

You and Your Family's Early Life Determine Your Health Because of Epigenetics

Robert H. Lane MD MS
Professor and Chair, Department of Pediatrics
Associate Director of Epigenomics
Genomic Science Personalized Medicine Center
Medical College of Wisconsin

Pediatrician in Chief
The Barri L. and David J. Drury Chair in Pediatrics
Children's Hospital of Wisconsin

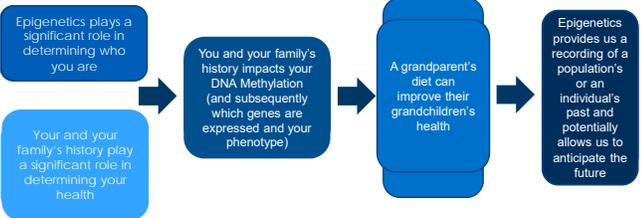


Main Message

Your family's history and your perinatal environment impact your epigenetics, and this impact influences your health throughout your life



Roadmap of our Chat

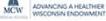


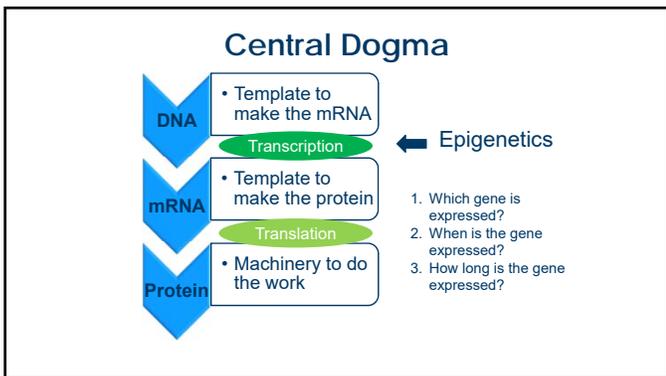
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DEFINE EPIGENETICS







Epigenetics Regulates Gene Expression and Subsequently Determines Cell Type

Stem cell

Conversion of Genes to Epigenetics

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Your Chromatin is the Palette that Provides the Molecular Paints that Determines how a Cells Function

DNA

Chromatin

Histones

Nucleosome

Conversion of Genes to Epigenetics

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Epigenetics Determines where the Paint Brush Goes

Transcription Machinery

Transcription Machinery

Conversion of Genes to Epigenetics

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Epigenetics Directs the Paint Brush by Modifying the Nucleosome

These modifications take a significant effort to change

Histone Proteins

DNA Methylation

N-terminal tails

- Methylation
- Acetylation
- Phosphorylation

Conversations with Scientists

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Epigenetics and Transcription

- Epigenetics regulates the three characteristics of transcription
 - Initiation
 - Elongation rate
 - Termination
- Epigenetics regulates transcription in varying degrees by being a template of the whole gene

DNA

Transcription

mRNA

- Template to make the mRNA
- Template to make the protein

Conversations with Scientists

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Transcription Machinery

Conversations with Scientists

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Epigenetic Mechanisms Define our Epigenetics Biology

- Epigenetics determines....
 - ...tissue specific gene expression
 - ...developmental gene expression
 - ...gender specific gene expression
 - ...how well we adapt to our environment



Epigenetics Occurs Throughout our Whole Genome

- 2% of the human genome encodes protein coding genes (exomes)
- 98% contains vast stretches of **non-protein coding DNA** that supervise expression



Non-Protein Coding DNA Defines our Species

- Non-Coding regions determine our developmental complexity
- The higher the ratio of non-protein encoding DNA to protein encoding DNA the more 'complex' a species you are



Non-Protein Coding DNA Plays a Large Part in Determining our Health

- The ENCODE project is the product of an international research consortium, which is funded by the National Genome Research Institute
- The aim of this research consortium is to identify the functional elements of the human genome
- 90% of common variants associated with disease lie outside of protein encoding regions



<http://www.genome.gov/encode/>



Roadmap of our Chat

Epigenetics plays a significant role in determining who we are

Describe Developmental Origins of Disease Theory/ Life Course Theory



You and Your Family's Early Life Determine Your Health Because of Epigenetics

DESCRIBE DEVELOPMENTAL ORIGINS OF DISEASE THEORY/ LIFE COURSE THEORY



Developmental Origin of Health and Life Course Theory are very Similar

- The 'school' of Developmental Origins of Health focuses upon the importance of a vulnerable period that appears to exist during pregnancy and for a short time after delivery
- The 'school' of Life Course Theory focuses upon the importance of family history and 'weathering'

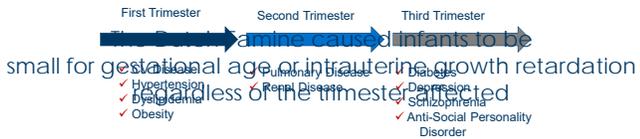


Developmental Origins of Health: Dutch Famine of 1944-1945

- The famine lasted 5 months
 - Calories dropped from 1800/day to 600/day
 - After liberation, calories increased > 2000 calories/day

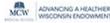


Developmental Origins of Health Started with the Dutch Famine



Developmental Origins of Health: The Chinese Famine (1959 – 1961)

- Largest in human history
- Epidemiologically similar to the Dutch Famine in that there was an increase in 'small for gestational age' or intrauterine growth retardation in the **1st generation**
- Epidemiologically different from "Dutch Famine"
 - Superimposed on widespread chronic under nutrition
 - Severity varied across regions and affected rural regions disproportionately



Consequences of Chinese Famine (1959 – 1961)

- Different than Dutch Famine
 - Affected neurodevelopmental outcomes
 - Increased incidence of 'large for gestational age (LGA)' infants in **second generation***
- Mothers with obesity and diabetes are more likely to have LGA infants.



Life Course Model and Racial Disparities

- High infant mortality in the US is due in large part to the rates among African Americans
- A maternal grandmother's exposure to neighborhood poverty predicts risk for growth restriction and prematurity in the grandchild
 - This risk is independent of the mother's status
 - Further risk (25%) can be statistically attributed to generational residence in low income neighborhoods



Roadmap of our Chat

Epigenetics plays a significant role in determining who we are

Your and your family's history play a significant role in determining your health

Provide Examples of Personal and Family Histories that are Known to Affect Epigenetics

Conversations with Scientists

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You and Your Family's Early Life Determine Your Health Because of Epigenetics

PROVIDE EXAMPLES OF PERSONAL AND FAMILY HISTORIES THAT ARE KNOWN TO AFFECT EPIGENETICS

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DNA Methylation has been the most Frequently Studied Epigenetic Characteristic

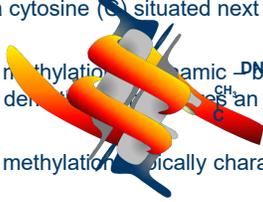
- DNA methylation studies lend themselves toward high throughput techniques that are easy to apply to human studies
 - DNA methylation studies require little sample
 - DNA methylation studies appear easy to interpret

Conversations with Scientists

MCW ADVANCING A HEALTHIER WISCONSIN ENDORSEMENT

DNA CpG Methylation

- DNA CpG methylation involves placing a methyl group (CH₃) on a cytosine (C) situated next to a guanidine (G)
- DNA CpG methylation is a dynamic process - so demethylation requires an energy expenditure
- DNA CpG methylation typically characterizes silenced genes



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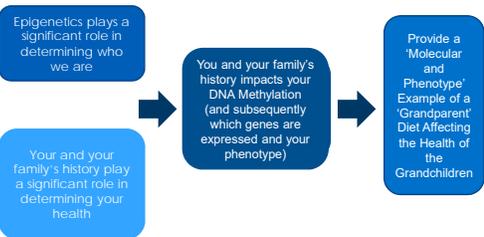
These Parental 'Conditions' Change DNA Methylation in the Offspring and are Associated with Adult Diseases such as Insulin Resistance and Obesity

- | | |
|---------------------------|----------------------|
| • Maternal diabetes | • Paternal habits |
| • Maternal obesity | • Mode of conception |
| • Maternal macronutrient | • Mode of delivery |
| • Maternal micronutrient | • Gestational age |
| • Environmental exposures | • "Size" at birth |
| • Maternal smoking | • Womb mates |



MCW ADVANCING A HEALTHIER WISCONSIN ENDORSEMENT

Roadmap of our Chat



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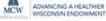
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PROVIDE A 'MOLECULAR AND PHENOTYPE' EXAMPLE OF 'GRANDPARENT' DIET AFFECTING THE HEALTH OF THE GRANDCHILDREN



Small for Gestational Age and/or Intrauterine Growth Retardation (IUGR)

- In the US, 3-10% of pregnancies are complicated by IUGR
- In the US, IUGR accounts for 20% of perinatal morbidity and mortality
- In the US, the most common causes are environmental



Multiple Clinical Observations Link IUGR to Adult Disease

- Poor postnatal growth
- Insulin resistance
- Obesity
- Dyslipidemia
- Hypertension
- Cardiovascular disease
- Immunodeficiency
- Renal insufficiency and failure
- Neurodevelopmental delay
- ADHD
- Alzheimer's
- Chronic lung disease
- Divorce



We Can Stop the Transmission of the Insulin Resistance and Obesity Across Generations

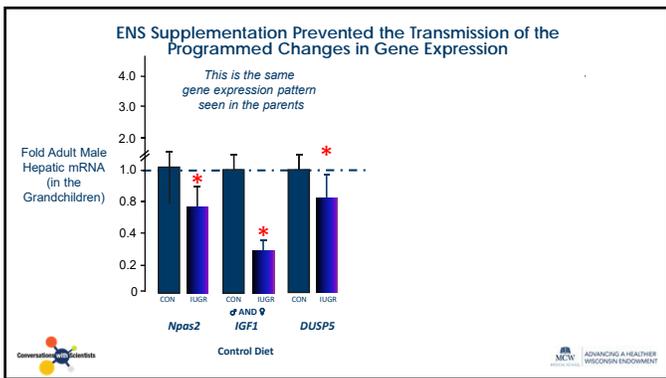
The two primary questions that we are asking....

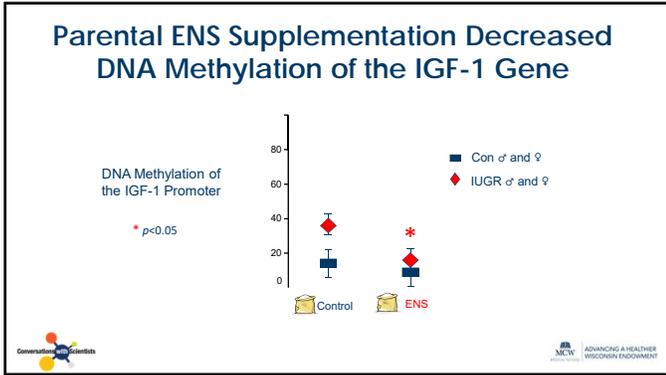
<p><u>Generation</u></p> <p>(1) Because of your grandparent's environment - if your parent(s) are IUGR and are raised in a 'normal' environment with a 'normal diet', do you still have the same predisposition to insulin resistance and obesity as your parents?</p> <p>(2) Because of your grandparent's environment - if your parent(s) are IUGR and are raised in a 'normal' environment with a supplemented diet, are you protected from that predisposition to insulin resistance and obesity?</p>	<p><u>Diet</u></p> <p>(IUGR environment)</p> <p>Normal (NL)</p> <p>Supplemented (ENS)</p> <p>Choline</p> <p>Betaaine</p> <p>Animals</p> <p>from the</p> <p>all four crosses</p>
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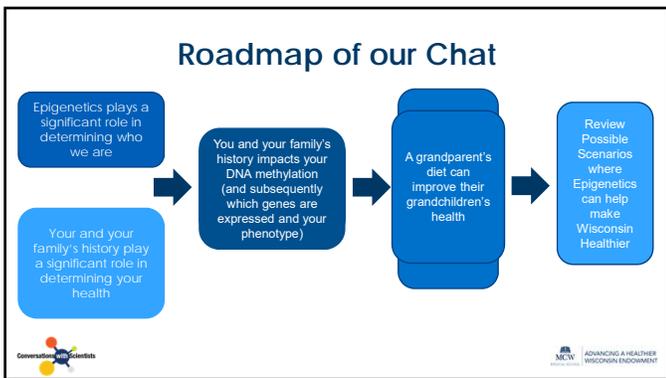
The 'ENS Diet in the Parent Generation Influenced the Health of the Grandchildren

- ✓ Grandchildren whose IUGR parents were on the normal diet are both insulin resistant and obese
- ✓ Grandchildren whose IUGR parents were on the ENS diet have normal glucose metabolism and are lean

.....but stinky







You and Your Family's Early Life Determine Your Health Because of Epigenetics

REVIEW POSSIBLE SCENARIOS WHERE EPIGENETICS CAN HELP MAKE WISCONSIN HEALTHIER

Logos: Conversation with Scientists, MCW, ADVANCING A HEALTHIER WISCONSIN ENDORSEMENT

Social Policy/ Population Health

- We can use epigenetics as a quantifiable biological measure of the impact of social and political initiatives within our region
- We can potentially use epigenetics to identify populations or neighborhoods that stand at risk for 'weathering' diseases if current and future research makes the necessary advancements

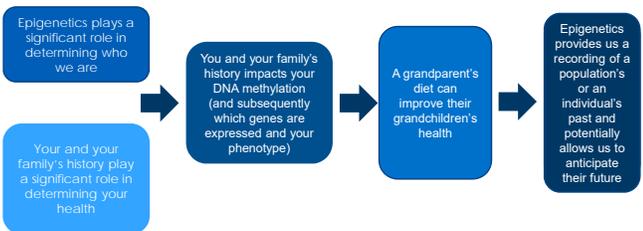


Personalized /Precision Medicine

- We can potentially use epigenetics as an anticipatory 'biomarker' in individuals if current and future research makes the necessary advancements
- We can potentially use epigenetics in individuals to track the effectiveness of interventions (e.g. diet) if current and future research makes the necessary advancements

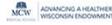


Roadmap of our Chat



Main Message

Your family's history and your perinatal environment impacts your epigenetics, and this impact influences your health throughout your life



Healthy citizens are the greatest asset the world can have...

- Winston Churchill

You can't chose your parents, but you can chose your epigenetics...

- Genevieve and Henry Lane



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THANK YOU