

# Understanding the Dynamic Relationship between Genetics, Environment, and Early Childhood Development on Risk of Obesity

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IOM OBESITY SOLUTIONS ROUNDTABLE

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# Genomics

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We have 22-24,000 active genes, but Pinor Noir has 29,000- more doesn't mean more functional complexity

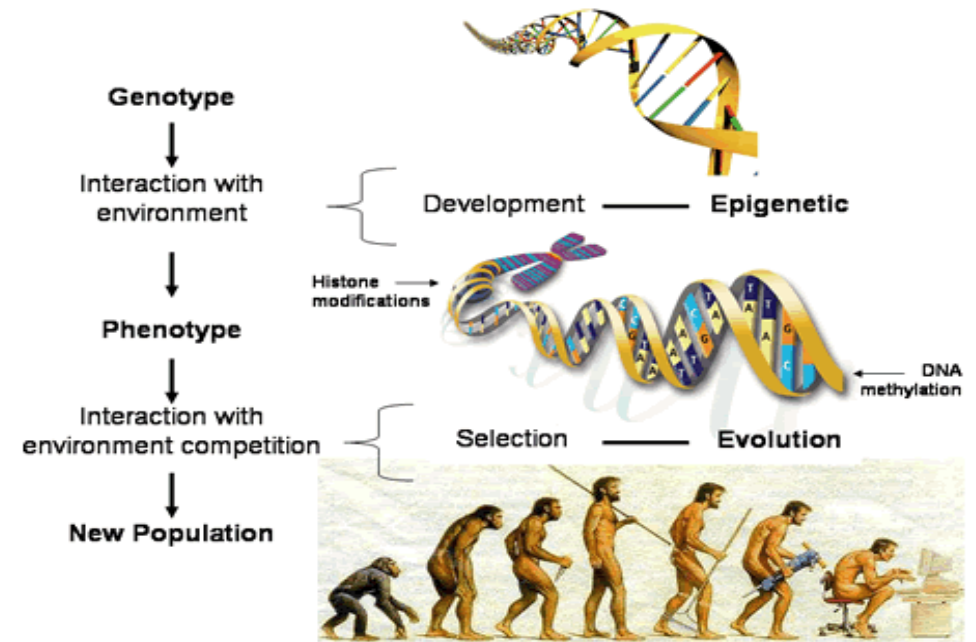
Our genetic code is a record of our past (with more than 120,000 silent genes) and a record of our present, what determines our future?

If 99.9% of all human beings have the same genetics, why are there so many differences?

# Genetics x Environment x Development

Epigenetics: changes in gene expression via post-translational and post-transcriptional modifications.

➤ You can't change your genes, but you can change the way your genes behave



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FANTASIA  
on a Theme by Thomas Tallis.

R. Vaughan Williams.

Largo sostenuto. 4/4 (♩ = 120)

Violin I solo.  
Violin II solo.  
Viola solo.  
Violoncello solo.

Orchestra I.  
Violin I.  
Violin II.  
Viola.  
Violoncello (tutti).  
Violoncello (last desk).  
Contrabass.

Orchestra II.  
Violin I (i desk).  
Violin II (i desk).  
Viola (i desk).  
Violoncello (i desk).  
Contrabass (i player).

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Copyright 1921 in U.S.A. by Goodwin & Tubb, Ltd.  
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# Genetics x Environment

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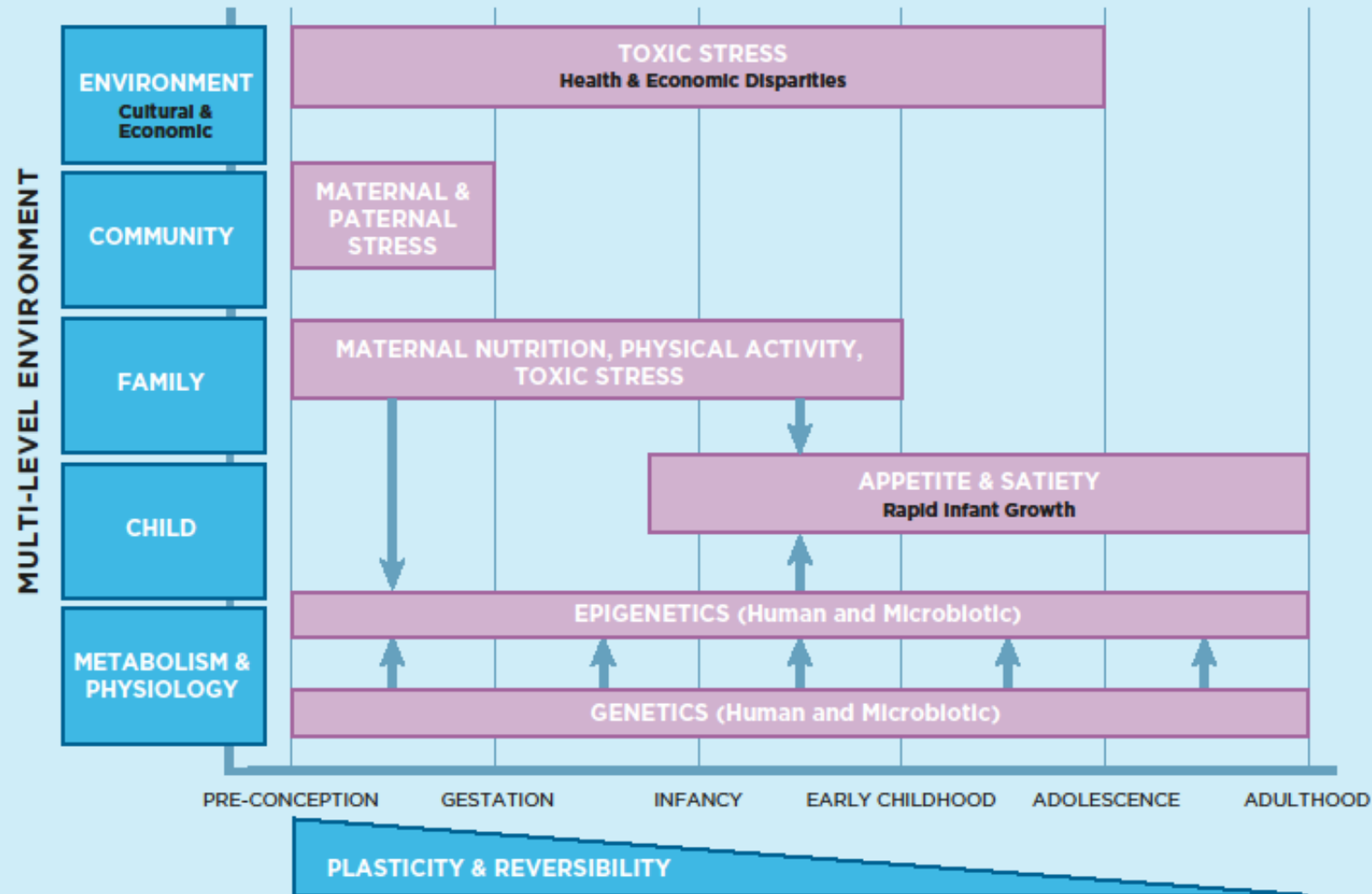
In all living species, environment affects gene expression. The social life of genes can be short or long acting.

- The case of the Killer bees versus European bees



# EARLY ORIGINS OF OBESITY

## The Role of Epigenetics and Opportunities for Intervention



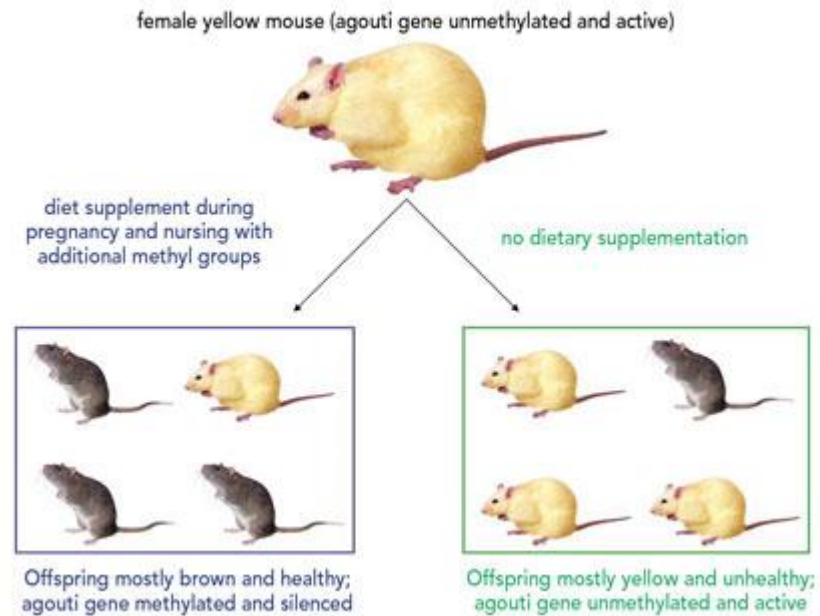
The model presented is intended to highlight the workshop objectives, rather than to be fully comprehensive. All levels of the internal and external environment interact with each other in a dynamic manner.



# Epigenetics in Pediatric Obesity- Maternal Nutrition (1)



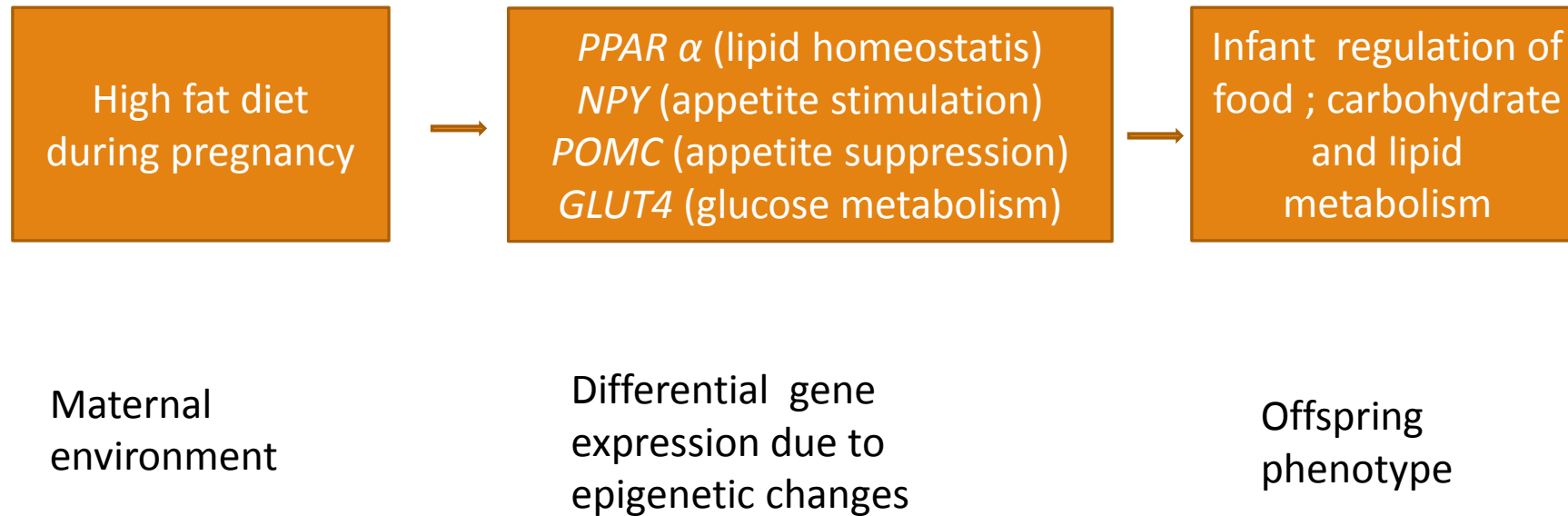
Genetically identical, same aged mice  
Different pre-natal diets: Yellow mouse fed a normal diet; Brown mouse supplemented with **choline, folic acid, and vitamin B12** (affected methylation at the agouti locus)



<http://archive.hudsonalpha.org/education/outreach/basics/epigenetics>

# Epigenetics in Pediatric Obesity- Maternal Nutrition (2)

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# Epigenetics and Pediatric Obesity: Infant Microbiome

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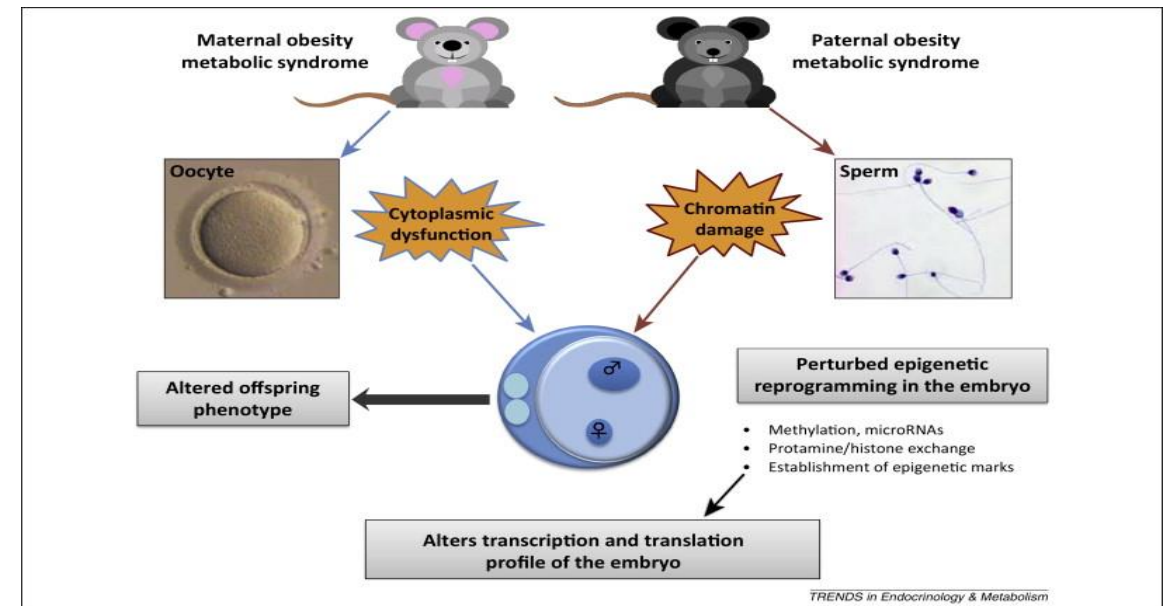
- Maternal obesity in breastfeeding mothers affects the infant microbiome that affects infant adiposity via epigenetic mechanisms
- Mother on a Western diet more often has a shift in microbiome species, this affects lipid metabolism and inflammatory response
- Composition of the microbiome affects leptin and insulin levels, as well as n6/n3 fatty acid ratios
- Exposure to a maternal western diet through breastmilk appears to pattern the microbiome and affect a pro-inflammatory state in infants.



Friedman 2014; Kumar, 2014

# Epigenetics and Pediatric Obesity: Paternal Nutrition

- Epigenetic mediation through sperm and the paternal line
- High fat paternal diet increases beta cell dysfunction in female offspring
- Paternal obesity affects the metabolic and reproductive health of the offspring for multiple generations.



Ng, *Nature*, 2010; Lane, *Trends in Endocrinology and Metabolism*, 2015.

# What can we learn from epigenetics to better understand childhood obesity?

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- Godfrey (2011) examined longitudinal cohorts of children and epigenetic signatures of their umbilical cord tissue, examining fat distribution with a DEXA scan at age 9
  - Increased methylation of: *RXRA; NOS3; SOD1; IL-8; PIK3CD*
  - *RXRA was confirmed as differentially methylated for those children with later increased adiposity in an independent sample of children*
  - *No causal mechanism identified*
  - *Changed methylation pattern associated with later childhood adiposity*
  - *Conclusion: Perinatal epigenetics can assess individual vulnerability to childhood obesity*

Godfrey, *Diabetes*, 2011

# Opportunities for Intervention and Prevention (1)

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- **Maternal malnourishment (over or under) increases the risk for childhood obesity**
  - Animal models have examined maternal supplements such as choline that change methylation patterns and is able to reverse early metabolic dysfunction.
  - These relationships depend on age, gender, and maternal nutritional status
- **Regardless of maternal BMI, a high fat maternal diet during pregnancy results in increased inflammatory cytokine production in the placenta and the fetus.**
  - Some of these effects are mitigated if post-natal nutrition has normal fat composition
- **Paternal nutrition increases the risk for childhood obesity**
  - Some of these effects could be addressed with improved paternal nutrition

# Opportunities for Intervention and Prevention (2)

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- Epigenetics could provide an approach to:
  - Identify at-risk children
  - Understand mechanisms to shed light on factors that could be potentially mitigated

# The IOM Workshop Planning Committee: Examining a Developmental Approach to Childhood Obesity

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Ann Yaktine, Director of the Board of Food and Nutrition

Kimber Bogard, Director of the Board of Children, Youth, and Families

## Planning Committee:

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