GIBT ES EIN GENETISCHES MENOPAUSENPROGRAMM ?

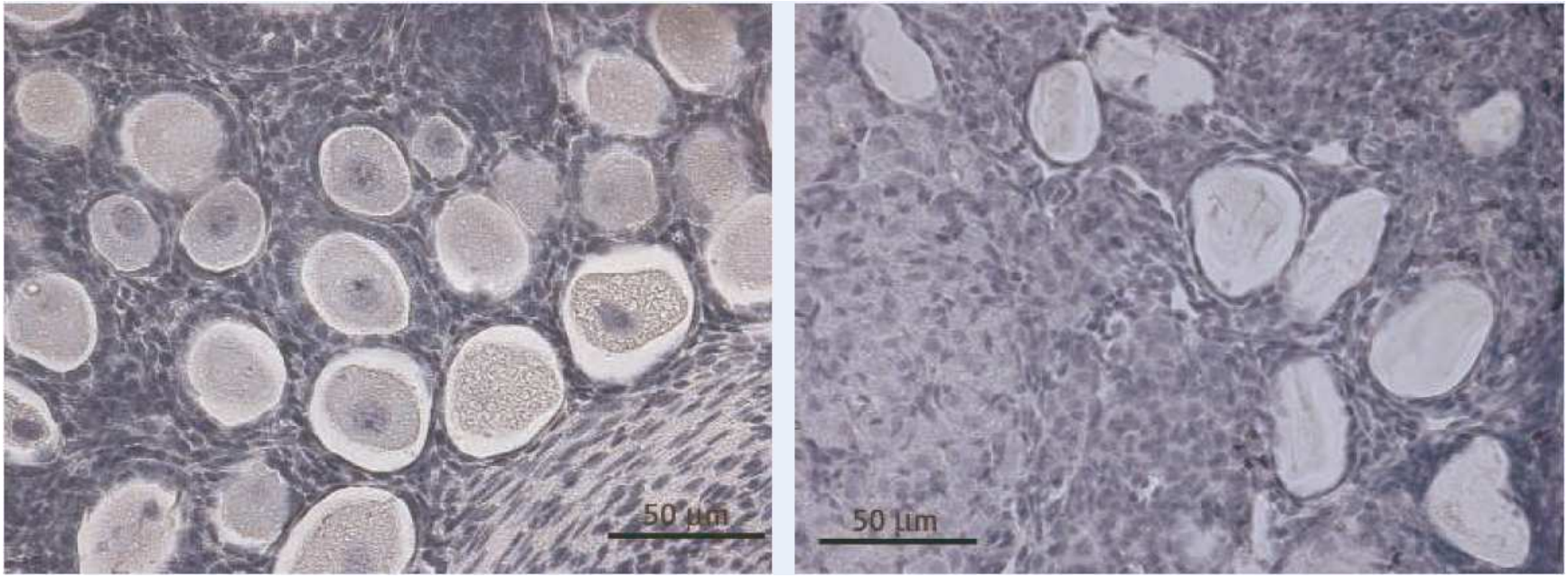
DEVELOPMENTAL BIOLOGY

Aging of the Ovary Linked to PTEN Pathway

When a woman is born, her ovaries already contain a full supply of the immature eggs she will need in her reproductive lifetime. Normally, these eggs begin ripening at about age 13 and are gradually released, usually at the rate of one per month, until she is about 50 years old. But in a small minority of women, perhaps 1 in 100, the ovaries stop releasing eggs much earlier in premature ovarian failure (POF) in humans.

"It is a very nice piece of work that shows the importance of the PTEN pathway" in controlling follicle maturation in mice, says reproductive geneticist Aleksandar Rajkovic of Baylor College of Medicine in Houston, Texas. If *PTEN* also controls human egg maturation, the finding may aid the design of improved infertility treatments.

Marx J, Science. 2008 Feb 1;319(5863):558-9.

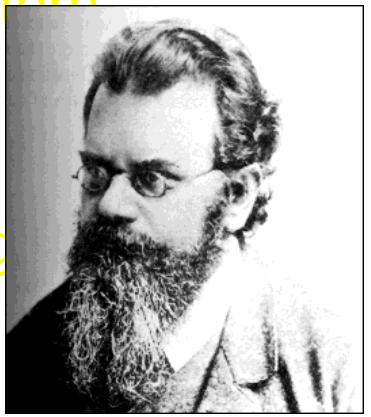


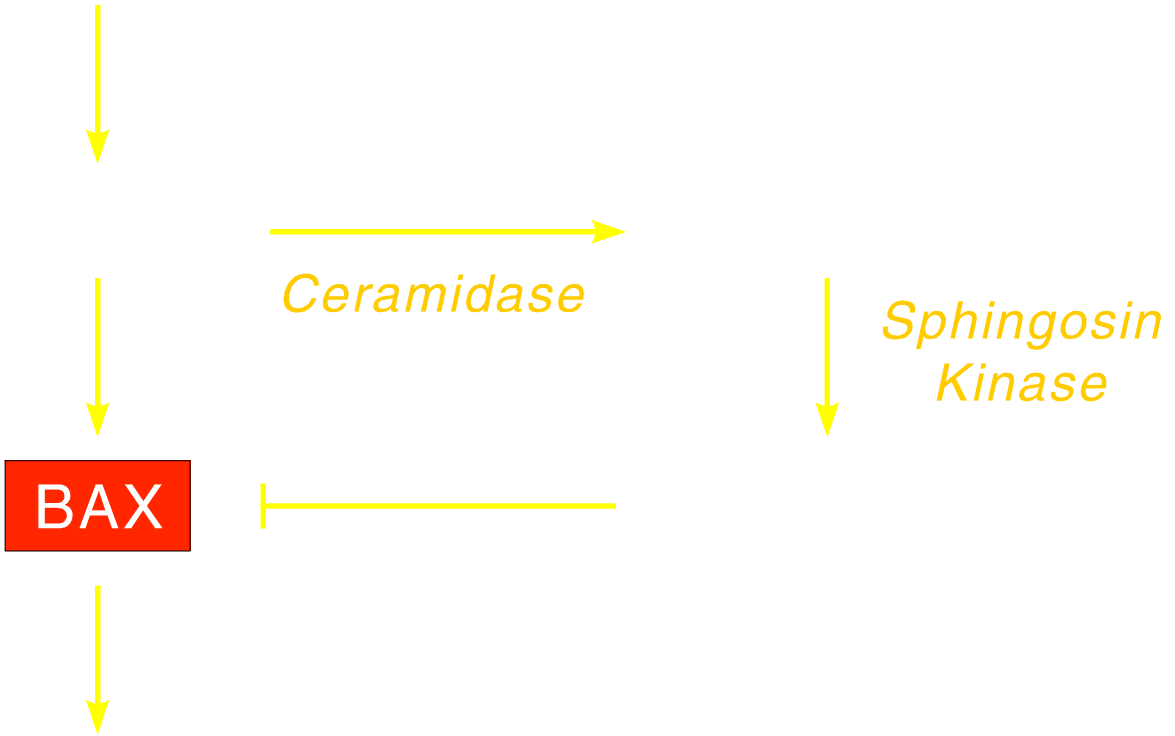
Mouse ovarian tissue in which *Pten* was inactivated in oocytes (*left*) shows many activated follicles just 8 days after birth.
But by 12 weeks (*right*), the mouse ovaries are depleted of follicles.

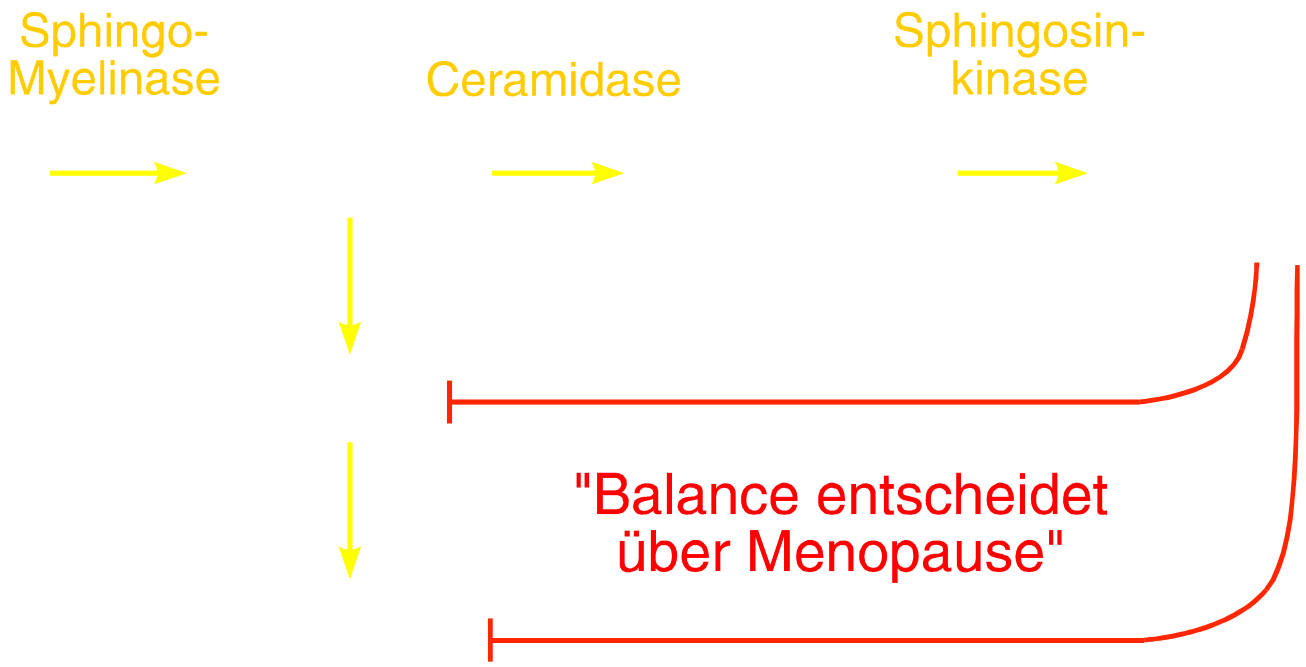
Marx J, Science. 2008 Feb 1;319(5863):558-9.

Lebensdauer korreliert mit notwendiger Brutpflege

- Reproduktives Altern hängt mit somatischen Altern zusammen
- Keimdrüsen altern nicht zufällig
- Endogene Programme der Keimdrüsenalterung hängen mit somatischer Alterung zusammen.
- Zentrale Peptide scheinen beides zu steuern




Ceramidase
Sphingosin
Kinase
BAX



Nature Medicine 6, 1101

Absence of the proapoptotic Bax protein extends fertility and alleviates age-related health complications in female mice

Gloria I. Perez*†, Andrea Jurisicova‡, Lisa Wise‡, Tatiana Lipina‡, Marijana Kanisek‡, Allison Bechard‡, Yasushi Takai*, Patricia Hunt§, John Roder‡, Marc Grynpas‡, and Jonathan L. Tilly*¶

*Vincent Center for Reproductive Biology, Vincent Obstetrics and Gynecology Service, Massachusetts General Hospital/Harvard Medical School, Boston, MA 02114; ‡Samuel Lunenfeld Research Institute, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada M5G 1X5; and §Center for Reproductive Biology and School of Molecular Biosciences, Washingston State University, Pullman, WA 99164

Proc Natl Acad Sci U S A. 2007 Mar 20;104(12):5229-34. Epub 2007 Mar 8.

Die Anhebung des weiblichen Menopausenalters würde zahlreiche somatische Funktionen des weiblichen Körpers optimieren.

KO / WT

Keine Unterschiede

in Tumorgenese

Perez GI et al. Proc Natl Acad Sci U S A. 2007 Mar 20;104(12):5229-34. Epub 2007 Mar 8.

Further, ovariectomy studies show that the health benefits gained by aged females from Bax deficiency reflect a complex interplay between ovary-dependent and -independent pathways. Importantly, and contrary to popular belief, prolongation of ovarian function into advanced age by Bax deficiency did not lead to an increase in tumor incidence. Thus, the development of methods for postponing ovarian failure at menopause may represent an attractive option for improving the quality of life in aging females.

Perez GI et al. Proc Natl Acad Sci U S A. 2007 Mar 20;104(12):5229-34. Epub 2007 Mar 8.

Die mit zunehmender Lebenszeit vermehrt auftretenden chromosomalen Aberrationen in den Oozyten entstehen nicht zufällig – sie sind sind Folge eines aktivierten Apoptoseprogrammes

Preliminary studies showed that the incidence of aneuploidy in oocytes of WT females increased from 1.4 to 4.5% between 1 (n 72 oocytes) and 8 (n 67 oocytes) mo of age, although this difference was not statistically different (P 0.05) by χ^2 analysis.
Further, the incidence of aneuploidy in oocytes of KO females remained relatively constant between 1 (3.7%, n54 oocytes) and 8 mo (3.1%, n 32 oocytes) of age, and thus the observed genotype-dependent differences in reproductive capacity could not be attributed to differences in aneuploidy.

Perez GI et al. Proc Natl Acad Sci U S A. 2007 Mar 20;104(12):5229-34. Epub 2007 Mar 8.

KO - Mäuse

Zunehmende Fertilität
mit zunehmendem Lebensalter

Alter:	2 Monate	25% wurden schwanger
	9 Monate	90% wurden schwanger (WT 20%)

(später – aber länger reproduktionsfähig)

Perez GI et al. Proc Natl Acad Sci U S A. 2007 Mar 20;104(12):5229-34. Epub 2007 Mar 8.

Absence of the proapoptotic Bax protein extends fertility and alleviates age-related health complications in female mice

Gloria I. Perez*†, Andrea Jurisicova‡, Lisa Wise‡, Tatiana Lipina‡, Marijana Kanisek‡, Allison Bechard‡, Yasushi Takai*, Patricia Hunt§, John Roder‡, Marc Grynpas‡, and Jonathan L. Tilly*¶

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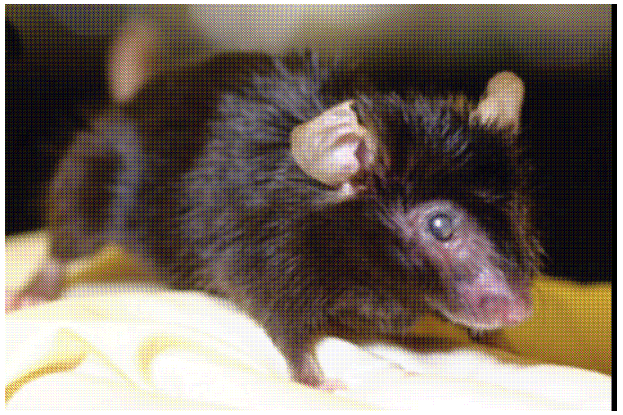
Therefore, development of methods for postponing ovarian failure at menopause may represent an attractive option for improving the quality of life in aging females.

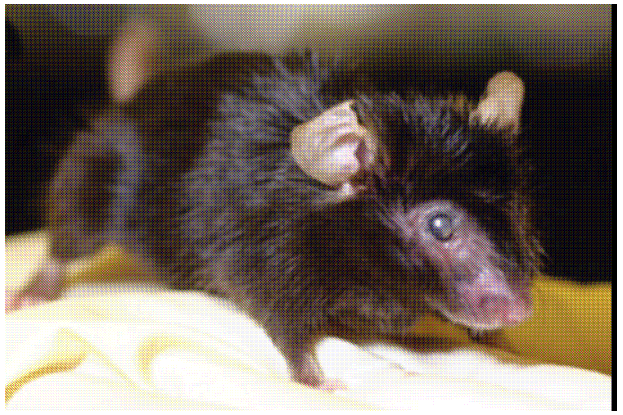


Perez GI et al. Proc Natl Acad Sci U S A. 2007 Mar 20;104(12):5229-34. Epub 2007 Mar 8.

KO / WT

Signifikante Unterschiede in

- Alopezie
- Katarakt
- Rektaler Prolaps
- Hautdicke



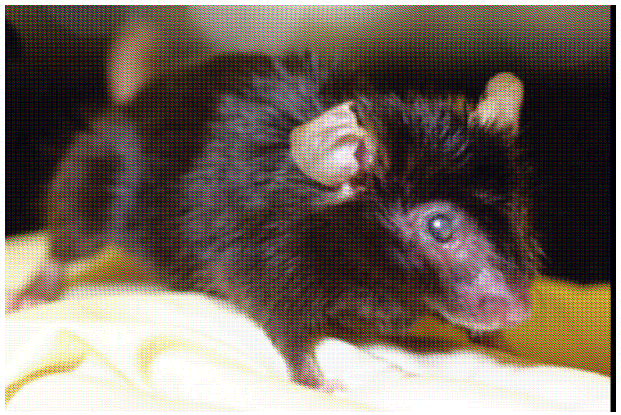
Perez GI et al. Proc Natl Acad Sci U S A. 2007 Mar 20;104(12):5229-34. Epub 2007 Mar 8.

KO / Mäuse

Höhere Vigilanz

besseres Gedächtnis

schärfere Hörfunktionen

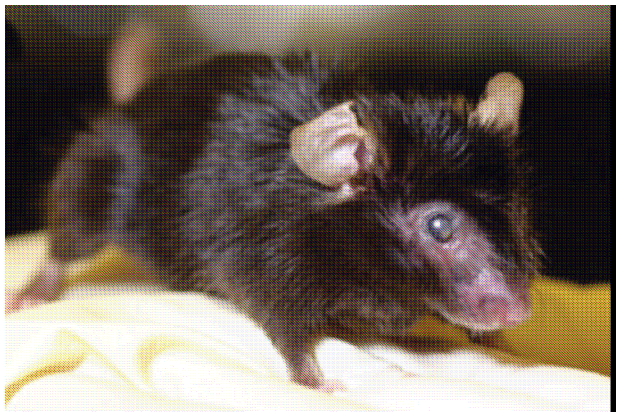


Perez GI et al. Proc Natl Acad Sci U S A. 2007 Mar 20;104(12):5229-34. Epub 2007 Mar 8.

KO / Mäuse

Trabekulare Knochenmasse

signifikant besser



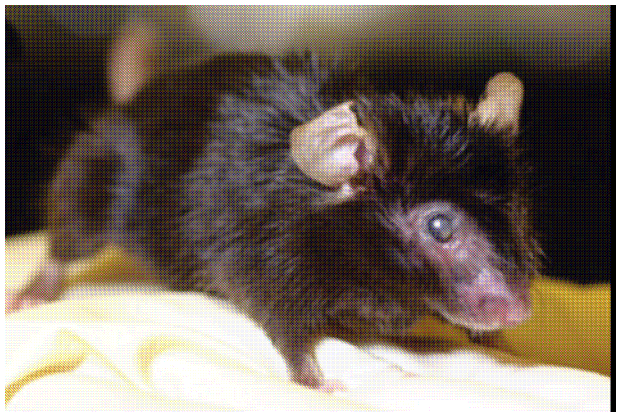
Perez GI et al. Proc Natl Acad Sci U S A. 2007 Mar 20;104(12):5229-34. Epub 2007 Mar 8.

WT / KO

keine Muskel

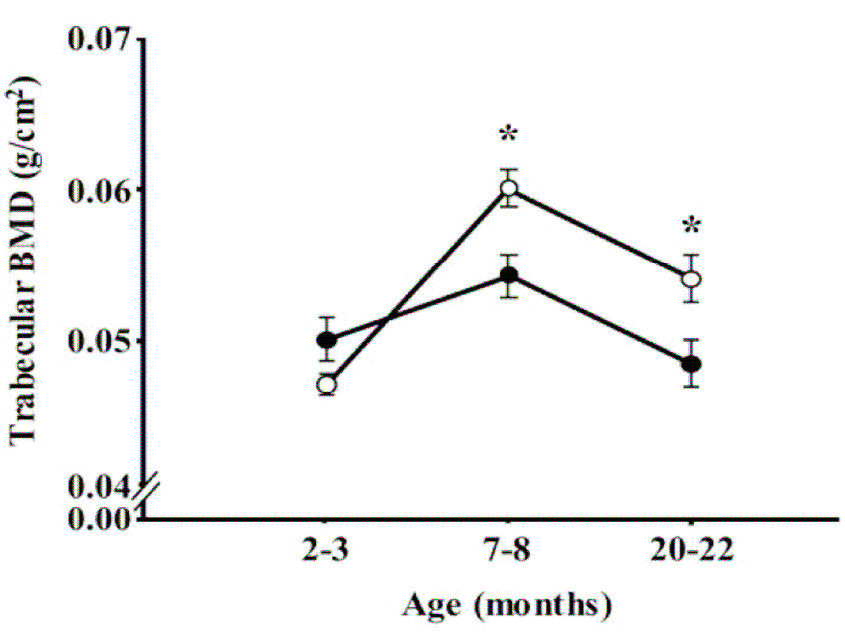
zu Fettverschiebung

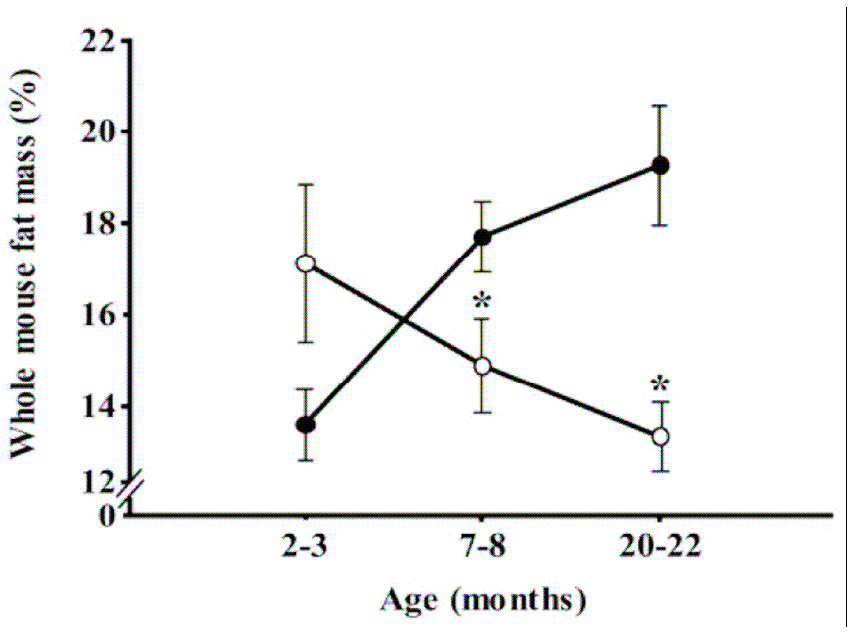
in KO - Mäusen



Perez GI et al. Proc Natl Acad Sci U S A. 2007 Mar 20;104(12):5229-34. Epub 2007 Mar 8.

Changes in body composition with age

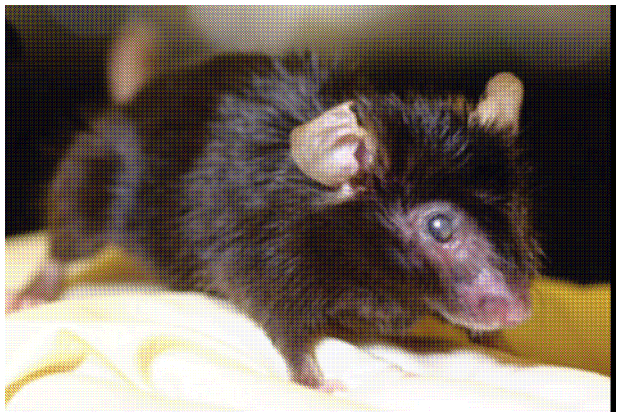




KO / Mäuse

Kein FSH – Anstieg

im Alter



Perez GI et al. Proc Natl Acad Sci U S A. 2007 Mar 20;104(12):5229-34. Epub 2007 Mar 8.

Chronologie der ovariellen Insuffizienz

1. Inhibin B ↓
2. FSH ↑
3. Östradiol ↓

Martin TJ et al. Nat Med. 2006 Jun;12(6):612-3.

BEI FEHLENDEM BAX BLEIBT DER FSH ANSTIEG AUS

SOLL MAN DEN FSH ANSTIEG VERHINDERN ?

Effects of pretreatment with estrogens on ovarian stimulation with gonadotropins in women with premature ovarian failure: a randomized, placebo-controlled trial

Massimo Tartagni, M.D.,[a] *Ettore Cicinelli, M.D.,*[b] *Giovanni De Pergola, M.D.,*[c] *Maria Antonietta De Salvia, Ph.D.,*[d] *Cristina Lavopa, M.D.,*[a] *and Giuseppe Loverro, M.D.*[a]

[a] Clinica Ostetrica e Ginecologica III, [b] Clinica Ostetrica e Ginecologica, [c] Istituto di Clinica Medica, Endocrinologia, e Malattie Metaboliche, and [d] Sezione di Farmacologia, Dipartimento di Farmacologia e Fisiologia Umana, Policlinico di Bari, Università di Bari, Bari, Italy

Fertil Steril. 2007 Apr;87(4):858-61. Epub 2007 Jan 29.

Characteristics and basal hormonal assessment in patients of group 1 and group 2.

No. of patients	Age (y)	Amenorrea (mo)	BMI (kg/m^2)	Family history	FSH (mIU/mL)
25 (group 1)	32.9 ± 3.9[a]	16.9 ± 9.05[a]	22.9 ± 5.7[a]	5	68.24 ± 20.03[a]
25 (group 2)	32.5 ± 4.8[a]	16.6 ± 9.99[a]	22.7 ± 5.9[a]	4	67.8 ± 19.5[a]

[a] Values are mean ± SD.

Tartagni. Estrogens and pregnancy in POF. Fertil Steril 2007.

Follicle-stimulating hormone and E_2 assessment at pretherapy and at beginning of stimulation.

	Group 1	Group 2
Patients (n)	25	25
FSH (mUI/mL), pretherapy	68.32 ± 20.01[a]	67.80 ± 19.58[a]
FSH (mUI/mL) beginning of stimulation	15.64 ± 5.34[a,b]	65.44 ± 14.85[a]
E_2 (pg/mL), beginning of stimulation	13.52 ± 5.1[a]	14.24 ± 4.47[a]
Average FSH (IU), responder patients	4,125	
Average FSH (IU), nonresponder patients	5,800	5,800
Ovulation rate (%)	32[c]	0
Pregnancy rate (%)	50	0

[a] Values are expressed as mean ± SD. NS = not significant.
[b] FSH at beginning of stimulation is $P<.001$, versus pretherapy in group 1.
[c] Ovulation rate in group 1 is $P<.005$, versus group 2.

Tartagni. Estrogens and pregnancy in POF. Fertil Steril 2007.

- 50 MCG EE 3x1/d für 2 Wochen
- FSH 200 IV/d

Fertility and Sterility, 2007;87(4).

FSH ANSTIEG IST
FÜR DIE VERSTÄRKTE
OSTEOKLASTENAKTIVITÄT
VERANTWORTLICH

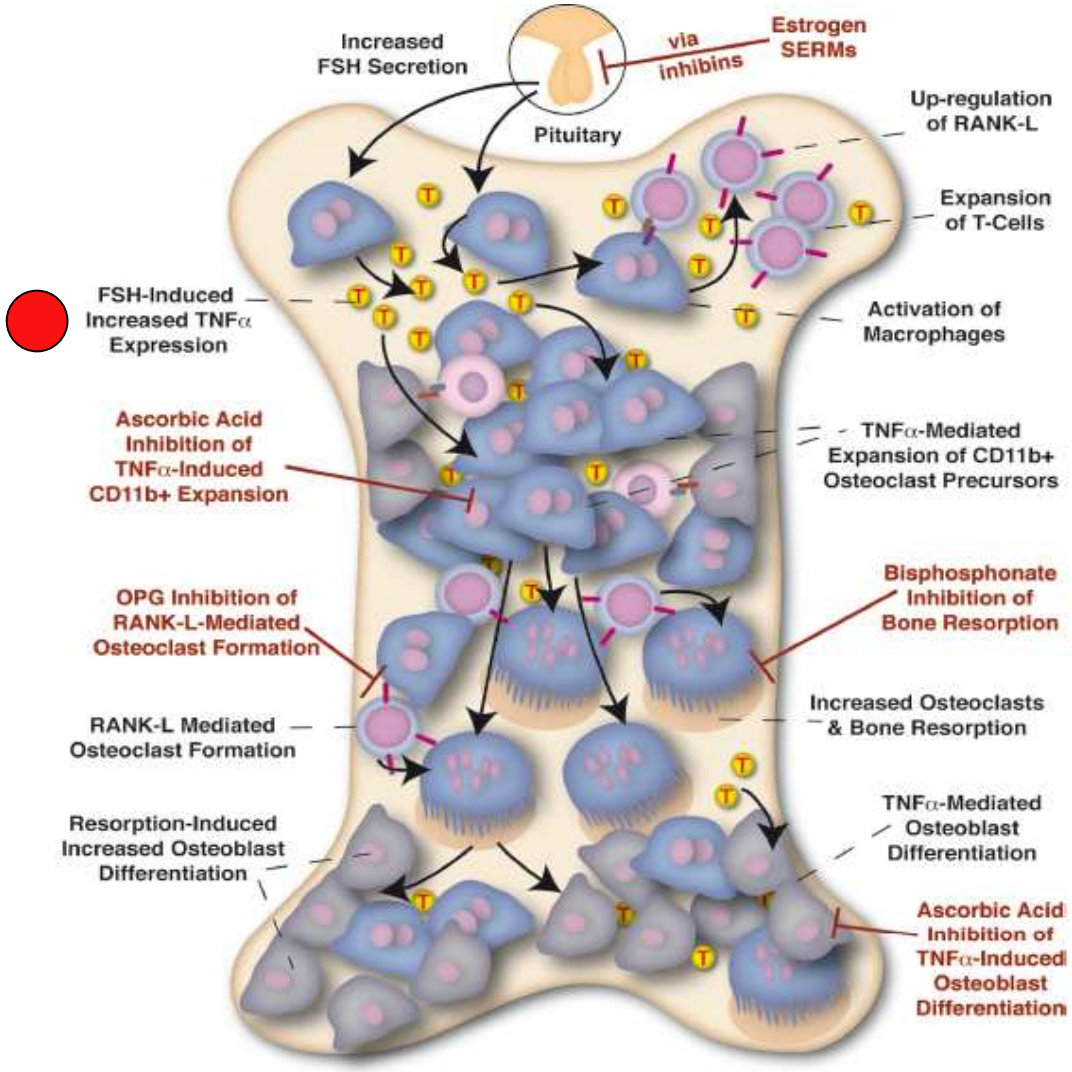
Follicle-stimulating hormone stimulates TNF production from immune cells to enhance osteoblast and osteoclast formation

Jameel Iqbal*, Li Sun*, T. Rajendra Kumar†, Harry C. Blair‡, and Mone Zaidi*§

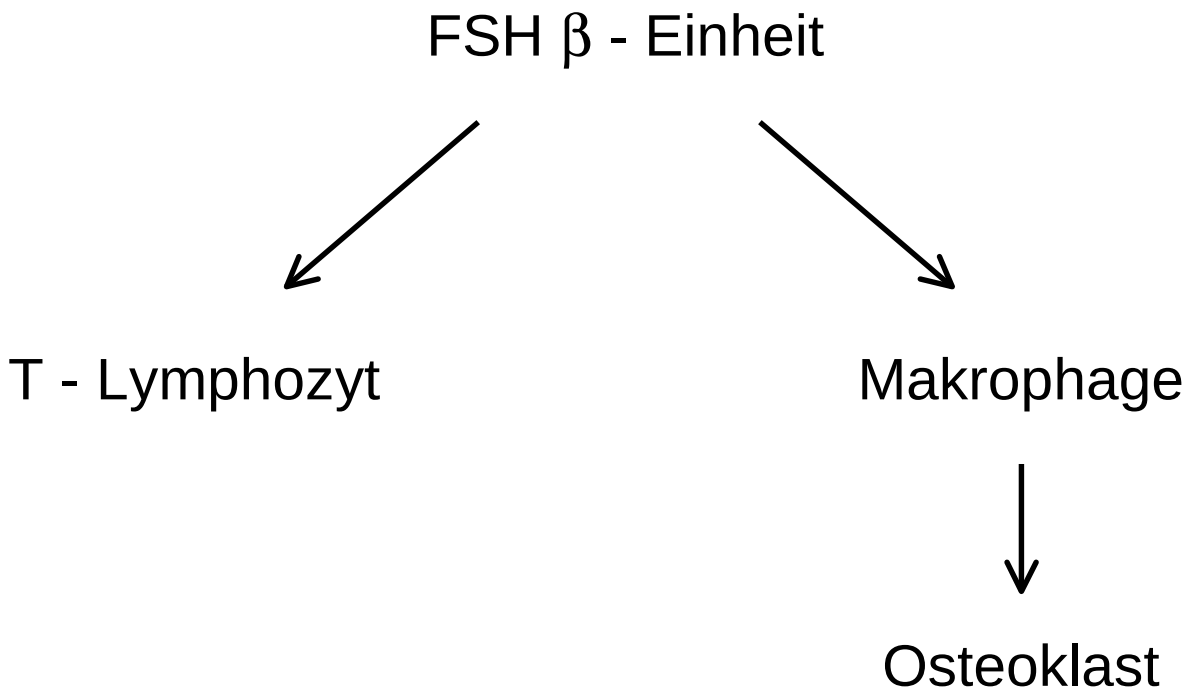
*Mount Sinai Bone Program, Department of Medicine, Mount Sinai School of Medicine, New York, NY 10029; †Department of Molecular and Integrative Physiology, University of Kansas Medical Center, Kansas City, KS 66160; and ‡Departments of Pathology and Cell Biology, University of Pittsburgh School of Medicine and Pittsburgh Veterans Affairs Medical Center, Pittsburgh, PA 15261

Proc Natl Acad Sci U S A. 2006 Oct 3;103(40):14925-30. Epub 2006 Sep 26.

Integrated hypothesis for hypogonadal bone loss



Iqbal J et al. Proc Natl Acad Sci U S A. 2006 Oct 3;103(40):14925-30. Epub 2006 Sep 26.



Iqbal J et al. Proc Natl Acad Sci U S A. 2006 Oct 3;103(40):14925-30. Epub 2006 Sep 26.

FSH Directly Regulates Bone Mass

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

[1]Mount Sinai Bone Program, Department of Medicine and Department of Orthopedics, Mount Sinai School of Medicine, New York, NY 10029, USA

[2]Departments of Pathology and Cell Biology, University of Pittsburgh, Pittsburgh, PA 15261, USA

[3]VA Medical Center, Pittsburgh, PA 15261, USA

[4]Department of Anatomy and Histology, University of Bari, 70124 Bari, Italy

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[7]Department of Pathology, University of California, Los Angeles, Los Angeles, CA 90095, USA

*Contact: hcblair@imap.upitt.edu (H.C.B.); mone.zaidi@mssm.edu (M.Z.)

DOI 10.1016/j.cell.2006.01.051

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

Pathophysiologically, the results suggest that the bone loss during early menopause and in hypogonadism, which has been attributed solely to declining sex hormone levels, may result at least in significant part from elevated circulating FSH. There is no correlation between the serum levels of estrogen and markers of bone resorption (Riggs et al., 2002; Khosla et al., 1998). Instead, there is a strong correlation between rising serum FSH levels and elevated bone resorption markers in early menopause (Sowers et al., 2003). Furthermore, BMD is lower in hypergonadotrophic amenorrheic women with high circulating FSH compared with amenorrheic females with normal or low FSH levels (Devleta et al., 2004). Postmenopausal serum FSH levels (Padmanabhan et al., 1989) correspond to concentrations that stimulate human osteoclasts in vitro. Finally, reduced FSH levels and increased BMD correlate well following estrogen replacement therapy (Kawai et al., 2004). Thus, we speculate that a high circulating FSH causes postmenopausal and hypogonadal osteoporosis.

Sun L et al. Cell. 2006 Apr 21;125(2):247-60.

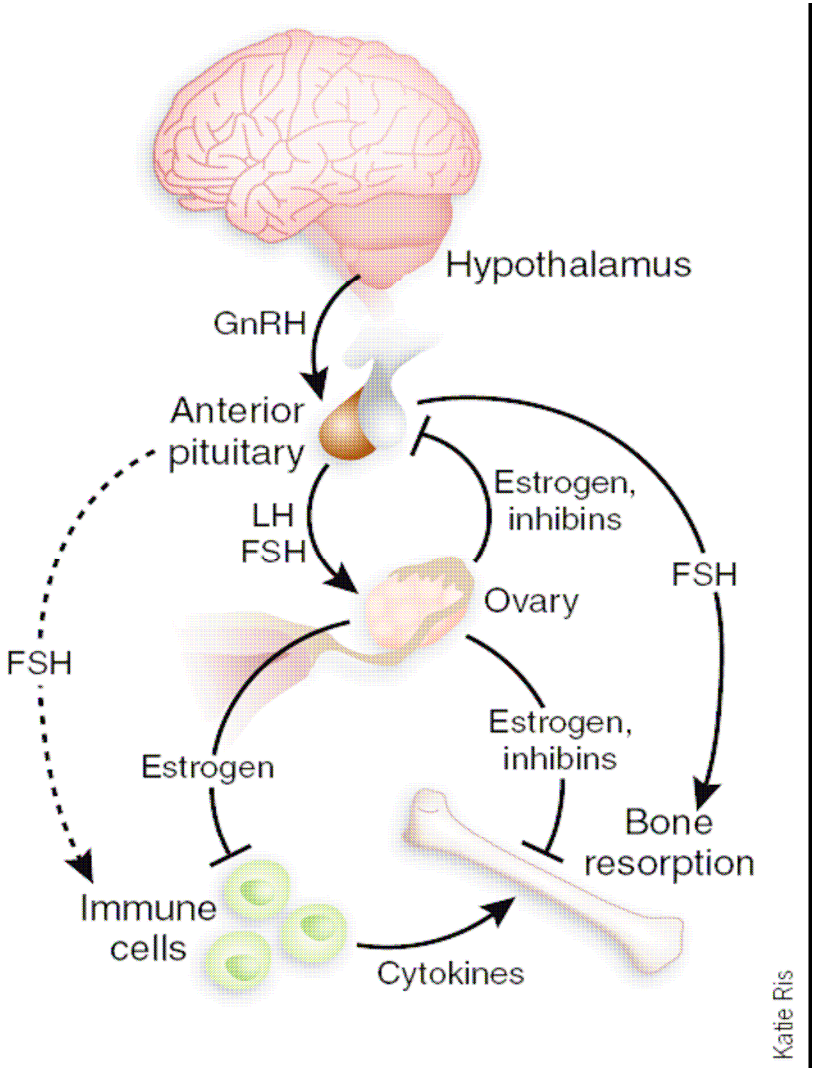
Bone loss goes beyond estrogen

T John Martin & Dana Gaddy

The central position of estrogen in the physiological and pharmacological control of bone resorption is now challenged by evidence from mouse genetics of estrogen-independent control by pituitary FSH.

Nat Med. 2006 Jun;12(6):612-3

The potential effects of FSH on the skeleton *in vivo*, either directly upon bone or indirectly



Martin TJ et al. Nat Med. 2006 Jun;12(6):612-3

FSH - Rezeptoren

in Osteoklasten –

jedoch nicht in Osteoblasten

Martin TJ et al. Nat Med. 2006 Jun;12(6):612-3.

RANK-Ligand

stimuliert FSH-Rezeptoren

in Osteoklast

FSH Rezeptor ist inflammatorische Adresse

Martin TJ et al. Nat Med. 2006 Jun;12(6):612-3.

Mangel an FSH-Rezeptoren

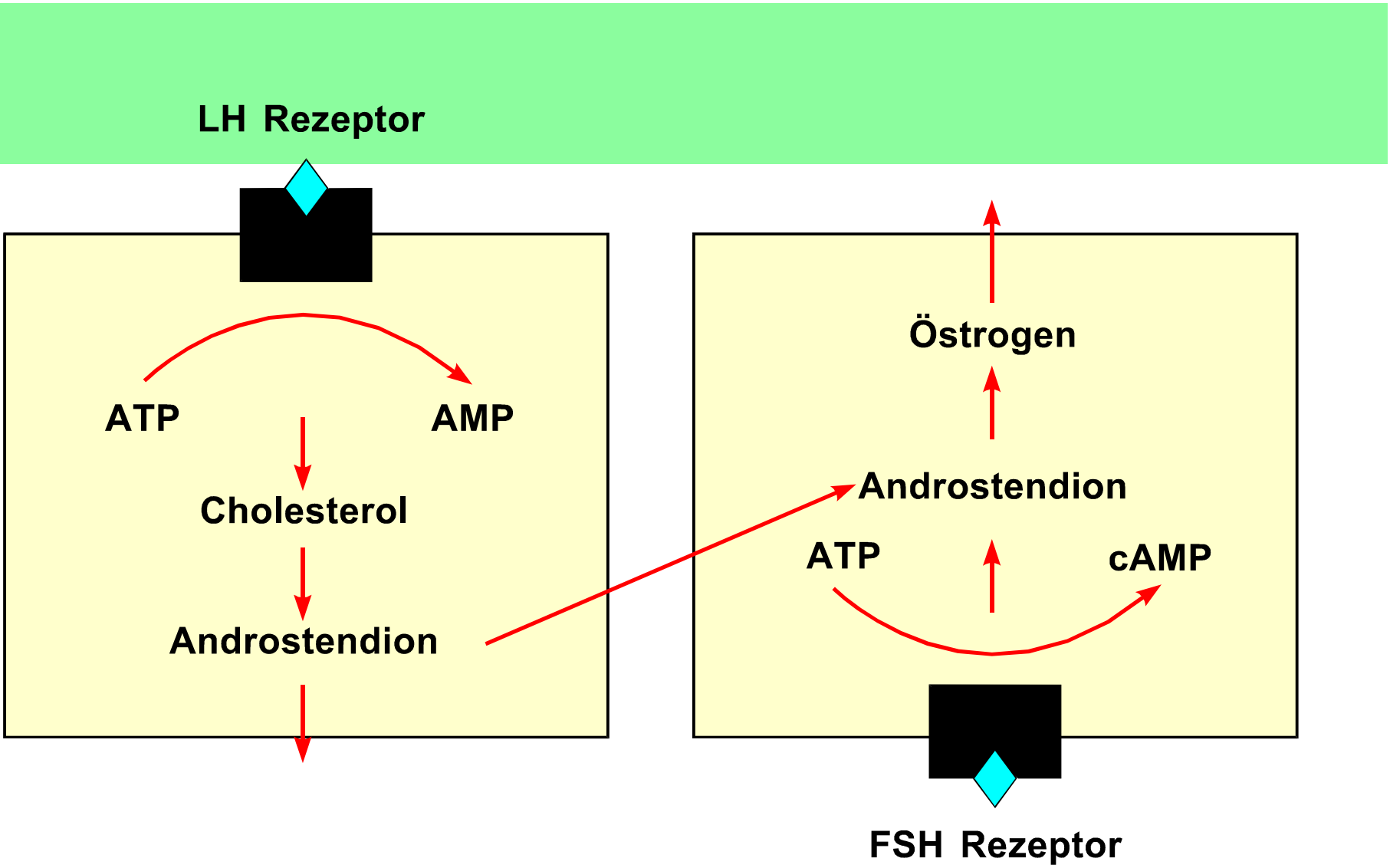
erhöht

Testosteronkonzentration

um das Zehnfache

Testosteron – anabol FSH katabol

Martin TJ et al. Nat Med. 2006 Jun;12(6):612-3.


LH Rezeptor
ATP
AMP
Cholesterol
Androstendion
Östrogen
Androstendion
ATP
cAMP
FSH Rezeptor

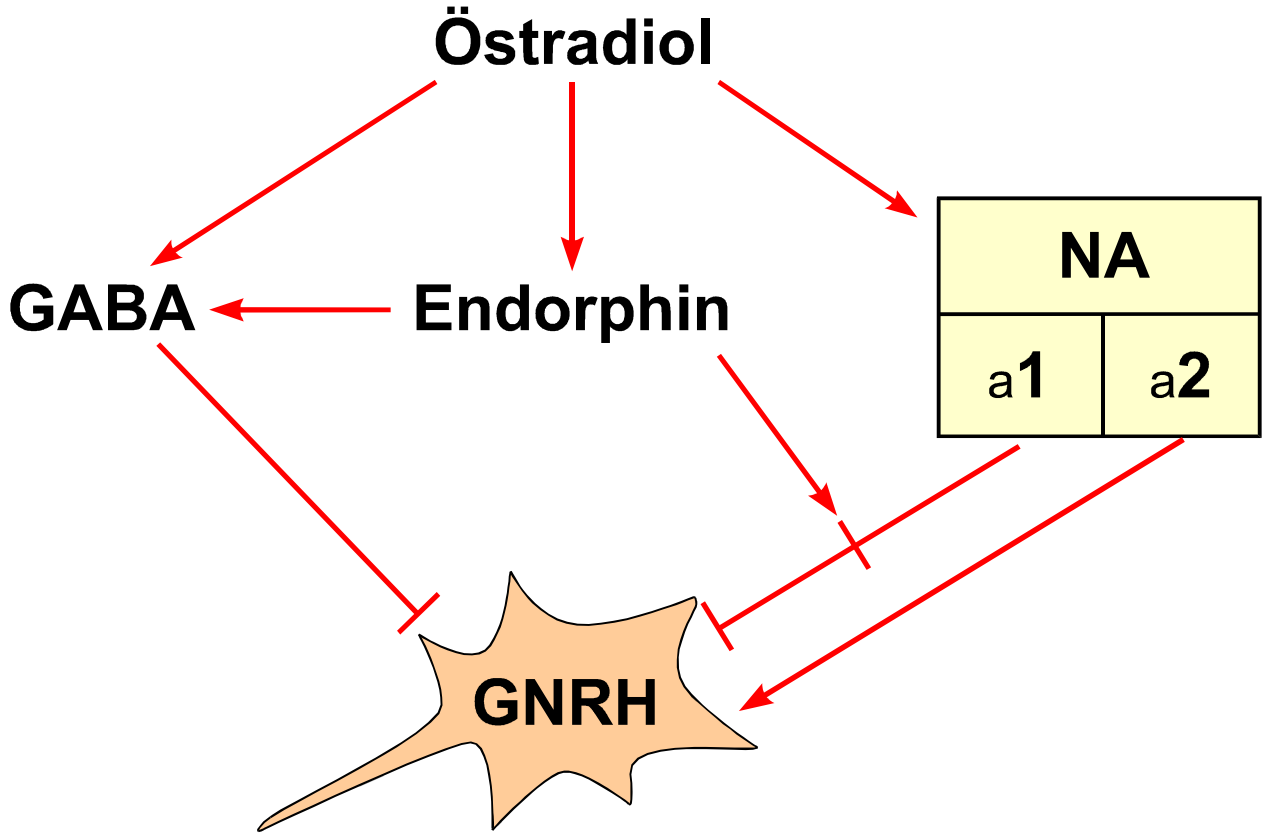
Hypoöstrogene

FSH - O - Mäuse

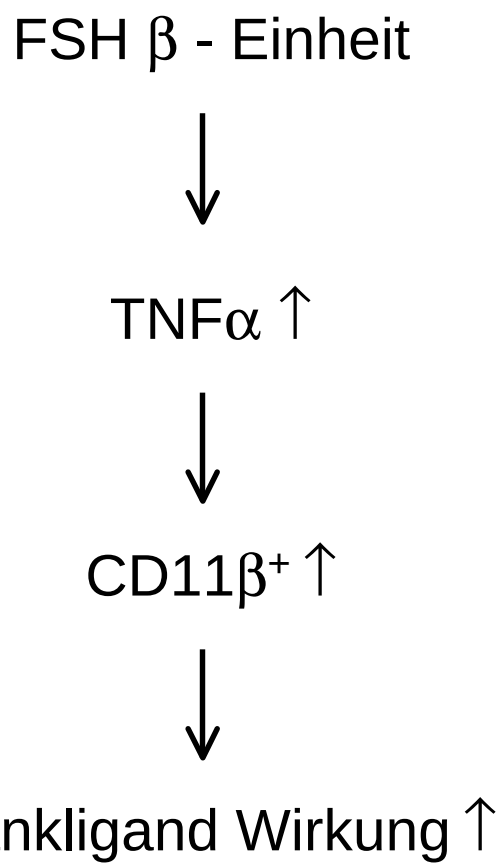
haben keine Osteoporose,

wenn Androgene normal

Iqbal J et al. Proc Natl Acad Sci U S A. 2006 Oct 3;103(40):14925-30. Epub 2006 Sep 26.



Die GNRH Impulshöhe beeinflußt die Gonadotropin-Kettenexpression; Psyche und Katabolismus



Iqbal J et al. Proc Natl Acad Sci U S A. 2006 Oct 3;103(40):14925-30. Epub 2006 Sep 26.

Hypergonadotropinämie erzeugt

proinflammatorisches Milieu

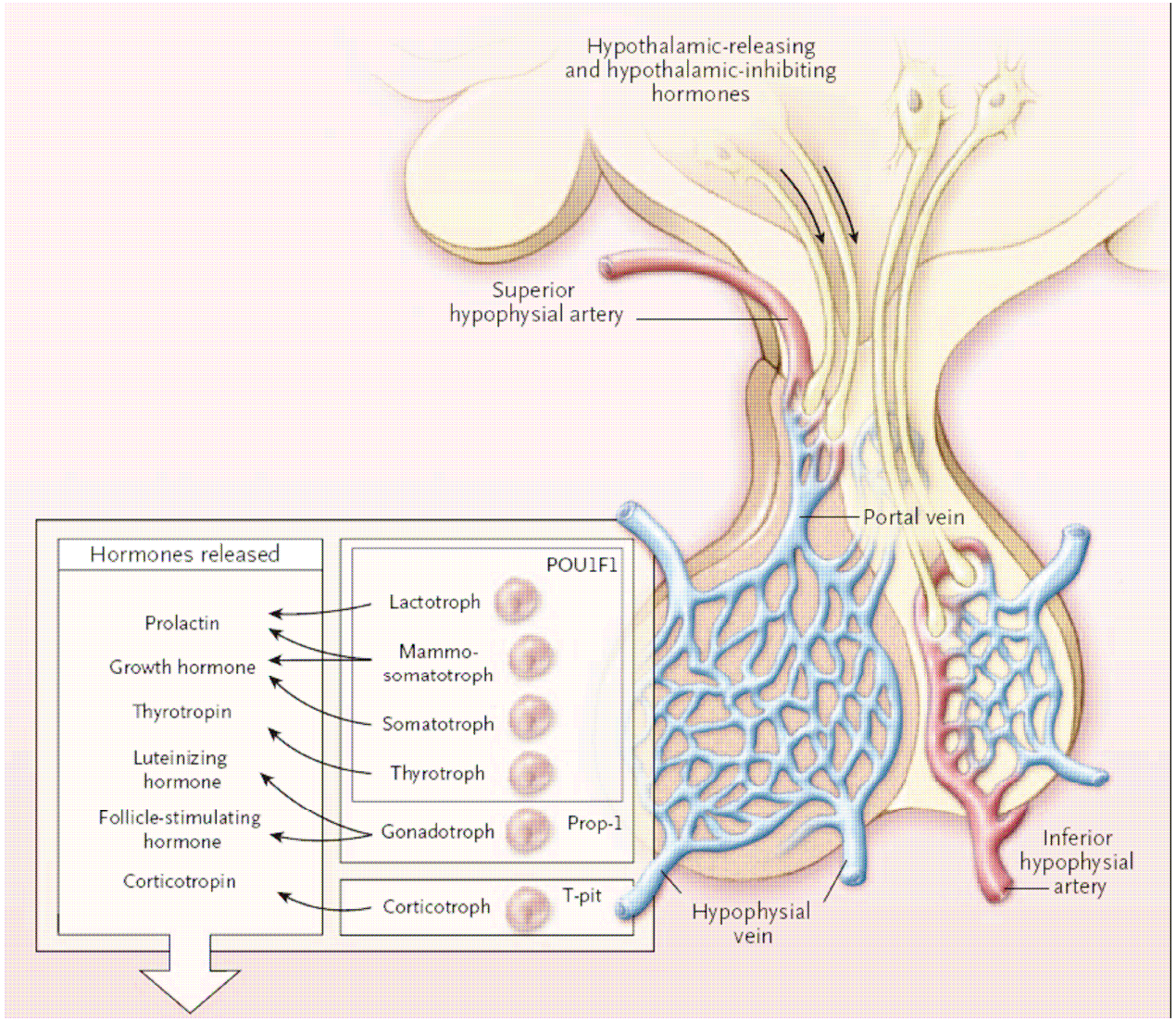
Iqbal J et al. Proc Natl Acad Sci U S A. 2006 Oct 3;103(40):14925-30. Epub 2006 Sep 26.

Ascorbin hemmt

TNFα induzierten

CD11β^{+} Anstieg

Iqbal J et al. Proc Natl Acad Sci U S A. 2006 Oct 3;103(40):14925-30. Epub 2006 Sep 26.


Hypothalamic-releasing and hypothalamic-inhibiting hormones
Superior hypophysial artery
Portal vein
Hormones released
Prolactin
Growth hormone
Thyrotropin
Luteinizing hormone
Follicle-stimulating hormone
Corticotropin
POU1F1
Lactotroph
Mammo-somatotroph
Somatotroph
Thyrotroph
Gonadotroph
Prop-1
Corticotroph
T-pit
Hypophysial vein
Inferior hypophysial artery

Wenn das Mutterherz versagt

Lebensbedrohliche Störung im Wochenbett: Ein Enzym als Übeltäter entlarvt

Den Ursachen eines tragischen, bislang schwer behandelbaren Herzleidens stillender Mütter scheint ein internationales Forscherteam unter deutscher Leitung auf die Spur gekommen zu sein. Die Rede ist von der Postpartum-Kardiomyopathie, einer meist kurz vor oder nach der Niederkunft auftretenden seltenen Herzerkrankung. Bedingt durch eine stark eingeschränkte Durchblutung des Herzmuskelgewebes kommt es dabei zu einer nachhaltigen, oftmals tödlichen Schwächung des Kreislauforgans. Besonders groß ist die Gefahr eines endgültigen Herzversagens bei jenen Frauen, bei denen diese Störung nicht zum ersten Mal auftritt. Denn mit jeder weite-

Enzym Cathepsin D derart außer Kontrolle gerät, konnten die Forscher in weiteren Experimenten aufklären. Der Ursprung allen Übels ist demnach ein von aggressiven Sauerstoffverbindungen ausgehender, übermäßiger oxidativer Stress. Während der Schwangerschaft und der Stillzeit muss sich das Herz in besonderem Maße gegen die Attacken der gefährlichen Sauerstoffabkömmlinge wehren, zumal in diesem Zeitraum – bedingt durch die erhöhte Beanspruchung des Organismus – extrem hohe Mengen solcher Aggressoren anfallen.

Üblicherweise kann der erhöhte oxidative Stress dem Herzen nichts anha-

vollständig abwenden. Vergleichbar günstige Wirkungen hatten auch antioxidative Mittel.

Im zweiten Teil ihrer Untersuchungen wollten die Wissenschaftler herausfinden, inwieweit sich diese Beobachtungen auf den Menschen übertragen lassen. Wie sie berichten, fanden sie bei fünf Müttern, die sich aufgrund einer schweren Postpartum-Kardiomyopathie einer Herztransplantation unterziehen mussten, die gleichen Veränderungen wie bei den herzkranken Mäusen. So enthielt der Herzmuskel der betroffenen Frauen zu geringe Mengen an antioxidativen Eiweißstoffen und deren Blut zu-

Frankfurter Allgemeine Zeitung, 14.Feb 2007, Nr. 38, Seite N2

A Cathepsin D-Cleaved 16 kDa Form of Prolactin Mediates Postpartum Cardiomyopathy

Denise Hilfiker-Kleiner,[1,*] Karol Kaminski,[1] Edith Podewski,[1] Tomasz Bonda,[1] Arnd Schaefer,[1] Karen Sliwa,[3] Olaf Forster,[3] Anja Quint,[1] Ulf Landmesser,[1] Carola Doerries,[1] Maren Luchtefeld,[1] Valeria Poli,[4] Michael D. Schneider,[5] Jean-Luc Balligand,[6] Fanny Desjardins,[6] Aftab Ansari,[7] Ingrid Struman,[8] Ngoc Q.N. Nguyen,[8] Nils H. Zschemisch,[1] Gunnar Klein,[1] Gerd Heusch,[9] Rainer Schulz,[9] Andres Hilfiker,[1,2] and Helmut Drexler[1]

[1]Department of Cardiology and Angiology
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[3]Department of Cardiology, Chris-Hani-Baragwanath Hospital, University of the Witwatersrand, 2013 Soweto, South Africa
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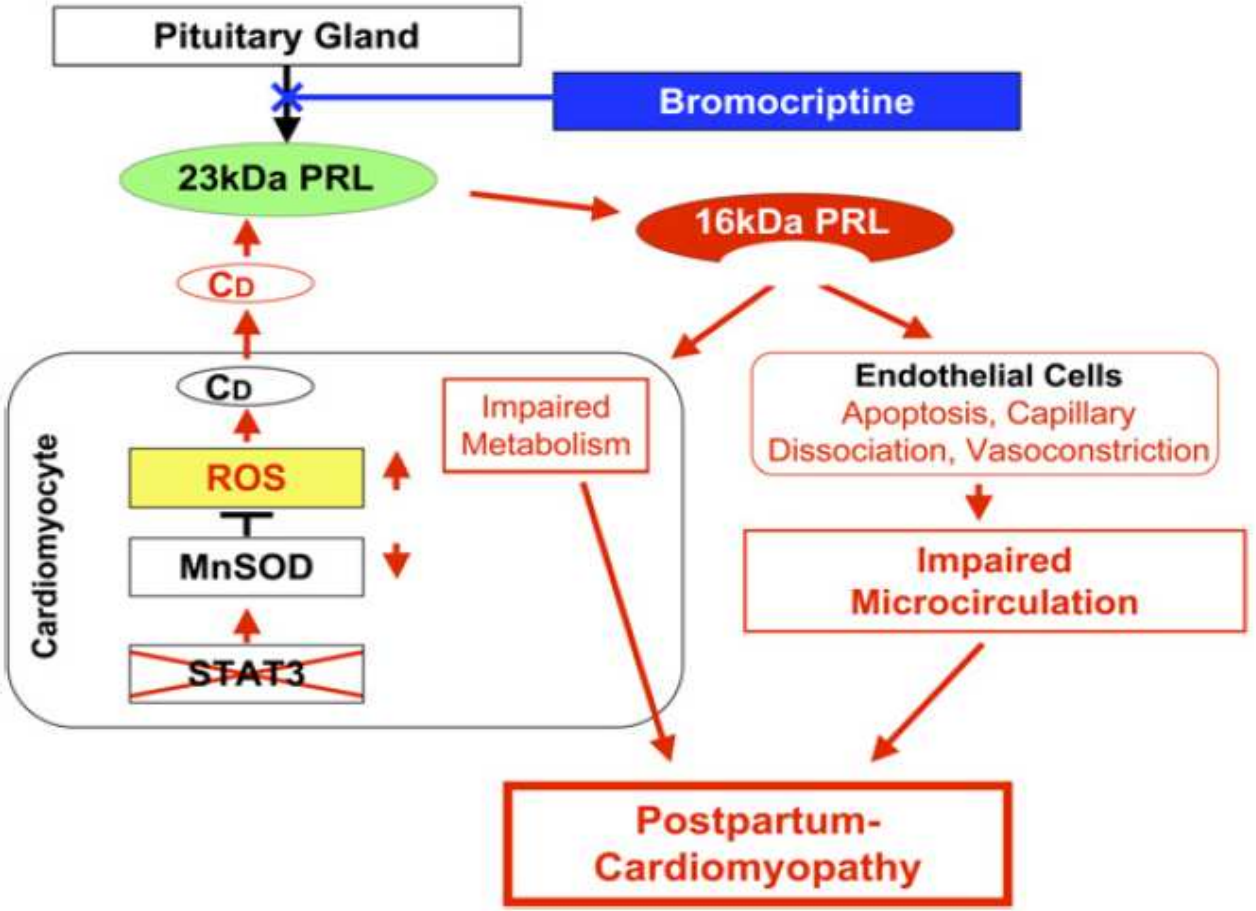
[6]Department of Pharmacology and Therapeutics, University of Louvain Medical School, 1200 Brussels, Belgium
[7]Department of Pathology and Laboratory Medicine, Emory University, Atlanta, GA 30322, USA
[8]Centre of Biomedical Integrative Genoproteomics, Université de Liege, 4000 Sart Tilman, Belgium
[9]Department of Pathophysiology, Universitaetsklinikum, Essen, 45122 Essen, Germany
*Correspondence: hilfiker.denise@mh-hannover.de
DOI 10.1016/j.cell.2006.12.036

Cell. 2007 Feb 9;128(3):589-600.

Schematic Model for the Development of PPCM



Hilfiker-Kleiner D et al. Cell. 2007 Feb 9;128(3):589-600.

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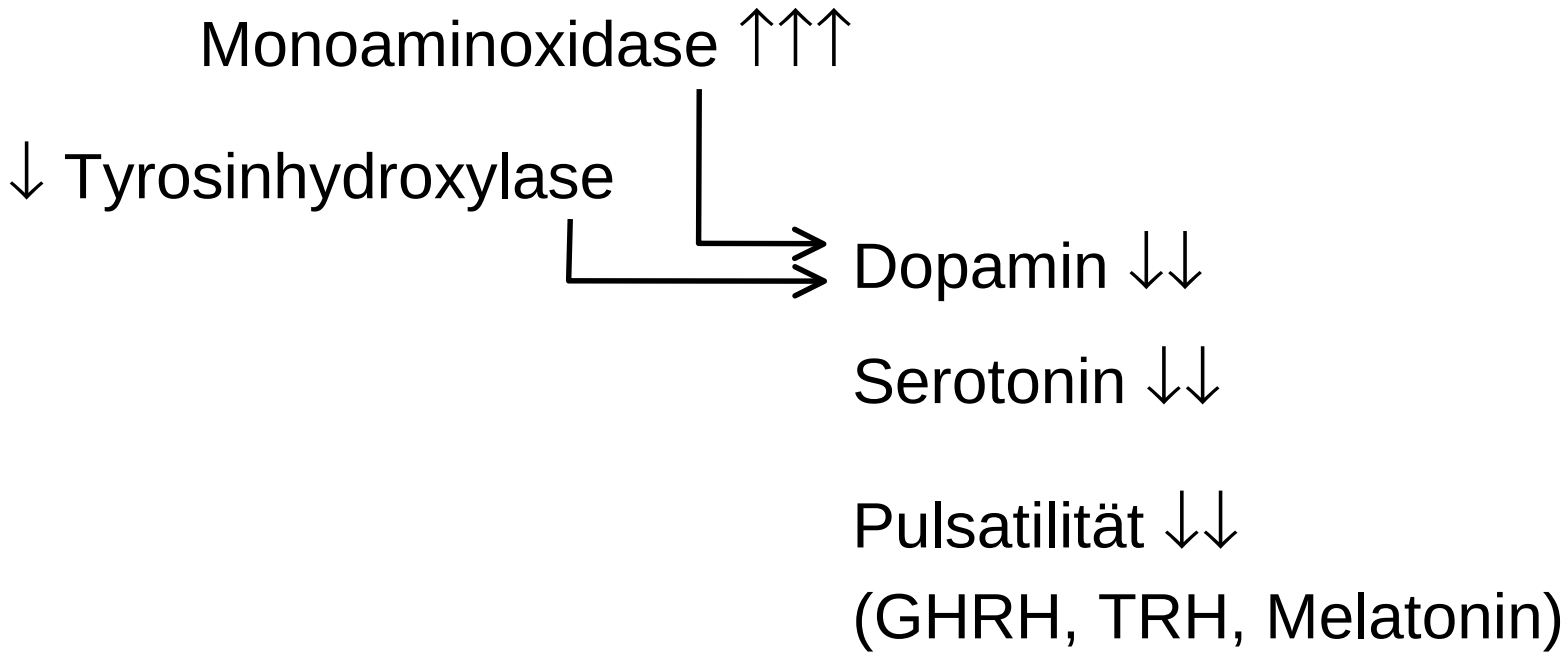


L-Dopa rejuviniert

GHRH – Pulsatilität

TRH – Pulsatilität

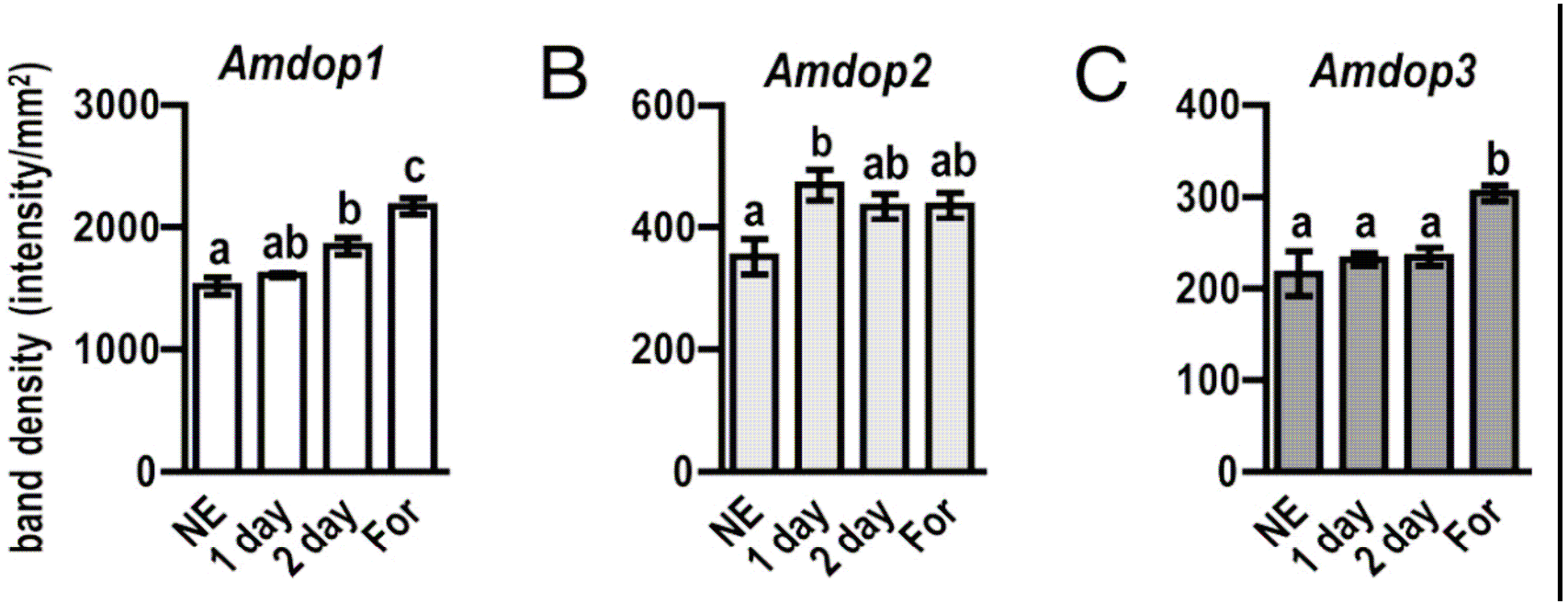
Queen pheromone modulates brain dopamine function in worker honey bees

Kyle T. Beggs*, Kelly A. Glendining*, Nicola M. Marechal*, Vanina Vergoz*, Ikumi Nakamura*, Keith N. Slessor†‡, and Alison R. Mercer*§

*Department of Zoology, University of Otago, P.O. Box 56, Dunedin, New Zealand; and †Department of Chemistry, Simon Fraser University, Burnaby, BC, Canada V5A 1S6

Edited by Gene E. Robinson, University of Illinois at Urbana–Champaign, Urbana, IL, and approved December 18, 2006 (received for review September 19, 2006)

Age-related changes in dopamine receptor gene mRNA levels quantified by Northern blot analysis



Beggs LT et al. PNAS 2007;104(7):2460-2464.

Pergamon

Journal of Insect Physiology 44 (1998) 685–692

Journal of Insect Physiology

Queen mandibular gland pheromone influences worker honey bee (*Apis mellifera* L.) foraging ontogeny and juvenile hormone titers

T. Pankiw [a,*], Z-.Y. Huang [b], M.L. Winston [c], G.E. Robinson [b]

[a] *Department of Entomology, University of California, Davis, CA, 95616, USA*
[b] *Department of Entomology, University of Illinois, Urbana, IL, 61801, USA*
[c] *Department of Biological Sciences, Simon Fraser University, Burnaby, B.C., V5A 1S6, Canada*

Cysteamin unterdrückt

Somatostatin

Adenosin

↓

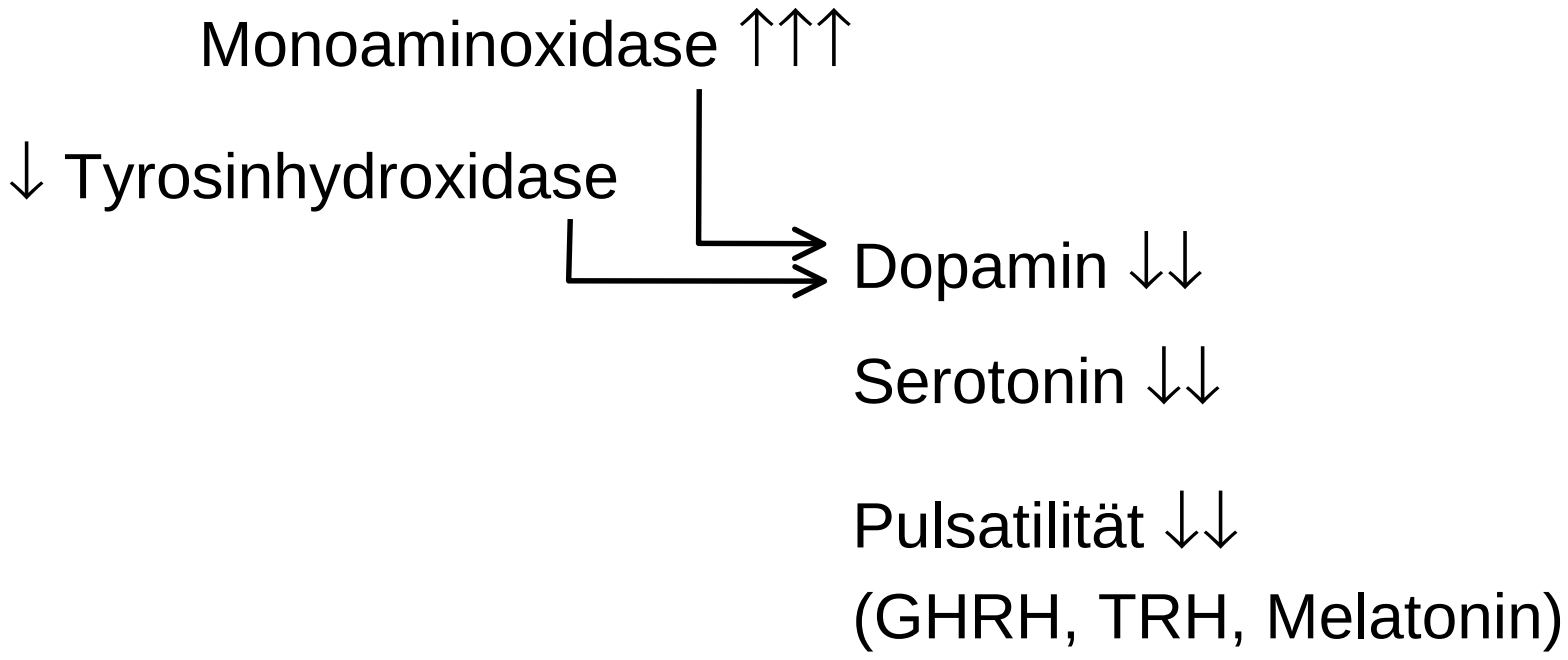
Tyrosinhydroxylase

↓

Katecholamine ↑

Dopamin ↑

Zentrales Altern



Monoaminoxydasehemmer :
Deprenyl

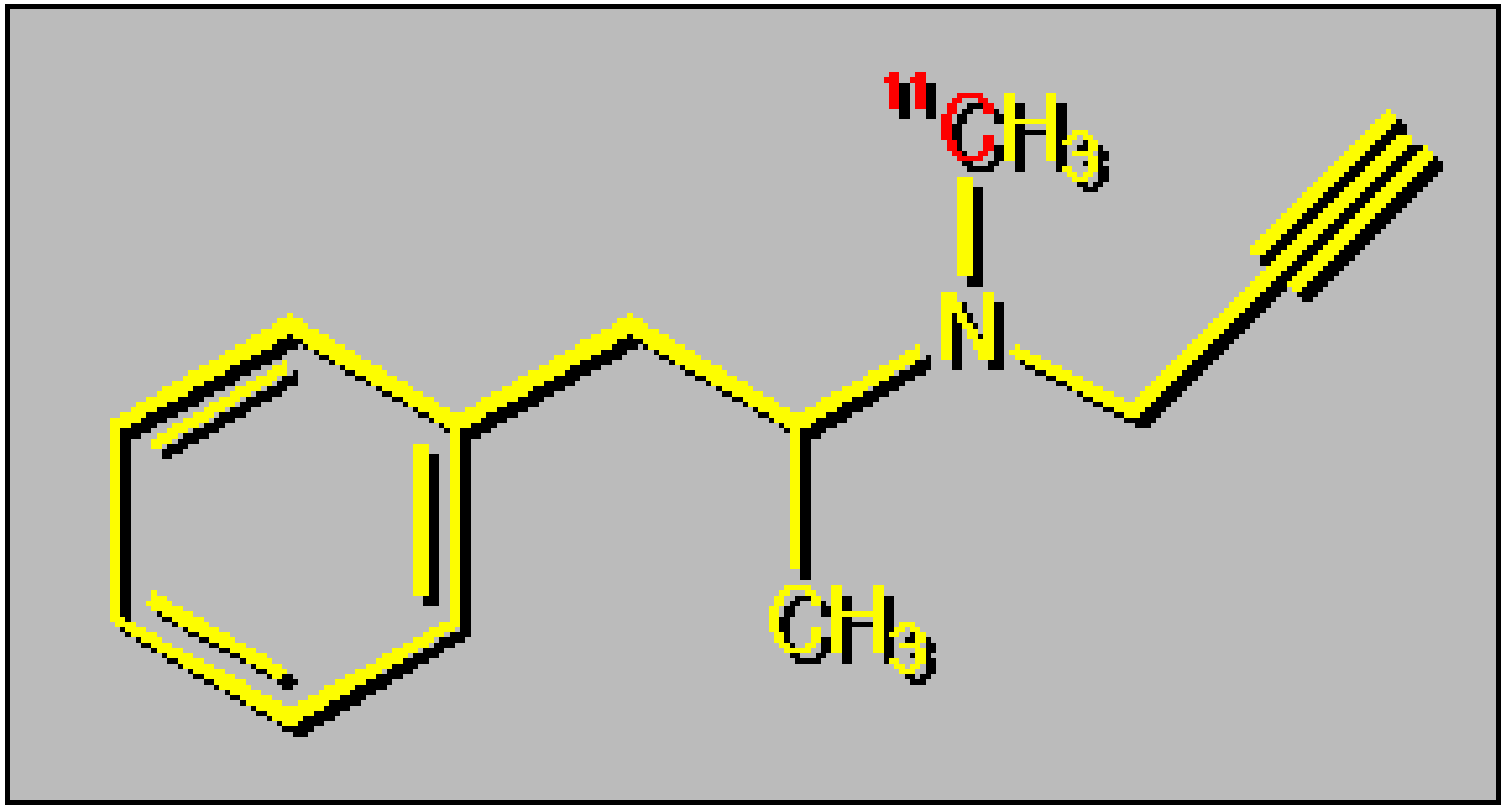
Katalase ↑
Sod ↑

Pharmacological Interventions in Aging and Age-associated Disorders

Potentials of Propargylamines for Human Use

KENICHI KITANI,[a] CHIYOKO MINAMI,[a] TAKAKO YAMAMOTO,[a]
SETSUKO KANAI,[b] GWEN O. IVY,[c] AND MARIA-CRISTINA CARRILLO[d]

Birkmayer and coworkers in a retrospective study initially reported that patients with Parkinson's disease who received levodopa and deprenyl lived for a significantly longer period than control patients who received levodopa and placebo.[17]


11CH3
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ELSEVIER

Mechanisms of Ageing and Development
123 (2002) 1065–1079

mechanisms of ageing and development

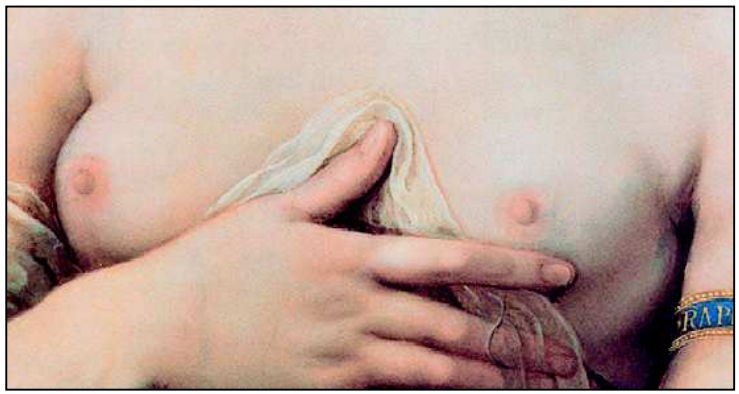
www.elsevier.com/locate/mechagedev

Review

Modulation of neuroendocrine–immune signaling by L-deprenyl and L-desmethyldeprenyl in aging and mammary cancer

Srinivasan ThyagaRajan *, David L. Felten

Susan Samueli Center for Complementary and Alternative Medicine, University of California Irvine, UCI Medical Center, Bldg. 55, Room 314, 101 The City Drive, Orange, CA, 92868, USA



DEPRENYL

- STIMULIERT SOD
- STIMULIERT KATALASE
- SENKT BRUSTKREBSINZIDENZ IM TIERVERSUCH

Thyagarajan S et al. 1995,
Endocrinology 136:1103-1110

Knoll J et al. 1992,
J Am Geriatr Soc40:839-847

Ann N Y Acad Sci. 2002 Apr;959:295-307.

Pharmacological interventions in aging and age-associated disorders: potentials of propargylamines for human use.

Kitani K, Minami C, Yamamoto T, Kanai S, Ivy GO, Carrillo MC.

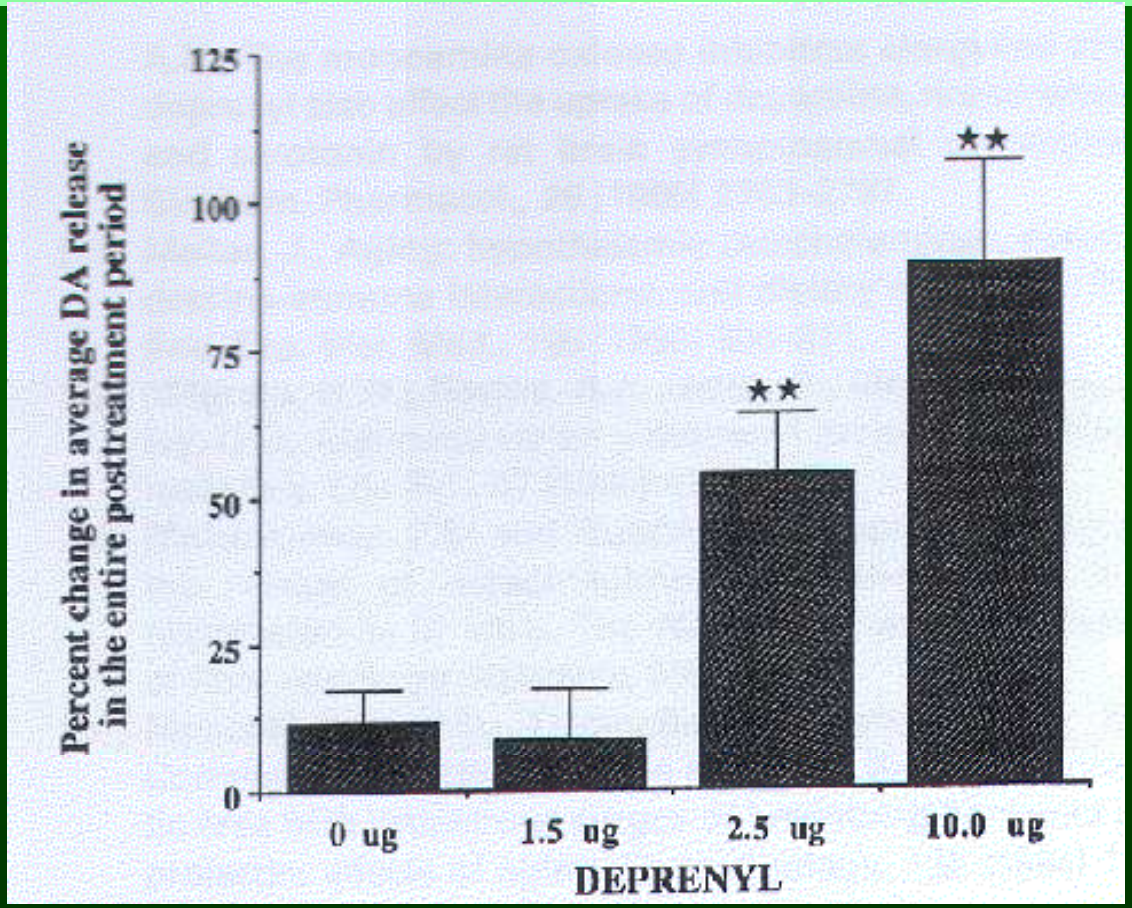
Deprenyl increases natural killer (NK) cell functions and interferon-gamma,

L-Deprenyl stimulates the release of catecholamines in the rat medial basal hypothalamus in vivo

Srinivasan ThyagaRajan*, S. Kaleem Quadri

while DA release was augmented after infusion of 10.0 μg of deprenyl. There were no significant alterations in the release of NE and DA in the control and 1.5 μg deprenyl groups. These results suggest that deprenyl-induced in vivo release of catecholamines in the MBH may be involved in the reversal of some of the reproductive aging processes.

S. ThyagaRajan, S.K. Quadri / Neuroscience Letters 270 (1999) 79–82



S. ThyagaRajan, S.K. Quadri / Neuroscience Letters 270 (1999) 79–82

MONOAMIN-OXIDASE B INHIBITOR **DEPRENYL** ERHÖHT DOPAMIN UND NA STEIGERT LIBIDO

Knoll J et al. 1988

Mech Ageing Dev 46:237-262

ELSEVIER

Neuroscience Letters 354 (2004) 225–228

Neuroscience Letters

www.elsevier.com/locate/neulet

Positive effects of deprenyl and estradiol on spatial memory and oxidant stress in aged female rat brains

Müge Kiray*, Nazan Uysal, Ataç Sönmez, Osman Açıkgöz, Sevil Gönenç

Department of Physiology, Dokuz Eylul University Medical School, Balçova, Izmir 35340, Turkey

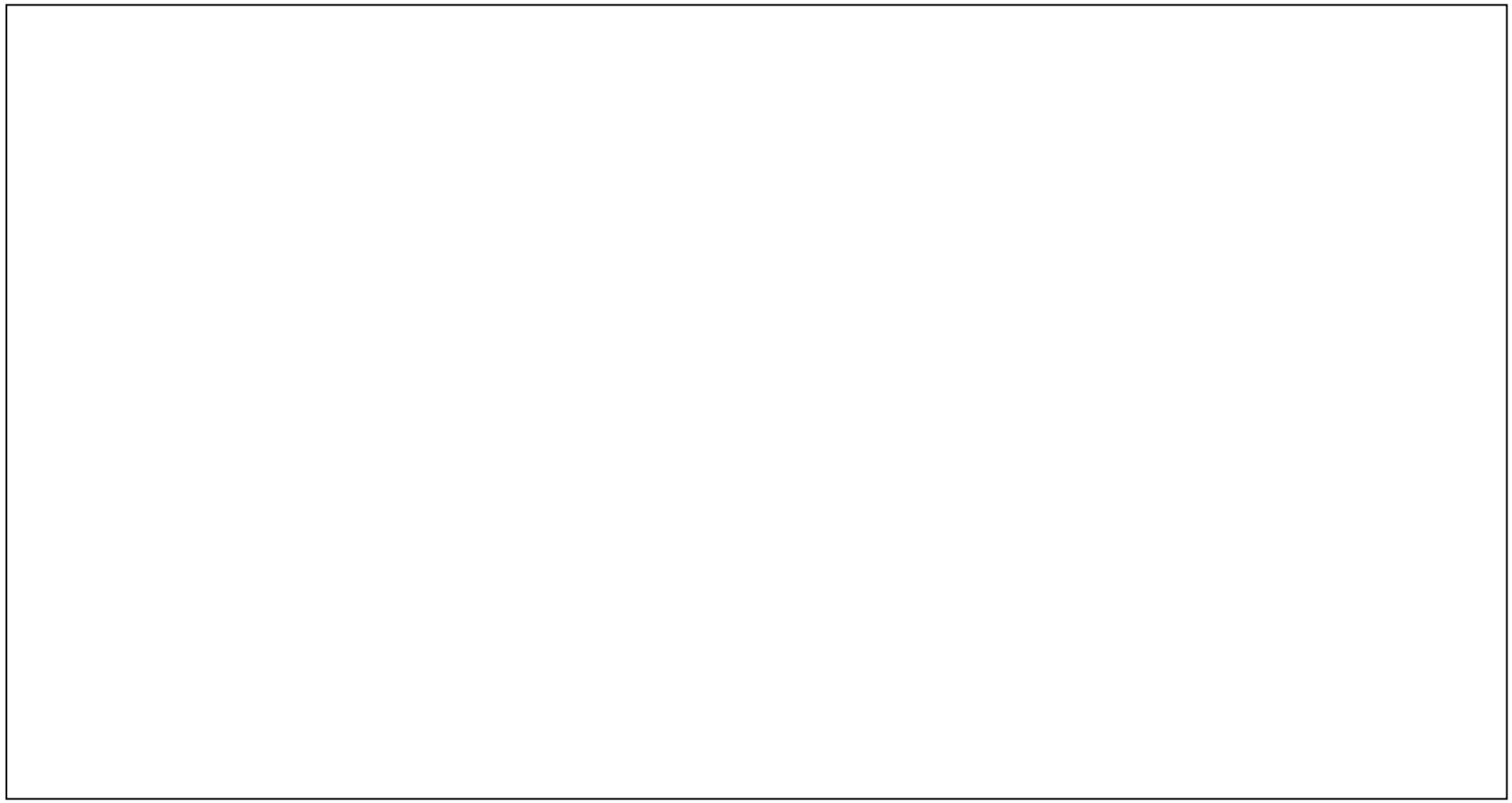
Received 2 September 2003; received in revised form 9 October 2003; accepted 15 October 2003

Ann. N.Y. Acad. Sci. 959: 508–516 (2002).

on antioxidant status when applied alone. Therefore, we think that positive effects of deprenyl and estradiol on spatial memory may occur due to different actions other than their antioxidant actions. It is possible that neurotrophic actions of deprenyl are responsible for this effect [13]. Estradiol can enhance the cholinergic transmission and density of hippocampal dendritic spines. Estradiol may improve the spatial memory by these effects [8]. Further studies are needed to find novel pharmacological approaches that can be used for preventing or retarding the harmful effects of neurodegenerative disorders and aging.

Neuroscience Letters 354 (2004) 225–228

dle age. The cyclic increase in norepinephrine activity associated with the LH surge begins to diminish during middle age and disappears completely in old age to coincide with cessation of estrous cycles. Reinduction of cycling is possible by treating old rats with the drug deprenyl. Deprenyl is speculated to restore estrous cycles by increasing dopamine and epinephrine production and by reducing serum prolactin levels (386).

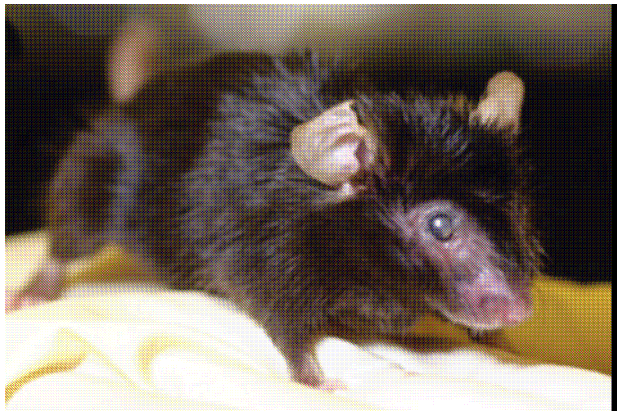


Absence of the proapoptotic Bax protein extends fertility and alleviates age-related health complications in female mice

Gloria I. Perez*†, Andrea Jurisicova‡, Lisa Wise‡, Tatiana Lipina‡, Marijana Kanisek‡, Allison Bechard‡, Yasushi Takai*, Patricia Hunt§, John Roder‡, Marc Grynpas‡, and Jonathan L. Tilly*¶

*Vincent Center for Reproductive Biology, Vincent Obstetrics and Gynecology Service, Massachusetts General Hospital/Harvard Medical School, Boston, MA 02114; ‡Samuel Lunenfeld Research Institute, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada M5G 1X5; and §Center for Reproductive Biology and School of Molecular Biosciences, Washingston State University, Pullman, WA 99164

Therefore, development of methods for postponing ovarian failure at menopause may represent an attractive option for improving the quality of life in aging females.



Perez GI et al. Proc Natl Acad Sci U S A. 2007 Mar 20;104(12):5229-34. Epub 2007 Mar 8.

Ovarian Tissue Banking

cryopreservation of the ovarian tissue (primordial follicle reserve)

↓

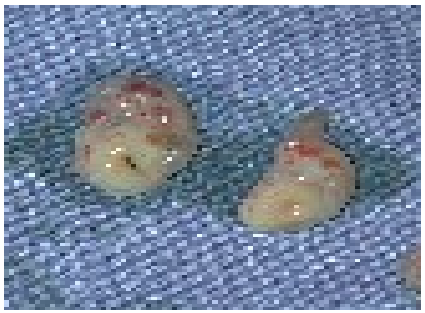
therapy of malignancies
e.g.: Leukaemia

↓

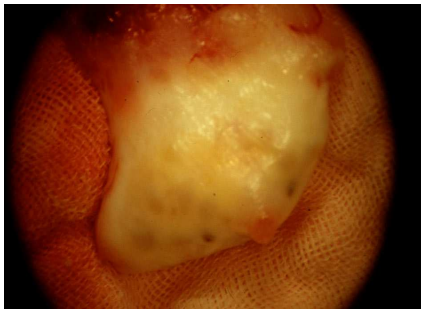
restoration of fertility and hormone - production after retransplantation of ovarian tissue

Ovarian Tissue Banking
- Withdrawal -

- slices



- whole ovary



Cryopreservation of the Whole Ovary

advantage:

- **increased primordial-follicle-pool**
- **immediate blood perfusion after TX (microanastomosis)**
- **normal conception possible**

problems:

- **freezing procedure difficult**
- **reimplanation of malignant cells**

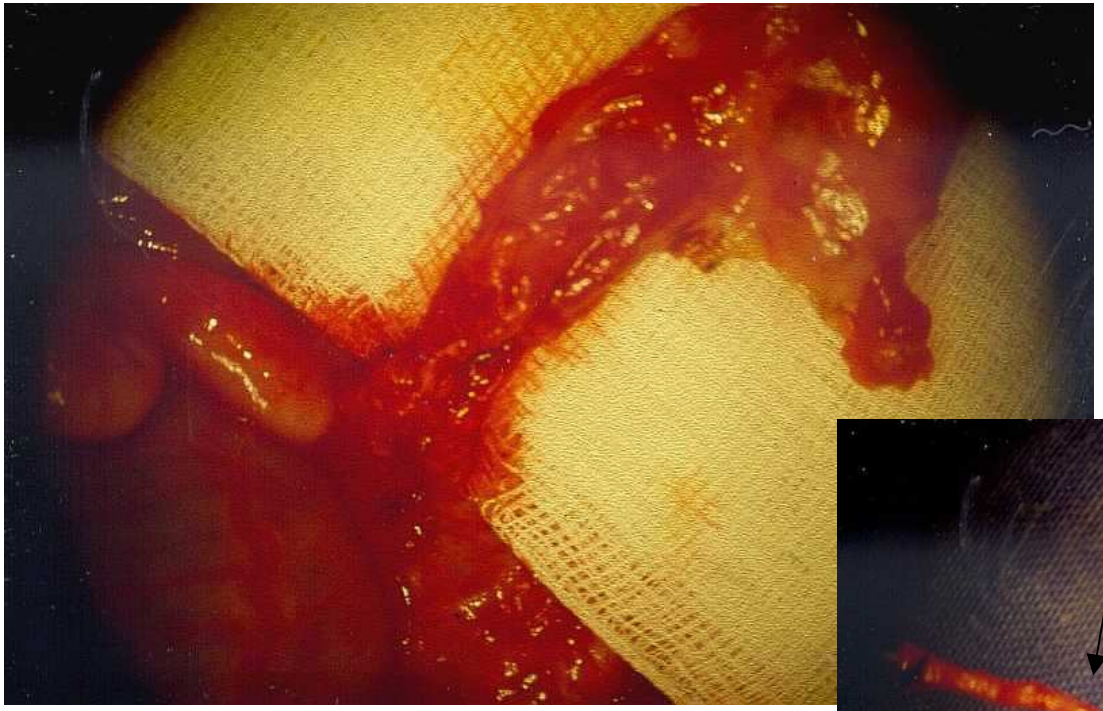
Cryopreservation of a Whole Ovary
- Transplantation of Sheep Ovaries -

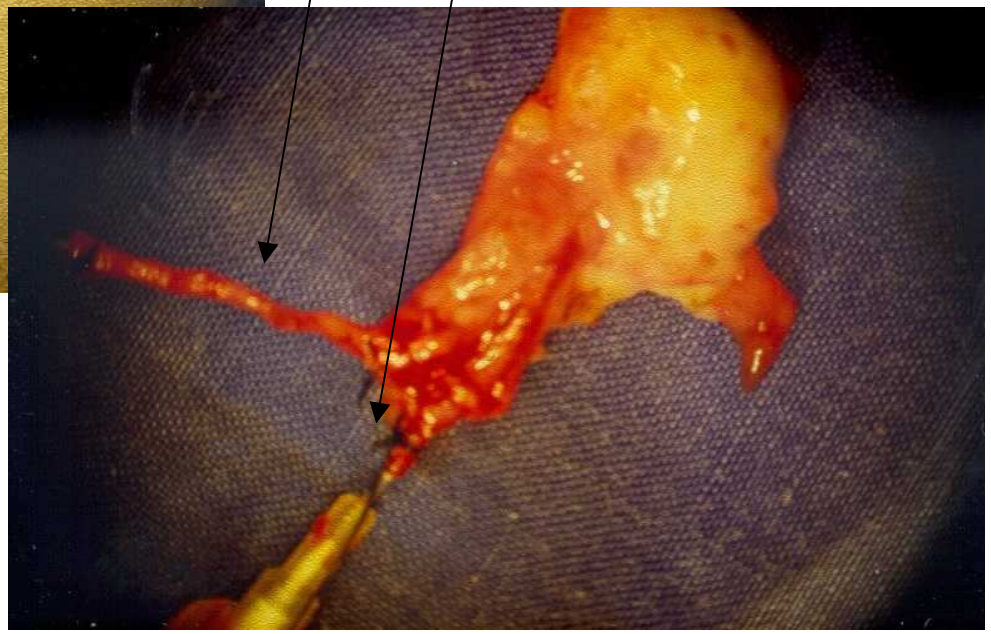
step I: - unilateral ovarectomy
- cryopreservation

step II: - 3 weeks later: contralaterale orthotopic reimplantation with microanastomosis of the ovarian vessels

- laparoscopic biopsy after 2 months
- FSH-, progesterone and ultrasonic follicle screening
- pregnancy

Transplantation of a Whole Ovary
- Vessel Preparation -





Ovarian Tissue Banking
- Applications in humans -

Several reimplantations

z.B. Oktay K, Buyuk E, Veeck L, Zaninovic N, Xu K, Takeuchi T, Opsahl M, Rosenwaks Z: Embryo development after heterotopic transplantation of cryopreserved ovarian tissue. Lancet. 2004 Mar 13;363(9412):837-40.

Localisation forearm, abdomen, peritoneum, uterus

Results: Follicule growth, hormonal production