About OMICS Group

OMICS Group is an amalgamation of Open Access publications and worldwide international science conferences and events. Established in the year 2007 with the sole aim of making the information on Sciences and technology 'Open Access', OMICS Group publishes 500 online open access scholarly journals in all aspects of Science, Engineering, Management and Technology journals. OMICS Group has been instrumental in taking the knowledge on Science & technology to the doorsteps of ordinary men and women. Research Scholars, Students, Libraries, Educational Institutions, Research centers and the industry are main stakeholders that benefitted greatly from this knowledge dissemination. OMICS Group also organizes 500 International conferences annually across the globe, where knowledge transfer takes place through debates, round table discussions, poster presentations, workshops, symposia and exhibitions.

About OMICS International Conferences

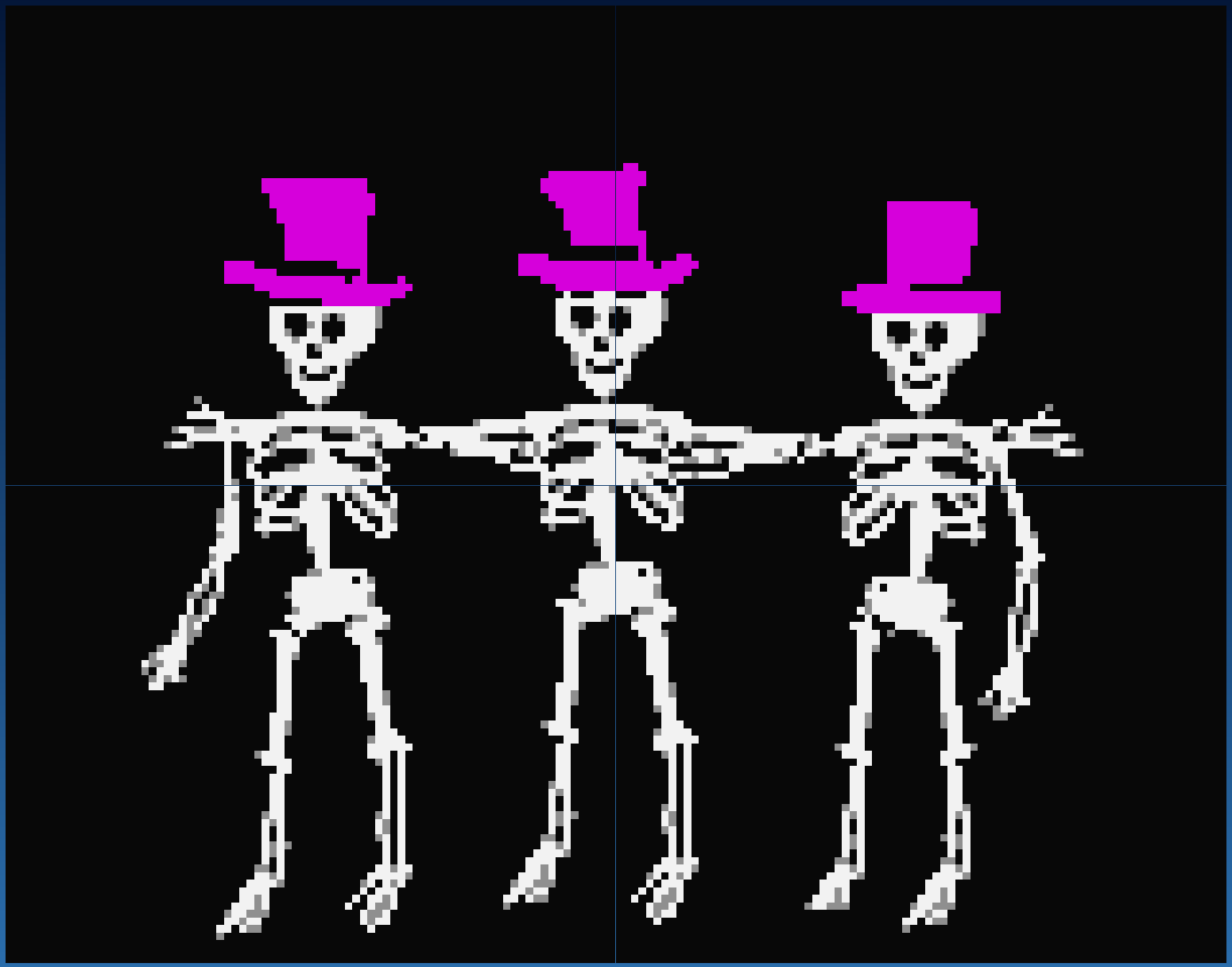
OMICS International is a pioneer and leading science event organizer, which publishes around 500 open access journals and conducts over 500 Medical, Clinical, Engineering, Life Sciences, Pharma scientific conferences all over the globe annually with the support of more than 1000 scientific associations and 30,000 editorial board members and 3.5 million followers to its credit.

OMICS Group has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

Identifying new targets to improve skeletal formation in human

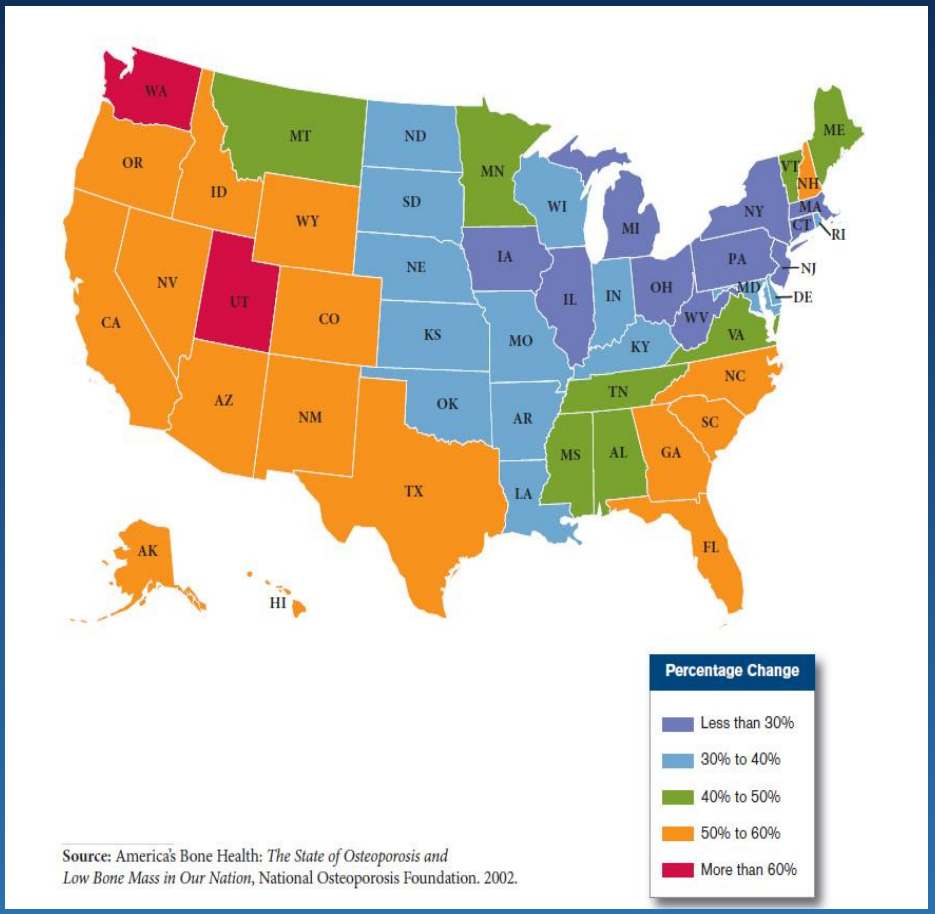
Anja Nohe, PhD,

University of Delaware



Facts about Osteoporosis

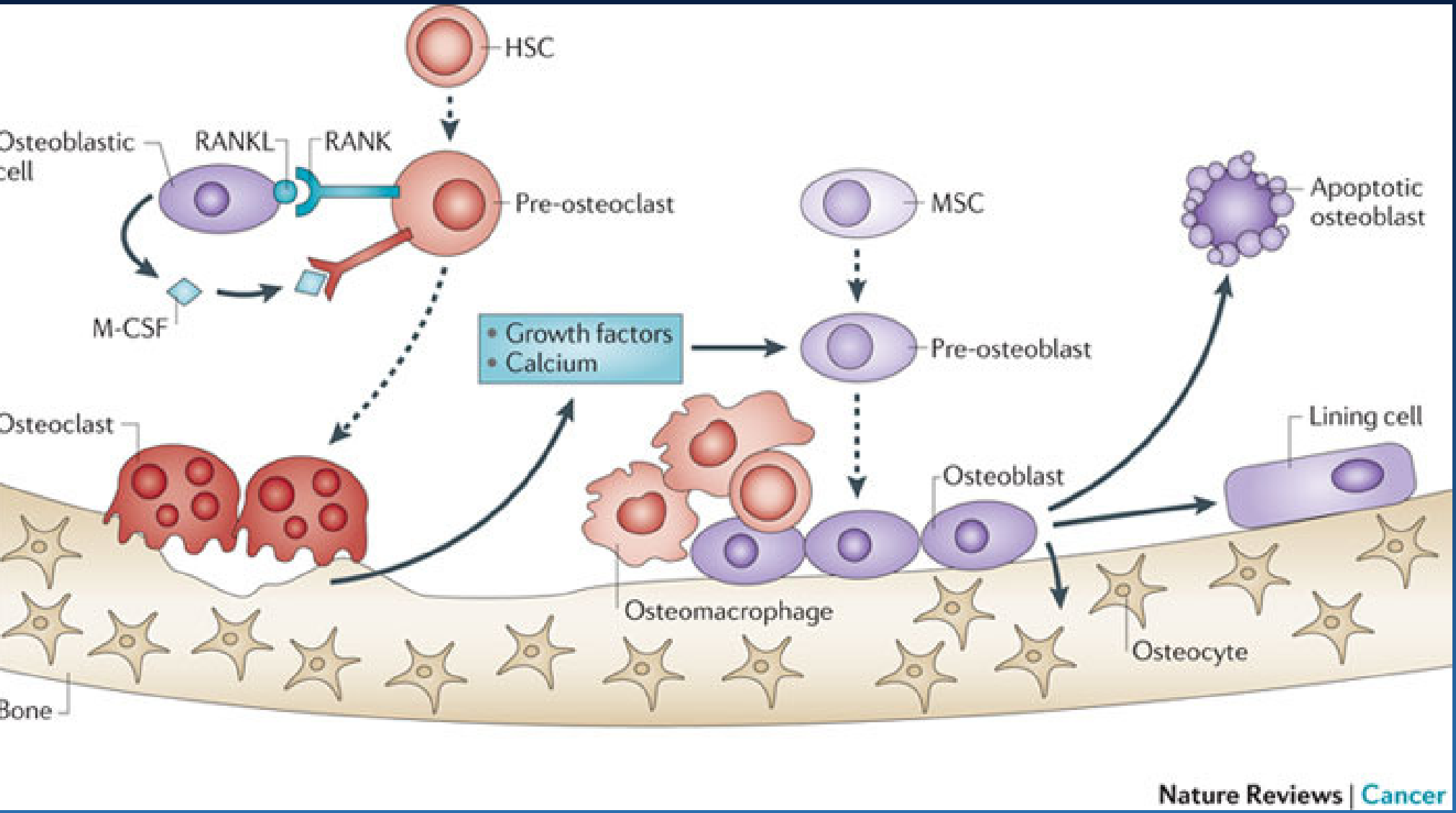
- Osteoporosis is a disease characterized by weak and porous bones with a low bone mass density (BMD) level. The World Health Organization defines osteoporosis as having a BMD at or below -2.5 on the BMD T-score test and having a fracture



Source: America's Bone Health: *The State of Osteoporosis and Low Bone Mass in Our Nation*, National Osteoporosis Foundation. 2002.

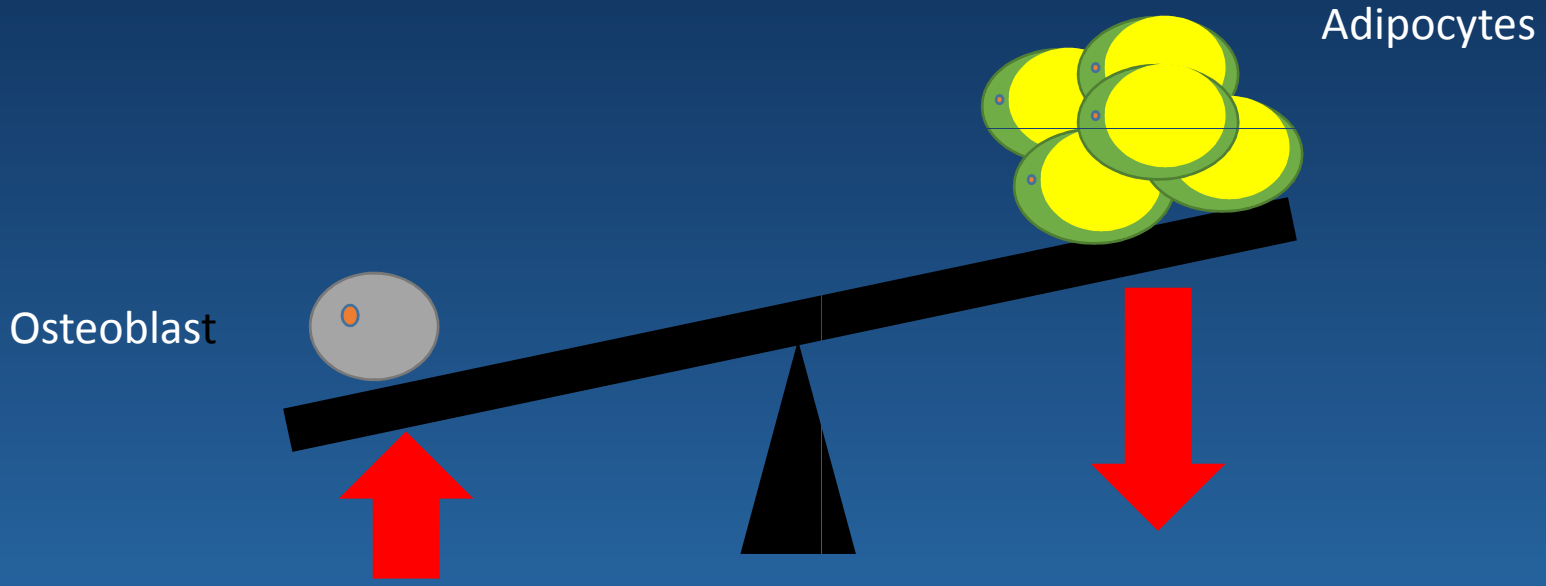
- One in two women and one in four men will be affected.
- Costs: above $18 billion in America and are expected to double by 2050.
- Most common fractures: hip and vertebrae.
- Hip fractures have a mortality rate between 12 and 20 percent after six months, and affect women more often than men by a ratio of nearly three to one. Hip fractures severely compromise a person's quality of life.
- 90 percent of adult bone mass is developed by age 18 in women and age 20 in men, meaning early years are critical for healthy bones.
- Only 35 percent of adults in America receive the daily recommended value of calcium

Bone Re-modelling

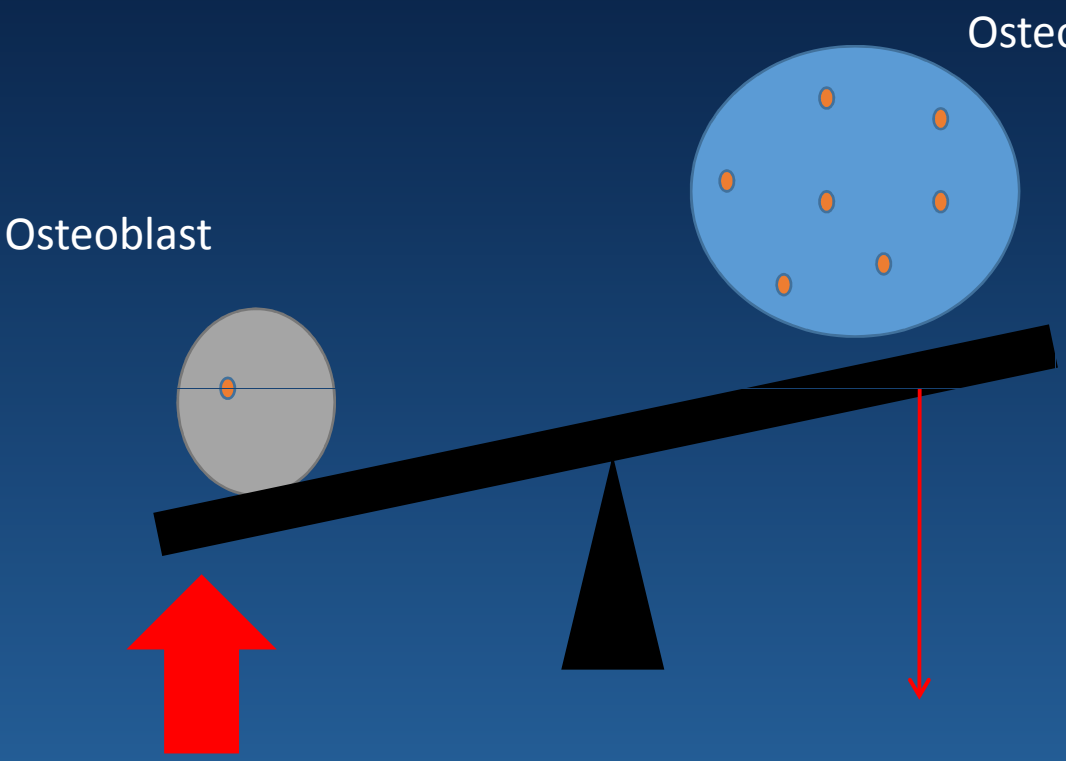


Nature Reviews Cancer. 2011 11, 411-425
Current Opinion in biotechnology 2012, 4, (2

Strategy: To Reduce Adipocytes Number and Increase Osteoblasts



Strategy: to Reduce Osteoclast Activity or Number and Increase Osteoblasts

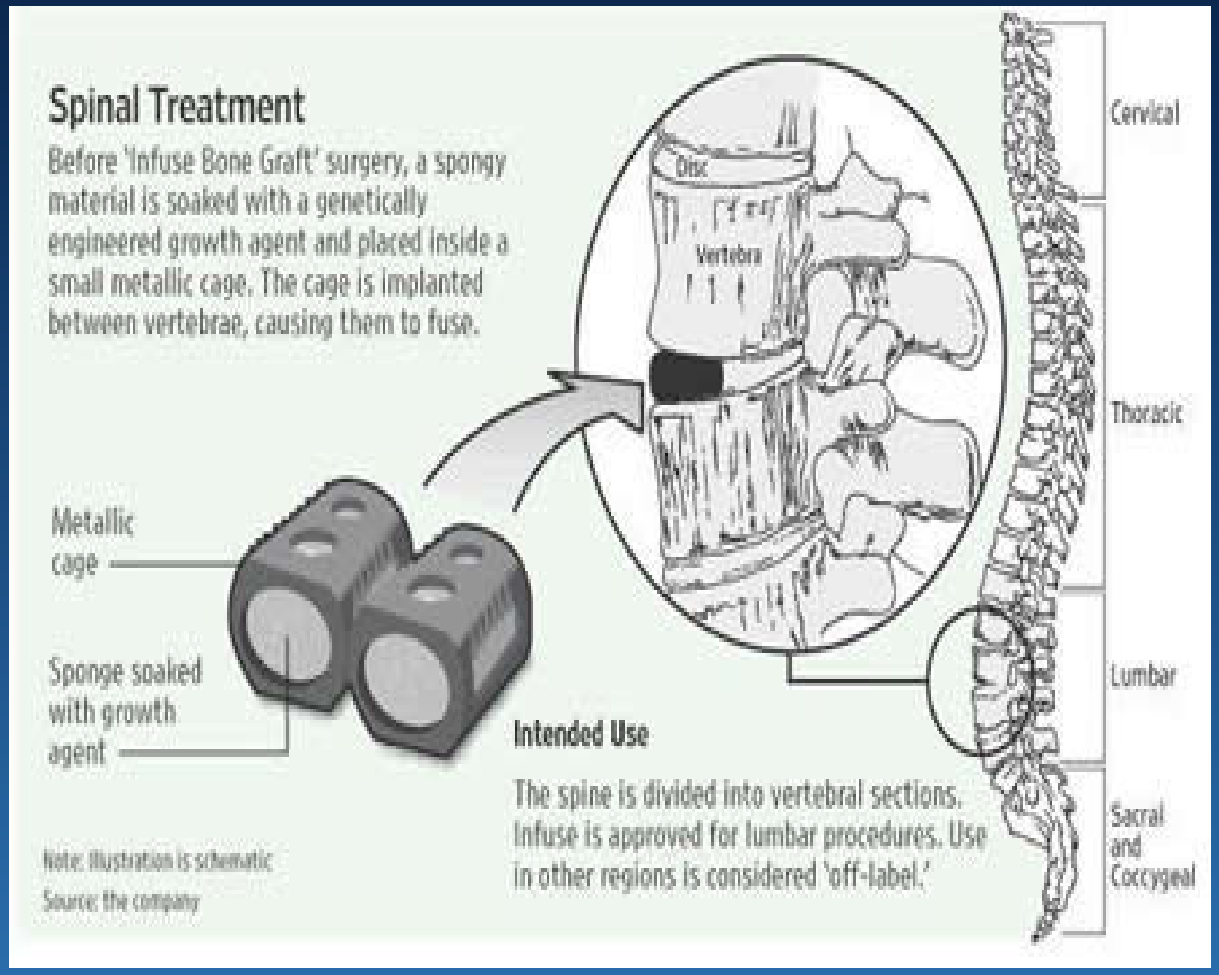


Drug	Advantage	Disadvar
Bisphosphonates	FDA approved, decrease fractures, administered orally	Affects only oste does not induce growth by osteo
Parathyroid Hormone (PTH)	Osteoanabolic – increase new bone, BMD, and decrease fractures	Administered th injections, poor compliance
Denosumab	Effects wide range of fracture sites	Increased poten side effects inclu eczema
SERM	Multiple non-FDA approved drugs in development that affects different fracture sites in late stage testing	Only one drug is approved - affec vertebral fractur
Cathepsin K Inhibitor	Effects multiple site and many in development	Affects osteocla possible serious skin effects
Sclerostin Inhibitor	Great promise in pre-clinical studies	Phase I trials ur development

Dose-Dependent Effect of Keratose-Delivered BMP-2 for Induction of Ectopic Bone in Mouse Leg Muscles.

Roche C. de Guzman et al., 2013. Biomaterials, 34, (6

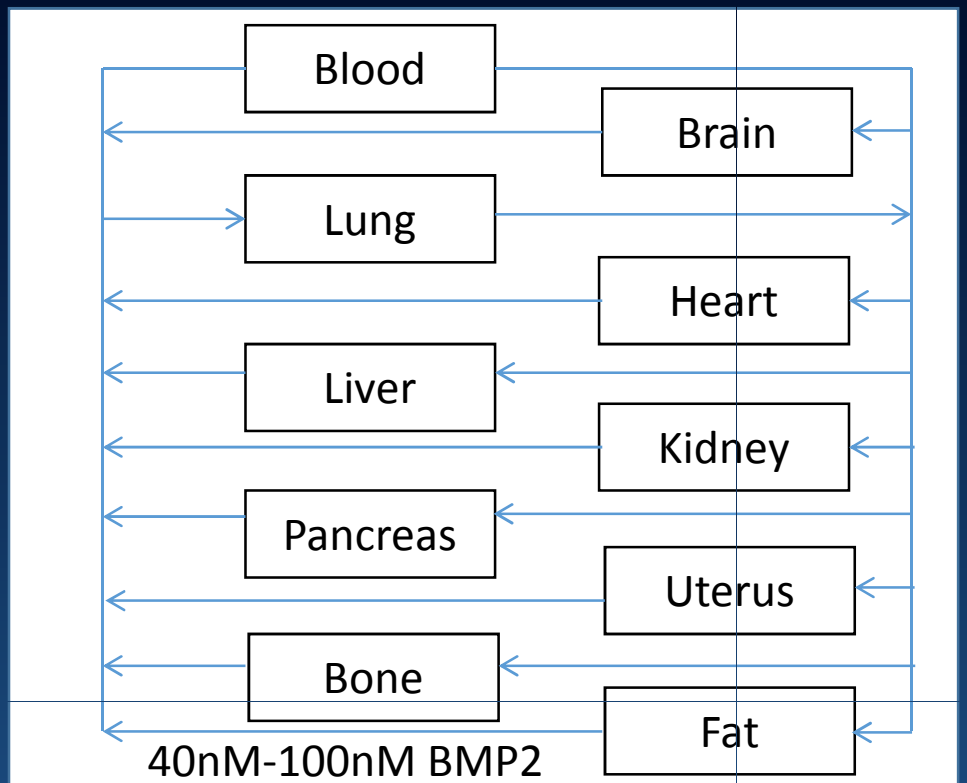
BMP2: The Bad: Example Infuse

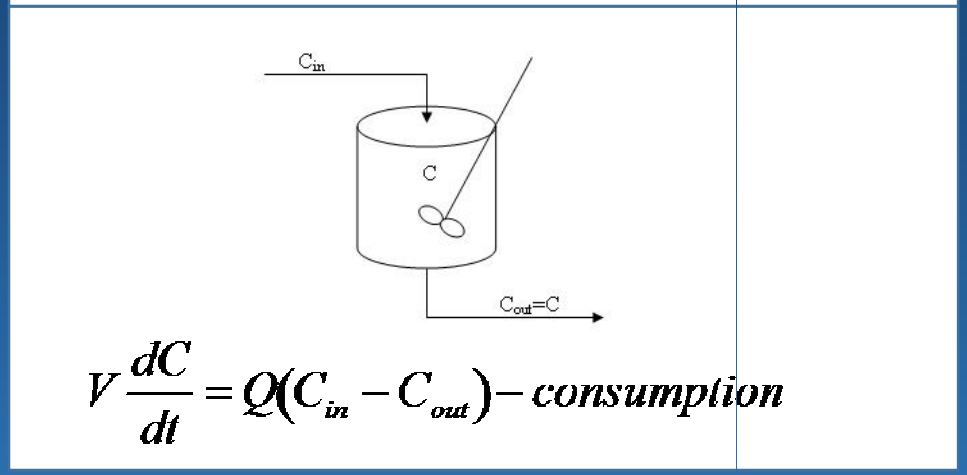


Side Effects
- Dysphagia
- Infection
- Nerve damage
- Retrograde ejaculation
- Male sterility
- Osteolysis
- Cancer risks

Medtronic's Infuse No Better Than Bo Graft With Risk

PBPK Modelling of the Distribution of BMP2





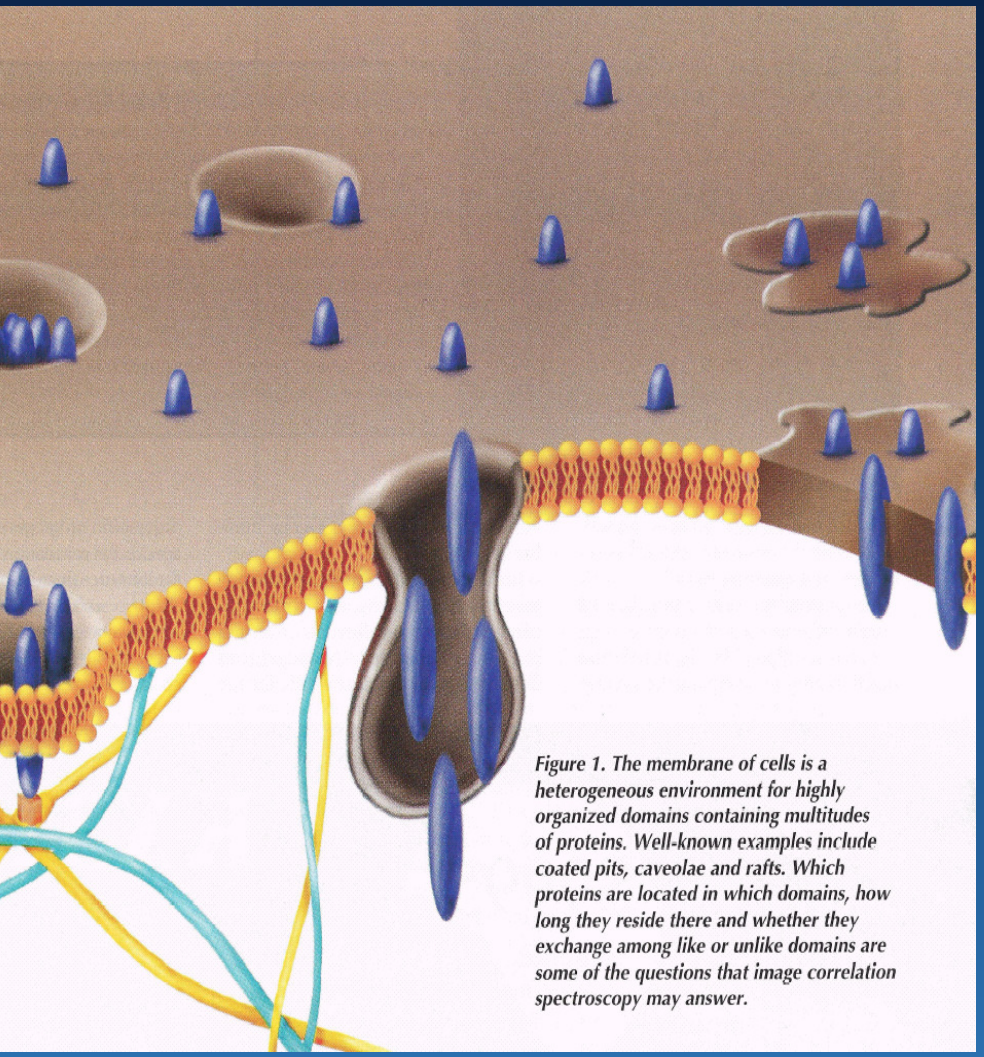
BMP2	Normalized	Conc. (mol/L)	Sou
Brain	9.266	3.94E-06	Wu
Lung	2.718	1.15E-06	Ex
Heart	0.974	4.14E-07	Ex
Liver	2.891	1.23E-06	Ex
Pancreas	0.647	2.75E-07	Wu
Kidney	1.000	4.25E-07	Ex
Bone	5.855	2.49E-06	Wu
Fat	0.900	3.82E-07	Wu
Uterus	2.200	9.34E-07	Wu
Blood	9.429	3.88E-09	Wu

	Receptor Expression		R_i	
	Relative	Normalized	Conc. (mol/L)	
Brain	688.14	4.6524	3.85E-08	V
Lung	160.16	1.0828	8.96E-09	V
Heart	273.47	1.8489	1.53E-08	V
Liver	147.91	1.0000	8.28E-09	V
Pancreas	64.95	0.4391	3.63E-09	V
Kidney	156.07	1.0552	8.73E-09	V
Bone	24.85	0.1680	1.39E-09	V
Fat	272.33	1.8412	1.52E-08	V
Uterus	213.82	1.4456	1.20E-08	V
Blood	110.24	0.7453	6.17E-09	V

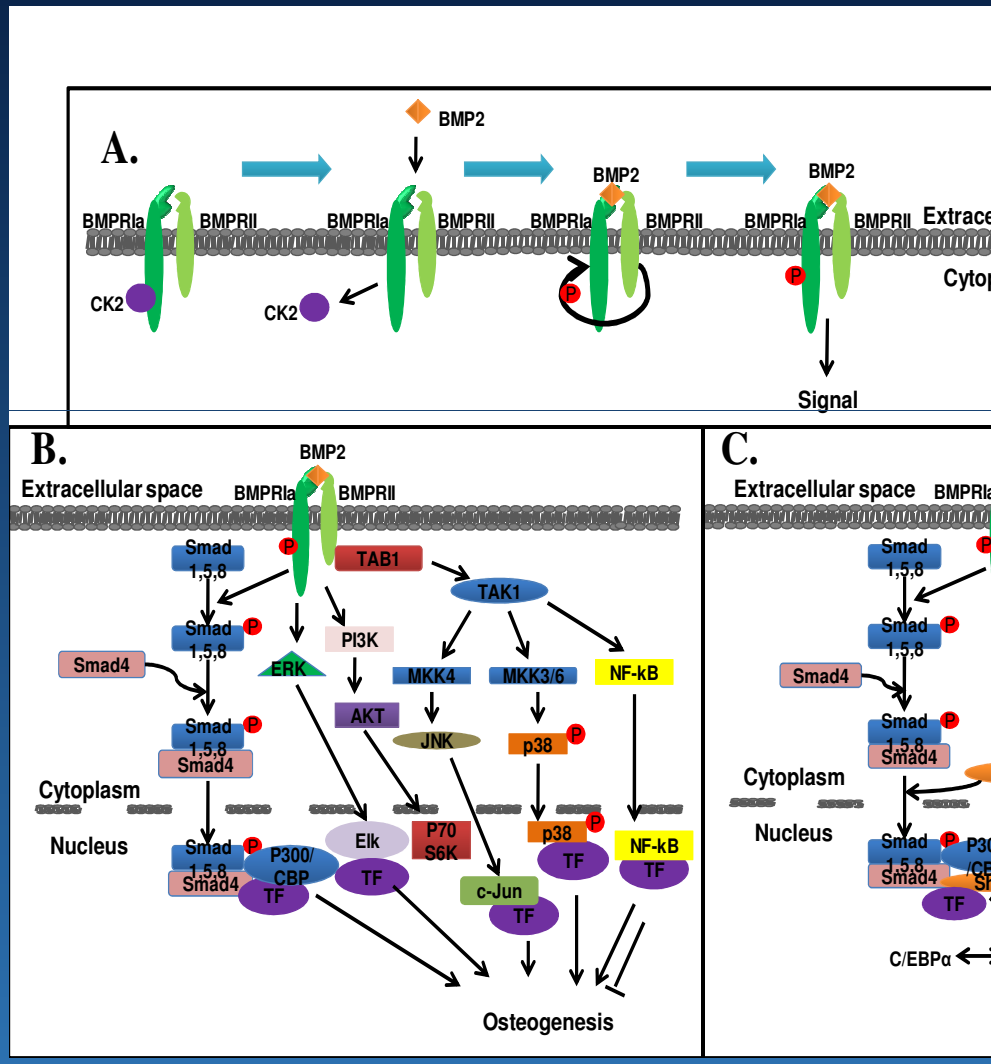
Organ	Protein Turnove
Brain	5.05E-05
Lung	1.41E-06
Heart	6.20E-06
Liver	1.10E-05
Pancreas	1.37E-06
Kidney	1.23E-06
Bone	7.27E-06
Fat (Brown)	9.32E-06
Uterus	2.22E-06
Blood	2.85E-08

Utturkar A, Paul B, Akkiraju H, Bonor J, Dhurjati P, et al. (2013) Development of Physiologically Based Pharmacokinetic Model (PBPK) of BMP2 in Mice. Biol Syst 2: 123. doi:10.4172/2329-6577.1000123

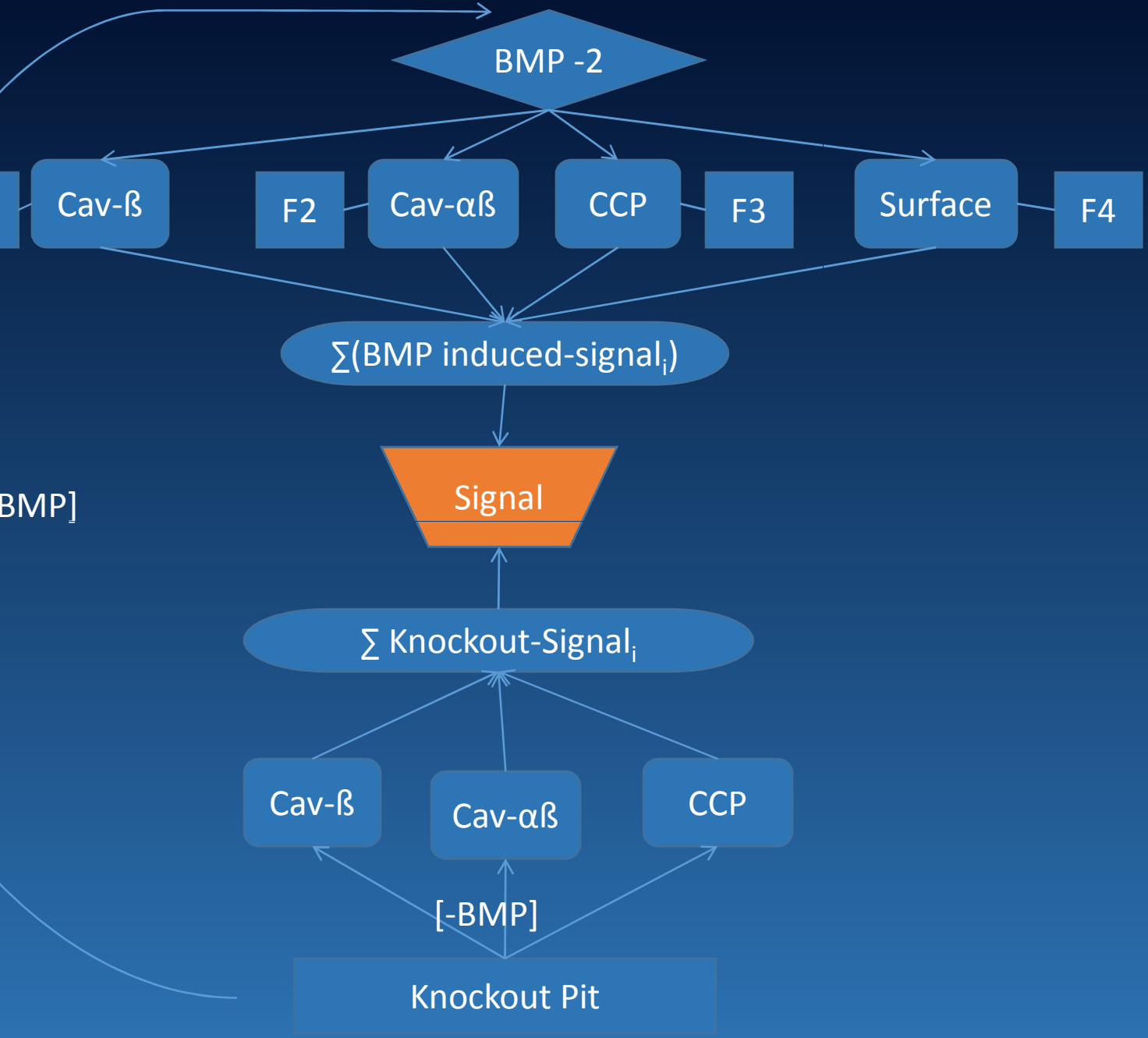
Multiple effects on BMP2 on cells. Why?



Nohe A. and Petersen NO. Biophotonics 2002, **9**:39-52.



Moseychuck et al



S. Saldanha, et al.,(2013). *Journal of Cellular Physiology*, **228** (5): 1

	Co-localized with	-BMP	+BMP
BRIa	CCP	45	66
	cav-αß	12	25
	cav-ß	12	8
	other	31	0
BRII	CCP	75	76
	cav-αß	11	19
	cav-ß	13	5
	other	1	0
CCP	BRIa	31	40
	BRII	44	52
	other	25	8
CAV-ß	BRIa	8	0
	BRII	6	4
	other	87	96
CAV-αß	BRIa	20	30
	BRII	14	16
	other	66	54

	CCP	caveolae
BRIa	3.35	1.79
BRII	4.67	1.50

Cluster Density	-BMP	+BMP
BRIa	7.45	4.71
BRII	6.23	2.66
cav-ß	2.65	0.90
cav-αß	7.82	12.2
CCP	14.2	14.2

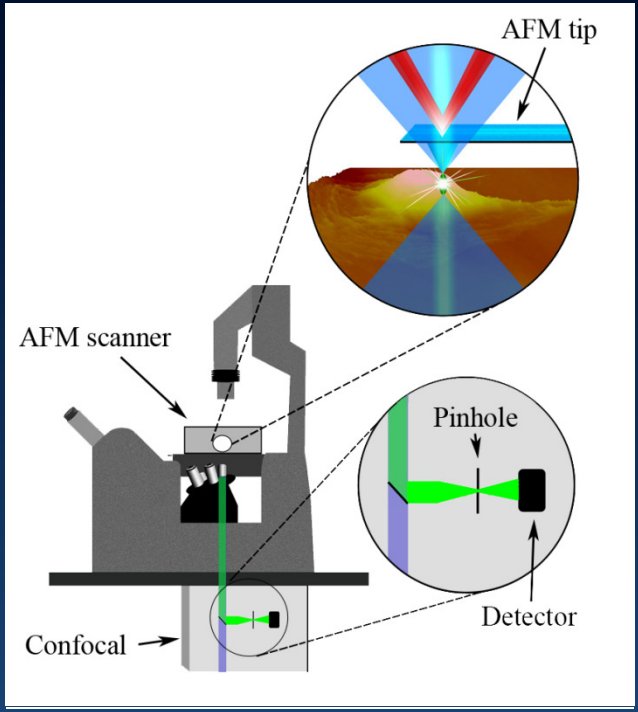
SMAD signal	-BMP	+BMP
No disruption	0	1.3
CCP	1.7	2.7
CAV	1.4	0.8
CAV+CCP	3.1	2.8

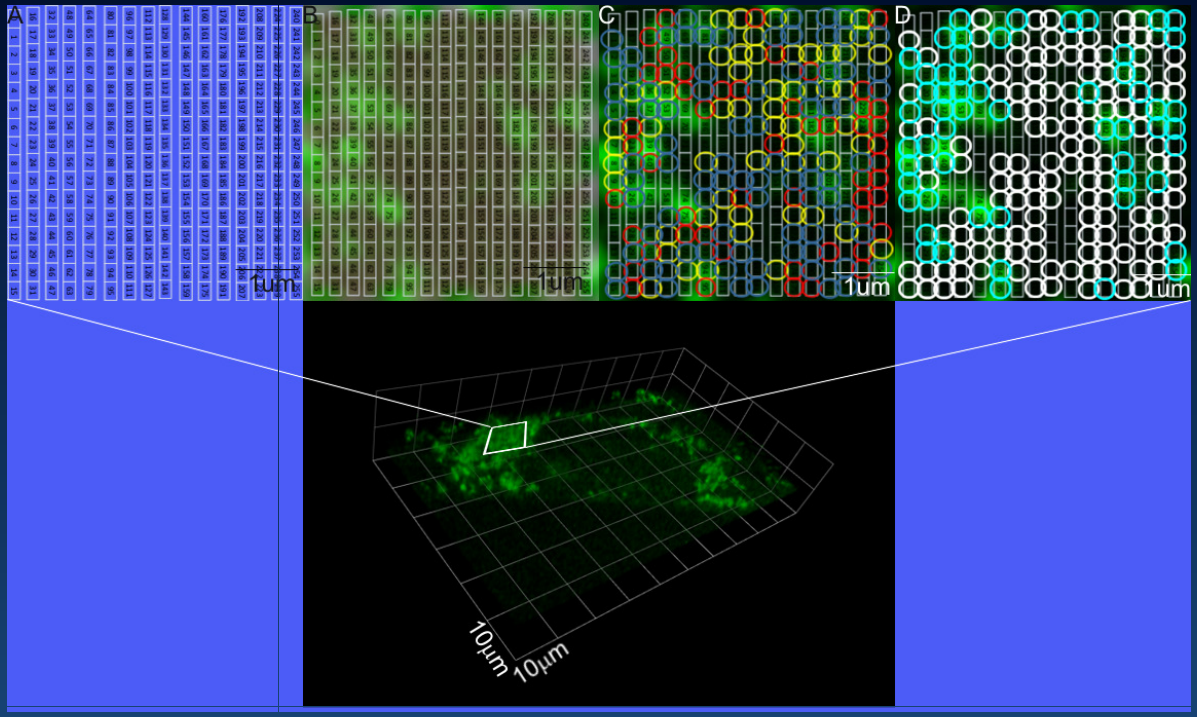
Distribution of BMP Receptors in Membrane Domains

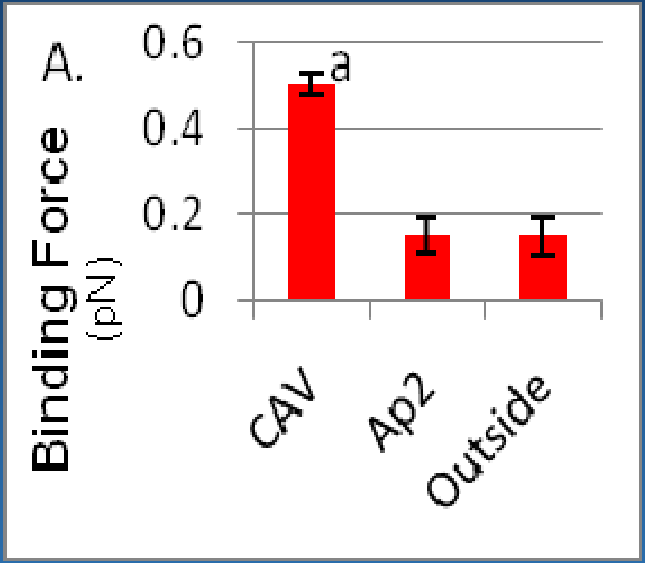
	Value	% contribution
A_{ccp}	4.1504	35.10
A_{cav}	7.6737	64.90
$A_{cav-\alpha ß}$	101.6842	
$A_{cav-ß}$	-25.5712	

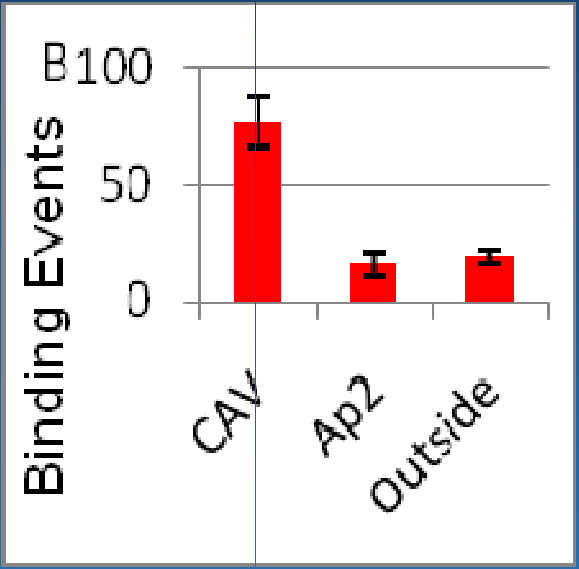
$$[SMAD\ Signal] = [Ks_{tot}] = [Ks_{cav+ccp}] = A_{CCP}\frac{([BRIa])_{CCP}}{C.D._{CCP}}[Ks_{CCP}] + \left\{A_{cav-\alpha ß}\frac{([BRII])_{cav-\alpha ß}}{C.D._{cav-\alpha ß}} + A_{cav-ß}\frac{([BRII])_{cav-ß}}{C.D._{cav-ß}}\right\}[Ks_{cav}]$$

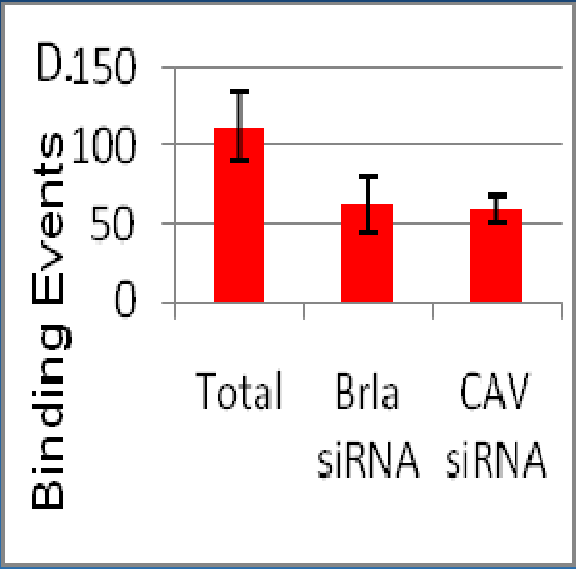
S. Saldanha, et al.,(2013). *Journal of Cellular Physiology*, **228** (5): 1





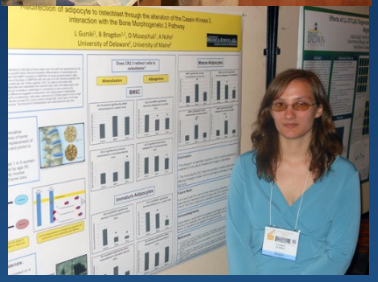


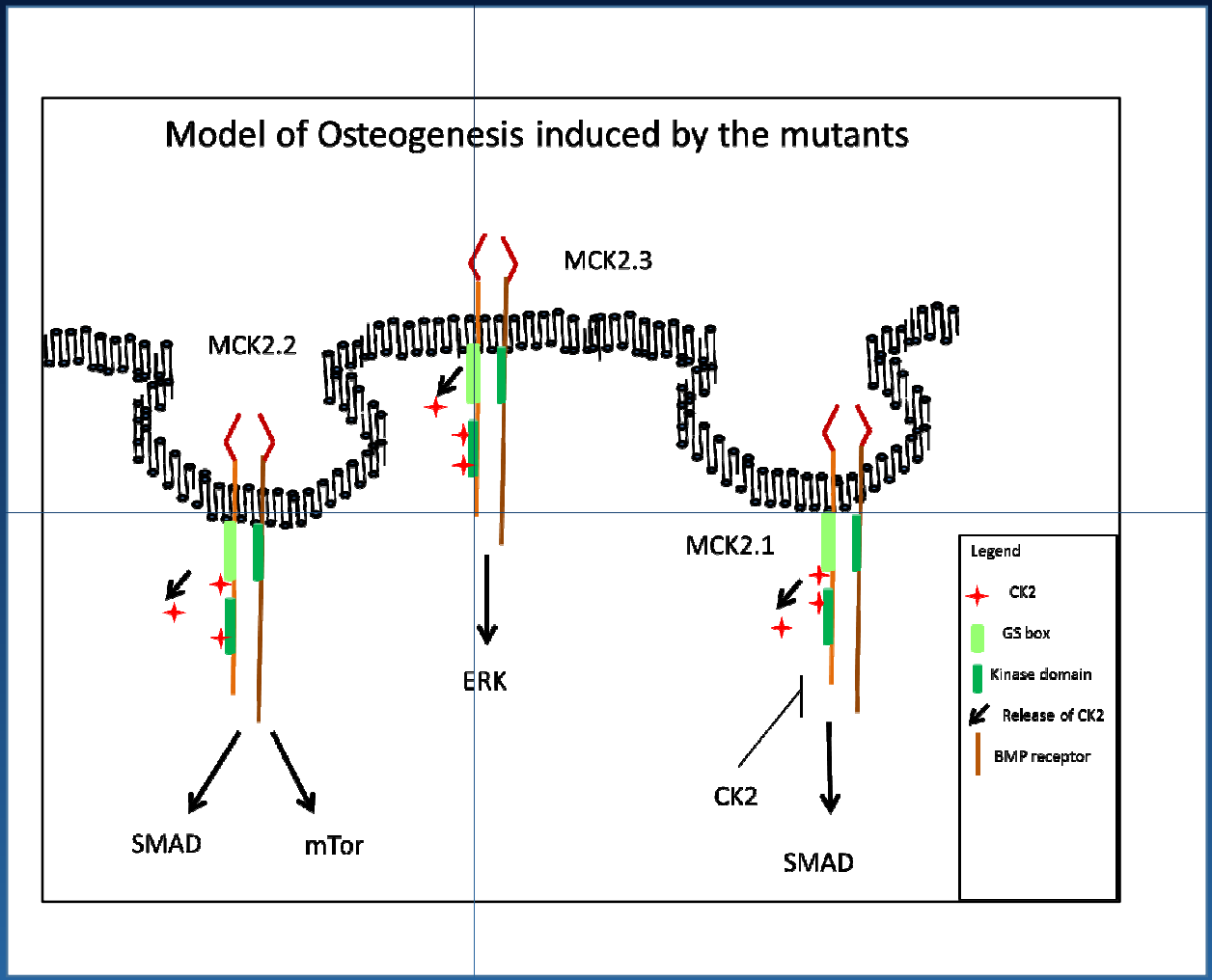




J. Bonor, E. L. Adams, B. Bragdon, O. Moseychuk, K. J. Czymmek, and A. Nohe. *J Cell Physiol*. 2012 Jul;227(7):2880-8. doi: 10.1002/*JCP*23032

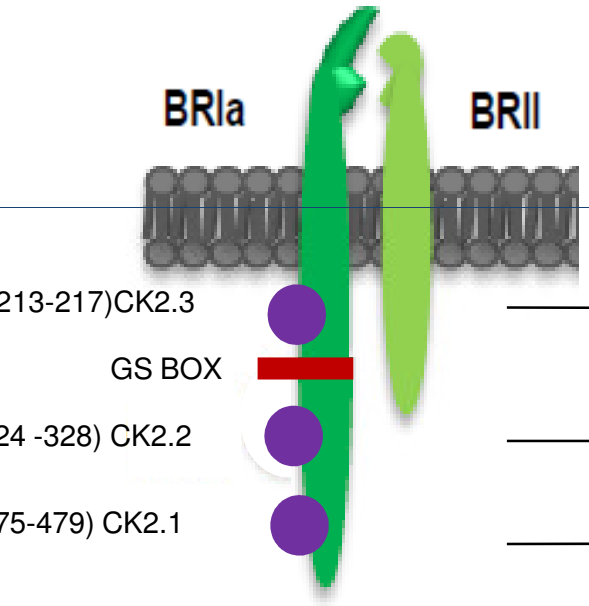
BMP2 Signaling Pathway





Bragdon B, et al. Biophysical Jou
Bragdon et al., Bone, 2011
Moseychuck et al., JCCS, 2013
Akkiraju et al., in preparation

CK2 is a Key Switch of BMP2 Dependent Stem Cel Differentiation



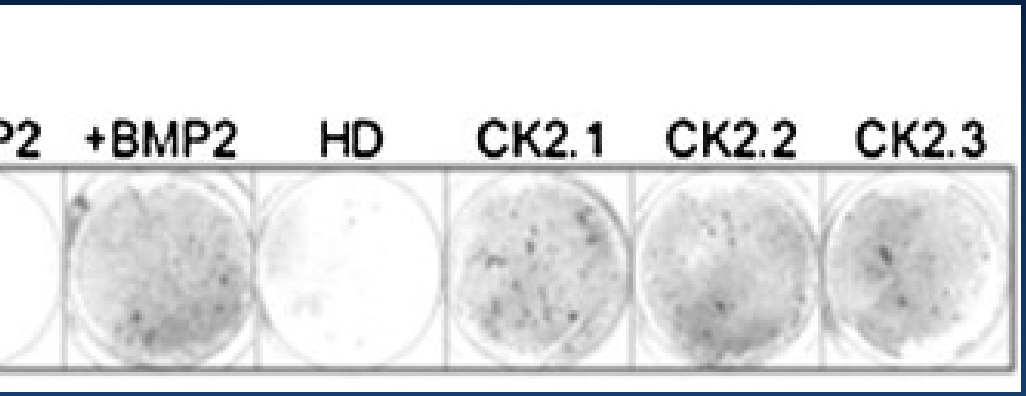
Osteogenesis (Smad and Caveolin-1 independent, MEK depen

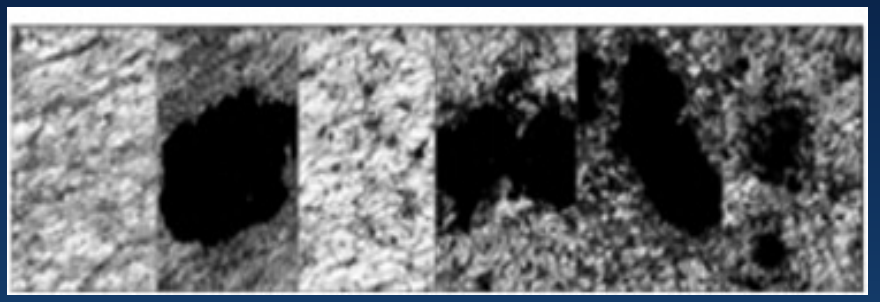
Osteogenesis/Adipogenesis (Smad, Caveolin-1 mTOR/MEK)

Osteogenesis/Chondrogenesis (Smad, Caveolin-1/?, MEK/?)

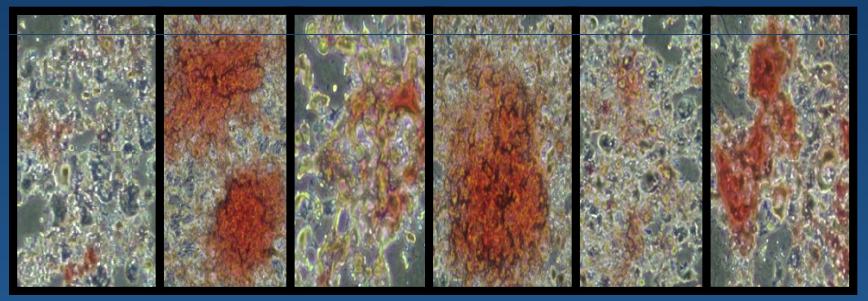
Bragdon B, et al. Biophysical J
Bragdon et al., Bone, 2011
Moseychuck et al., JCCS, 2013
Akkiraju et al., in preparation

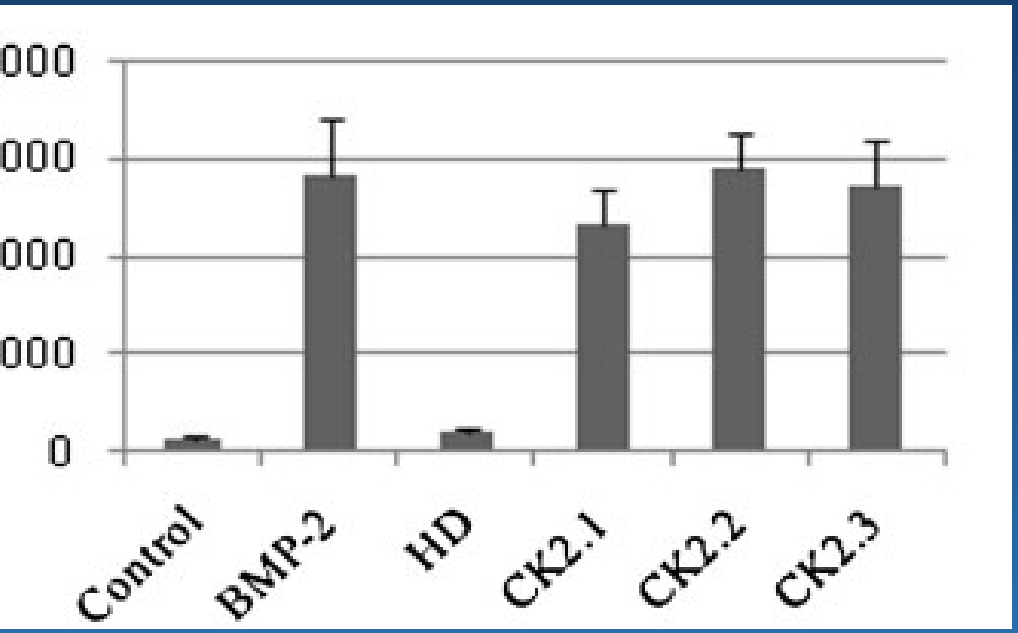
Loss of CK2 interaction with BRIa regulates osteogenesis and adipogenesis





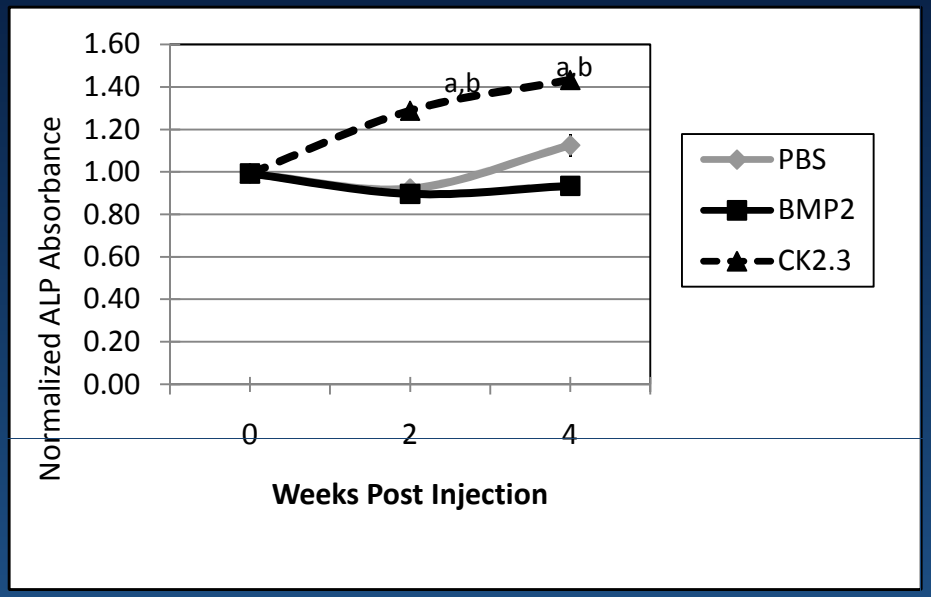
- BMP2 +BMP2 HD CK2.2 CK2.3 CK2.1

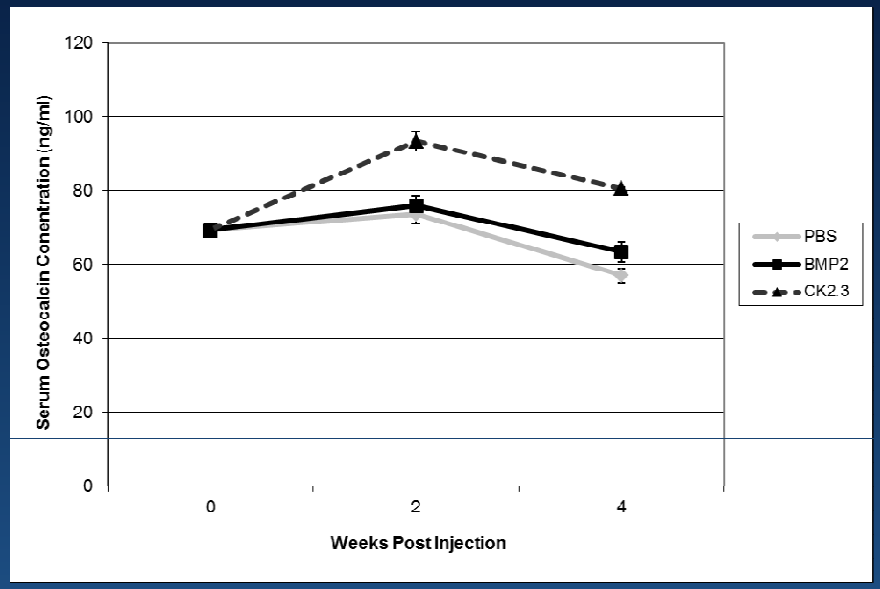


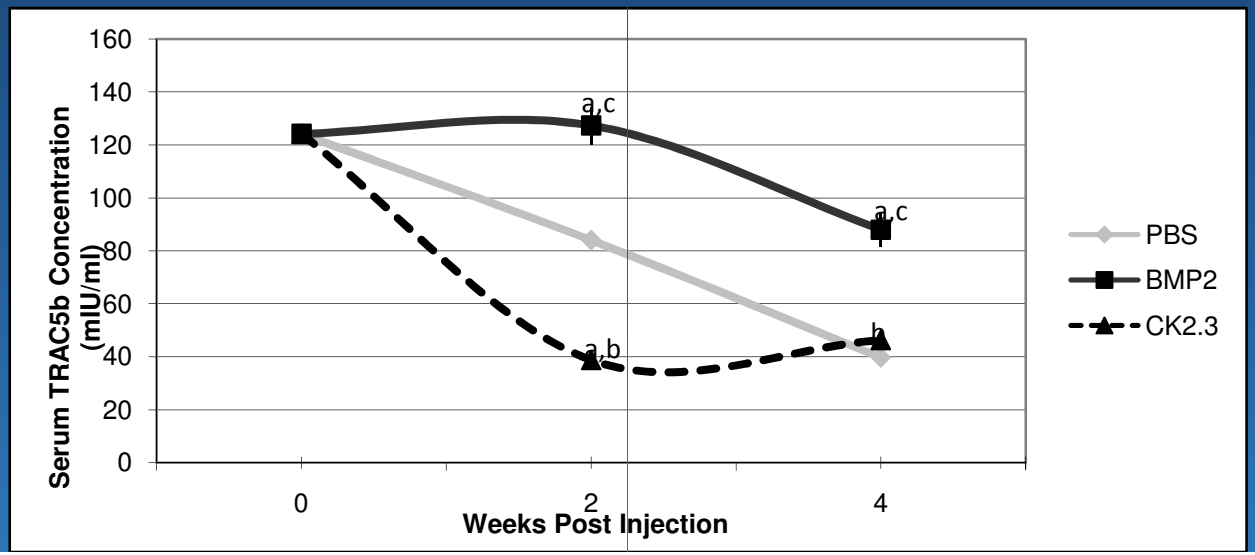


Bragdon B, et al. Biophysical
Moseychuck et al., JCCS, 201

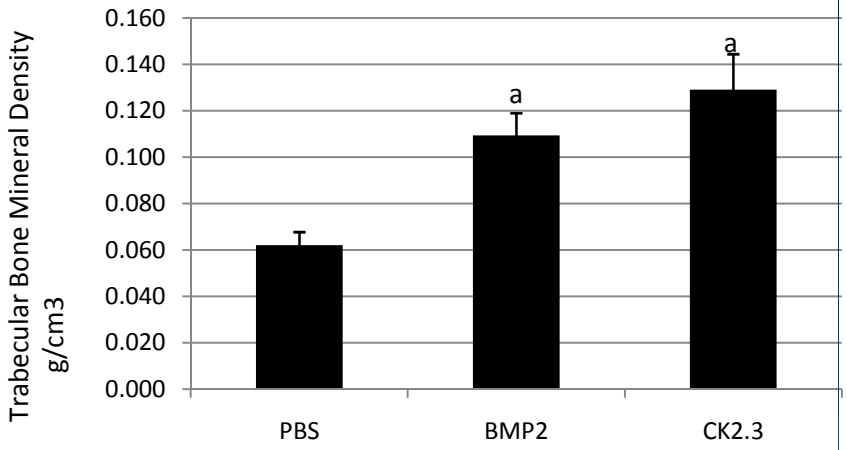
Serum Markers for Osteoblast Differentiation are Increased and Decreased for Osteoclast Activity

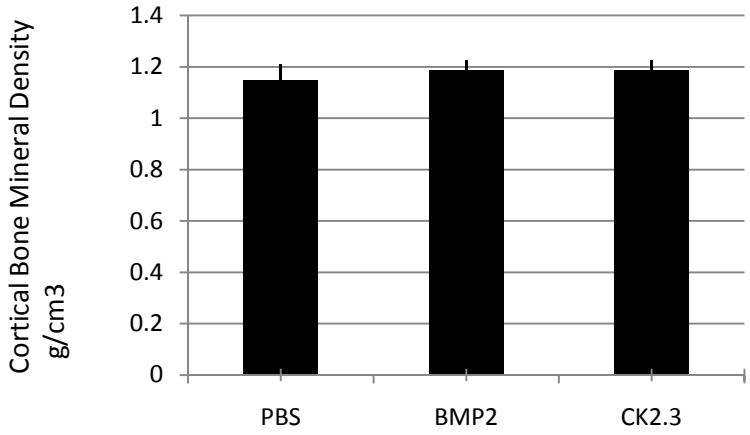


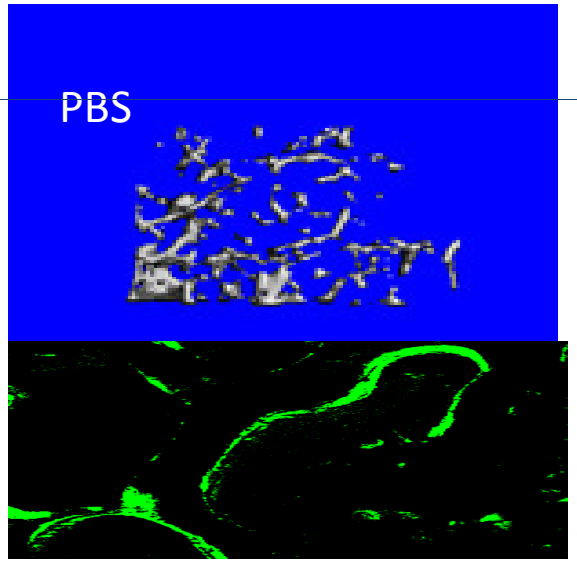


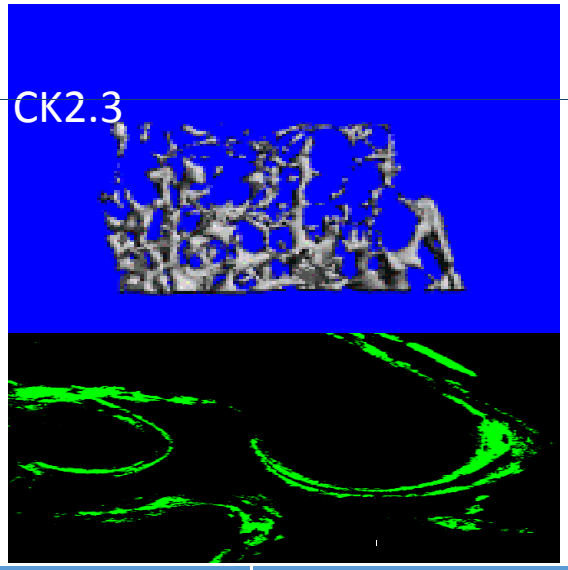


Trabecular Bone Mineral Density is Increased



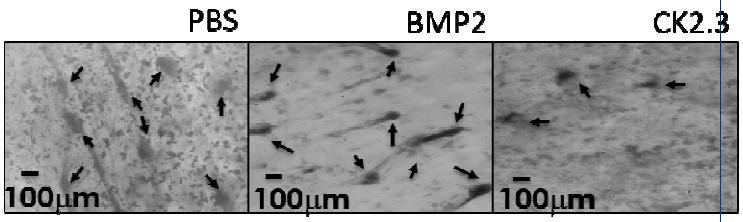


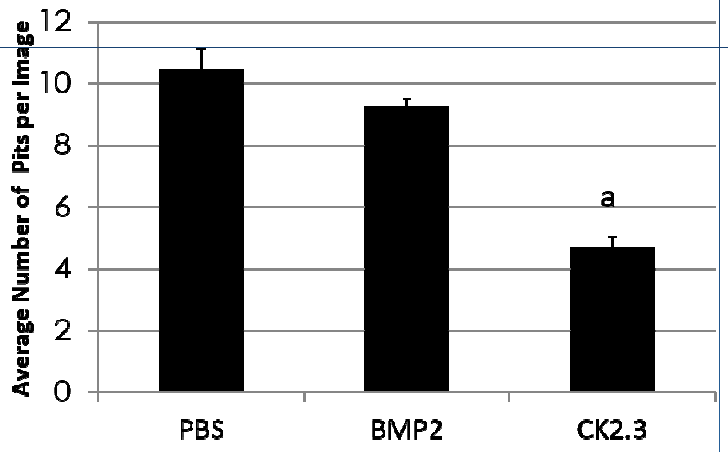


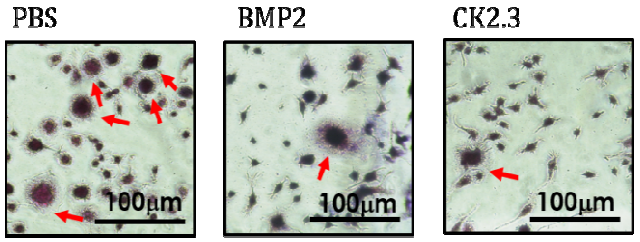


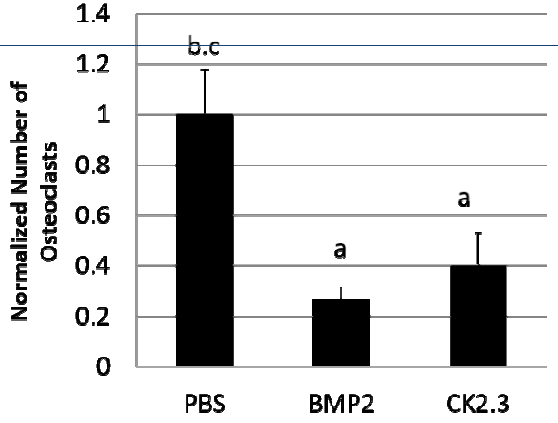
	BV/TV in %	TB.N (1/mm)	Tb.Th (mm)	Tb.Sp (mm)	MAR mm/day
PBS	23.3+/- 3.8	2.67+/-0.16	0.042+/-0.004	0.38+/-0.026	0.6+/-0.3
CK2.3	38.9+/-0.35*	3.19+/-0.13*	0.048+/-0.003	0.32+/-0.010*	2.2+/-0.3

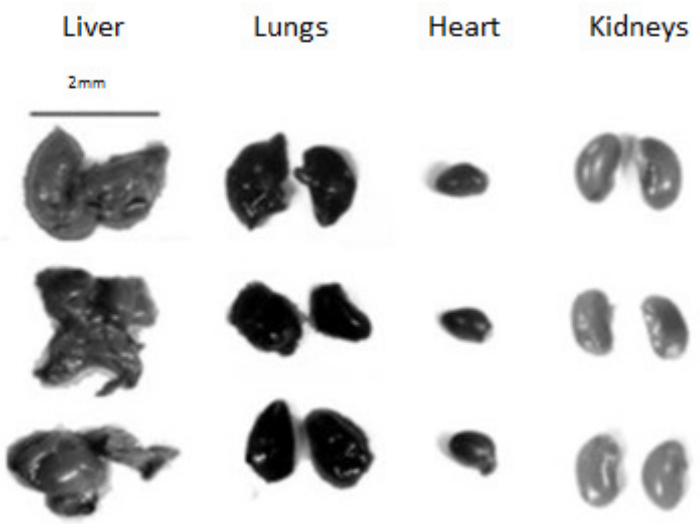
Osteoclast Number and Activity is Decreased in Mice Injected with CK2.3

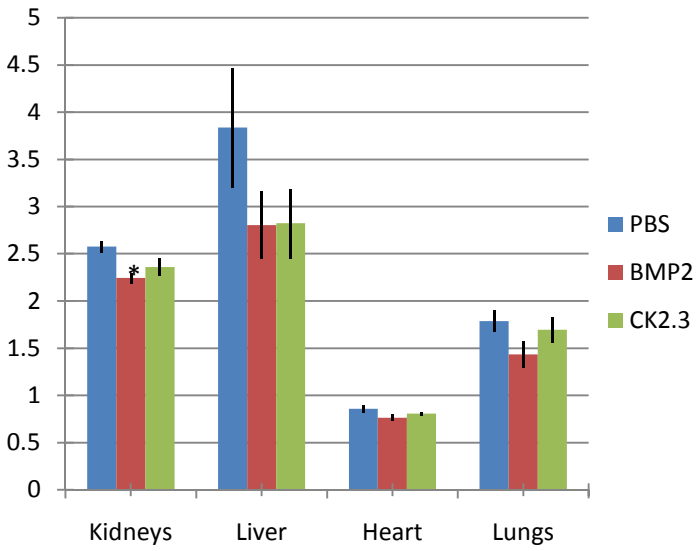






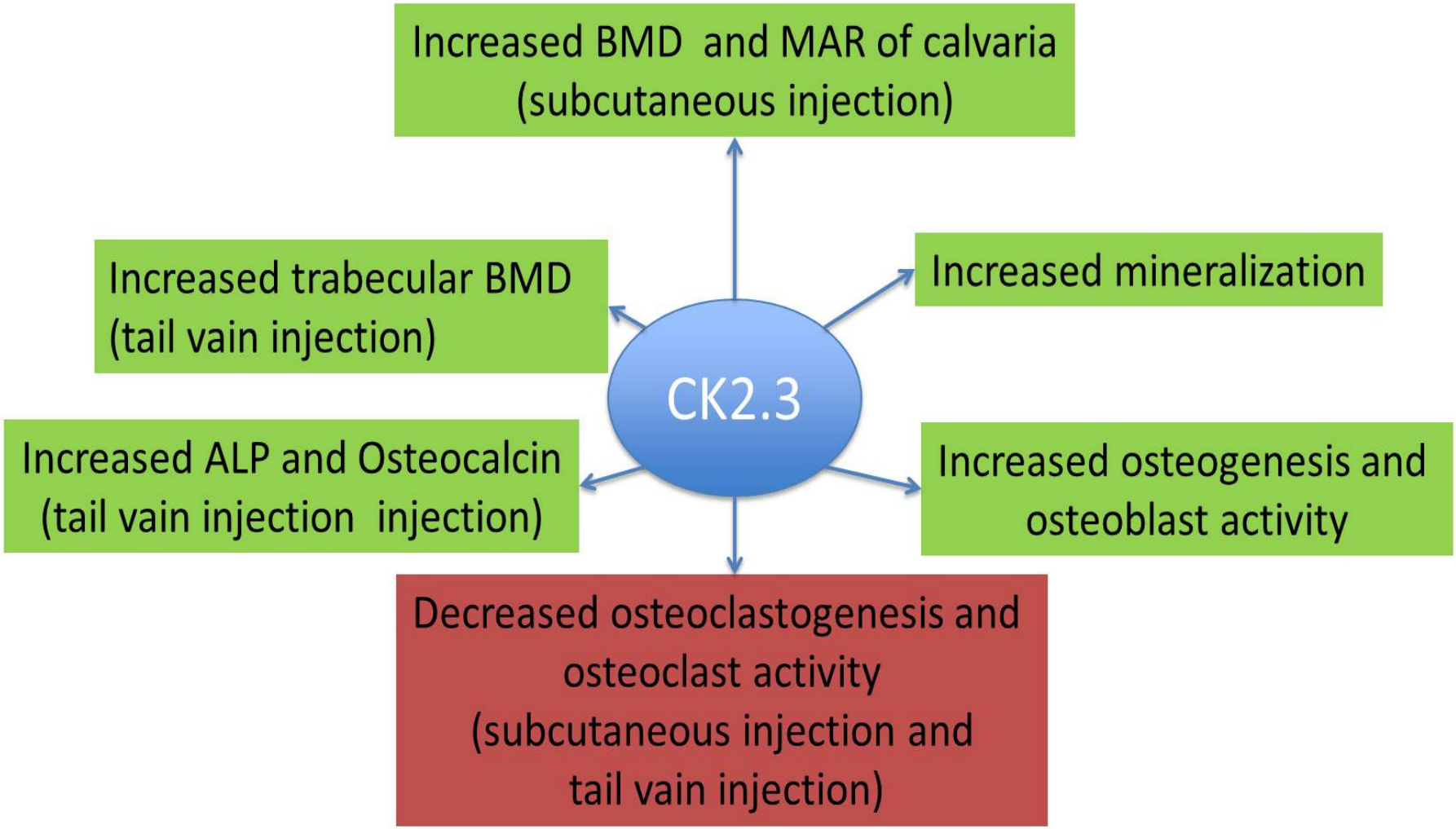






	PBS	BMP-2	CK2.3	Mean Rang
Chol (mg/dl)	107	103	98	55-1
TRG (mg/dl)	108	133	116	75-2
ALT (u/l)	30	30	28	27-1
AST (u/l)	80	105	98	43-3
ALK (u/l)	117	101	94	44-2
GLU (mg/dl)	162	180	167	93.7-219
PHOS (mg/dl)	7.7	6.4	5.9	4.5-7
TRP (g/dl)	5.9	5.4	5.8	4.8-7
CAL (mg/dl)	9.1	9.3	9.2	8.5-9
BUN (mg/dl)	21	25	19	5-
CRE (mg/dl)	0.2	0.3	0.2	0.2-0
ALB (g/dl)	3.4	3.6	3.6	2.4-4

Proven Biological Functions of CK2.3

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