

# Healthy Lifestyle | Healthy Sperm | Healthy Children

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# Structure of the Workshop

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1. Four sessions with each lasting no more than 15 minutes
  - I. Story telling with real life examples for all major concepts
  - II. Use lay language as much as possible
  
2. Two experiments:
  - I. Compare mouse and human sperm
  - II. Sperm motility activation
  
3. Q&A session

# Where do we come from?

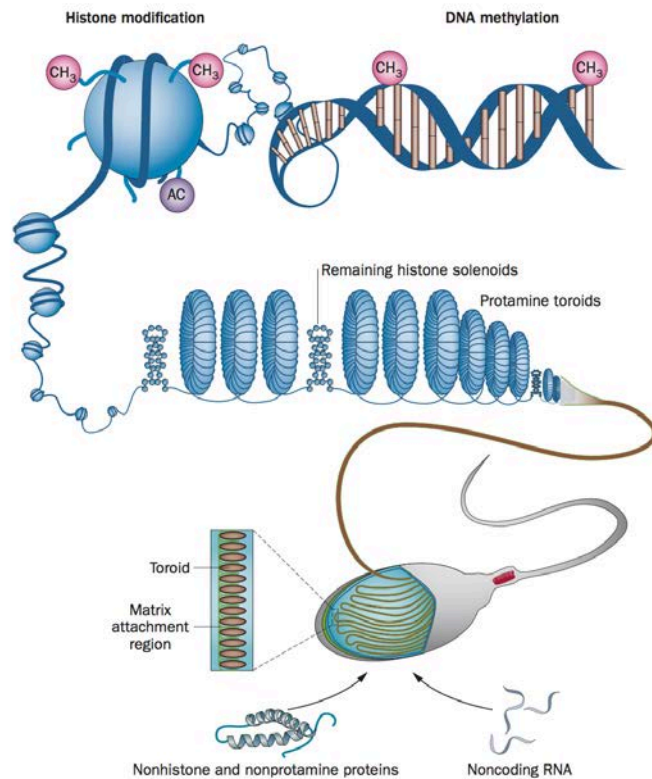
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- How are sperm formed?
- How are eggs/oocytes formed?
- Fertilization: Fusion of a sperm and an egg/oocyte
- Embryonic development

# What is inside sperm?

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## Genetic materials:

- DNA: double helix, large molecules
- Genetic code: combinations of four bases (A,C,T and G)

## Epigenetic information:

- Chemically modified DNA: DNA methylation
- Chemically modified proteins: histone marks
- RNAs: large or small; coding or noncoding
- Chemically modified RNAs: m6A

# Role of genetic materials in sperm

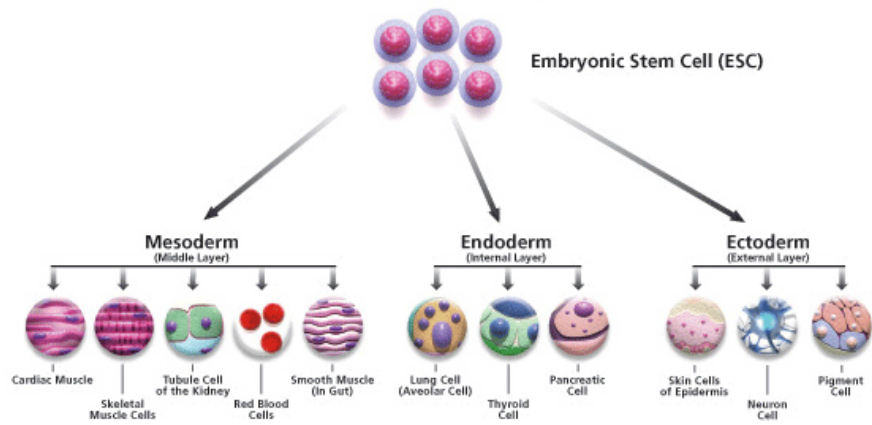
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- Embryonic development
- Fetal development
- Prepubertal development
- Puberty
- Adult life

# Epigenetic information within sperm

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- Software (epigenetics) for the hardware/computer (genetics)
- Adaptive and responsive to environment, diet, physical activities
- Acquired traits: good vs. bad
- Inheritable or not?

# Consequences of genetic defects

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Prader-Willi Syndrome



Carey et al: Medical Genetics, 4th Edition.  
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Angelman Syndrome



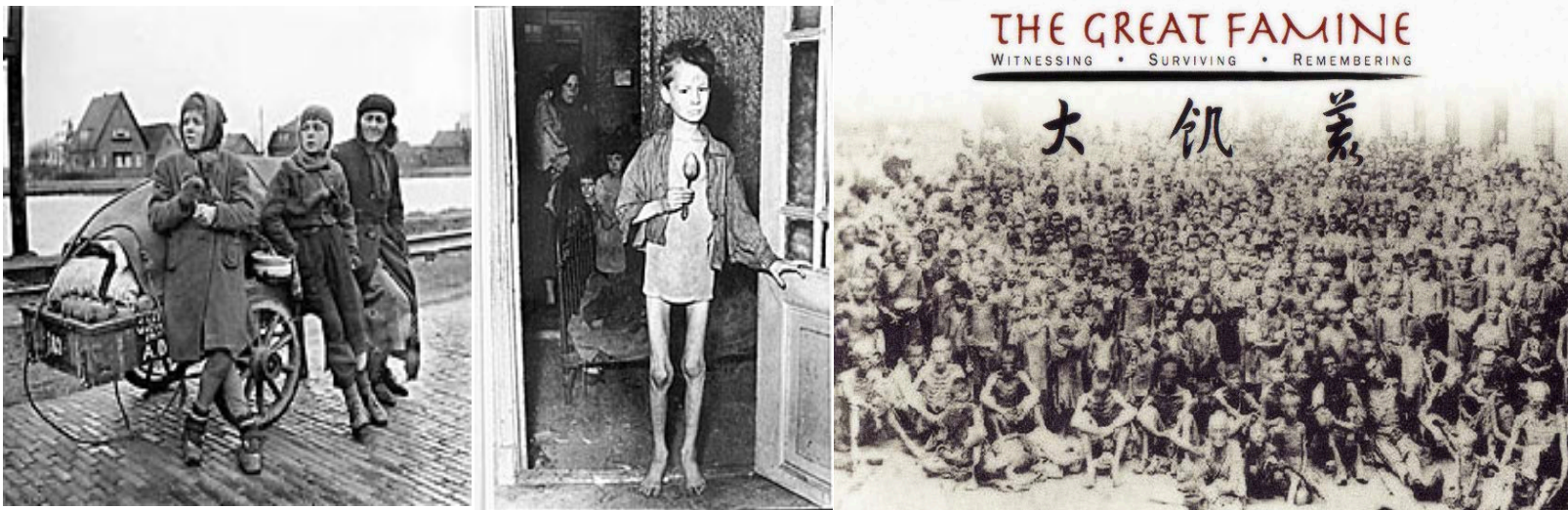
Carey et al: Medical Genetics, 4th Edition.  
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- Infertility
- Abortion
- Birth defects
- Congenital diseases
- Single vs. multiple genetic defects



# Effects of epigenetic alterations

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- Disease tendency
- Latent/Adult onset
- Intergenerational vs. transgenerational inheritance



# Acquired Paternal Traits in Offspring

nature  
neuroscience

## Parental olfactory experience influences behavior and neural structure in subsequent generations

Brian G Dias<sup>1,2</sup> & Kerry J Ressler<sup>1-3</sup>

Using olfactory molecular specificity, we examined the inheritance of parental traumatic exposure, a phenomenon that has been frequently observed, but not understood. We subjected F0 mice to odor fear conditioning before conception and found that subsequently conceived F1 and F2 generations had an increased behavioral sensitivity to the F0-conditioned odor, but not to other odors. When an odor (acetophenone) that activates a known odorant receptor (*Olf151*) was used to condition F0 mice, the behavioral sensitivity of the F1 and F2 generations to acetophenone was complemented by an enhanced neuroanatomical representation of the *Olf151* pathway. Bisulfite sequencing of sperm DNA from conditioned F0 males and F1 naive offspring revealed CpG hypomethylation in the *Olf151* gene. In addition, *in vitro* fertilization, F2 inheritance and cross-fostering revealed that these transgenerational effects are inherited via parental gametes. Our findings provide a framework for addressing how environmental information may be inherited transgenerationally at behavioral, neuroanatomical and epigenetic levels.

ARTICLES

nature  
medicine

## Multigenerational epigenetic adaptation of the hepatic wound-healing response

Müjdat Zeybel<sup>1</sup>, Timothy Hardy<sup>1</sup>, Yi K Wong<sup>2</sup>, John C Mathers<sup>2</sup>, Christopher R Fox<sup>1</sup>, Agata Gackowska<sup>1</sup>, Fiona Oakley<sup>1</sup>, Alastair D Burt<sup>1</sup>, Caroline L Wilson<sup>1</sup>, Quentin M Anstee<sup>1</sup>, Matt J Barter<sup>1</sup>, Steven Masson<sup>1</sup>, Ahmed M Elsharkawy<sup>1</sup>, Derek A Mann<sup>1,3</sup> & Jelena Mann<sup>1,3</sup>

Scienceexpress

Research Articles

## Disruption of histone methylation in developing sperm impairs offspring health transgenerationally

Keith Siklenka,<sup>1\*</sup> Serap Erkek,<sup>1,2,3\*</sup> Maren Godmann,<sup>1,2</sup> Romain Lambrot,<sup>4</sup> Serge McGraw,<sup>4</sup> Christine Lafleur,<sup>4</sup> Tamara Cohen,<sup>4</sup> Jiangbo Xia,<sup>1,2\*</sup> Matthew Suderman,<sup>2</sup> Michael Hallett,<sup>1</sup> Jacquetta Trasler,<sup>4,5</sup> Antoine H. F. M. Peters,<sup>1,2,6,7\*</sup> Sarah Kimmins<sup>1,8,9\*</sup>

ditional epigenetic inheritance (Fig. 1). Maternal and paternal transmission of such effects has been related to alterations of DNA methylation in germ cells (7, 8-12). DNA methylation occurs at the 2-position of cytosine residues and associates with heritable gene silencing when promoter sequences containing multiple CpG dinucleotides (CpG islands; CGIs) are methylated. Likewise, DNA methylation sup-

nature  
genetics

## Epigenetic germline inheritance of diet-induced obesity and insulin resistance

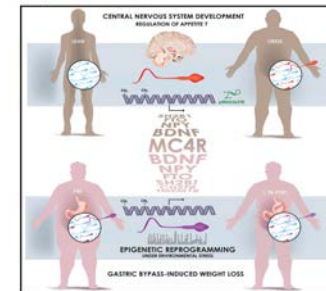
Peter Huypens<sup>1-3</sup>, Steffen Sass<sup>4</sup>, Moya Wu<sup>1,2</sup>, Daniela Dyckhoff<sup>1-3</sup>, Matthias Tschöp<sup>3,5,6</sup>, Fabian Theis<sup>1,7</sup>, Susan Marshall<sup>1,2</sup>, Martin Hrabě de Angelis<sup>1-3,8,9</sup> & Johannes Beckers<sup>1-3,8,9</sup>

Short Article

## Cell Metabolism

### Obesity and Bariatric Surgery Drive Epigenetic Variation of Spermatozoa in Humans

Graphical Abstract



Authors

Ida Donkin, Soetkin Versteijhe, Lars R. Ingerslev, ..., Christopher T. Workman, Julieen R. Zierath, Romain Barrès

Correspondence

barrès@sund.ku.dk

In Brief

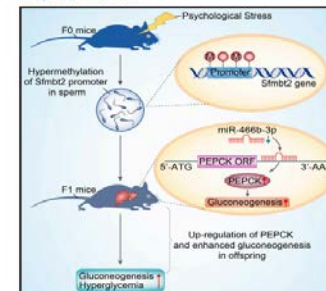
Donkin et al. show that spermatozoa from obese men carry a distinct epigenetic signature compared to lean men, in particular at genes controlling brain development and function. The sperm methylome is dynamically remodeled after gastric-bypass-induced weight loss, notably at gene regions implicated in the central control of appetite.

Short Article

## Cell Metabolism

### Paternal Psychological Stress Reprograms Hepatic Gluconeogenesis in Offspring

Graphical Abstract



Authors

Ling Wu, Yan Lu, Yang Jiao, ..., Jieli Lu, Xuejin Chen, Xiaoying Li

Correspondence

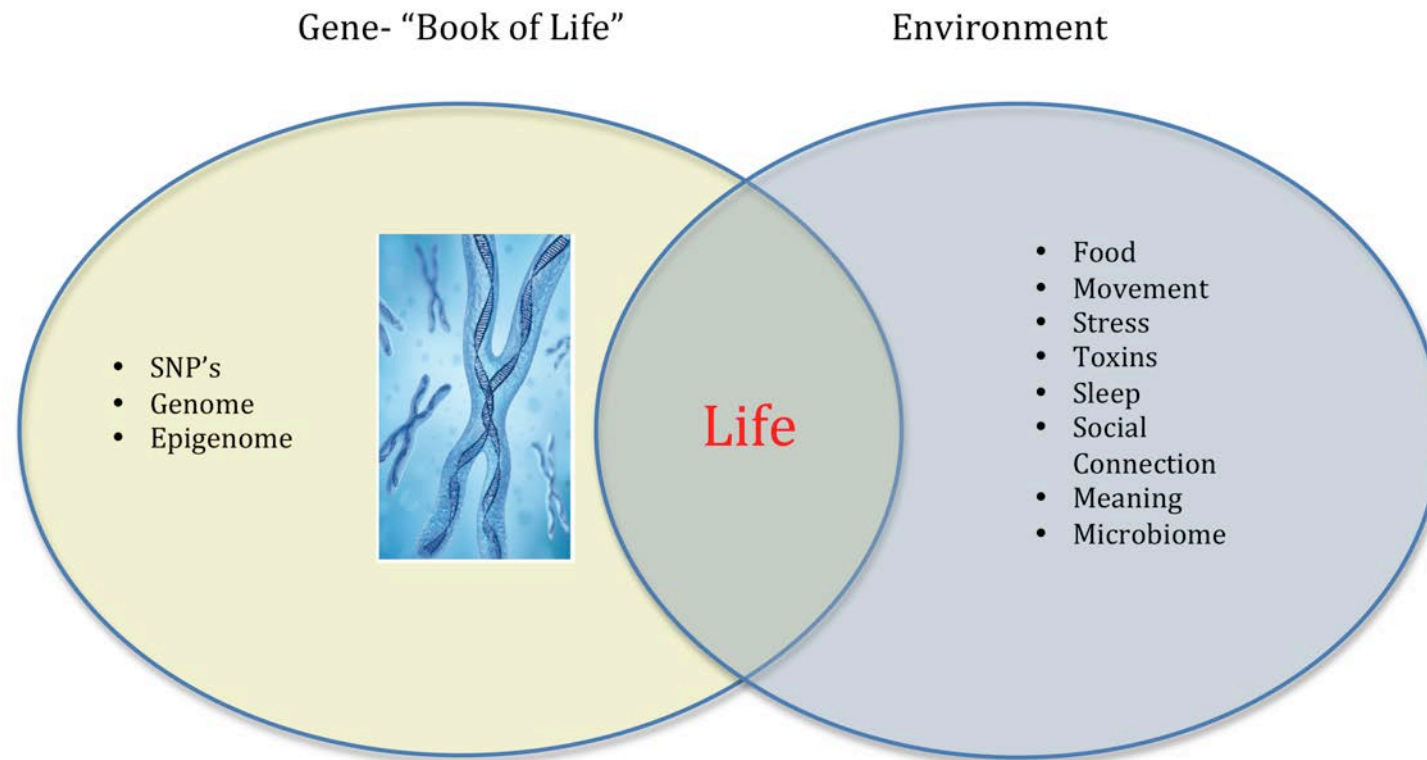
chenxuejin@shsmu.edu.cn (X.C.), lixy@sibs.ac.cn (X.L.)

In Brief

Using a mouse model of restraint stress, Wu et al. uncover the intergenerational effects of paternal psychological stress on glucose metabolism in offspring. Paternal stress epigenetically downregulates miR-466b-3p expression, leading to increased PEPCK expression and hepatic gluconeogenesis in hyperglycemic F1 mice.

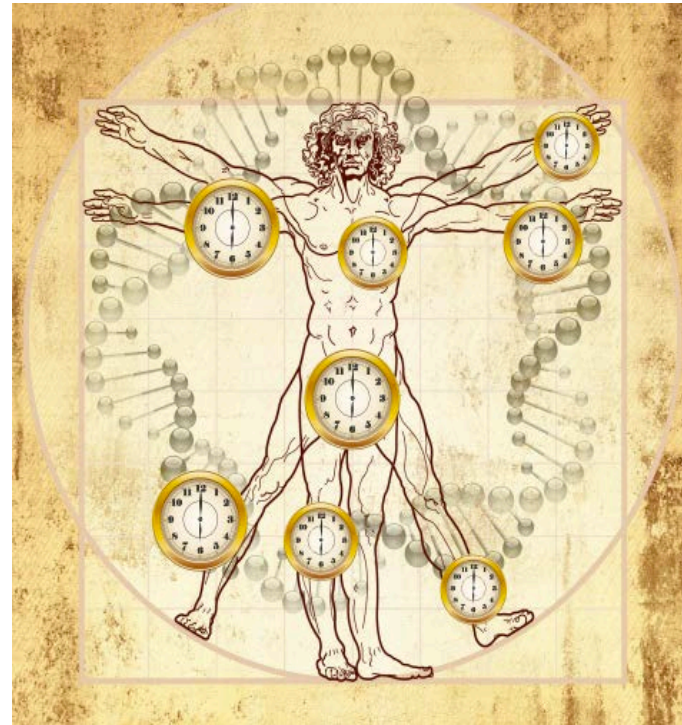
# Our genome constantly interacts with environments

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# “Growth ring” in humans -Aging and the methylome

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# Representative Clinical Conditions with Epigenetic Origins

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- Type 2 DM and Metabolic Syndrome
- Coronary artery disease
- Autoimmune Diseases
- Cancer
- Allergic Disorders
- Depression
- Neurologic: Alzheimer's, PD, ALS, Autism
- Infertility

# Lifestyle/Behavioral Factors Shown to Have Health-Promoting Epigenomic Influences

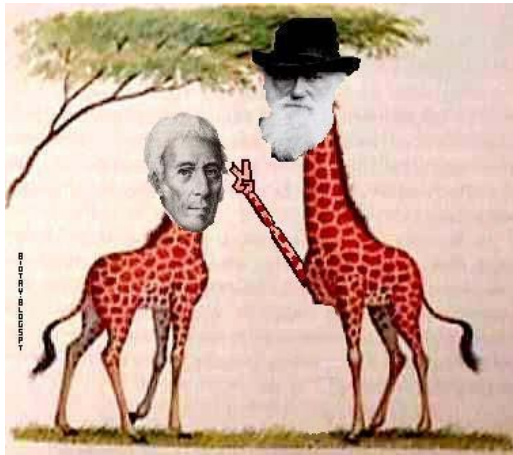
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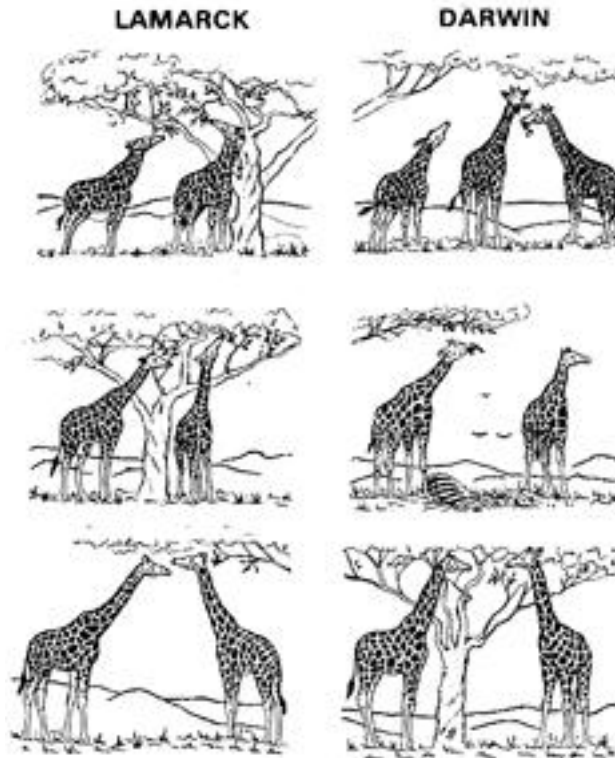
- Plant-based, unprocessed foods
- Movement
- Mindfulness
- Bonding-social connection
- Reduction in environmental toxin exposure
- Microbiome



# Evolution Theories



Lamarck	Darwin
❖ Use and disuse	❖ Variation
❖ Transmission of acquired characteristics	❖ Inheritance
❖ Increasing complexity	❖ Differential survival
❖ No extinction	❖ Extinction





Thank You!

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