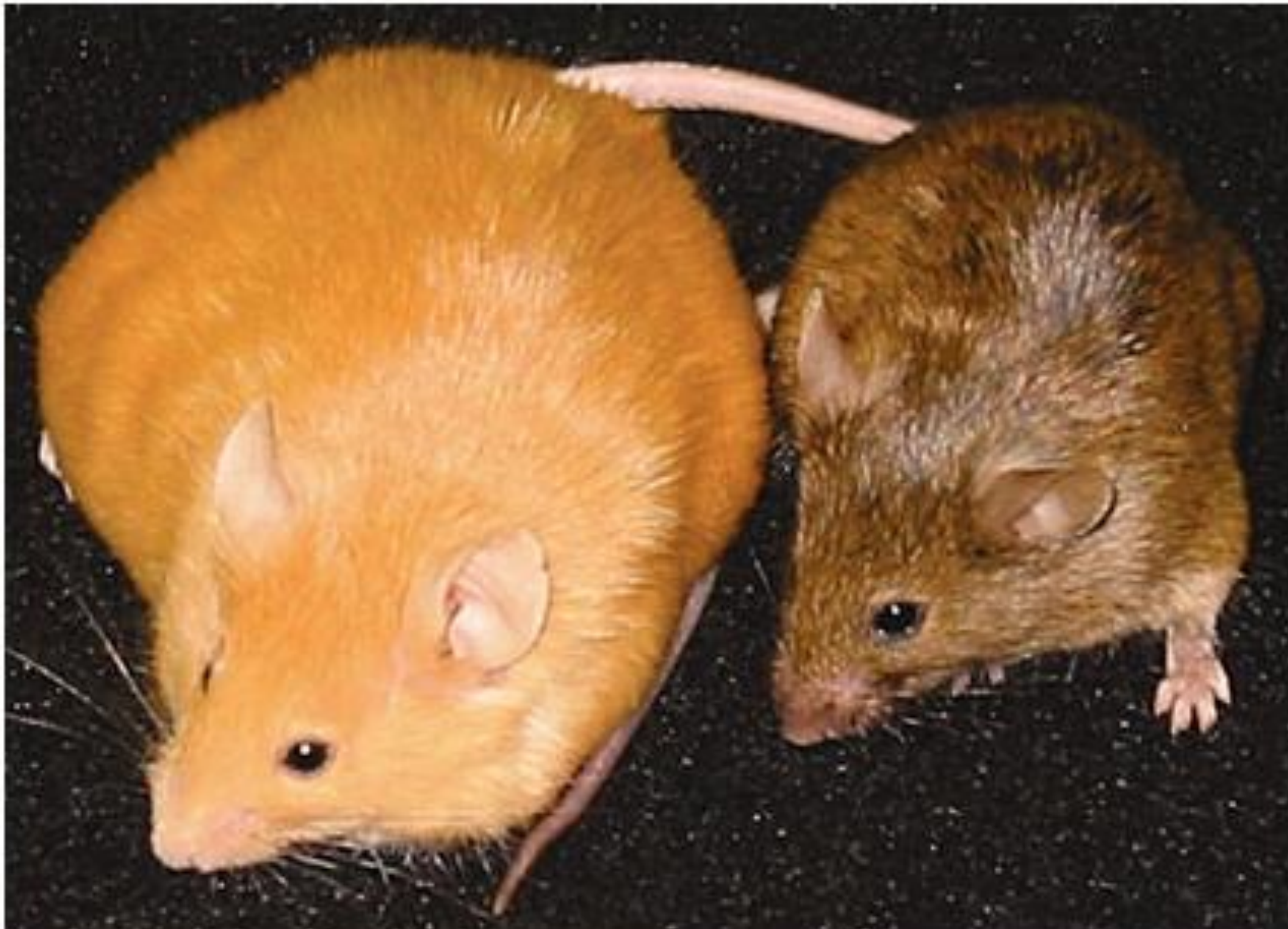
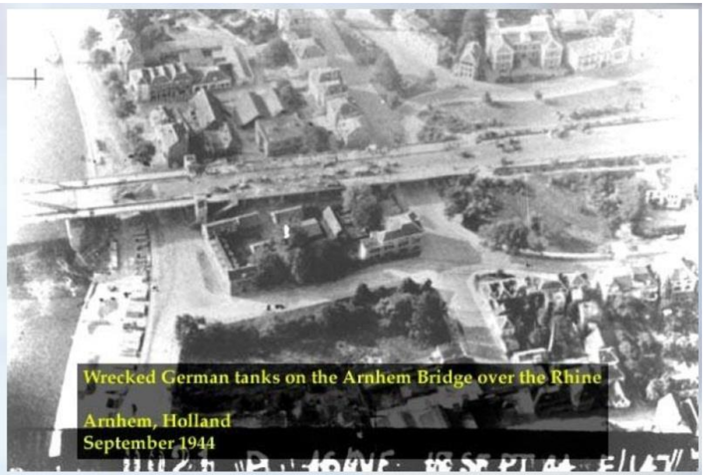
Epigenetic modifications: which environmental agents?



II World War: nazist embargo in the Netherlands. 30.000 death for famine.



60 years later….

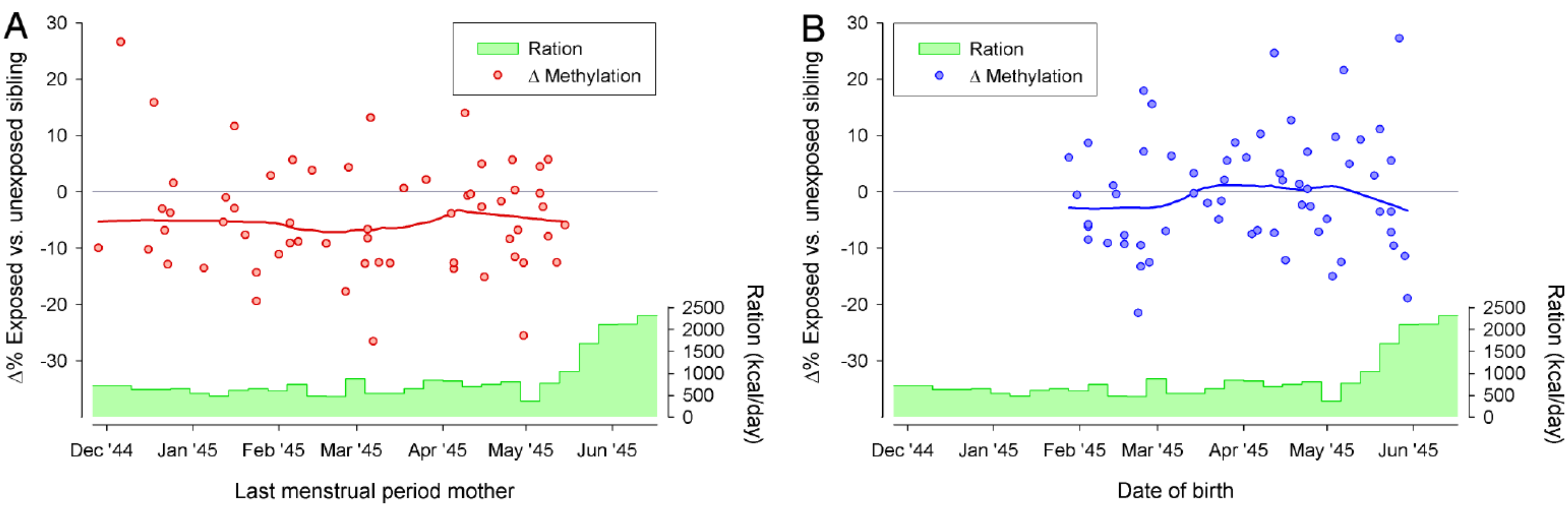
PNAS

Persistent epigenetic differences associated with prenatal exposure to famine in humans

Bastiaan T. Heijmans[a,1,2], Elmar W. Tobi[a,2], Aryeh D. Stein[b], Hein Putter[c], Gerard J. Blauw[d], Ezra S. Susser[e,f], P. Eline Slagboom[a], and L. H. Lumey[e,1]

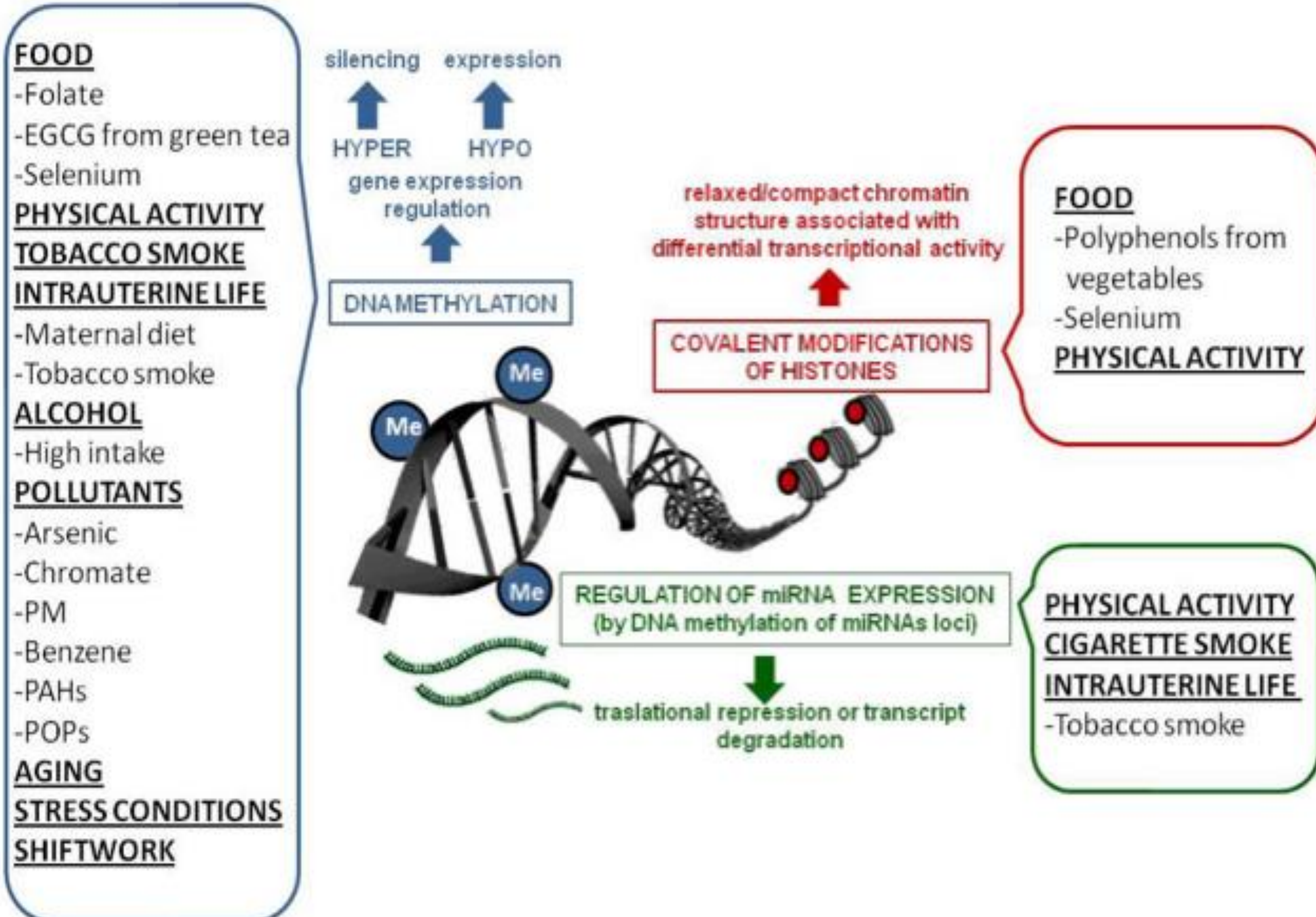
Departments of [a]Molecular Epidemiology, [c]Medical Statistics, and [d]Gerontology and Geriatrics, Leiden University Medical Center, Leiden, The Netherlands; [b]Hubert Department of Global Health, Rollins School of Public Health, Emory University Atlanta, GA 30322; [e]Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY 10032; and [f]New York State Psychiatric Institute, New York, NY 10032

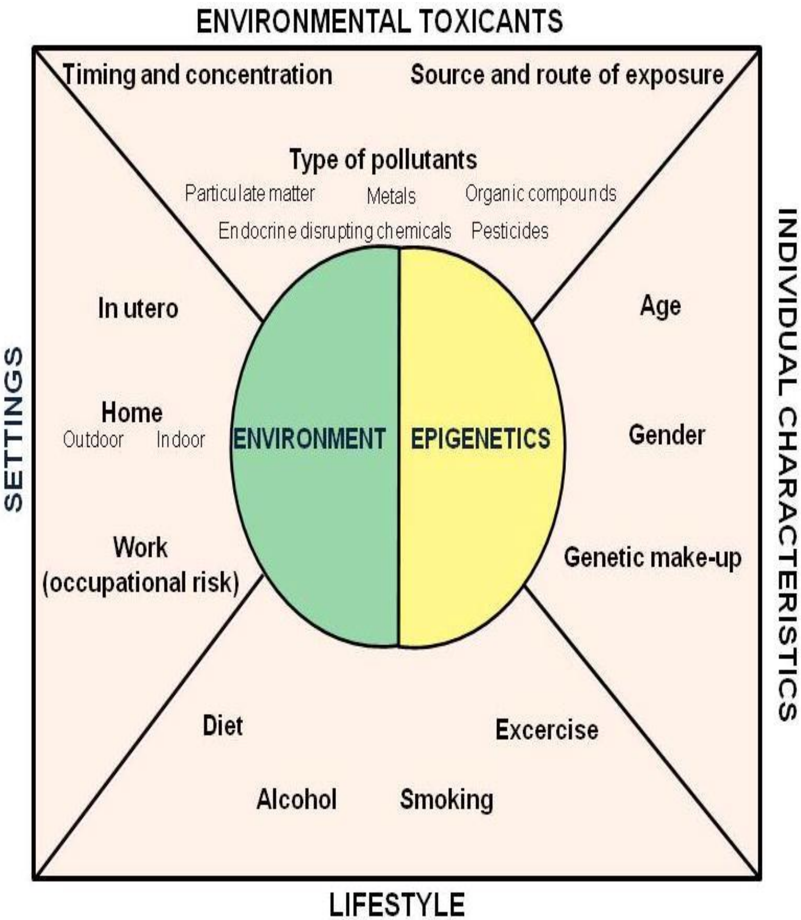
Edited by Charles R. Cantor, Sequenom Inc., San Diego, CA, and approved September 17, 2008 (received for review July 7, 2008)

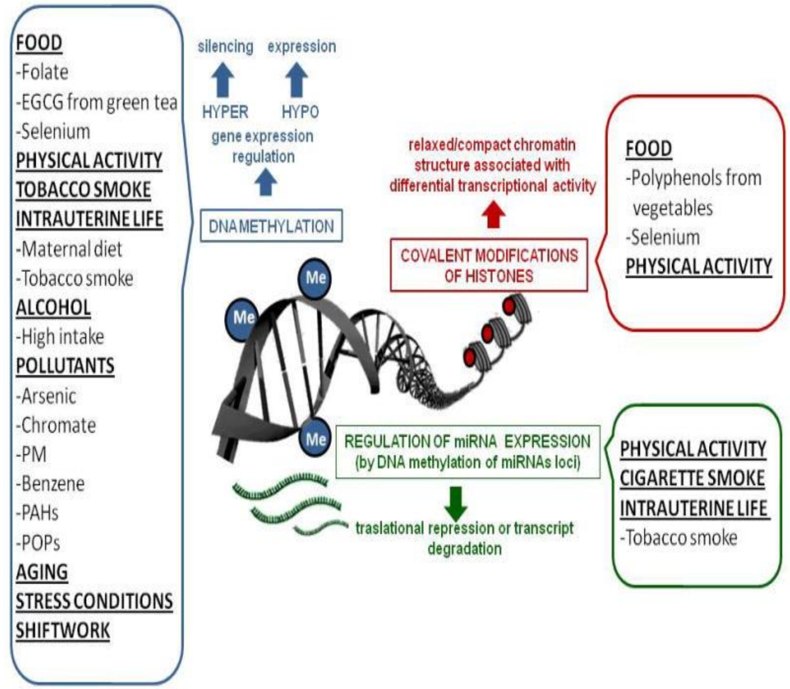


Ridotta metilazione del gene IGF2 negli individui concepiti durante la carestia

Epigenomics. 2011 June ; 3(3): 267–277.







NIH Public Access
Author Manuscript
Epigenomics. Author manuscript; available in PMC 2013 August 26.

Published in final edited form as:
Epigenomics. 2011 June ; 3(3): 267–277. doi:10.2217/epi.11.22.

Epigenetics and lifestyle

Jorge Alejandro Alegría-Torres[1], **Andrea Baccarelli**[2], and **Valentina Bollati**[3,*]

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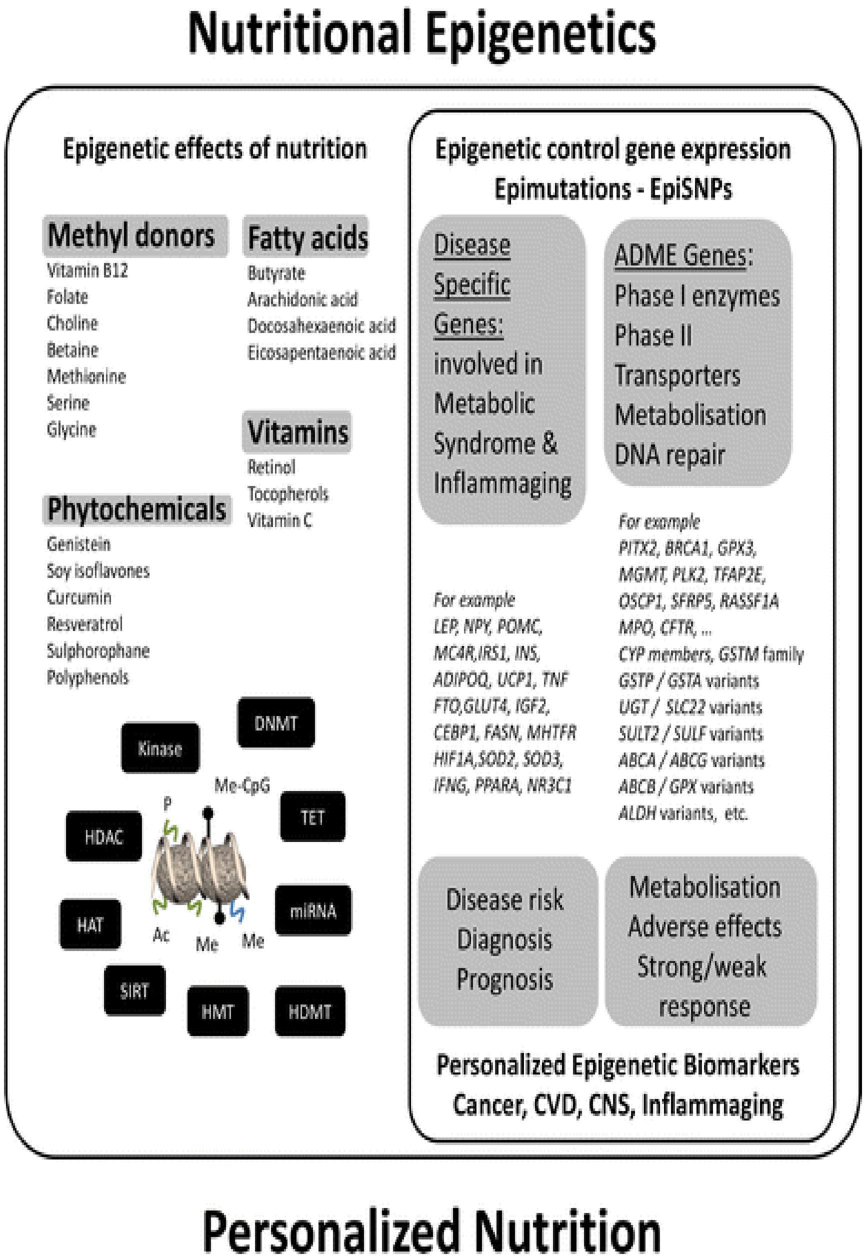
Overview of the mechanisms and consequences of epigenetic regulation by nutritional compounds



vel Szic et al. Clinical Epigenetics (2015) 7:33
DOI 10.1186/s13148-015-0068-2
CLINICAL EPIGENETICS

REVIEW Open Access

From inflammaging to healthy aging by dietary lifestyle choices: is epigenetics the key to personalized nutrition?

Katarzyna Szarc vel Szic[1], Ken Declerck[1], Melita Vidaković[2] and Wim Vanden Berghe[1]*

Diabetologia (2017) 60:778–783
DOI 10.1007/s00125-016-4187-x

REVIEW

Genetics of obesity: can an old dog teach us new tricks?

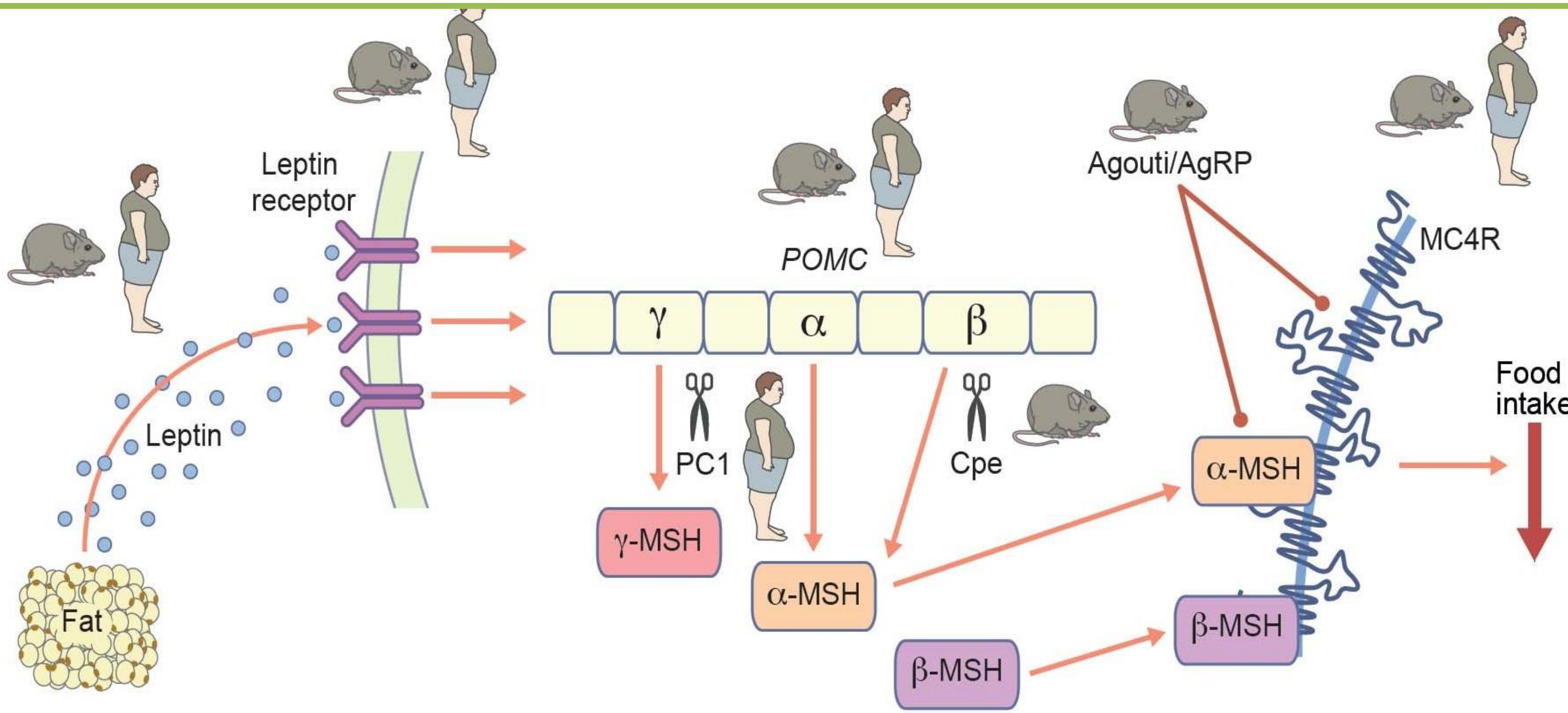
Giles S. H. Yeo[1]

Why do some people eat more than others?

The old dog

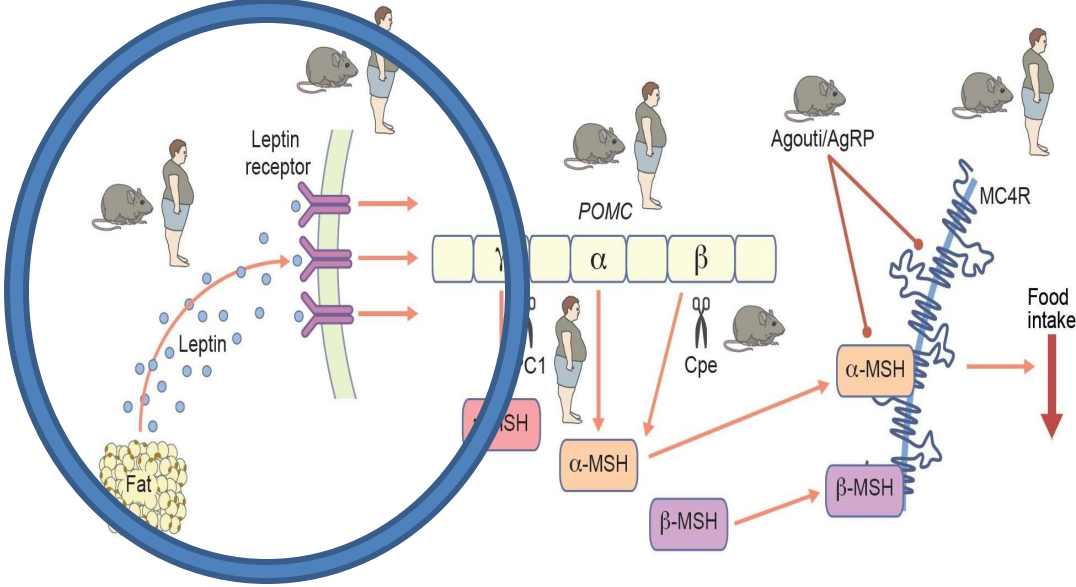
Numerous pathways within the brain play a role in the control of food intake: best characterized the **Leptin–Melanocortin pathway**

- Study in twin and adoption revealed that genetic heritability of fat mass is between 30% and 70%
- The majority of monogenic disorders in severe obesity in both mouse and man involve genetic disruption of the **Leptin–Melanocortin pathway**



© The Author 2016 Diabetologia DOI 10.1007/s00125-016-4187-x

Leptin pathway



- **1997**: the first report that two young cousins with severe early onset obesity had mutations in the gene of leptin (LEP).

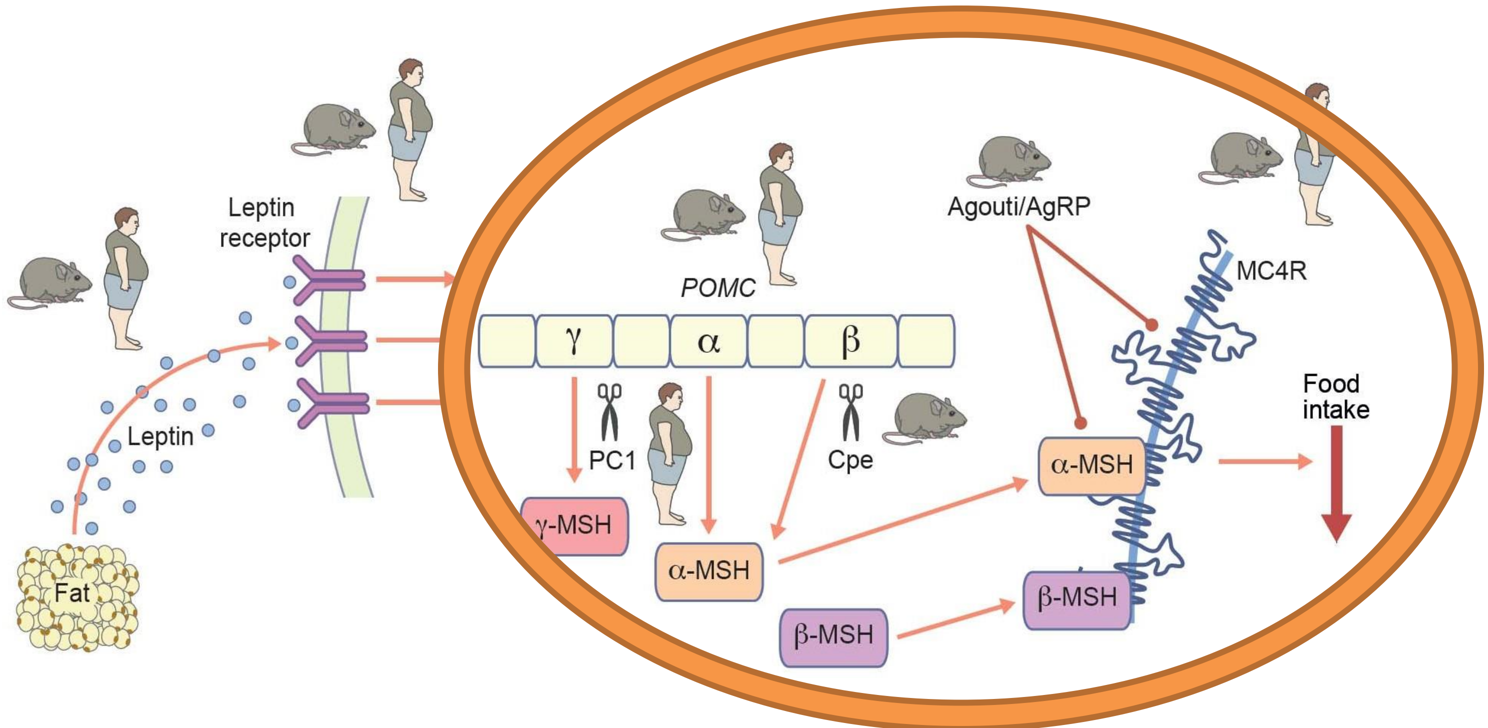
- Leptin is secreted by white adipose tissue and is a key indicator if fat deposits are sufficient.
Is not a satiety signal!

- If fat deposits are enough inhibits the growth of adipose tissue through decreased appetite and lipogenesis and increased energy expenditure and lipolysis.

- Patients with leptin deficiency are exceptionally sensitive to leptin administration, anyone with an intact system will not respond to leptin, certainly with regards to food intake and loss of bodyweight.

Melacortin pathway

- Is one of the key mechanisms of leptin signaling in the brain.
- The central component of the pathway is pro-opiomelanocortin (POMC).
- MC4R mutations remain the most common monogenic form of obesity, with pathogenic mutations found in up to 5% of cases of severe childhood obesity and up to 1% of the general population with a BMI >30 kg/m2.

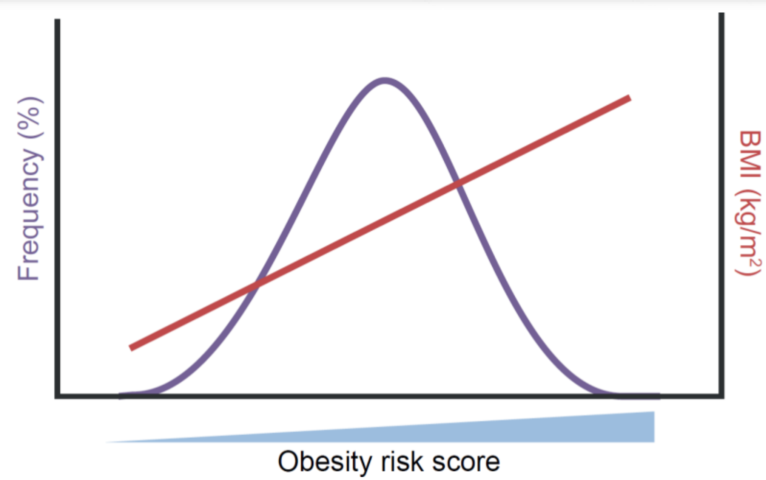


GWAS of Obesity

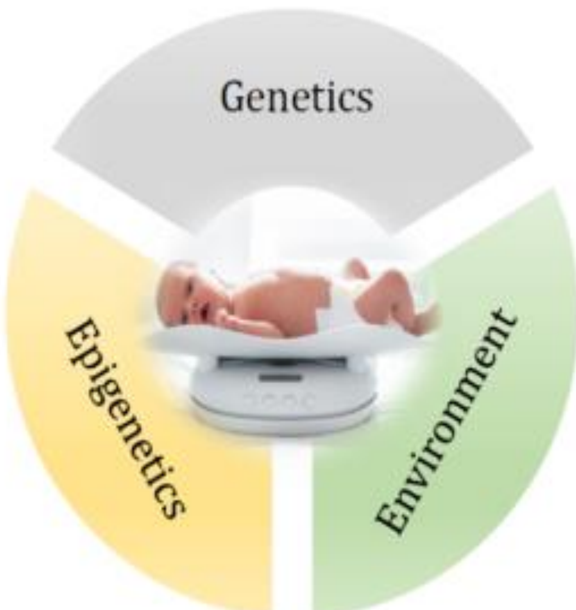
- SNPs associated with waist (hip ratio) tend to be primarily expressed in fat;
- SNPs associated with BMI are primarily expressed in the central nervous system:

From these SNPs can generate an obesity risk score → score of 2 (homozygous for risk allele), 1 (heterozygous) or 0 (homozygous for non-risk allele);
When plotted against a large population: increasing risk score is directly related to increasing BMI;
Some of these genes members of the leptin–melanocortin pathway → like **POMC** and **MC4R**.

Obesity risk score is directly related to BMI in the population



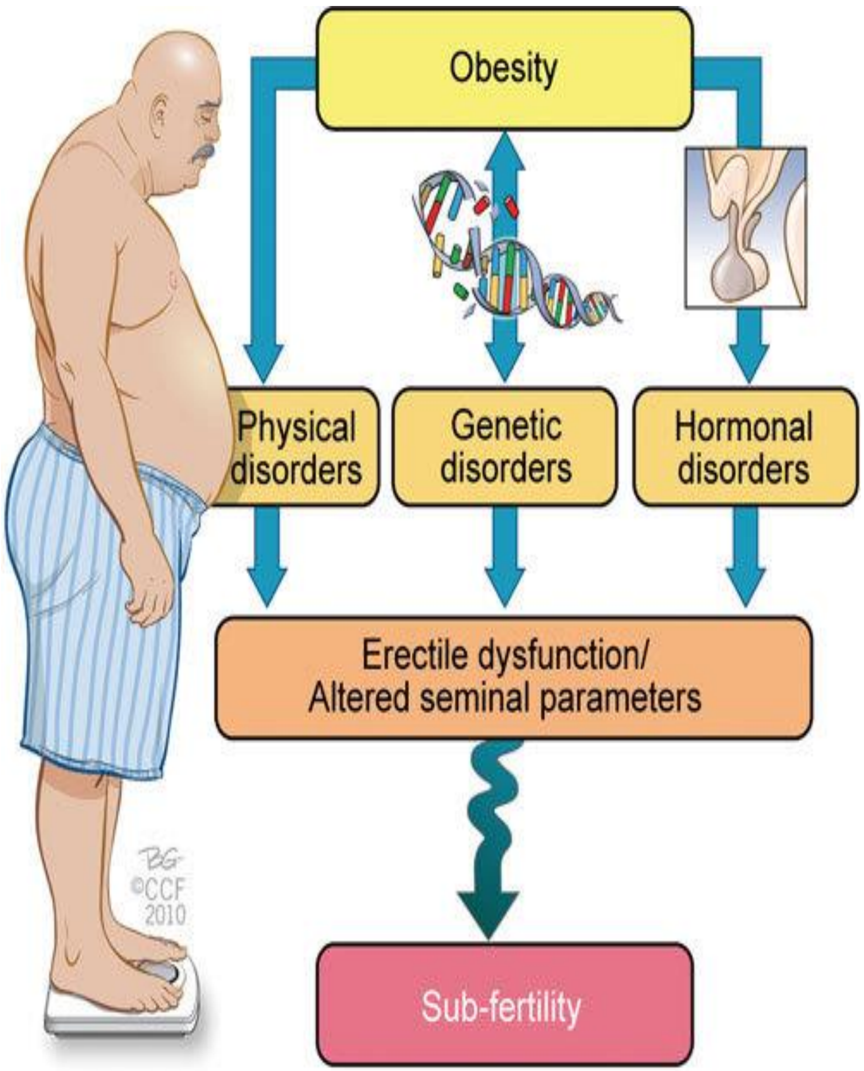
In post-genomics' world, can new genetic information influence the treatment of obese patients? The answer is… 'it depends'



- **For monogenic forms of obesity (1% of people with BMI >30 kg/m²) the answer is <u>YES</u>.**
  We can now treat the that harbour genetic mutations within the leptin–melanocortin pathway.

- **While…for common polygenic obesity, as the predictive value of these SNPs and risk scores are still very poor for any given individual specific treatment → it is difficult to quantify the influence of the genetic and environmental component.**

The effects of obesity on male infertility and the mechanisms involved




Asian Journal of Andrology (2010) 12: 480–489

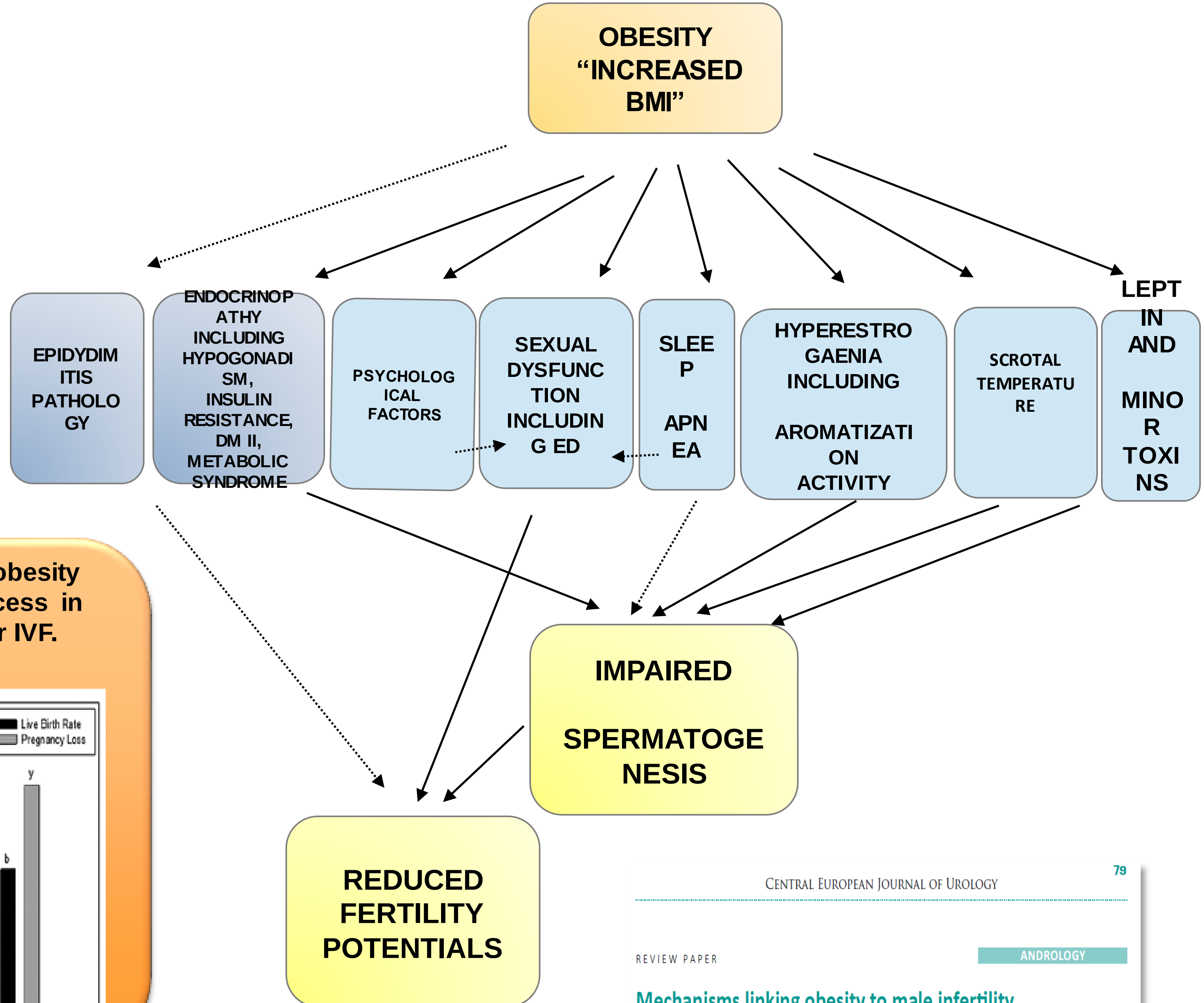
www.nature.com/aja

Review

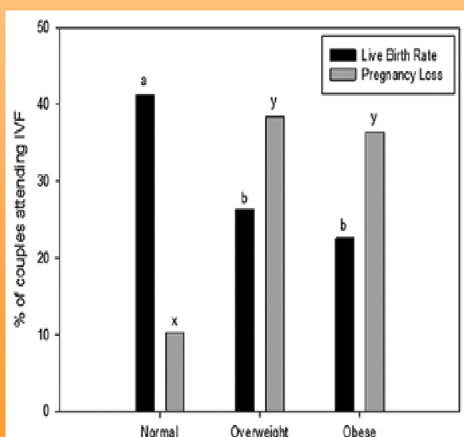
Obesity: modern man's fertility nemesis

Stephanie Cabler[1], Ashok Agarwal[1], Margot Flint[2], Stefan S. Du Plessis[2]

[1] Center for Reproductive Medicine, The Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195, USA
[2] Division of Medical Physiology, Faculty of Health Sciences, Stellenbosch University, PO Box 19063, Tygerberg 7505, South Africa



The effect of male obesity on conception success in couples going for IVF.



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Central European Journal of Urology

REVIEW PAPER

ANDROLOGY

Mechanisms linking obesity to male infertility

Atif Katib

Soubry *et al. Clinical Epigenetics* (2016) 8:51
DOI 10.1186/s13148-016-0217-2

Clinical Epigenetics

RESEARCH Open Access

Obesity-related DNA methylation at imprinted genes in human sperm: Results from the TIEGER study

Adelheid Soubry[1*], Lisa Guo[2], Zhiqing Huang[2], Cathrine Hoyo[3], Stephanie Romanus[1], Thomas Price[4] and Susan K. Murphy[2,5*]

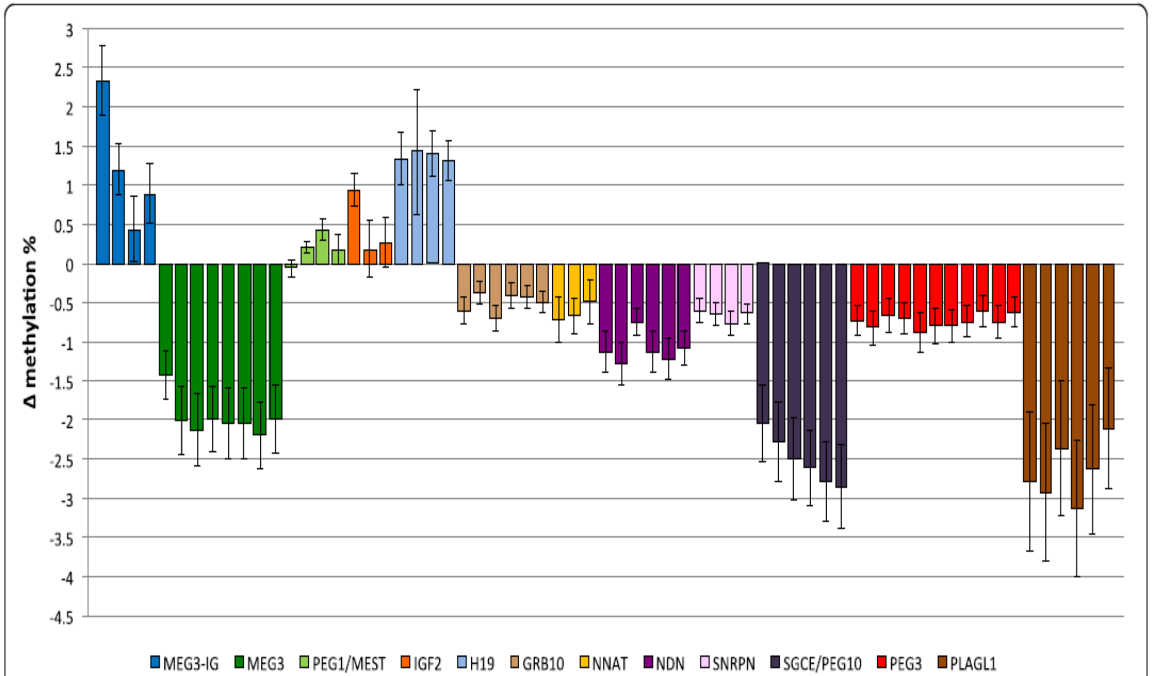

Fig. 1 Methylation differences in sperm from overweight/obese men versus normal weight men at imprinted genes. Differences in methylation percentages between overweight/obese men and men of normal weight are shown by CpG site for each DMR studied, adjusted for age and patient status at the Duke Fertility Center. *Bars* represent SE

Mediterranean diet and fertility

The preconception Mediterranean dietary pattern in couples undergoing in vitro fertilization/intracytoplasmic sperm injection treatment increases the chance of pregnancy

Marijana Vujkovic, B.Sc.,[a] Jeanne H. de Vries, Ph.D.,[g] Jan Lindemans, Ph.D.,[b] Nick S. Macklon, Ph.D.,[a,h,i] Peter J. van der Spek, Ph.D.,[c] Eric A. P. Steegers, Ph.D.,[a] and Régine P. M. Steegers-Theunissen, Ph.D.[a,d,e,f]

Vujkovic M et al., 2010

Taking a Mediterranean Diet in the pre-conception period in couples who undergo IVF/ICSI contributes to achieving success in the pregnancy.

Mediterranean and western dietary patterns are related to markers of testicular function among healthy men

A. Cutillas-Tolín[1,*,†], L. Mínguez-Alarcón[1,†], J. Mendiola[1], J.J. López-Espín[2], N. Jørgensen[3], E.M. Navarrete-Muñoz[4,5], A.M. Torres-Cantero[1,6,7], and J.E. Chavarro[8,9]

Cutillas-Tolìn A. et al., 2015

The traditional Mediterranean Diet can have a positive impact on male reproductive potential.