Endocrinologia, longevità e invecchiamento
IPOTIROIDISMO SUBCLINICO

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ITALIAN CHAPTER

16° Congresso Nazionale AME

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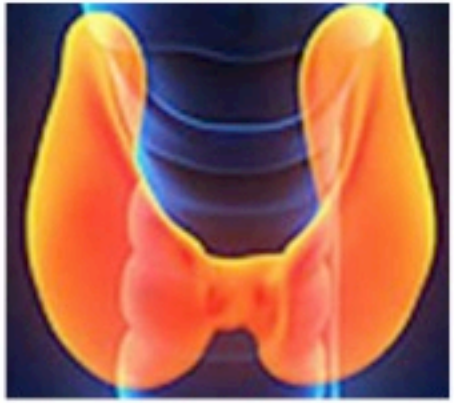
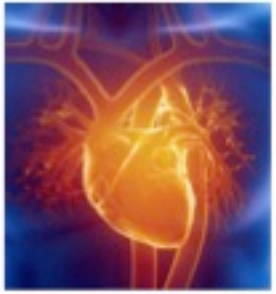
Roma

Ipotiroidismo subclinico e longevità





adnkronos

Fatti Soldi Lavoro Salute Sport Cultura Intrattenimento Magazine

Archivio . AdnSalute . 2009 . 06 . 13

MEDICINA

LONGEVITA': TIROIDE PIGRA? FORSE E' IL SEGRETO PER VIVERE 100 ANNI

Ipotiroidismo subclinico e longevità:
modelli animali

Journal of Gerontology: BIOLOGICAL SCIENCES
2005, Vol. 60A, No. 11, 1369–1377

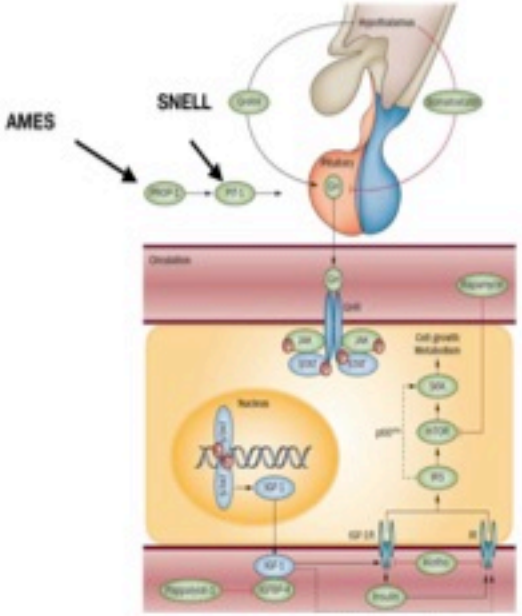
An elderly breeding pair of naked mole-rats. The animal standing is a 24-year-old breeding female that is midway through gestation, and the animal sleeping is her 28.3-year-old naked mole-rat mate. This picture was taken a few days before he died.

Species	LQ*	Thyroxine (mg/dl)	IGF-1 (ng/ml)	Glycated Hemoglobin, %	Source
Laboratory mice	1	5.0 ± 0.2	591 ± 25	10.2 ± 1.2	Miller et al., 2002
Majuro mice	1.1	2.3 ± 0.1	464 ± 48	20.2 ± 1.0	Miller et al., 2002
Idaho mice	1.2	4.4 ± 0.3	300 ± 27	3.8 ± 0.2	Miller et al., 2002
Naked mole-rats	5.0	0.004 ± 0.001	NAD	5.5 ± 0.3	This study

Note: *Based on allometric equation of Austad and Fisher (4).

LQ = longevity quotient; IGF-1 = insulin-like growth factor-1; NAD = no available data.

Ipotiroidismo subclinico e longevità:
modelli animali



Dimensioni ridotte e pubertà ritardata

Curr. Top. Dev. Biol. 2004; 63:189

Durata di vita 40 – 70% più del wild type

J. Gerontol. A Biol. Sci. Med. Sci. 2004; 59: 1244

Meno frequenti le patologie età correlate

J. Gerontol. A Biol. Sci. Med. Sci. 2003; 58: 291

Somministrazione di tiroxina a lungo termine riduce significativamente la sopravvivenza

J. Gerontol. A Biol. Sci. Med. Sci. 2004; 59: 1244

Ipotiroidismo subclinico e longevità:
modelli animali

ELSEVIER

Mechanisms of Ageing and Development

Volume 33, Issue 3, February 1986, Pages 275-282

Effects of chronic hyperthyroidism on the lifespan of the rat

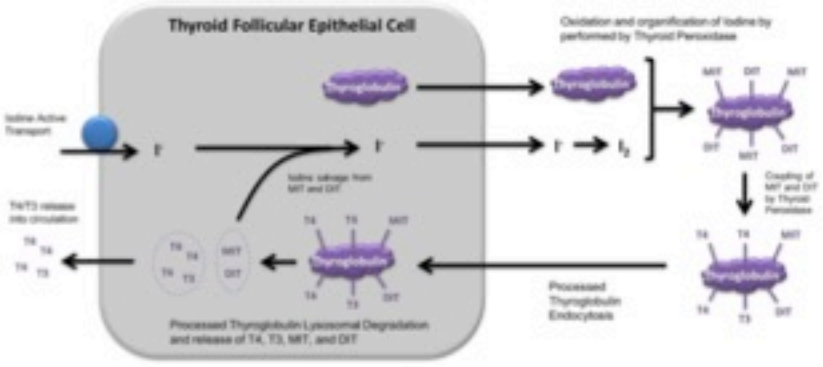
Hiroshi Ooka, Tadashi Shinkai

Inducendo ipotiroidismo nel ratto Wistar si allunga la sopravvivenza di circa 28 mesi; al contrario l'ipertiroidismo ne riduce la vita media

L'ipotiroidismo risulta associato a ridotta generazione di ROS e minore danno ossidativo, mentre l'ipertiroidismo induce effetti opposti

Ipotiroidismo subclinico e longevità:
modelli sperimentali

Il ruolo giocato dagli ormoni tiroidei nella longevità potrebbe essere legato allo stress ossidativo



Antioxid Redox Signal. 2008 Sep;10(9):1577-92. doi: 10.1089/ars.2008.2054.

Peroxides and peroxide-degrading enzymes in the thyroid.

Schweizer U1, Chiu J, Köhrle J.

Abstract

Iodination of thyroglobulin is the key step of thyroid hormone biosynthesis. It is catalyzed by thyroid peroxidase and occurs within the follicular space at the apical plasma membrane. ***Hydrogen peroxide produced by thyrocytes as an oxidant for iodide may compromise cellular and genomic integrity of the surrounding cells, unless these are sufficiently protected by peroxidases***. Thus, peroxidases play two opposing roles in thyroid biology. Both aspects of peroxide biology in the thyroid are separated in space and time and respond to the different physiological states of the thyrocytes. **Redox-protective peroxidases in the thyroid are peroxiredoxins, glutathione peroxidases, and catalase.** Glutathione peroxidases are selenoenzymes, whereas selenium-independent peroxiredoxins are functionally linked to the selenoenzymes of the thioredoxin reductase family through their thioredoxin cofactors. Thus, selenium impacts directly and indirectly on protective enzymes in the thyroid, a link that has been supported by animal experiments and clinical observations. In view of this relationship, it is remarkable that rather little is known about selenoprotein expression and their potential functional roles in the thyroid. Moreover, selenium-dependent and -independent peroxidases have rarely been examined in the same studies. Therefore, we review the relevant literature and present expression data of both selenium-dependent and -independent peroxidases in the murine thyroid

Ipotiroidismo subclinico e longevità:
modelli sperimentali

Il ruolo giocato dagli ormoni tiroidei nella longevità potrebbe essere legato allo stress ossidativo

Effect of thyroid state on lipid peroxidation, antioxidant defences, and susceptibility to oxidative stress in rat tissues

P Venditti, M. Balestrieri, S Di Meo and T De Leo

Abstract

The effects of altered thyroid states on lipid peroxidation, antioxidant capacity, and susceptibility to oxidative stress of rat tissues were examined. Hyperthyroidism was induced by administering methimazole in drinking water for 15 days. Hypothyroidism was elicited by a 10-day treatment of hypothyroid rats with tri-iodothyronine (10 μg/100 g body weight). In peroxidation was r rats lipid peroxidat in skeletal muscle increased significan rats and in muscle reductase activity thyroid and hypo

whole antioxidant capacity of tissues decreased, but significantly only in liver and heart. The results obtained studying the response to oxidative stress in vitro indicated that the susceptibility to oxidative challenge was increased in all tissues of hypothyroid rats and in heart and muscle of hypothyroid animals. These results are explainable in haemoprotein content and/or so it has been reported that protection against free radical ch an effect could be due to ular defence systems different

Table 2 Lipid peroxidation in tissues of rats in different thyroid states. Values are means ± S.E.M. For each value, eight rats were used

	Parameter	Group: Euthyroid	Hypothyroid	Hyperthyroid
Liver	MDA	81.61 ± 2.89	67.72 ± 3.71	73.70 ± 3.77 %
	HPs	1.31 ± 0.08	1.35 ± 0.05	1.92 ± 0.07 %
Heart	MDA	82.73 ± 1.62	88.55 ± 2.72	80.69 ± 1.63 %
	HPs	0.72 ± 0.03	0.68 ± 0.02	0.80 ± 0.03 %
Muscle	MDA	23.08 ± 1.62	17.63 ± 1.37	28.99 ± 1.08
	HPs	0.47 ± 0.02	0.40 ± 0.02	0.62 ± 0.03 %

Abbreviations: MDA, was measured in whole tissue. Hydroperoxides (HP) were measured in acid homogenates per g tissue.
*Significant (P<0.05) versus euthyroid rats. Significant (P<0.05) versus hypothyroid rats.

Table 3 Effect of thyroid state on level of antioxidants in rat tissues. Values are means ± S.E.M. For each value, eight rats were used

	Parameter	Group: Euthyroid	Hypothyroid	Hyperthyroid
Liver	GPX	39.56 ± 1.39	49.68 ± 2.56	41.73 ± 2.33
	GR	17.98 ± 2.21	21.12 ± 1.61	23.09 ± 1.76
	Vit E	0.92 ± 0.10	0.98 ± 0.09*	0.98 ± 0.08*
	C_{18}	0.28 ± 0.02*	0.30 ± 0.12*	0.76 ± 0.13*
Heart	GPX	11.98 ± 0.96	13.98 ± 0.62*	12.43 ± 0.43*
	GR	4.73 ± 0.61	3.10 ± 0.26	4.67 ± 1.04*
	Vit E	0.26 ± 0.01	0.46 ± 0.04*	0.94 ± 0.14*
	C_{18}	0.02 ± 0.02	0.04 ± 0.02*	0.11 ± 0.02*
Muscle	GPX	3.86 ± 0.15	4.72 ± 0.19*	4.64 ± 0.19*
	GR	1.16 ± 0.13	1.13 ± 0.14	1.50 ± 0.10
	Vit E	1.45 ± 1.20	12.27 ± 1.10	14.23 ± 1.30
	C_{18}	0.14 ± 0.02	0.04 ± 0.02	0.11 ± 0.01

GPX, glutathione peroxidase (μmol NADPH/min per g tissue); GR, glutathione reductase (μmol NADPH/min per g tissue); Vit E, vitamin E (mmol/g tissue); C_{18}, antioxidant capacity (expressed as mmol/g tissue).
*Significant (P<0.05) versus euthyroid rats (significant (P<0.05) versus hypothyroid rats.

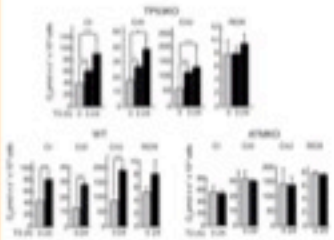
L'induzione dell'ipotiroidismo non aumenta la perossidazione dei lipidi, mentre aumenta nei ratti in cui si induce ipertiroidismo.

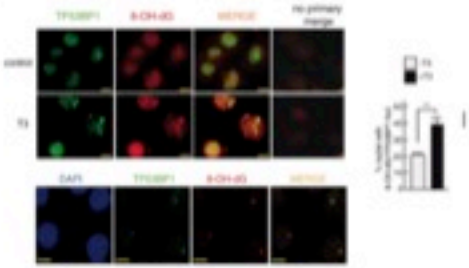
La capacità antiossidante si riduce in entrambi i gruppi rispetto agli eutiroidei, ma solo a livello del fegato e cuore

The thyroid hormone receptor β induces DNA damage and premature senescence

J Cell Biol. 2014 Jan 6; 204(1): 129–146.

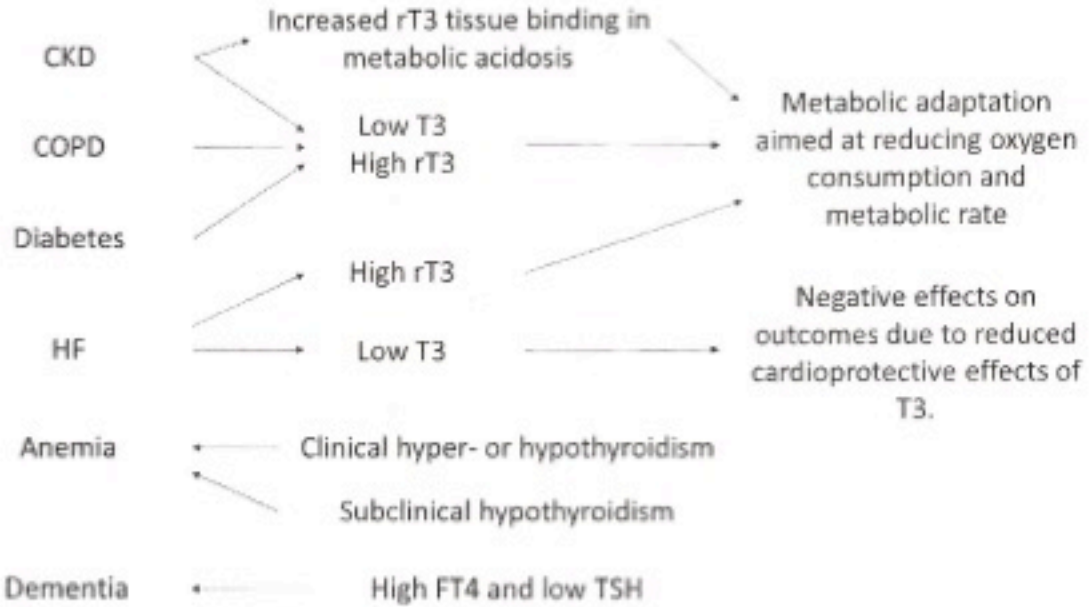
There is increasing evidence that the thyroid hormone (TH) receptors (THRs) can play a role in aging, cancer and degenerative diseases. In this paper, we demonstrate that binding of TH T3 (triiodothyronine) to THRB induces senescence and deoxyribonucleic acid (DNA) damage in cultured cells and in tissues of young hyperthyroid mice. T3 induces a rapid activation of ATM (ataxia telangiectasia mutated/PRKAA (adenosine monophosphate-activated protein kinase) signal transduction and recruitment of the NRF1 (nuclear respiratory factor 1) and THRB to the promoters of genes with a key role on mitochondrial respiration. Increased respiration leads to production of mitochondrial reactive oxygen species, which in turn causes oxidative stress and DNA double-strand breaks and triggers a DNA damage response that ultimately leads to premature senescence of susceptible cells. Our findings provide a mechanism for integrating metabolic effects of THs with the tumor suppressor activity of THRB, the effect of thyroidal status on longevity, and the occurrence of tissue damage in hyperthyroidism.





Il legame della T3 al recettore beta incrementa la respirazione mitocondriale e la produzione di ROS con conseguente danno del DNA e senescenza prematura

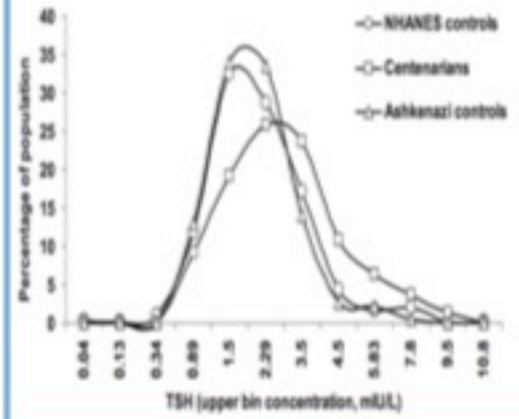
Ipotiroidismo subclinico e longevità:
studi nell'uomo



Ipotiroidismo subclinico e longevità:
studi nell'uomo

Extreme Longevity Is Associated with Increased Serum Thyrotropin

J Clin Endocrinol Metab 94: 1251–1254, 2009



Le concentrazioni sieriche di TSH nei centenari sono significativamente più elevate rispetto ai controlli di più giovane età

Genetic Predisposition to Elevated Serum Thyrotropin Is Associated with Exceptional Longevity

J Clin Endocrinol Metab. 2009 Dec; 94(12): 4768–4775.

	Controls	Offspring	Probands
n (females/males)	163 (79/84)	366 (185/181)	232 (166/66)
Age (yr)			
All	70 (53–80)	69 (59–79)	97 (95–103)
Females	67 (52–80)	68 (59–79)	97 (95–103)
Males	74 (59–80)	69 (59–79)	97 (95–103)
TSH (mIU/liter)			
All	1.55 (0.63–3.93)	1.68 (0.65–4.79)[a]	1.97 (0.42–7.15)[a]
Females	1.60 (0.60–4.7)	1.72 (0.51–6.3)[a]	2.00 (0.53–7.34)[a]
Males	1.50 (0.55–4.50)	1.68 (0.65–5.9)[a]	1.93 (0.61–6.9)[a]
FT4 (ng/dl)			
All	1.00 (0.69–1.7)	1.03 (0.67–2.0)	1.02 (0.62–2.02)
Females	0.99 (0.74–1.5)	1.04 (0.66–1.9)[a]	1.04 (0.65–2.02)[a]
Males	1.00 (0.57–1.7)	1.02 (0.67–2.0)	0.95 (0.48–2.06)[a]

Data are expressed as median (97.5% CI).

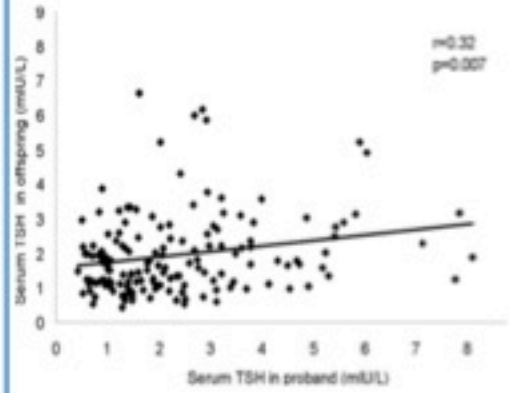
[a] $P < 0.05$ vs. controls.

Nonagenari o centenari e anche i loro figli hanno livelli sierici di TSH significativamente più elevati dei controlli

Ipotiroidismo subclinico e longevità:
studi nell'uomo

Genetic Predisposition to Elevated Serum Thyrotropin Is Associated with Exceptional Longevity

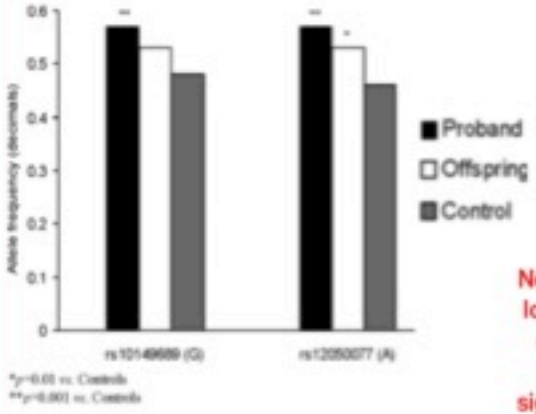
J Clin Endocrinol Metab. 2009 Dec; 94(12): 4768–4775]



L'analisi dell'ereditarietà mostra un moderato grado di ereditabilità (h2 =0.32; *P* = 0.007) dei valori sierici di TSH tra i centenari e i loro figli

Genetic Predisposition to Elevated Serum Thyrotropin Is Associated with Exceptional Longevity

J Clin Endocrinol Metab. 2009 Dec; 94(12): 4768–4775]



Nonagenari o centenari e anche i loro figli hanno una frequenza di due polimorfismi dei gene del recettore del TSH significativamente più elevata dei controlli

Ipotiroidismo subclinico e longevità:
studi nell'uomo

Sci Rep. 2015; 5: 11525.
Published online 2015 Jun 19. doi: 10.1038/srep11525
PMCID: PMC4473605

Human longevity is characterised by high thyroid stimulating hormone secretion without altered energy metabolism

La secrezione di TSH in figli di nonagenari con almeno un fratello nonagenario è stata confrontata con quella dei coniugi.
Figli di nonagenari e rispettivi coniugi avevano livelli paragonabili di metabolismo basale.

Ipotiroidismo subclinico e longevità:
studi nell'uomo

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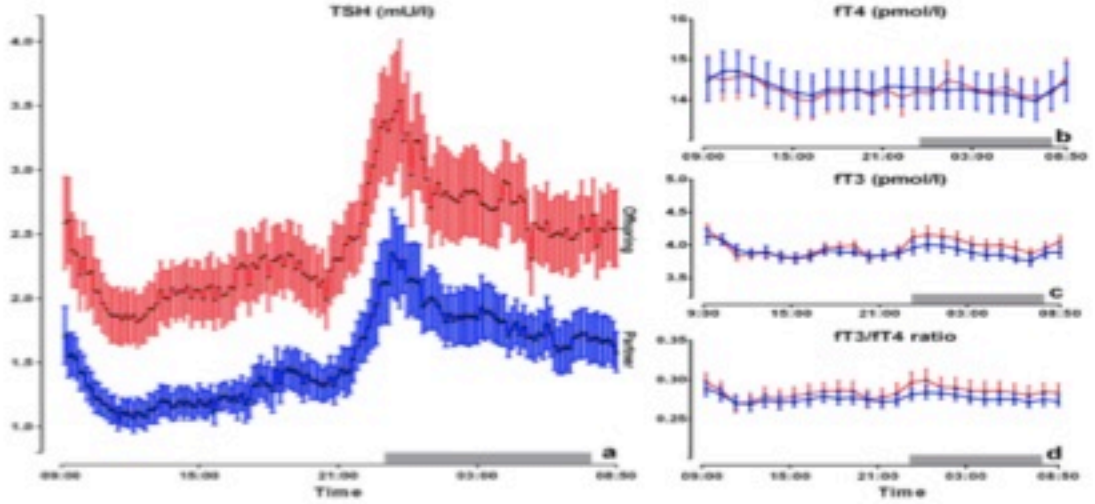
Sci Rep. 2015; 5: 11525.
Published online 2015 Jun 19. doi: 10.1038/srep11525
PMCID: PMC4473605

Human longevity is characterised by high thyroid stimulating hormone secretion without altered energy metabolism



Twenty-four hour profiles of TSH, fT4, fT3 and fT3/fT4 ratio in offspring from long-lived families and partners. In all the panels, data points represent means with standard error of the mean. The red lines depict 20 offspring and the blue lines depict 18 partners. (a) Ten minutes measurements of TSH. Hourly measurements of (b) fT4 (c) fT3 (d) fT3/fT4 ratio. The grey bars represent lights-off periods (from 23:00-08:00).

Ipotiroidismo subclinico e longevità:
studi nell'uomo

SCIENTIFIC REPORTS

Sci Rep. 2015; 5: 11525.
Published online 2015 Jun 19. doi: 10.1038/srep11525
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Human longevity is characterised by high thyroid stimulating hormone secretion without altered energy metabolism

Ridotta sensibilità della cellula follicolare al TSH ?

	Offspring (n = 61)	Partner (n = 51)	P-value
Hormone levels (rv)			
TSH (0.3–4.8 mU/l)[a]	2.1 (1.8–2.3)	1.6 (1.4–1.9)	**0.01**
fT4 (10–24 pmol/l)	16.1 (15.5–16.7)	16.5 (15.9–17.1)	0.36
fT3 (4.7–8.2 pmol/l)	4.7 (4.6–4.8)	4.6 (4.5–4.8)	0.49
T3 (1.1–3.1 nmol/l)[a]	1.66 (1.59–1.72)	1.62 (1.55–1.68)	0.37
rT3 (0.11–0.44 nmol/l)[a]	0.26 (0.24–0.28)	0.27 (0.25–0.29)	0.30
fT4xTSH product[a]	33.0 (29.0–37.4)	26.4 (23.0–30.3)	0.02
fT4/TSH ratio[a]	6.7 (5.2–8.6)	10.1 (7.7–13.2)	0.03
fT3/fT4 ratio	0.30 (0.29–0.31)	0.29 (0.27–0.30)	0.20
T3/rT3 ratio[a]	6.77 (6.28–7.25)	6.36 (5.84–6.88)	0.26

SCIENTIFIC REPORTS

Sci Rep. 2015; 5: 11525.
Published online 2015 Jun 19. doi: 10.1038/srep11525
PMCID: PMC4473605

Human longevity is characterised by high thyroid stimulating hormone secretion without altered energy metabolism

Aumentato turn over tessutale degli ormoni tiroidei ?

	Offspring (n = 61)	Partner (n = 51)	P-value
Hormone levels (rv)			
TSH (0.3–4.8 mU/l)[a]	2.1 (1.8–2.3)	1.6 (1.4–1.9)	**0.01**
fT4 (10–24 pmol/l)	16.1 (15.5–16.7)	16.5 (15.9–17.1)	0.36
fT3 (4.7–8.2 pmol/l)	4.7 (4.6–4.8)	4.6 (4.5–4.8)	0.49
T3 (1.1–3.1 nmol/l)[a]	1.66 (1.59–1.72)	1.62 (1.55–1.68)	0.37
rT3 (0.11–0.44 nmol/l)[a]	0.26 (0.24–0.28)	0.27 (0.25–0.29)	0.30
fT4xTSH product[a]	33.0 (29.0–37.4)	26.4 (23.0–30.3)	0.02
fT4/TSH ratio[a]	6.7 (5.2–8.6)	10.1 (7.7–13.2)	0.03
fT3/fT4 ratio	0.30 (0.29–0.31)	0.29 (0.27–0.30)	0.20
T3/rT3 ratio[a]	6.77 (6.28–7.25)	6.36 (5.84–6.88)	0.26

Ipotiroidismo subclinico e longevità:
studi nell'uomo

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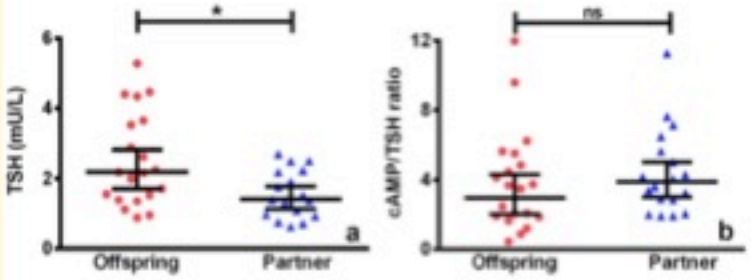
Human longevity is characterised by high thyroid stimulating hormone secretion without altered energy metabolism

Ridotta attività biologica del TSH ?



In vitro TSH bioactivity in offspring from long-lived siblings and partners. Red circles represent 20 offspring, blue triangles represent 18 partners. Solid lines represent (a) geometric mean with 95% CI of TSH levels (mU/l) (b) geometric mean with 95% CI of cAMP/TSH ratio. *P < 0.05; ns: not significant.

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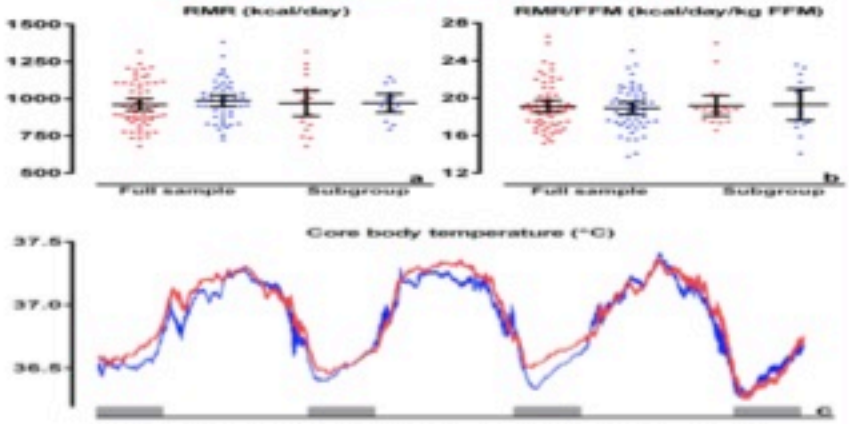
Human longevity is characterised by high thyroid stimulating hormone secretion without altered energy metabolism

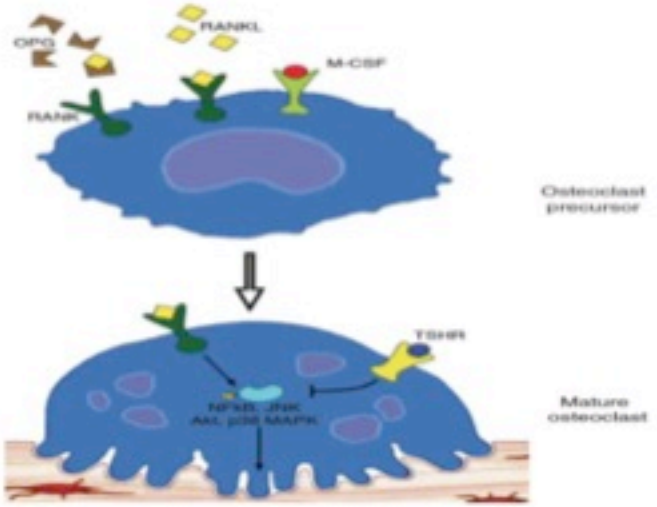
Differenze nel metabolismo energetico ?



Parameters of energy metabolism in offspring from long-lived siblings and partners. Red circles represent offspring (n = 61 for full study sample; n = 20 for subgroup) and blue triangles represent partners (n = 51 for full study sample; n = 18 for subgroup). (a) Mean (95% CI) resting metabolic rate (kcal/day). (b) Mean (95% CI) resting metabolic rate per kg fat free mass (c) Mean (SEM) core body temperature per 5 minutes over 3 days in full study sample offspring (red line) and partners (blue line). Grey blocks are the night periods (24.00h–07.00 h). RMR: resting metabolic rate; FFM: fat free mass. *P ≤ 0.05; **P ≤ 0.01; ns: not significant.

Ipotiroidismo subclinico e longevità:
studi nell'uomo

IL TSH sembra possedere effetti pleiotropici che favoriscono la longevità



Role of RANKL and TSH in osteoclast maturation. Osteoclast precursors mature when receptor activator of nuclear factor kappa B ligand (RANKL) binds to its receptor (RANK) together with activation of the macrophage colony-stimulating factor (M-CSF) receptor. When RANKL is bound to osteoprotegerin (OPG), no activation can take place. In the mature osteoclast, survival, differentiation, and activation are maintained via activation of NFkB, MAPKs, and Akt. Binding of TSH to its receptor (TSHR) antagonizes RANKL signalling via inhibition of all pathways. N, nucleus.

Role of TSH in the immune system

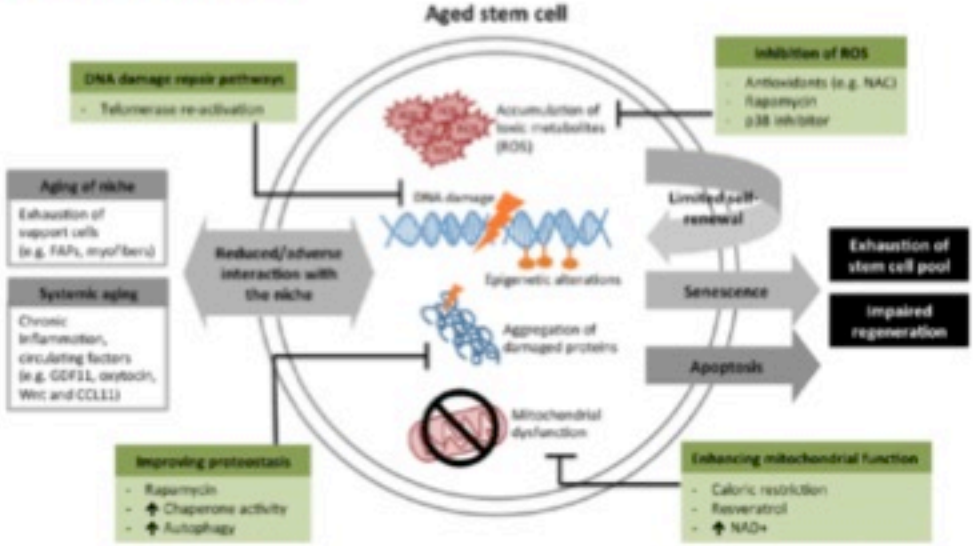
The relatively high frequency of autoimmune diseases of the thyroid gland suggests a link between the thyroid and immune systems.
Asymptomatic autoimmune thyroiditis (Hashimoto's disease) has been identified in postmortem studies in 27% of adult women and 7% of adult men .
Graves' disease has a prevalence of 0.28–1.2% in women and 0–2% in men.

Thyroid and thymus also share a common ontogenetic origin and impairments in TSH production in the pituitary gland and immune cells have been shown to occur in parallel.

Several effects of TSH on immune cells have been identified so far.
- TSH supported T-cell development in the thymus , enhanced antibody production , and improved natural killer cell activity.
- Intraepithelial lymphocyte development in the intestinal epithelium, which does not take place in athymic mice, can be induced by exogenous application of TSH.
- TSH regulated the activity of the intraepithelial immune system on infection with rotavirus . The pattern of TSH-immunoreactive cells in the mucosa changed from their presence in the upper and lower parts of the intestinal crypts to the presence of stained cells at the apical region of the villi on infection with rotavirus.
- On stimulation with TSH, thymocytes responded in a time-dependent manner; application at 09.00 h was efficient while application at 18.00 h did not induce proliferation . This finding underscores the importance of circadian changes in TSH levels and TSH receptor expression, addressed in the section 'TSH levels in

Ipotiroidismo subclinico e longevità:
studi nell'uomo

IL TSH sembra possedere effetti pleiotropici che favoriscono la longevità
effetti sul turn over tissutale



Common pathways contributing to stem cell loss and dysfunction in the aging process. Common aging phenotypes within the stem cell are shown in orange, in the niche in pink, and the strategies by which to target and hopefully reverse these mechanisms in blue.

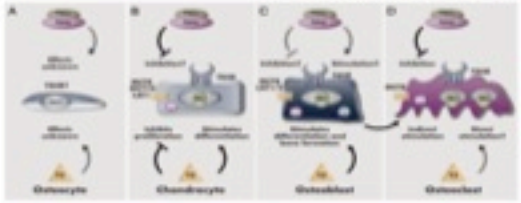
Nat Med. 2014 August 6; 20(8): 870–880.

Ipotiroidismo subclinico e longevità:
studi nell'uomo

IL TSH sembra possedere effetti pleiotropici che favoriscono la longevità
effetti sul turn over tissutale

Role of Thyroid Hormones in Skeletal Development and Bone Maintenance

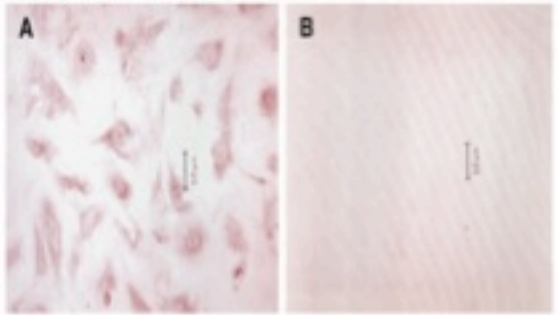
Endocrine Reviews, April 2018, 37(2):135–187



Actions of T3 and TSH in skeletal cells.
A, T3 and TSH actions in osteocytes have not been investigated, and it is unknown whether osteocytes express thyroid hormone transporters, deiodinases, TRs, or the TSHR.
B, Chondrocytes express MCT8, MCT10, and LAT1 transporters, DIO3 (D3), TRs (predominantly TR1), and TSHR. T3 inhibits proliferation and stimulates prehypertrophic and hypertrophic chondrocyte differentiation, whereas TSH might inhibit proliferation and matrix synthesis.
C, Osteoblasts express MCT8 and LAT1/2 transporters, the DIO2 (D2) and D3, TRs (predominantly TR1), and TSHR. Most studies indicate that T3 stimulates osteoblast differentiation and bone formation. Contradictory data suggest that TSH may stimulate, inhibit, or have no effect on osteoblast differentiation and function.
D, Osteoclasts express MCT8, D3, TRs and the TSHR. Currently, it is unclear whether T3 acts directly in osteoclasts or whether indirect effects in the osteoblast lineage mediate its actions. Most studies indicate that TSH inhibits osteoclast differentiation and function.

The Expression of Thyrotropin Receptor in the Brain

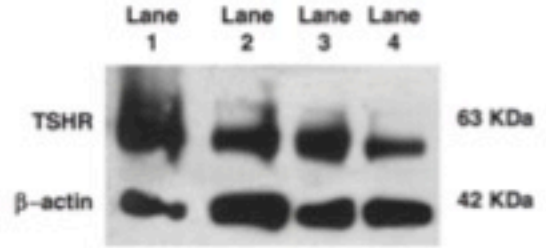
Endocrinology 142: 813–822, 2001



Expression of the TSH receptor in human primary cultured astrocytes. Cultured astrocytes were fixed with ice-cold acetone, then incubated with either nonspecific preimmune mouse IgG1 immunoglobulin; B) or anti-TSH receptor antibody (TSHR34; A). Binding was detected with peroxidase-coupled antibody and peroxidase-catalyzed color reaction (A and B). Preincubation of TSHR34 antibody with purified extracellular domain of the TSH receptor gave a result similar to that obtained in A

Expression of thyrotropin and thyroid hormone receptors in adipose tissue of patients with morbid obesity and/or type 2 diabetes: effects of weight loss

International Journal of Obesity (2009) 33, 1001–1006



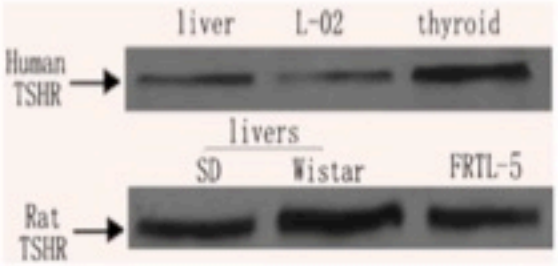
Thyroid-stimulating hormone receptor (TSHR) and beta-actin protein expression by western blot analysis. Lane 1, subcutaneous adipose tissue (SAT) of a control subject; lane 2, SAT of an obese subject; lane 3, visceral adipose tissue VAT of a control subject; lane 4, VAT of an obese subject

Ipotiroidismo subclinico e longevità:
studi nell'uomo

IL TSH sembra possedere effetti pleiotropici che favoriscono la longevità
effetti sul turn over tissutale

Presence of thyrotropin receptor in hepatocytes

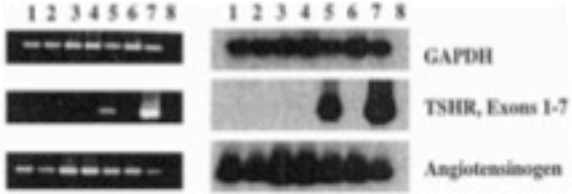
J. Cell. Mol. Med. Vol 13, No 11-12, 2009 pp. 4636-4642



TSHR protein is present in human or rat samples. The presence of TSHR protein was detected by immunoprecipitation using anti-human TSHR or anti-rat TSHR antibodies as described in the Materials and Methods. Human thyroid tissue and rat thyroid FRTL-5 cell line were positive controls. Data are representative of three separate experiments

Extrathyroidal Manifestations of Graves' Disease: The Thyrotropin Receptor Is Expressed in Extraocular, But Not Cardiac, Muscle Tissues*

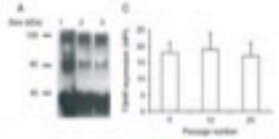
J Clin Endocrinol Metab 86: 2315–2319, 2001)

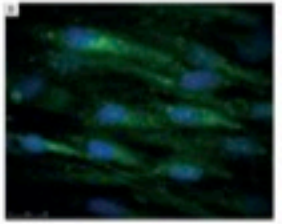


High stringency RT-PCR (left) and Southern blot (right) results. GAPDH and angiotensinogen are present in all tissue types tested. TSHR mRNA transcripts are present in thyroid and EOM only. Exons 1–7 of the TSHR are represented above; the other exons investigated gave the same results. The water blank was consistently negative. 1, Left ventricle; 2, right ventricle; 3, left atrium; 4, right atrium; 5, extraocular muscle; 6, abdominal muscle; 7, thyroid; 8, water blank.

TSH-induced gene expression involves regulation of self-renewal and differentiation-related genes in human bone marrow-derived mesenchymal stem cells

Journal of Endocrinology (2012) **212**, 169–178





Determination of TSHR expression. TSHR expression on the cell surface of hMSCs was determined by three different methods. (A) Western blot: lane 1, TSHR in human thyroid cells; lane 2, TSHR in hBMSCs from the first donor; and lane 3, TSHR in hBMSCs from the second donor. (B) In fluorescence con focal microscopy studies, cells were stained with the primary antihuman TSHR antibody and FITC-conjugated secondary Ab plus Hoechst to stain the nuclei. Inverted Leica DM4000 with 4-laser Leica confocal microscope system (Leica GE) and software, Wetzlar, Germany.
(C) TSHR expression was also assessed by flow cytometry.

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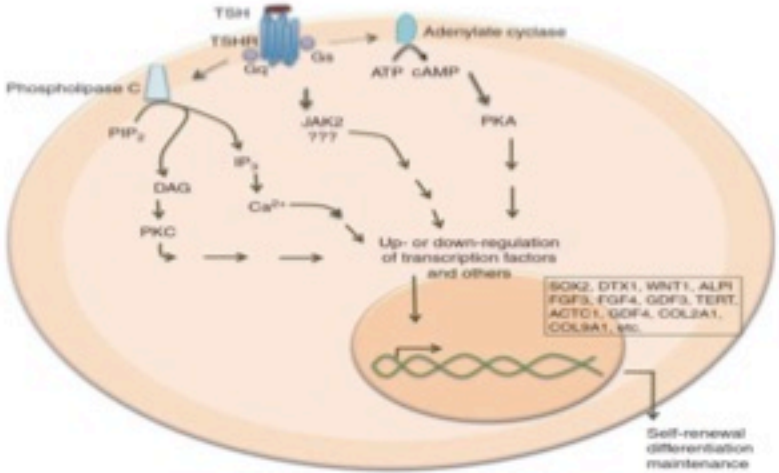

Sicuramente il TSH induce l'espressione di geni nelle cellule staminali mesenchimali che sono determinanti per il destino delle cellule stesse in termini di auto rinnovamento, differenziazione e funzionamento

CONCLUSIONI

- LA LONGEVITA' SEMBRA CARATTERIZZATA DA UNA MAGGIORE SECREZIONE DI TSH SENZA MODIFICHE DELLE CONCENTRAZIONI EMATICHE DEGLI ORMONI TIROIDEI E SENZA MODIFICHE DEL METABOLISMO ENERGETICO
- GLI EFFETTI PLEIOTROPICI DEL TSH POTREBBERO ESERCITARE UN'AZIONE PROTETTIVA SULLE FAMIGLIE DI LONGEVI
- IL RUOLO DEL TSH POTREBBE ESSERE LEGATO AL TURN OVER TESSUTALE; IN PARTICOLARE ALLA VITA DELLE CELLULE STAMINALI TESSUTALI