Epigenetics and its Implications for Public Health

Lisa Marriott, PhD
Assistant Professor, OHSU/PSU School of Public Health
marriott@ohsu.edu
Before we begin, please answer the following questions.

1. Have you heard about epigenetics before?
   - Yes
   - No
   - Not sure

<table>
<thead>
<tr>
<th></th>
<th>Initial Fair (n=125)</th>
<th>To Date (n=1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Students:</td>
<td>8.4%</td>
<td>Overall 14.6%</td>
</tr>
<tr>
<td>Teachers:</td>
<td>36.4%</td>
<td></td>
</tr>
</tbody>
</table>

2. How well do you think you could explain epigenetics to someone else?
   - Not at all
   - Not very well
   - Neutral
   - Well
   - Completely
   - Not sure

<table>
<thead>
<tr>
<th></th>
<th>Initial Fair (n=125)</th>
<th>To Date (n=1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Students:</td>
<td>0.8%</td>
<td>Overall 3%</td>
</tr>
<tr>
<td>Teachers:</td>
<td>9.1%</td>
<td></td>
</tr>
<tr>
<td>% Answering “Well” or “Completely”</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
New to this research area?
You are not alone.

Patterns are Important. Trust Yourself.

Dr. Lars Olov Bygren
Overkalix

Norbotten, Sweden

<table>
<thead>
<tr>
<th>Year</th>
<th>Crop Report</th>
</tr>
</thead>
<tbody>
<tr>
<td>1800</td>
<td>Crop Failure</td>
</tr>
<tr>
<td>1801</td>
<td>Abundance</td>
</tr>
<tr>
<td>1802-1811</td>
<td>Normal</td>
</tr>
<tr>
<td>1812</td>
<td>Crop Failure</td>
</tr>
<tr>
<td>1813-1820</td>
<td>Normal</td>
</tr>
<tr>
<td>1821</td>
<td>Crop Failure</td>
</tr>
<tr>
<td>1822</td>
<td>Abundance</td>
</tr>
<tr>
<td>1823-1827</td>
<td>Normal</td>
</tr>
<tr>
<td>1828</td>
<td>Abundance</td>
</tr>
<tr>
<td>1829-1835</td>
<td>Normal</td>
</tr>
<tr>
<td>1836</td>
<td>Crop Failure</td>
</tr>
<tr>
<td>1837-1843</td>
<td>Normal</td>
</tr>
<tr>
<td>1844</td>
<td>Abundance</td>
</tr>
<tr>
<td>1845-1855</td>
<td>Normal</td>
</tr>
<tr>
<td>1856</td>
<td>Crop Failure</td>
</tr>
<tr>
<td>1856-1862</td>
<td>Normal</td>
</tr>
<tr>
<td>1863</td>
<td>Abundance</td>
</tr>
</tbody>
</table>

**Nutrition affects generations**

- Grandsons of Overkalix boys (aged 9-12) who had overeaten in **abundant** years **died six years earlier** than the grandsons of those who had endured a poor harvest.
  - 32 years after controlling for SES
  - Diabetes mortality among grandsons: OR=4.1
- **Sex-linked effects:**
  - Paternal grandfather experiences only predicted mortality in grandsons
  - Paternal grandmother experiences only predicted mortality in granddaughters
- **Established importance of the** "Slow Growth Period" before puberty (ages 8-10 in girls; 9-12 in boys)

---

Dutch Hunger Winter

Increase in Coronary Heart Disease 50 Years Later

Critical Periods: The Heart

Critical Periods for Organ Development

From Susan Bagby, 2013
More Critical Periods

• "Slow Growth Period" before puberty (ages 8-10 in girls; 9-12 in boys)

Female
In utero – egg development

Male
Puberty – sperm development (though sperm production continues throughout life)
And the Patterns Continue....

“Of all reported outcomes, associations between prenatal famine and adult body size, diabetes, and schizophrenia show the most consistent pattern. For other outcomes, the pattern is more variable and inconsistent.”

Great Leap Forward
China, 1958-1960
20 million people died from starvation between 1959-1962

Your New Year’s Resolutions in Perspective

“She was sixteen years old, stood almost five foot six and weighed eighty-eight pounds.”

Hepburn “suffered from asthma, jaundice and other illnesses caused by malnutrition, including acute anemia and a serious form of edema”

Epigenetics is a way to change the ‘volume’ of gene expression.
## Genetic versus Epigenetic Changes

<table>
<thead>
<tr>
<th>From this</th>
<th>A Genetic Mutation</th>
<th>An Epigenetic Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATCGGGATTTCACG</td>
<td></td>
<td>ATCGGGGATTTCACG</td>
</tr>
<tr>
<td>To this</td>
<td>ATAGGGATTTCACG</td>
<td>ATCGGGGATTTCACG</td>
</tr>
</tbody>
</table>

*Denotes epigenetic change*
Gene Expression 101: DNA to protein

1. Transcription = DNA to RNA
   - DNA
   - RNA
   - Protein

2. Translation = RNA to protein
   - mRNA
   - Ribosome

Getting up to speed: http://learn.genetics.utah.edu/
### Genetic versus Epigenetic Changes

<table>
<thead>
<tr>
<th>From this</th>
<th>To this</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATCGGGATTTCACG</td>
<td>ATAGGGATTTCACG</td>
</tr>
</tbody>
</table>

**A Genetic Mutation**

- If a different amino acid is coded, a different protein results.

**An Epigenetic Change**

- ATCGGGATTTCACG
- ATCGGGATTTCACG

Same amino acid is coded, so same protein -- but it’s all about **access**.
The Patterns of Epigenetics

Ways to reduce or turn off (silence) gene expression

- methylate (methyl groups make it harder to access the DNA; DNA transcription is reduced)
- deacetylate (DNA is tightly wound around histones, making it harder to access the DNA; DNA transcription is reduced)

Ways to increase gene expression

- demethylate (no methyl groups allow for easier access to the DNA; DNA transcription is increased)
- acetylate (acetyl groups loosen the DNA from histones, making it easier for DNA transcription to increase)

"Is reducing gene expression good or bad?"

The valence depends on context

"Good"
Acclimatizing in high altitude increases oxygen transport in the blood (Julian et al., 2014)

"Depends"

Normal Cell Growth (skin cells, scab formation)

Abnormal Cell Growth (cancer)

"Bad"
99% of bees in hive are workers. Worker bees are either:

- **Nurses**
  - Take care of the larvae (baby bees).
  - They also build and clean the nest.

- **Foragers**
  - Collect pollen, nectar and water for the colony.

**Role in the hive:**

---

**Birth**

2-3 weeks

Epigenetics and Diet

Agouti Epigenetics and Diet

Agouti Epigenetics and Diet

Social Interactions

Epigenetics and the Social Context

Maternal behavior can alter the stress response of offspring (Meaney, 1997)

2004 research by Szyf and Meaney based on Agouti work – if diet can do it, what about...

EXPERIMENT #1
1. Very attentive mothers and very inattentive mothers bred
   - Inattentive mother raises biological pups
   - Attentive mother raises biological pups
2. Researchers examine the brains of grown pups
   - Genes rarely methylated
   - Genes highly methylated
   - Stress
   - Hippocampus

EXPERIMENT #2
1. Very attentive mothers and very inattentive mothers bred
   - Pups switched at birth
   - Mothers raise foster pups
2. Researchers examine the brains of grown foster pups
   - Genes rarely methylated
   - Genes highly methylated
   - Stress
   - Hippocampus

EXPERIMENT #3
1. Inattentive mothers bred
   - Inattentive mother raises biological pups
2. Brains of “damaged” pups treated with trichostatin A, a drug that removes methyl groups
3. Epigenetic changes disappear
   - Genes rarely methylated
   - Stress
   - Hippocampus

Hurley (2013). Grandma’s experiences leave a mark on your genes. Discover, May issue. (History of how they discovered it and image above)
If Patterns are Important

Epigenetics is a new lens for thinking about health

• If stress and diet are strongest so far:
• Traumatic experiences:
  – War (Now, Holocaust, Civil War)
  – Victims and offspring of massacres and famines
  – Ethnic displacements and migrations
  – Social: Alcoholic or abusive parents, school bullying -- research on suicide
• Environmental Systems & Health:
  – Pollution and toxins affecting masses

The activity was very well thought out. The organization of the task cards and included diagrams were very informative for the students. The students enjoyed having different roles to take on, work as a team of one job, and then share info back with the home team of mixed jobs. The aha moments when the pieces of info were put together were very exciting.

I used this activity as one of my final activities for my genetics unit and the students were able to bring in that info to the activity to help them understand what was going on with this group of people. It raised some interesting questions. The summative questions made my students stretch their learning, the Bees one more so than the Hurricane one. I had them do both. The web page is a great resource for the activity. Thank you for taking the time to share it. I will share with my colleagues. I am definitely going to do this activity again this year.

Cindy Lambert, MEd., NBCT
Trenton Elementary School
Trenton, ME 04605

From Students’ Perspectives
Scientists’ Key Understandings

1) the environment affects our genes;
2) you may have more control over your genes than previously thought;
3) epigenetics is a cutting edge science and there is a lot we don’t know yet;
4) epigenetics likely has a big role in a lot of areas (e.g. learning & memory, sleep, future disease risk, developmental origins of health and disease).

**Scientists’ Key Concern:**
Be careful to not focus on the specific mechanisms, which may become outdated as the science progresses.
Don’t Get Bogged Down in the Details

DNA → RNA → Protein

Your job is not to teach the public the mechanisms, it’s to teach them the concept

New Mechanisms:
- Histone methylation
- Histone ubiquitination
- Phosphorylation and ADP-ribosylation
- RNA methylation
- Non-coding RNAs

Simplify. Remember your patterns.
Patterns are Important

Every tissue in the body has its own epigenome
(Simplify: what would you predict based on what that organ does?)

Brena et al. (2006). Nature Genetics
Top Five Reasons for Teaching Epigenetics

1. It’s the science of why a person’s choices matter.
2. Science is constantly advancing – Shows the evolving “nature of science”.
3. Impact on Society – Famine, wartime stress, and pollution can all affect how DNA functions. Knowing this, we have a vast amount of information to frame the implications of world events. What obligations do we have to ourselves and others?
4. It helps to think how to be critical consumers of information – False claims with new products? Overreaching interpretations?
5. It is our past, present, and future – DOHAD message on disease risk

OHSU Teacher Advisory Board’s Warnings and Advice when teaching epigenetics

Teachers’ Primary Concerns:

1. **Social Determinants of Health**: Be careful when introducing the topic, as individuals from disadvantaged backgrounds may not have the ability to change their diet/stress due to socioeconomics or other factors
2. **Ethical and social justice considerations**: Some of these topics may be particularly sensitive to some minority groups (recently published example: DOHAD effects on Holocaust survivor offspring; Yehuda et al. 2015)
3. **Teachers are unprepared**: they don’t know this topic yet and will need materials and help

Teachers’ Advice:

1. Focus on the cutting edge aspect of epigenetics
2. Use avatars or characters rather than personal identities – especially if you’re talking about critical periods of development
3. Curriculum development will be very important – create briefing sheets and background packets for teachers and principals to talk with students and parents
Scientists’ and Teachers’ Agreed upon Learning Goals for Teaching Epigenetics

1) Students will be able to recognize the term

2) Students will understand that epigenetics can modify health outcomes in both directions – “good” and “bad”

3) Students will understand that the process of science (epigenetics) is more applicable than learning the specific mechanisms.

Resources to help you....
Let’s Get Healthy!’s Online Resources to Teach It

Let’s Get Healthy!’s Online Resources to Teach It

Where to get more information...

We have developed several printable handouts and manipulatives that you're welcome to use! Teachers, don't forget to see our lesson library for free, downloadable classroom lessons and activities about epigenetics.

- About Epigenetics
- Timeline — From Genes to Epigenetics
- Nutrition and Your Epigenome
- Epigenetics Flip Book
- Ideas for Epigenetic Manipulatives
- Epigenetics Glossary of Terms
- Briefing Sheet for Students
- Briefing Sheet for Parents
- Briefing Sheet for Teachers
- Briefing Sheet for Principals
- Online Resources for Epigenetics

http://www.letsgethealthy.org/about-the-research/station-descriptions/epigenetics/

DOHAD Lesson: Password is NSTA

http://www.letsgethealthy.org
Epigenetics Game

Pre-game questions

Level 1

Level 2

Level 3

Level 4

Post-game questions

True or False: 4 Questions

3. Gene expression can be turned on or off, much like the volume knob on a radio.

• True
• False

The correct answer is: True

Genes provide the instructions for making proteins that make your body work. The body can make more or less protein by turning these genes on or off.

Did you know? Genes make up only 2% of your DNA!

Next Question
Additional Manipulatives

DNA methylation

Analogy to your grandmother’s cookbook
Your DNA is like the original recipe, but how you make the recipe changes based on your experience and environment (your epigenetics)

FAQ Flip Board

DNA coiling around histones
Additional Teaching Resources

Online Resources
• Genetic Science Learning Center – University of Utah.
  • For their teacher site: www.teach.genetics.utah.edu;
  • For their student/learner site: www.learn.genetics.utah.edu
• Hank Green’s School-friendly YouTube Video about the power of epigenetics (SciShow; 9 minutes and 28 seconds; https://www.youtube.com/watch?v=kp1bZEUgqVI
• Moore Institute website and blog (http://betterthefuture.org)

Articles written for the lay public
Special Thanks!

Jackie Shannon, PhD, Leigh Coppola, Adam Lipus, MPH, Greg Heinonen

Funding for this project:
• Pilot project grant from OHSU Bob and Charlee Moore Institute for Nutrition and Wellness (2012)
• Subcontract from the Interdisciplinary Center for Epigenetics, Science and Society (NIH NHGRI - 5P20HG00551)
• Science Education Partnership Award (NIH OD R25 OD010496)

Advisory Boards
Epigenetics Expert Advisory Board
• Dr. Mitchell Turker (OHSU),
• Dr. Cathy Klein (NYU)
• Dr. Lisa Weasel (Portland State Univ)

DOHAD and Epigenetics Lesson Reviewers
• Dr. Kent Thornburg (OHSU; both)
• Dr. Susan Bagby (OHSU; DOHAD),
• Dr. Samantha Louey (OHSU; DOHAD)
• Dr. Mitchell Turker (OHSU; epigenetics)

Game Development
• Jason Laramie (Art Production) and Matt Steinwachs (Programming)
• OCTRI Bioinformatics for integration into Let’s Get Healthy! platform

Our teacher curriculum developers
Alison Charbonneau, June Poling, Kristin Allan, Debbie Frankel, Cheryl McGinnis and Berk Moss
Game play significantly increased self-reported ability to describe epigenetics to someone else

- Only 55.8% “enjoyed the game” (length cited as reason).
- However, 73.6% said the game “made them think more about how their choices affected their health”. These individuals were also significantly more likely to:
  - **Enjoy** the game ($p<0.001$)
  - **Knowledge**: Get more game questions correct (7.9 out of 10 vs 7.4; $p<0.012$)
  - **Intend to change** their...
    - diet ($p<0.01$),
    - sleep ($p<0.001$),
    - stress ($p<0.005$),
    - but not their air quality ($p=0.44$).