Physical Activity and Health Promotion

Costanzo Giulio Moretti
Unit of Endocrinology
Università di Roma TorVergata
St John Calibita Hospital Tiber Island Rome
Section of Reproductive Endocrinology

Lesson 7

Physical activity as prevention of endocrine disorders

EVIDENCE of INCREASED BMI

Prevalence in adolescents– obesity BMI >30 Kg/m^2

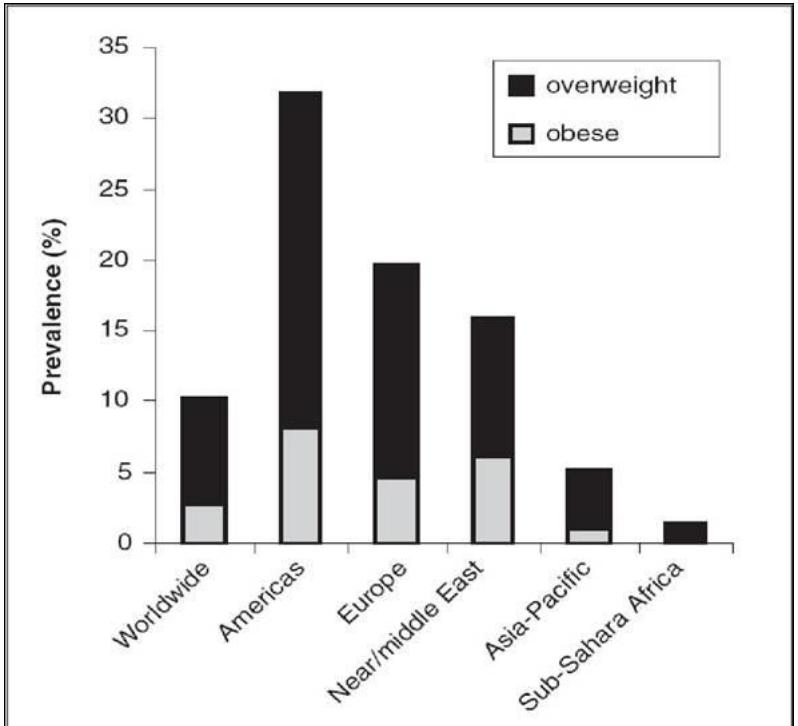
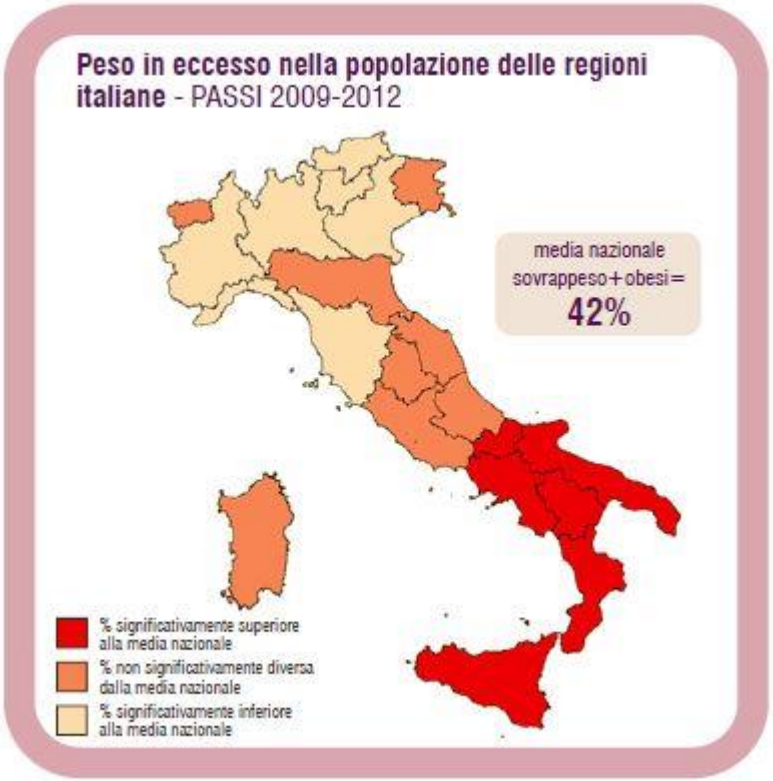
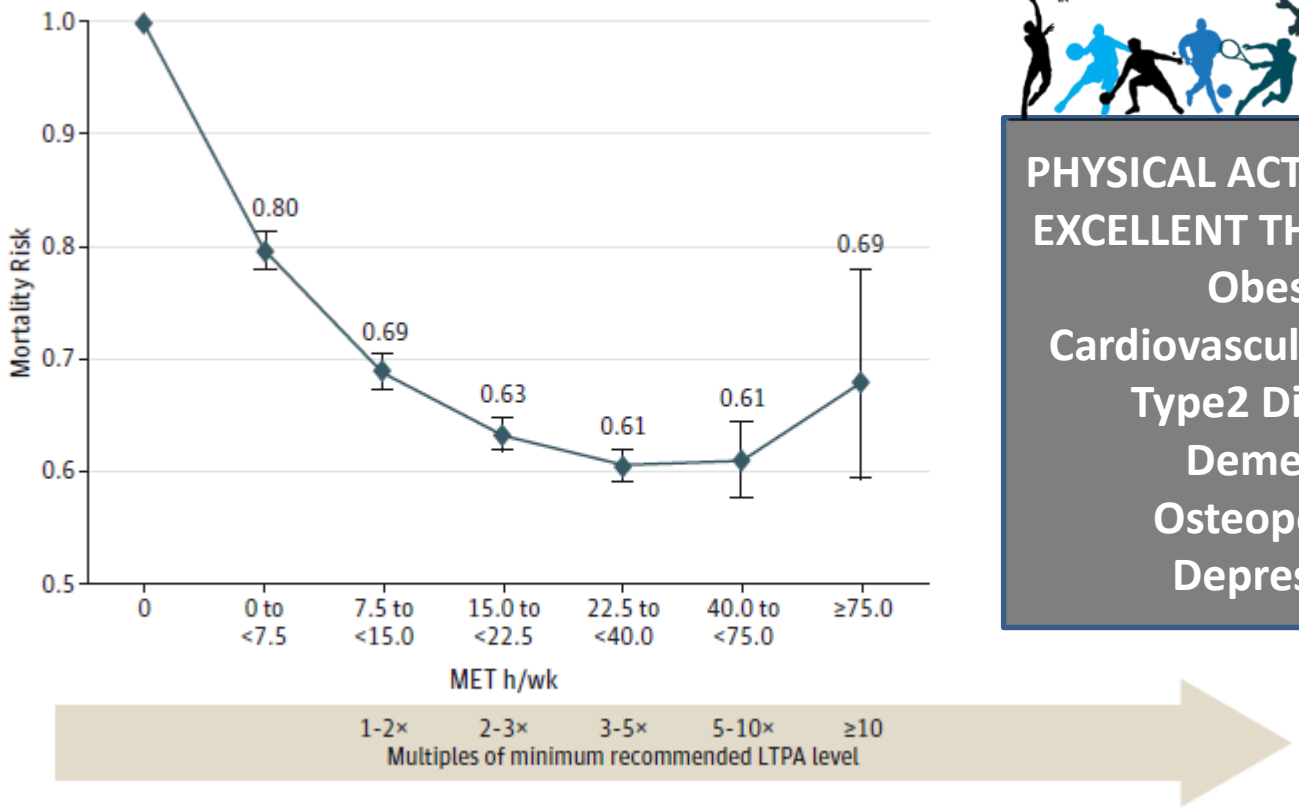


Figure 7 Prevalence of overweight and obesity among school-age children in global regions. Overweight and obesity defined by IOTF criteria. Children aged 5–17 years. Based on surveys in different years after 1990. Source: International Obesity Task Force data, based on populationweighted estimates from published and unpublished surveys, 1990–2002 (latest available) using IOTF-recommended cut-offs for overweight and obesity.



Relationship between moderate and intense physical activity and longevity

20% REDUCTION IN THE RISK OF ALL CAUSES OF MORTALITY FOR LEISURE TIME MODERATE- TO VIGOROUS-INTENSITY PHYSICAL ACTIVITY AND MORTALITY



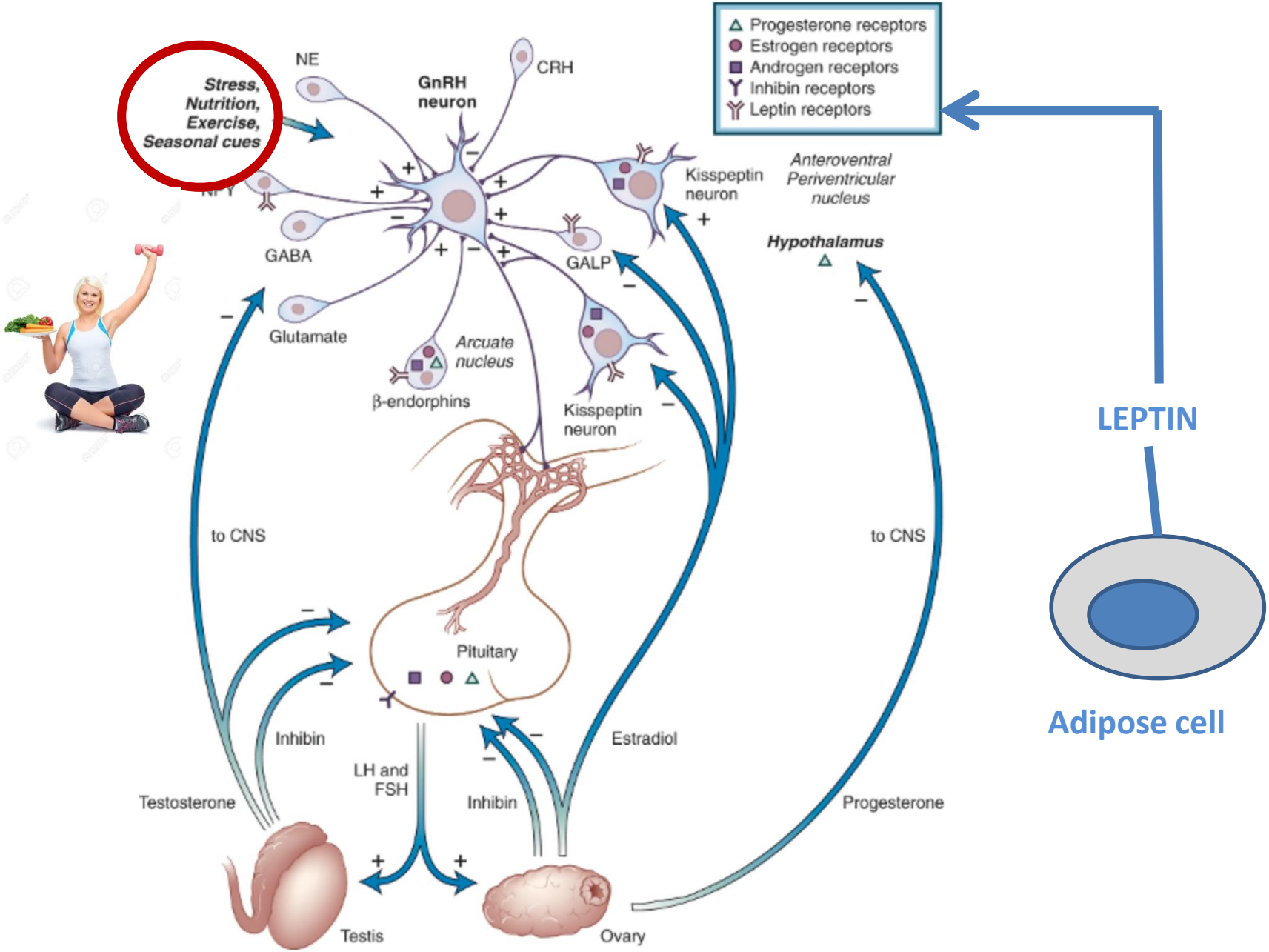
PHYSICAL ACTIVITY AS AN EXCELLENT THERAPY FOR
Obesity
Cardiovascular diseases
Type2 Diabetes
Dementia
Osteoporosis
Depression

Harem H et al JAMA Intern Med 2015

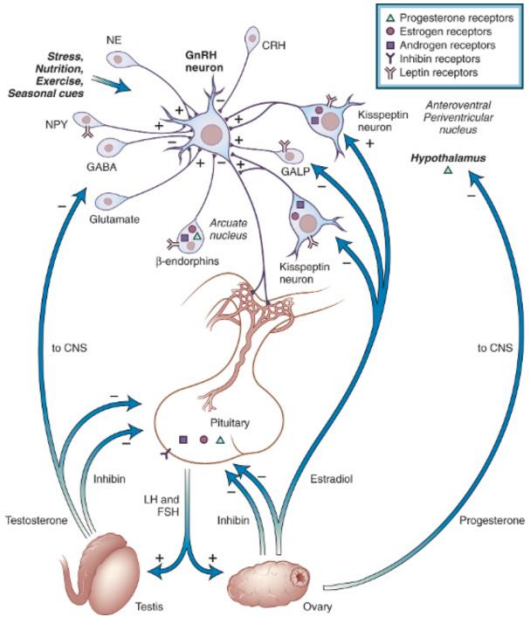
Physical activity and energy balance

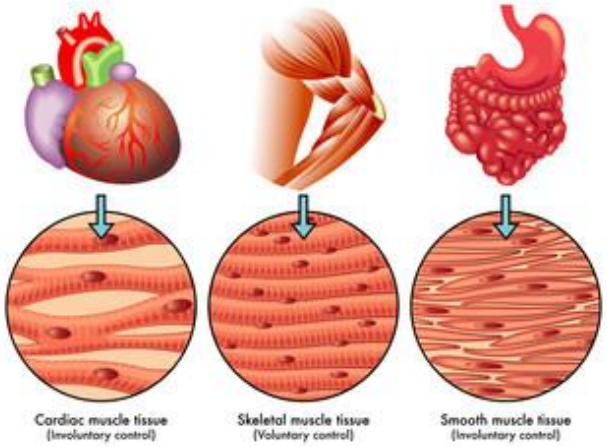
Hunger/satiety balance
Food availability
Caloric density
Macronutrients

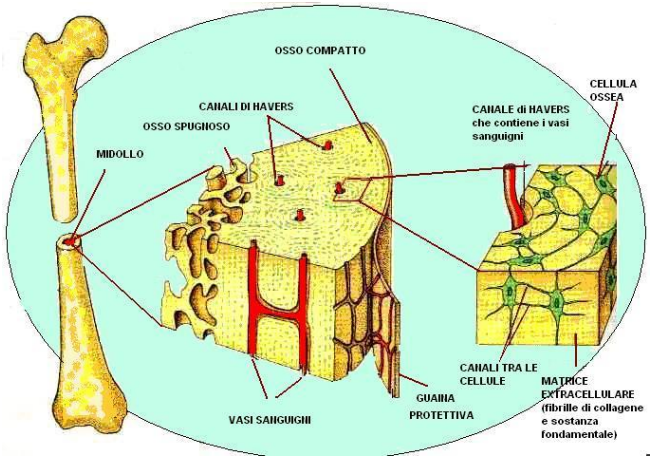
Resting Energy Expenditure **(REE)**
Wish to perform physical activity
Food energetic capacity
Termogenesis


Progesterone receptors
Estrogen receptors
Androgen receptors
Inhibin receptors
Leptin receptors
Stress, Nutrition, Exercise, Seasonal cues
NE
GnRH neuron
CRH
NPY
GABA
Glutamate
GALP
Kisspeptin neuron
Anteroventral Periventricular nucleus
Hypothalamus
Arcuate nucleus
β-endorphins
Kisspeptin neuron
to CNS
to CNS
Pituitary
Inhibin
LH and FSH
Inhibin
Estradiol
Testosterone
Progesterone
Testis
Ovary
LEPTIN
Adipose cell

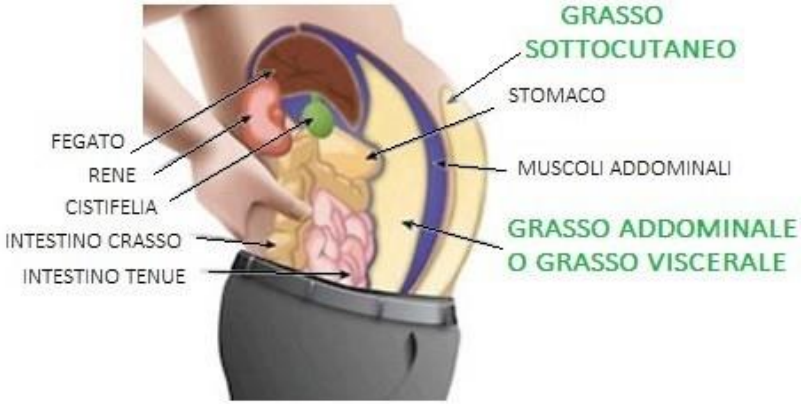
MUSCLE, BONE and ADIPOSE TISSUE AS IMPORTANT ENDOCRINE ORGANS

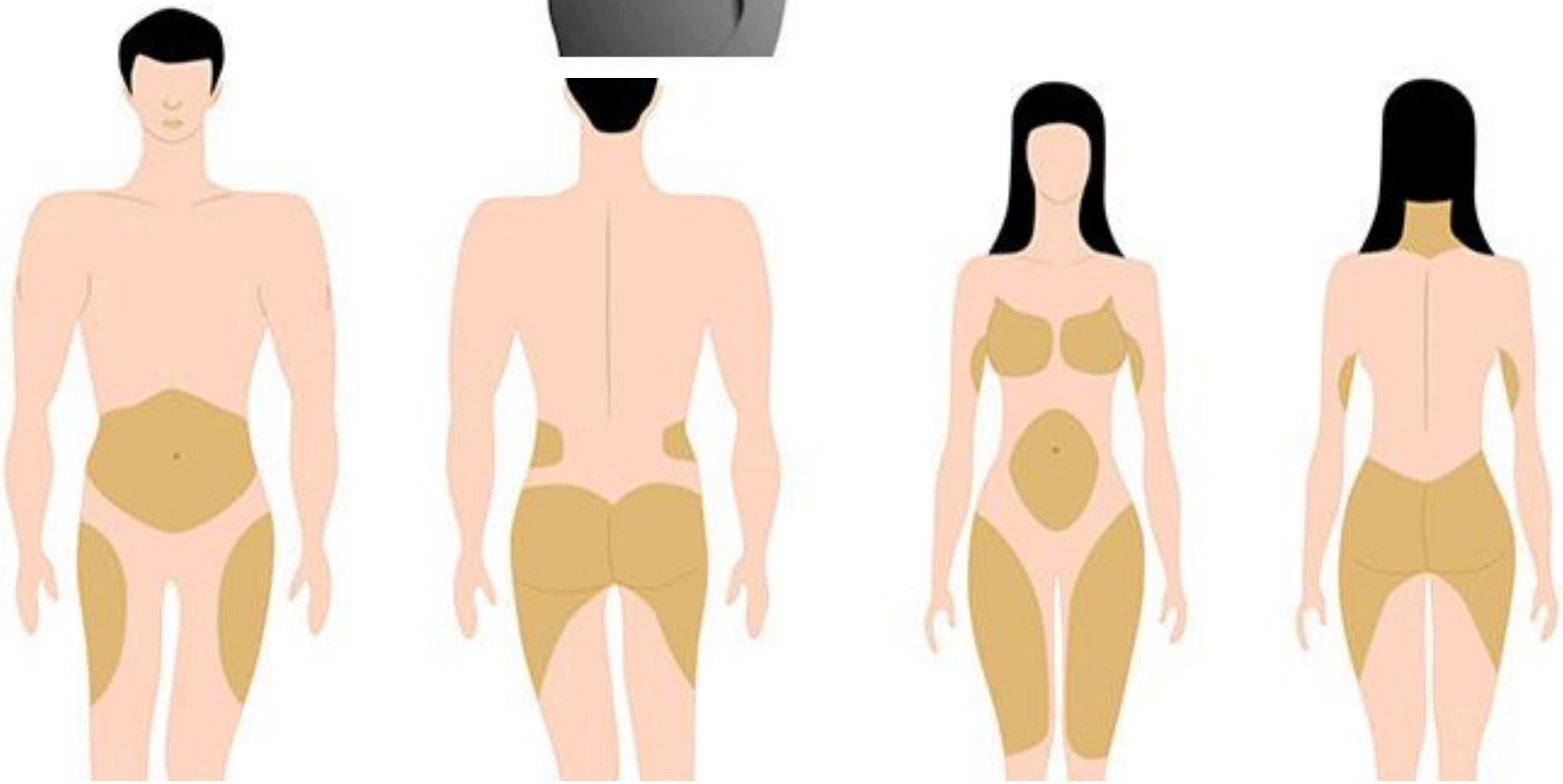






Adipose tissue

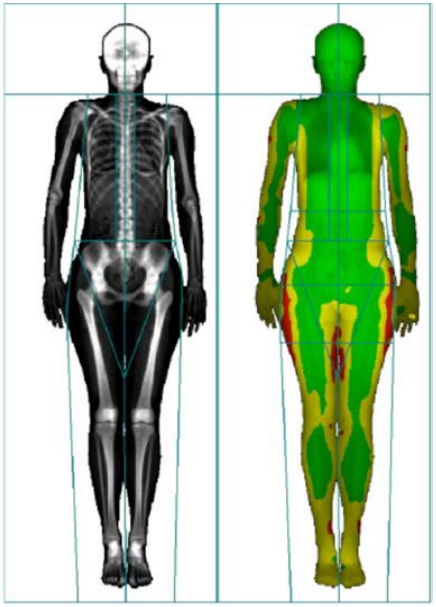


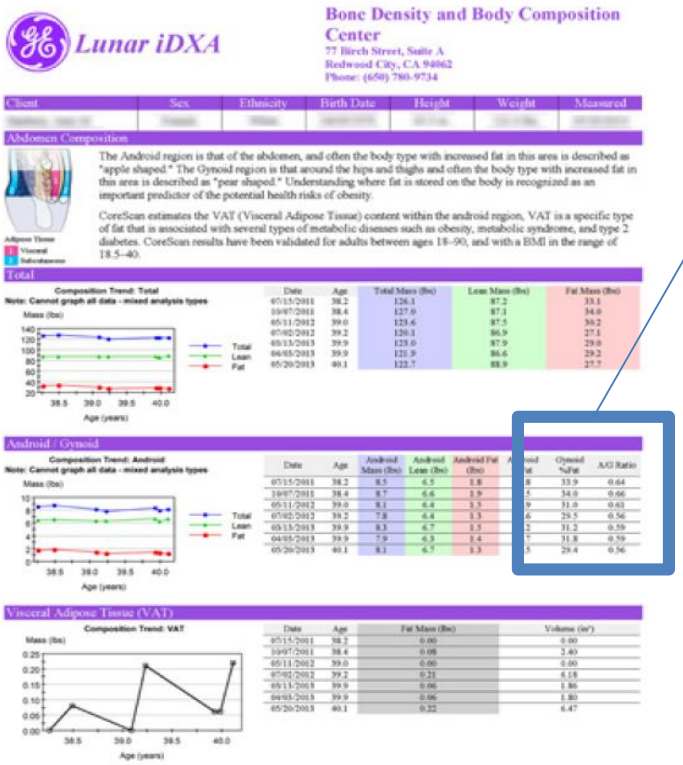


Evaluation of visceral fat

Volume 250.3±194.5 cm^3
Mass 235.9±183.1 gr
Cutoff visceral fat mass 350 gr

Endocrine 2014 (47)





Lunar iDXA

Bone Density and Body Composition Center
77 Birch Street, Suite A
Redwood City, CA 94062
Phone: (650) 780-9734

Client	Sex	Ethnicity	Birth Date	Height	Weight	Measured
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Abdomen Composition

The Android region is that of the abdomen, and often the body type with increased fat in this area is described as "apple shaped." The Gynoid region is that around the hips and thighs and often the body type with increased fat in this area is described as "pear shaped." Understanding where fat is stored on the body is recognized as an important predictor of the potential health risks of obesity.

CoreScan estimates the VAT (Visceral Adipose Tissue) content within the android region, VAT is a specific type of fat that is associated with several types of metabolic diseases such as obesity, metabolic syndrome, and type 2 diabetes. CoreScan results have been validated for adults between ages 18–90, and with a BMI in the range of 18.5–40.

Adipose Tissue
1 Visceral
2 Subcutaneous

Total

Composition Trend: Total
Note: Cannot graph all data - mixed analysis types

Date	Age	Total Mass (lbs)	Lean Mass (lbs)	Fat Mass (lbs)
07/15/2011	38.2	126.1	87.2	33.1
10/07/2011	38.4	127.0	87.1	34.0
05/11/2012	39.0	123.6	87.5	30.2
07/02/2012	39.2	120.3	86.9	27.1
05/13/2013	39.9	123.0	87.9	29.0
04/03/2013	39.9	121.9	86.6	29.2
05/20/2013	40.1	122.7	88.9	27.7

Android / Gynoid

Composition Trend: Android
Note: Cannot graph all data - mixed analysis types

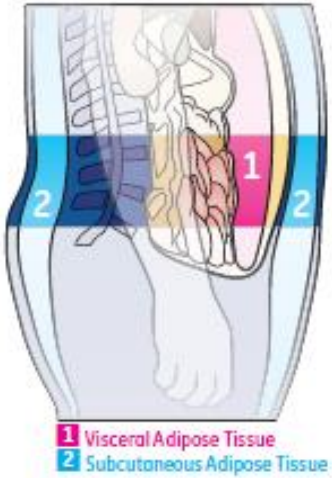
Date	Age	Android Mass (lbs)	Android Lean (lbs)	Android Fat (lbs)	Gynoid %Fat	A/G Ratio
07/15/2011	38.2	8.5	6.5	1.8	33.9	0.64
10/07/2011	38.4	8.7	6.6	1.9	34.0	0.66
05/11/2012	39.0	8.1	6.4	1.5	31.0	0.61
07/02/2012	39.2	7.8	6.4	1.3	29.5	0.56
05/13/2013	39.9	8.3	6.7	1.5	31.2	0.59
04/03/2013	39.9	7.9	6.3	1.4	31.8	0.59
05/20/2013	40.1	8.1	6.7	1.3	29.4	0.56

Visceral Adipose Tissue (VAT)

Composition Trend: VAT

Date	Age	Fat Mass (lbs)	Volume (in³)
07/15/2011	38.2	0.00	0.00
10/07/2011	38.4	0.08	2.40
05/11/2012	39.0	0.00	0.00
07/02/2012	39.2	0.21	6.18
05/13/2013	39.9	0.06	1.86
04/03/2013	39.9	0.06	1.80
05/20/2013	40.1	0.22	6.47

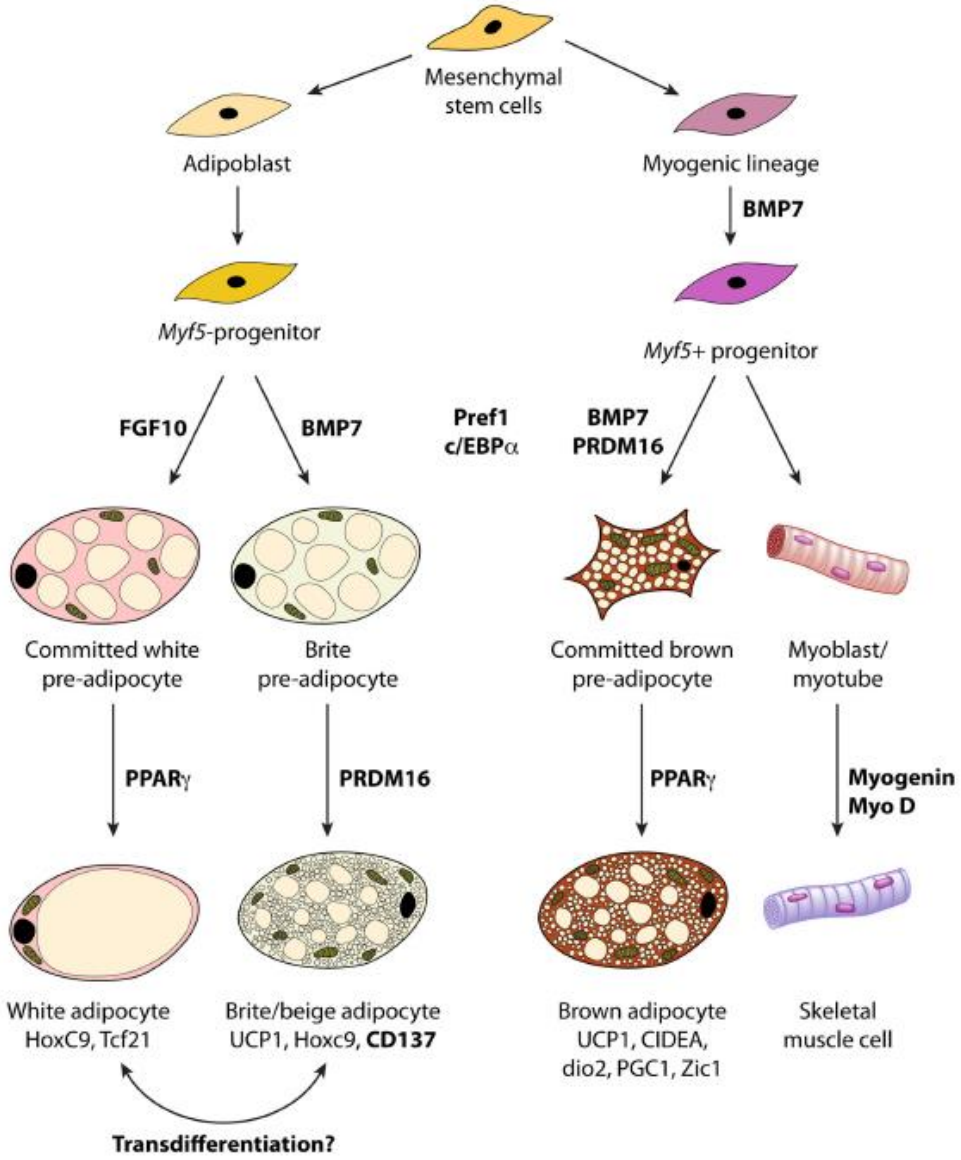
A/G Fat



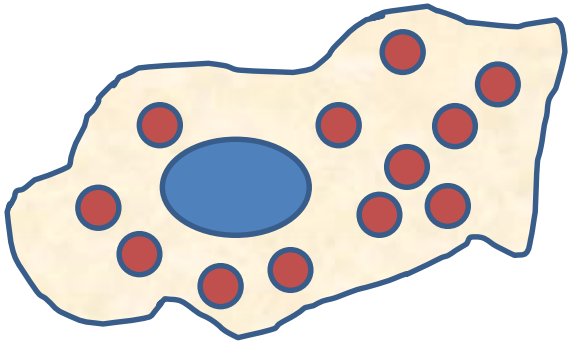
ADIPOKINES

Category	Proteins
Hormones	Leptin, resistin, angiotensinogen, adiponectin, estrogens, visfatin, angiopoietin4
Citokines	Interleukin 1,6,8,10 Interferon γ, TNFα
Extracellular matrix factors	Collagen-α1, Metalloproteinases, fibronectin,osteonectin, laminin, entactin, trombospondin 1 and 2
Complement's factors	Adipsin, C3, Factor B
Enzymes	Transfer protein for cholesterol esters, lipoprotein lipase
Acute response proteins	Acid glicoprotein A-1, Aptoglobin
Others	NEFA, plasminogen activator inhibitory factor, prostaciclina

WHITE, BROWN and «BRITE/BEIGE ADIPOCYTES

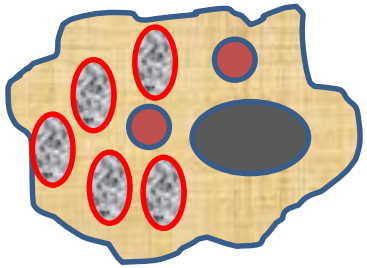


Obregon MJ. Frontiers in Physiology 5:479,2014



***WHITE* adipocyte**

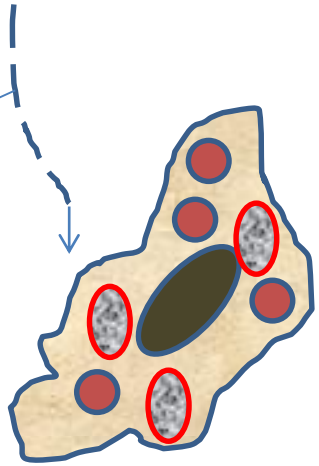
Triglicerydes (0.4-0.6 µgr)



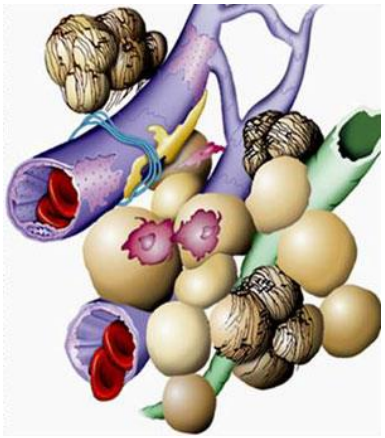
***BROWN* adipocyte**

Mitocondri

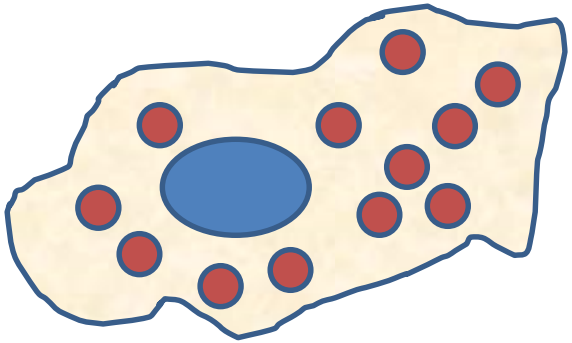
Transdifferentiation
(Browning)



***BRITE* adipocyte**



VEGF

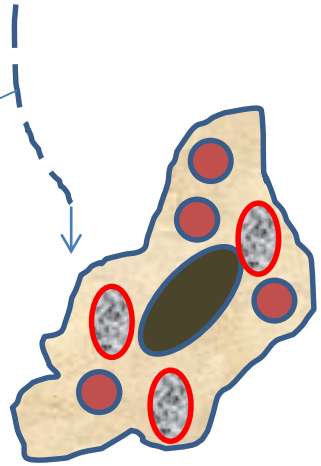


***WHITE* adipocyte**

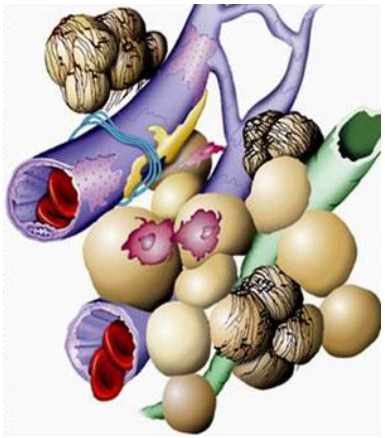
Triglicerydes (0.4-0.6 µgr)

ABILITY OF STORING ENERGY IN THE FORM OF TRIACYLGLYCEROL AND RELEASING ENERGY IN THE FORM OF FREE FATTY ACIDS

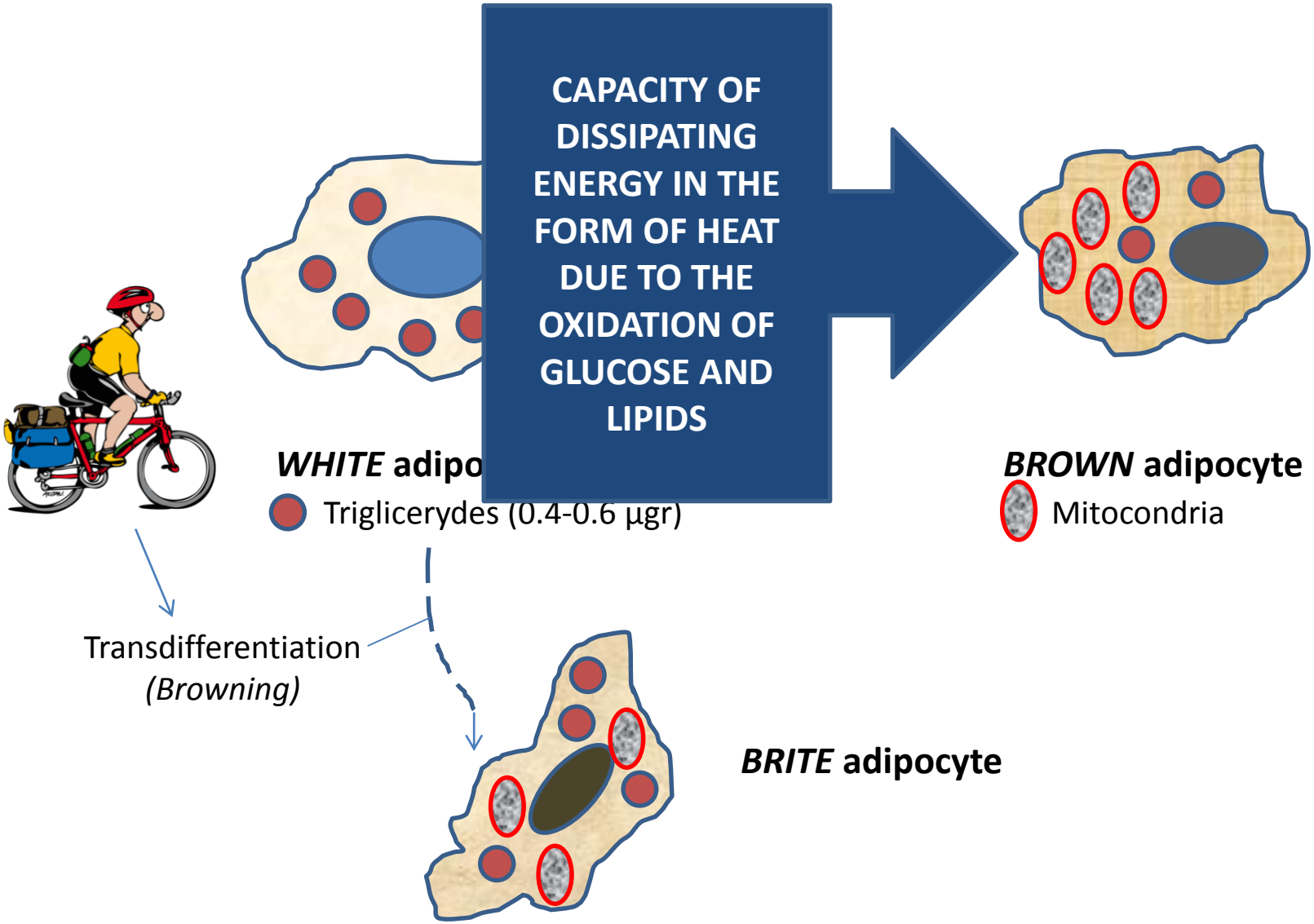
Transdifferentiation
(Browning)

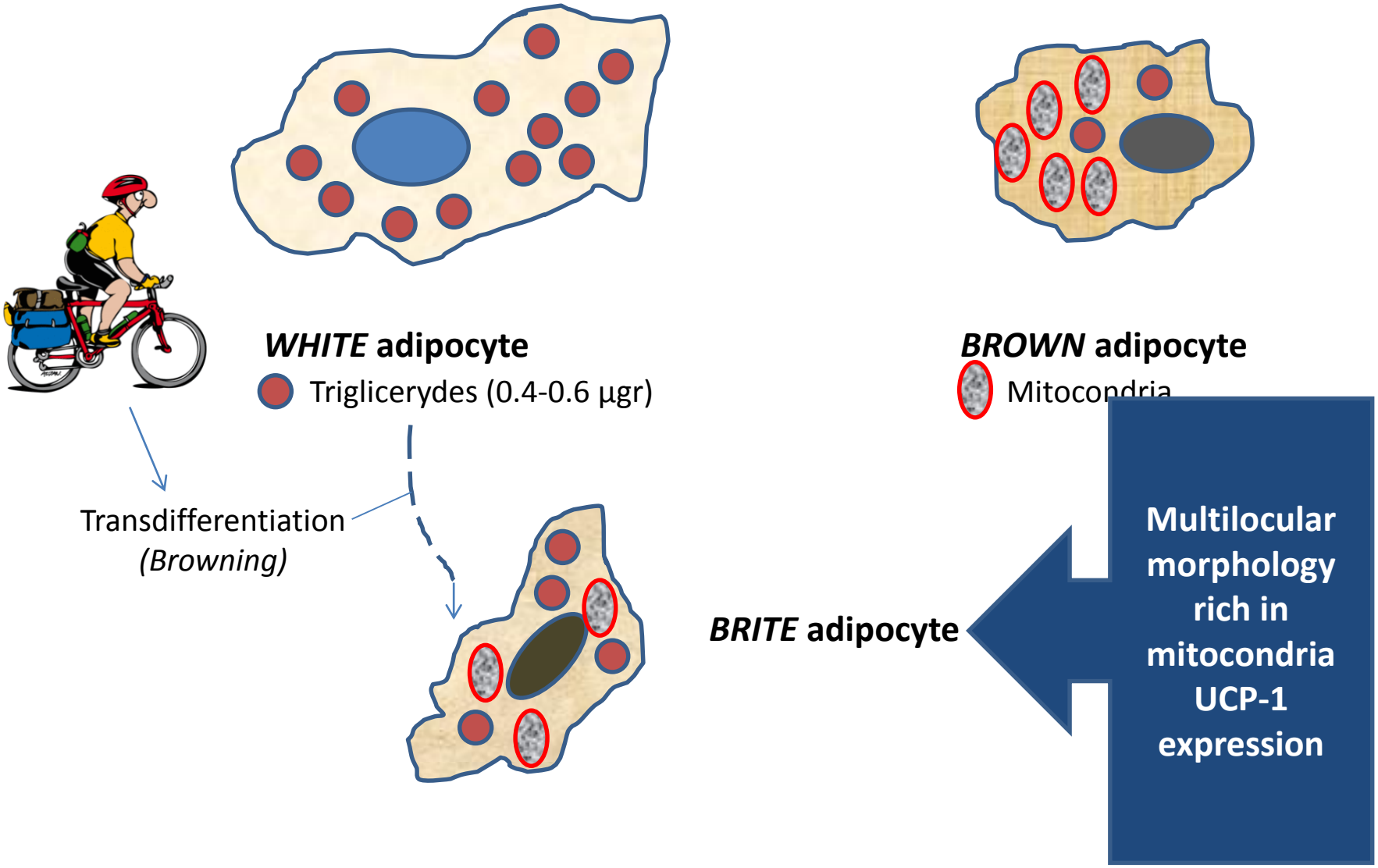


***BRITE* adipocyte**

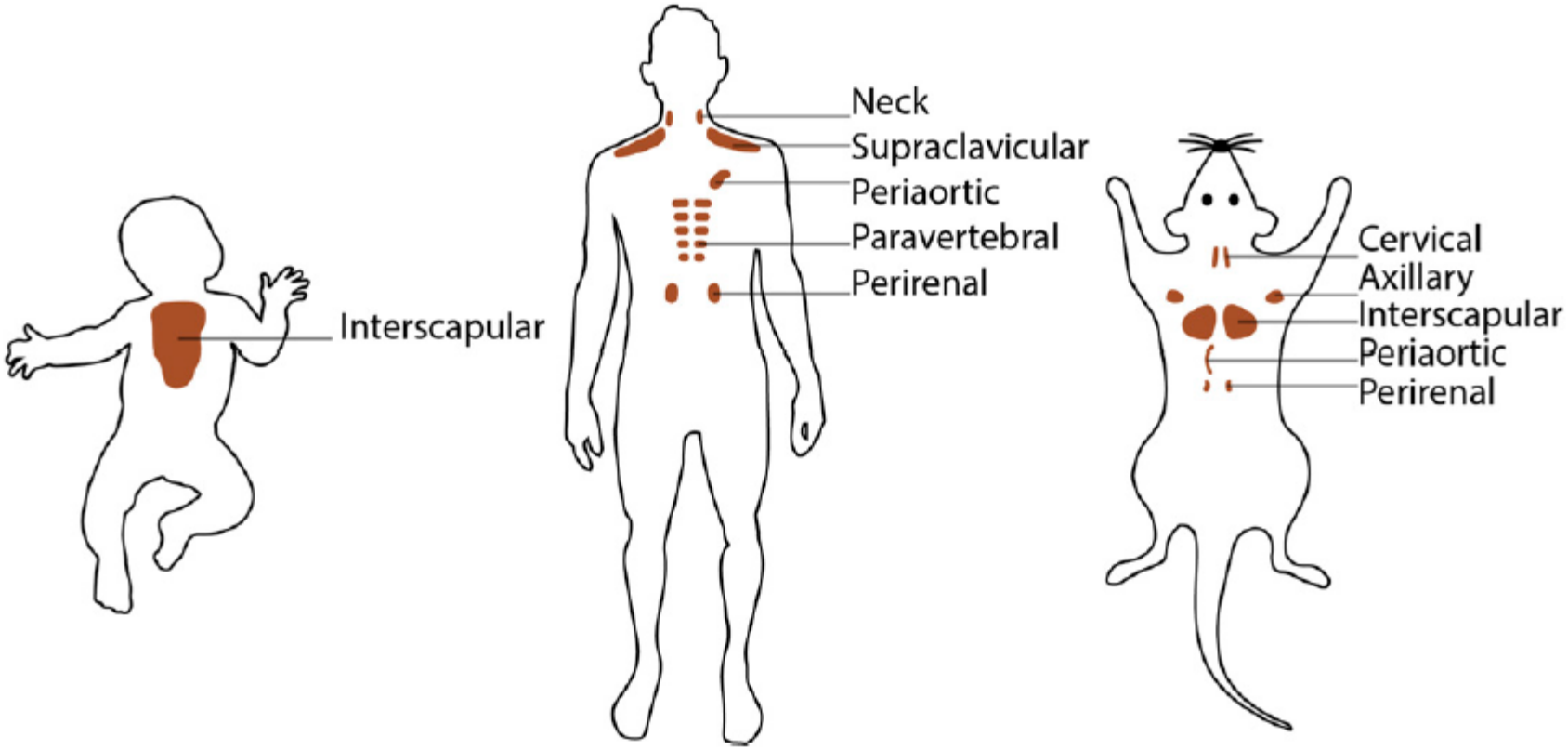


VEGF


CAPACITY OF DISSIPATING ENERGY IN THE FORM OF HEAT DUE TO THE OXIDATION OF GLUCOSE AND LIPIDS
WHITE adipo
Triglicerydes (0.4-0.6 µgr)
BROWN adipocyte
Mitocondria
Transdifferentiation
(Browning)
BRITE adipocyte

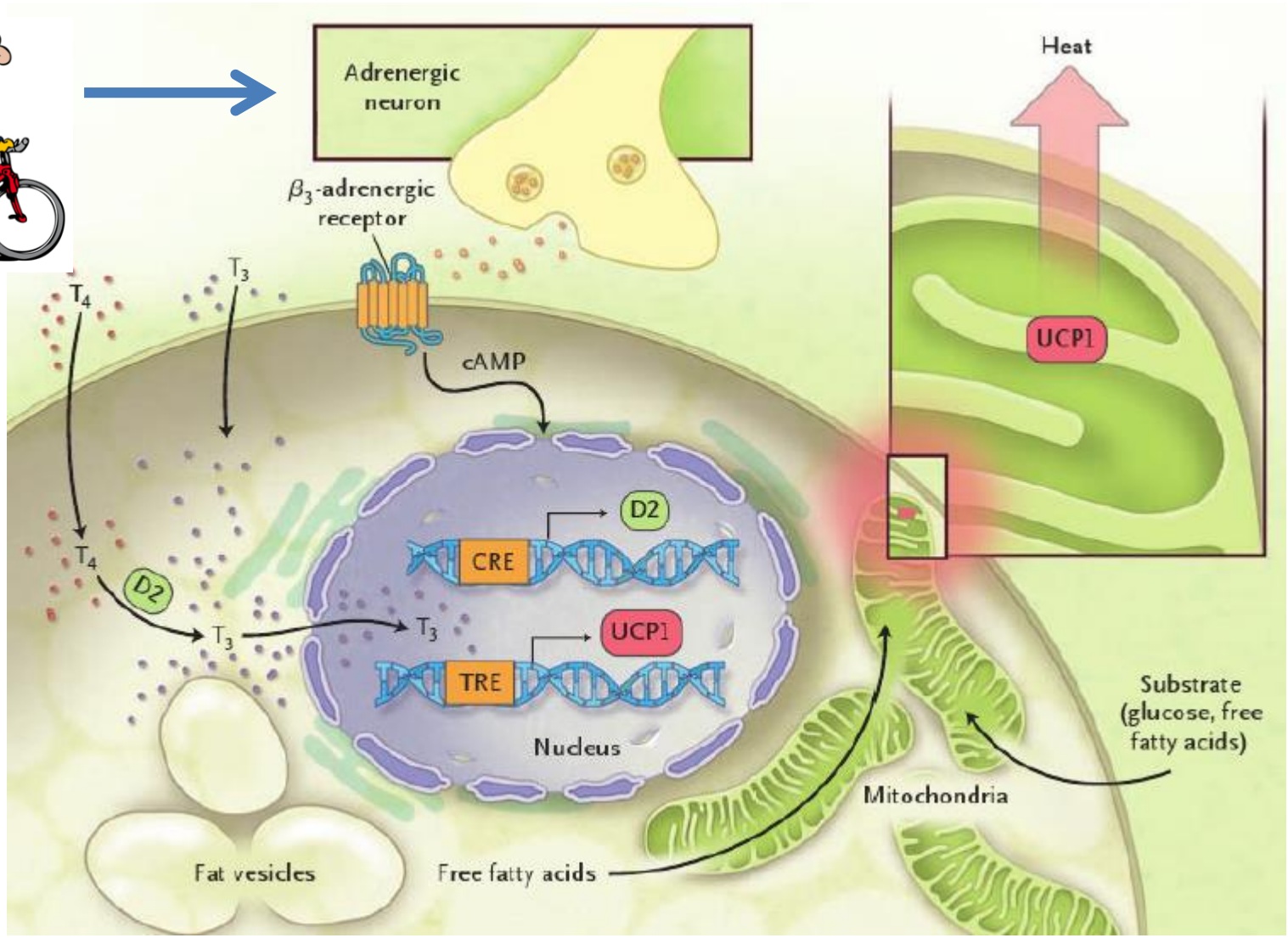

WHITE adipocyte
Triglicerydes (0.4-0.6 µgr)
BROWN adipocyte
Mitocondria
Transdifferentiation
(Browning)
BRITE adipocyte
Multilocular morphology rich in mitocondria UCP-1 expression

SITE OF BROWN ADIPOSE TISSUE IN HUMAN AND MICE



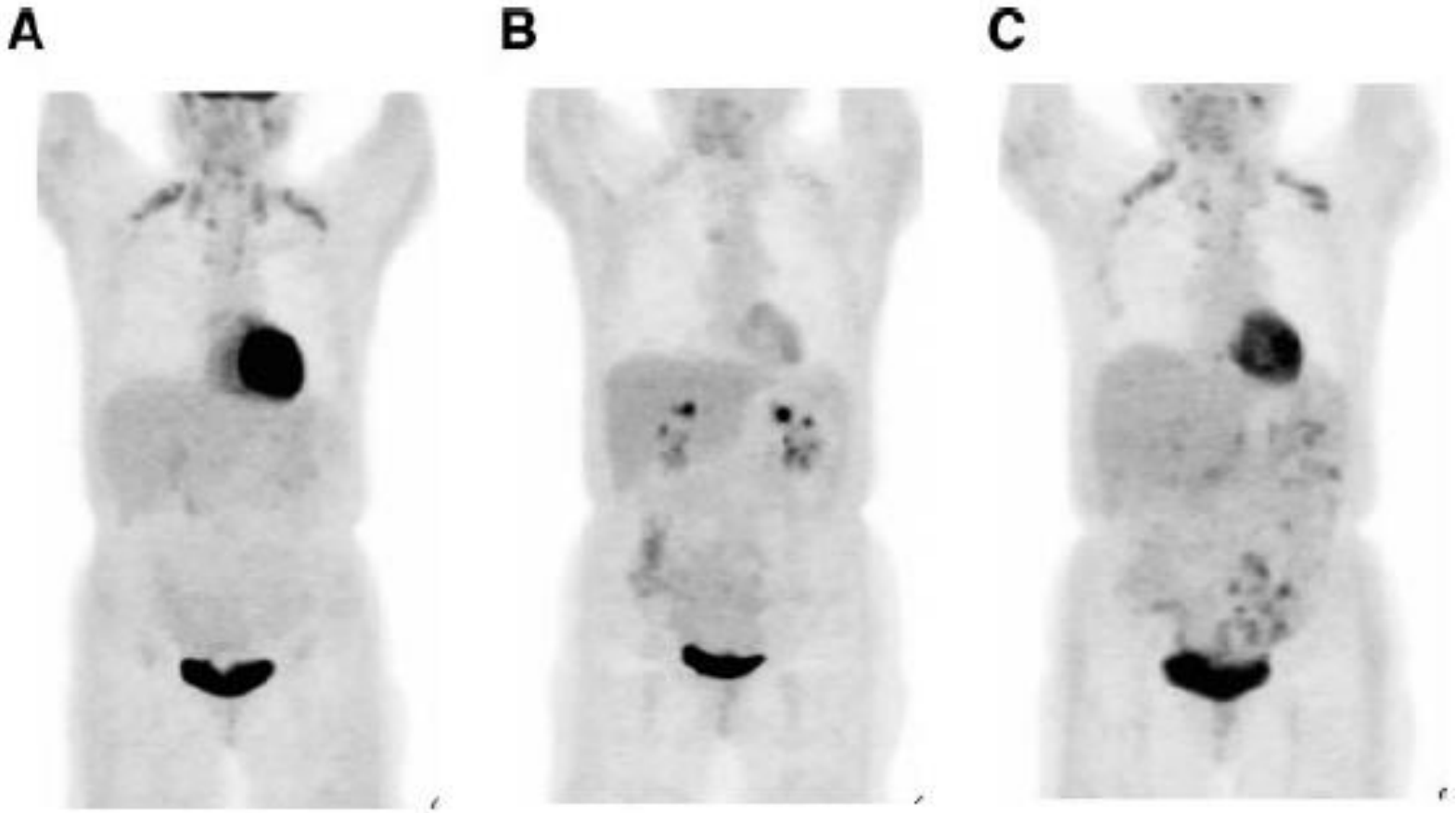
Van den Berg SM et al. Endocrine Review 38:46-68,2017

ACTIVATION OF BROWN FAT (UCP1)



Celi F. NEJM 2009

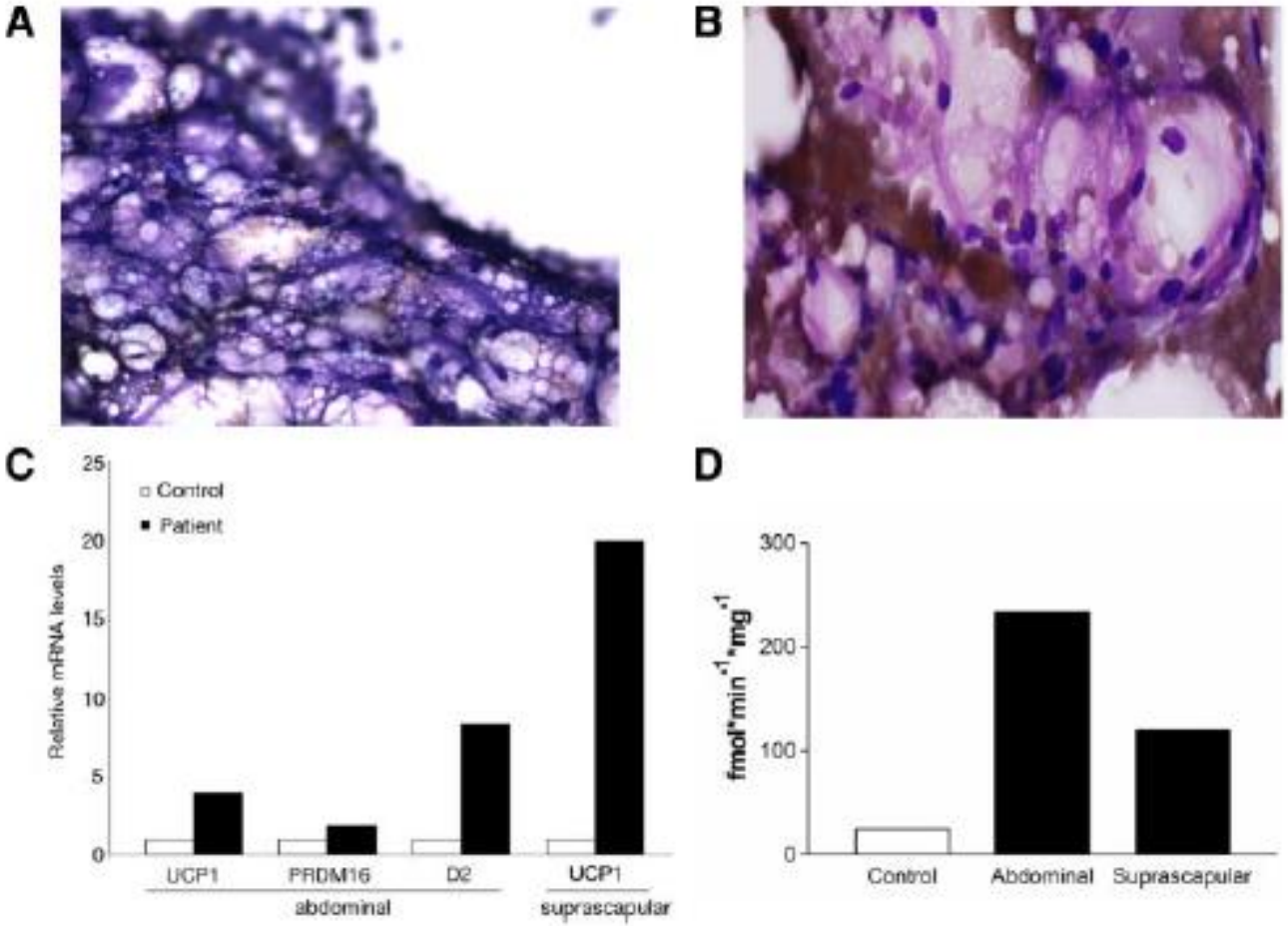
THYROID HORMONES AND BAT



fT4+ fT4- LT4+

Skarulis et al. JCEM 2010

HISTOLOGICAL AND MOLECULAR EVIDENCE OF THE EFFECT OF THYROID HORMONES ON BAT

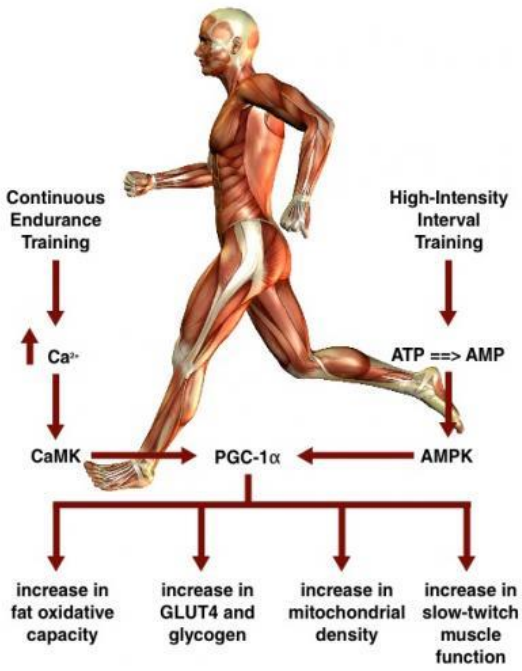


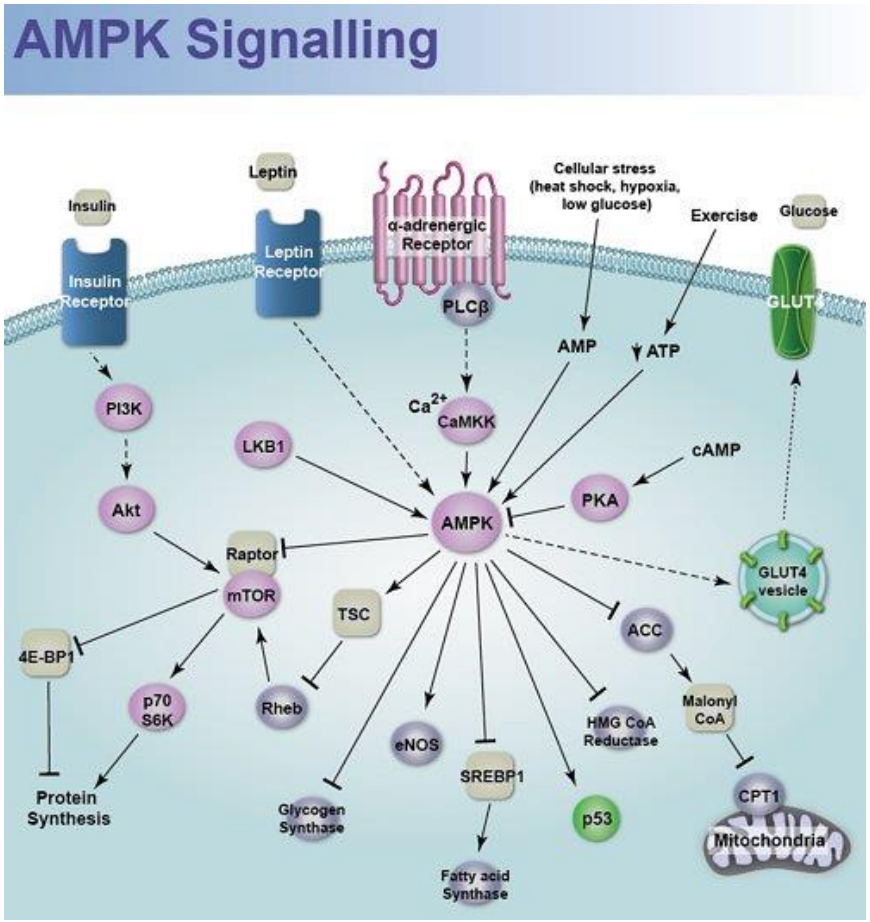
Skarulis et al. JCEM 2010

ATP consuption | ATP production

AMP:ATP

ENERGY EXPENSE

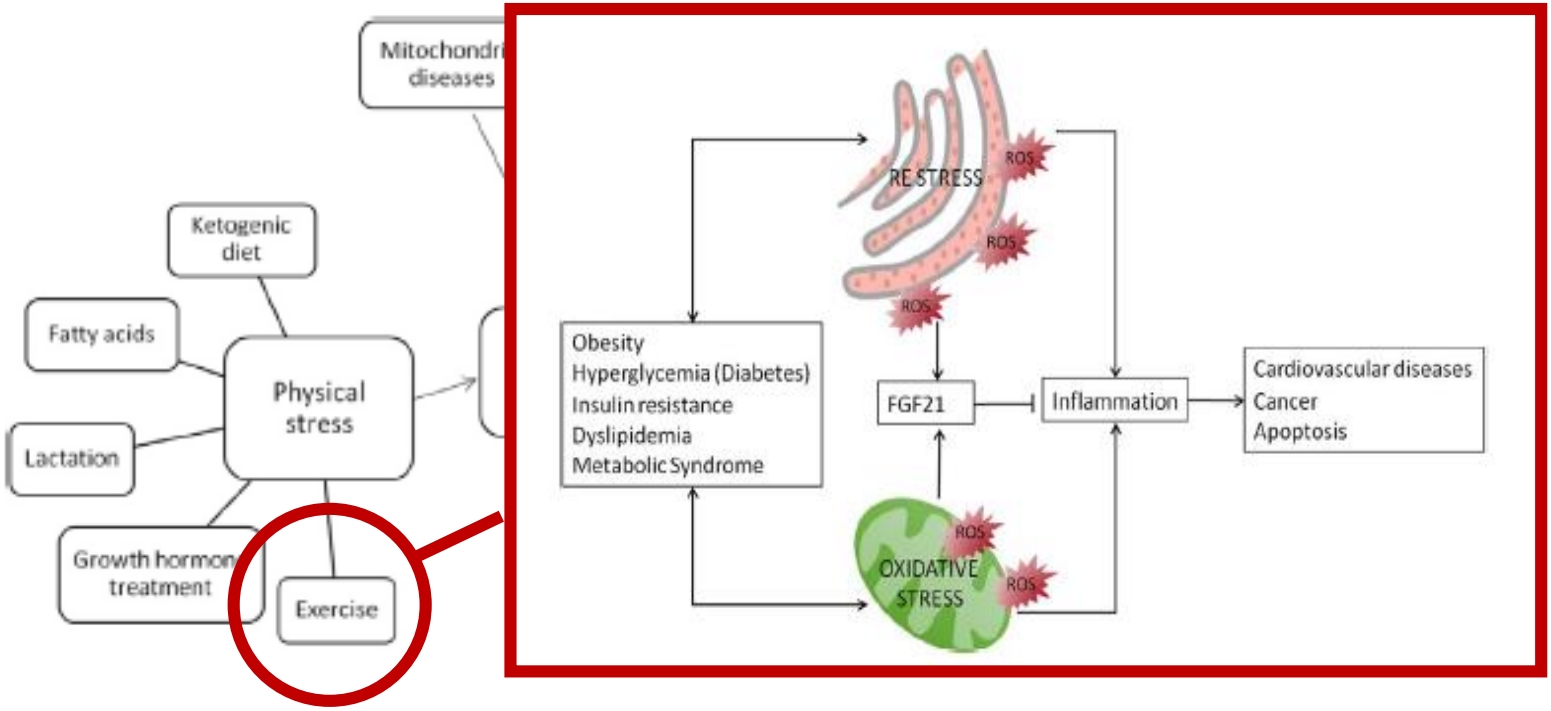




Fibroblast Growth Factor 21 is a 209 amino acid endocrine member of the FGF family synthesized in the liver and expressed in adipose tissue, muscle tissue and various other organs. FGF-21 is an important regulatory molecule of the homeostatic energy balance necessary to mediate the beneficial metabolic effects of physical exercise. It is expressed in WAT, BAT, pancreas, muscle tissue, cardiac endothelial cells and hypothalamus

CONDITIONS ASSOCIATED WITH THE INCREASED EXPRESSION OF FGF21

FGF21 inhibits inflammation in response to oxidative stress

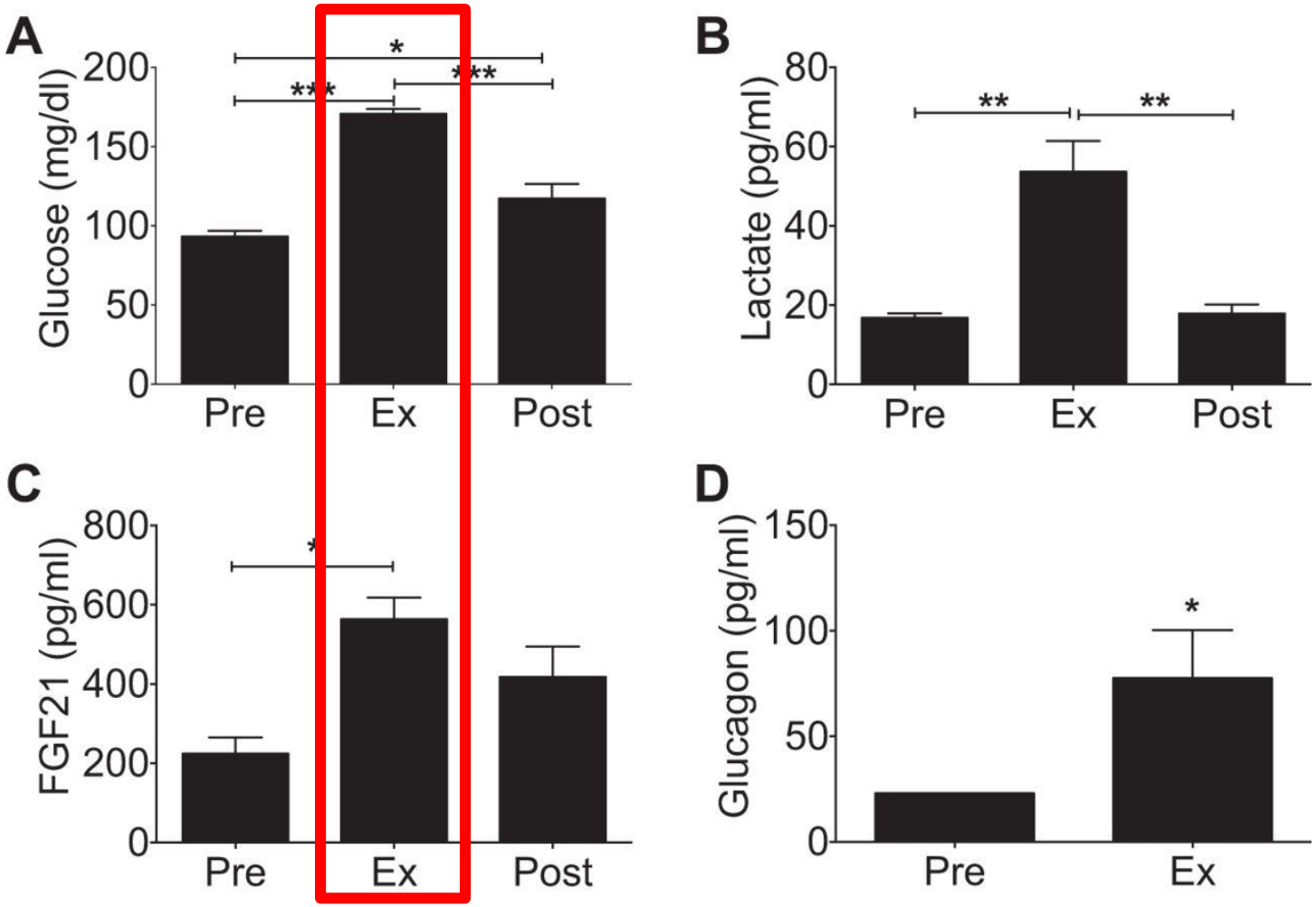


Gomez-Samano MA et al. Redox Biology 2017

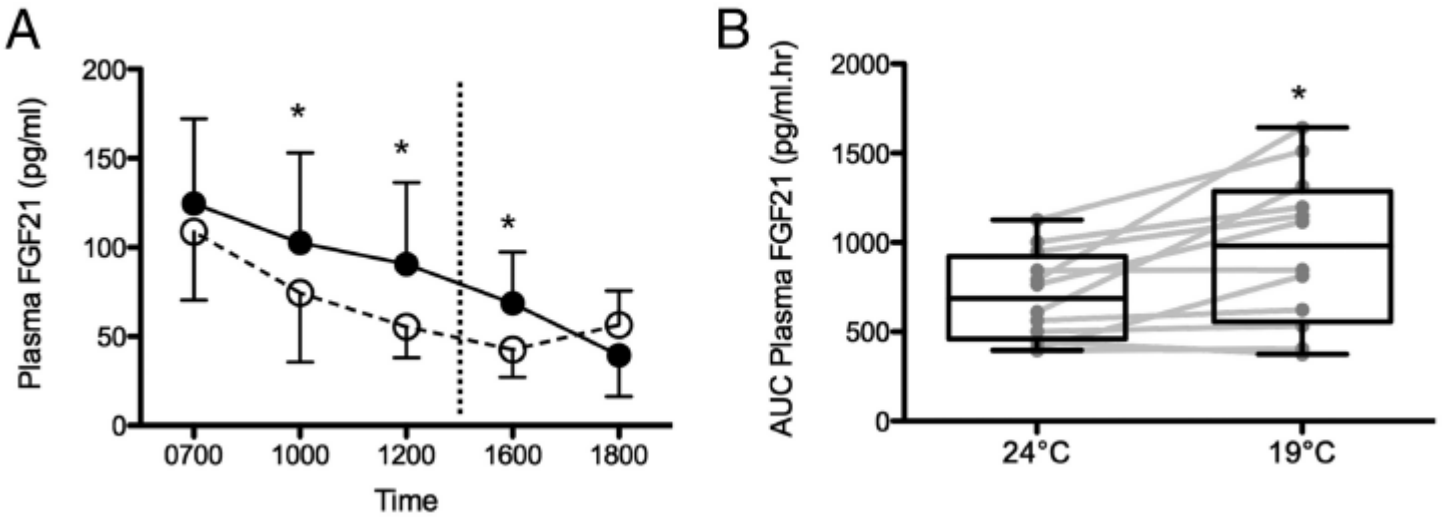
Fibroblast growth factor-21 is required for beneficial effects of exercise during chronic high-fat feeding in Wistar rats

Christine Loyd, I. Jack Magrisso, Michael Haas, Sowmya Balusu, Radha Krishna, Nobuyuki Itoh, Darleen A. Sandoval, Diego Perez-Tilve, Silvana Obici, Kirk M. Habegger

Journal of Applied Physiology Published 1 September 2016 Vol. 121 no. 3, 687-698

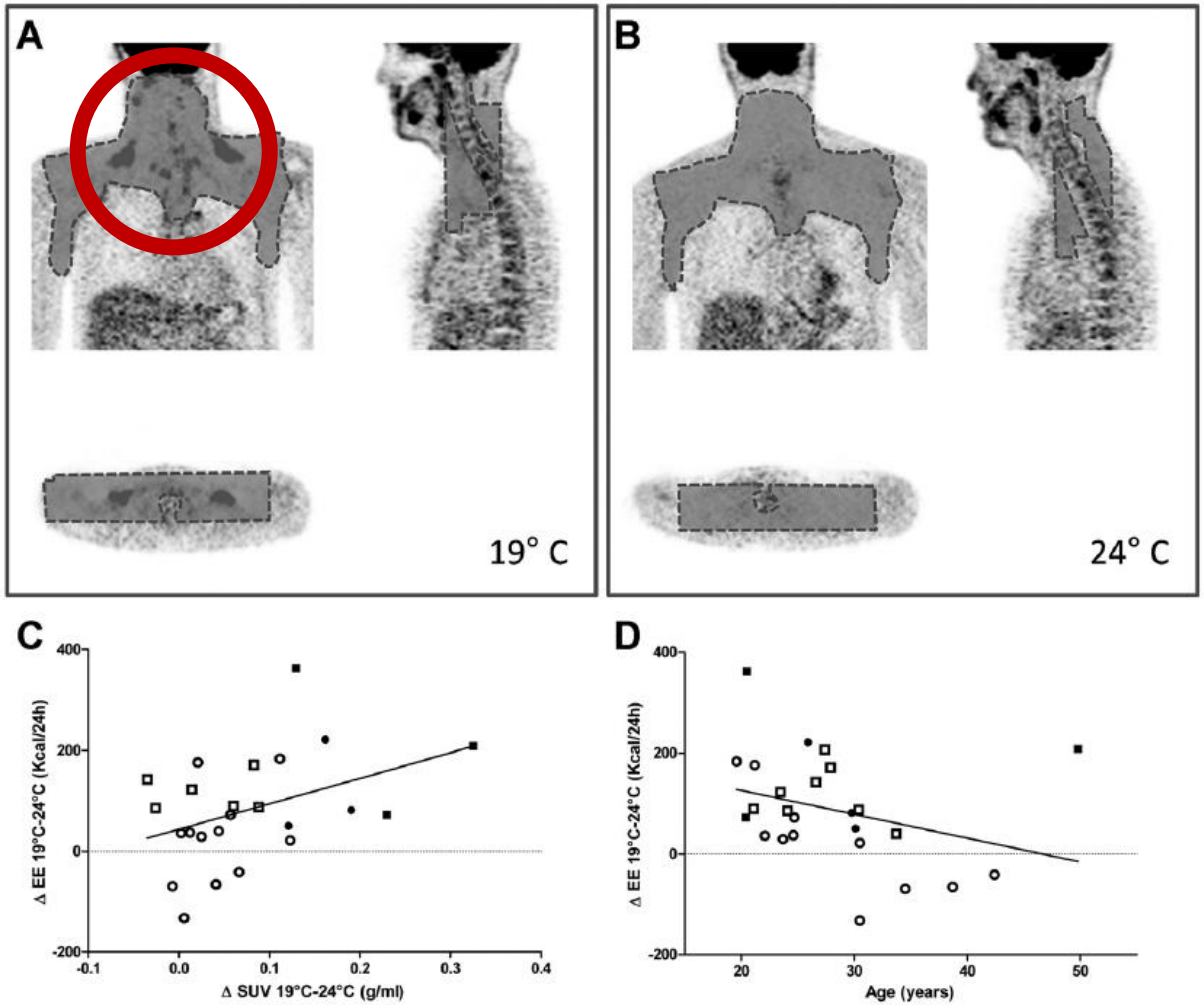


Circadian variations of FGF21 and its concentrations at different temperatures



Chen et al. JCEM 2013

PET IMAGES DEMONSTRATING 18F-FDG uptake IN LOCALIZED BAT DEPOSITS



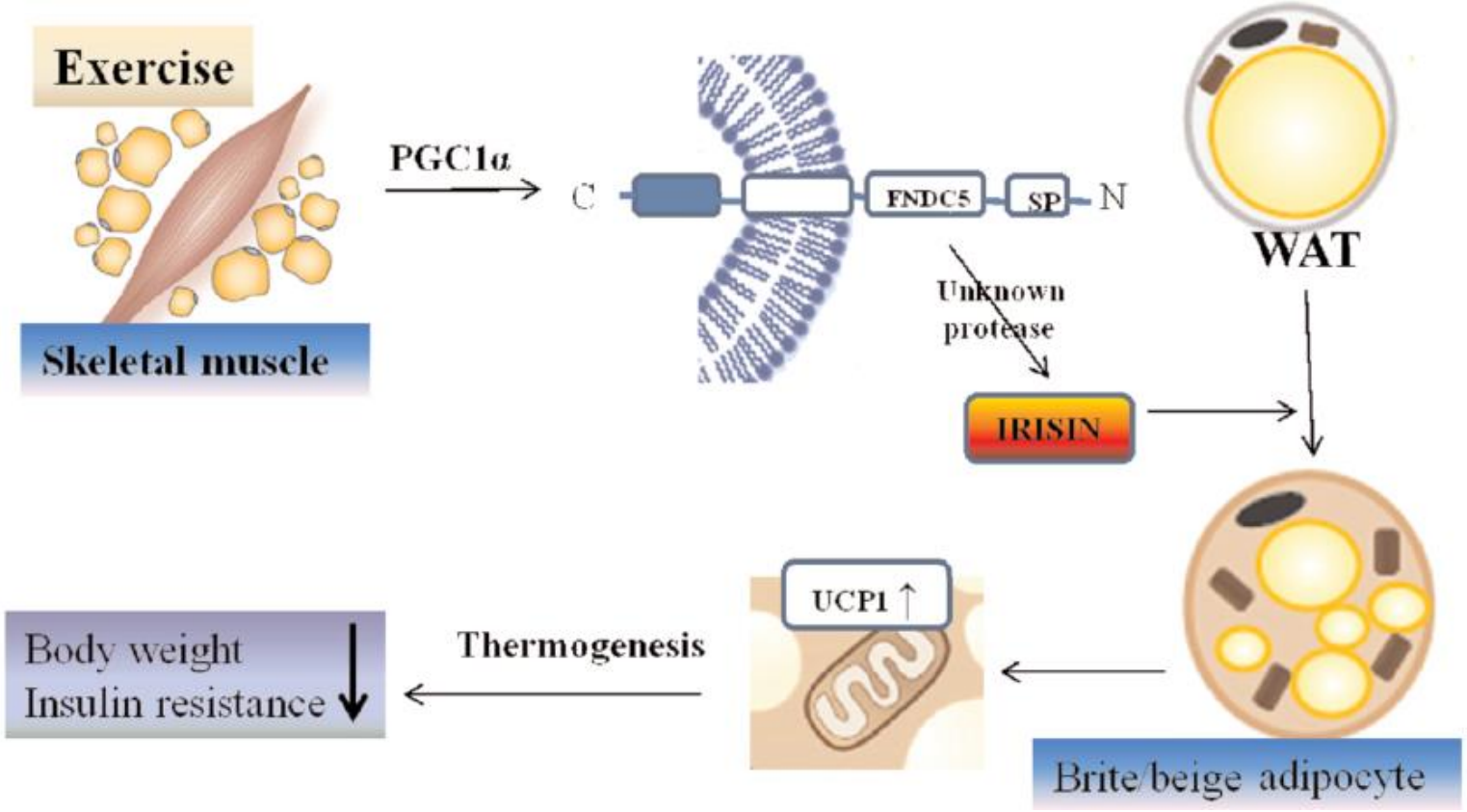
Chen et al. JCEM 2013

FDF-21 a stress response hormone

IRISIN

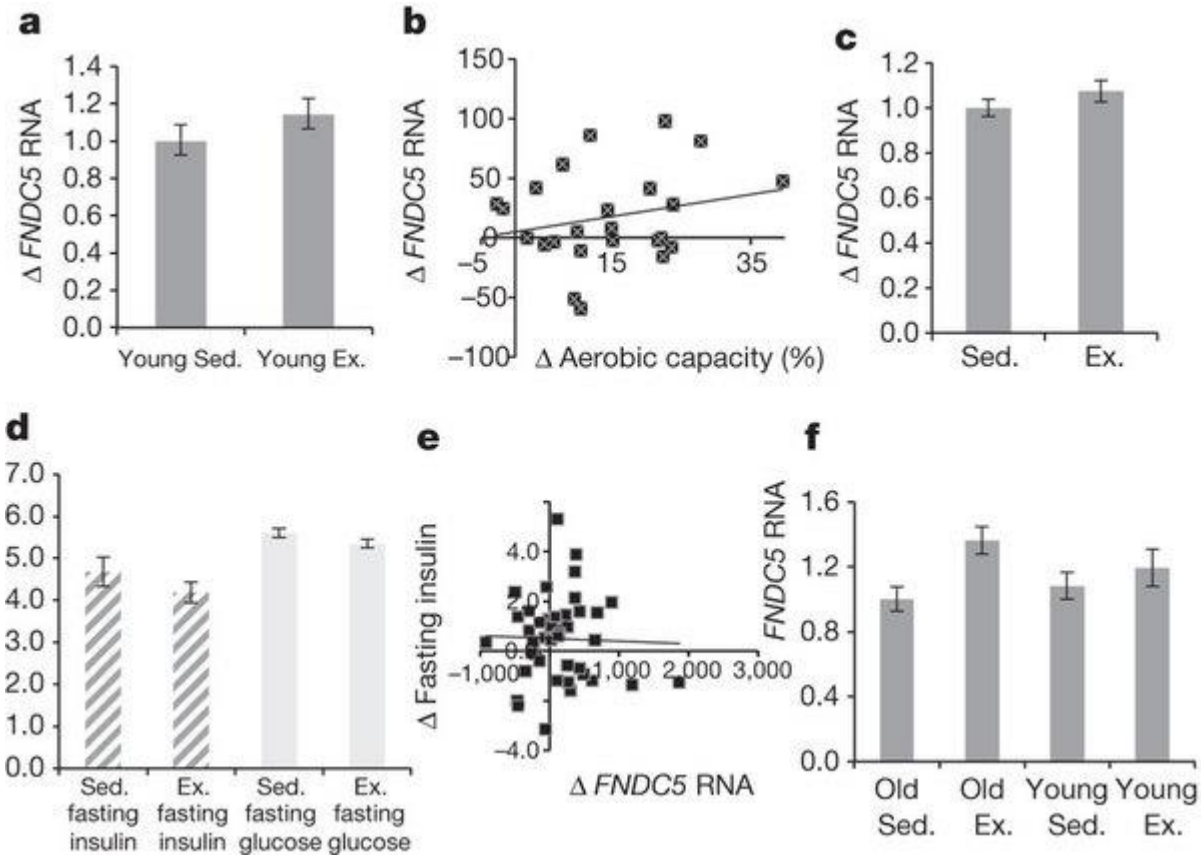
THE WELLNESS HORMONE

PHYSICAL EXERCISE INDUCES THE RELEASE OF PPARγ coactivator-1 ± (PGC1Î ±) FROM THE SKELETAL MUSCLE WHICH INCREASES THE EXPRESSION OF FIBRONECTIN TYPE III DOMAIN 5 (FNDC5) WHICH IN TURNS THROUGH THE ACTION OF UNKNOWN PROTEASES INDUCES THE RELEASE OF IRISIN

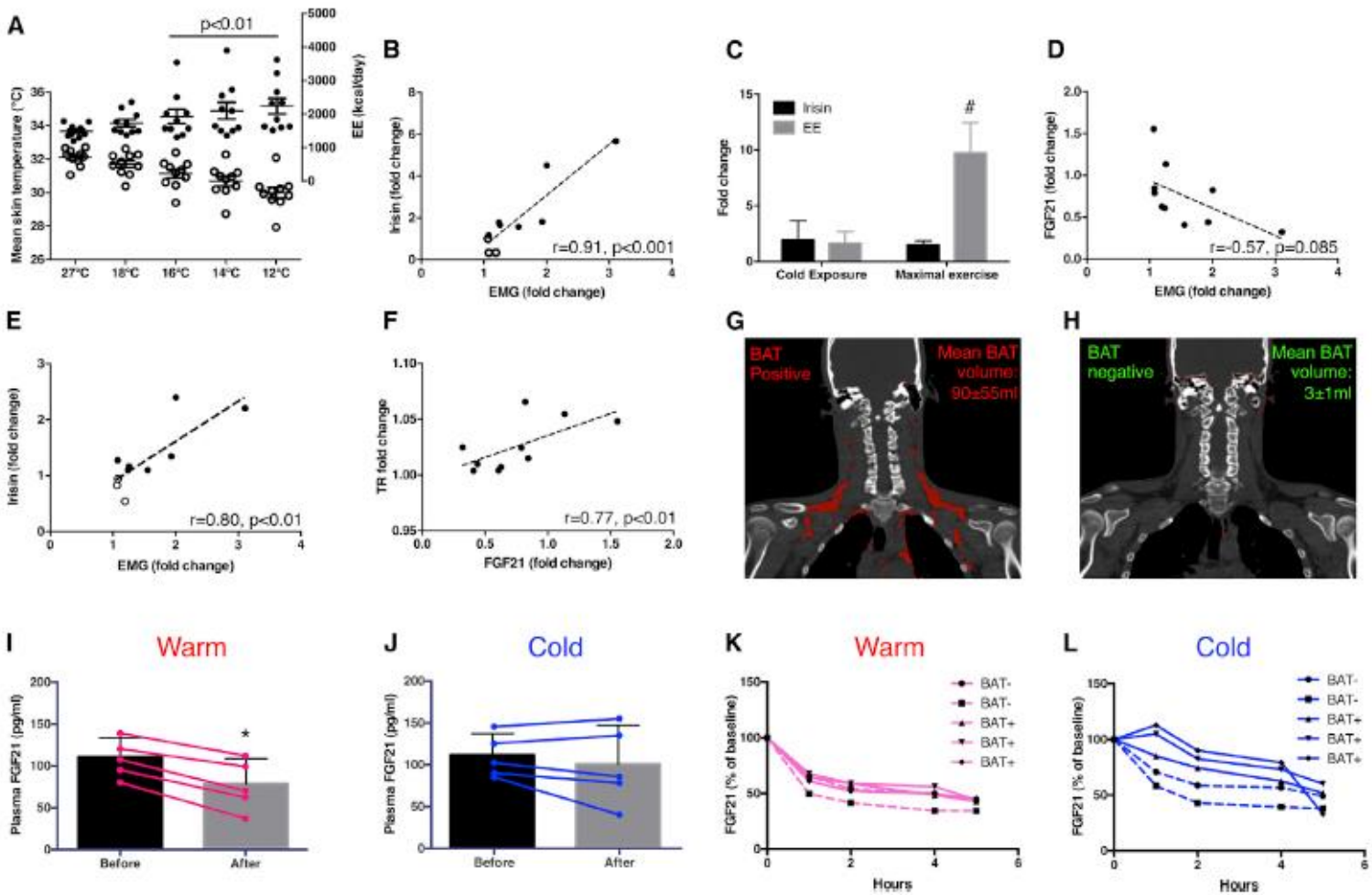


Panati K et al. ERMPS 2016

exercise training induces the expression of the *FNDC5* gene in human muscle, producing irisin, which can convert white fat into brown fat



THE REGULAR PHYSICAL EXERCISE AND THE COLD EXPOSURE ARE ASSOCIATED WITH AN INCREASE IN EE, IN A POSITIVE CORRELATION WITH THE RELEASE OF IRISIN and FGF21.



Lee P et al. Cell Metabolism 2014

IRISIN in PHYSIOPATHOLOGY

Inflammation

Marker of macrovascular pathology in Type 2 Diabetes

Cardiovascular pathologies in Type2 diabetes

Correlation between circulating irisin and endothelial dysfunction. Low levels of circulating irisin can be used as markers to identify an early state of angiopathy (12 pg / ml vs 40 pg / ml)

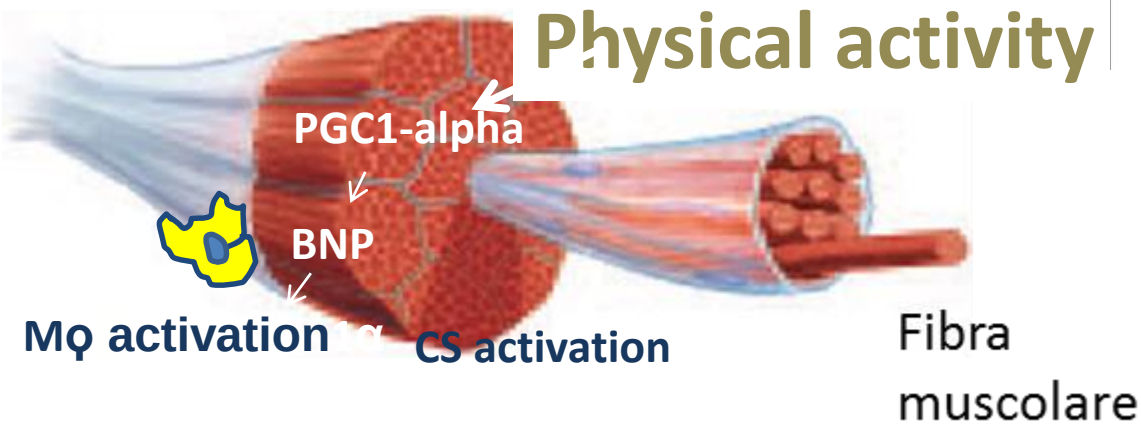
Kidney diseases

Low levels of irisin in severe kidney insufficiency

Metabolism

Biomarker for low or altered metabolic state in obese patients

NATRIURETIC PEPTIDES

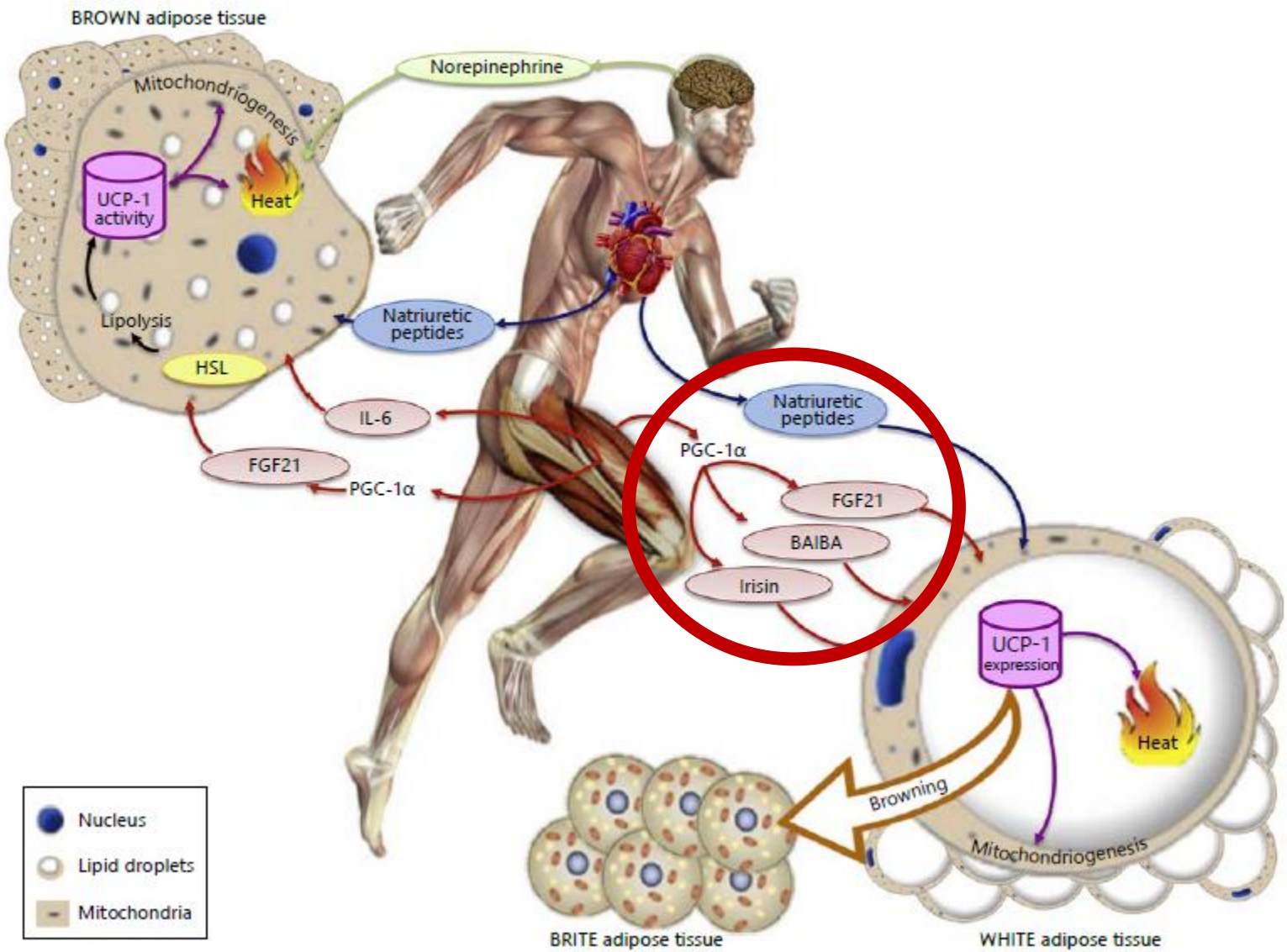


The levels of PGC-1α in the muscle are regulated by muscle activity through all the major signaling pathways involved in the contraction of muscle fibers and in turn they promote a high-strength muscle phenotype

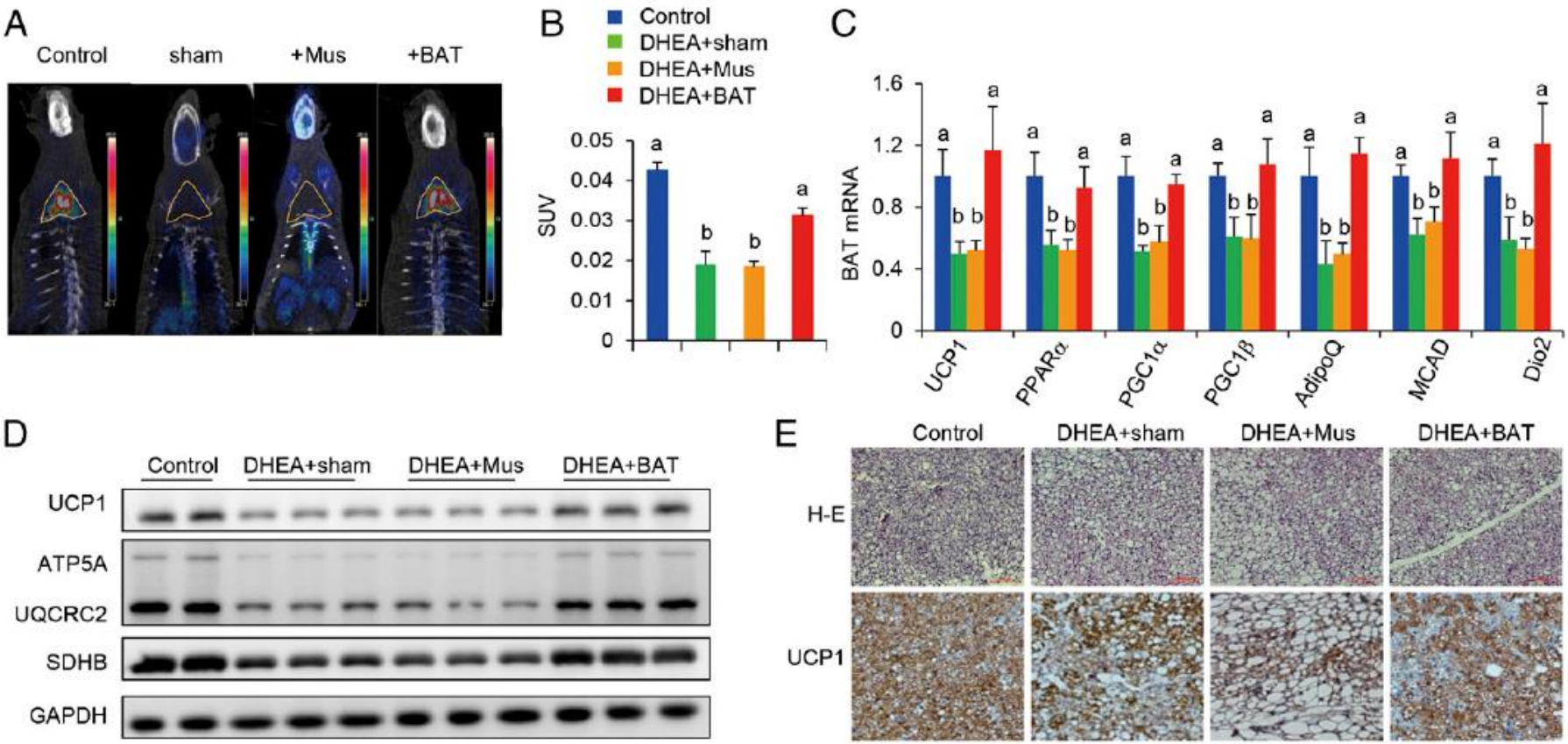
The over-expression of PGC-1Î promotes satellite cell (CS) activation by inducing a remodeling of the stem cell niche by upregulation of fibronectin

PGC-1α reduces pro-inflammatory gene programs in muscle fibers and promotes an increase in tissue macrophages, Brain Natriuretic Peptide (BNP) is the myokine that regulates cross-talk between muscle fibers and macrophages during physical activity downstream of PGC -1α

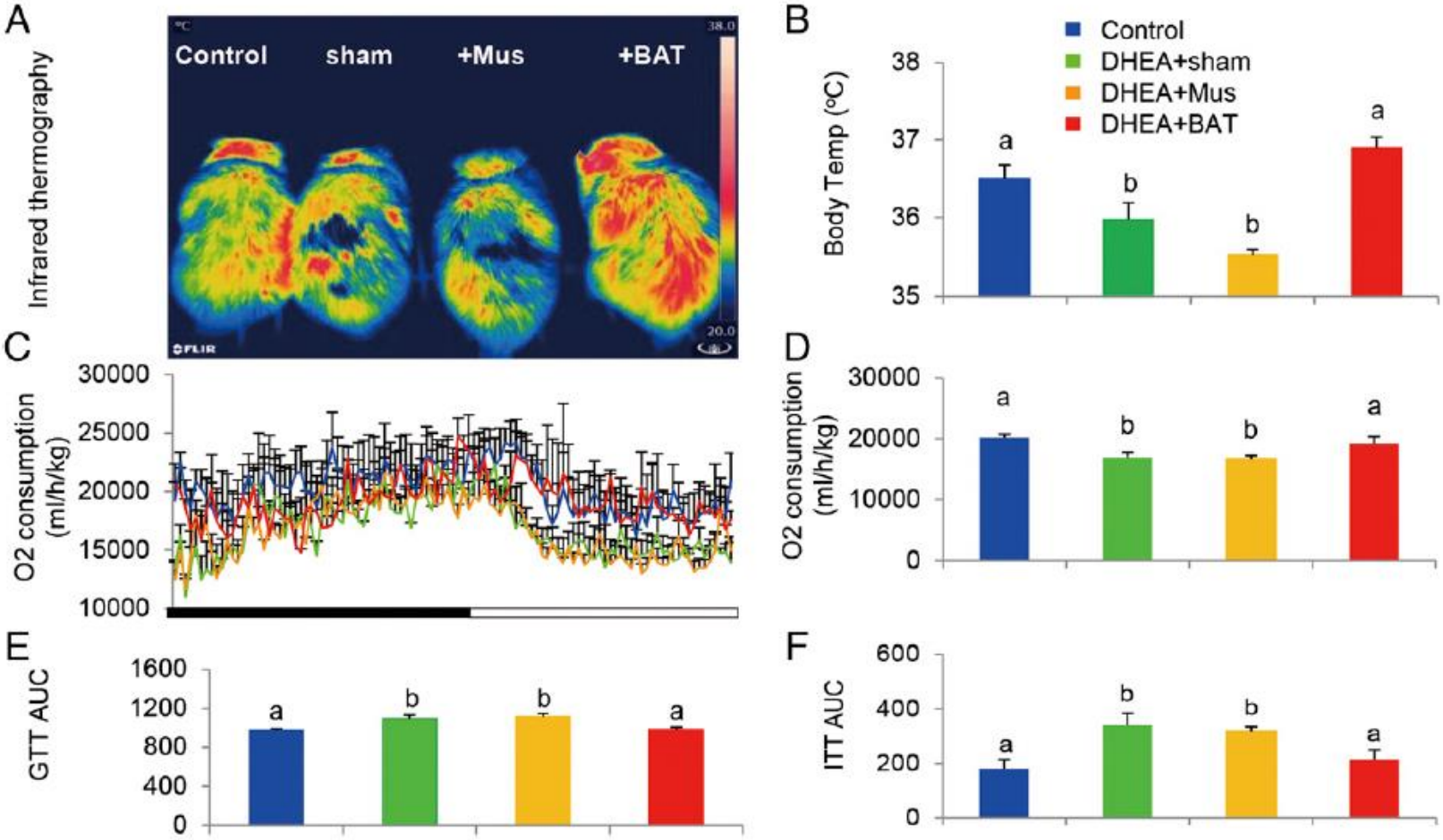
PHYSICAL ACTIVITY ACTIVATES BROWN FAT



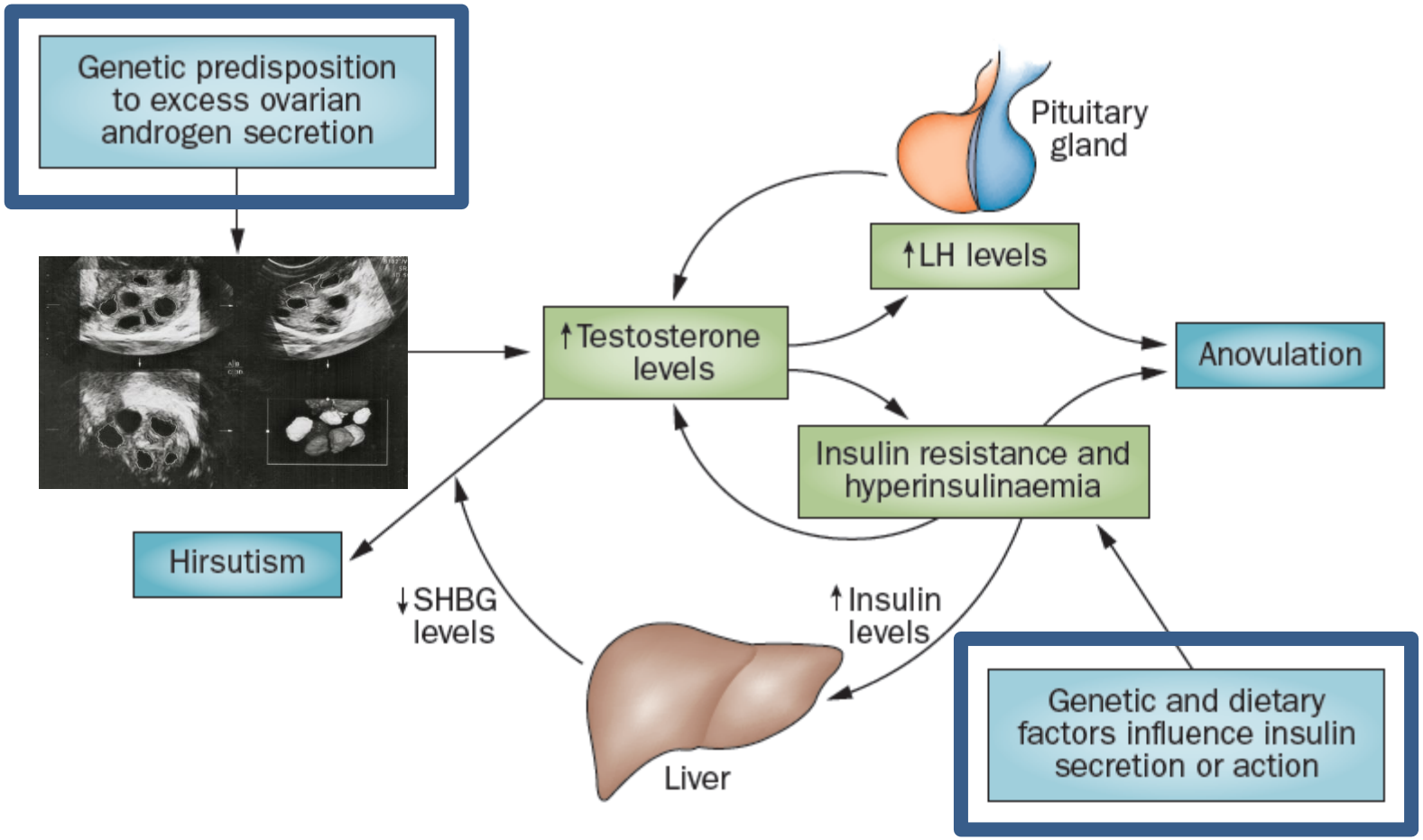
Brown adipose tissue transplantation ameliorates polycystic ovary syndrome



BAT TRANSPLANTATION REVERTS PCOS METABOLIC ABNORMALITIES



Genetic predisposition to PCOS and hirsutism



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FOCAL POINTS

Brown adipose tissue (BAT) is present in the human adult, involved in energy metabolism, glycemic regulation and lipid balance

Exercise can play a key role in the metabolism of BAT, recruiting it and activating it through SNS (norepinephrine) and myokines

In the mouse model a wide variety of stimuli activate BAT and adipose cell transdifferentiation

The transformation of BAT into WAT occurs in humans in response to aging, energy imbalance and other factors

The increase in BAT activity improves metabolism and its decrease is associated with metabolic dysfunction and obesity in the mouse

The increase in volume of WAT is characterized by infiltration of immune cells that participate in the activation of a condition of chronic low-grade inflammation, even if the same immune system can play in response to the cold a positive role in development, function and activity of the BAT and in the process of "beiging" of WAT, with a prominent role of eosinophils and alternative activation of macrophages, therefore also ways of activation of the immune system can open to potential new therapeutic strategies