

- 1 **Viewing Breastfeeding Beyond a Single Generation: The Potential Epigenetic Impact of Breastfeeding on Long Term Health**
By Laurel Wilson, IBCLC, CLE, CCCE, CLD
Author of The Greatest Pregnancy Ever and The Attachment Pregnancy
- 2 **Why am I interested in epigenetics?**
- 3 **It's About History and Herstory**
- 4 **What is epigenetics?**
 - Literally means above the gene.
 - Study of how our environment, internal and external influences genetic expression.
 - Genome=DNA
 - Epigenome=Phenotype
- 5 **What is epigenetics?**
- 6 **How does epigenetics work?**
- 7 **How does epigenetics work?**
 - Genome – Traditional Biology
- 8 **How does epigenetics work?**
 - Genetic Activity
- 9 **How does epigenetics work?**
 - Epigenome
 - Translator
 - Methylation
 - Histones
 - mRNA
- 10 **How does epigenetics work?**
 - DNA
 - Methylation
 - Approximately 30 million CpG Nucleotides that exist in an unmethylated or methylated state
- 11 **How does epigenetics work?**
 - Histones
 - Methylated or Acetylated
 - Tails are acetylated easy access to genes

- When deacetylated, they are highly charged and access to gene is difficult

- mRNA

- Messenger between DNA and Proteins that express genes through down regulation or translation

12 **How does Epigenetics Work?**

- Imprinting

13 **How does Epigenetics Work?**

- Imprinting

14 **How does epigenetics work?**

15 **Nutrigenomics**

- Nutrients can directly or via hormonal activity influence the expression of genes

- An entire new field now called nutrigenomics

- Nutrition changes gene expression (nutritional epigenetics)

- Metabolic processes of nutrients may vary and affect the state of health depending on the individual genotype (nutrigenetics)

- What is the most important first food?

16 **How does Epigenetics Work?**

- Why is this happening?

- Both male and female are in metabolic tug of war

- Male – very large, very strong progeny that will survive in competitive environment

- Female – small less energy “needy” progeny that won’t drain her of resources

- Many epigenetic effects during pregnancy and first years of life have to do with metabolism and growth (which is why we see impacts on metabolic disease – diabetes, obesity, etc.)

17 **Breastmilk and the microbiome**

- Breastmilk provides a stable microbiome in the human gut

- Microbes ferment dietary proteins and polysaccharides

- This fermentation process can change the methyl groups

available for translation of DNA

➤ These methyl groups can affect methylation and histone modification

➤ Non-species specific milk creates a completely different microbiome on the human gut than breastmilk

18 **Breastmilk and the microbiome**

➤ Breastfed infant has high levels of bifidobacterium which promotes positive digestion

➤ Formula fed infant have higher levels of E coli, streptococci, clostridia and bacterioides

➤ Formula fed infants also have completely different pH. Changes pH (5.9-7.3 allows putrefactive bacteria)

➤ These change the fermentation process and methyl groups available to body

19 **Breastmilk and the microbiome**

➤ To have optimal digestion and immune support from the food a baby takes in the following is required:

➤ Amino acids cysteine and methionine

➤ Uptake of selenium

➤ Breastmilk (not formula) is rich in sulfur containing amino acids

➤ Plasma cysteine levels are much higher in breastfed infants than formula fed

➤ Cysteine important for the “reading” of the genome

20 **Breastfeeding and the Phenotype**

21 **How does epigenetics work?**

➤ Epigenome

➤ Can be inherited

➤ The memory of the environment experienced is passed down

➤ Has been demonstrated in animal research up to 5 generations out

➤ Human research has found specific influence up to three generations – Hanger Winter 1944, Swedish 1890's (Kaati)

22 **Why does it work?**

➤ We are constantly adapting for optimal survival.

➤ The fetus is preparing for optimal survival outside the womb.

➤ The newborn is managing its new environment and adjusting

to cues.

- 23 **Breastfeeding and Epigenetics**
- During pregnancy and early postpartum life babies are programmed nutritionally to adapt to their environment.
 - Abundant resources, immune support, healthy food
 - Limited resources, immune challenge, poor nutrition
- 24 **How does epigenetics work?**
- You are what you eat?
 - You are what your mother and grandmother ate.
 - Diet of grandparents linked to longevity and disease variants in offspring for many generations
 - What is the impact of breastmilk?
 - The act of breastfeeding?
- 25 **Clear evidence that prenatal and early postpartum environment influences the child lifelong.**
- 26 **How does epigenetics work?**
- "Nutritional status can influence epigenetic profiles by inhibiting enzymes that catalyze DNA methylation or histone modifications or by influencing dietary availability of substrates necessary for these enzymatic processes."
Thayer, 2011
- 27 **Epigenetic Animal Studies**
- Mouse studies
 - What we are fed
 - Agouti mice (Jirtle, 2000)
- 28 **Breastmilk's Epigenetic Influence**
- Necrotizing Enterocolitis – gut microbiotica programming by suppressing the pathway involved in proinflammatory cytokine genes
 - Infectious Diseases and Disorders of Immune System - - expression of proinflammatory cytokine genes
 - Obesity – programming gut microbiotica and promoting oligosaccharides
- 29 **Breastmilk's Epigenetic Influence**

30  **Studies in Review**

- 1 Obermann-Borst et al. Duration of breastfeeding and gender are associated with methylation of the LEPTIN gene in very young children.
- 2 Ozkan et al.: Milk kinship hypothesis in light of epigenetic knowledge. Clinical Epigenetics 2012, 4-14.
- 3 Kosaka et al.: microRNA as a new immune-regulatory agent in breast milk. Silence, 2010,1:7.
- 4 Melnick, BC.: Milk: an exosomal microRNA transmitter promoting thymic regulatory T cell maturation preventing the development of atopy?

31  **1 Duration of Breastfeeding and LEP**

- “Duration of breastfeeding and gender are associated with methylation of the LEPTIN gene in very young children.” Obermann-Borst et al.
- DNA methylation of LEP, a non-imprinted gene
- Responsible for appetite regulation and fat metabolism

32  **1 Duration of Breastfeeding and LEP**

- Maternal Education, Breastfeeding Duration, Constitutional Factors at 17 mo. old
- Measured DNA methylation of LEP in whole blood and also serum leptin

33  **1 Duration of Breastfeeding and LEP**

- Findings
 - No assoc. maternal education and duration of bf
 - Breastfeeding at least 1-3 had higher serum concentrations of leptin (low methylation)

- 2.8 vs. 2.6 mmol/l; P=0.025
- Boys overall had lower methylation

34 **2 Milk Kinship and Epigenetics**

- Ozkan et al.: Milk kinship hypothesis in light of epigenetic knowledge. *Clinical Epigenetics* 2012, 4-14.
- Does wet nursing or milk sharing cause consanguinity?

35 **2 Milk Kinship and Epigenetics**

- Wet nursing or milkshare and milk kinship
- Why is this a possibility?
 - Exosomes in breastmilk
 - Tiny endosome-derived membrane vesicles (approximately 30 to 100 nm in diameter) that are released into the extracellular environment
 - Genetic material such as microRNA
 - Stem Cells
 - Organic substances affecting epigenetic regulation mechanisms

36 **2 Milk Kinship and Epigenetics**

37 **3 miRNA in Breastmilk**

- MicroRNA in Breastmilk
- Kosaka et al.: "microRNA as a new immune-regulatory agent in breast milk." *Silence*, 2010,1:7.
- High levels of miRNA in breastmilk in first six months of lactation
- Suggest that humans can transfer genetic material other than sexual reproduction

38 **3 miRNA in Breastmilk**

39 **3 miRNA in Breastmilk**

- Period of Influence is Strongest Before age of 2
 - Inadequacy of immune system to reject genetic material
 - Increased plasticity
 - Increased vulnerability of epigenome during developmental period
 - Approximately 1.3×10^7 copies/liter/day of miR-181a are received by a breastfed infant.

40 **4mRNA in Breastmilk**

- Melnik, 2014 Milk: an exosomal microRNA transmitter promoting thymic regulatory T cell maturation preventing the development of atopy?
- Boiling of milk abolishes milk's exosomal miR-mediated bioactivity (mRNA 155)
 - Formula therefore cannot protect against development of atopic disease
 - Formula is deficient in bioactive exosomal miRs promoting thymic regulatory T cell maturation
 - Another example of breastmilk promoting positive epigenetic regulation

41 **Questions to Ponder**

- Very clear data that stress has epigenetic impact, and is multigenerational.
- Very clear evidence that social standing and hierarchy has very clear impact on health gradient.
- Very clear evidence that in western societies, low income, higher stressed mothers have shorter duration of breastfeeding?
- What epigenetic influence is this cumulative effect having on babies and their future offspring?

42 **Thank You**

- Questions:
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