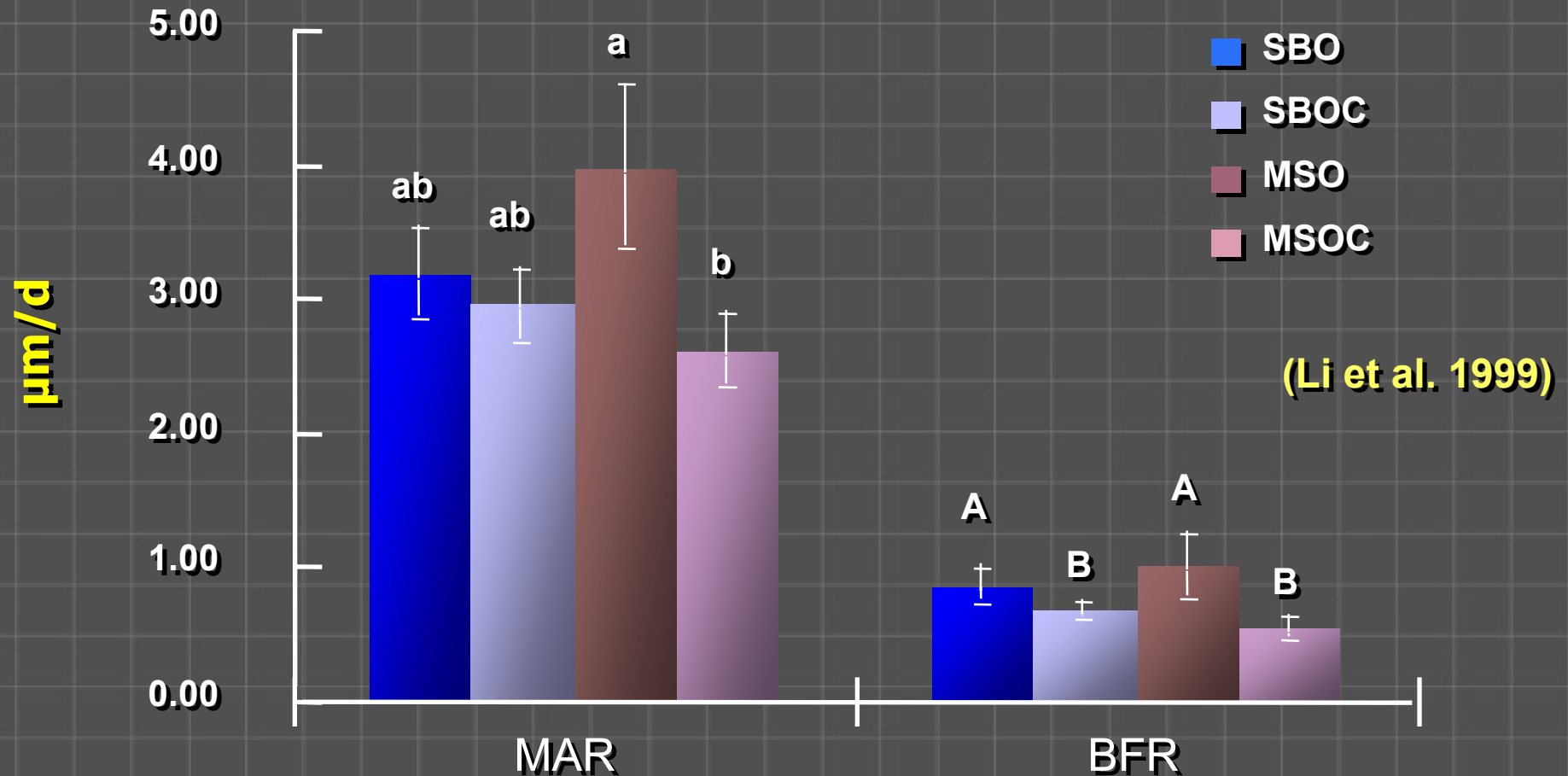


Effect of CLA and n-6, n-3 PUFA on IGFBPs in Rat Serum



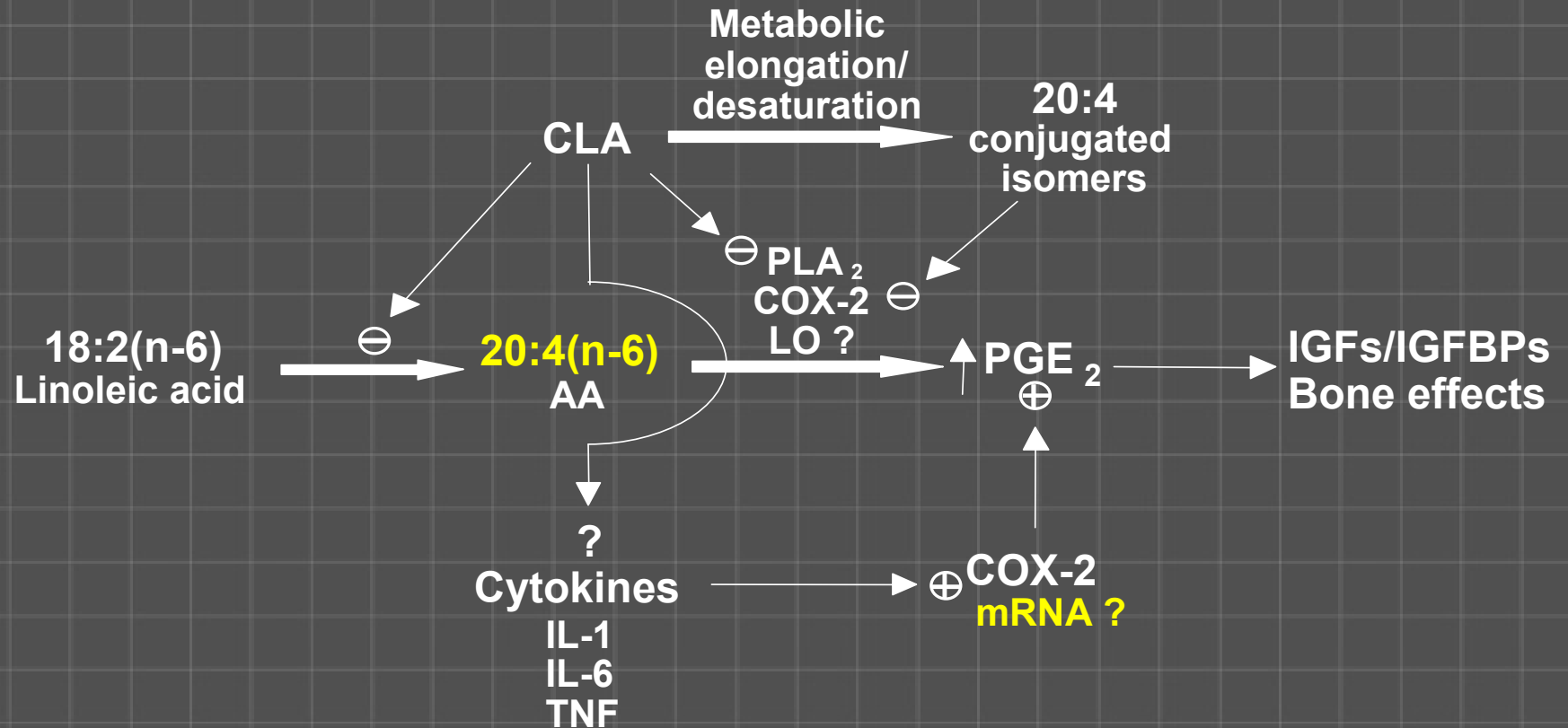
(Li et al. 1999)

Effect of CLA and PUFA (n-6 & n-3) on Bone Formation (MAR and BFR) in Rats

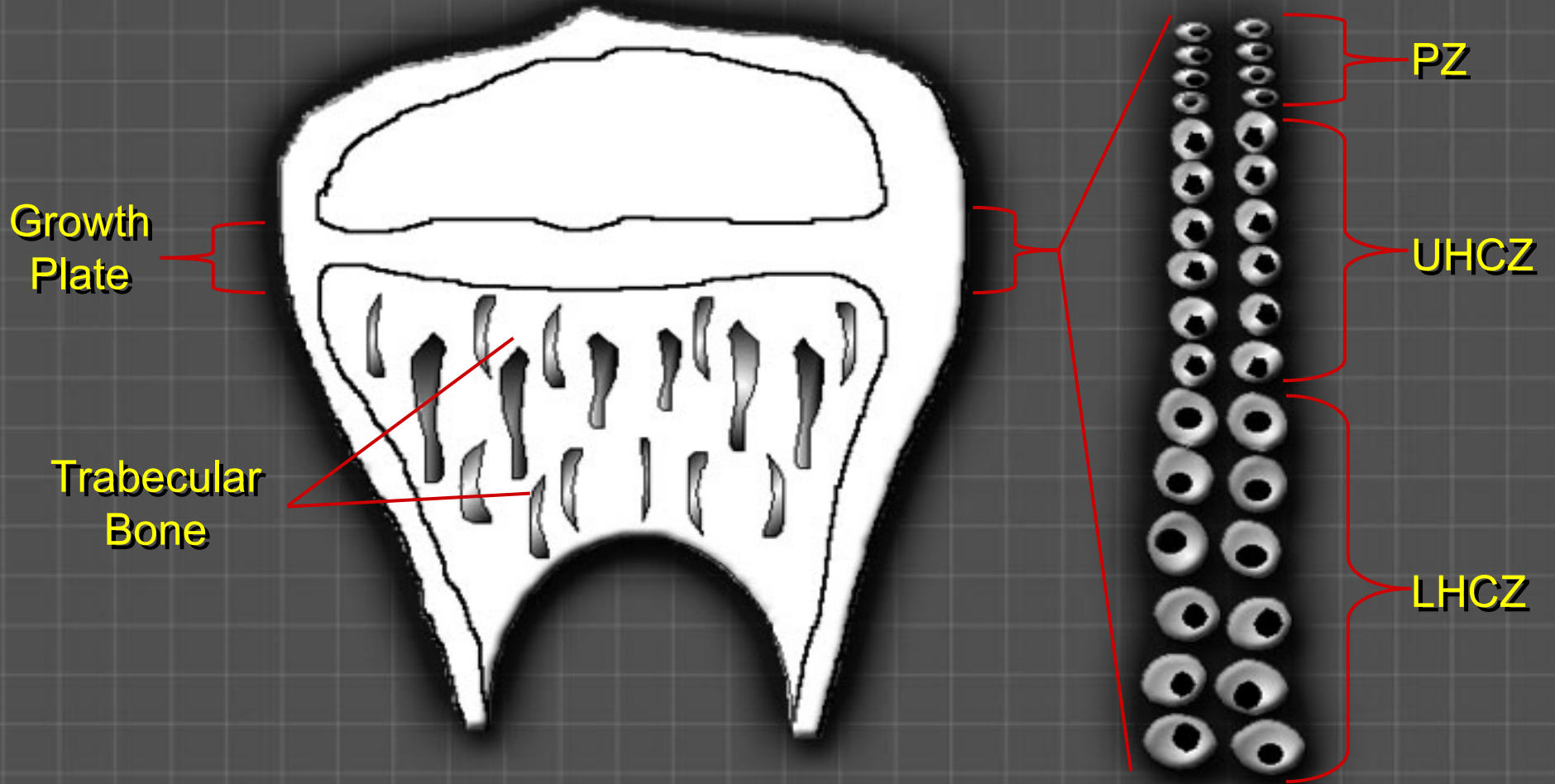


Proposed Actions of CLA on PGE₂ Production and Bone Metabolism

(Watkins et al. 1999)

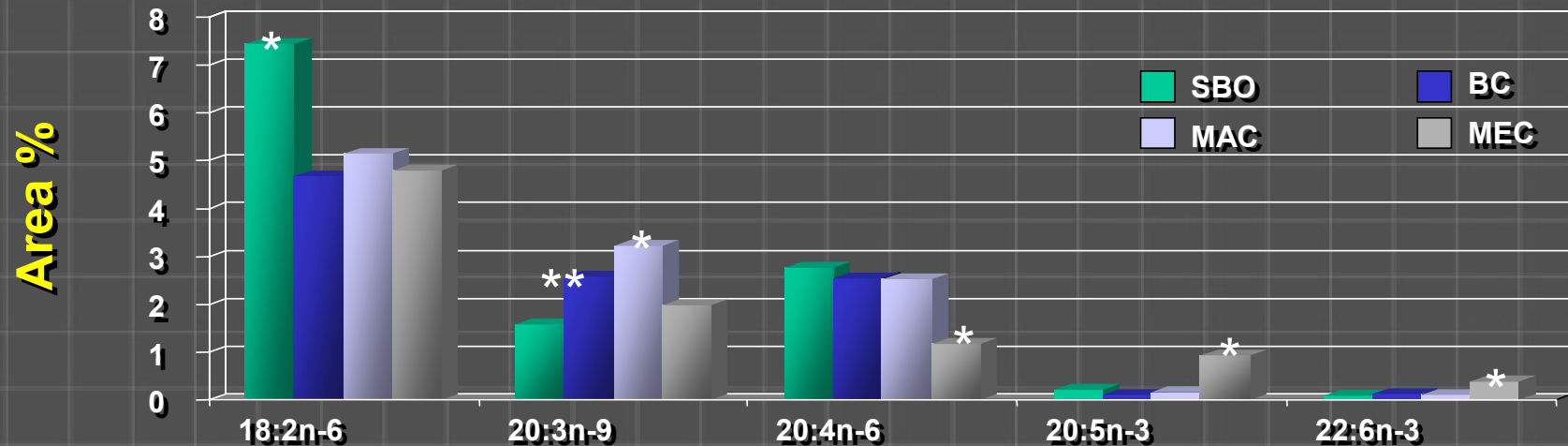
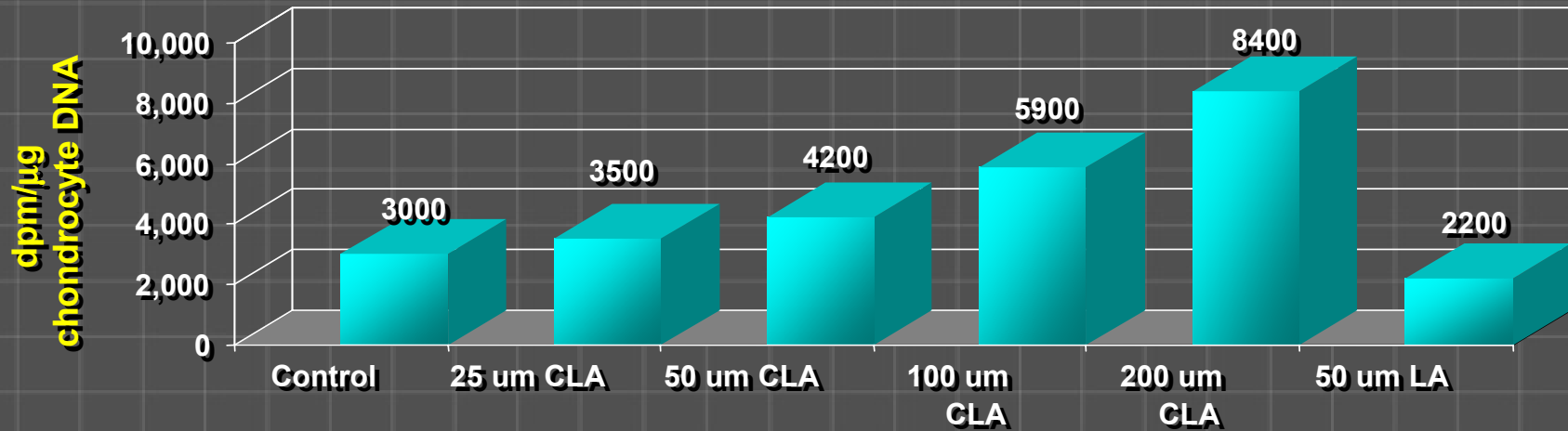


Epiphyseal Growth Plate Cartilage and Trabecular Bone

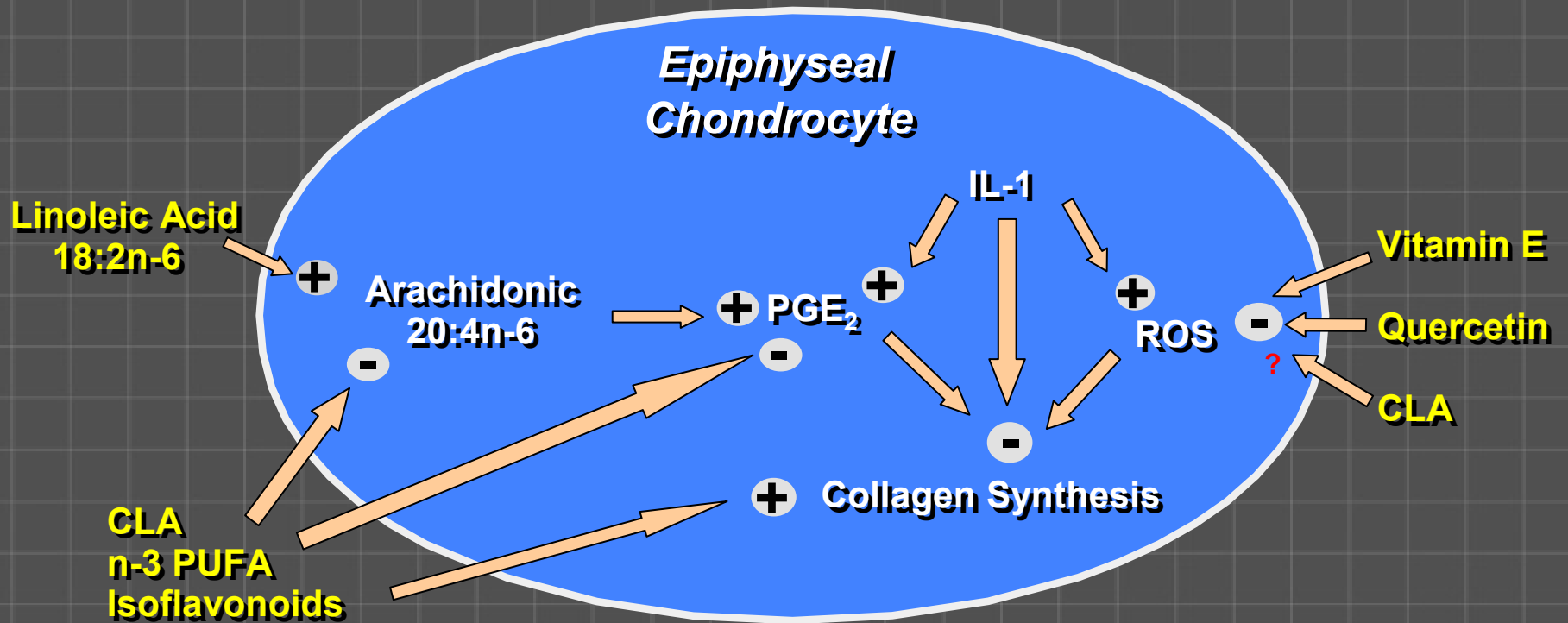


CLA and LA Effects on Epiphyseal Chondrocyte Function

(Xu et al. 1994)



Actions of Dietary PUFA, CLA and Antioxidants on Collagen Synthesis in Epiphyseal Chondrocytes



Model for Understanding the Mechanism of CLA Action on Bone Formation – Osteoblast (OB)

Purpose: to study the actions of PUFA on developmental regulation of bone modeling/remodeling, directing differentiation of progenitor cells, and to minimize bone loss

Targets: OB

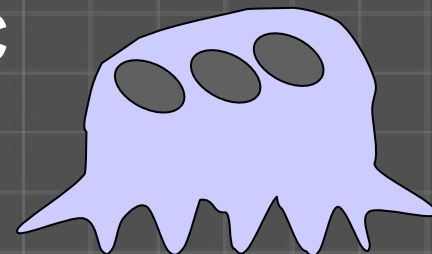
COX-2 - OB activity, chronic bone loss

Cbfa1 transcription factors - differentiation of OB

osteocalcin genes in OB - proliferation, maturation, mineralization

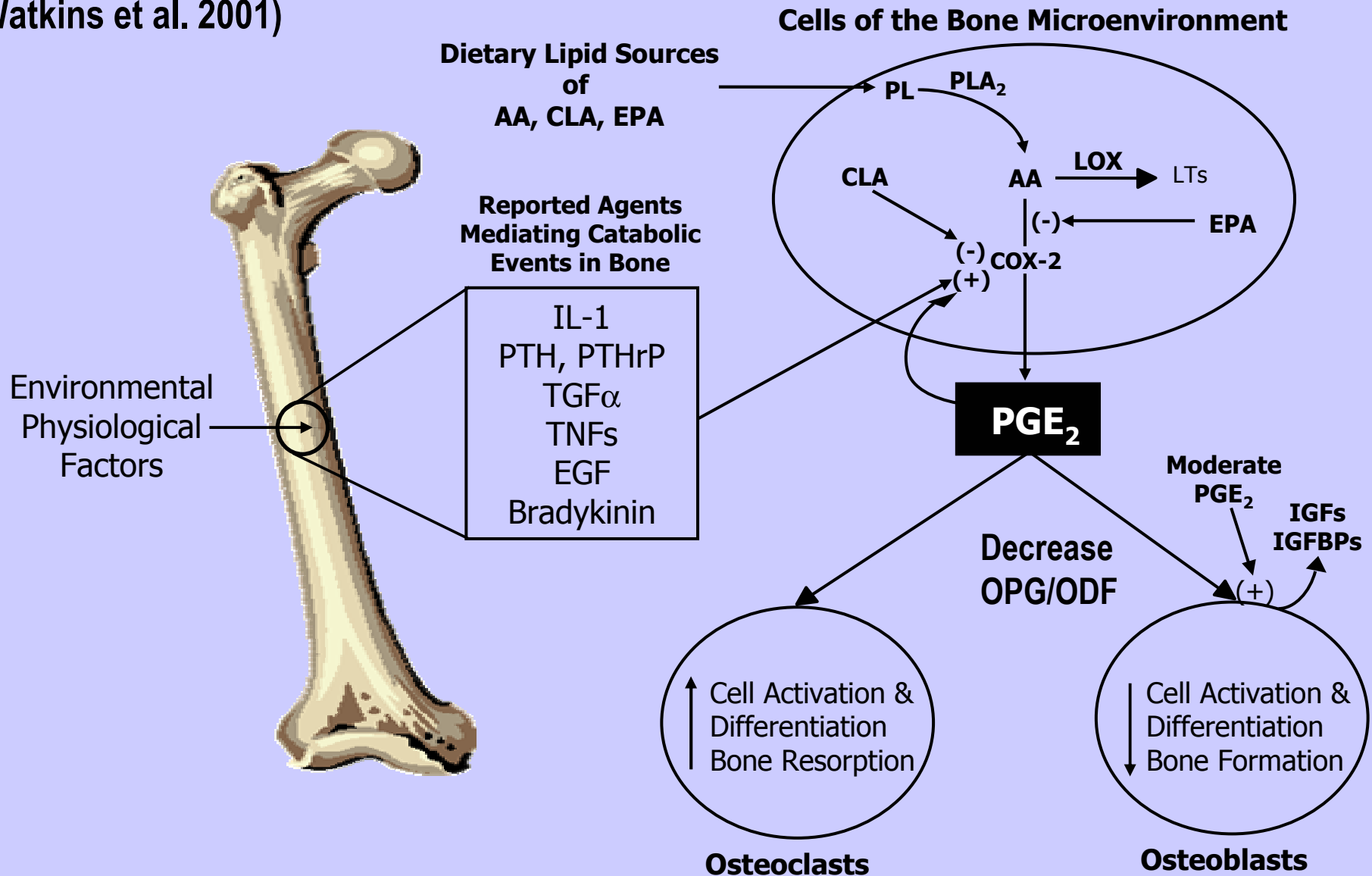
ODF and OPG signaling proteins - differentiation of OC

(Watkins et al. 2001 Exp Biol Med & Prog Lipid Res)



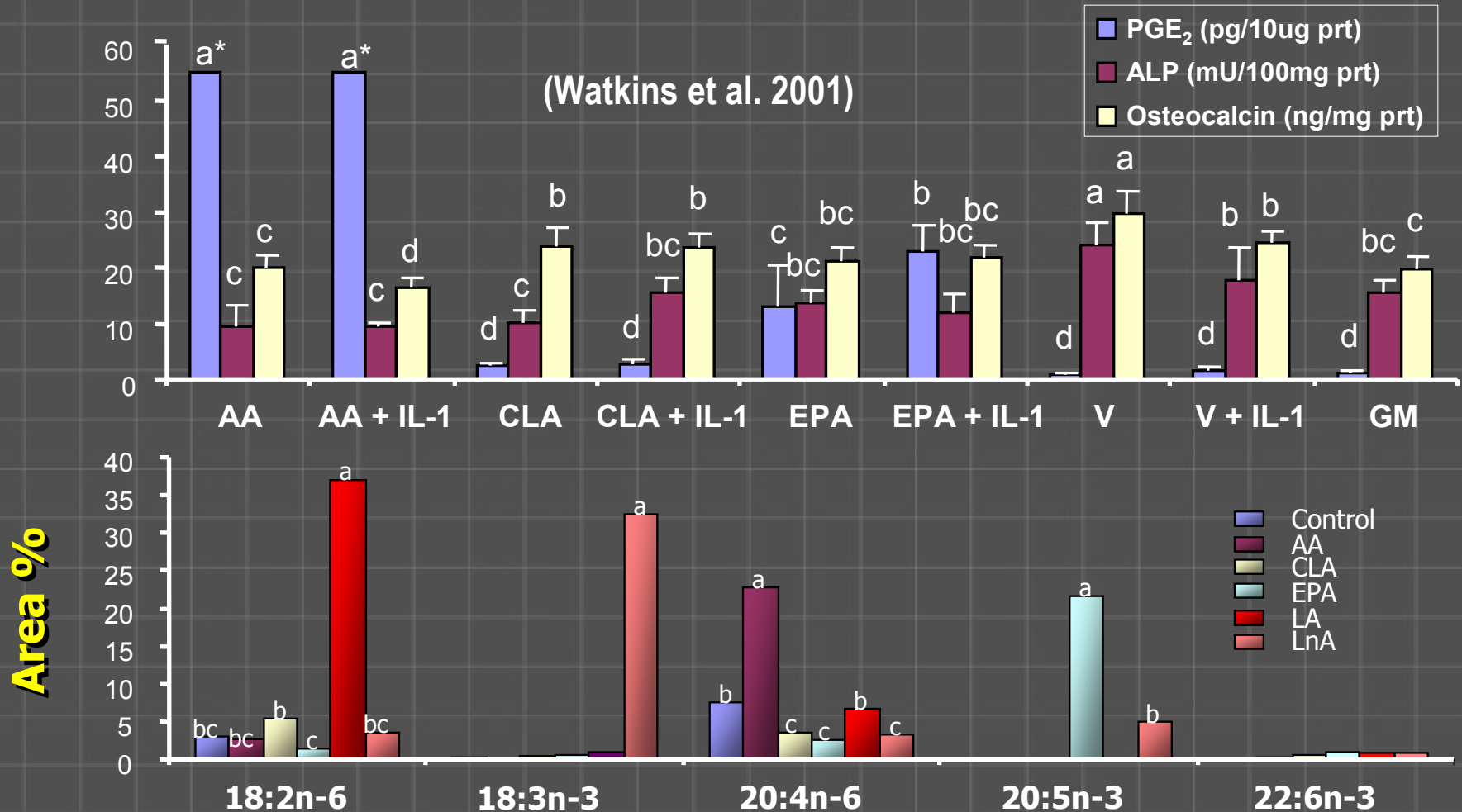
Molecular Targets for Moderating Catabolic Events in Aging Bone

(Watkins et al. 2001)

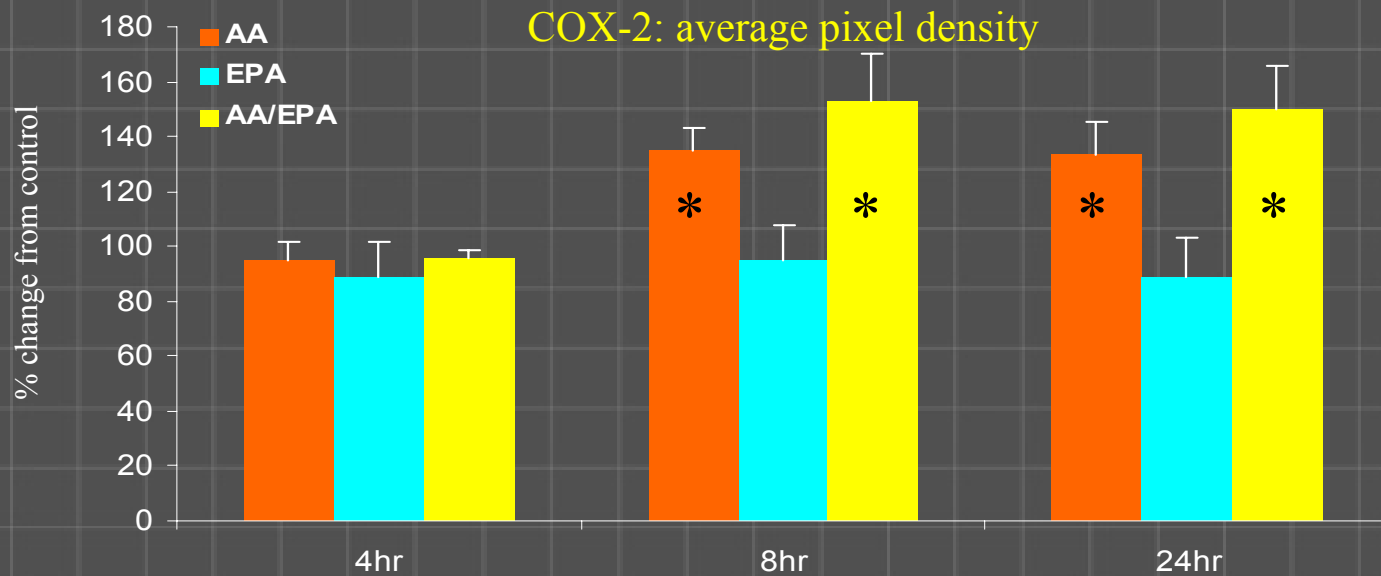
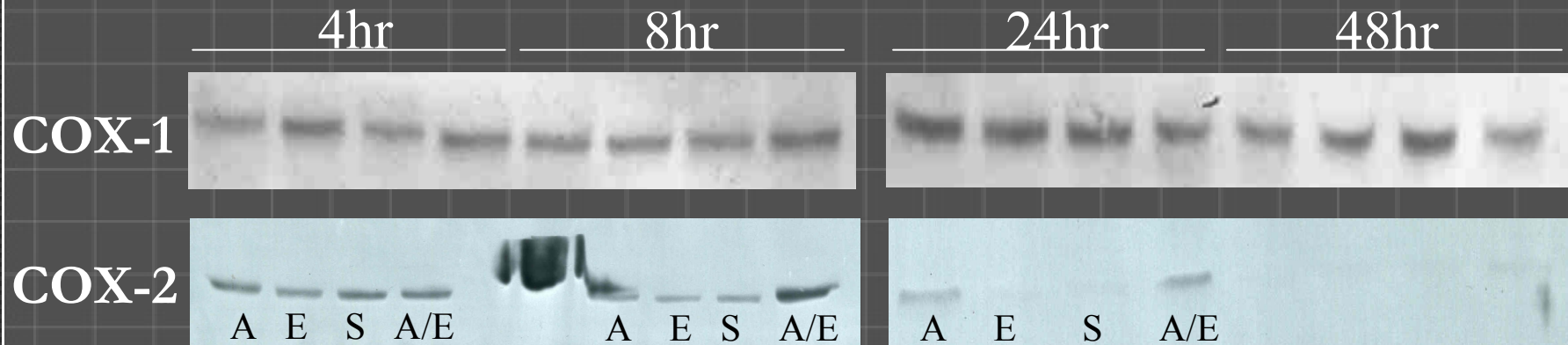


Osteoblast Activity (matrix/mineral formation)

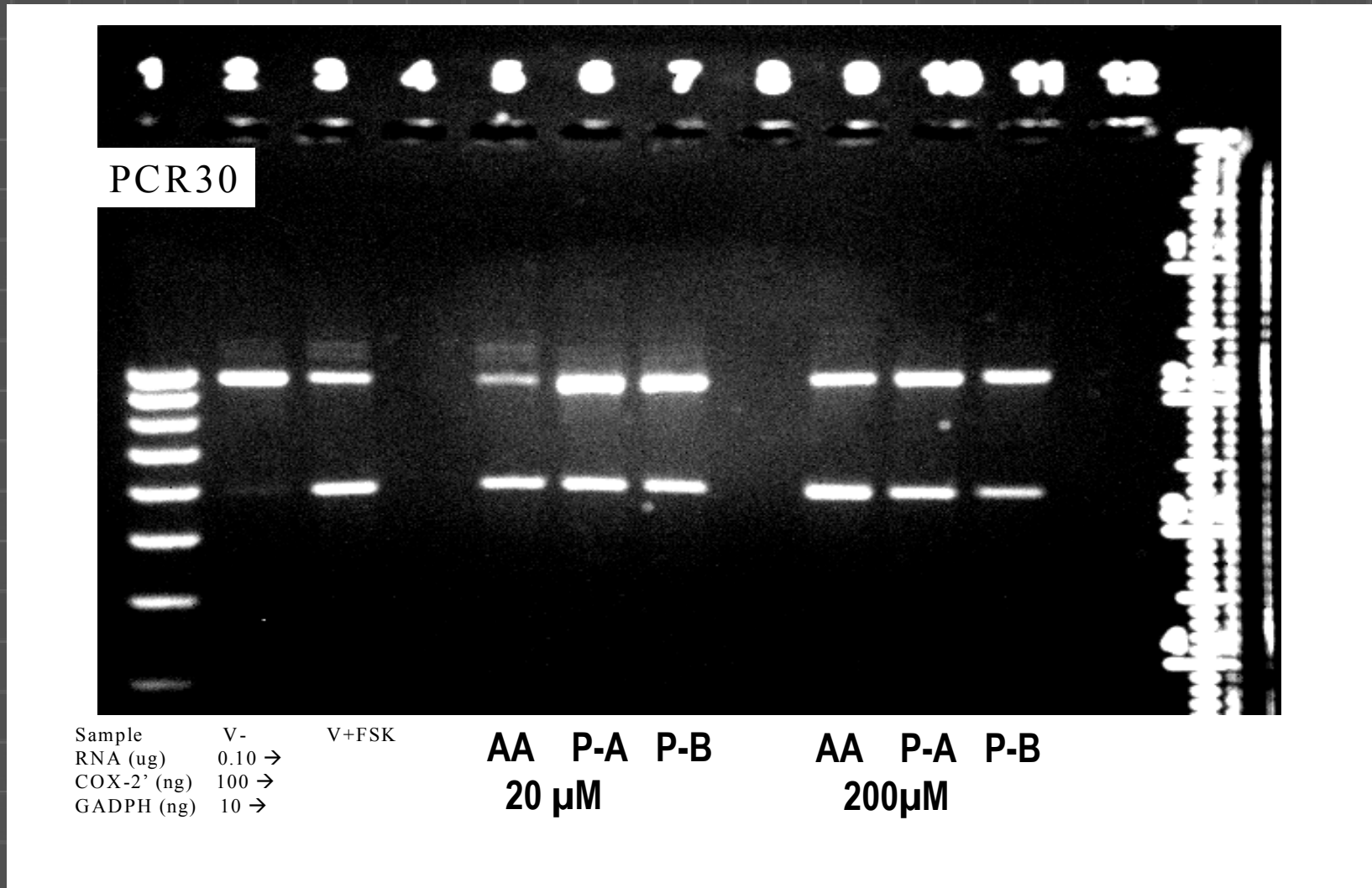
Effects of PUFA (AA, EPA, CLA) on MC3T3-E1 Cells



Osteoblast COX-2 Expression (PUFA Effects: AA, EPA)

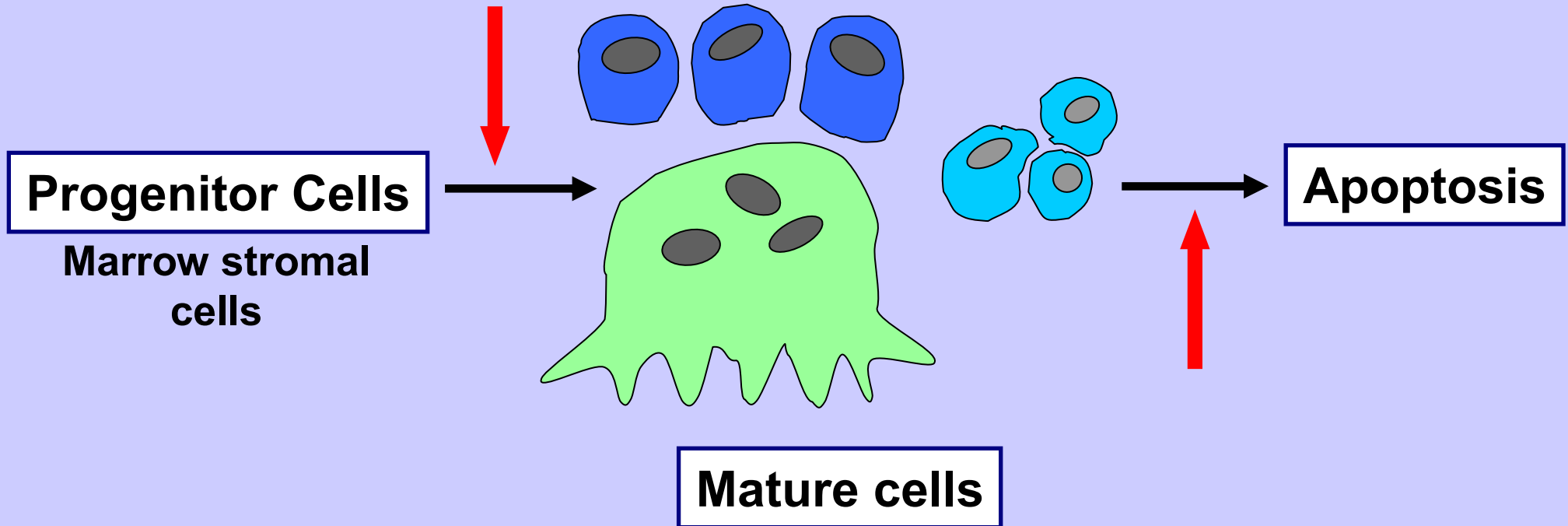


Osteoblasts COX-2 mRNA Expression: A = arachidonate, PUFA mixtures A and B

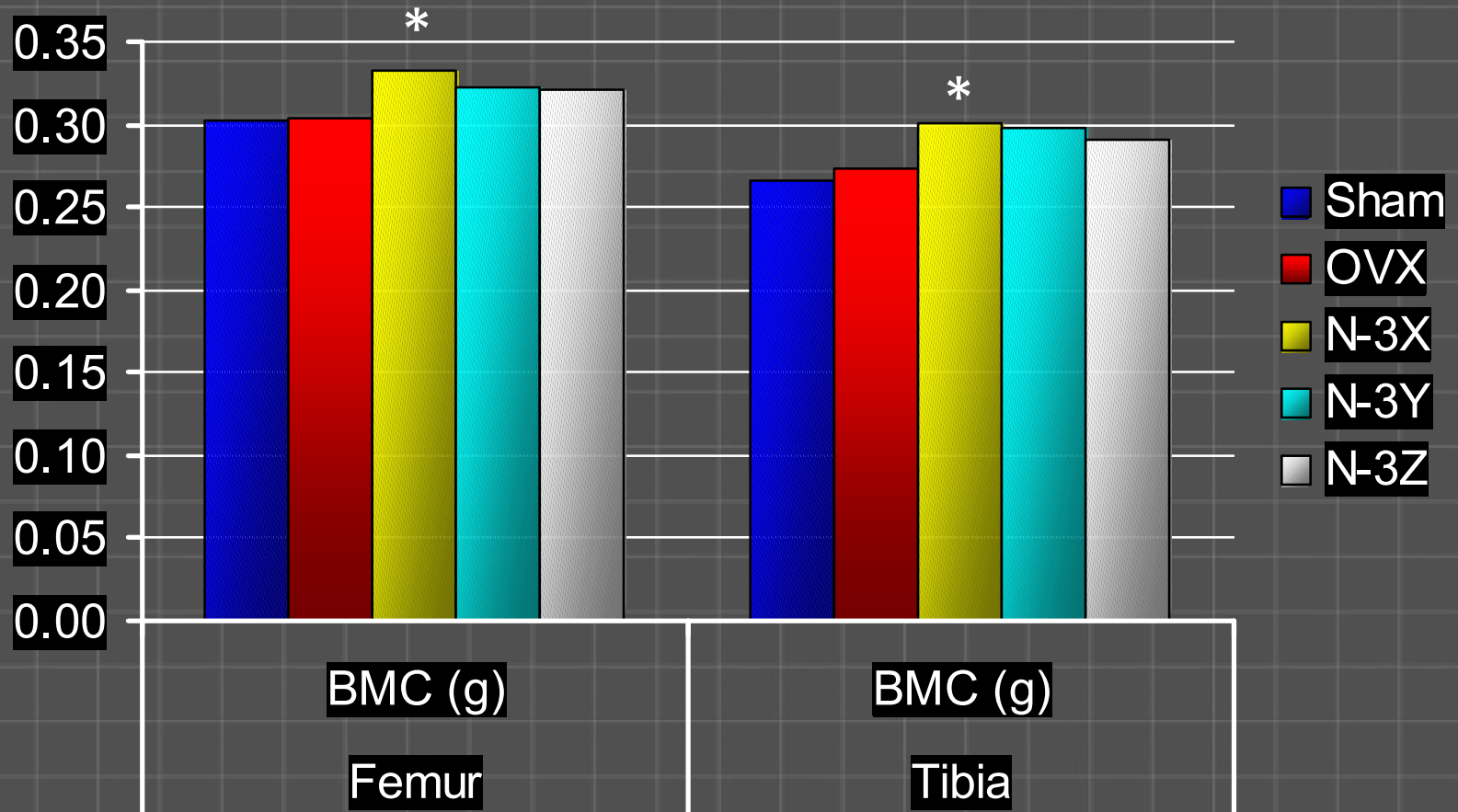


Gene Targets for Bone Health: Potential Actions of CLA on Cells of the Bone Microenvironment

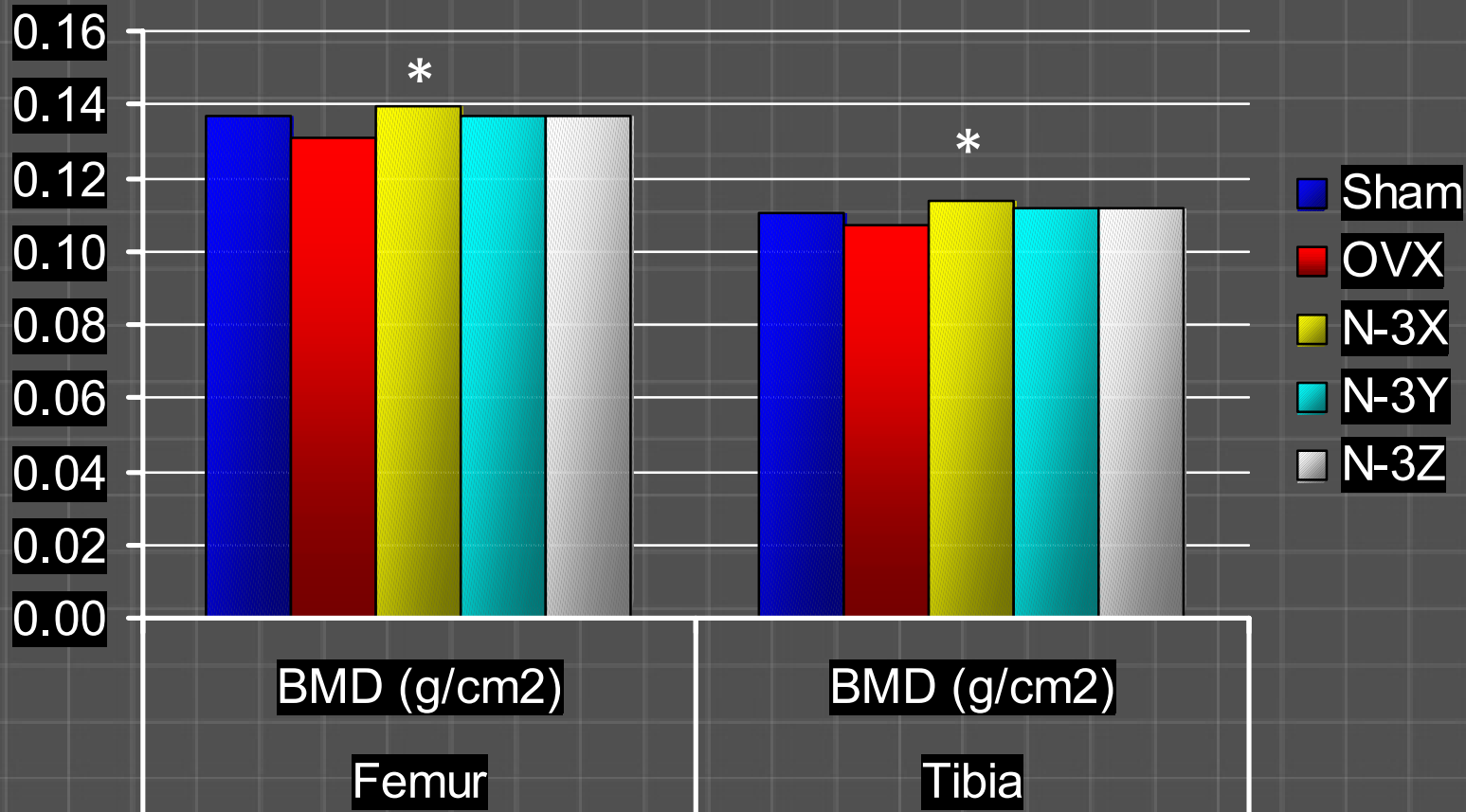
Transcription factors
Receptor- ligand



Effect of PUFA-CLA Mixtures on Bone Mineral Content (BMC) in OVX Rats (7 wks dietary treatment)



Effect of PUFA-CLA Mixtures on Bone Mineral Density (BMD) in OVX Rats (7 wks dietary treatment)



Conclusions: Modulation of Gene Expression in Osteoblasts (OB)

Bone CLA Research Opportunities:

- **The Cbfa-1 transcription factor – expression influenced by fatty acids, directed differentiation of marrow stromal cells (mouse)**
- **COX-2 activity and mRNA expression in OB modified by fatty acids and LC-PUFA; supported by data on ex vivo PGE production and bone histomorphometry (rat)**
- **Genes expressed during OB maturation (BALP) appear to be up-regulated by specific PUFA; supported by data on BALP in vivo and in OB cultures (dog, rat)**
- **Genes expressed during mineralization appear to be influenced by n-6/n-3 PUFA; supported by OB culture studies and in vivo bone modeling experiments (rat)**

Acknowledgments

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