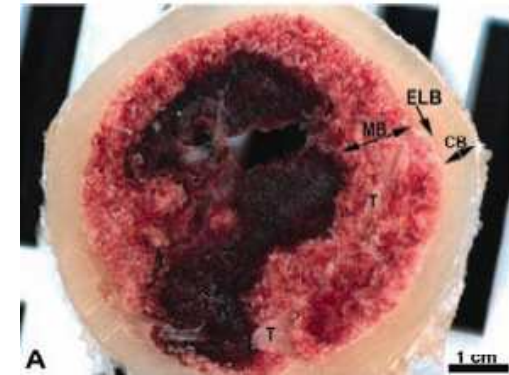
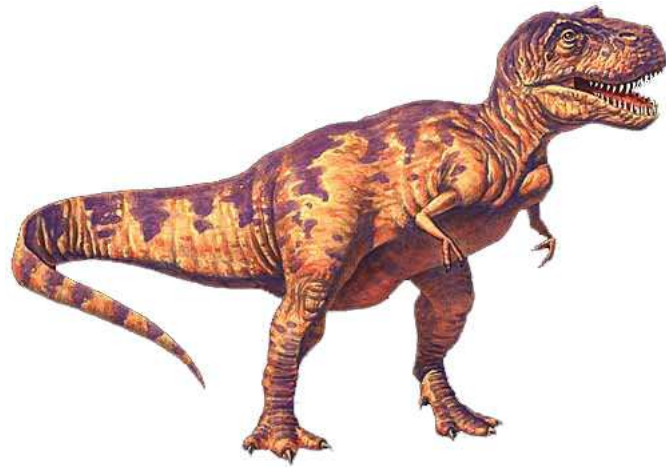


REPORTS

# Gender-Specific Reproductive Tissue in Ratites and *Tyrannosaurus rex*

Mary H. Schweitzer,<sup>1,2,3\*</sup> Jennifer L. Wittmeyer,<sup>1</sup> John R. Horner<sup>3</sup>

Unambiguous indicators of gender in dinosaurs are usually lost during fossilization, along with other aspects of soft tissue anatomy. We report the presence of endosteally derived bone tissues lining the interior marrow cavities of portions of *Tyrannosaurus rex* (Museum of the Rockies specimen number 1125) hindlimb elements, and we hypothesize that these tissues are homologous to specialized avian tissues known as medullary bone. Because medullary bone is unique to female birds, its discovery in extinct dinosaurs solidifies the link between dinosaurs and birds, suggests similar reproductive strategies, and provides an objective means of gender differentiation in dinosaurs.



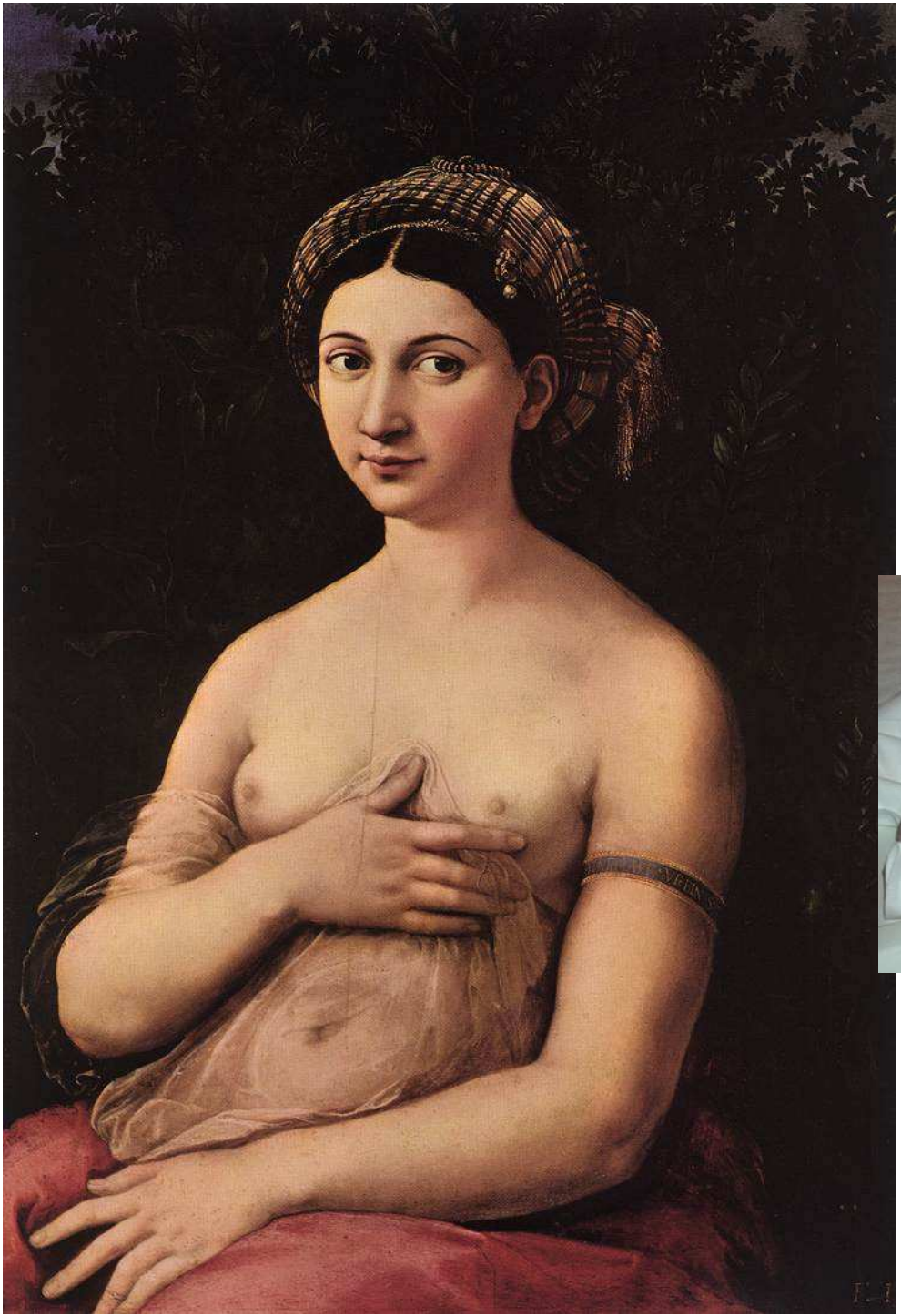
REPORTS

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Science 3 June 2005 Vol. 308. no. 5727, pp. 1456 - 1460



## On mammary stem cells

Wendy A. Woodward<sup>1,\*</sup>, Mercy S. Chen<sup>2,\*</sup>, Fariba Behbod<sup>2</sup> and Jeffrey M. Rosen<sup>2,†</sup>

<sup>1</sup>Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX 77030-3498, USA

<sup>2</sup>Department of Molecular and Cellular Biology, Baylor College of Medicine, One Baylor Place, M638a DeBakey, Houston, TX 77030, USA

\*These authors contributed equally to this work

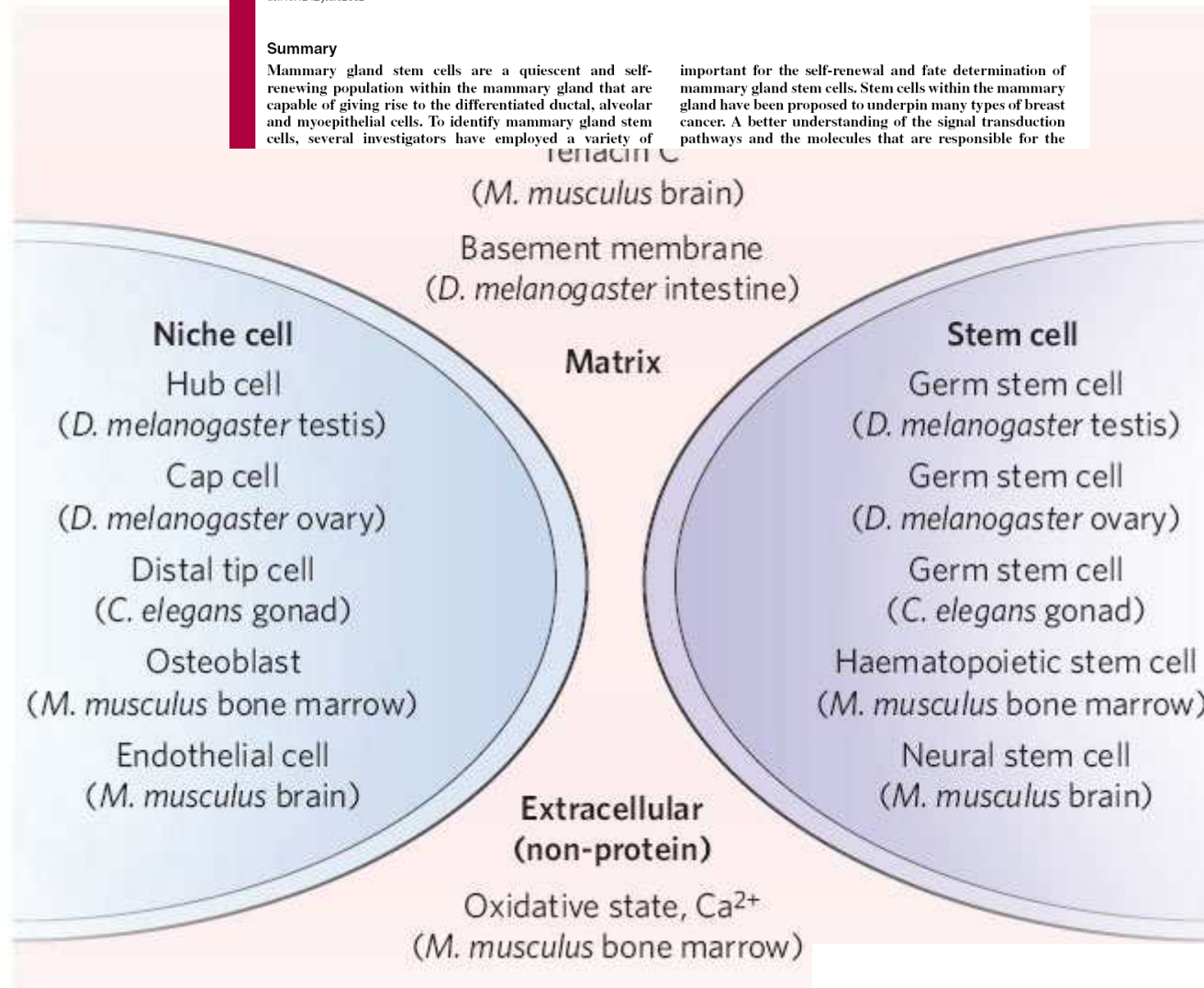
†Author for correspondence (e-mail: jrosen@bcm.edu)

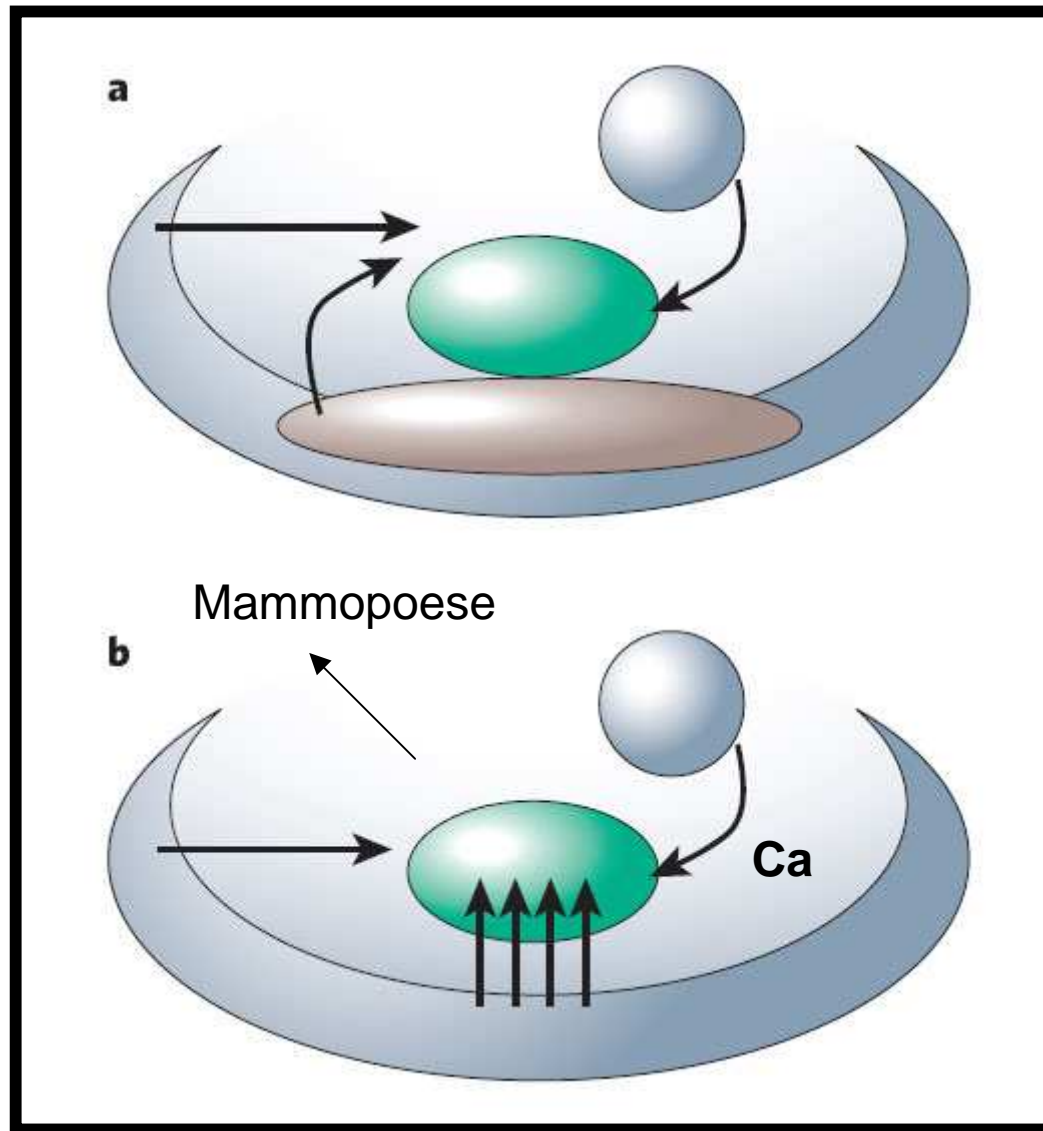
*Journal of Cell Science* 118, 3585-3594 Published by The Company of Biologists 2005  
doi:10.1242/jcs.02532

### Summary

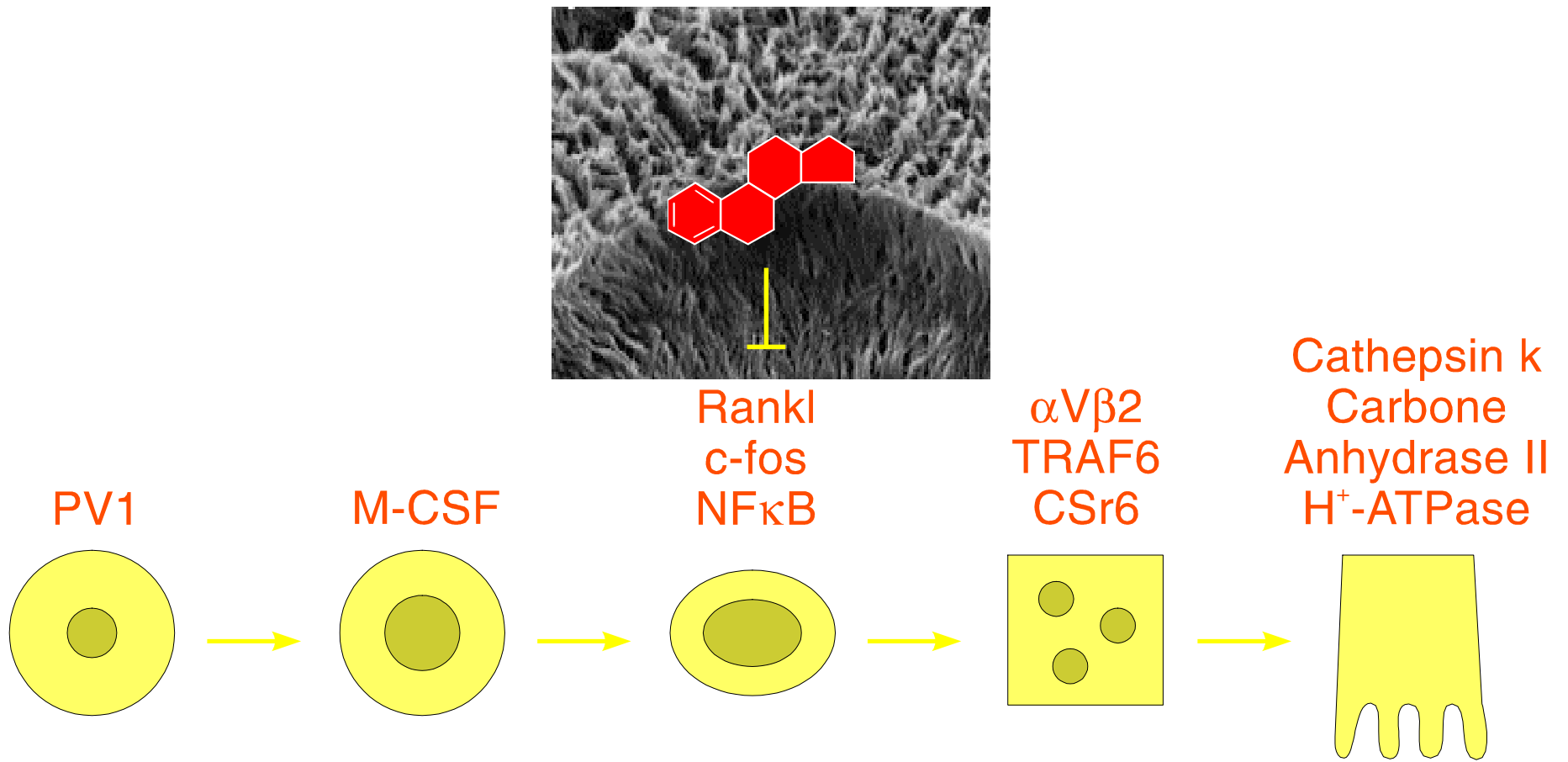
Mammary gland stem cells are a quiescent and self-renewing population within the mammary gland that are capable of giving rise to the differentiated ductal, alveolar and myoepithelial cells. To identify mammary gland stem cells, several investigators have employed a variety of

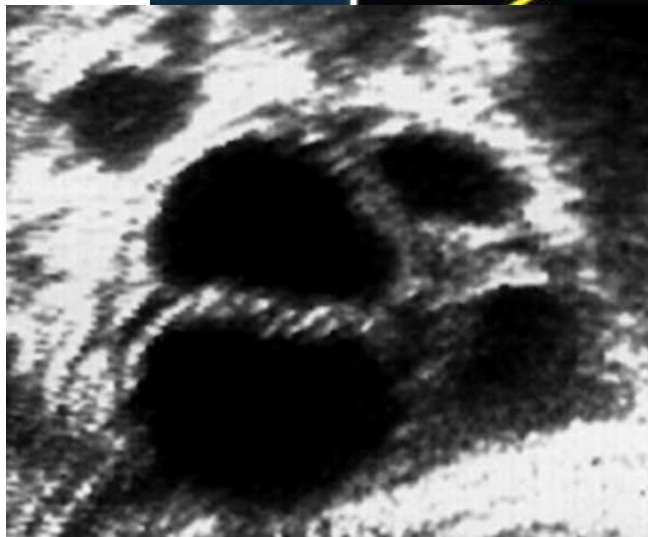
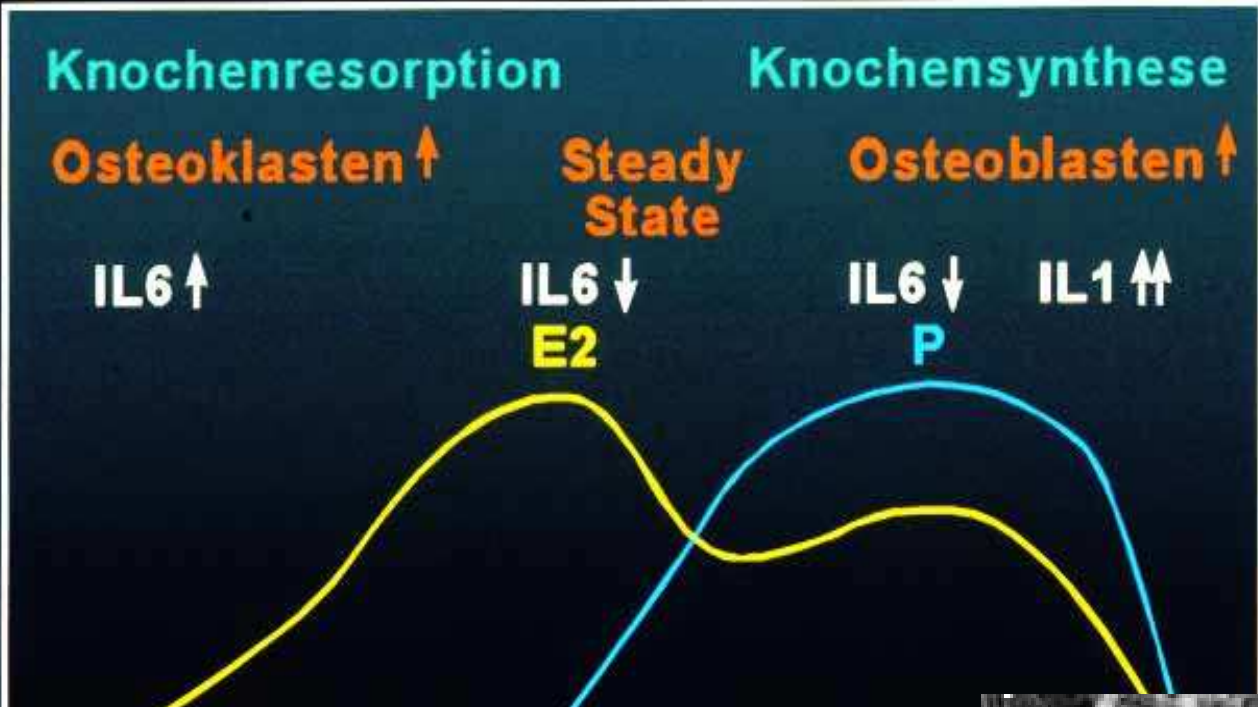
important for the self-renewal and fate determination of mammary gland stem cells. Stem cells within the mammary gland have been proposed to underpin many types of breast cancer. A better understanding of the signal transduction pathways and the molecules that are responsible for the



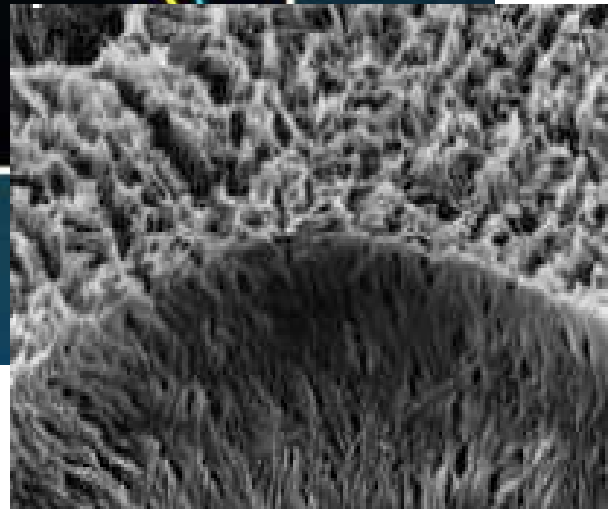


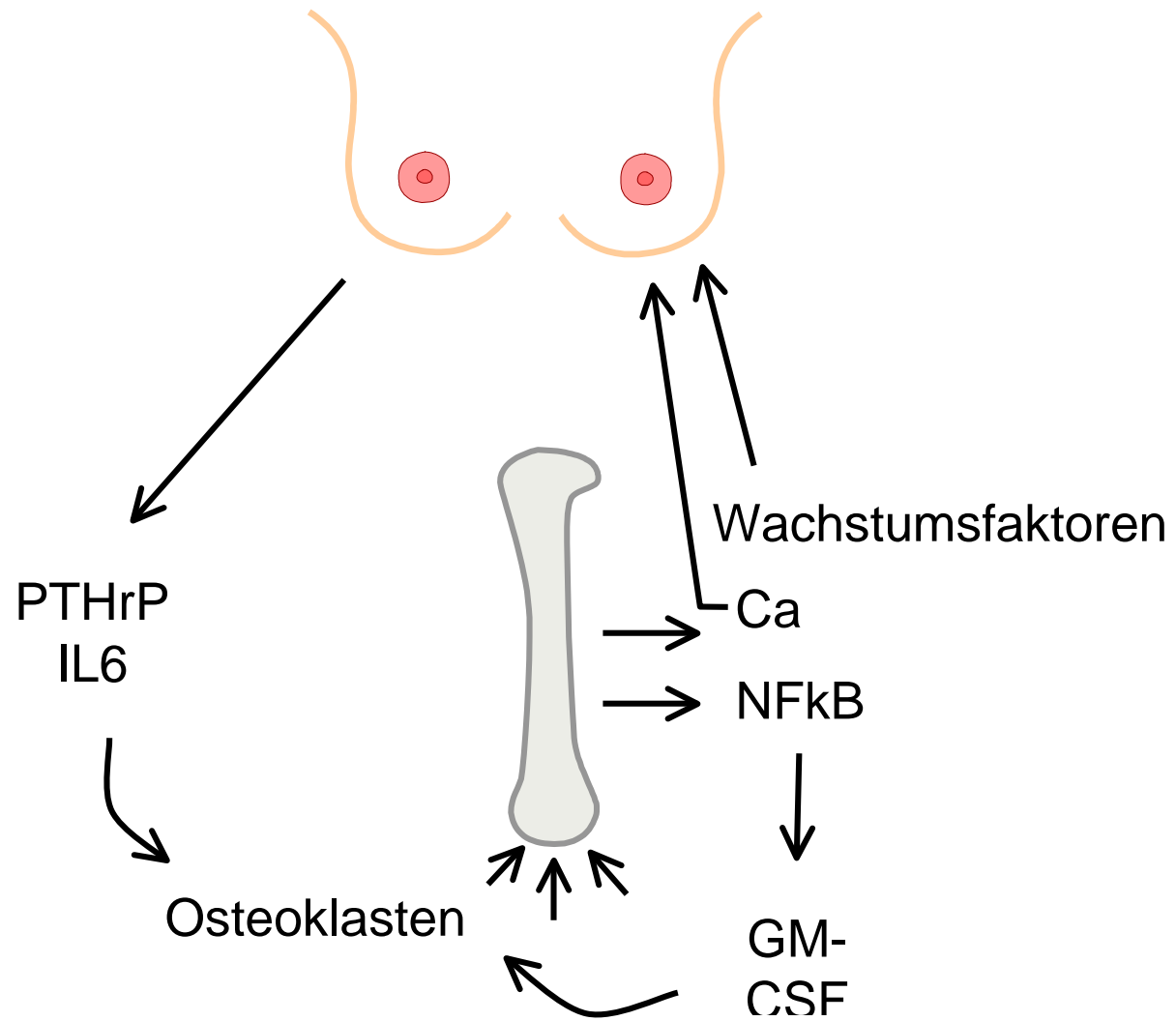
RANK Ligand





Ovulation



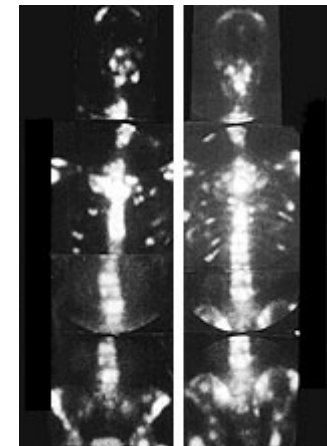
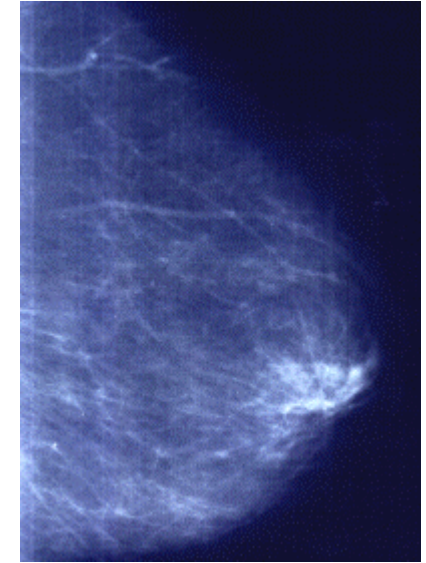




# Nuclear factor- $\kappa$ B in cancer development and progression

Michael Karin<sup>1</sup>

Nuclear factor- $\kappa$ B (NF- $\kappa$ B) transcription factors and the signalling pathways that activate them are central coordinators of innate and adaptive immune responses. More recently, it has become clear that NF- $\kappa$ B signalling also has a critical role in cancer development and progression. NF- $\kappa$ B provides a mechanistic link



Lancet, 360, 2061

Fornarina

## LETTERS

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## Regulation of cancer cell migration and bone metastasis by RANKL

D. Holstead Jones<sup>1,2,3\*</sup>†, Tomoki Nakashima<sup>1\*</sup>, Otto H. Sanchez<sup>4†</sup>, Ivona Kozieradzki<sup>1,2,3</sup>, Svetlana V. Komarova<sup>5</sup>, Ildiko Sarosi<sup>6</sup>, Sean Morony<sup>6</sup>, Evelyn Rubin<sup>2,3</sup>, Renu Sarao<sup>1</sup>, Carlo V. Hojilla<sup>4</sup>, Vukoslav Komnenovic<sup>1</sup>, Young-Yun Kong<sup>7</sup>, Martin Schreiber<sup>8</sup>, S. Jeffrey Dixon<sup>9</sup>, Stephen M. Sims<sup>9</sup>, Rama Khokha<sup>2,4</sup>, Teiji Wada<sup>1</sup> & Josef M. Penninger<sup>1,2,3</sup>

... to  
... for photography, V.  
... and materials, Spring-

... and M. J. Hattingh  
... Republic of South Africa) for g  
... plants, X.-H. Jiang and B. J. Sneath for pre  
... nary research from which this work develop  
... and M. Haus for preparation of the manuscript

27 January 1992; accepted 27 May 1992

**Increased Osteoclast Development After Estrogen  
Loss: Mediation by Interleukin-6**

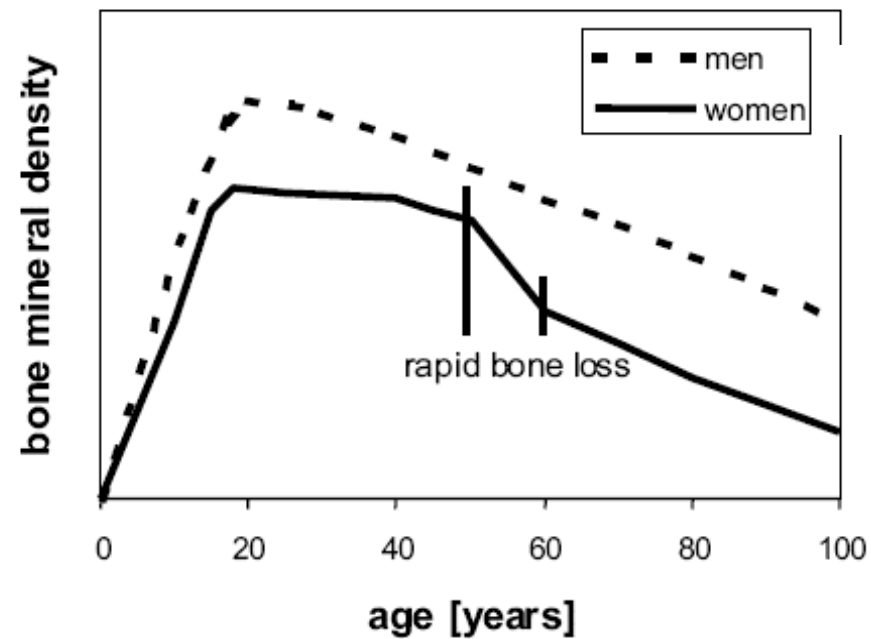
Robert L. Jilka, Giao Hangoc, Giuseppe Girasole,  
Giovanni Passeri, Daniel C. Williams, John S. Abrams,  
Brendan Boyce, Hal Broxmeyer, Stavros C. Manolagas\*

teoclasts, the cells that resorb bone, develop from hematopoietic precursors of the bone  
marrow under the control of factors produced in their microenvironment. The cytokine  
interleukin-6 can promote hematopoiesis and osteoclastogenesis. In mice, estrogen  
depletion (ovariectomy) increased the number of colony-forming units for granulocytes and  
macrophages, enhanced osteoclast development in ex vivo cultures of marrow cells, and  
increased the number of osteoclasts in trabecular bone. These changes were blocked by  
estradiol or an antibody to interleukin-6. Thus, estrogen-mediated stimulation of osteoclastogenesis  
and bone resorption in postmenopausal women is mediated by interleukin-6.

## Osteoporosis: Gender-specific aspects

Peter Pietschmann<sup>1,3</sup> and Katharina Kersch-Schindl<sup>2</sup>

<sup>1</sup>Department of Pathophysiology and <sup>2</sup>Department of Physical Medicine and Rehabilitation, Medical University of Vienna, and <sup>3</sup>Ludwig Boltzmann Institute of Aging Research, Vienna, Austria



**Fig. 1.** Bone gain and bone loss in men and women. Adapted from R. Bartl, 2001 [9]

## DEXA measurement for osteoporosis in patients between 50 - 60

Gruppe	1	2	3	4	5	6	7	8	Gesamt
patients total	4.115	5.935	6.007	5.896	4.684	3.605	2.134	1.312	33.688
T-score below -2,5	694	594	646	580	559	475	313	190	4.051
T-score below -2,5 in %	16,87	10,01	10,75	9,84	11,93	13,18	14,67	14,48	12,03%
T-score below -3,0	322	261	308	281	270	233	166	103	1.944
T-score below -3,0 in %	7,83	4,40	5,13	4,77	5,78	6,46	7,78	7,85	5,77%

## **The effect of age and bone mineral density on the absolute, excess, and relative risk of fracture in postmenopausal women aged 50–99: results from the National Osteoporosis Risk Assessment (NORA)**

E. S. Siris · S. K. Brenneman · E. Barrett-Connor ·  
P. D. Miller · S. Sajjan · M. L. Berger · Y.-T. Chen

**Both the absolute and the excess risks of fracture were similar among women aged 50-59 and aged 60-69 for osteoporotic fractures overall, wrist/forearm, rib, and, to a lesser extent, vertebral fractures in the NORA cohort.**

**Prevention of bone loss in younger postmenopausal women may be an effective way to prevent or delay fractures in postmenopausal women as they age. **When women aged 50-60 present a T-score < -2.0, their long-term risk for future fracture is likely to be high, since bone loss would be expected to continue indefinitely without intervention.****

**One strategy to reduce fracture risk in older women is long-term intervention to prevent bone loss in women started around the time of menopause, when rates of bone loss are the highest.**

## Risikorechner

Bitte beantworten Sie die untenstehenden Fragen für die Berechnung der 10-Jahres-Wahrscheinlichkeit für eine Fraktur

Land: Österreich

Name / ID: [Mehr zu den Risikofaktoren](#) 

### Fragebogen:

1. Alter (zwischen 40 und 90 Jahren) oder Geburtsdatum

Alter:   
Geburtsdatum: J:  M:  T: 2. Geschlecht  Männlich  Weiblich3. Gewicht (kg) 4. Körpergröße (cm) 5. Vorausgehende Fraktur  Nein  Ja6. Hüftfraktur eines Elternteils  Nein  Ja7. Gegenwärtiges Rauchen  Nein  Ja10. Sekundäre Osteoporose  Nein  Ja11. Alkohol 3 und mehr Einheiten  Nein  Ja12. Knochenmineraldichte (g/cm<sup>2</sup>)Auswahl DXA 

Löschen

Rechnen

### Weight Conversion

Pounds  Kgs

Convert

### Height Conversion

Inches  Cms

Convert





# FSH Directly Regulates Bone Mass

Li Sun,<sup>1</sup> Yuanzhen Peng,<sup>1</sup> Allison C. Sharrow,<sup>2,3</sup> Jameel Iqbal,<sup>1</sup> Zhiyuan Zhang,<sup>1</sup> Dionysios J. Papachristou,<sup>2,3</sup> Samir Zaidi,<sup>1</sup> Ling-Ling Zhu,<sup>1</sup> Beatrice B. Yaroslavskiy,<sup>2,3</sup> Hang Zhou,<sup>1</sup> Alberta Zallone,<sup>4</sup> M. Ram Sairam,<sup>5</sup> T. Rajendra Kumar,<sup>6</sup> Wei Bo,<sup>7</sup> Jonathan Braun,<sup>7</sup> Luis Cardoso-Landa,<sup>1</sup> Mitchell B. Schaffler,<sup>1</sup> Baljit S. Moonga,<sup>1</sup> Harry C. Blair,<sup>2,3,\*</sup> and Mone Zaidi<sup>1,\*</sup>

<sup>1</sup> Mount Sinai Bone Program, Department of Medicine and Department of Orthopedics, Mount Sinai School of Medicine, New York, NY 10029, USA

<sup>2</sup> Departments of Pathology and Cell Biology, University of Pittsburgh, Pittsburgh, PA 15261, USA

<sup>3</sup> VA Medical Center, Pittsburgh, PA 15261, USA

<sup>4</sup> Department of Anatomy and Histology, University of Bari, 70124 Bari, Italy

<sup>5</sup> Clinical Research Institute of Montreal, Montreal, QC H2W 1R7, Canada

<sup>6</sup> Department of Molecular and Integrative Physiology, University of Kansas, Kansas City, KS 66160, USA

<sup>7</sup> Department of Pathology, University of California, Los Angeles, Los Angeles, CA 90095, USA

\*Contact: [hclair@imap.upitt.edu](mailto:hclair@imap.upitt.edu) (H.C.B.); [mone.zaidi@mssm.edu](mailto:mone.zaidi@mssm.edu) (M.Z.)

DOI 10.1016/j.cell.2006.01.051

Cell. 2006 Apr 21;125(2):247-60.

# Endogenous Sex Hormones, Sex Hormone-Binding Globulin, and the Risk of Incident Vertebral Fractures in Elderly Men and Women: The Rotterdam Study

HERMIEN W. GODERIE-PLOMP, MARJOLEIN VAN DER KLIFT, WILLEM DE RONDE, ALBERT HOFMAN, FRANK H. DE JONG, AND HUIBERT A. P. POLS

*Departments of Internal Medicine (H.W.G.-P., M.v.d.K., W.d.R., F.H.d.J., H.A.P.P.) and Epidemiology and Biostatistics (H.W.G.-P., M.v.d.K., A.H., H.A.P.P.), Erasmus Medical Center, 3000 DR Rotterdam, The Netherlands*

In an age-matched, case-control study, we investigated the association between endogenous sex steroid hormones and incident vertebral fractures in both elderly men and women (aged  $67.7 \pm 6.8$  yr). Drawn from the Rotterdam Study, participants required radiographs of the lumbar spine at both baseline and follow-up (average time of follow-up, 6.5 yr) and frozen blood samples, taken at baseline. One hundred and seventy-eight men (45 cases) and 454 women (115 cases) were thus selected. Serum estradiol, SHBG, testosterone, and insulin were measured, along with bone mineral density at both spine and hip. Women in the lowest tertile of serum estradiol ( $\leq 15.5$  pmol/liter) had a 2.1 times increased risk (95% confidence interval, 1.3–3.5) of incident vertebral fractures, inde-

pendently of bone mineral density measured at either site. SHBG levels in the lowest two tertiles were associated with a 50% reduction in incident vertebral fracture risk. Women with a combination of both low estradiol and high SHBG had a 7.8 times higher risk of an incident vertebral fracture (95% confidence interval, 2.7–22.5;  $P < 0.001$ ), adjusted for age and weight. This increased risk did not change when non-SHBG-bound estradiol was used instead of total estradiol. For men, no clear association was found, possibly due to insufficient power. No clear association between testosterone and incident vertebral fractures was observed in either men or women. (*J Clin Endocrinol Metab* 89: 3261–3269, 2004)

# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

MAY 13, 2004

VOL. 350 NO. 20

## Homocysteine Levels and the Risk of Osteoporotic Fracture

Joyce B.J. van Meurs, Ph.D., Rosalie A.M. Dhonukshe-Rutten, M.Sc., Saskia M.F. Pluijm, Ph.D., Marjolein van der Klift, M.D., Ph.D., Robert de Jonge, Ph.D., Jan Lindemans, Ph.D., Lisette C.P.G.M. de Groot, Ph.D., Albert Hofman, M.D., Ph.D., Jacqueline C.M. Witteman, Ph.D., Johannes P.T.M. van Leeuwen, Ph.D., Monique M.B. Breteler, M.D., Ph.D., Paul Lips, M.D., Ph.D., Huibert A.P. Pols, M.D., Ph.D., and André G. Uitterlinden, Ph.D.

### ABSTRACT

#### BACKGROUND

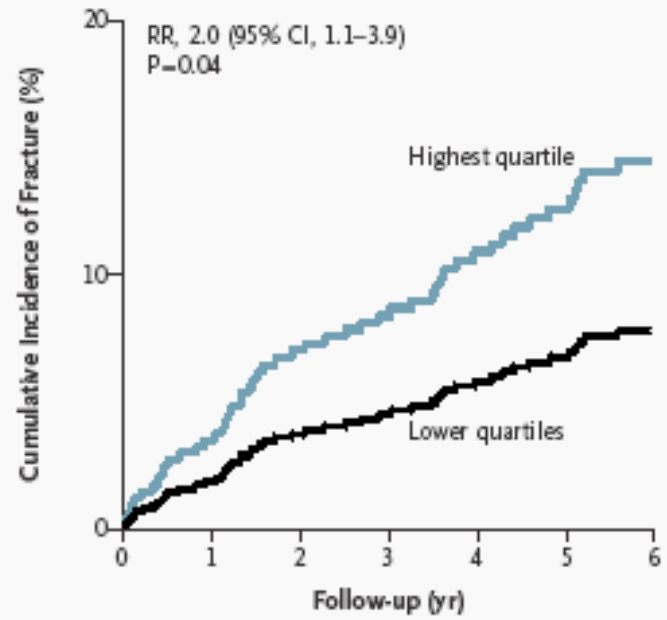
Very high plasma homocysteine levels are characteristic of homocystinuria, a rare autosomal recessive disease accompanied by the early onset of generalized osteoporosis. We therefore hypothesized that mildly elevated homocysteine levels might be related to age-related osteoporotic fractures.

#### METHODS

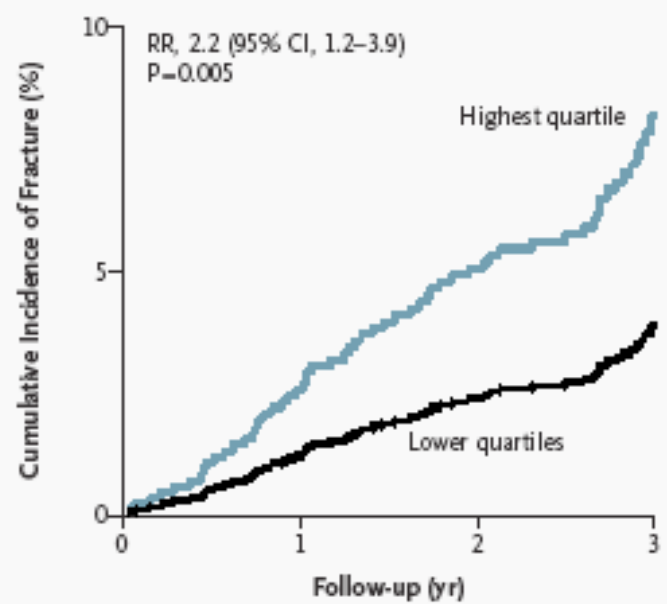
We studied the association between circulating homocysteine levels and the risk of incident osteoporotic fracture in 2406 subjects, 55 years of age or older, who participated in two separate prospective, population-based studies. In the Rotterdam Study, there were two independent cohorts: 562 subjects in cohort 1, with a mean follow-up period of 8.1 years; and 553 subjects in cohort 2, with a mean follow-up period of 5.7

From the Departments of Internal Medicine (J.B.J.M., M.K., J.P.T.M.L., H.A.P.P., A.G.U.), Epidemiology and Biostatistics (A.H., J.C.M.W., M.M.B.B., H.A.P.P., A.G.U.), and Clinical Chemistry (R.J., J.L., A.G.U.), Erasmus Medical Center, Rotterdam; the Division of Human Nutrition, Wageningen University, Wageningen (R.A.M.D.-R., L.C.P.G.M.G.); and the Institute for Research in Extramural Medicine and the Department of Endocrinology, Vrije Universiteit Medical Center, Amsterdam (S.M.F.P., P.L.) — all in the Netherlands. Address reprint requests to Dr. van Meurs

**B Rotterdam Study, Cohort 2**

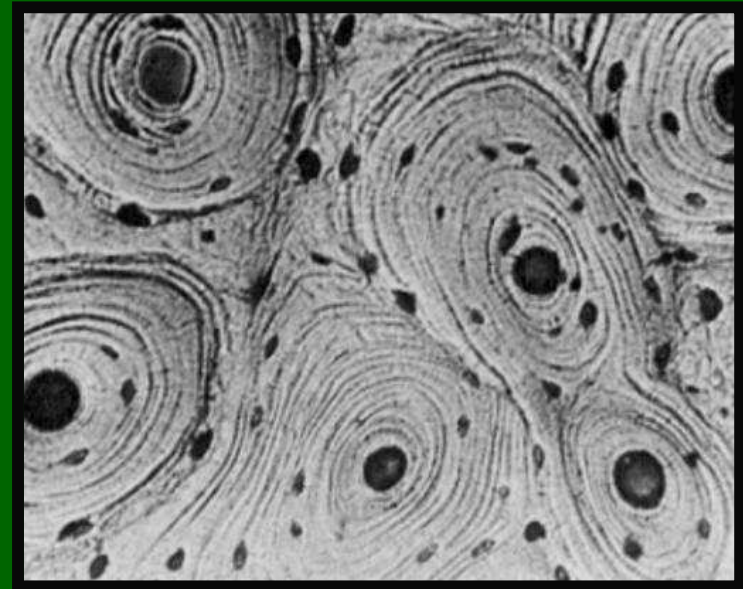


**C LASA**



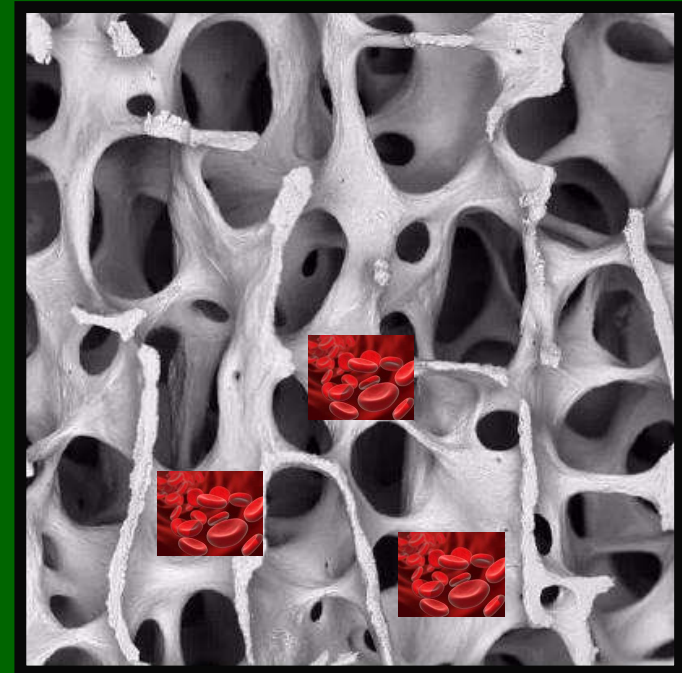
# Cortical Bone

- Dense outer shell of compact bone; defines bone shape
- 80% of skeletal mass
- Essential functions
  - Provides biomechanical strength
  - Attachment site for tendon and muscle



# Trabecular Bone

- A sponge-like network of delicate plates of bone known as trabeculae
- 20% of skeletal mass
- Essential functions
  - Mineral metabolism
  - Strength and elasticity
- Higher turnover rate compared to cortical bone



Howship lacunae

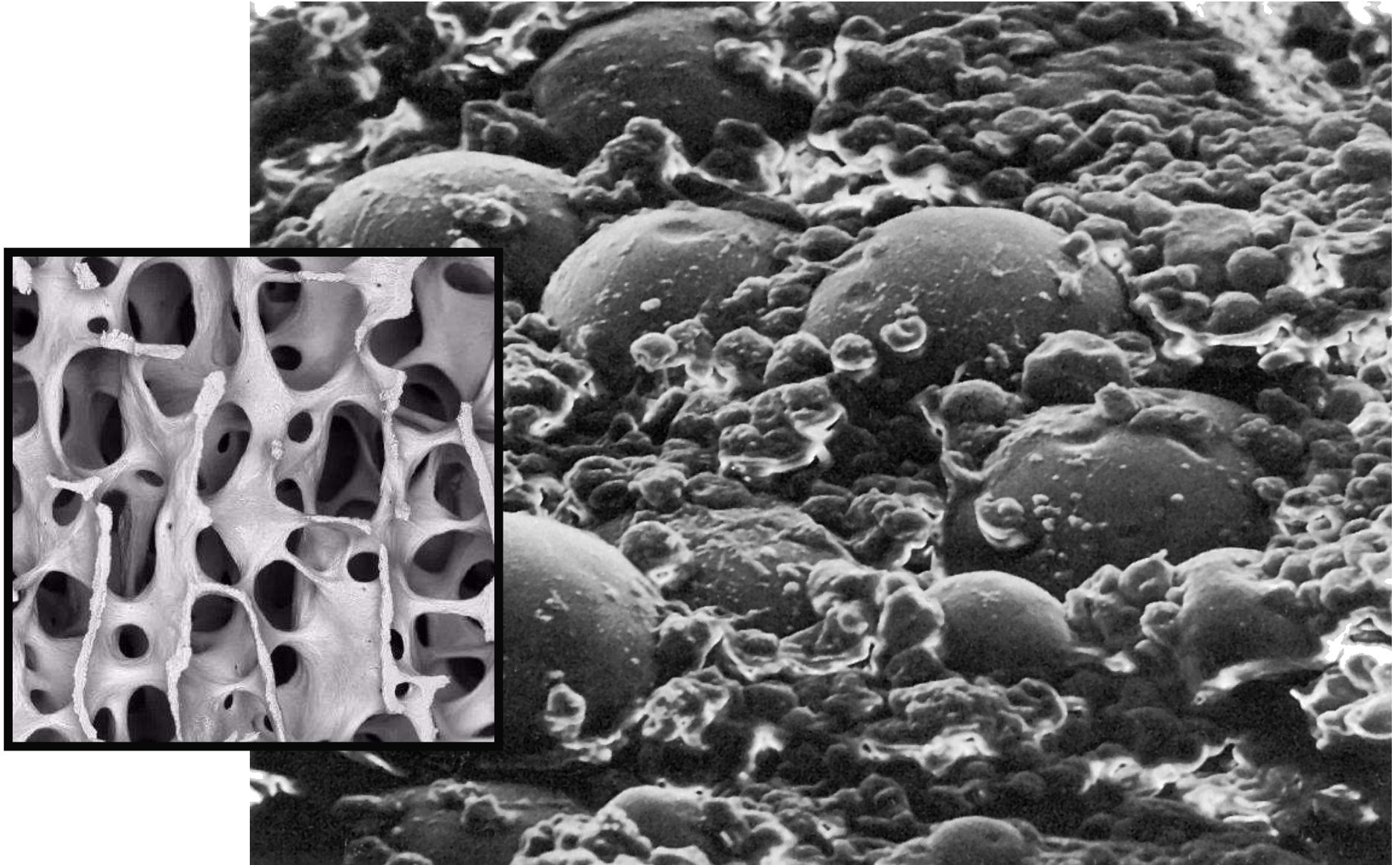
Dempster DW. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism*. 6th ed. 2006: 7-11;  
Image courtesy of A. Boyde

## ARTICLES

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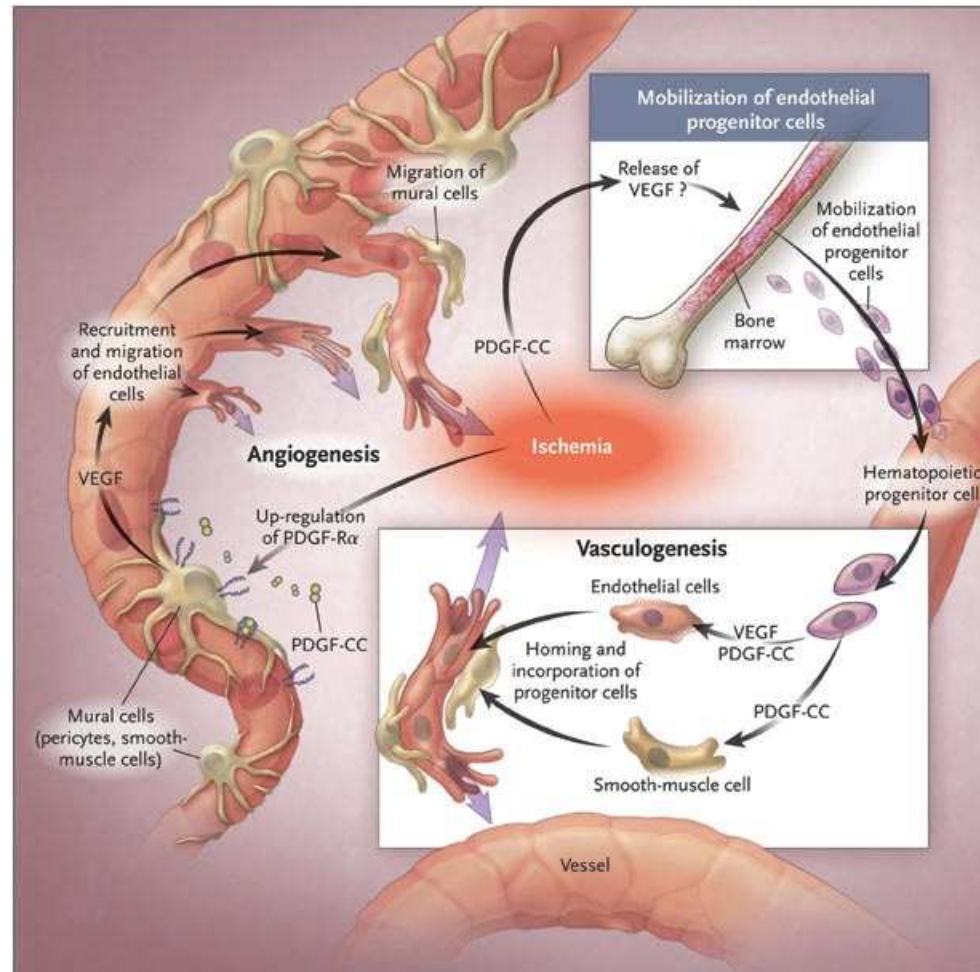
# Mesenchymal and haematopoietic stem cells form a unique bone marrow niche

Simón Méndez-Ferrer<sup>1,2†</sup>, Tatyana V. Michurina<sup>3</sup>, Francesca Ferraro<sup>4</sup>, Amin R. Mazloom<sup>5</sup>, Ben D. MacArthur<sup>5†</sup>, Sergio A. Lira<sup>1</sup>, David T. Scadden<sup>4</sup>, Avi Ma'ayan<sup>5</sup>, Grigori N. Enikolopov<sup>3</sup> & Paul S. Frenette<sup>1,2,6</sup>



Quelle: Mehdi Tavassoli, Joseph Mendel Yoffey,  
Bone Marrow Structure and Function  
Alan R. Liss, Inc. 1983

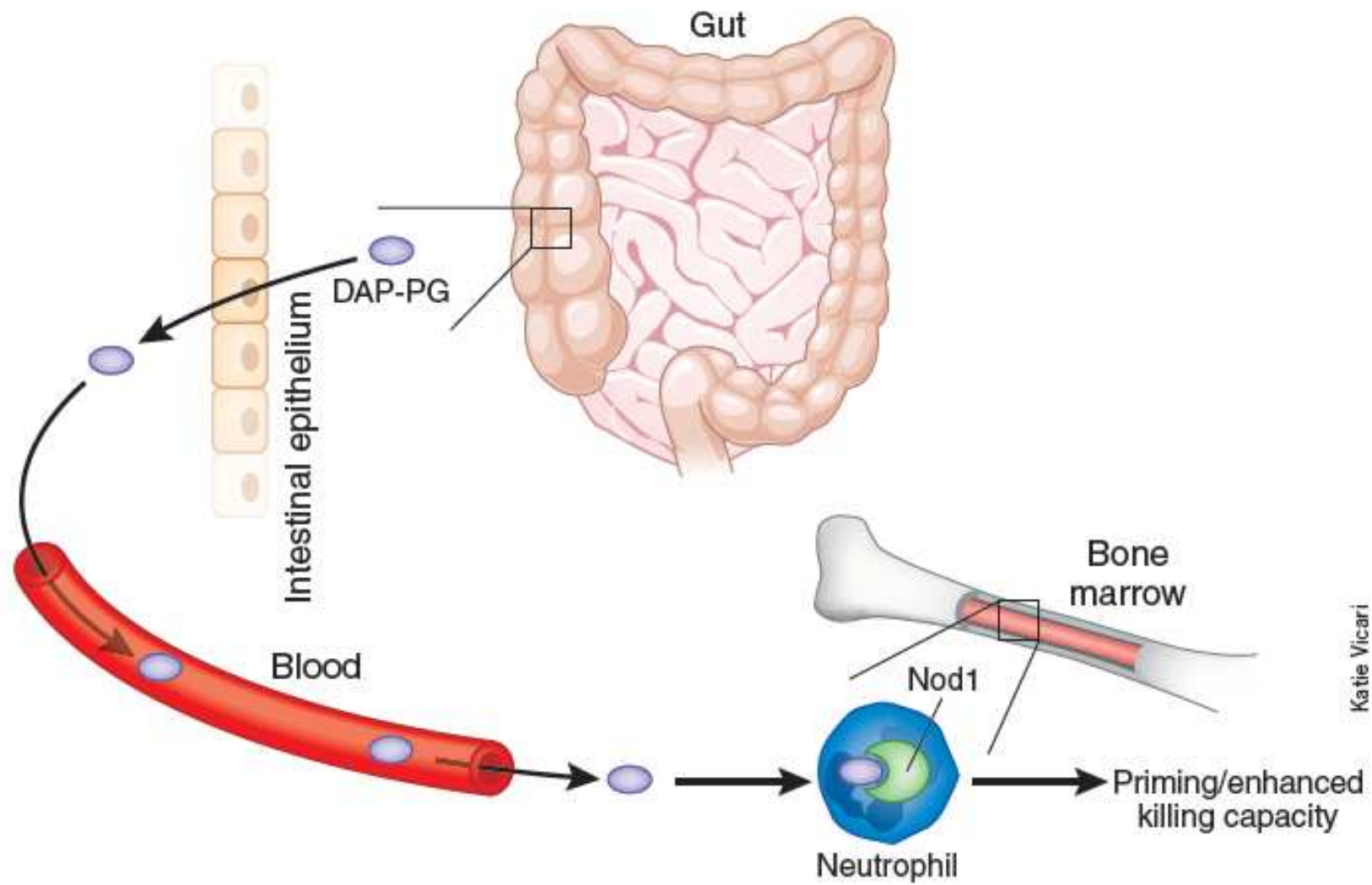




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# **Osteoblastic cells regulate the haematopoietic stem cell niche**

**L. M. Calvi<sup>1,2</sup>, G. B. Adams<sup>3,4</sup>, K. W. Weibrecht<sup>3</sup>, J. M. Weber<sup>1</sup>, D. P. Olson<sup>3</sup>,  
M. C. Knight<sup>4</sup>, R. P. Martin<sup>3</sup>, E. Schipani<sup>4</sup>, P. Divieti<sup>4</sup>, F. R. Bringhurst<sup>4</sup>,  
L. A. Milner<sup>2</sup>, H. M. Kronenberg<sup>4</sup> & D. T. Scadden<sup>3</sup>**



Katie Vicari

# Gut microbes extend reach to systemic innate immunity

Dana J Philpott & Stephen E Girardin

**MICROFLORA**



**DIAMINOPIMETIC SÄURE PEPTIDOGLYCAN**



**NEUTROPHILE AKTIVITÄT**

# Endocrine Regulation of Energy Metabolism by the Skeleton

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

<sup>1</sup> Department of Genetics & Development

<sup>2</sup> Department of Pathology

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

<sup>3</sup> CHO-A Biotechnology Research Institute, CHO-A Pharm. Co., Seoul 143-701, Korea

<sup>4</sup> Ecole Normale Supérieure de Lyon, UMR5161, Laboratoire d'Endocrinologie Moléculaire et Différenciation Hématopoïétique et Osseuse, 69364 Lyon, France

<sup>5</sup> Centre for Stem Cell Research, University of Cambridge, Cambridge CB2 1TN, United Kingdom

<sup>6</sup> Faculty of Dentistry, and Department of Anatomy and Cell Biology, McGill University, Montreal, QC, Canada H3A 2B2

<sup>7</sup> Department of Cellular & Molecular Physiology, Penn State Medical Center, Hershey, PA 17033

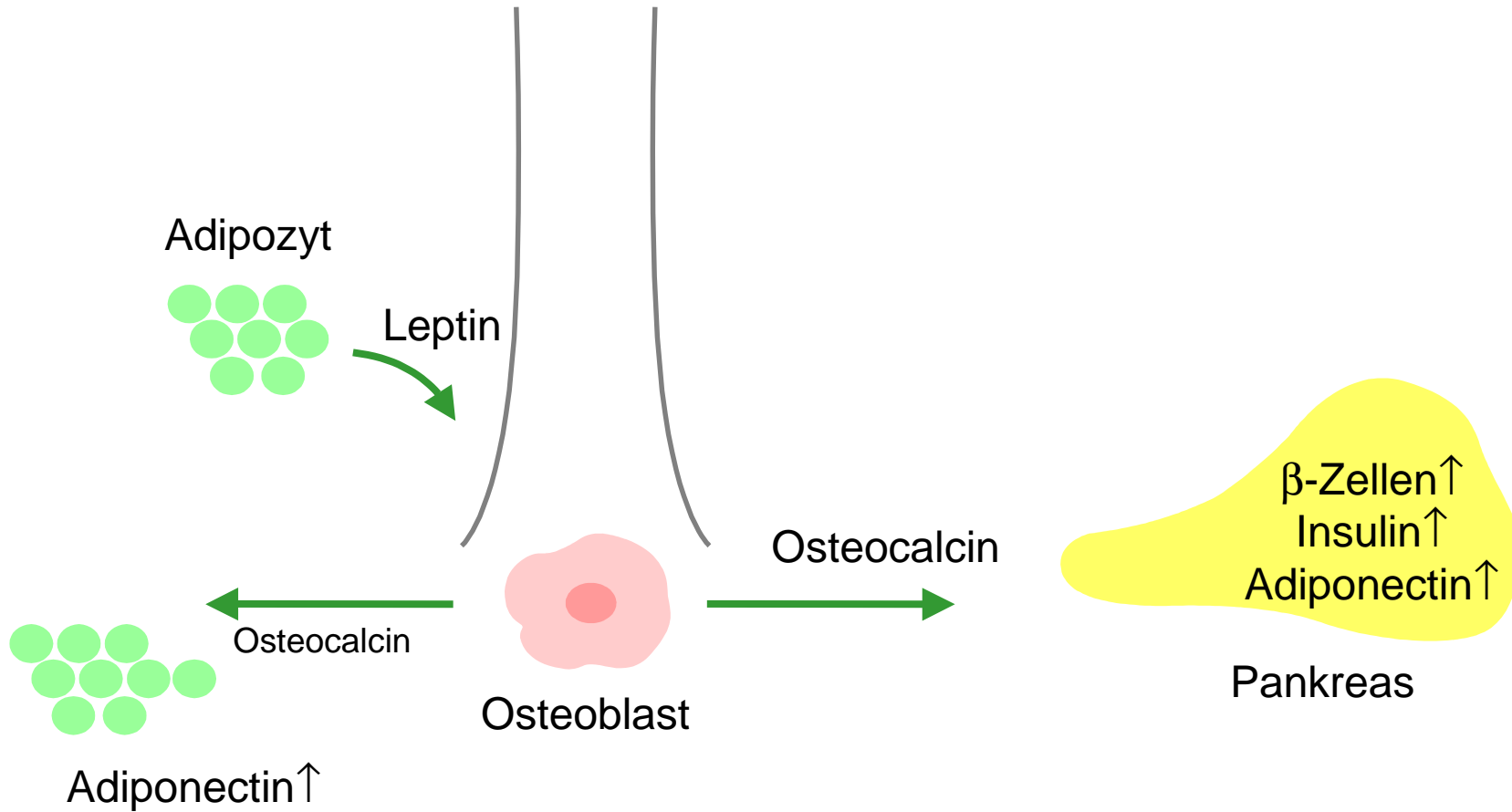
<sup>8</sup> Department of Medicine, Northwestern University School of Medicine, Chicago, IL 60611, USA

\*Correspondence: [gk2172@columbia.edu](mailto:gk2172@columbia.edu)

DOI 10.1016/j.cell.2007.05.047

# The bones of contention

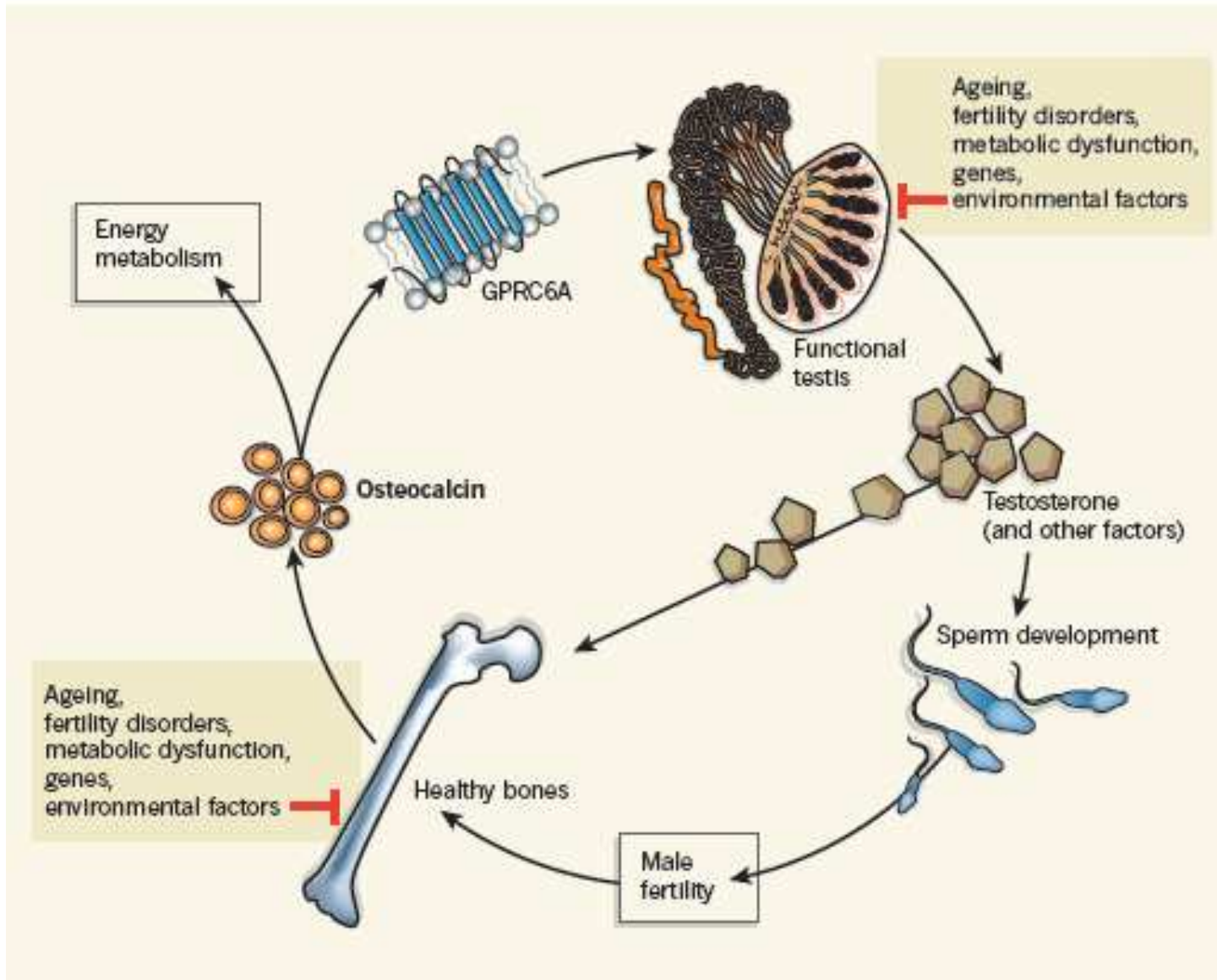
The skeleton may provide more than just structural support. **Alla Katsnelson** investigates the rise of bone as a metabolic regulator.



# Endocrine Regulation of Male Fertility by the Skeleton

Franck Oury,<sup>1,6</sup> Grzegorz Sumara,<sup>1,6</sup> Olga Sumara,<sup>1</sup> Mathieu Ferron,<sup>1</sup> Haixin Chang,<sup>3</sup> Charles E. Smith,<sup>4</sup> Louis Hervo,<sup>4</sup> Susan Suarez,<sup>3</sup> Bryan L. Roth,<sup>5</sup> Patricia Ducy,<sup>2</sup> and Gerard Karsenty<sup>1,\*</sup>





# Do neural signals remodel bone?

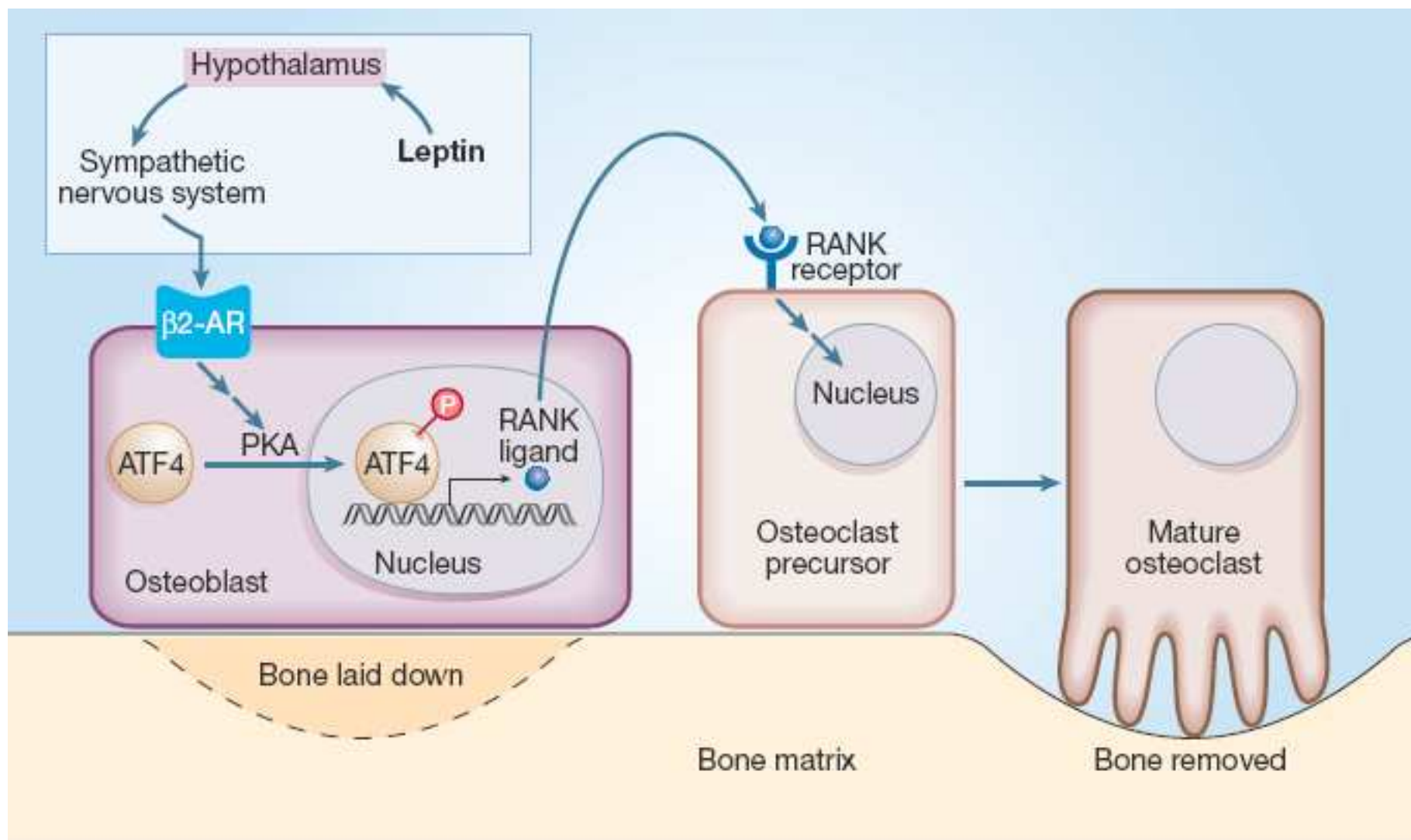
Joel K. Elmquist and Gordon J. Strewler

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The hormone leptin is best known for its influence on body weight. But it also controls bone mass, and recent work in mice is beginning to uncover the neuroendocrine systems involved.

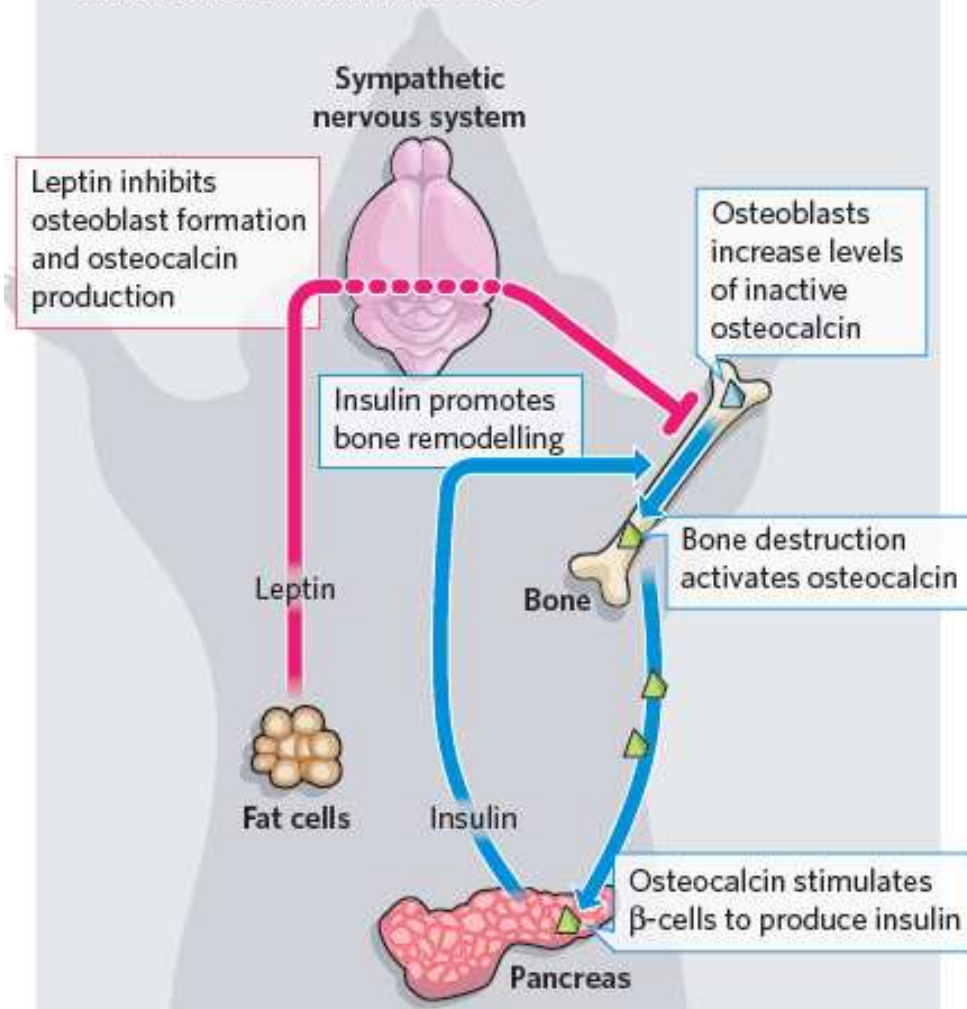
**T**he hypothalamus is the part of the brain that maintains homeostasis, which includes regulating the autonomic nervous system — the unconscious system for monitoring and controlling the state of the body's internal organs. A key input to the hypothalamus is leptin, a hor-

for the effects of leptin on bone mass. The authors examined mice lacking the  $\beta$ 2-adrenergic receptor ( $\beta$ 2-AR) — one of several adrenergic receptors that respond to noradrenaline, a neurotransmitter released by sympathetic neurons. The mutant mice are resistant to the bone-reducing effects

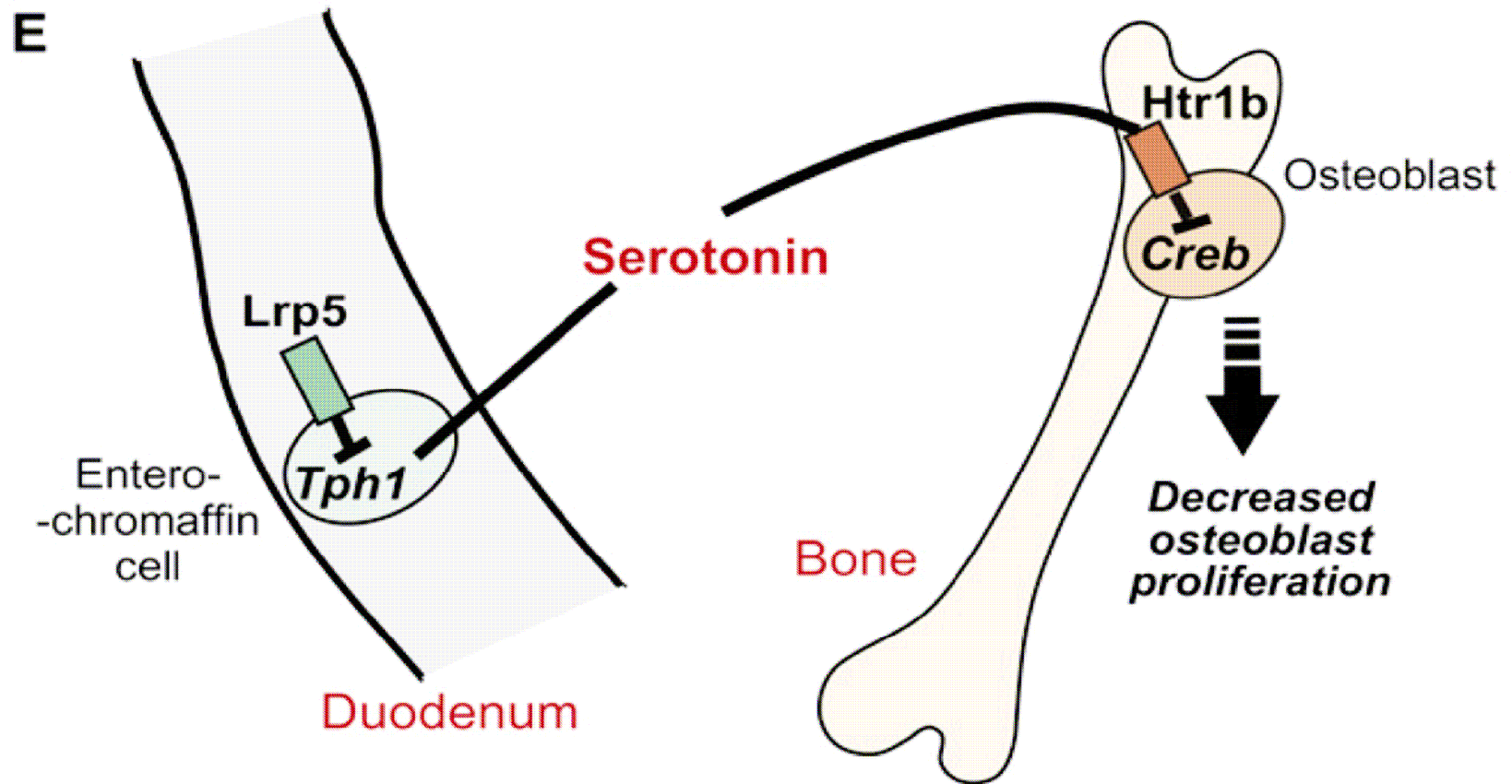


## CLOSE TO THE BONE

Bone remodelling includes both building of bone (by cells called osteoblasts) and destruction of bone (by osteoclasts). This dynamic, energy-intensive process seems to interact with metabolism in multiple ways.



# Genetic Interaction between Lrp5 and Serotonin



# Use of Antidepressants and Rates of Hip Bone Loss in Older Women

## *The Study of Osteoporotic Fractures*

Susan J. Diem, MD, MPH; Terri L. Blackwell, MA; Katie L. Stone, PhD; Kristine Yaffe, MD; Elizabeth M. Haney, MD; Michael M. Bliogotes, MD; Kristine E. Ensrud, MD, MPH

**Background:** Serotonin transporters have recently been described in bone, raising the possibility that medications that block serotonin reuptake could affect bone metabolism.

**Methods:** We assessed current use of selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs) and obtained serial bone mineral density (BMD) measurements in a cohort of 2722 older women (mean age, 78.5 years) participating in the Study of Osteoporotic Fractures, a prospective cohort study of community-dwelling women. Hip BMD was measured at the sixth examination and an average of 4.9 years later at the eighth examination. We categorized women as nonusers (used no SSRIs or TCAs at either examination; n=2406), SSRI users (used SSRIs but no TCAs at either examination; n=198), or TCA users (used TCAs but no SSRIs at either examination; n=118). Depressive symp-

toms were identified using a cutoff score of at least 6 on the Geriatric Depression Scale.

**Results:** After adjustment for potential confounders, including the Geriatric Depression Scale score, mean total hip BMD decreased 0.47% per year in nonusers compared with 0.82% in SSRI users ( $P<.001$ ) and 0.47% in TCA users ( $P=.99$ ). Higher rates of bone loss were also observed at the 2 hip subregions for SSRI users. Results were not substantially altered when women who scored at least 6 on the Geriatric Depression Scale were excluded from the analysis.

**Conclusion:** Use of SSRIs but not TCAs is associated with an increased rate of bone loss at the hip in this cohort of older women.

*Arch Intern Med.* 2007;167:1240-1245

# WIRKUNG VON SSRI AUF KNOCHEN

## CANADIAN MULTICENTER OSTEOPOROSIS STUDY

**OR 2,1 (1,3-3,4)**

*Richards JB, CMOSRSG 2007 The impact of selective serotonin reuptake inhibitors on the risk of fracture. Arch Intern Med 167:188–194*

## ROTTERDAM STUDY

**OR 2,35 (1,37-1,48)**

*Ziere G, 2008 Selective serotonin reuptake inhibiting antidepressants are associated with an increased risk of nonvertebral fractures. Clin Psychopharmacol 28:411–417*

# Ultralow-Dose Micronized 17 $\beta$ -Estradiol and Bone Density and Bone Metabolism in Older Women

## A Randomized Controlled Trial

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Karen M. Prestwood, MD

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Anne M. Kenny, MD

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Alison Kleppinger, MS

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Martin Kulldorff, PhD

**Context** Estrogen therapy is known to prevent osteoporosis, but studies have shown that conventional doses increase adverse events. Whether lower doses, one quarter of standard treatment, prevent bone loss is not known.

**Objective** To examine the effect of 3 years of treatment with 0.25 mg/d of micronized 17 $\beta$ -estradiol on bone mineral density (BMD) and bone turnover in healthy older postmenopausal women.



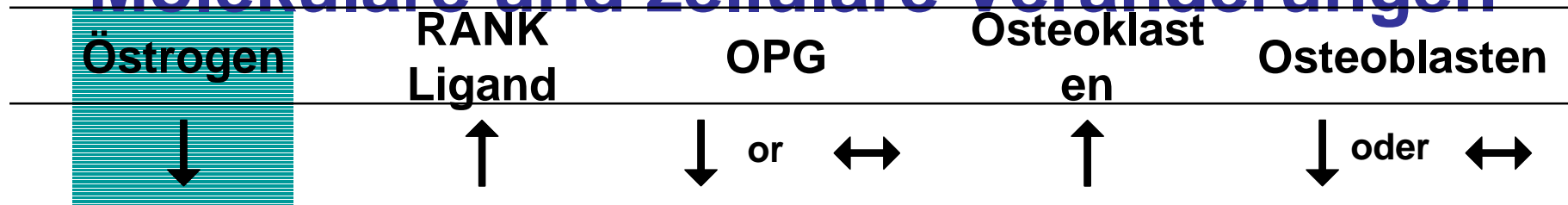
# Supra low estrogen replacment therapy

- estradiol-valerat oder benzoat 0.025
  - ethanol 96 % 4,0
  - propylenglycol ad 10,0 ad
- 
- MDS: estradiol-drops
  - 10 drops are 1 mg estradiol
  - Event.Sacch.Natrium 0.05 g



# auf den Knochenstoffwechsel auswirken

## Molekuläre und zelluläre Veränderungen

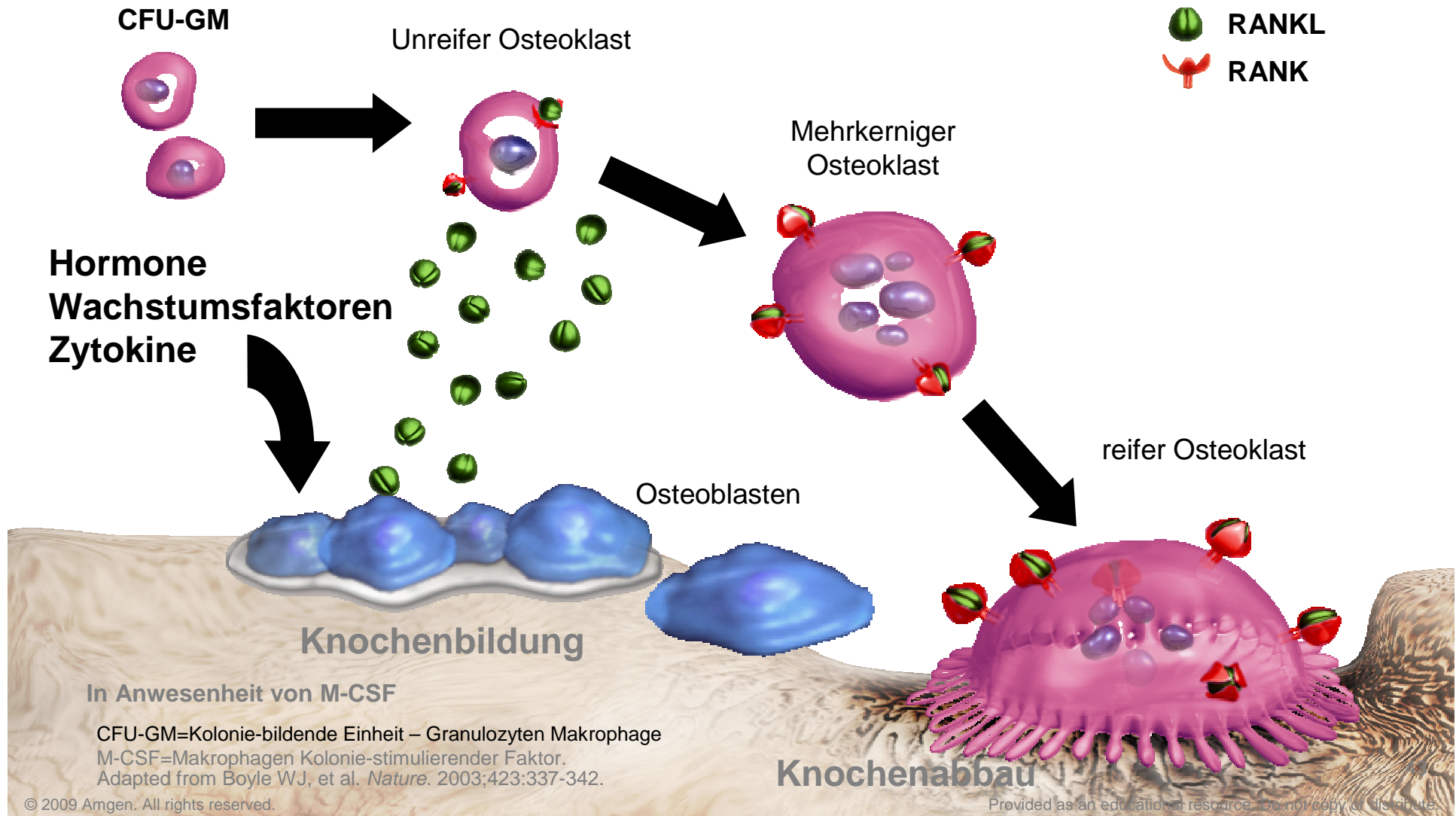


## Veränderungen der Mikrostruktur

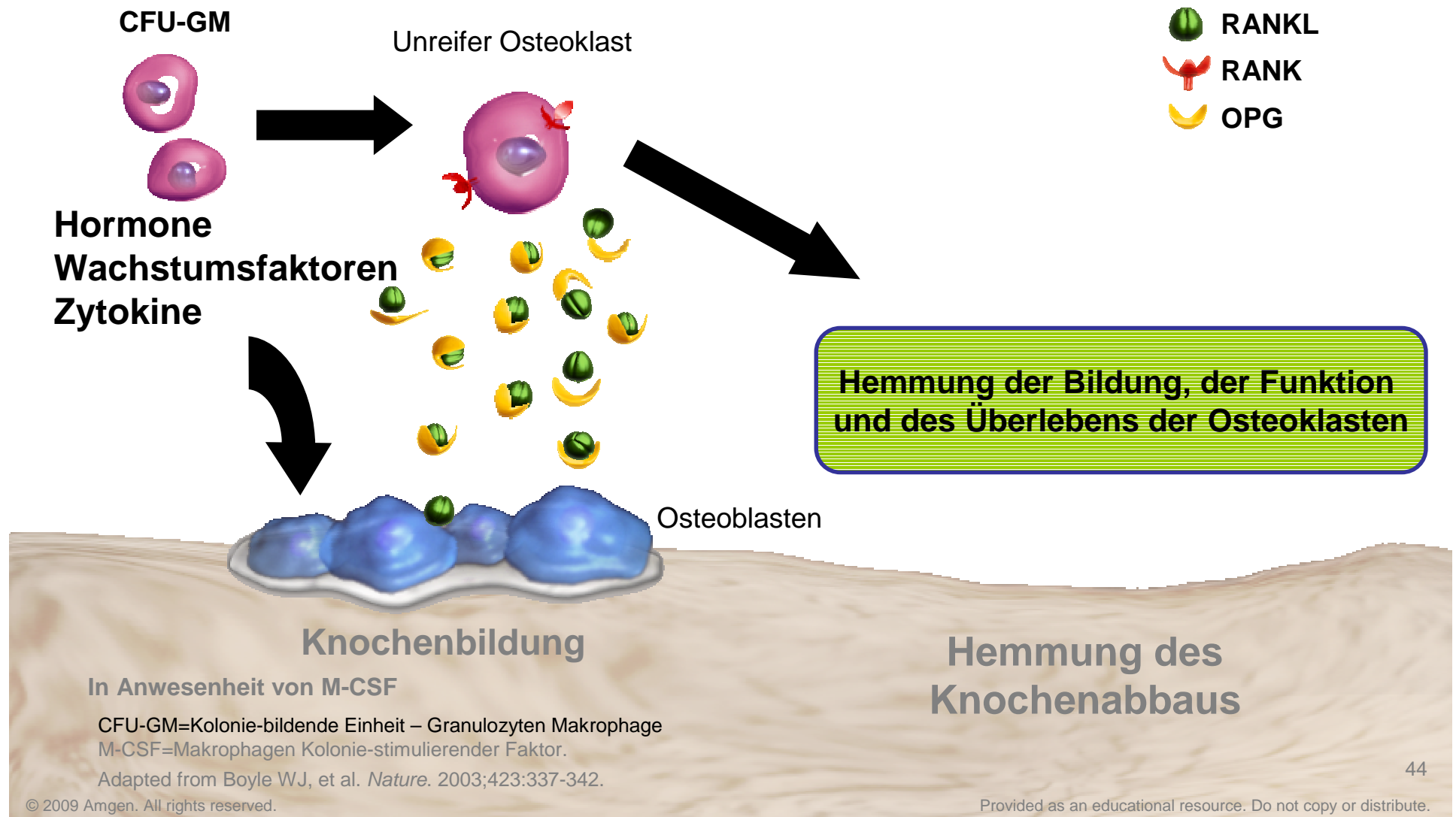


Eghbali-Fatourehchi G, et al. *J Clin Invest.* 2003;111:1221-1230.  
 Hofbauer LC, et al. *Endocrinology.* 1999;140:4367-4370.  
 Shevde NK, et al. *Proc Nat Acad Sci.* 2000;97:7829-7834.  
 Riggs BL, et al. *J Bone Miner Res.* 1998;13:763-773.  
 Chavassieux P, et al. *Endocrine Rev.* 2007;28:151-164.

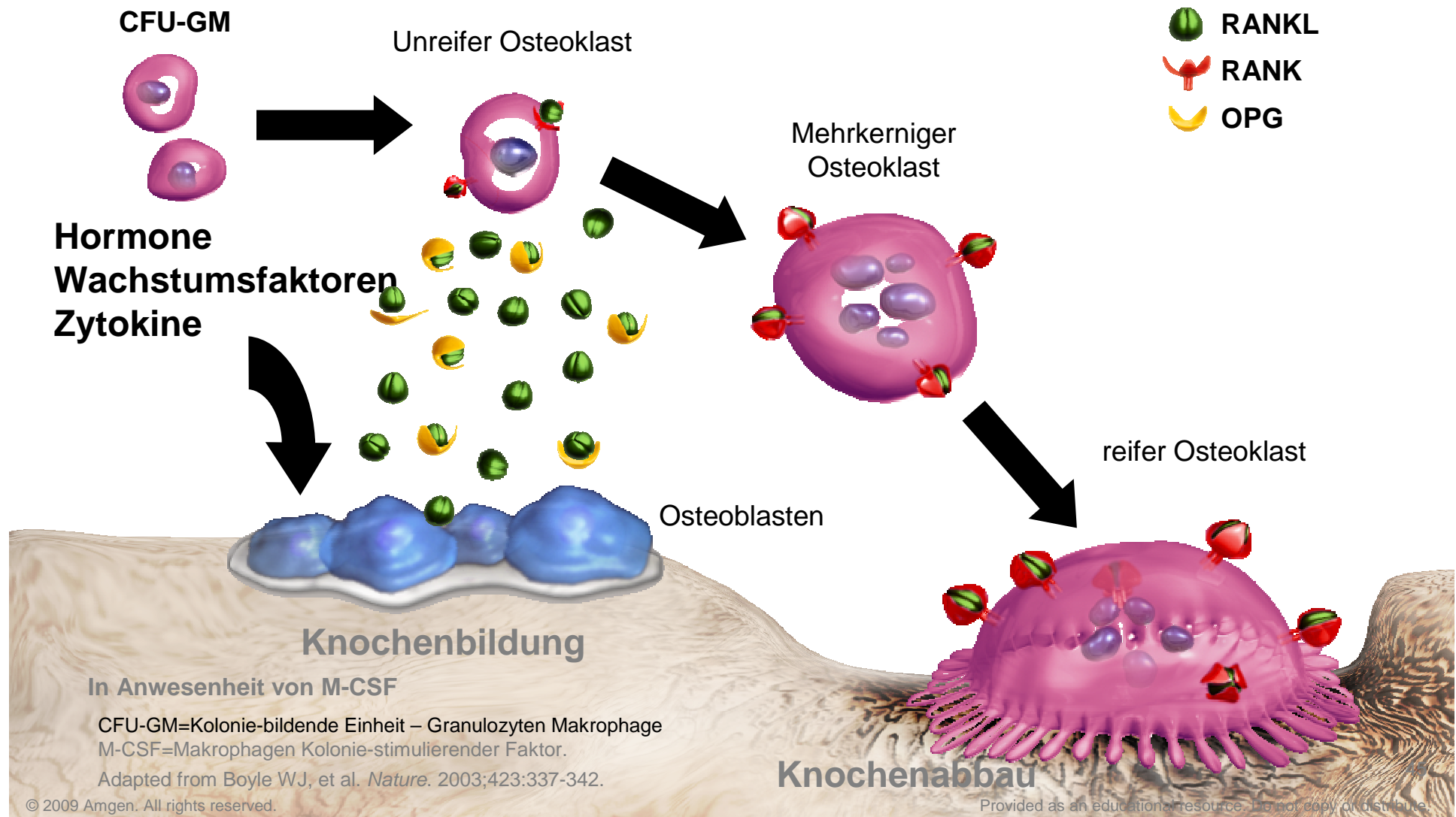
# RANK Ligand ist Mediator des Knochenabbaus



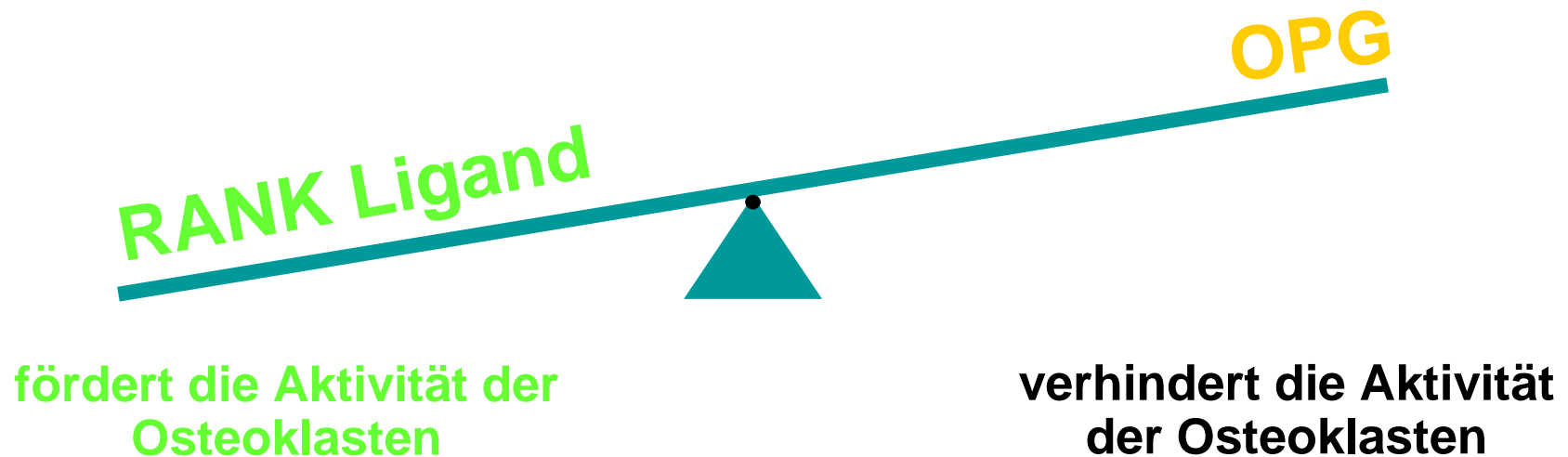
# Osteoprotegerin (OPG) schützt vor Knochenabbau



# vom Verhältnis der OPG- und RANKL Expression ab



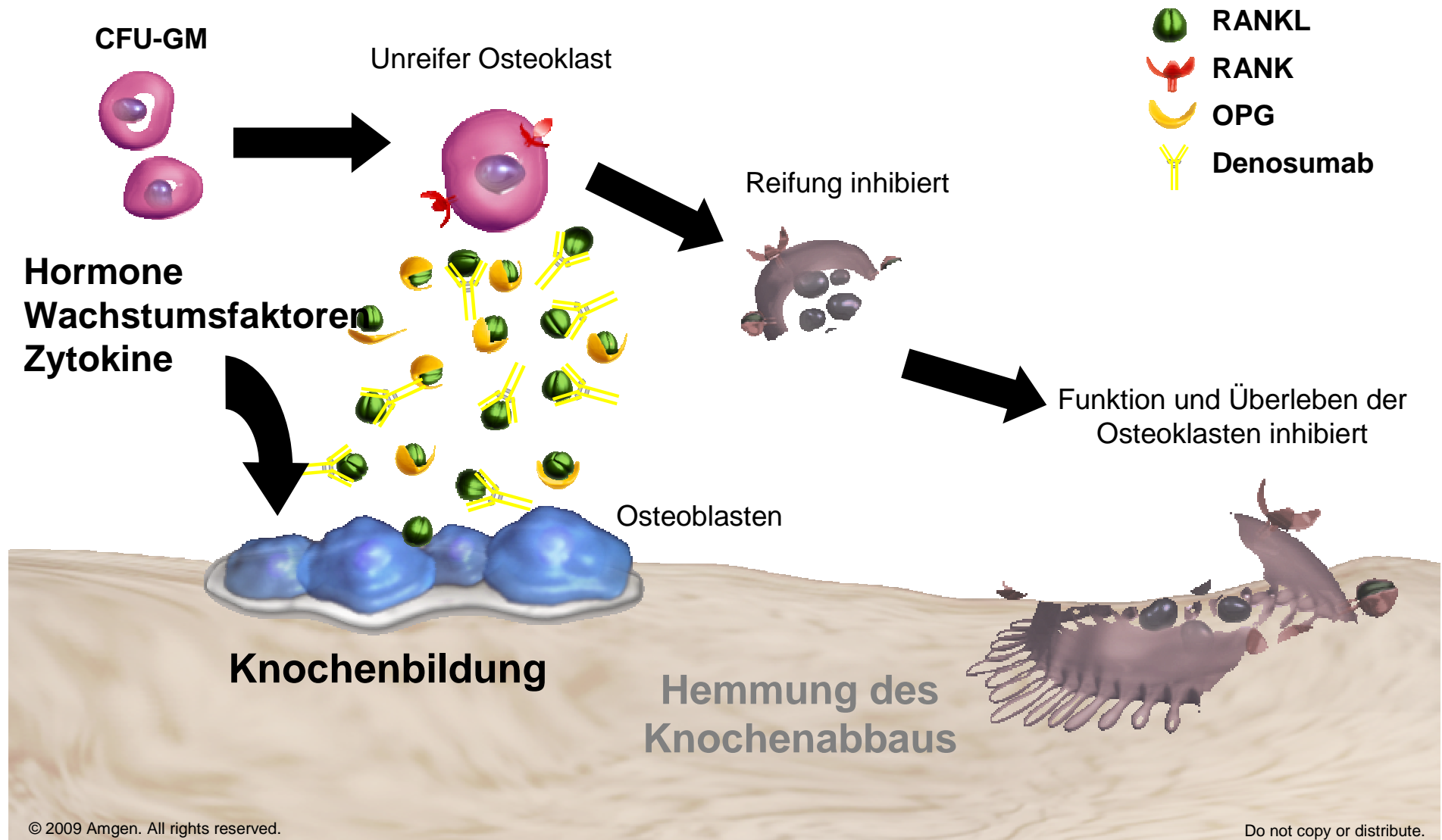
# führt zu einer erhöhten Knochenresorption



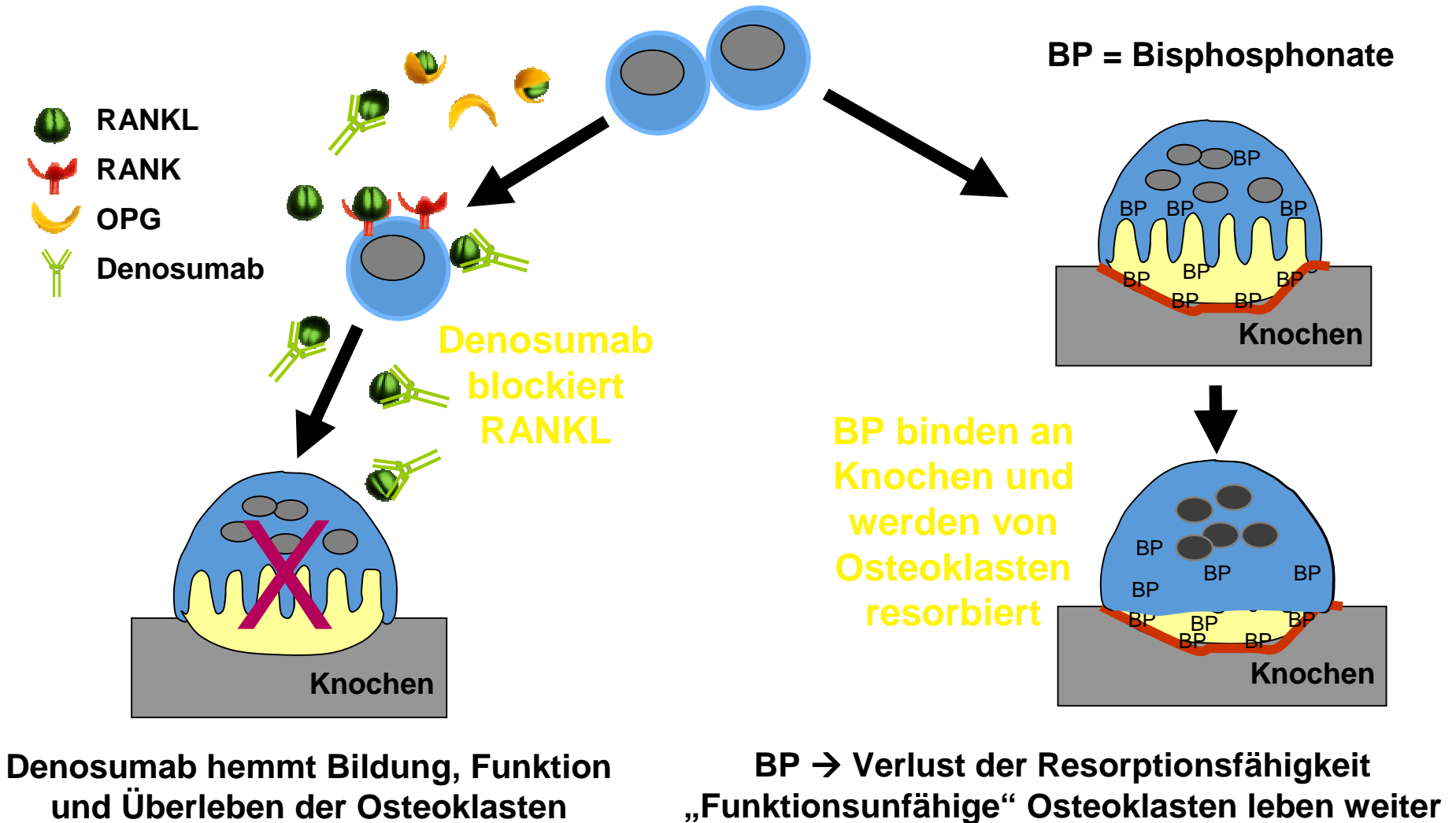
## Aktivität der Osteoklasten

Hofbauer L *et al.* *JAMA* 2004; 292: 490-495; Lacey D *et al.* *Cell* 1998; 93: 165-176; Boyle W *et al.* *Nature* 2003; 423: 337-342

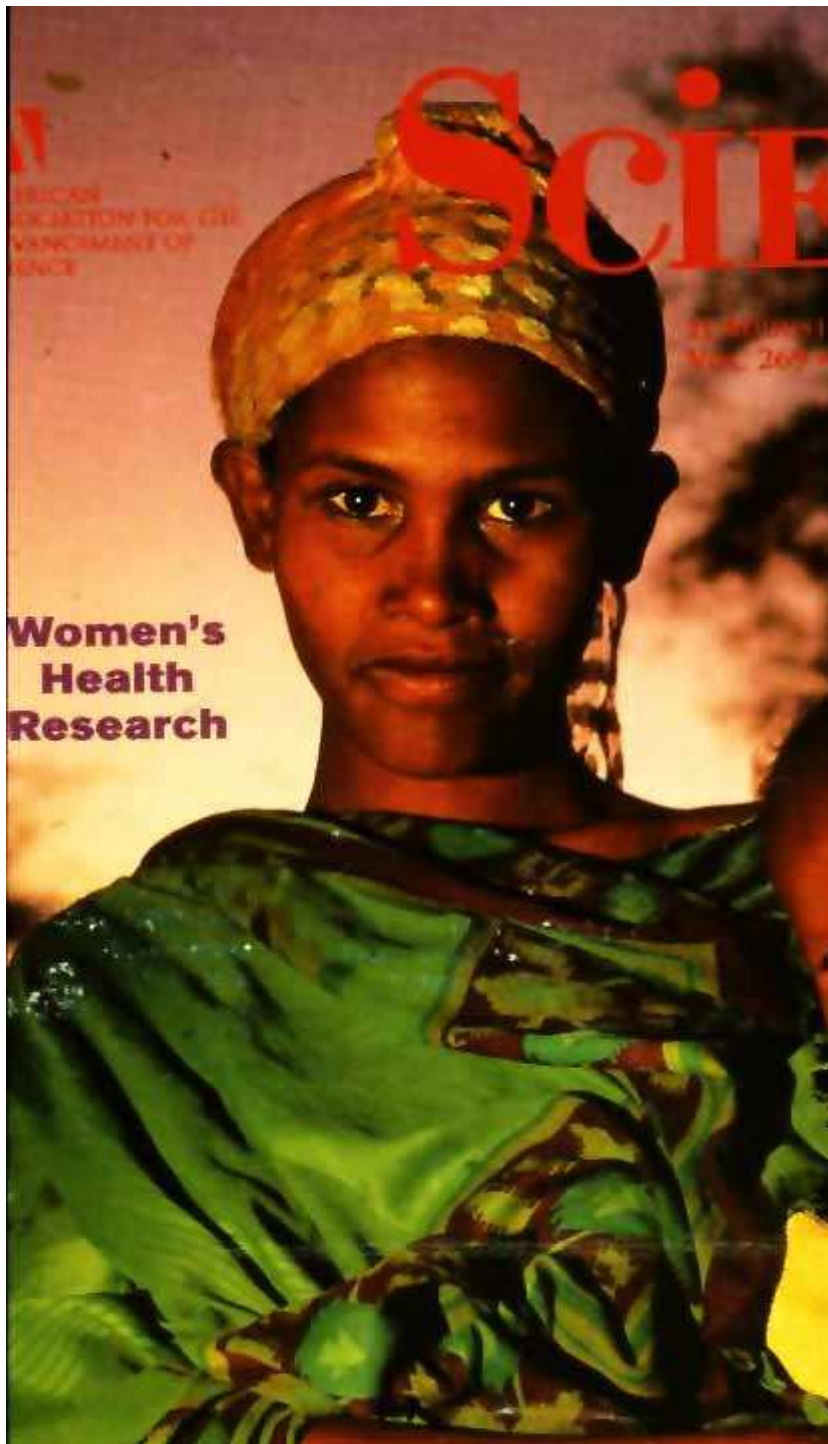
# Denosumab hemmt RANKL und Knochenabbau



# sich grundlegend im Wirkmechanismus







*Gynecol Endocrinol* 1998;12:1-6.

## Gender-specific medicine. The new profile of gynecology

*D. M. Gruber and J. C. Huber*

*Department of Gynecology and Obstetrics, Division of Gynecological Endocrinology and Reproductive Medicine, University of Vienna, Vienna, Austria*

Key words: GENDER-SPECIFIC MEDICINE, ENDOCRINE SYSTEM, REPRODUCTION

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### ABSTRACT

*The science of gynecology is undergoing a change and is promoted the vaginal radical hysterectomy. Two*