associació catalana de diabetis 12º CONGRESO

GIRONA | 14 y 15 de marzo de 2013
Auditorio Palacio de Congresos

Hueso & Diabetes

Javier Gómez-Ambrosi
Laboratorio de Investigación Metabólica
Clínica Universidad de Navarra

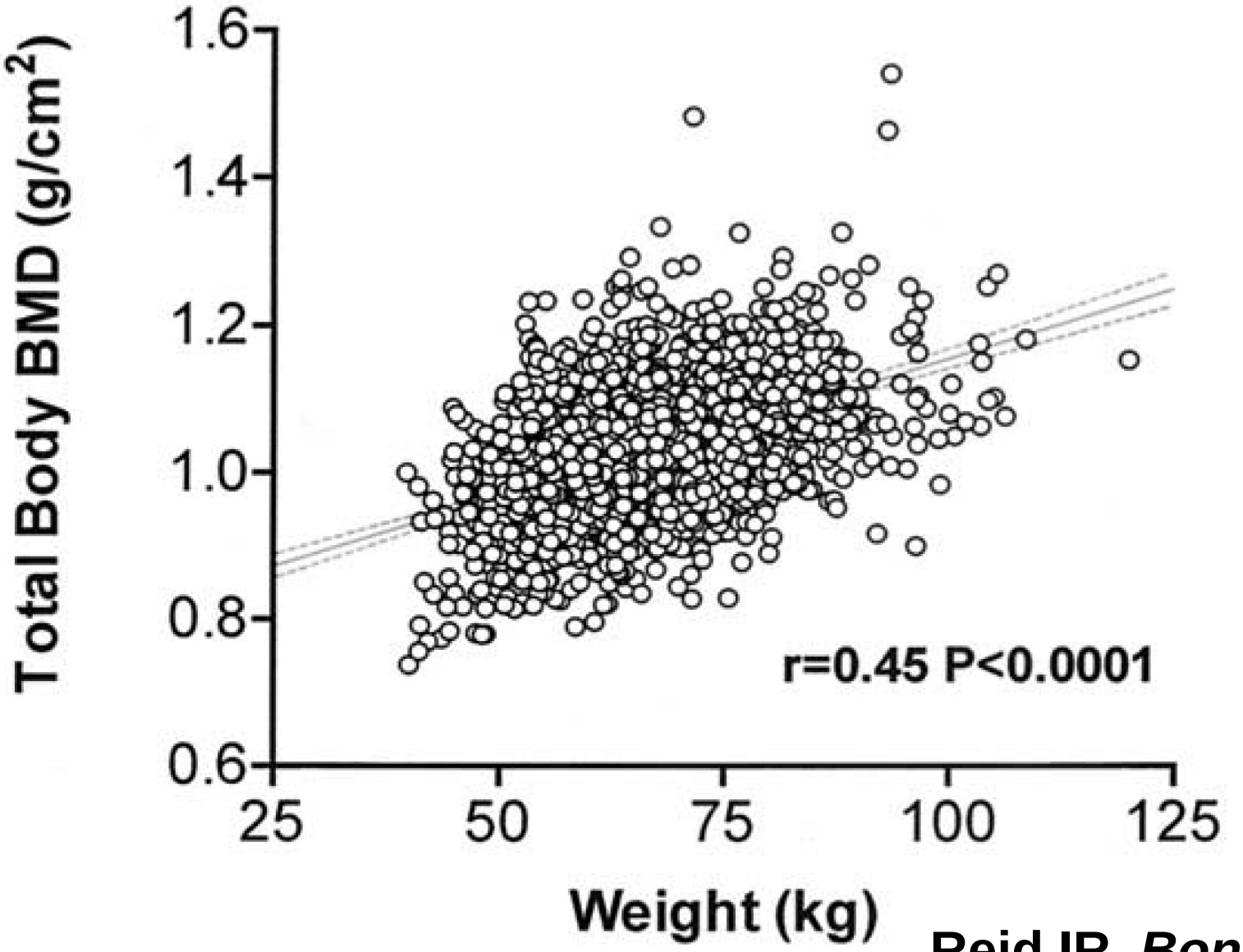
15 de Marzo de 2013

ciberobn

GOBIERNO DE ESPAÑA · MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD · Instituto de Salud Carlos III

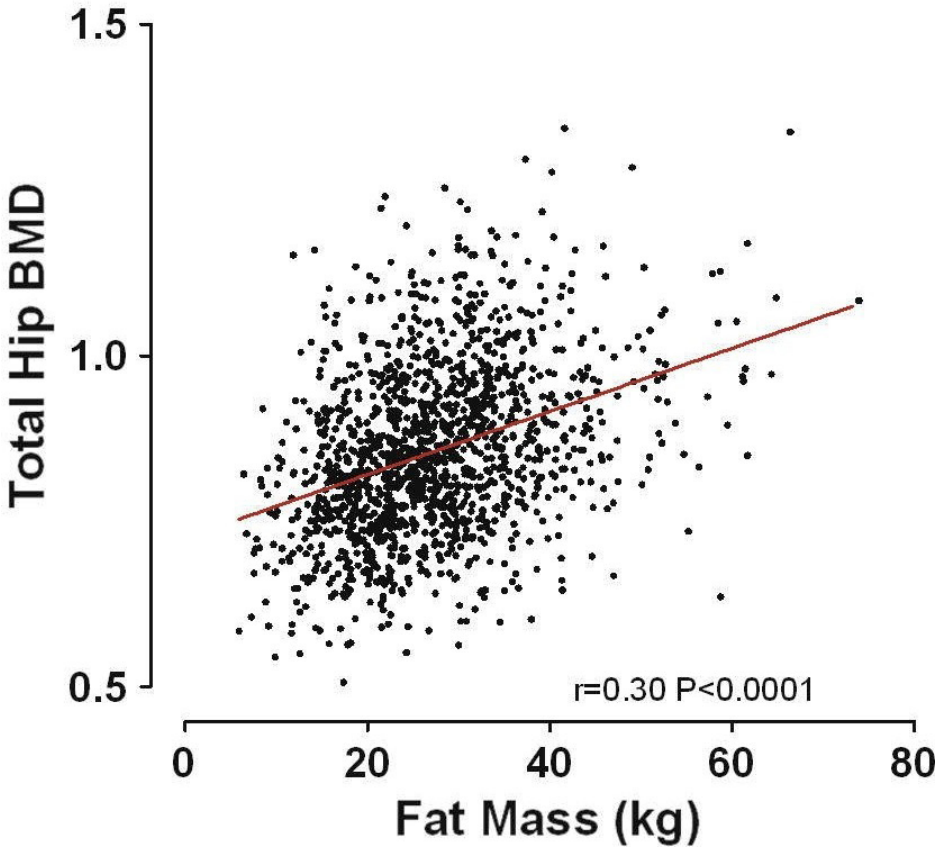
Clínica Universidad de Navarra

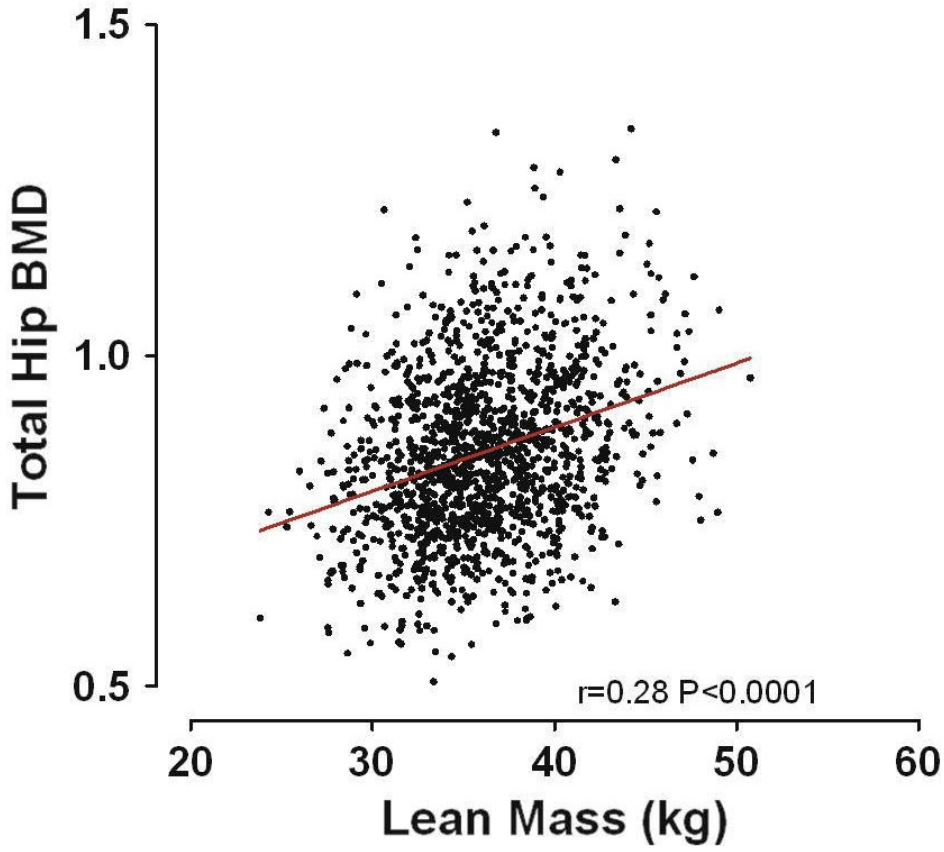
Body weight & BMD



Reid IR. *Bone* 2002

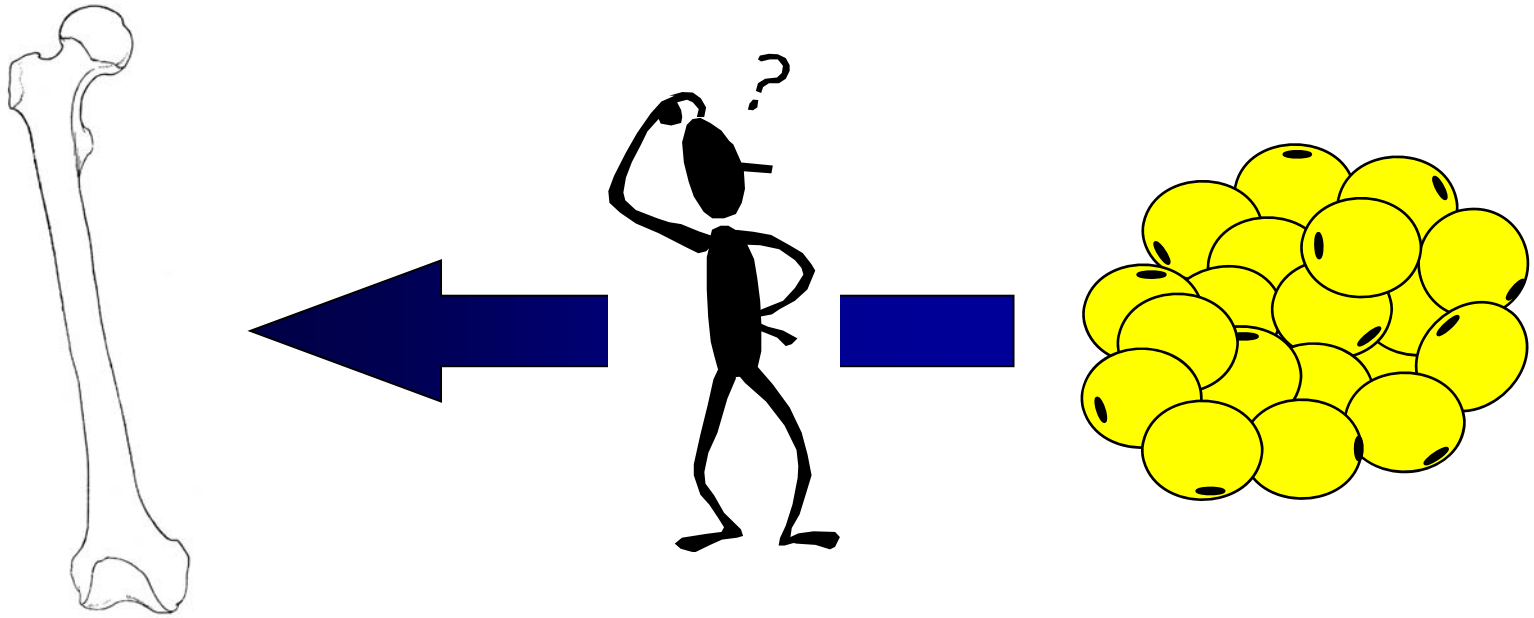
Body composition & BMD





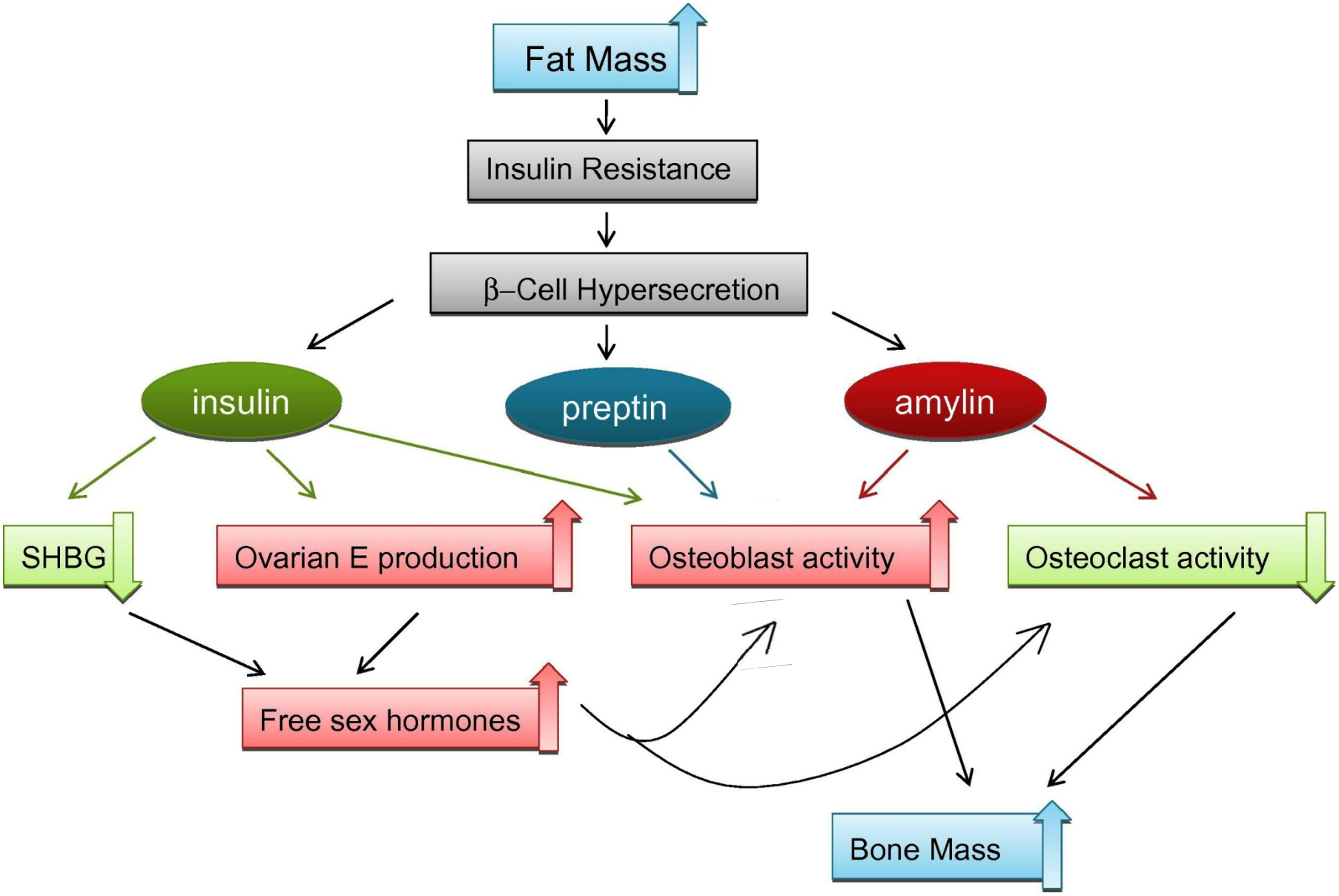
Reid IR. *Arch Biochem Biophys* 2010

The bone-adipose axis



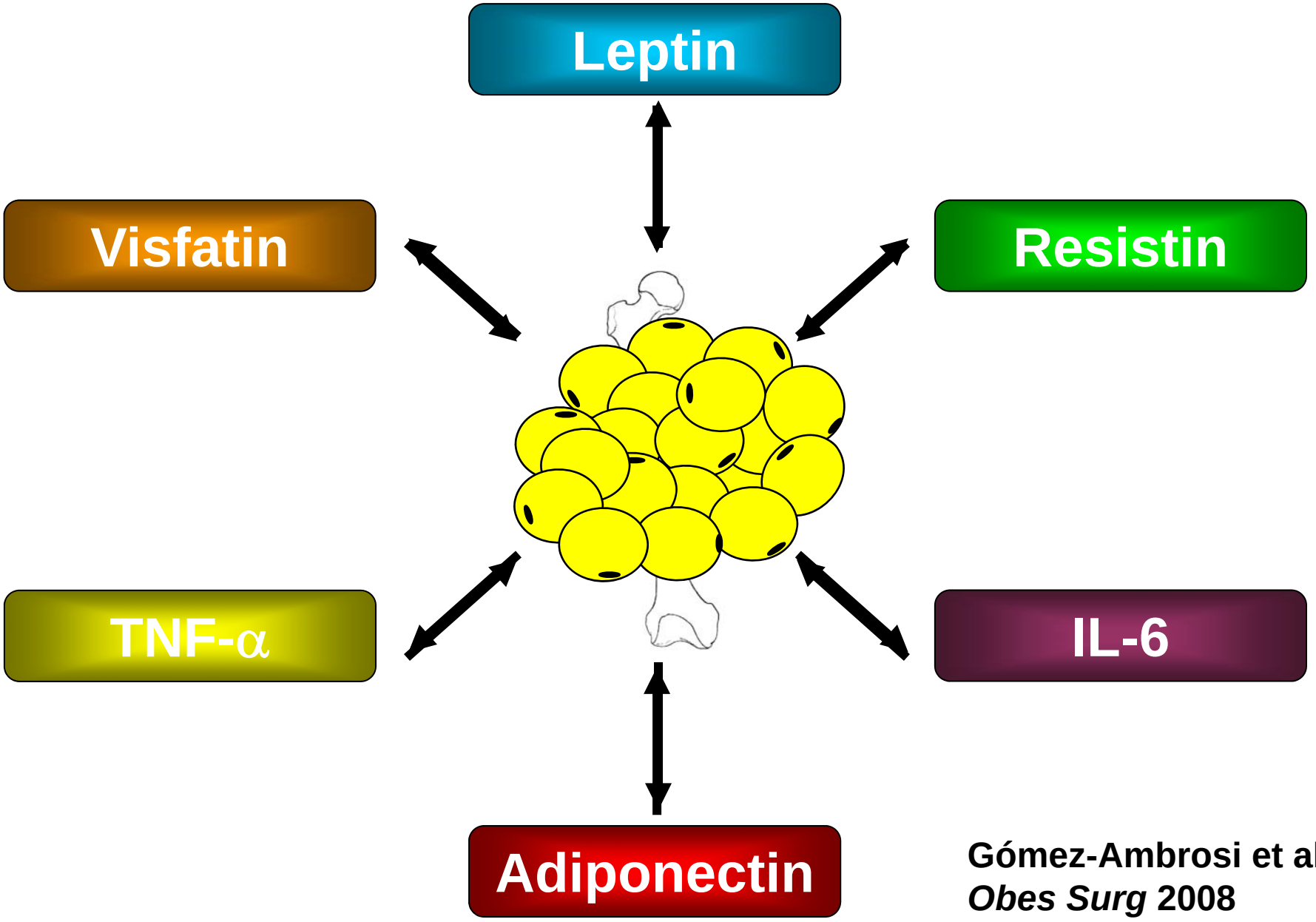
Gómez-Ambrosi et al. *Obes Surg* 2008

Fat mass & bone mass - Pancreas



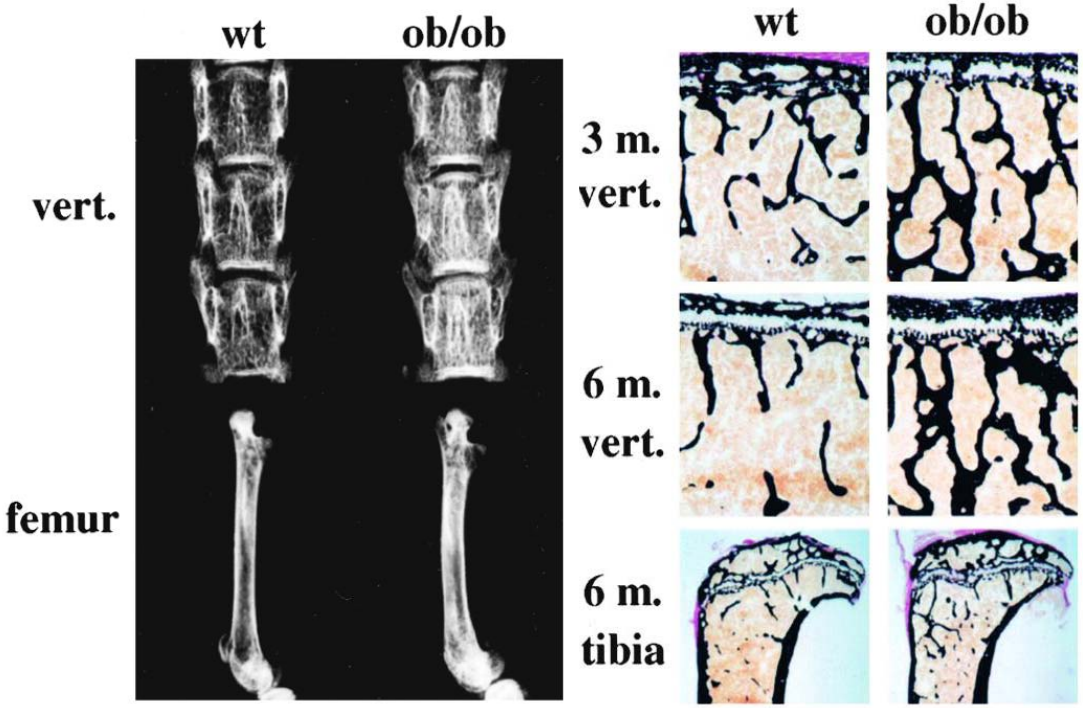
Reid IR. *Arch Biochem Biophys* 2010

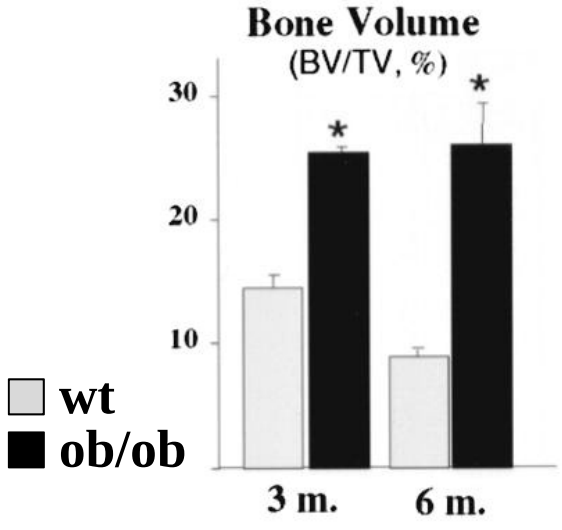
Adipokines & Bone

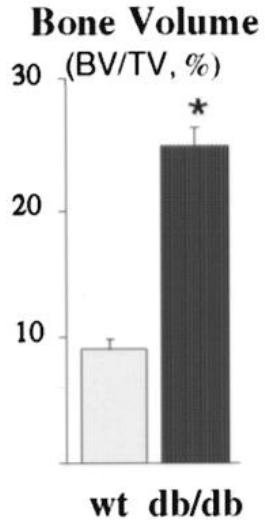


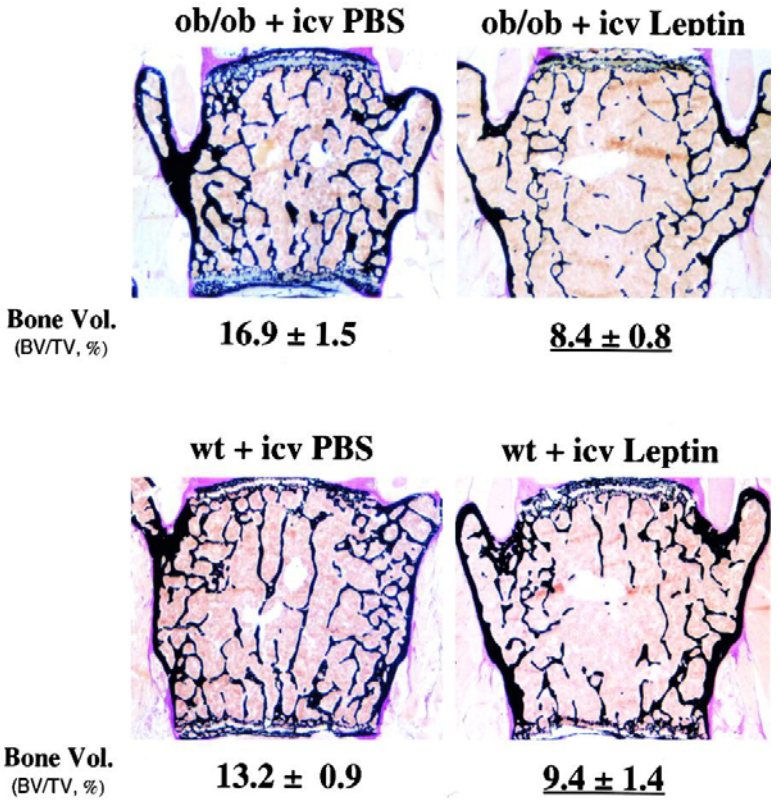
Gómez-Ambrosi et al.
Obes Surg 2008

Leptin & Bone



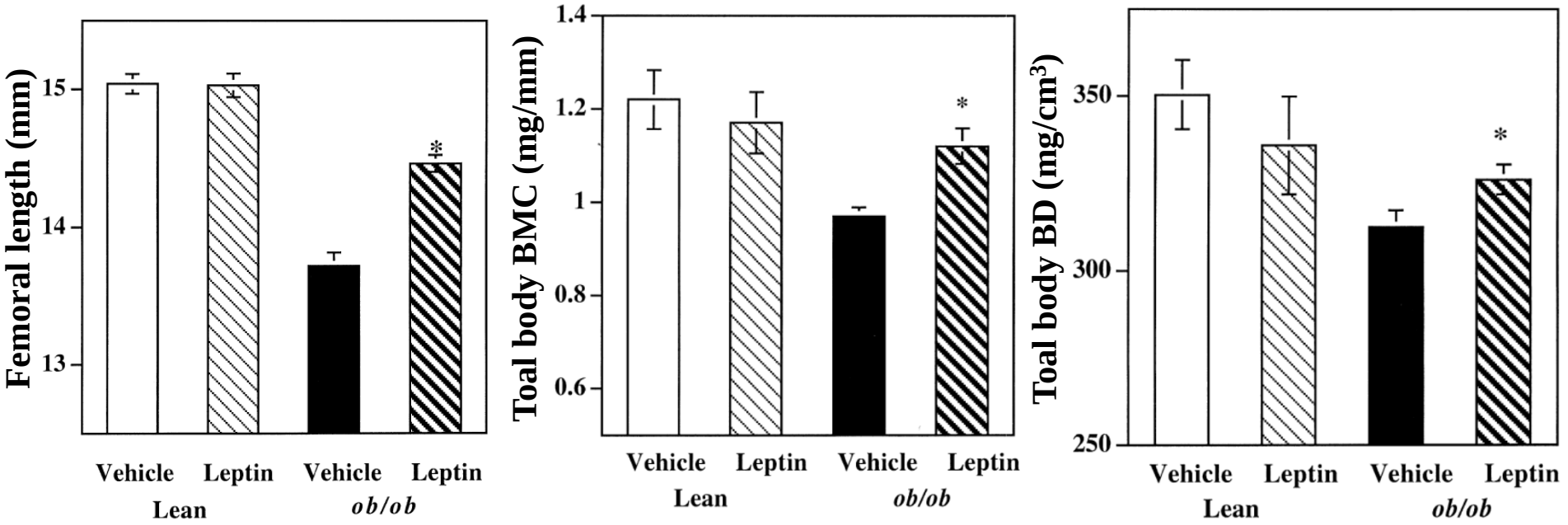






Ducy et al. *Cell* 2000

Leptin & Bone

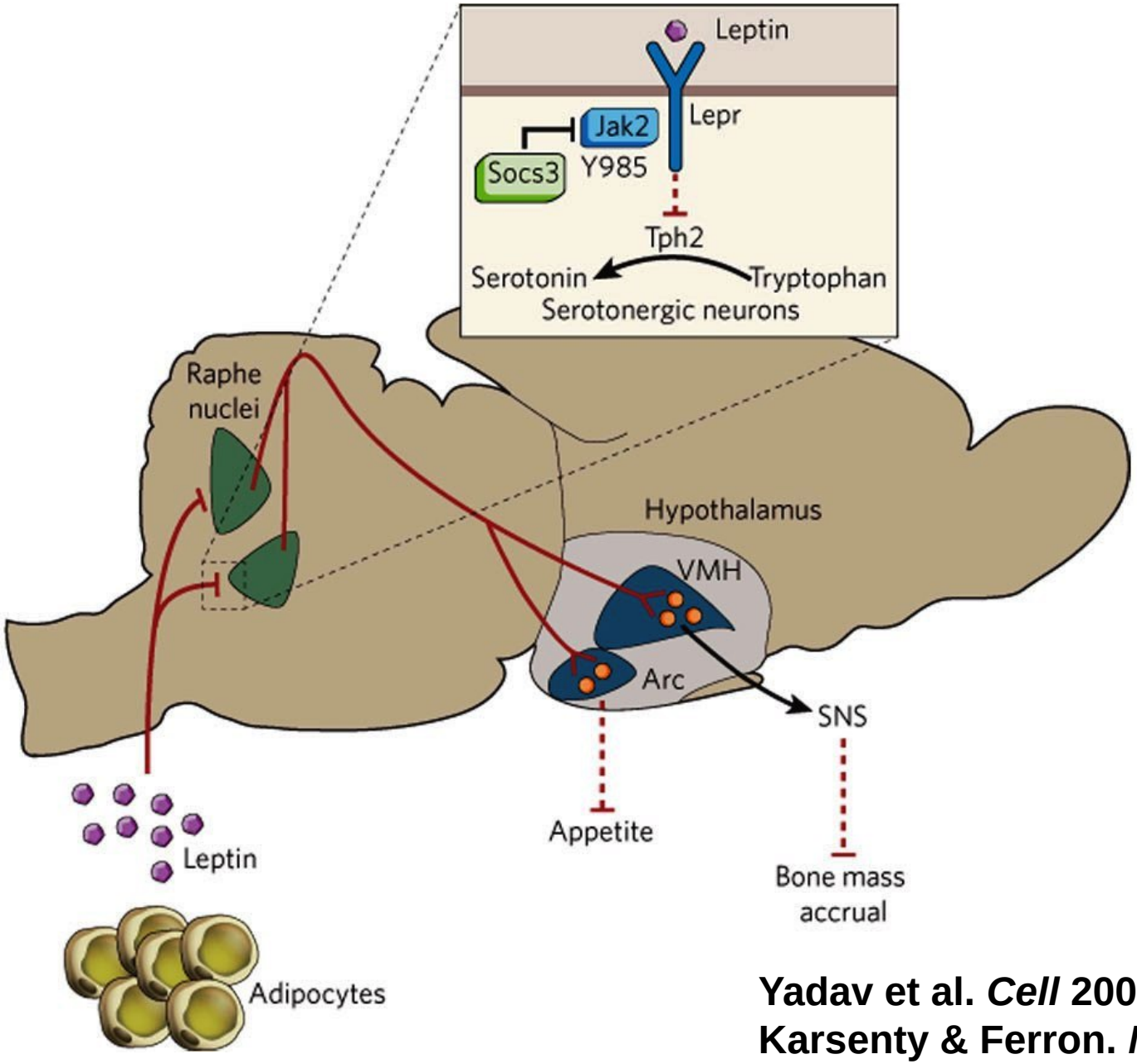


Steppan et al. *Regul Pept* 2000

Parameter	*Lean (saline)*	*Lean (L10)*	*Ob/Ob (saline)*	*Ob/Ob (L10)*
Body mass	24.9 ± 0.94^{a}	22.1 ± 0.86^{a}	57.9 ± 5.4^{b}	38.7 ± 2.9^{c}
Fat mass (g)	2.5 ± 0.8^{a}	1.5 ± 0.18^{a}	34.6 ± 3.3^{b}	19.7 ± 2.8^{d}
BMC (g)	0.49 ± 0.4^{a}	0.49 ± 0.05^{a}	0.36 ± 0.04^{b}	0.48 ± 0.18^{a}
BMD (g/cm^2)	0.053 ± 0.004^{a}	0.052 ± 0.004^{a}	0.047 ± 0.004^{b}	0.052 ± 0.007^{a}

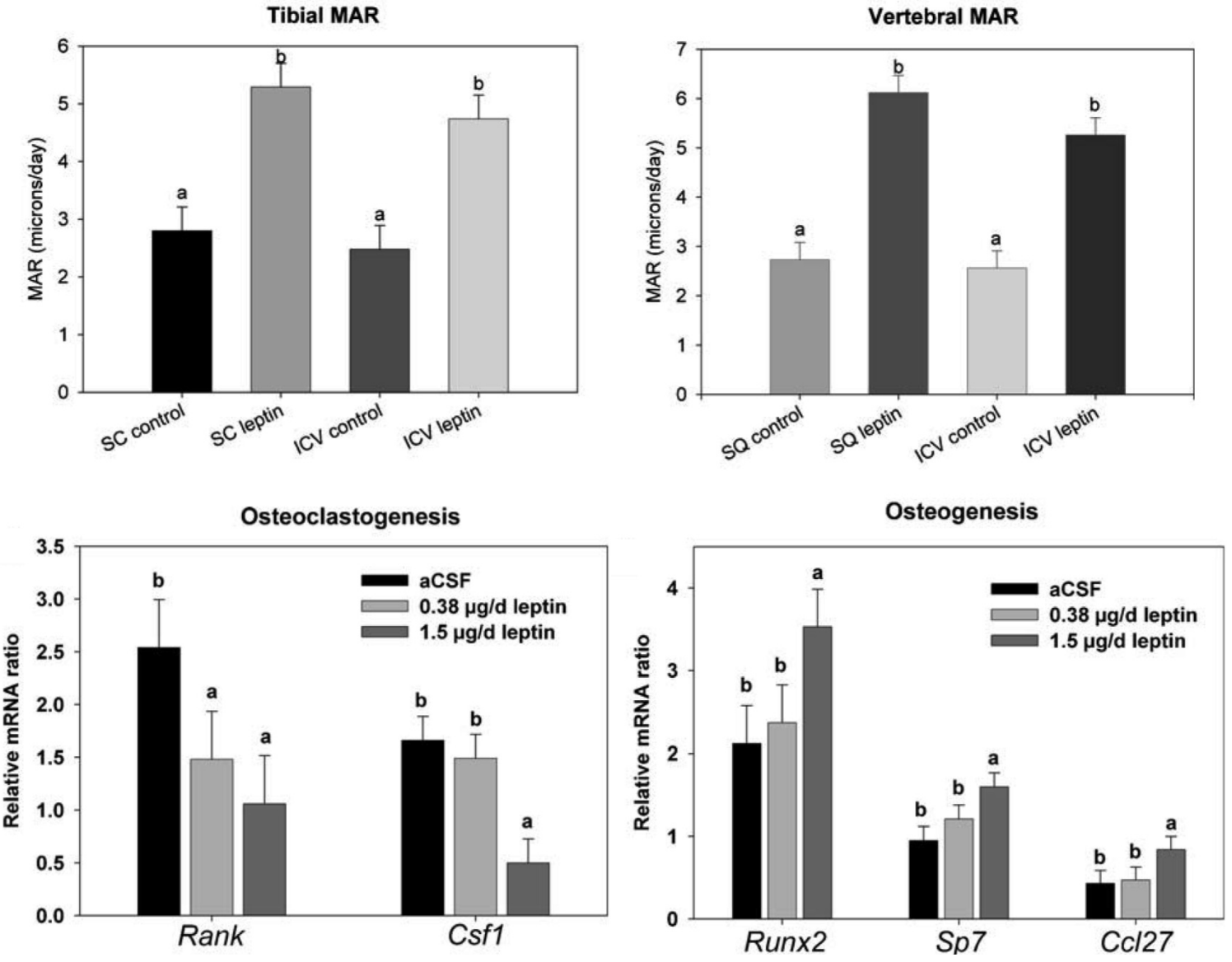
Hamrick et al. *J Bone Miner Res* 2005

Leptin & Bone



Yadav et al. *Cell* 2009
Karsenty & Ferron. *Nature* 2012

Leptin & Bone



Bartell et al. *J Bone Miner Res* 2011

Leptin & Bone

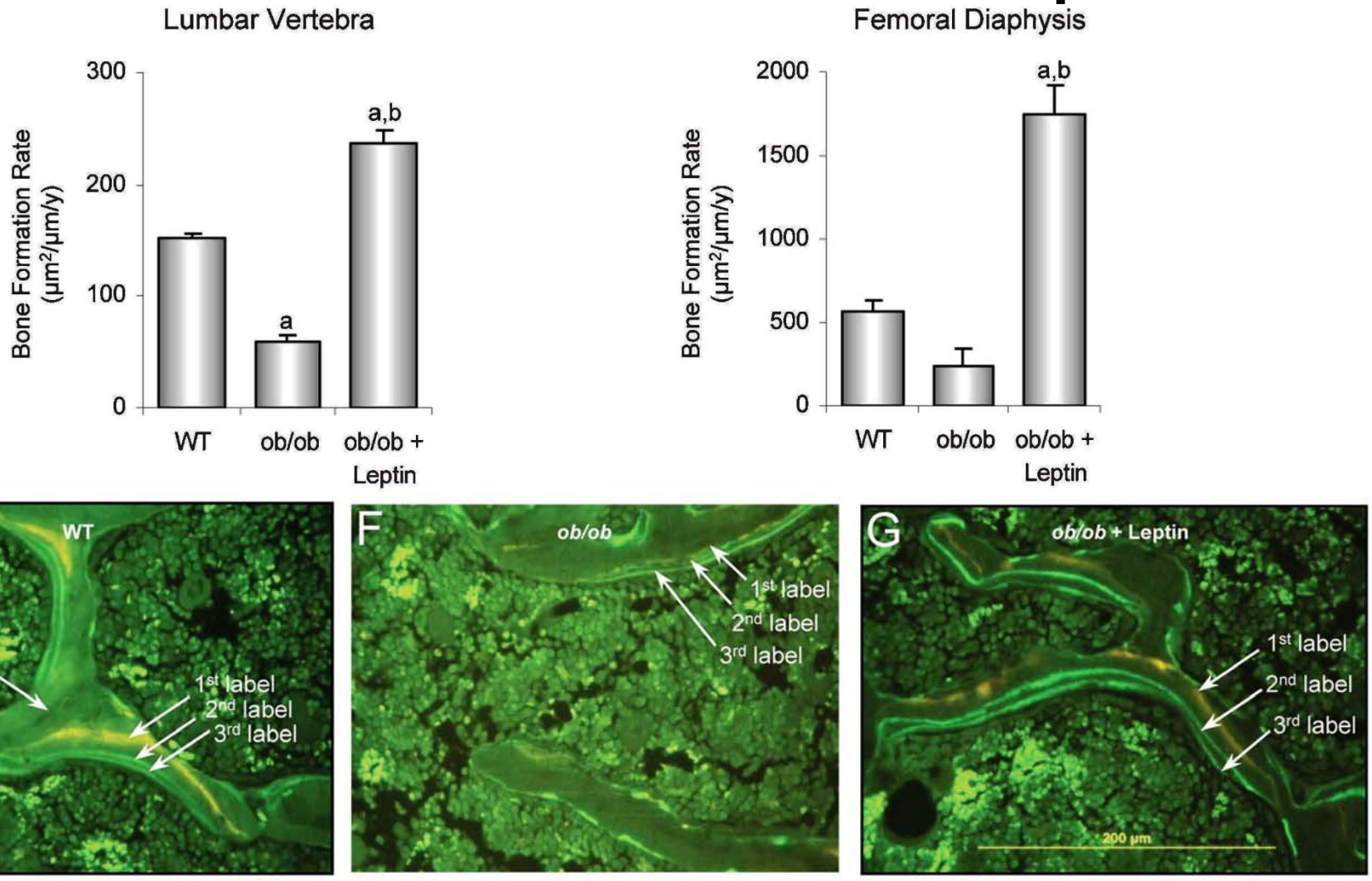
Experimental dynamics and variables potentially governing leptin-bone-fat interactions

	Experimental parameters
Dynamics	Experimental model: In vitro versus in vivo
	Scope of gene mutation: Tissue-specific versus whole-body (global) mutation
	Site of action: Central versus peripheral
	Route of administration: intracerebroventricular versus subcutaneous
	Bone site (gross): Appendicular versus axial
	Bone site (micro): Cortical versus trabecular
	Age: Young versus old
Variables	Dose level of leptin
	Animal gender
	Animal age
	Delivery mechanism and frequency
	Circadian

Gimble JM. *J Bone Miner Res* 2011

Leptin & Bone

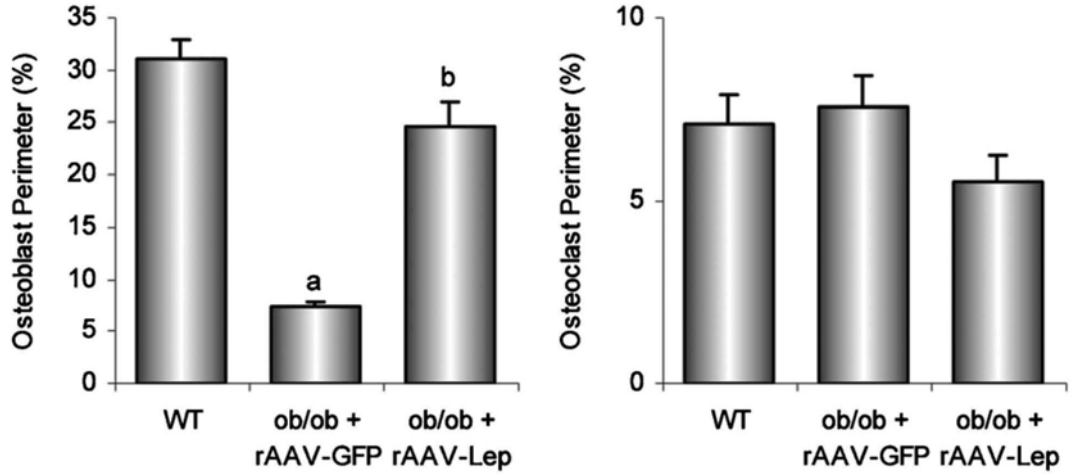
Subcutaneous administration of leptin



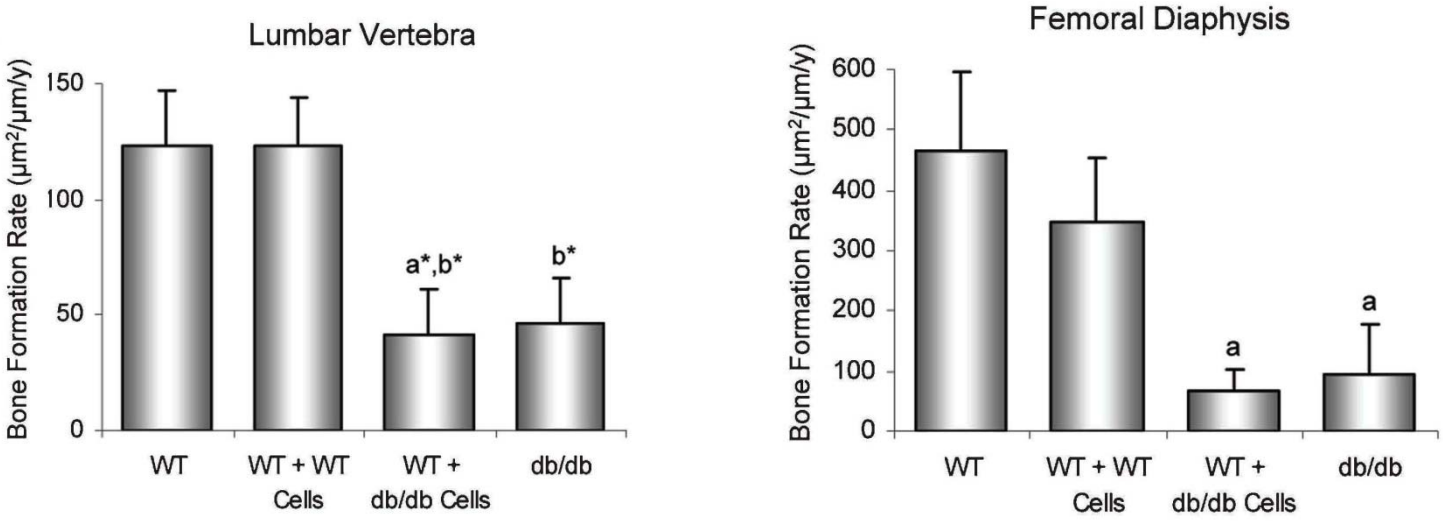
Turner et al. *J Bone Miner Res* 2013

Leptin & Bone

Hypothalamic administration of leptin

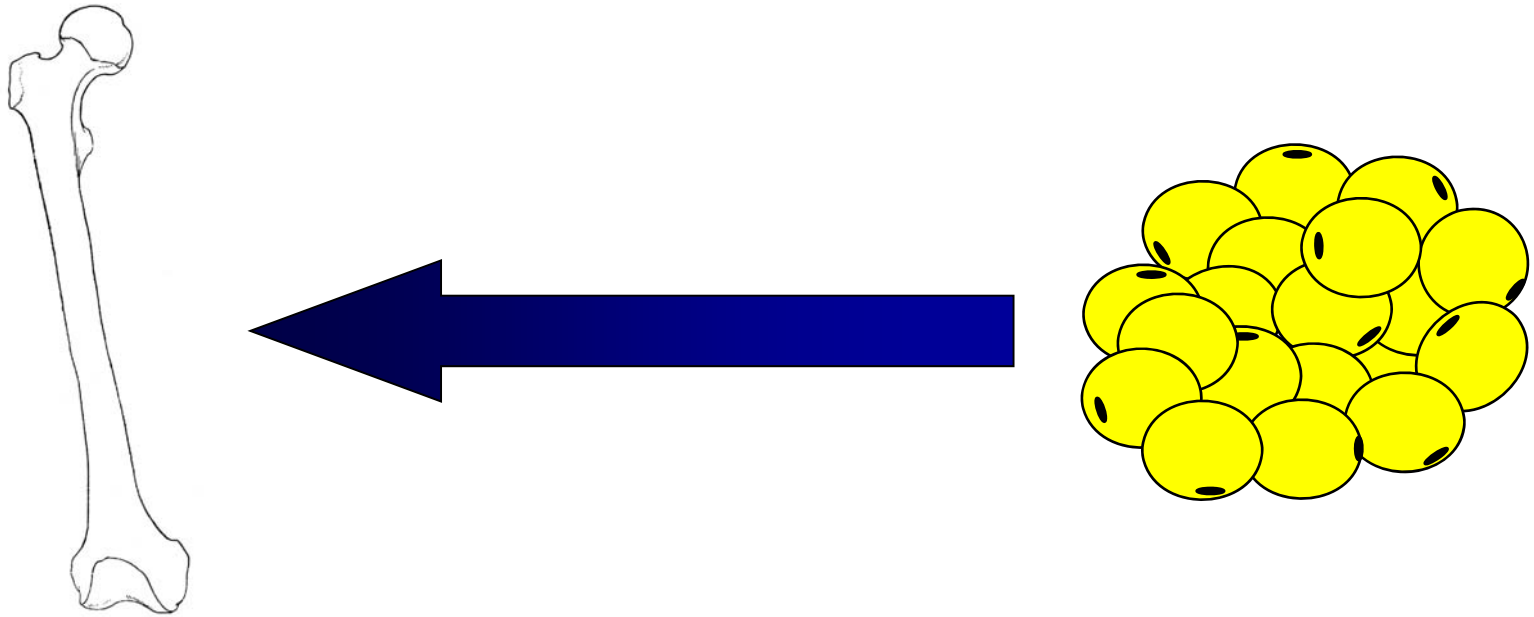


Transplantation of bone marrow WT-*db/db* mice



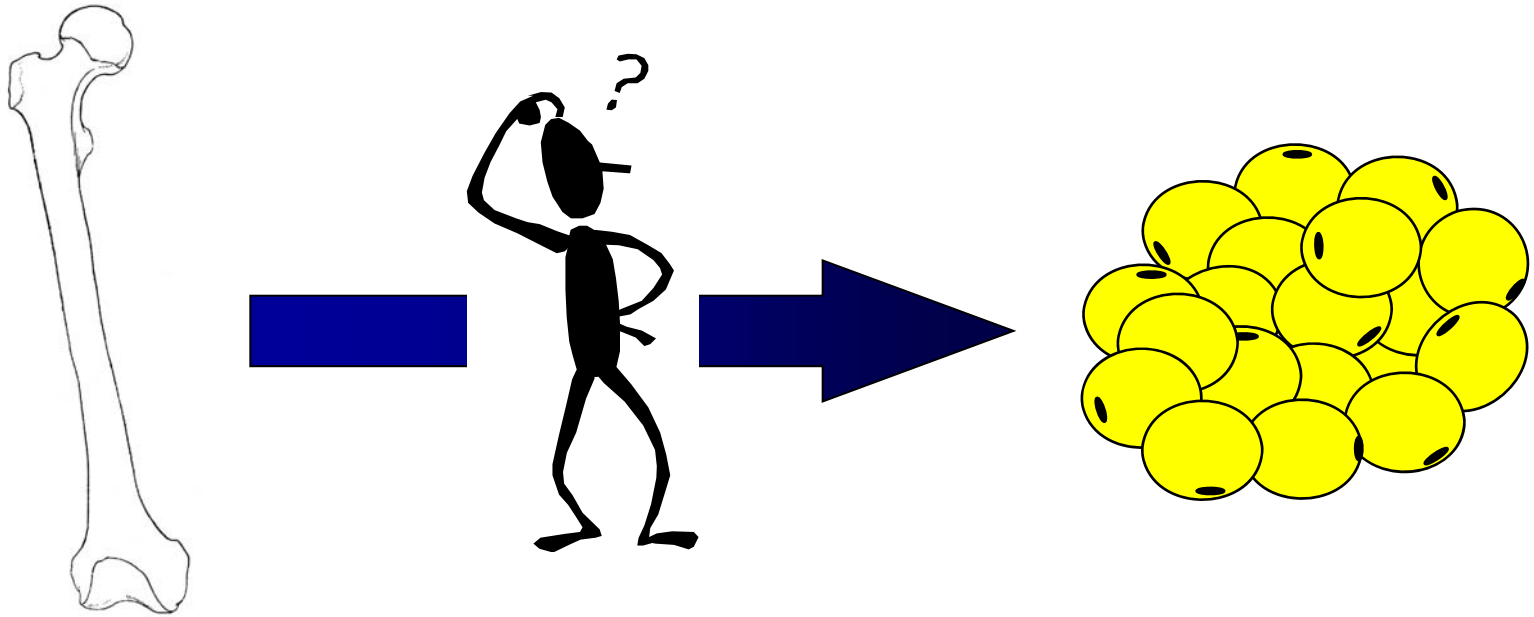
Turner et al. *J Bone Miner Res* 2013

The bone-adipose axis



Gómez-Ambrosi et al. *Obes Surg* 2008

The bone-adipose axis



Gómez-Ambrosi et al. *Obes Surg* 2008

Cell

Endocrine Regulation of Energy Metabolism by the Skeleton

Na Kyung Lee,[1] Hideaki Sowa,[1] Eiichi Hinoi,[1] Mathieu Ferron,[1] Jong Deok Ahn,[3] Cyrille Confavreux,[1] Romain Dacquin,[4] Patrick J. Mee,[5] Marc D. McKee,[6] Dae Young Jung,[7] Zhiyou Zhang,[7] Jason K. Kim,[7] Franck Mauvais-Jarvis,[8] Patricia Ducy,[2] and Gerard Karsenty[1,*]

[1] Department of Genetics & Development

[2] Department of Pathology

College of Physicians and Surgeons, Columbia University, New York, NY 10032, USA

[3] CHO-A Biotechnology Research Institute, CHO-A Pharm. Co., Seoul 143-701, Korea

[4] Ecole Normale Supérieure de Lyon, UMR5161, Laboratoire d'Endocrinologie Moléculaire et Différenciation Hématopoïétique et Osseuse, 69364 Lyon, France

[5] Centre for Stem Cell Research, University of Cambridge, Cambridge CB2 1TN, United Kingdom

[6] Faculty of Dentistry, and Department of Anatomy and Cell Biology, McGill University, Montreal, QC, Canada H3A 2B2

[7] Department of Cellular & Molecular Physiology, Penn State Medical Center, Hershey, PA 17033

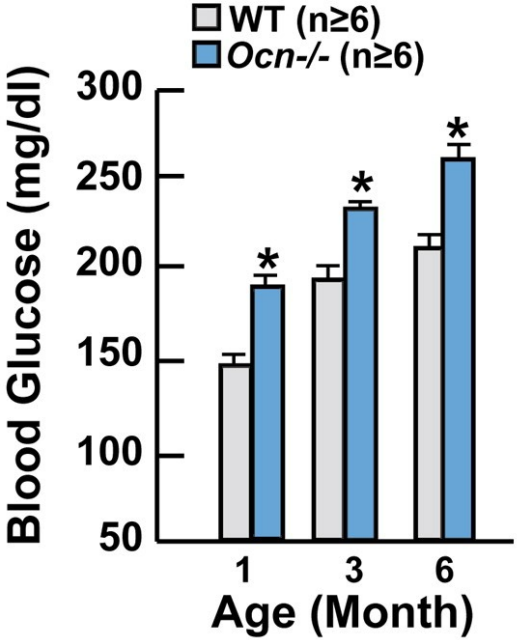
[8] Department of Medicine, Northwestern University School of Medicine, Chicago, IL 60611, USA

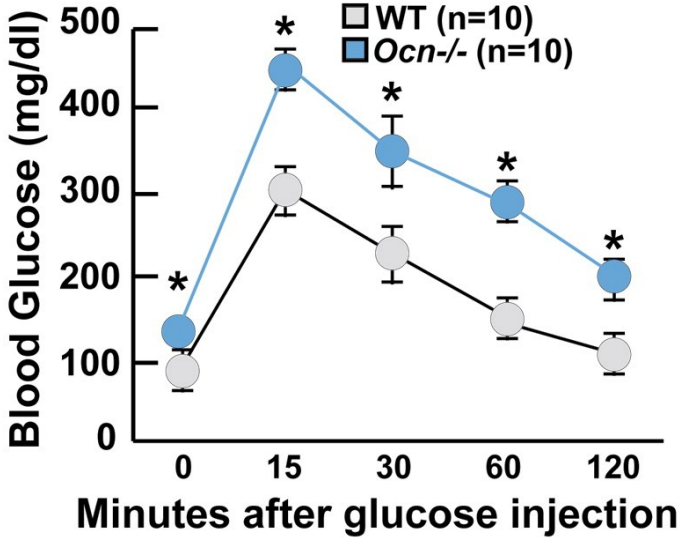
*Correspondence: gk2172@columbia.edu

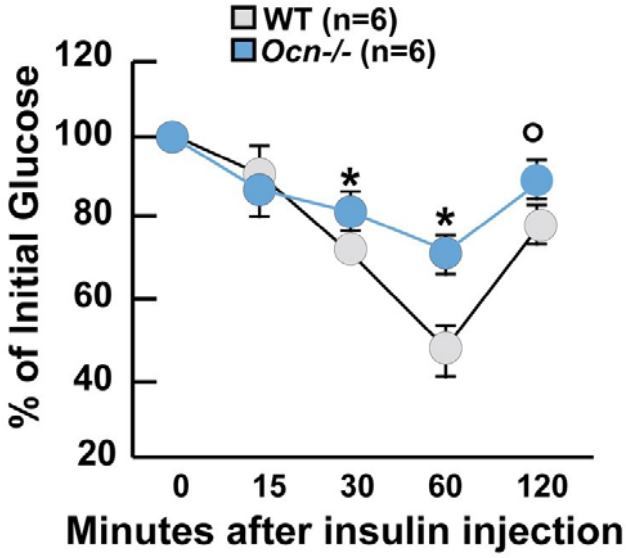
DOI 10.1016/j.cell.2007.05.047

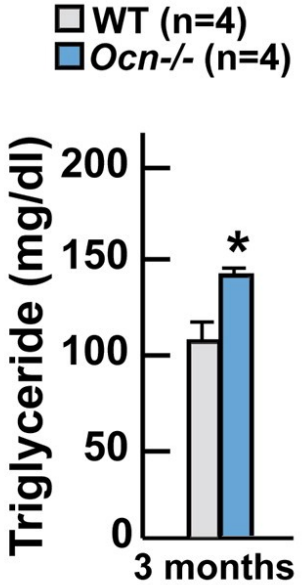
Cell 2007

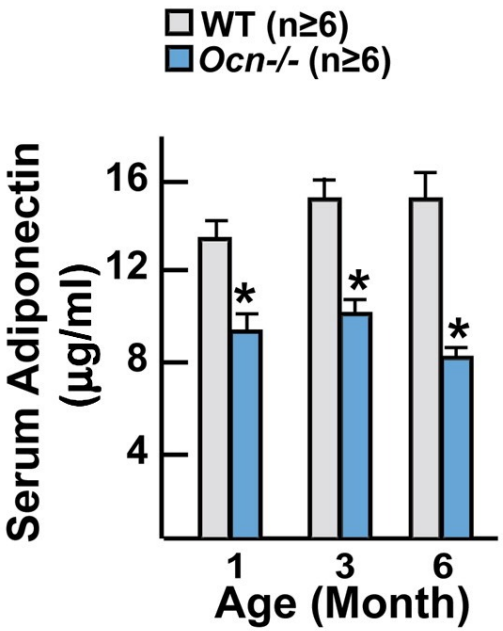
Endocrine regulation of energy metabolism by the skeleton

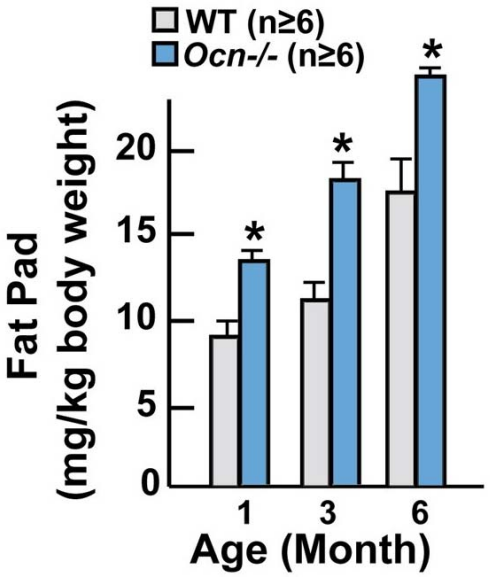


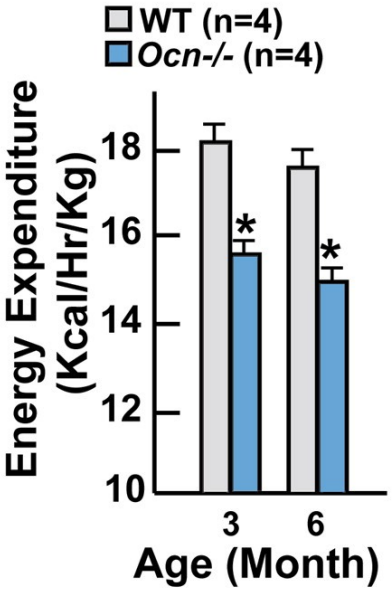






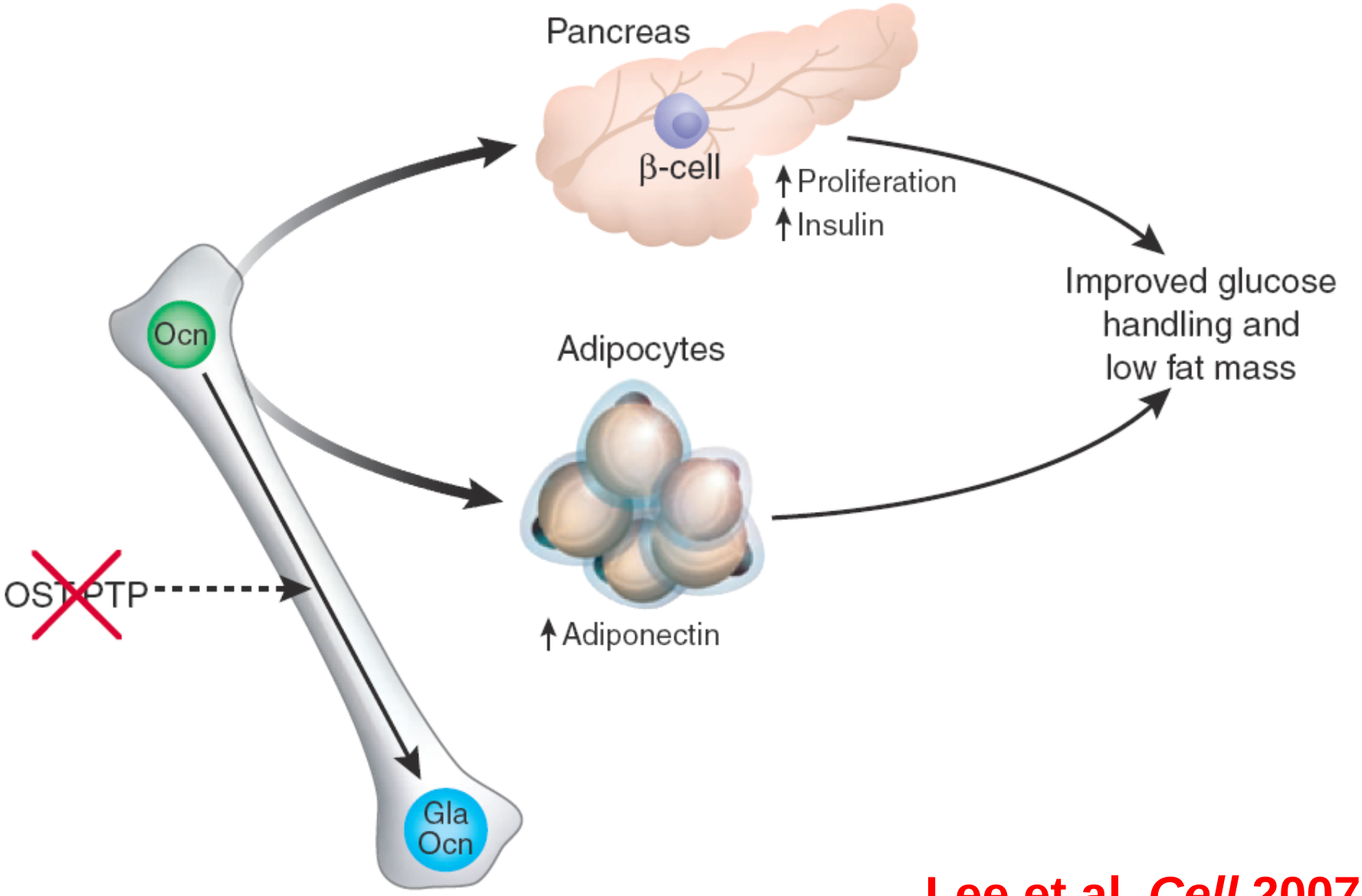






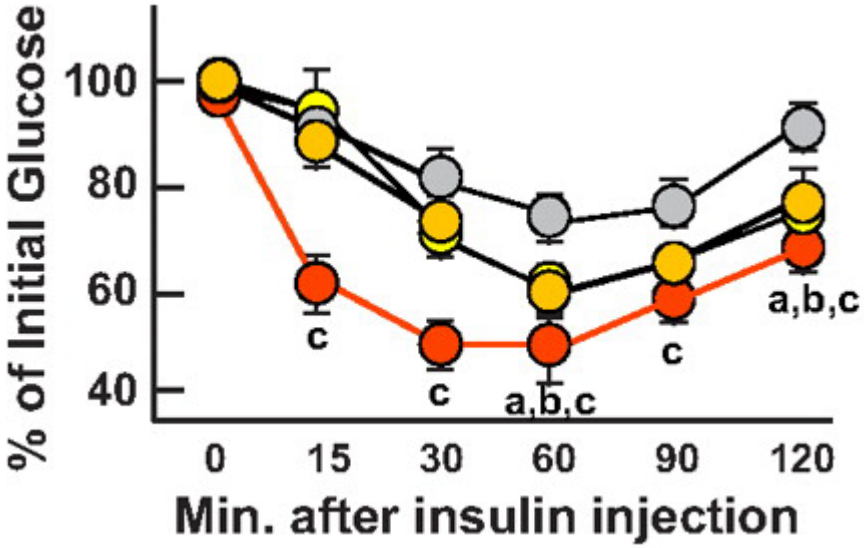
Lee et al. *Cell* 2007

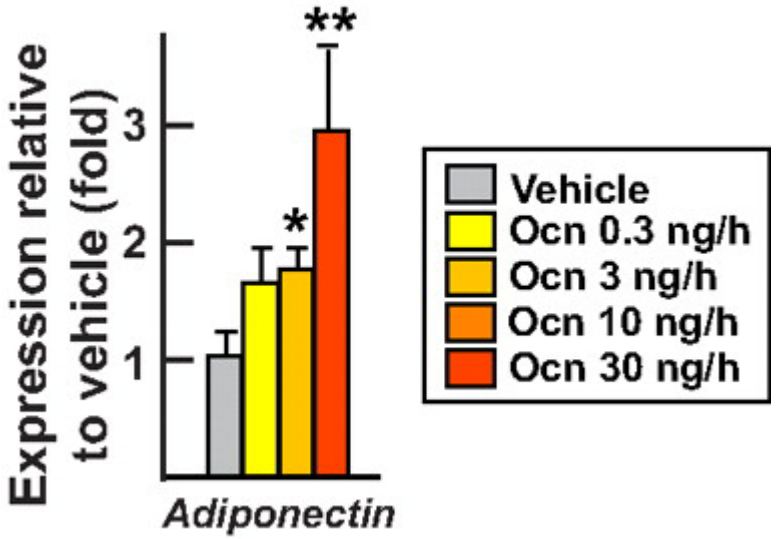
Endocrine regulation of energy metabolism by the skeleton

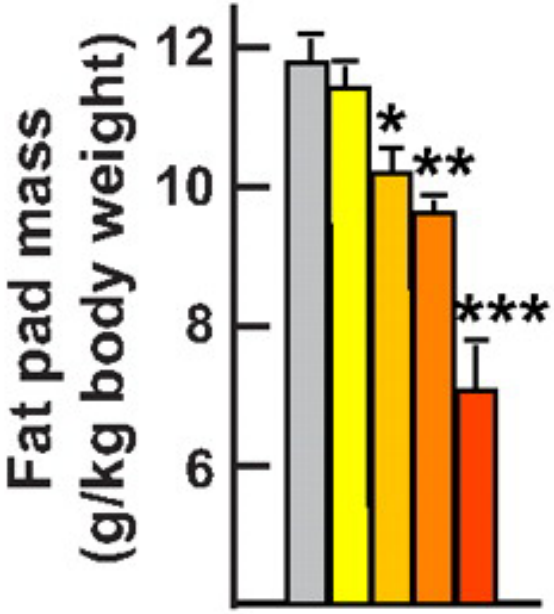


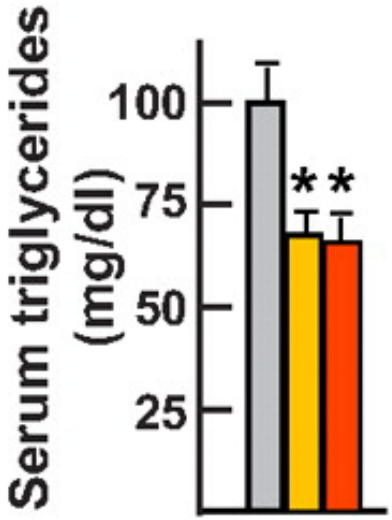
Lee et al. *Cell* 2007

Osteocalcin in the treatment of metabolic diseases



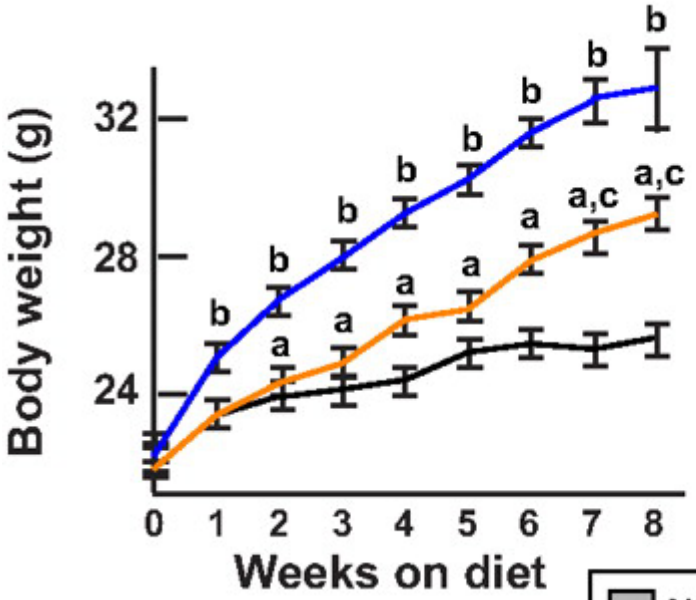


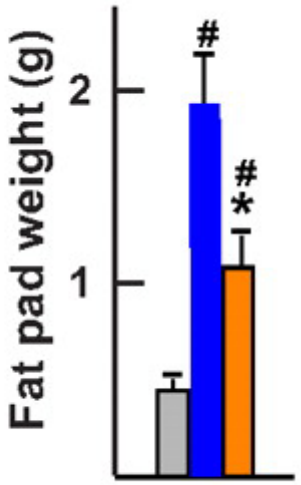


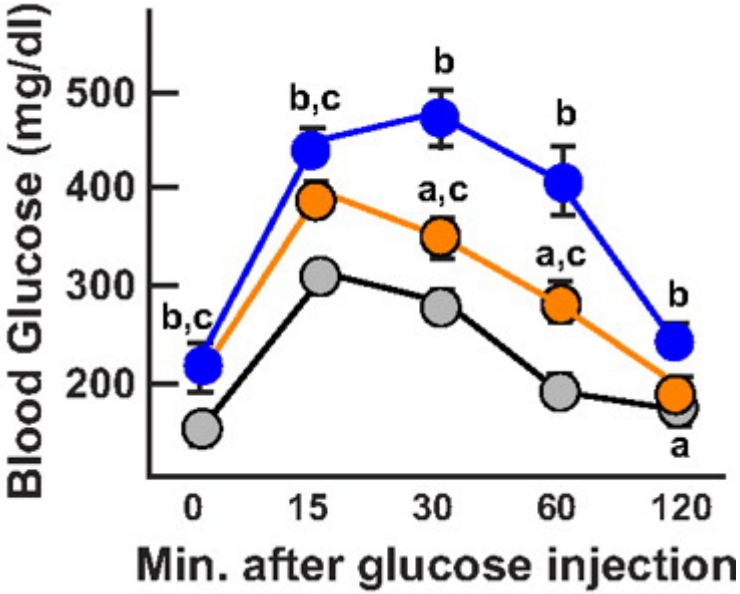


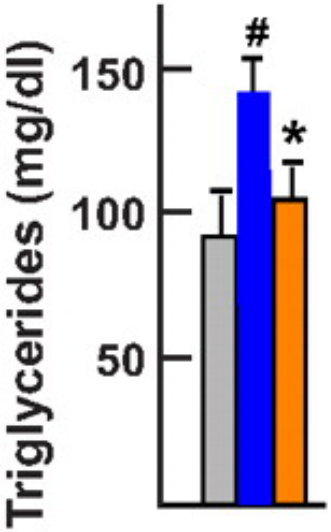
Ferron et al. *PNAS* 2008

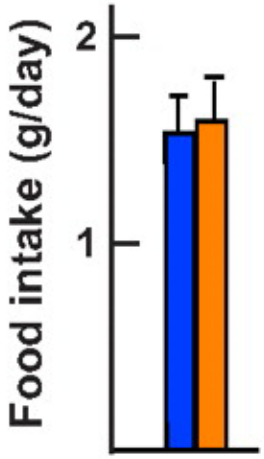
Osteocalcin in the treatment of metabolic diseases

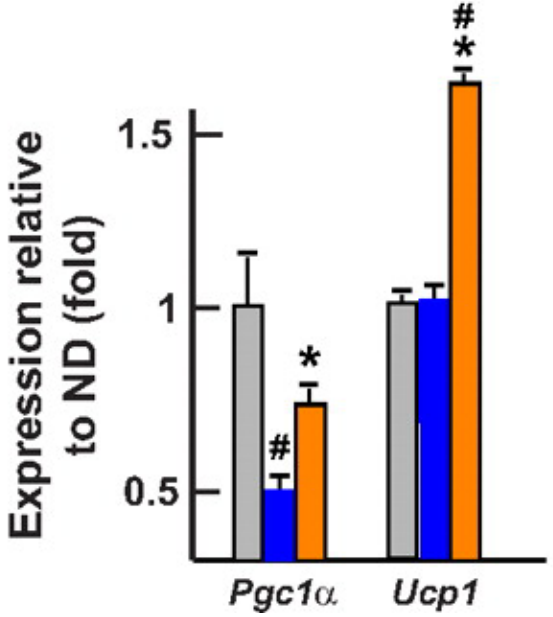






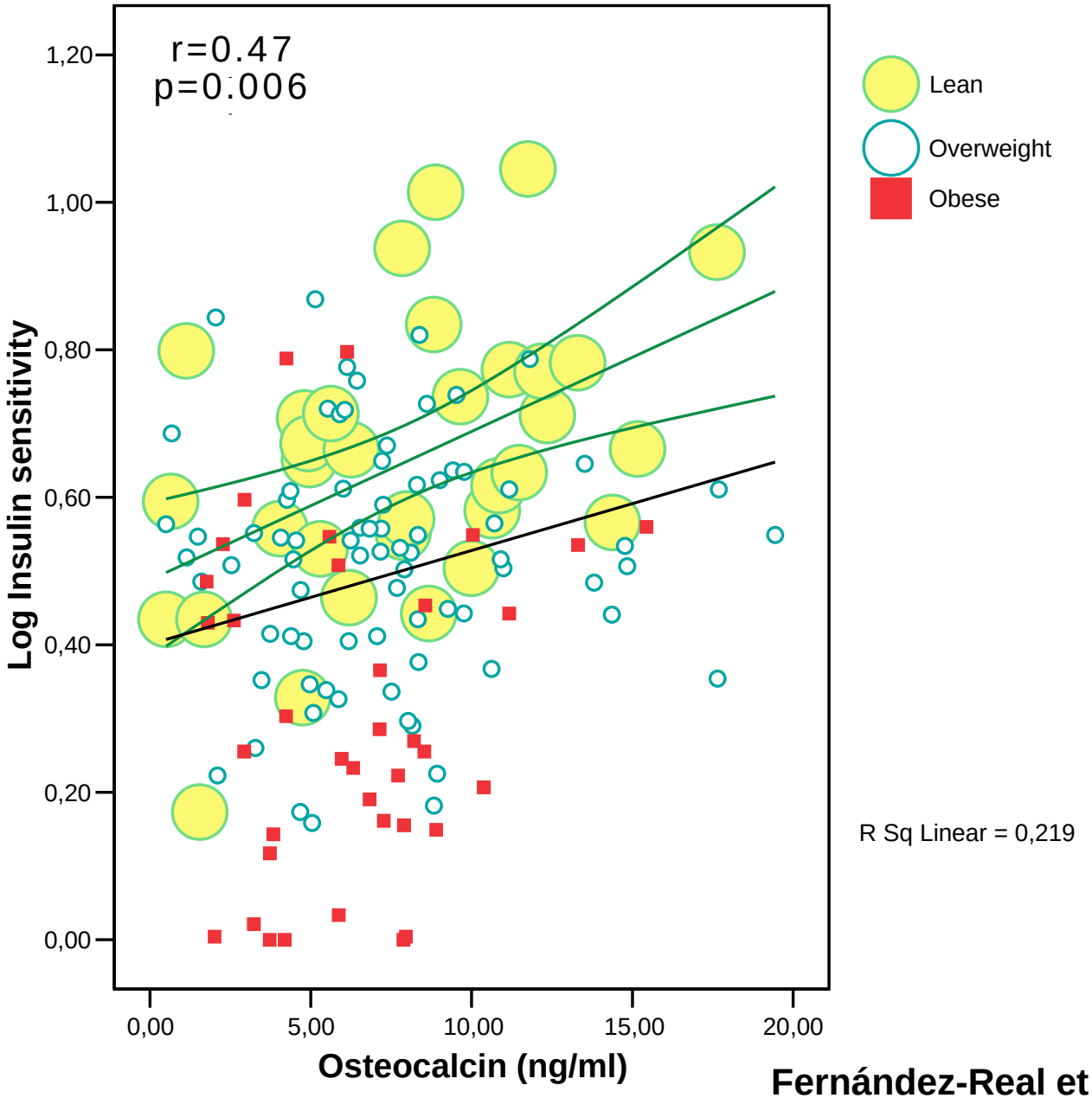






Ferron et al. *PNAS* 2008

The bone as an endocrine organ in humans



Fernández-Real et al. *JCEM* 2009

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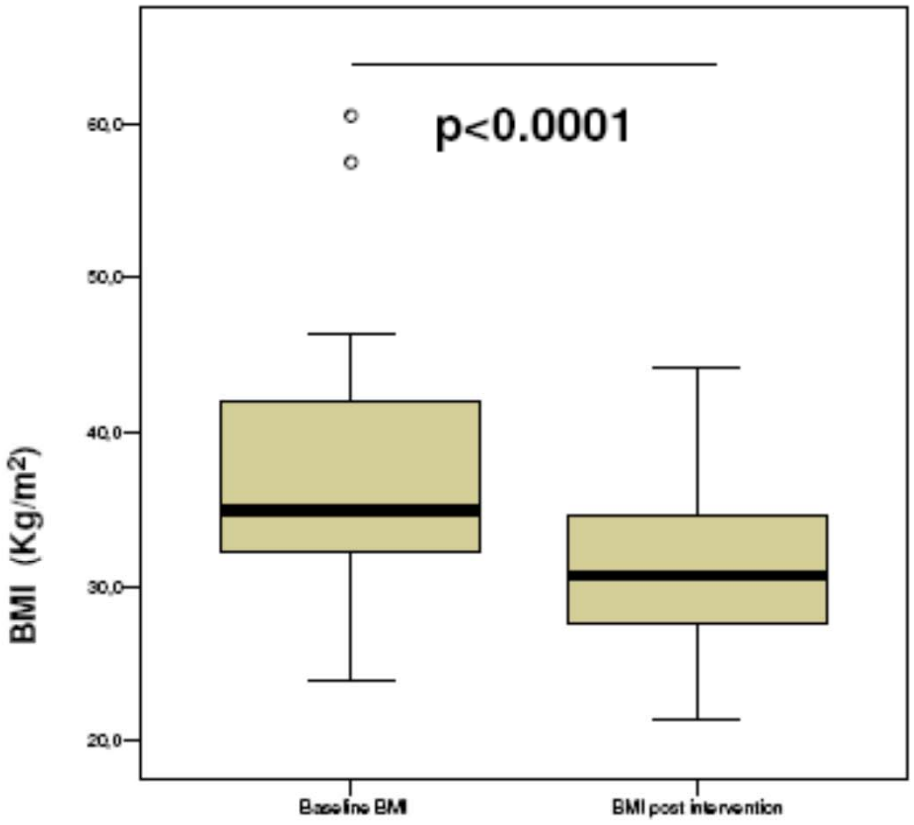
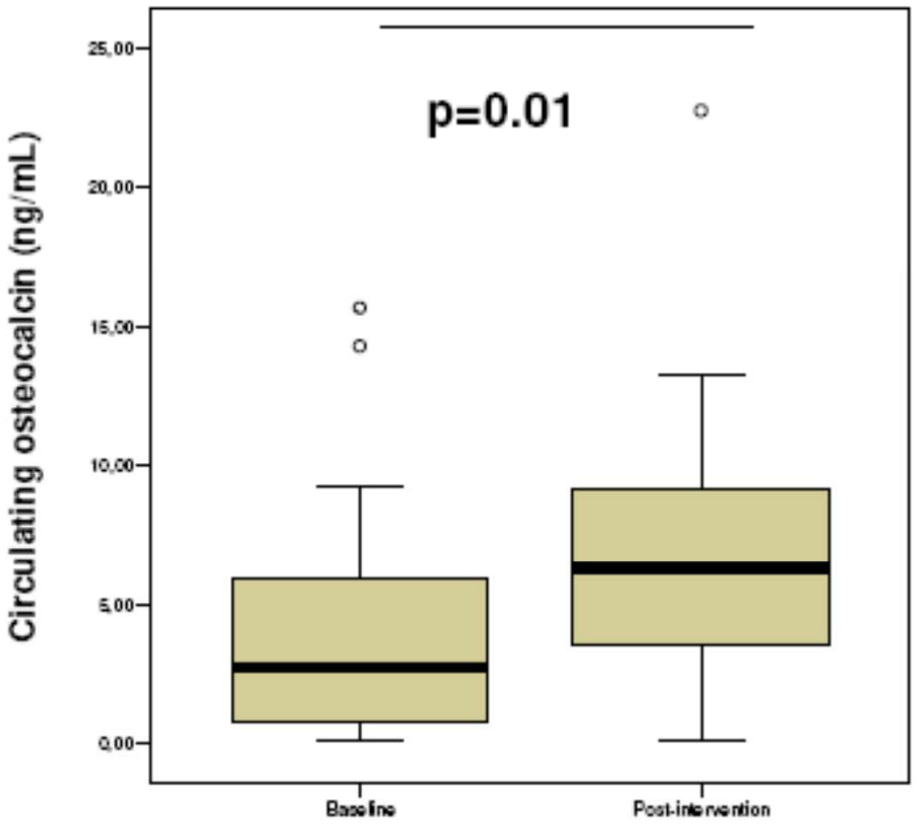
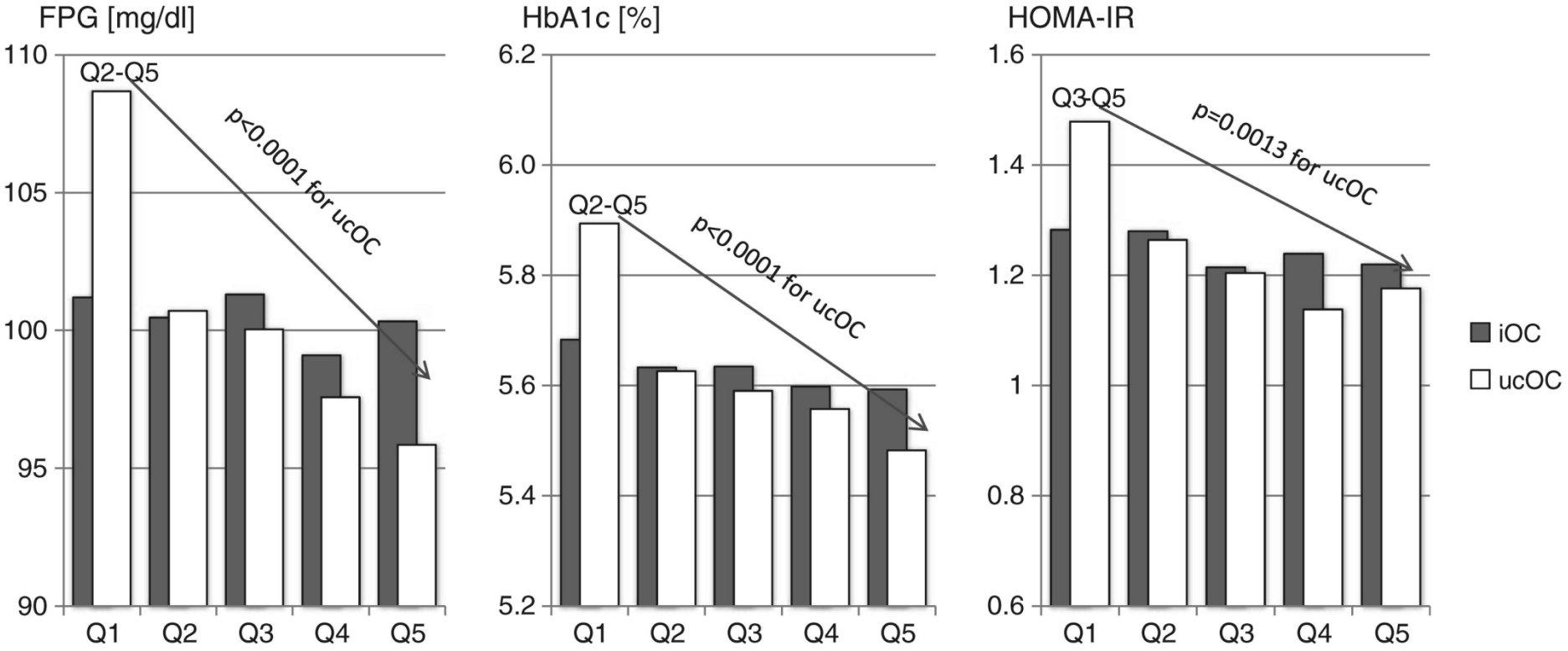




Fernández-Real et al. *JCEM* 2009

Osteocalcin and T2DM in humans

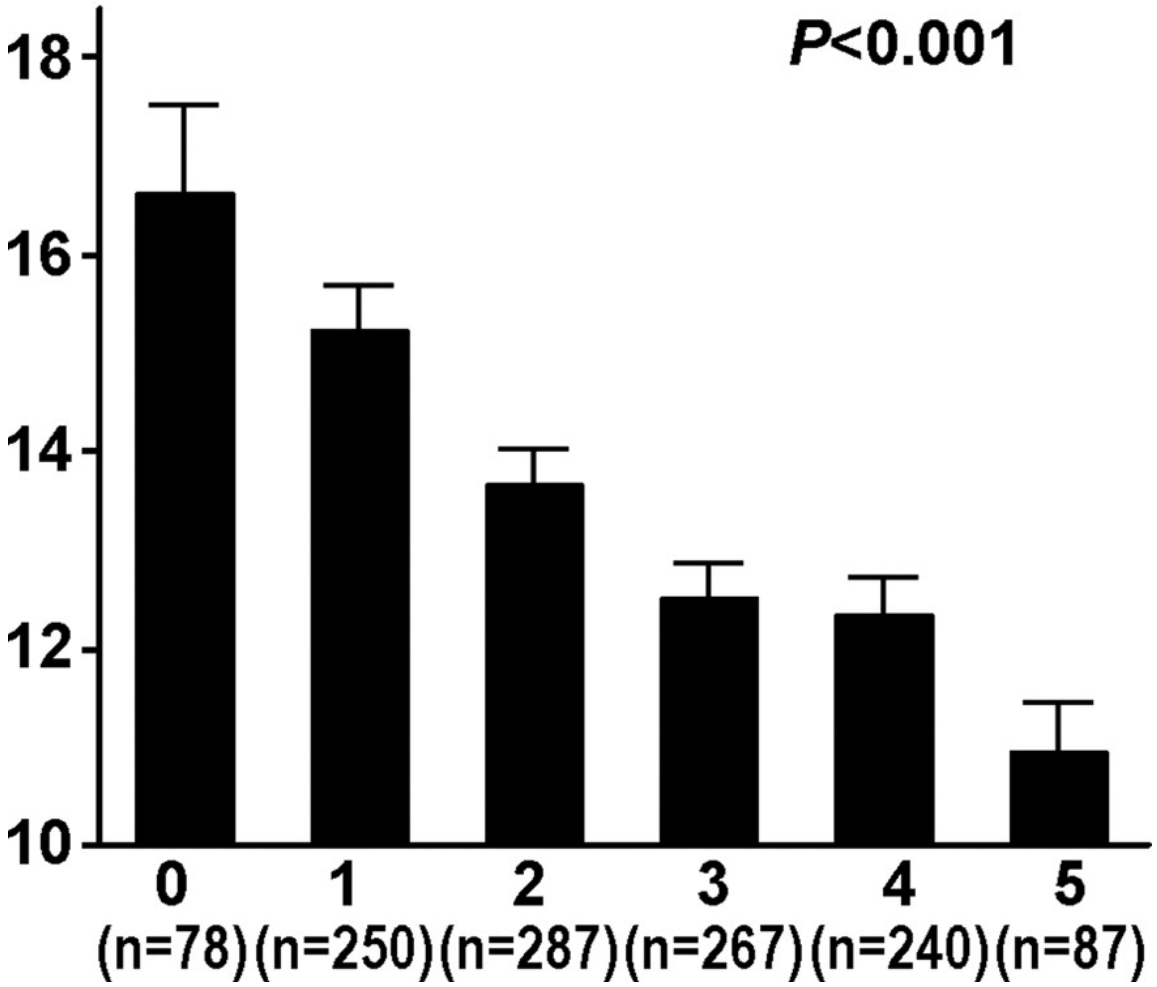
Osteocalcin & Insulin resistance



Iki et al. *Osteoporos Int* 2012

Osteocalcin and T2DM in humans

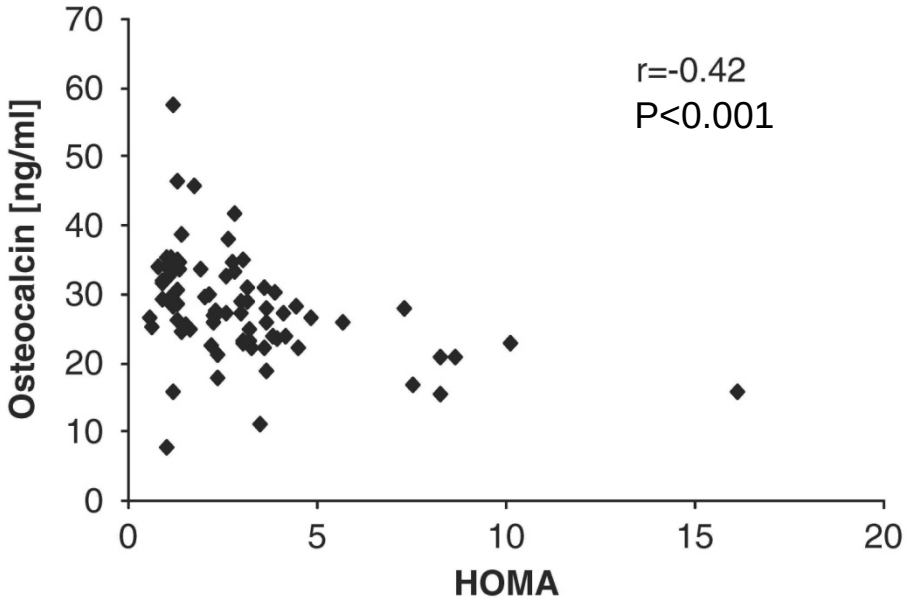
Osteocalcin & Metabolic Syndrome



Saleem et al. *ATVB* 2010

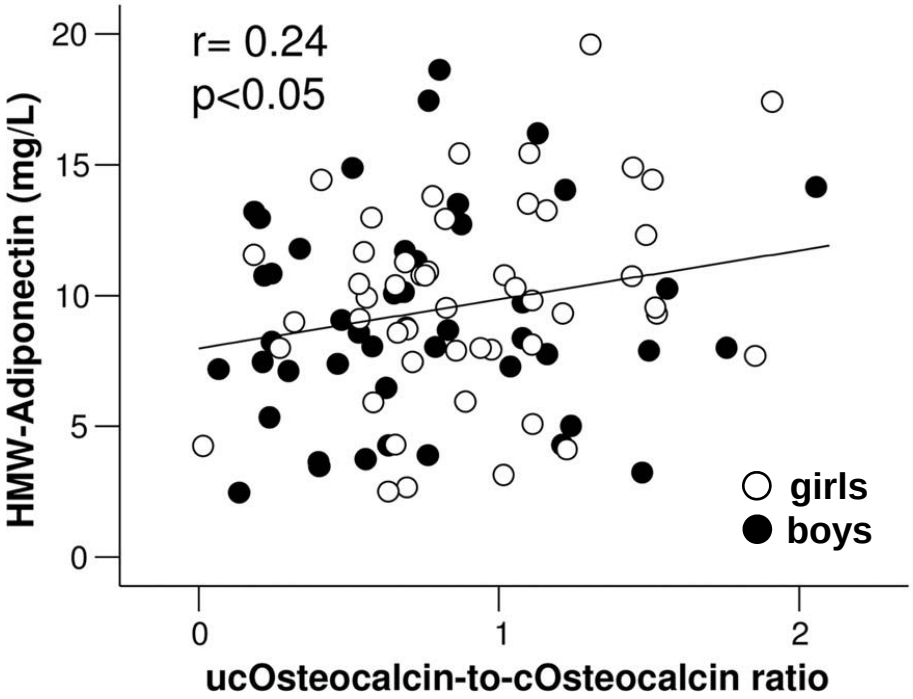
Osteocalcin and T2DM in children

Osteocalcin & HOMA



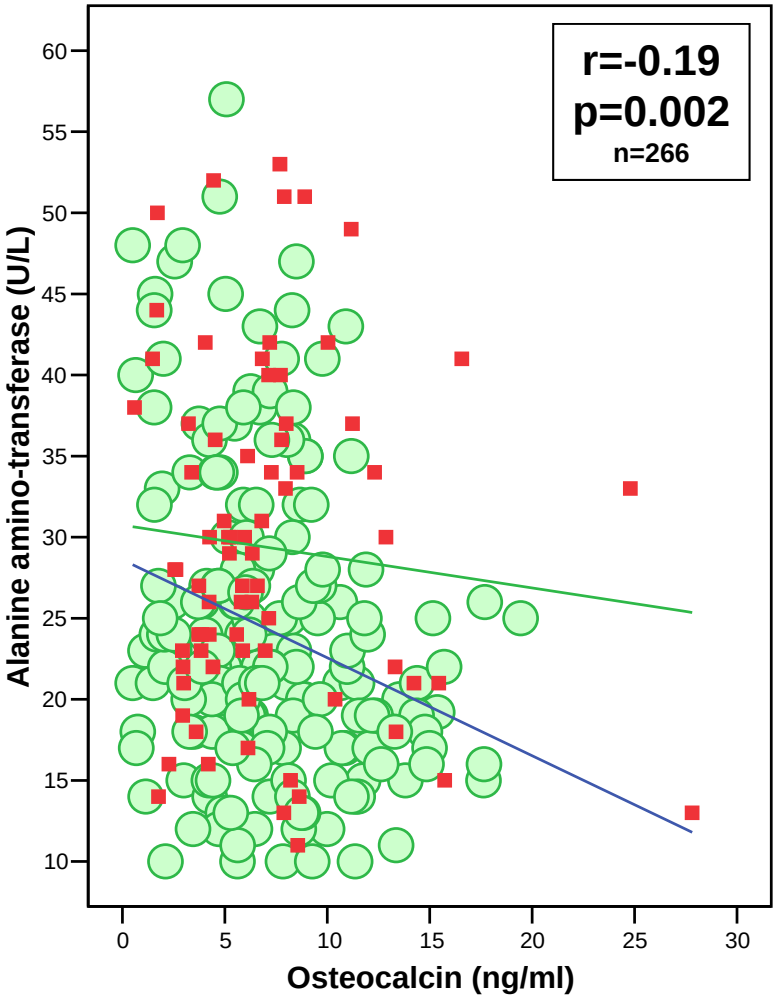
Reinehr et al. *Int J Obes* 2010

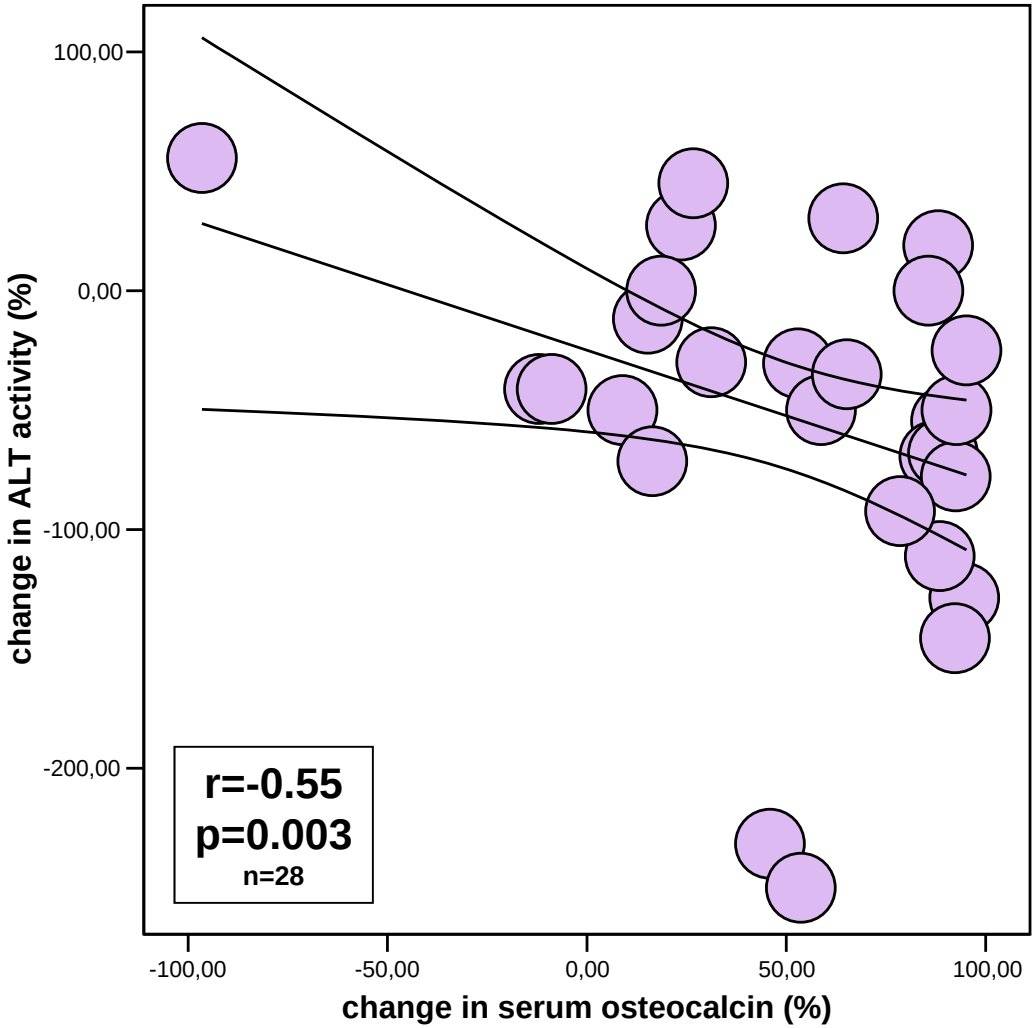
Osteocalcin & Adiponectin



Prats-Puig et al. *Diabetes Care* 2010

The bone as an endocrine organ in humans





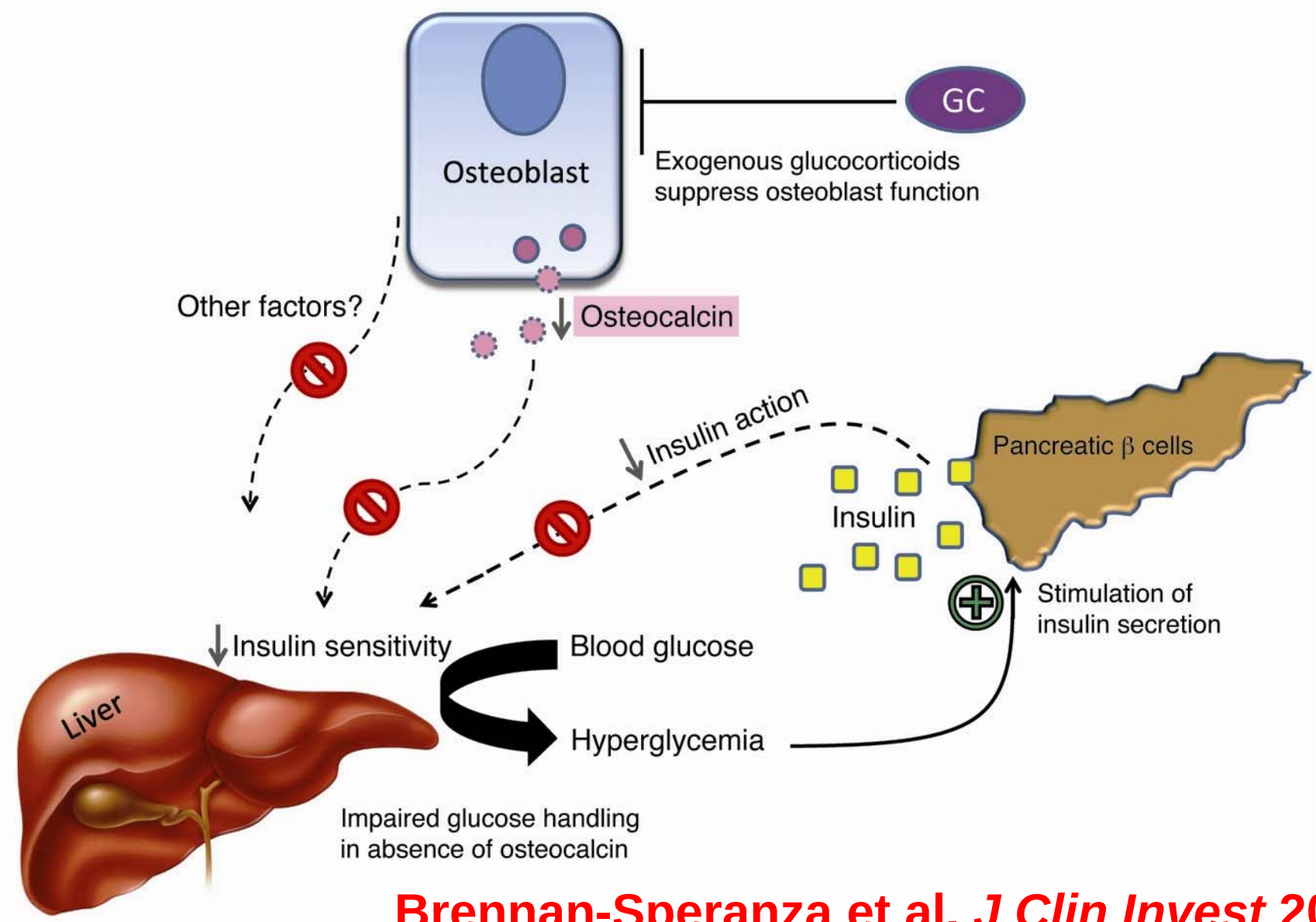
r=-0.23, p=0.002, n=191 non-obese subjects

r=-0.004, p=0.97, n=75 obese subjects

r=-0.41, p=0.04 after exclusion of the 3 outliers

Fernández-Real et al. *Osteoporos Int* 2010

Osteoblasts mediate the adverse effects of glucocorticoids on fuel metabolism



Brennan-Speranza et al. *J Clin Invest* 2012

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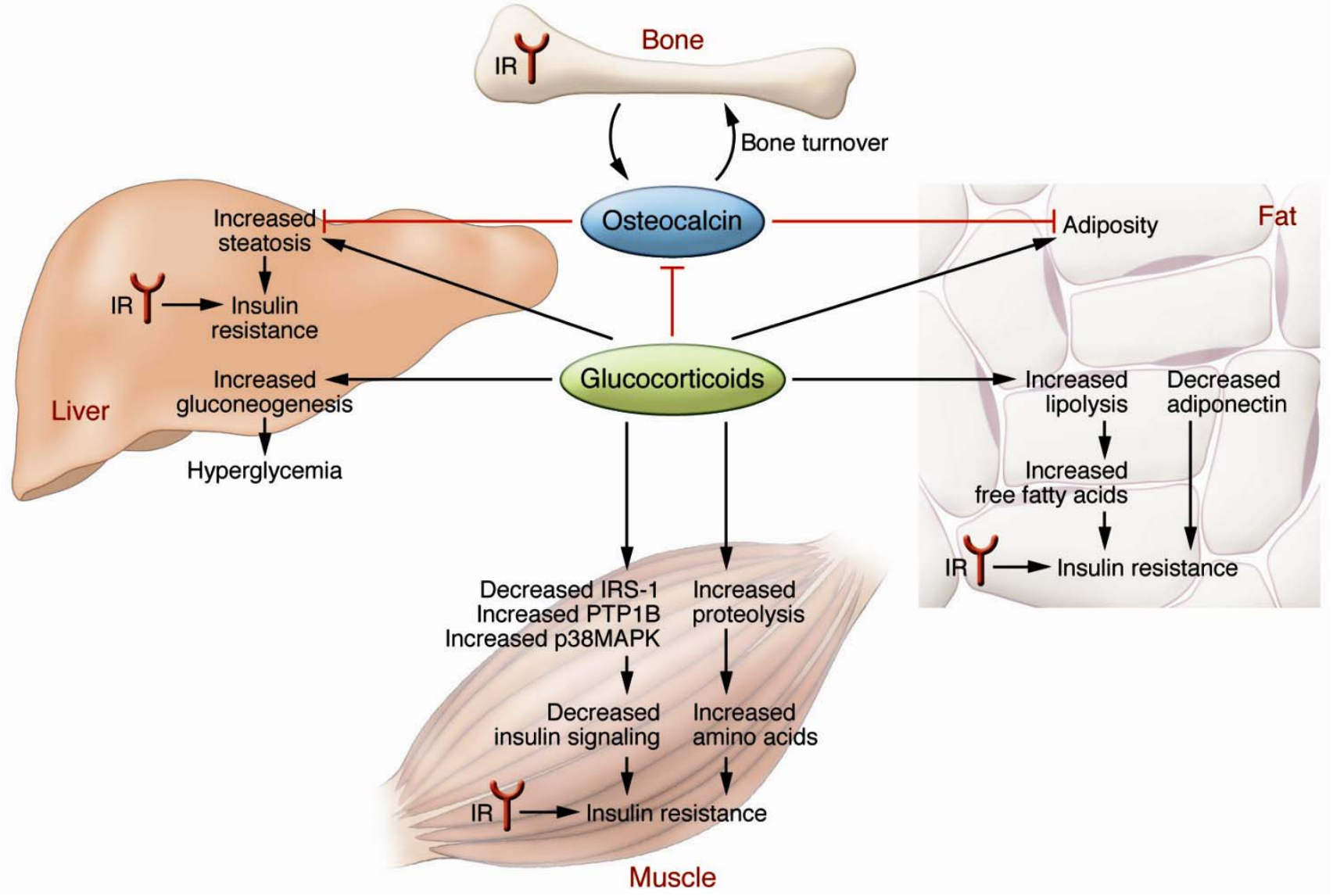
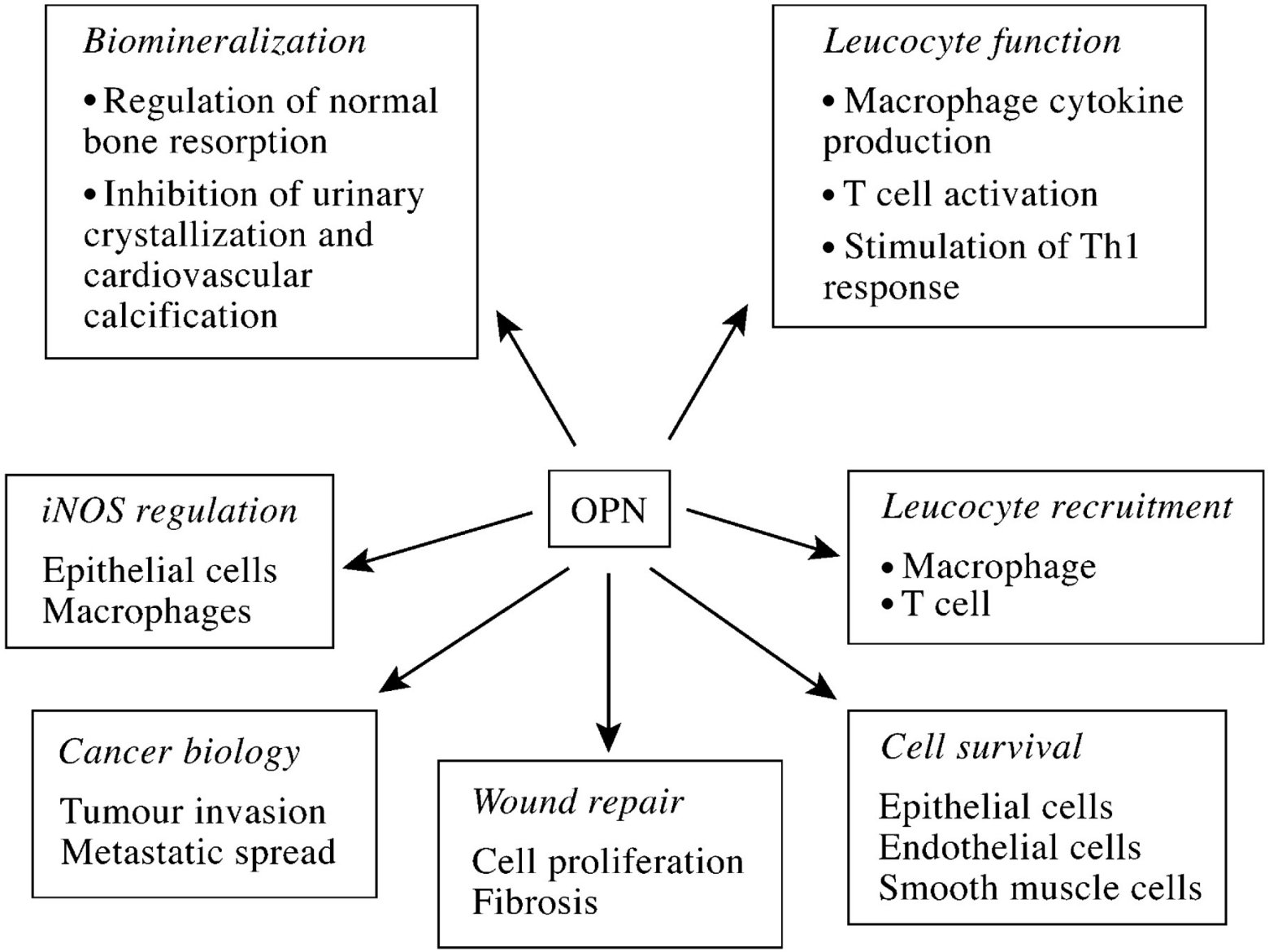


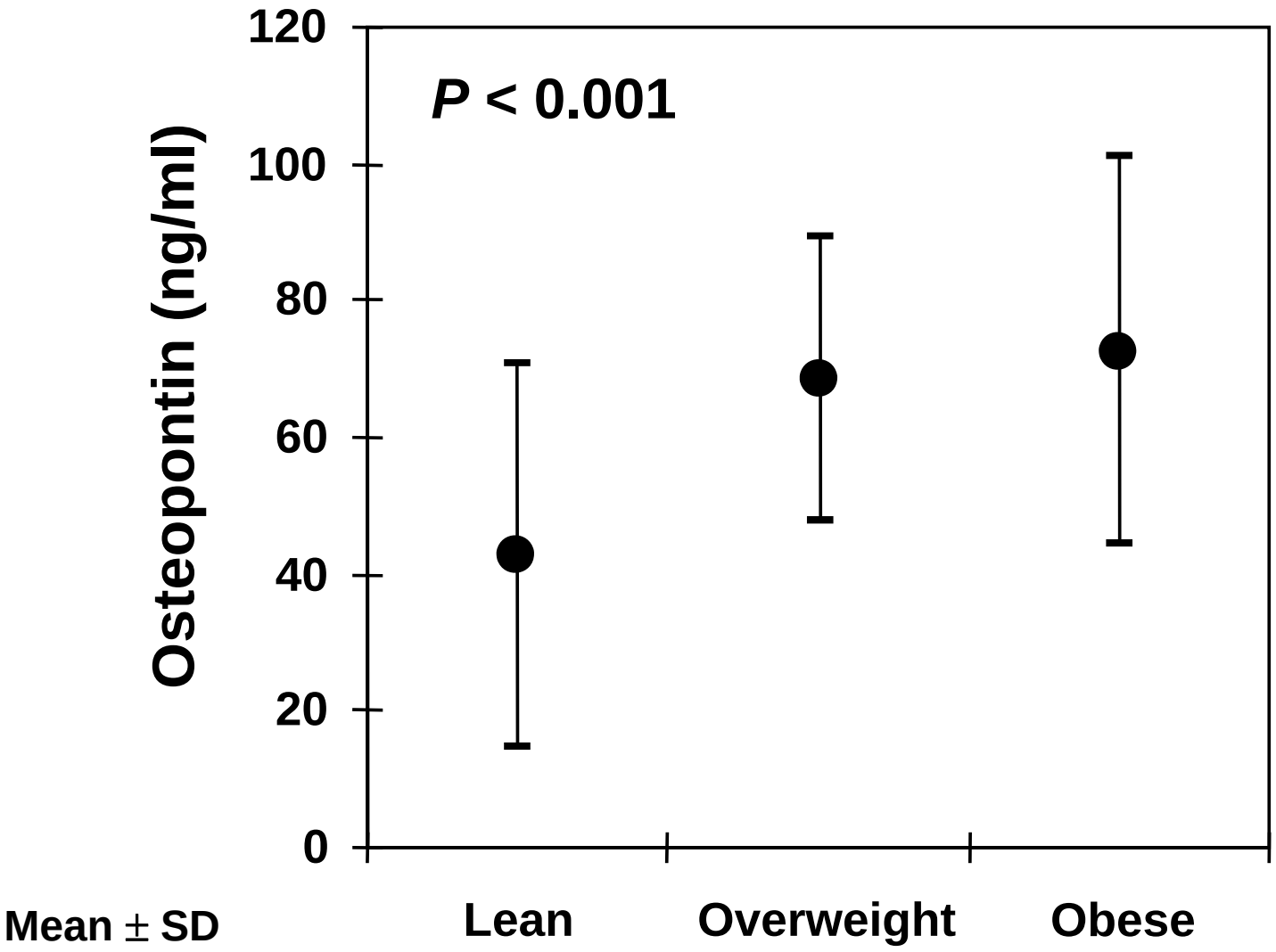
Brennan-Speranza et al. *J Clin Invest* 2012

Osteopontin (OPN) - Biological functions



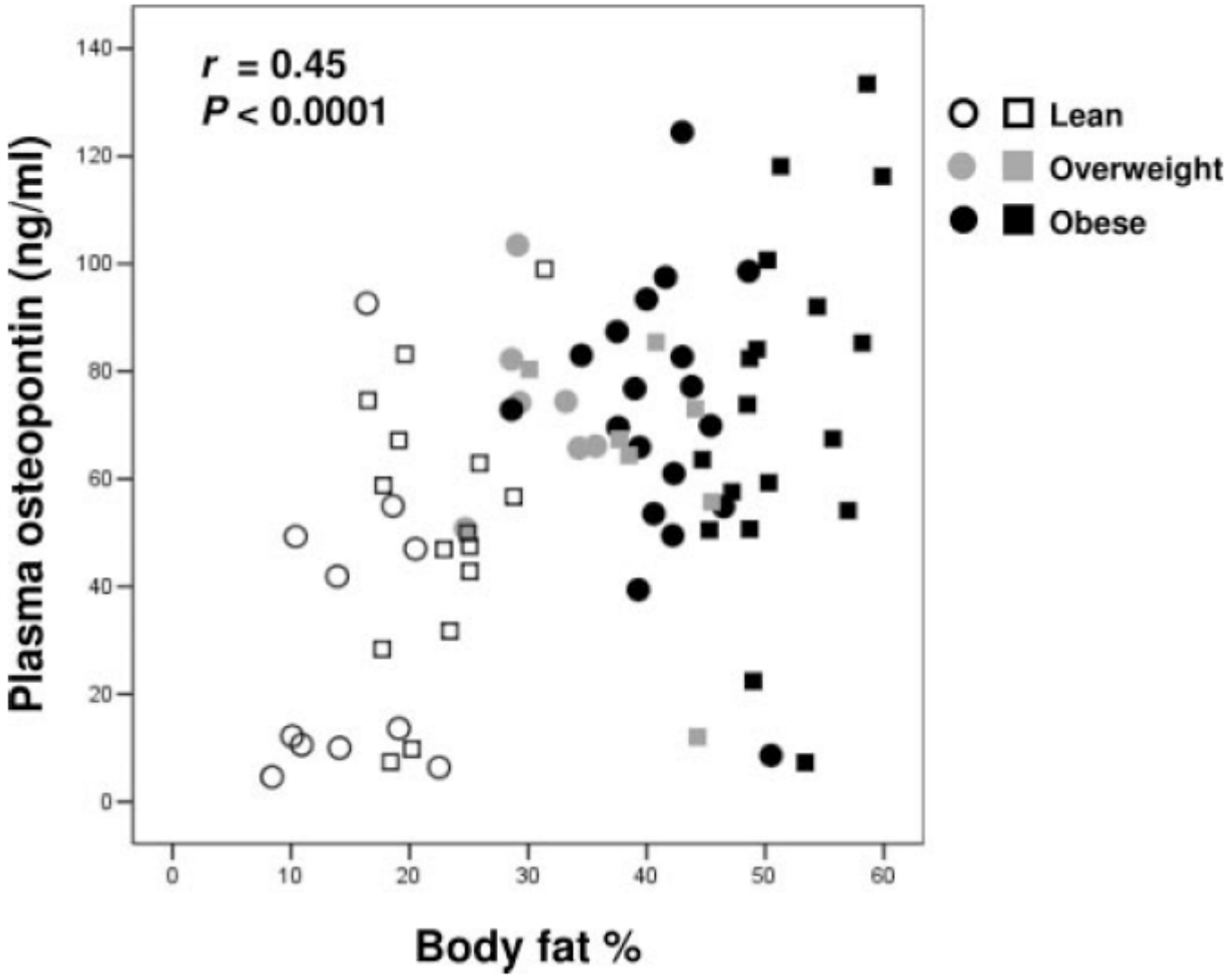
Mazzali et al. *QJM* 2002

Plasma OPN concentrations in human obesity



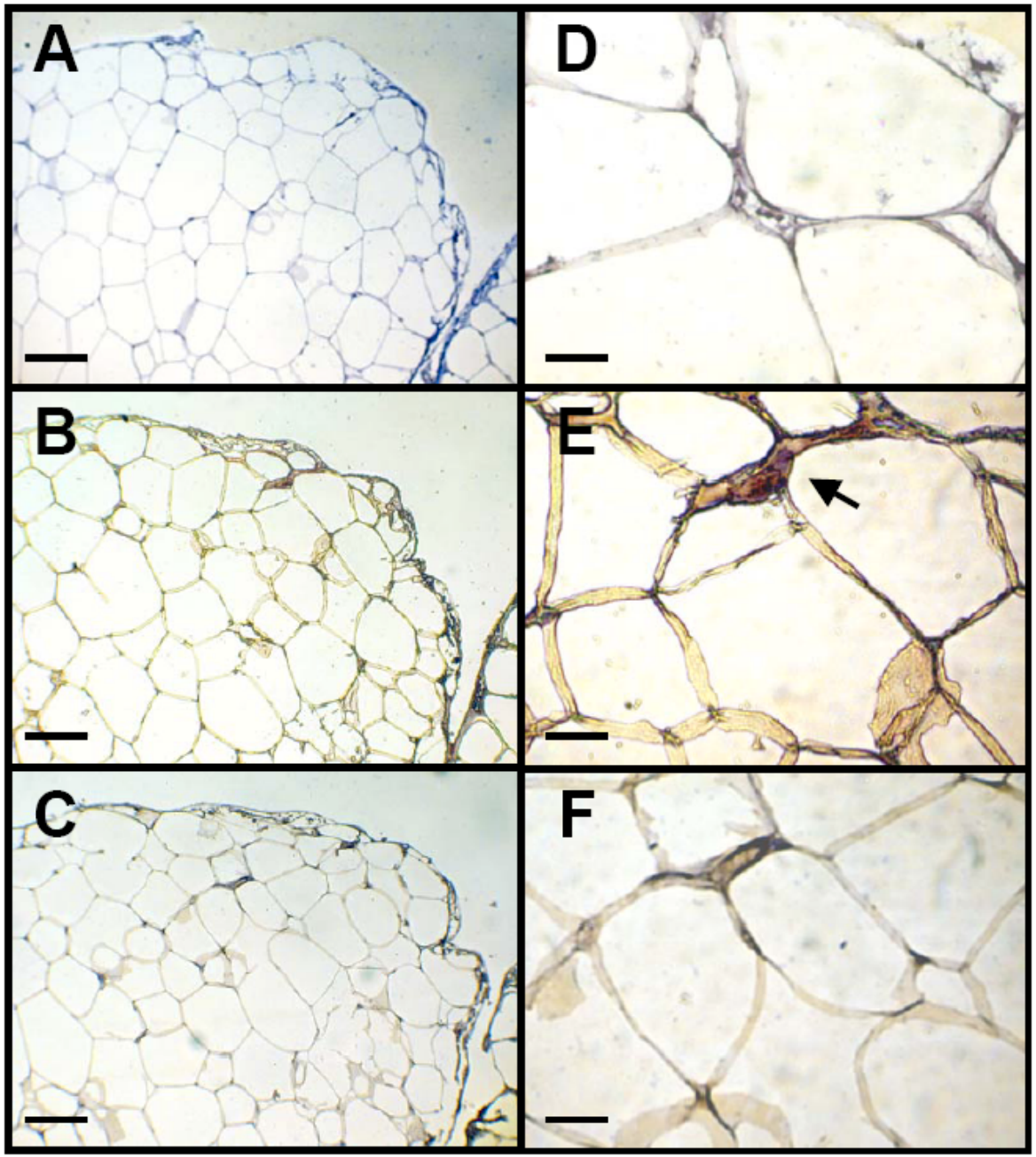
Gómez-Ambrosi et al.
J Clin Endocrinol Metab 2007

Plasma OPN correlates with body fat



Gómez-Ambrosi et al.
J Clin Endocrinol Metab 2007

Plasma OPN expression in human adipose tissue



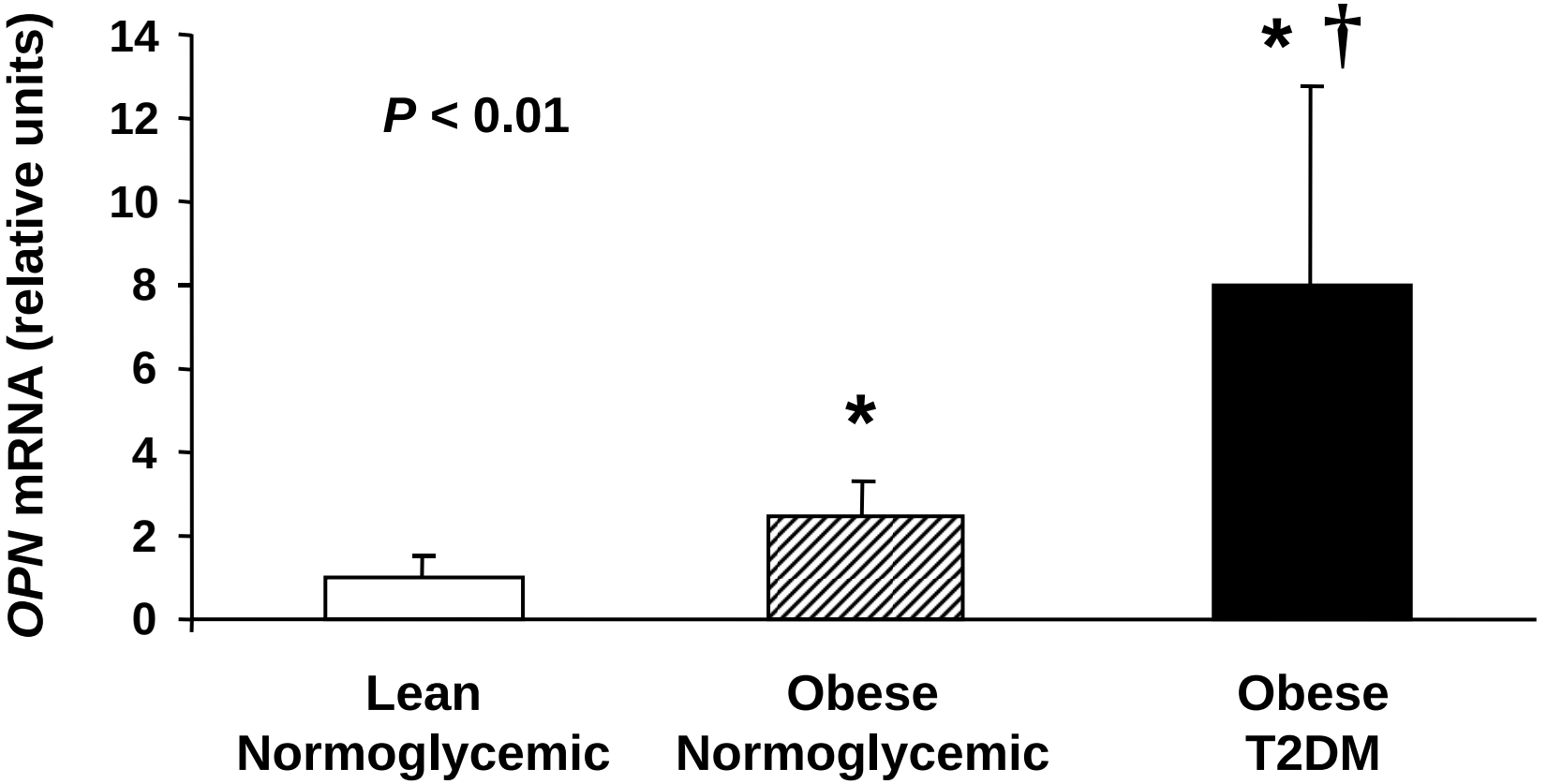
Control -

OPN+

CD68+

Gómez-Ambrosi et al.
J Clin Endocrinol Metab 2007

Plasma OPN expression in adipose tissue

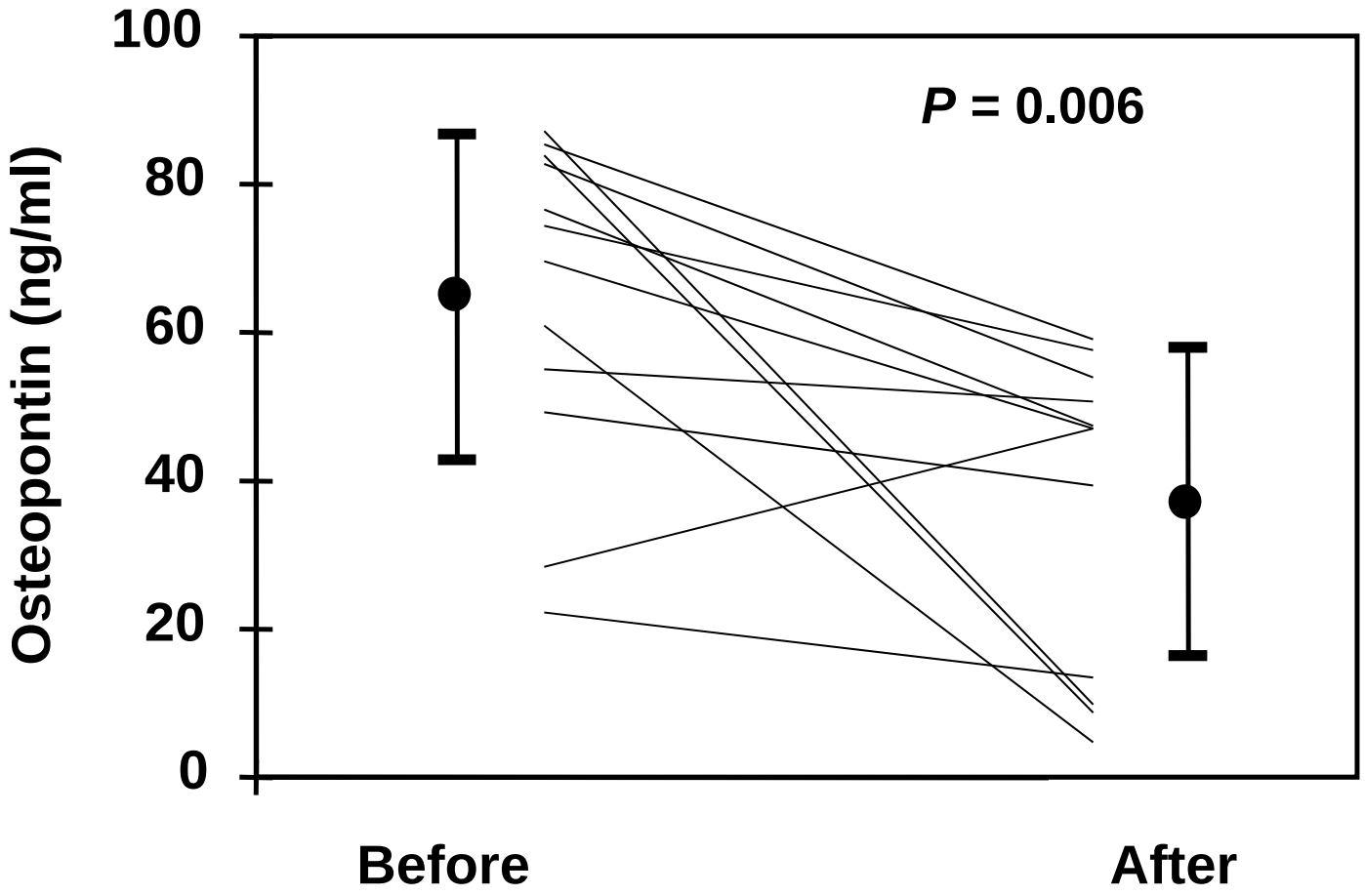


* *P* < 0.05 vs lean

† *P* < 0.05 vs obese NG

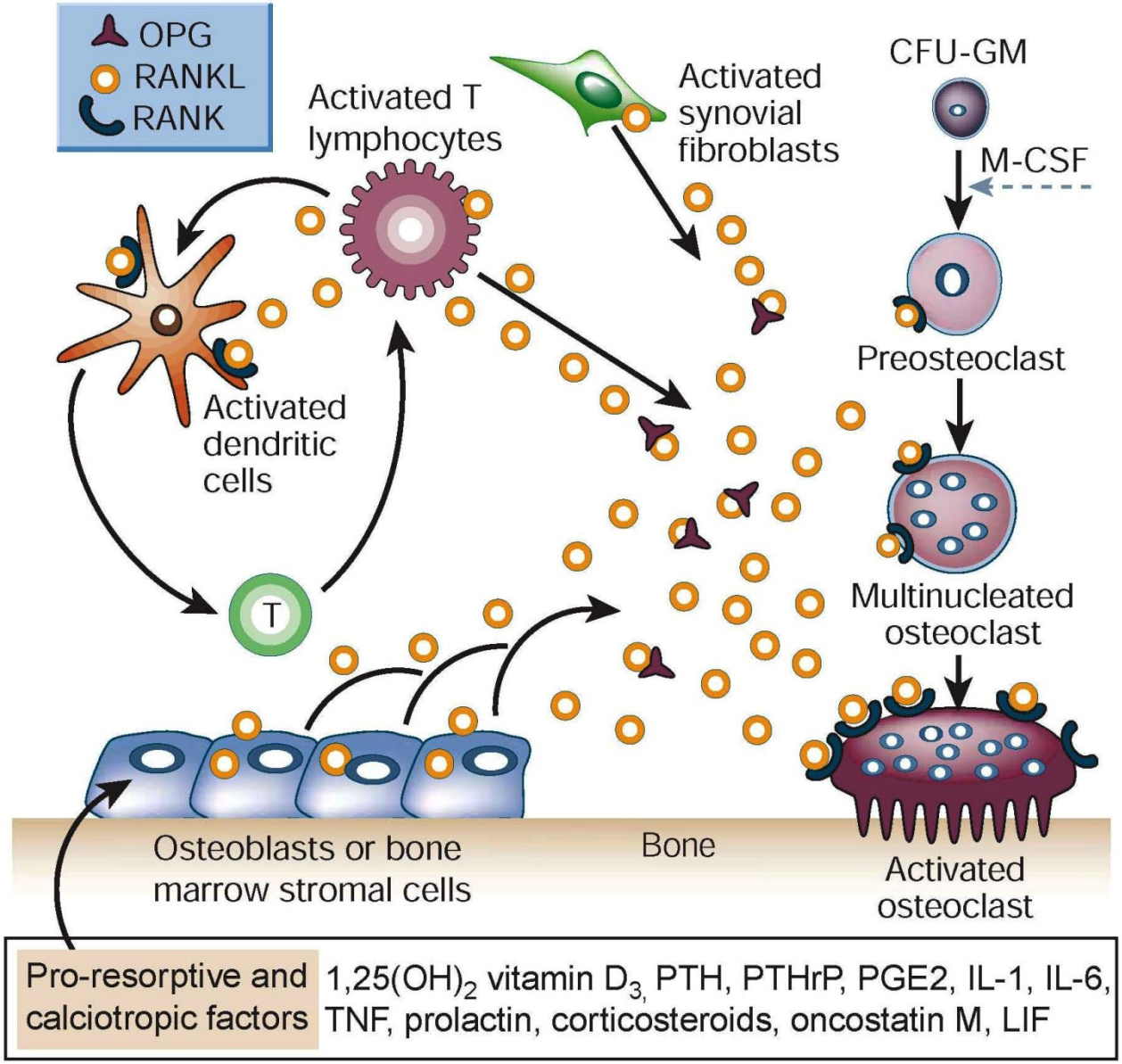
Gómez-Ambrosi et al.
J Clin Endocrinol Metab 2007

Plasma OPN decreases with weight loss



Gómez-Ambrosi et al.
J Clin Endocrinol Metab 2007

RANKL-RANK-OPG & Insulin Resistance



Boyle et al. *Nature* 2003

RANKL-RANK-OPG & Insulin Resistance

LETTERS

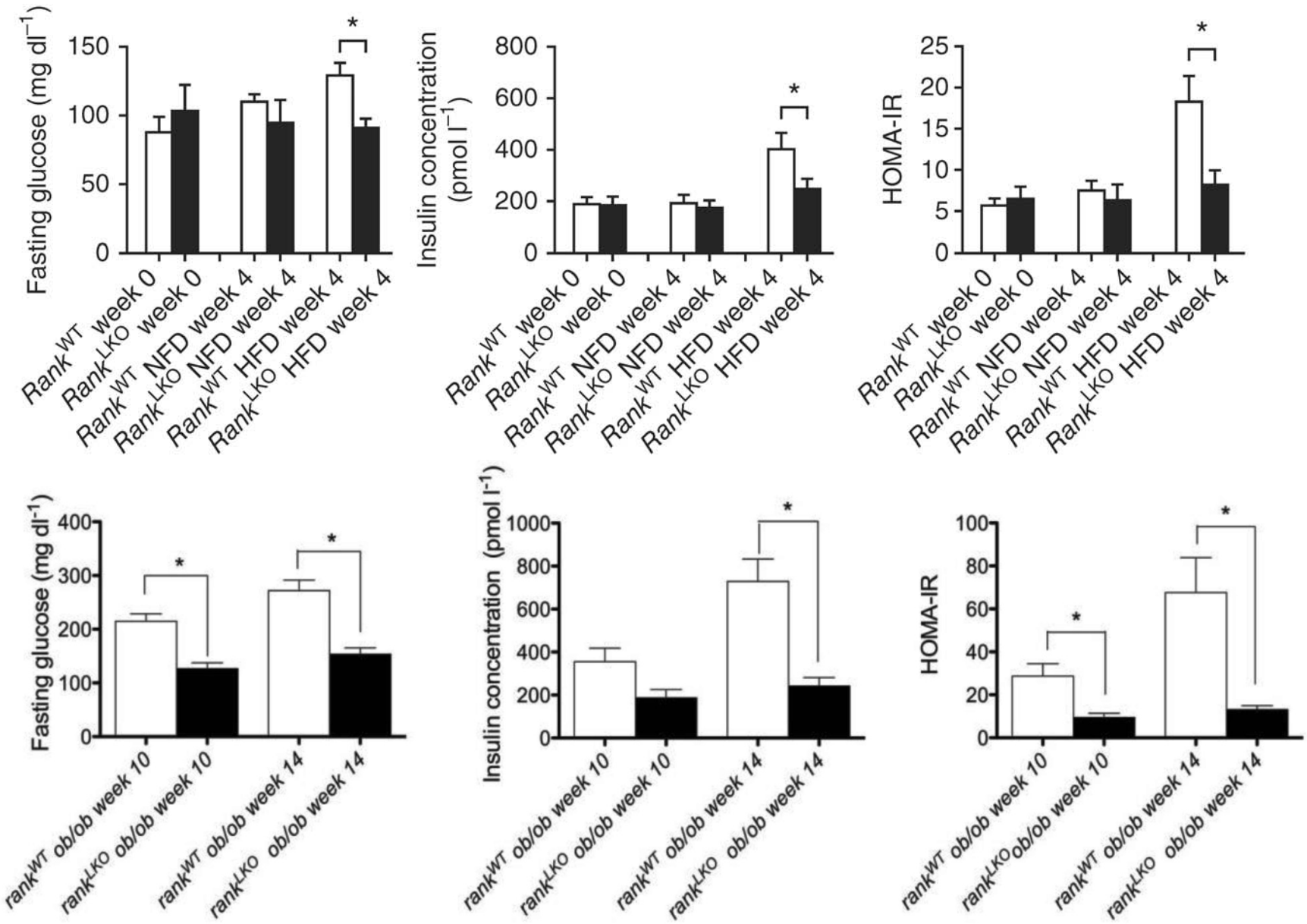
nature medicine

Blockade of receptor activator of nuclear factor-κB (RANKL) signaling improves hepatic insulin resistance and prevents development of diabetes mellitus

Stefan Kiechl[1,16], Jürgen Wittmann[2], Andrea Giaccari[3,4], Michael Knoflach[1], Peter Willeit[1,5], Aline Bozec[6], Alexander R Moschen[7], Giovanna Muscogiuri[3], Gian Pio Sorice[3], Trayana Kireva[6], Monika Summerer[8], Stefan Wirtz[9], Julia Luther[6], Dirk Mielenz[2], Ulrike Billmeier[9], Georg Egger[10], Agnes Mayr[11], Friedrich Oberhollenzer[10], Florian Kronenberg[8], Michael Orthofer[12], Josef M Penninger[12], James B Meigs[13,14], Enzo Bonora[15], Herbert Tilg[7], Johann Willeit[1] & Georg Schett[6,16]

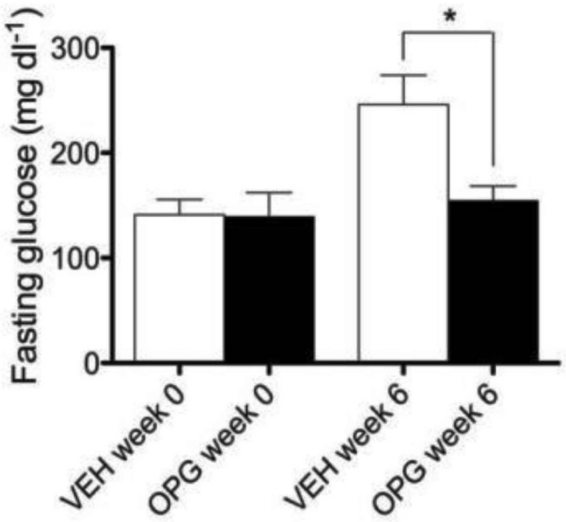
Kiechl et al. *Nat Med* 2013

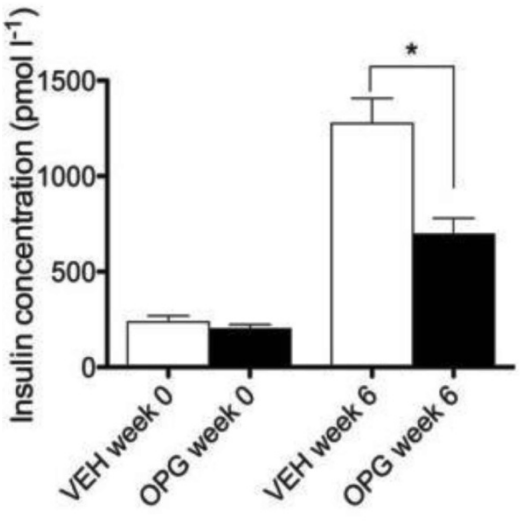
RANKL-RANK-OPG & Insulin Resistance

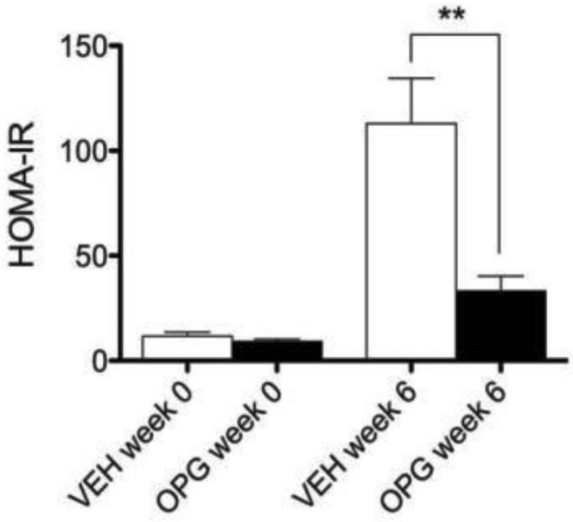


Kiechl et al. *Nat Med* 2013

RANKL-RANK-OPG & Insulin Resistance



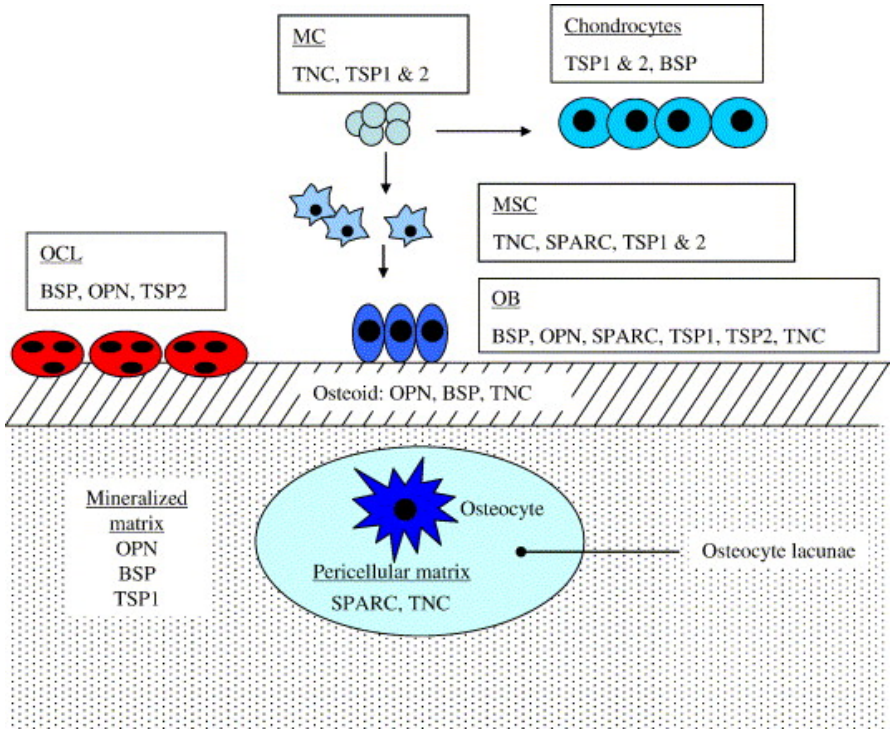




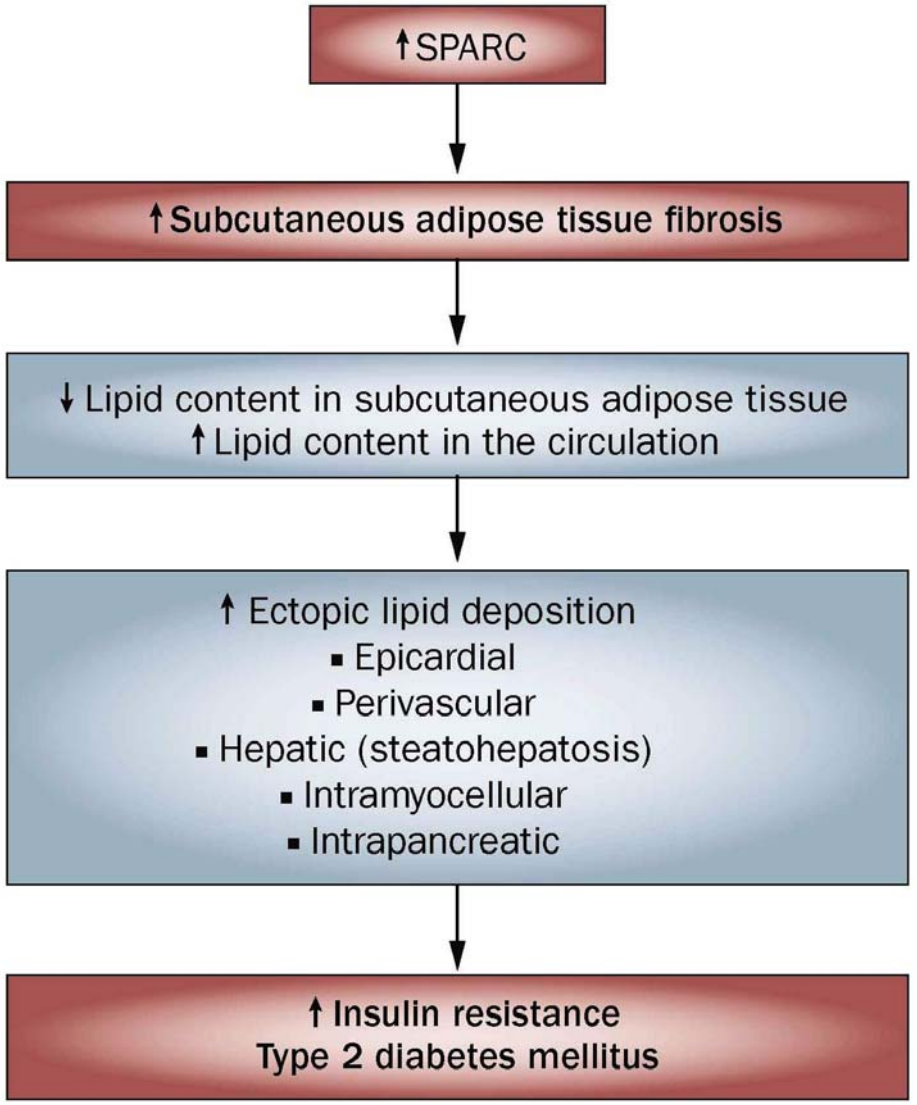
Kiechl et al. *Nat Med* 2013

SPARC (osteonectin) & Insulin Resistance

↑ Fortaleza ósea
↑ Riesgo CV
Implicado en cáncer
↑ En obesidad
↑ Resistencia a la insulina

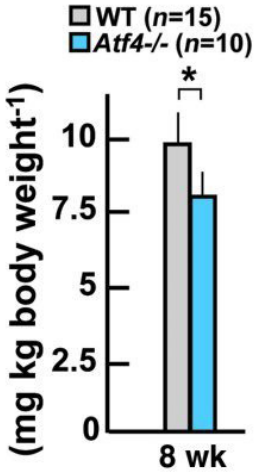


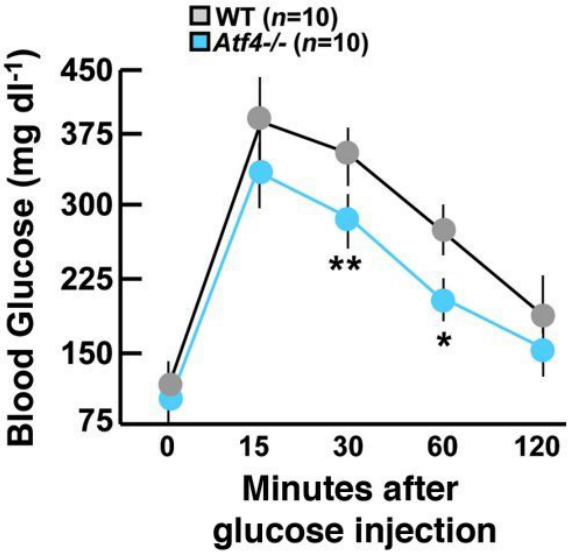
Alford & Hankenson. *Bone* 2006

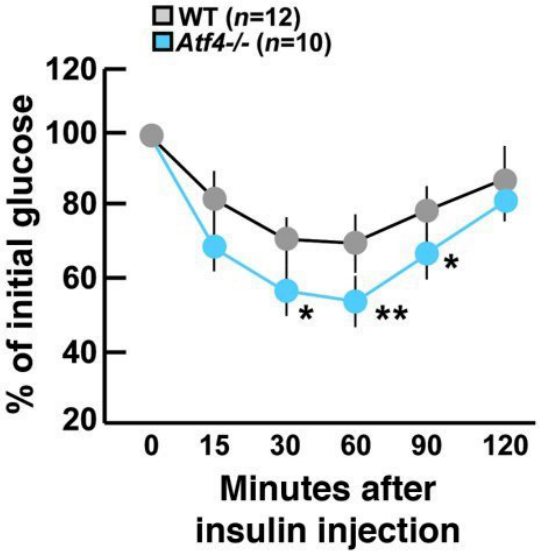


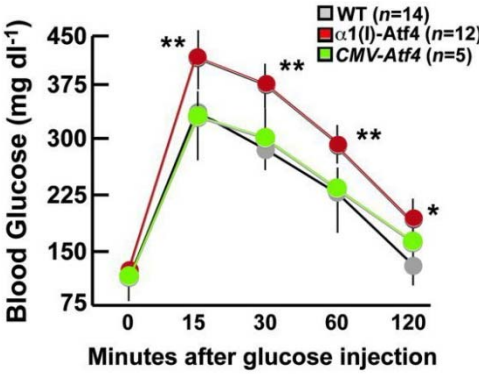
Kos & Wilding. *Nat Rev Endocrinol* 2010

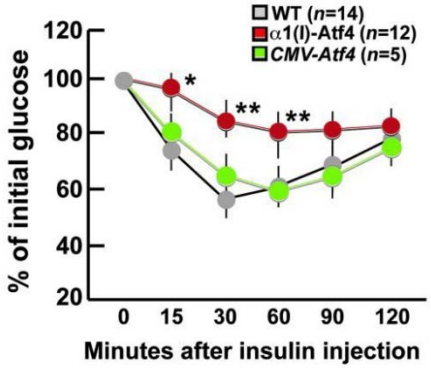
ATF4 & Glucose Metabolism

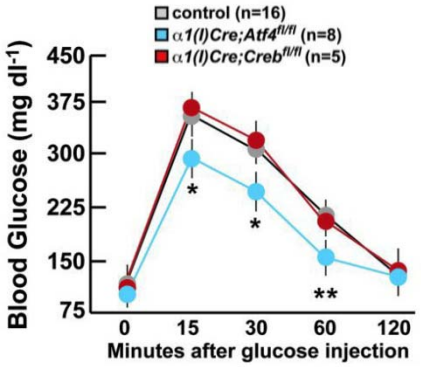


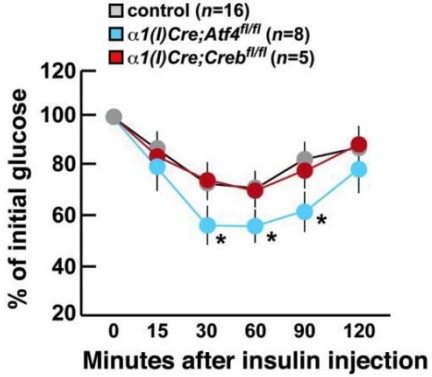


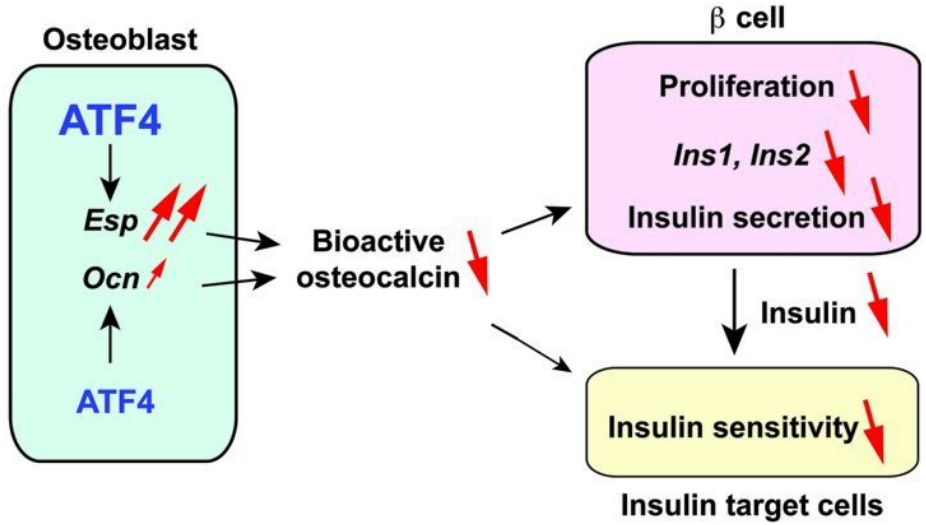






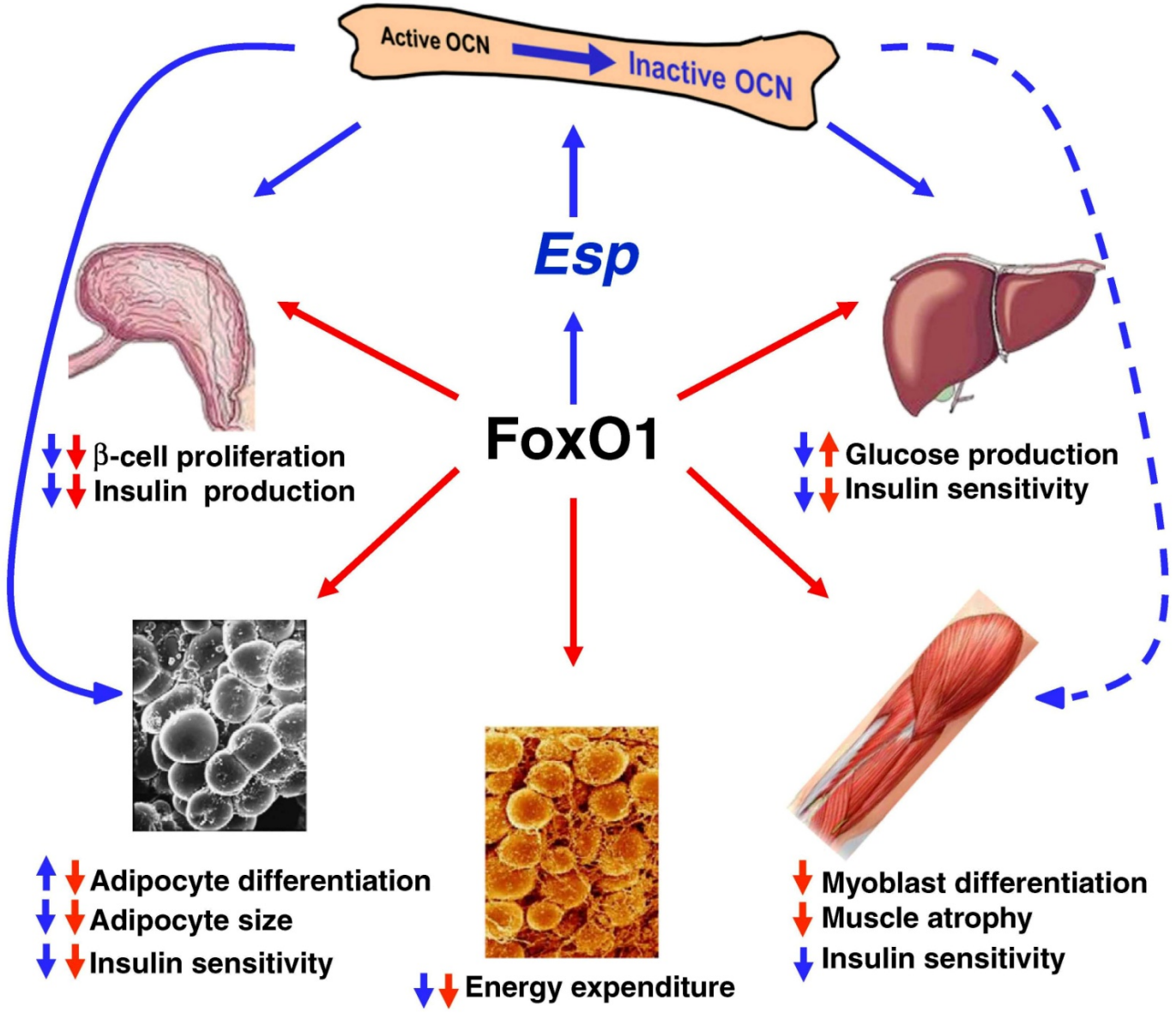






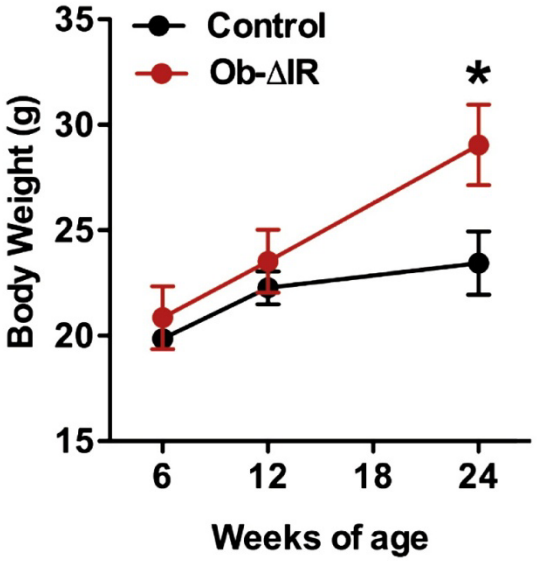
Yoshizawa. *J Clin Invest* 2009

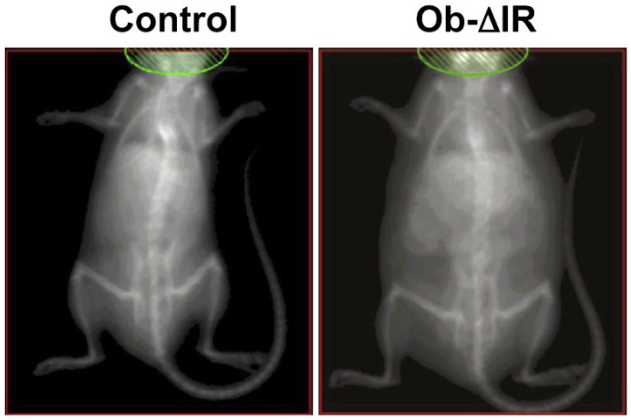
FoxO1 & Energy Metabolism

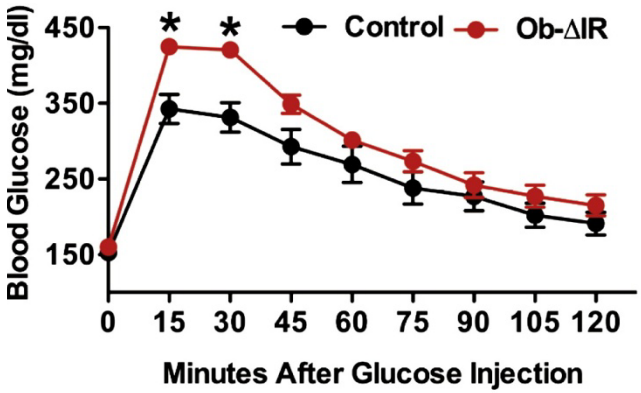


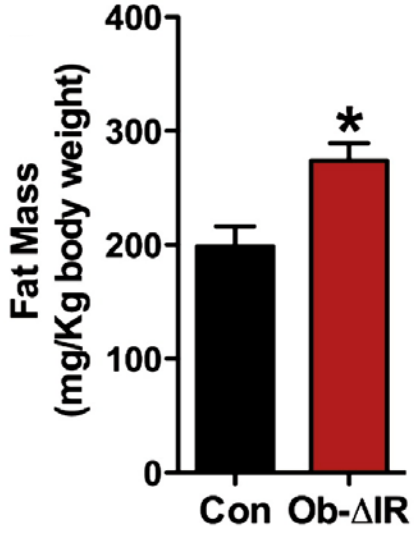
Kousteni. *Bone* 2012

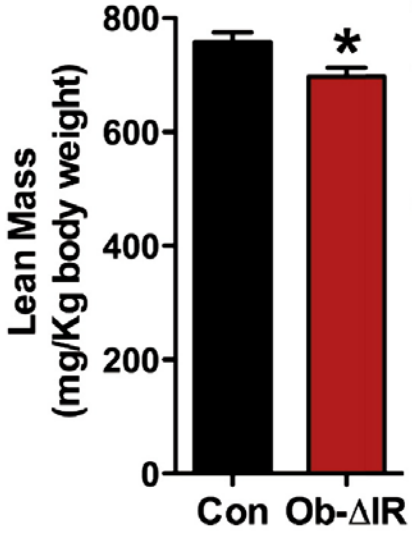
Insulin receptor signaling in osteoblasts regulates postnatal bone acquisition and body composition

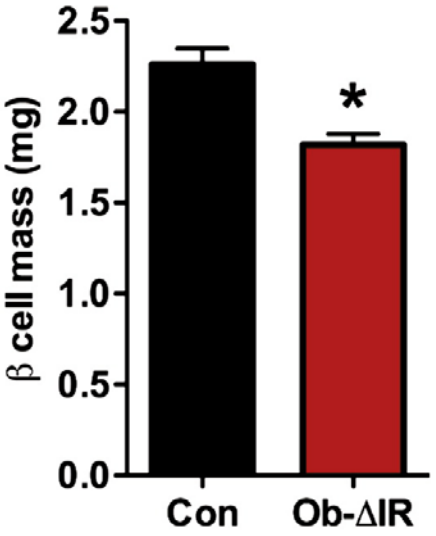


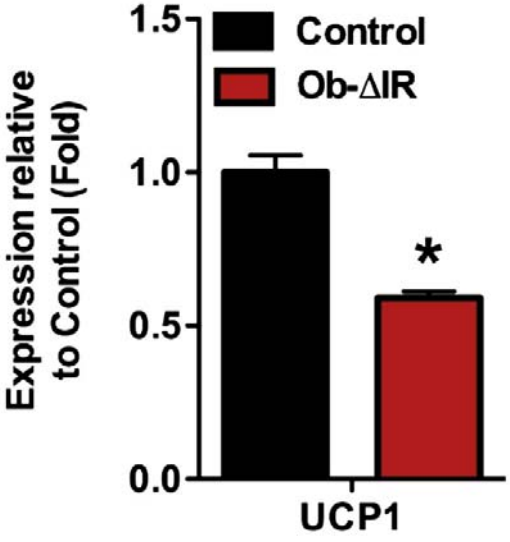




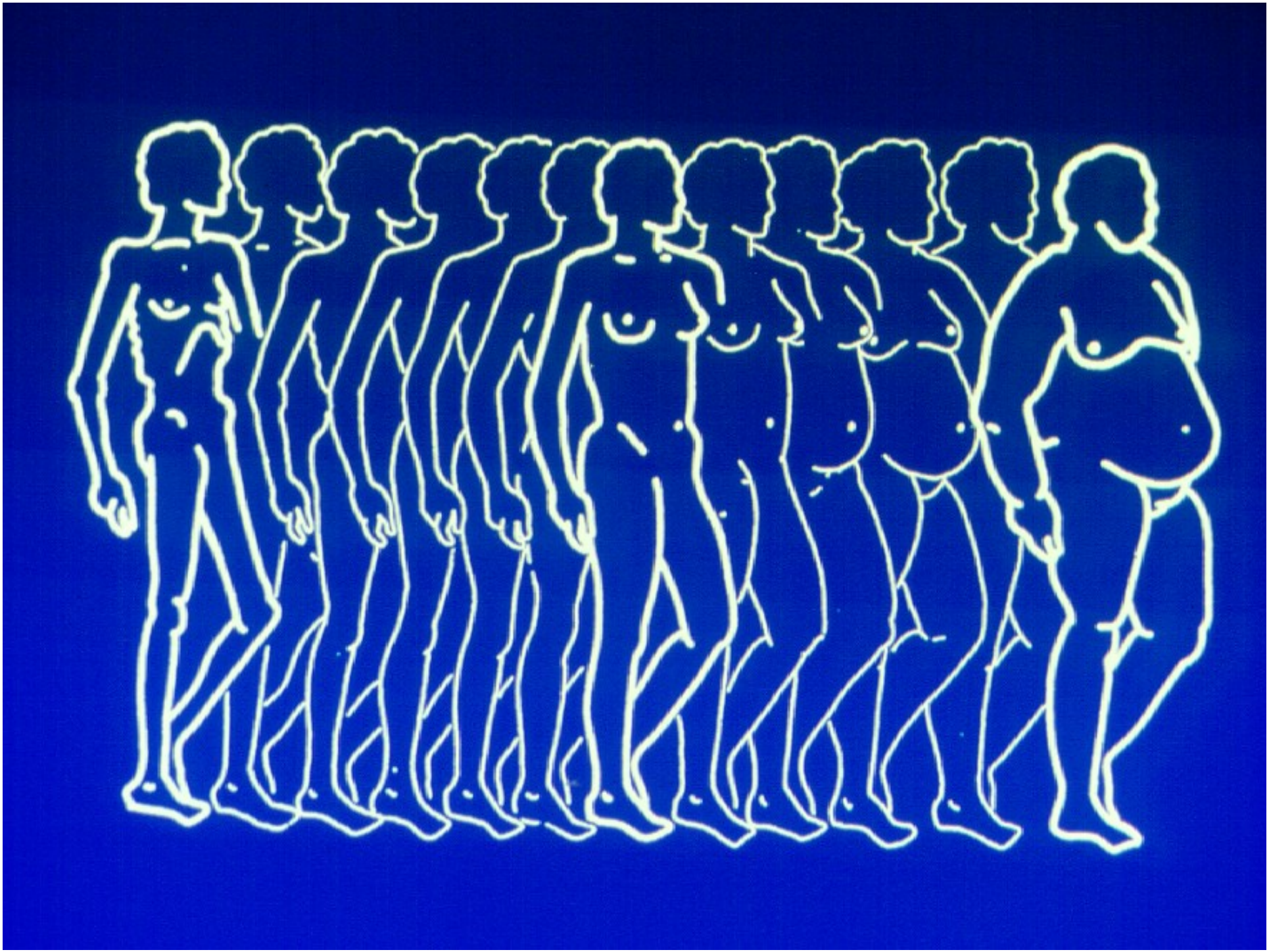




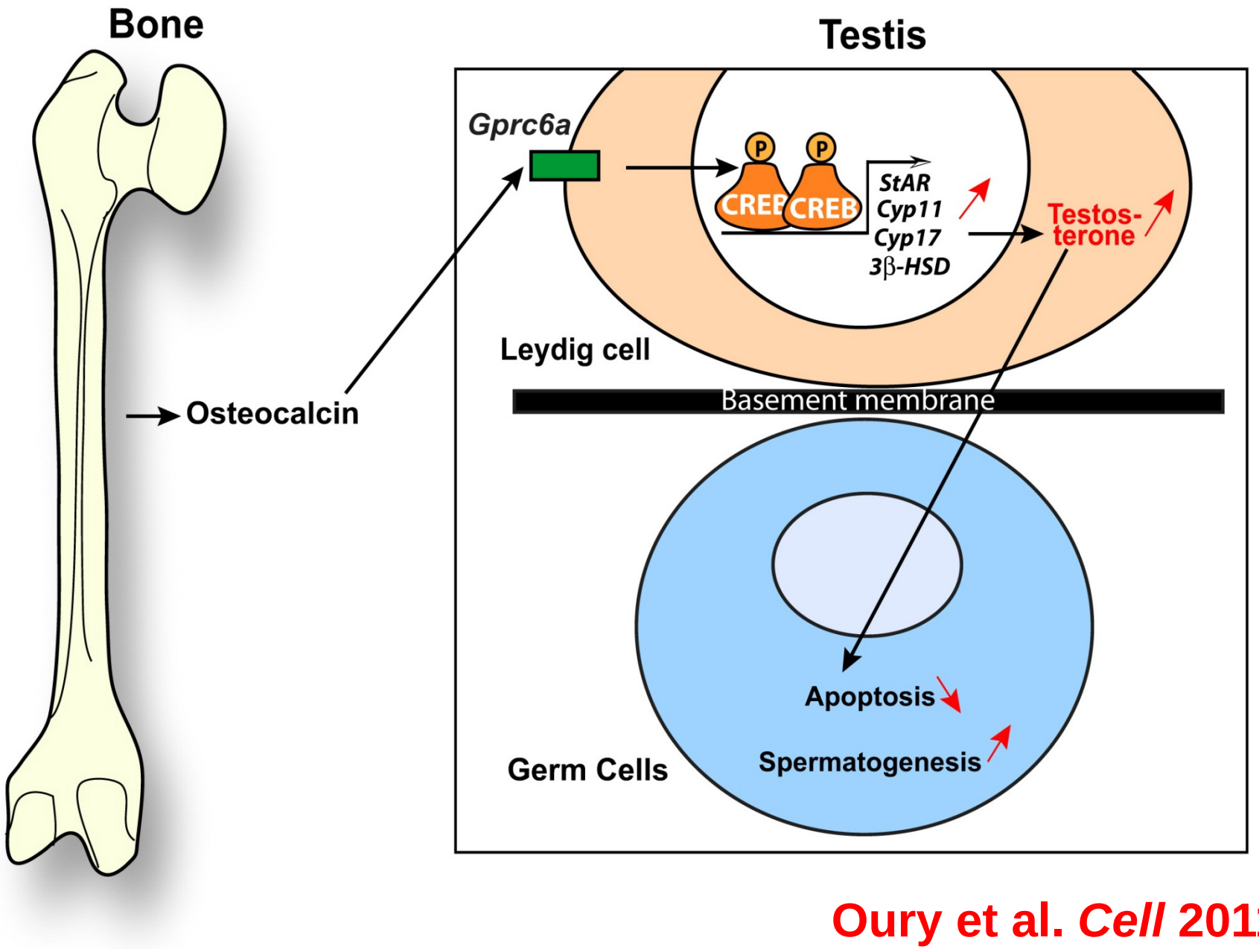




Fulzele et al. *Cell* 2010

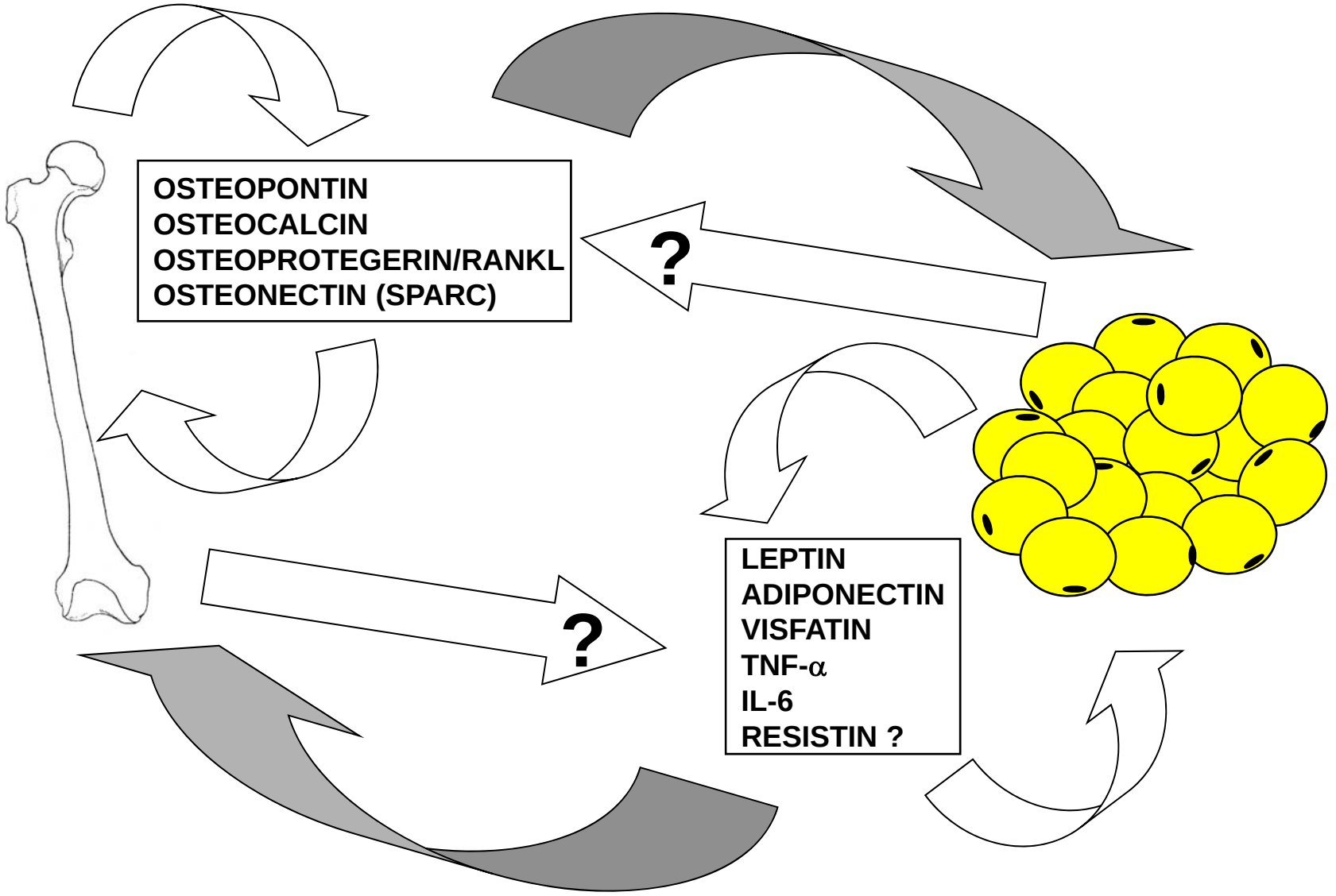


Endocrine regulation of male fertility in mice



Oury et al. *Cell* 2011

The bone-adipose axis



Gómez-Ambrosi et al. *Obes Surg* 2008

Agradecimientos

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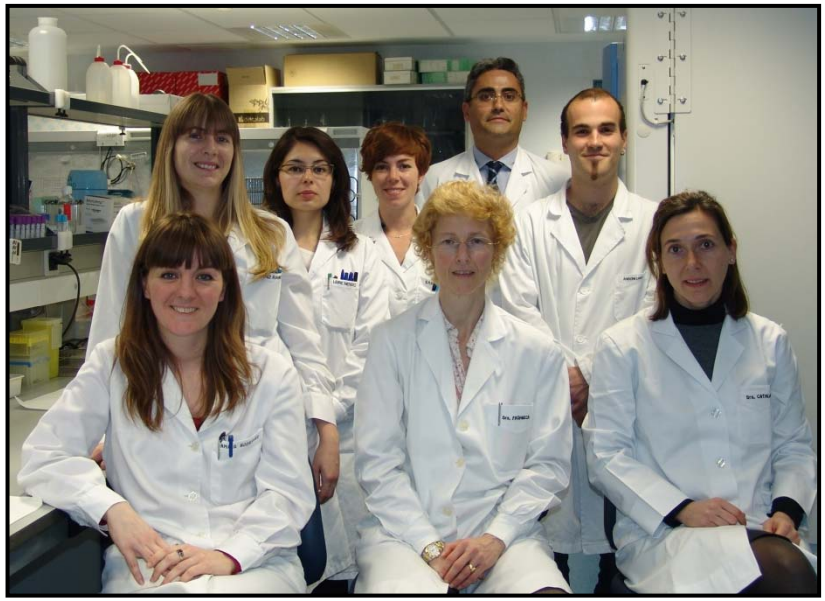

Lab. Investigación Metabólica

Gema Frühbeck
Amaia Rodríguez
Victoria Catalán
Leire Méndez
Beatriz Ramírez
Sara Becerril
Andoni Lancha
Javier Gurbindo

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