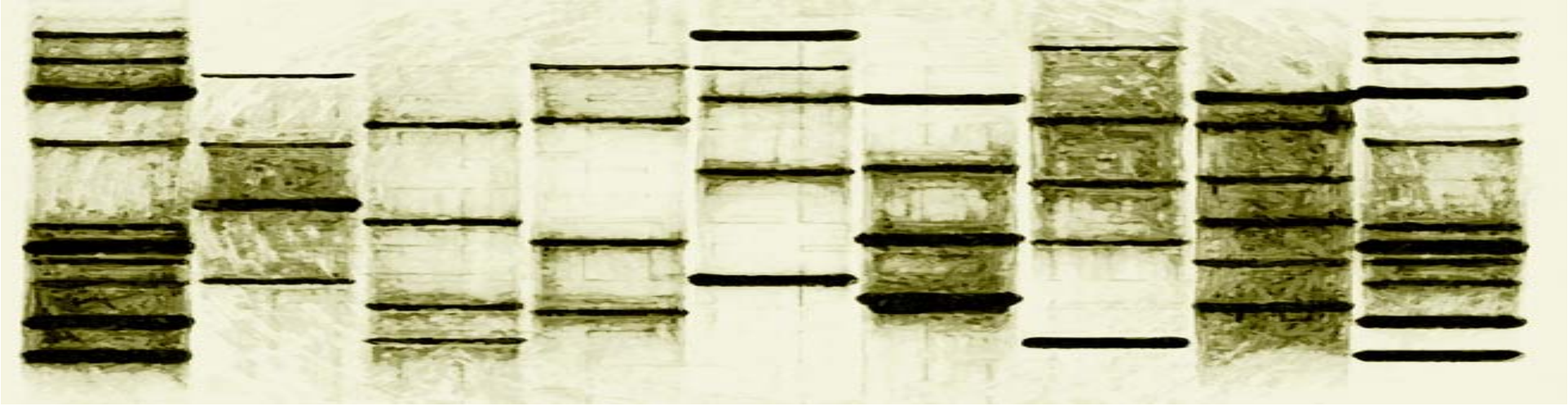
Epigenetics and its Implications for Public Health



OHSU Portland State University SCHOOL OF 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

Initial Fair (n=125)
Students: 8.4%
Teachers: 36.4%

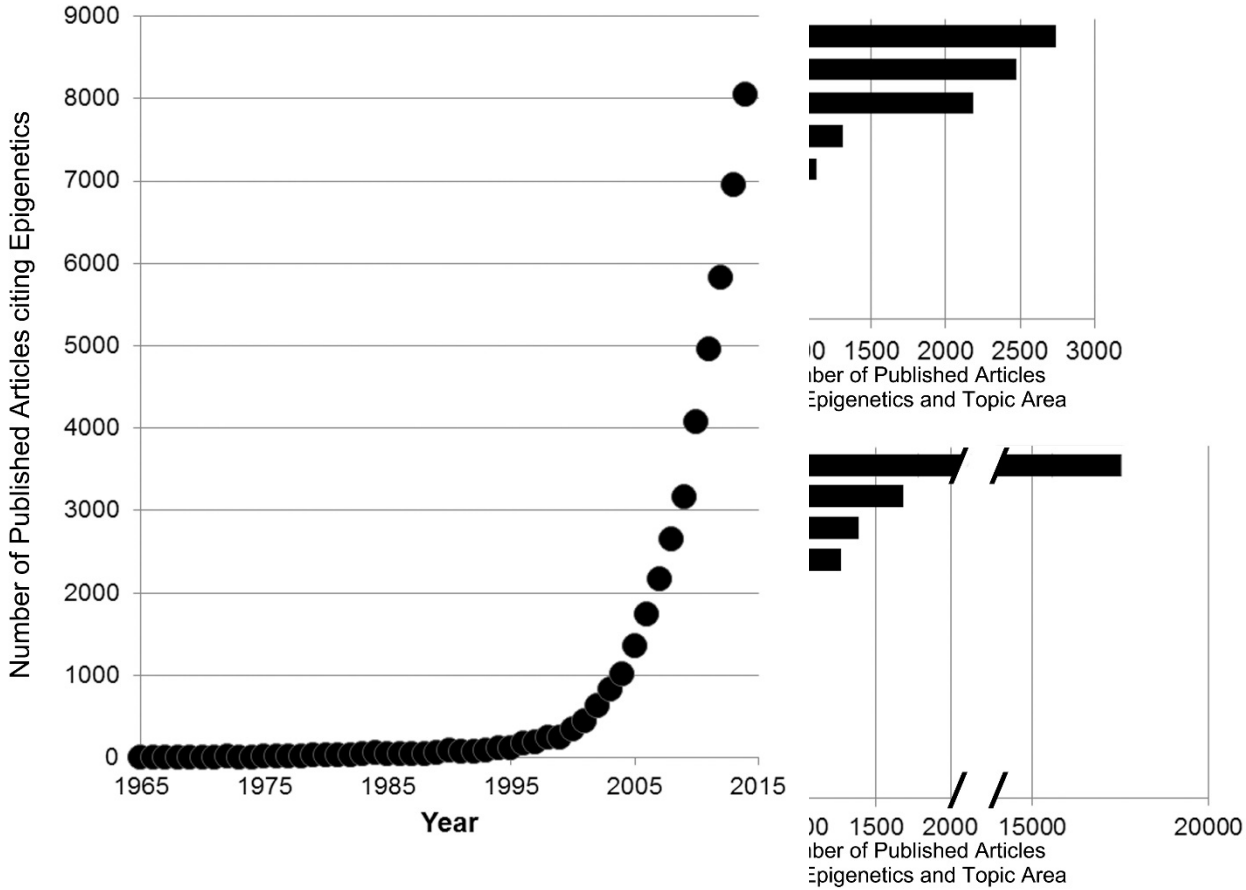
To Date (n=1000)
Overall 14.6%

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

Initial Fair (n=125)
Students: 0.8%
Teachers: 9.1%
% Answering "Well" or "Completely"

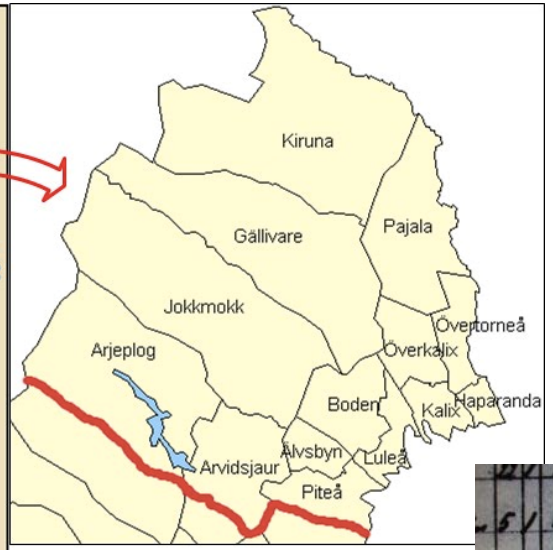
To Date (n=1000)
Overall 3%

New to this research area?
You are not alone.

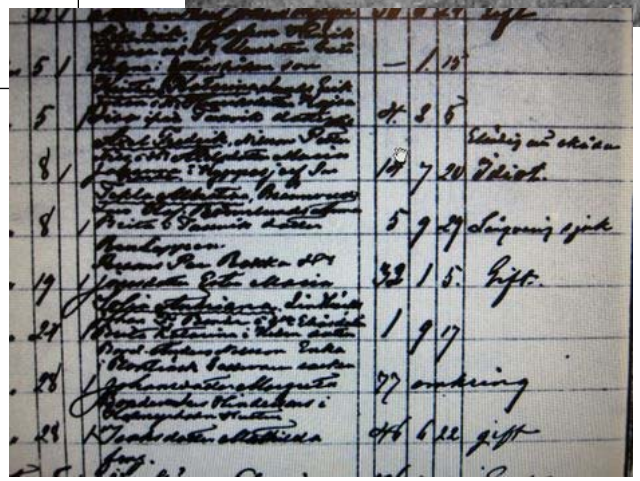


Marriott, L.K., Charbonneau, A., Moss, G.B., Shannon, J., Thornburg, K.L., and M.S. Turker (2016). "Epigenetics: A new science for middle school – and why you should teach it. *Science Scope*, February issue

Patterns are Important. Trust Yourself.



Dr. Lars Olov Bygren
Overkalix



http://www.radiolab.org/story/251885-you-are-what-your-grandpa-eats/ (2012)
http://blogs.biomedcentral.com/on-biology/2014/02/20/a-shock-of-change-felt-down-the-generations/

.

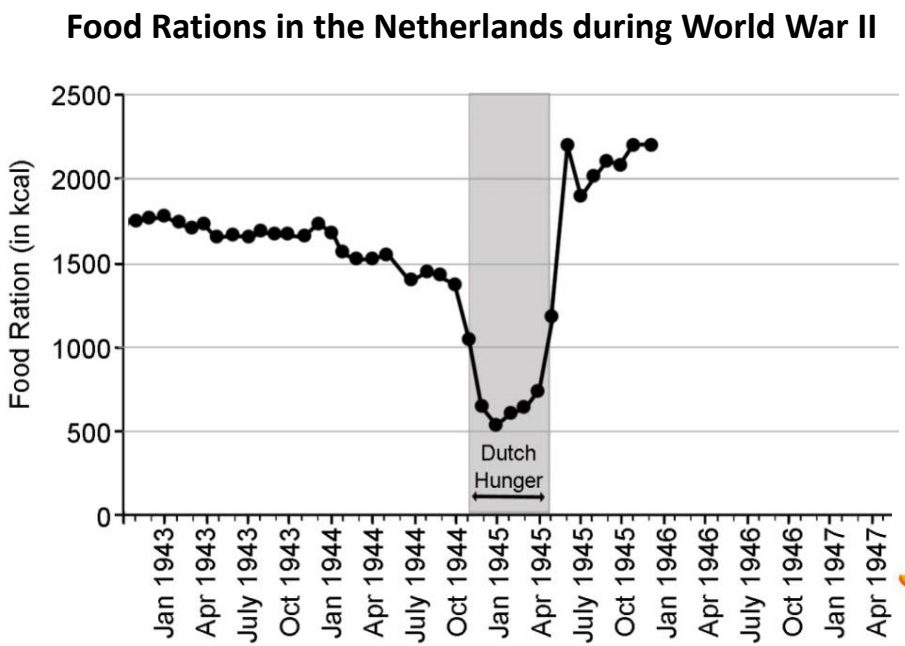
Year	Crop Report
1800	Crop Failure
1801	Abundance
1802-1811	Normal
1812	Crop Failure
1813-1820	Normal
1821	Crop Failure
1822	Abundance
1823-1827	Normal
1828	Abundance
1829-1835	Normal
1836	Crop Failure
1837-1843	Normal
1844	Abundance
1845-1855	Normal
1856	Crop Failure
1856-1862	Normal
1863	Abundance

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)

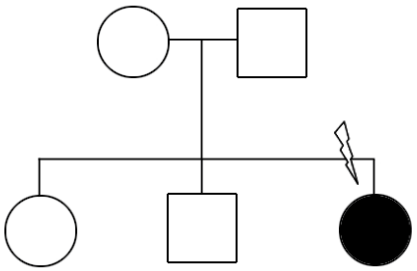
Cloud, J. "Why Your DNA Isn't Your Destiny." TIME. Time Inc., 6 Jan. 2010.
Pembrey, M., Saffery, R., Bygren, L. O., & Network in Epigenetic Epidemiology. (2014). Human transgenerational responses to early-life experience: potential impact on development, health and biomedical research.*Journal of Medical Genetics*, *51*(9), 563–572.

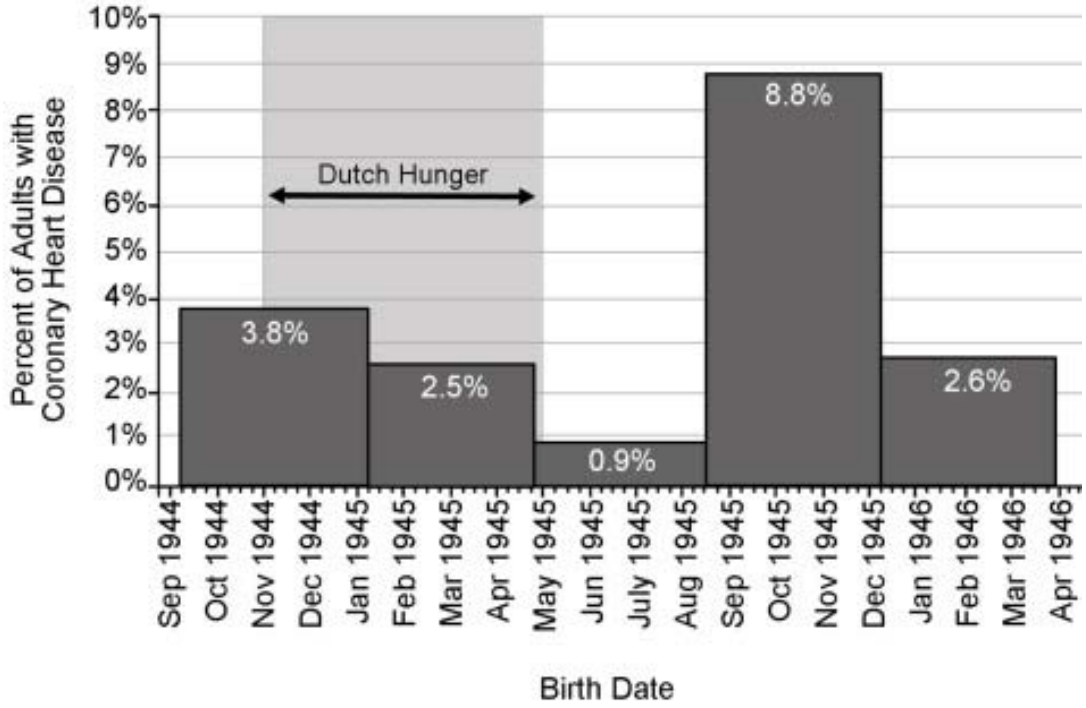
Dutch Hunger Winter



Charbonneau, A., Moss, G.B., and L.K. Marriott (2015). The surprising patterns of health and disease. *Science Scope, 3*, 64-70

Increase in Coronary Heart Disease 50 Years Later





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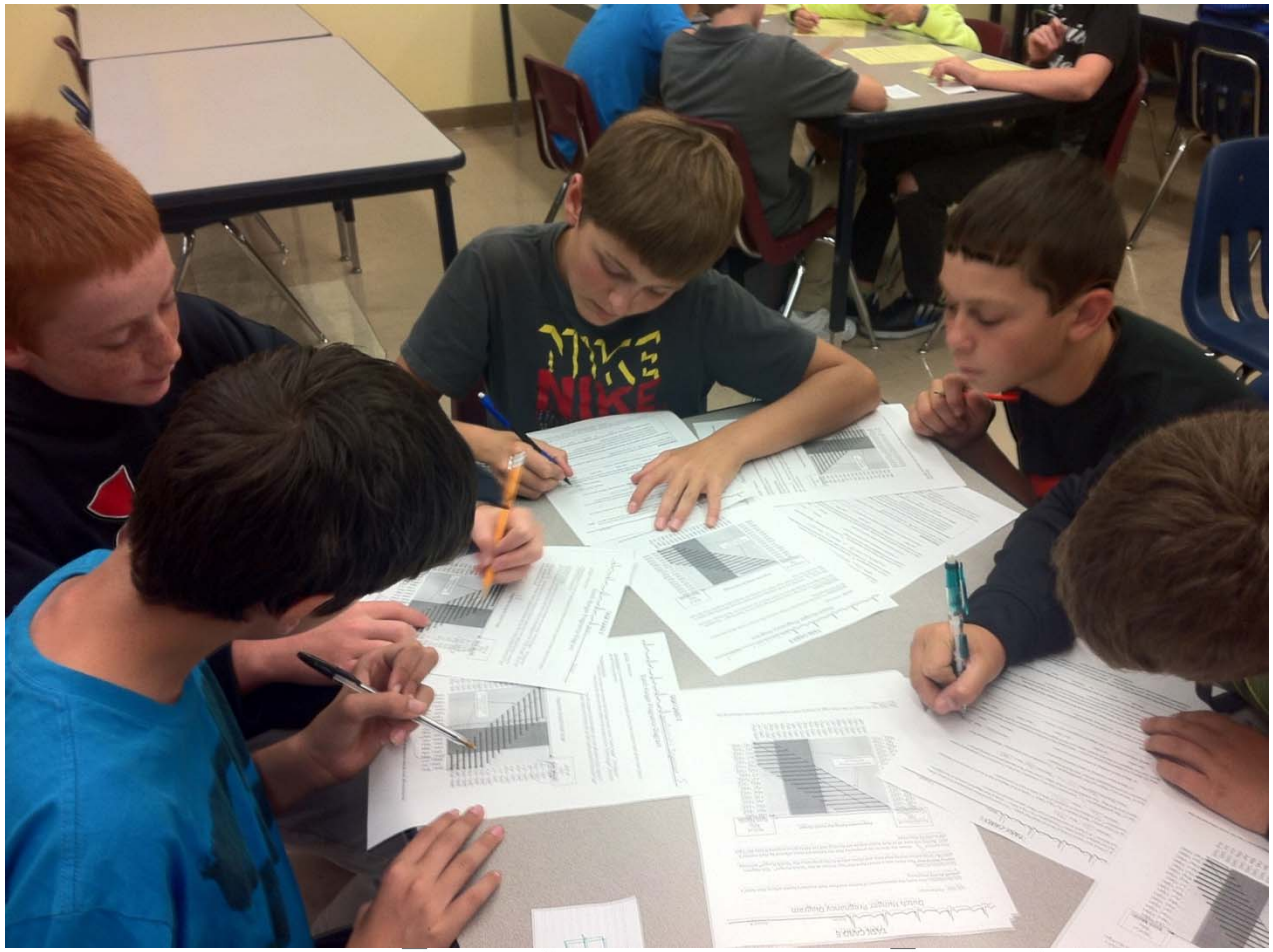
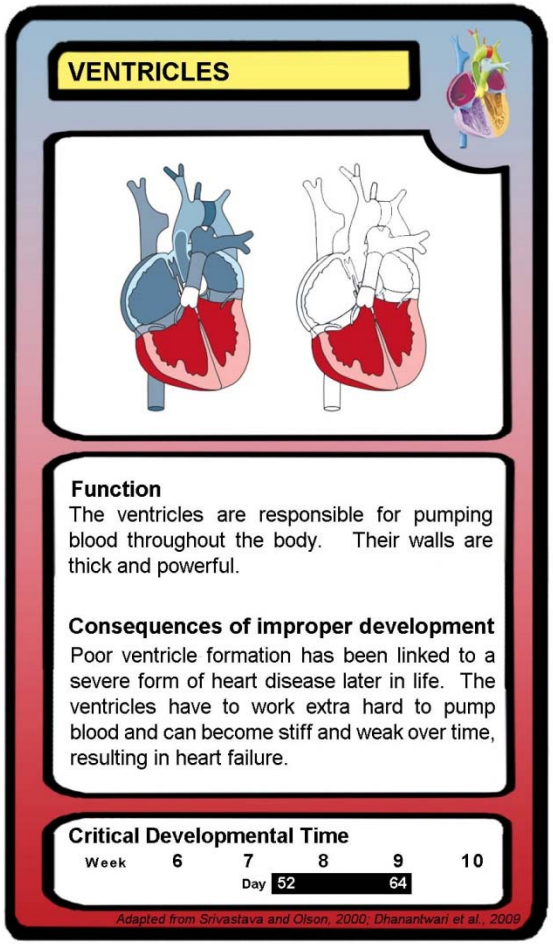
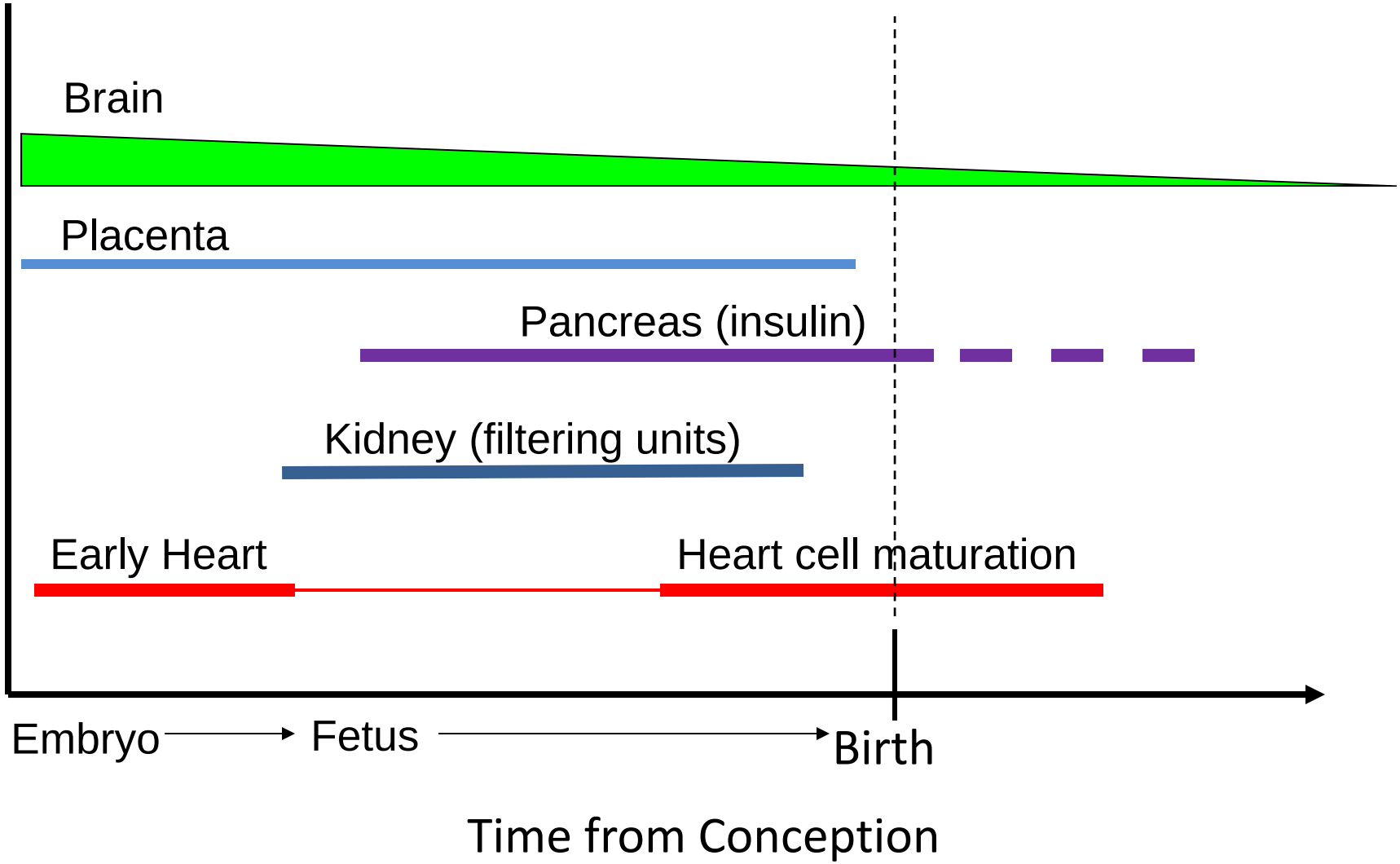
Critical Periods: The Heart





Charbonneau, A., Moss, G.B., and L.K. Marriott (2015). The surprising patterns of health and disease. *Science Scope, 3*, 64-70

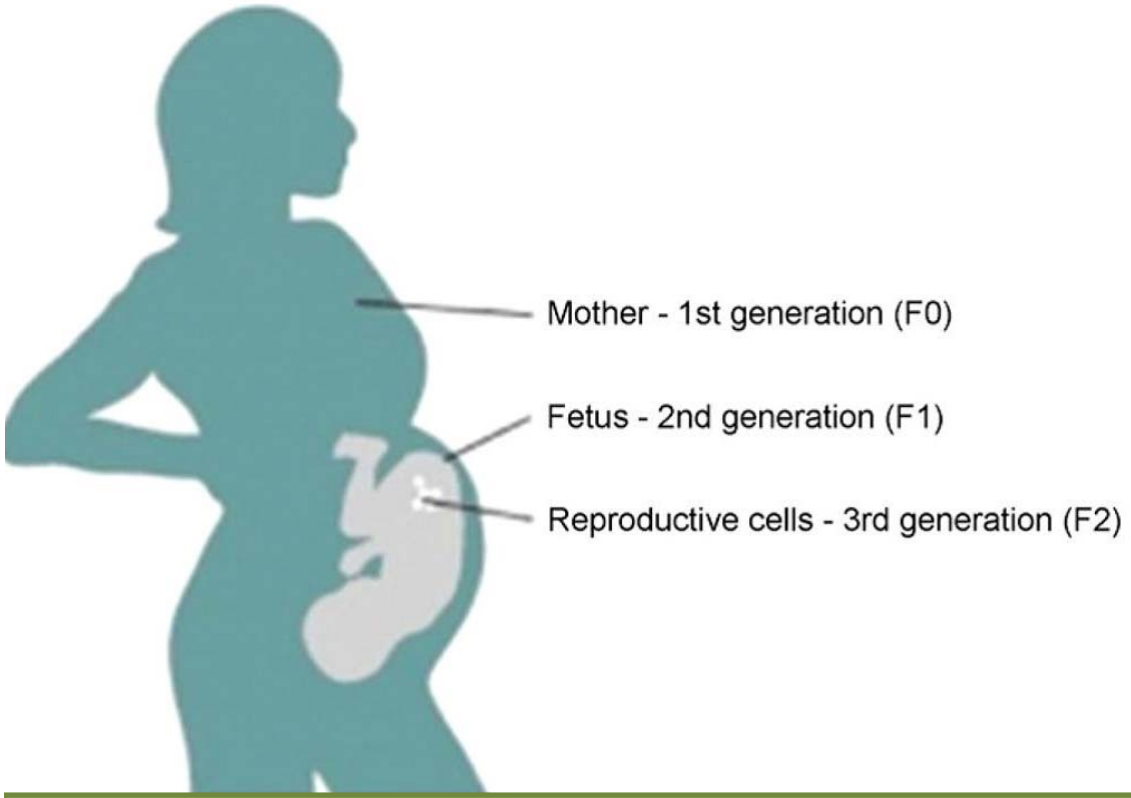
Critical Periods for Organ Development



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

Lumey, L.H. and F.W.A. van Poppel (2013). The Dutch Famine of 1944-45 as a human laboratory: changes in the early life environment and adult health. In: Early Life Nutrition and Adult Health and Development. Lumey, L.H. and A. Vaiserman, eds. Nova Science Publishers. Pages 59-76

Your New Year's Resolutions in Perspective

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

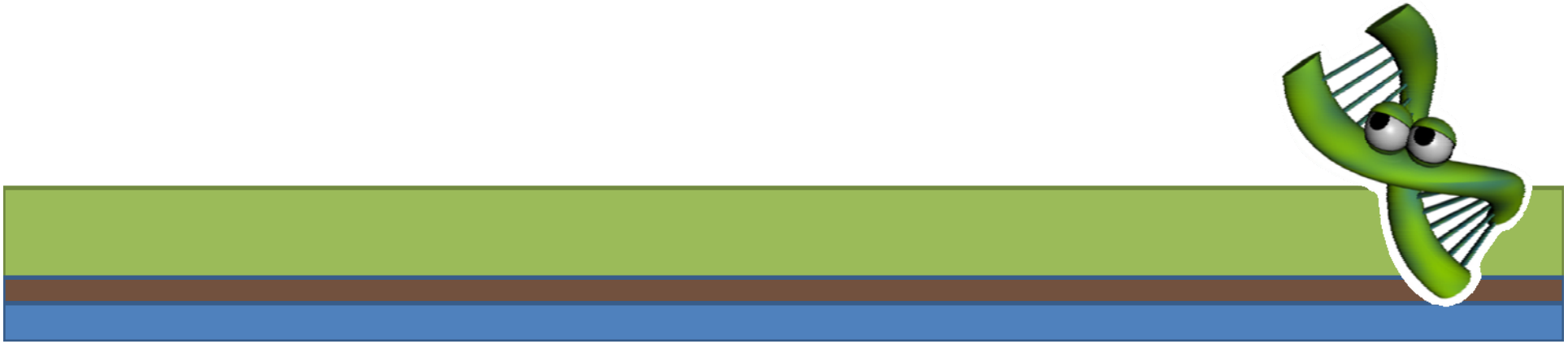
Hepburn "suffered from asthma, jaundice and other illnesses caused by malnutrition, including acute anemia and a serious form of edema"

Dotti, Luca (2015). Audrey at Home: Memories of my mother's kitchen with personal recipes, photographs, and memorabilia.
Smith, G.D. (2012). Epigenetics for the masses: more than Audrey Hepburn and yellow mice? Int. J. Epidemiology, 41(4), 303-8.

Epigenetics is a way to change the ‘volume’ of gene expression

Genetic versus Epigenetic Changes

	A Genetic Mutation	An Epigenetic Change
From this	ATCGGGATTCACG	ATCGGGATTCACG
To this	ATAGGGATTCACG	AT*CGGGATTCACG



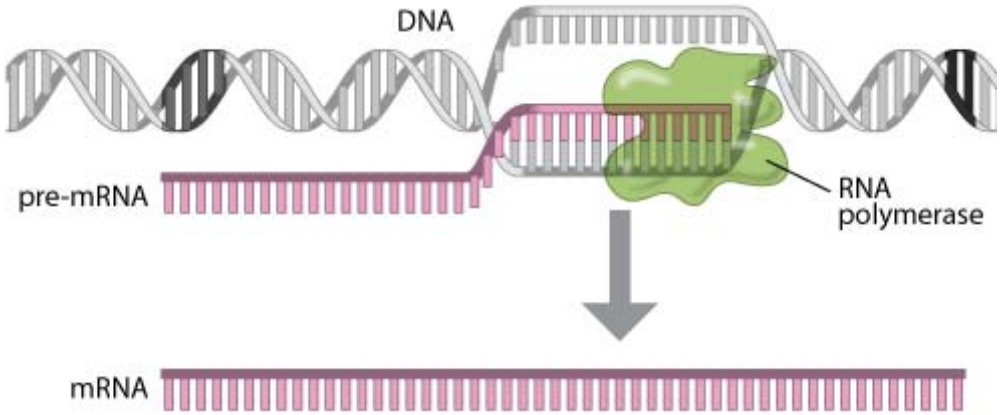
Gene Expression 101: DNA to protein

DNA

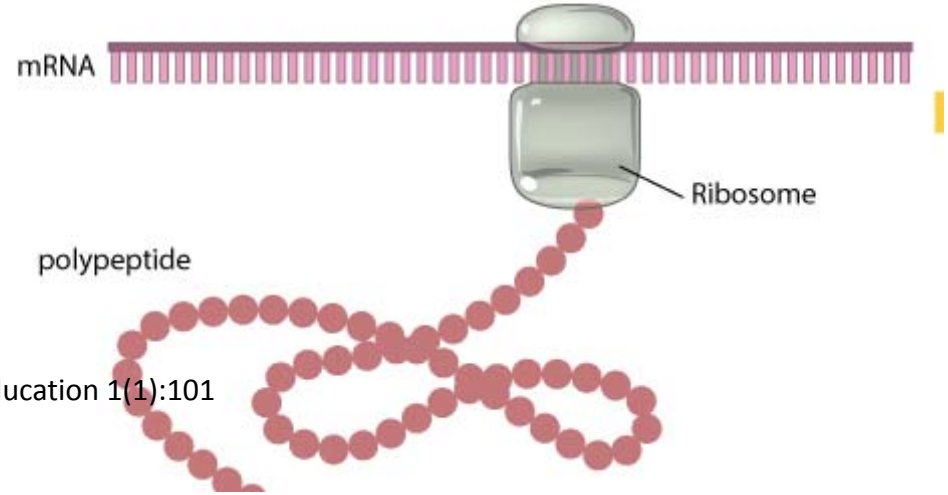
RNA

Protein

1. Transcription=DNA to RNA



2. Translation=RNA to protein

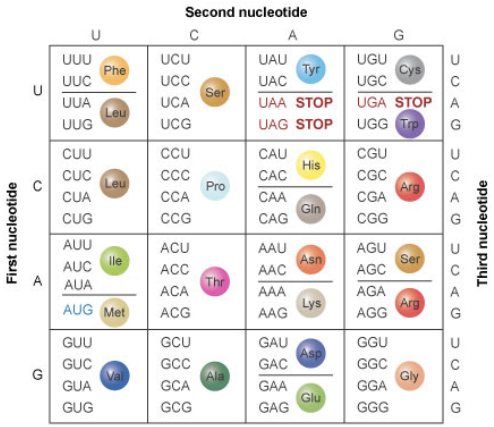


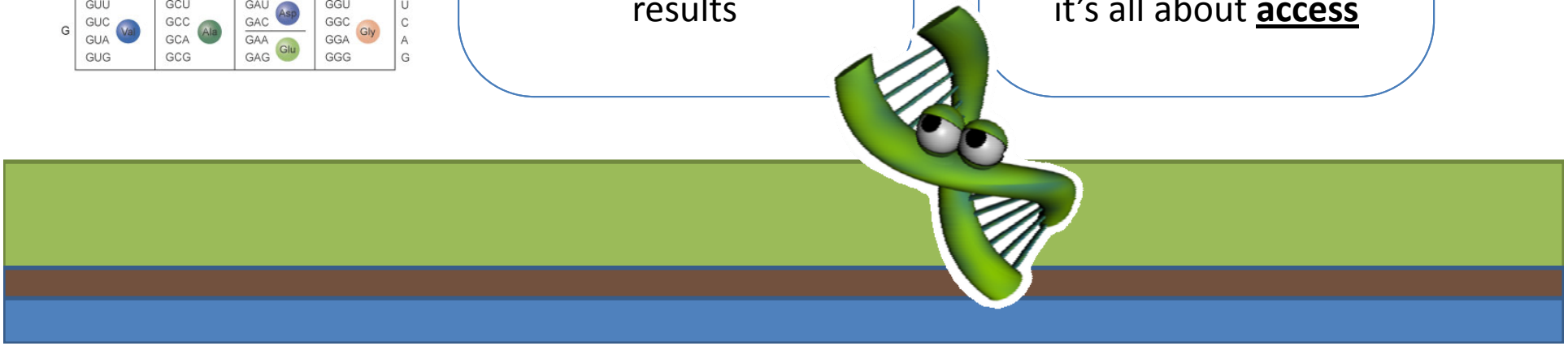
Clancy & Brown (2008) Translation: DNA to mRNA to Protein. Nature Education 1(1):101

Getting up to speed: http://learn.genetics.utah.edu/

Genetic versus Epigenetic Changes

	A Genetic Mutation	An Epigenetic Change
From this	ATCGGGATTCACG	ATCGGGATTCACG
To this	ATAGGGATTCACG	AT*CGGGATTCACG
	If a different amino acid is coded, a different protein results	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

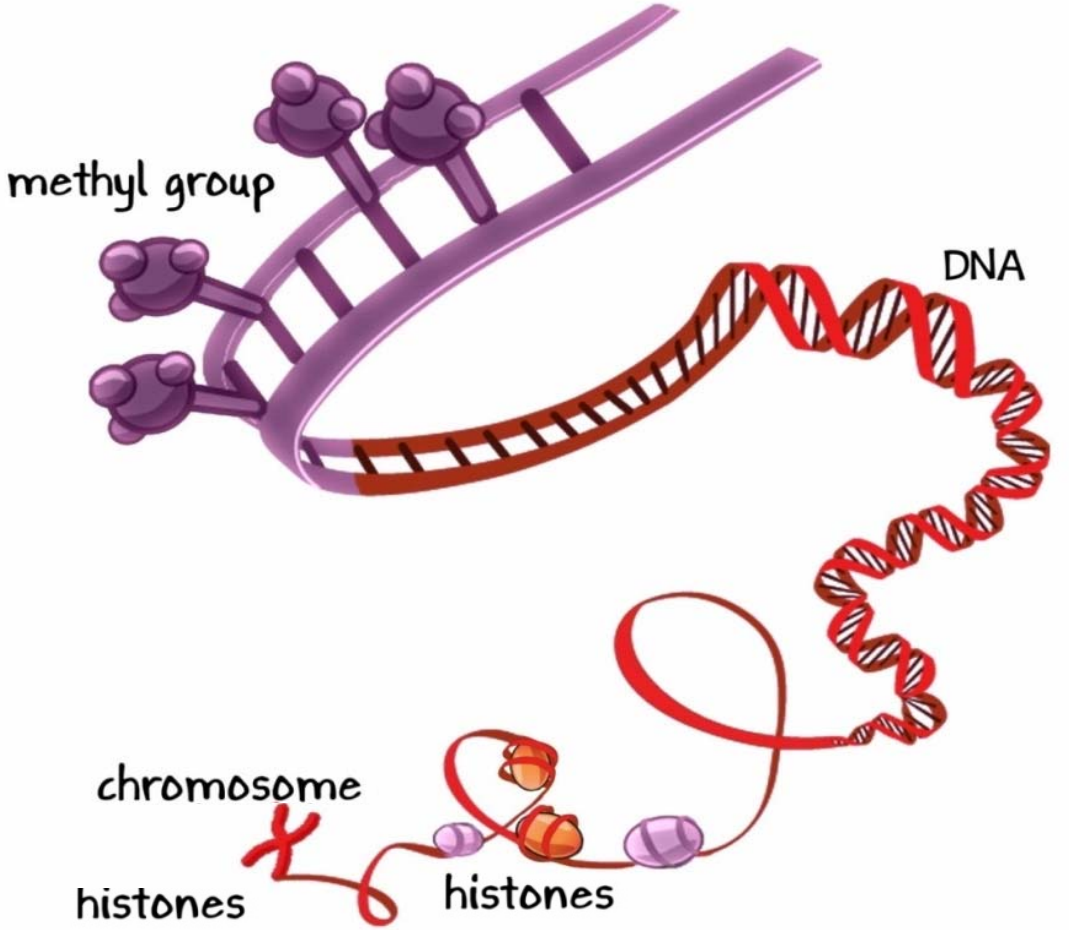
Ways to increase gene expression

methylate
(methyl groups make it harder to access the DNA; DNA transcription is reduced)

demethylate
(no methyl groups allow for easier access to the DNA; DNA transciption is increased)

deacetylate
(DNA is tightly wound around histones, making it harder to access the DNA; DNA transcription is reduced)

acetylate
(acetyl groups loosen the DNA from histones, making it easier f chromosome DNA transcription is increased)



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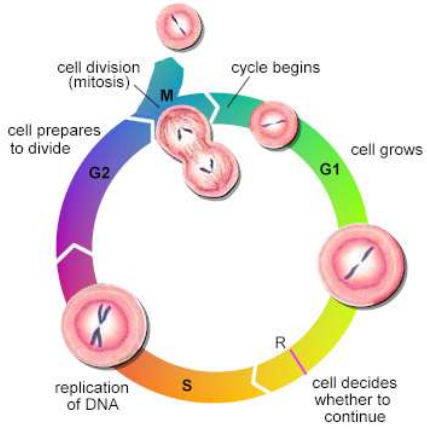
“Is reducing gene expression good or bad?”

The valence depends on context

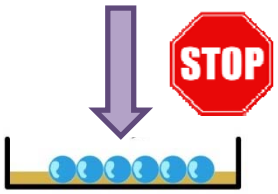
“Good”

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

“Depends”



Normal Cell Growth
(skin cells, scab formation)



p53 (tumor suppressor gene)

Abnormal Cell Growth
(cancer)

“Bad”

Epigenetics and Behavior

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

ATCGGGATTCACG
ATCGGGATTCACG

Foragers
Collect pollen, nectar and
water for the colony.

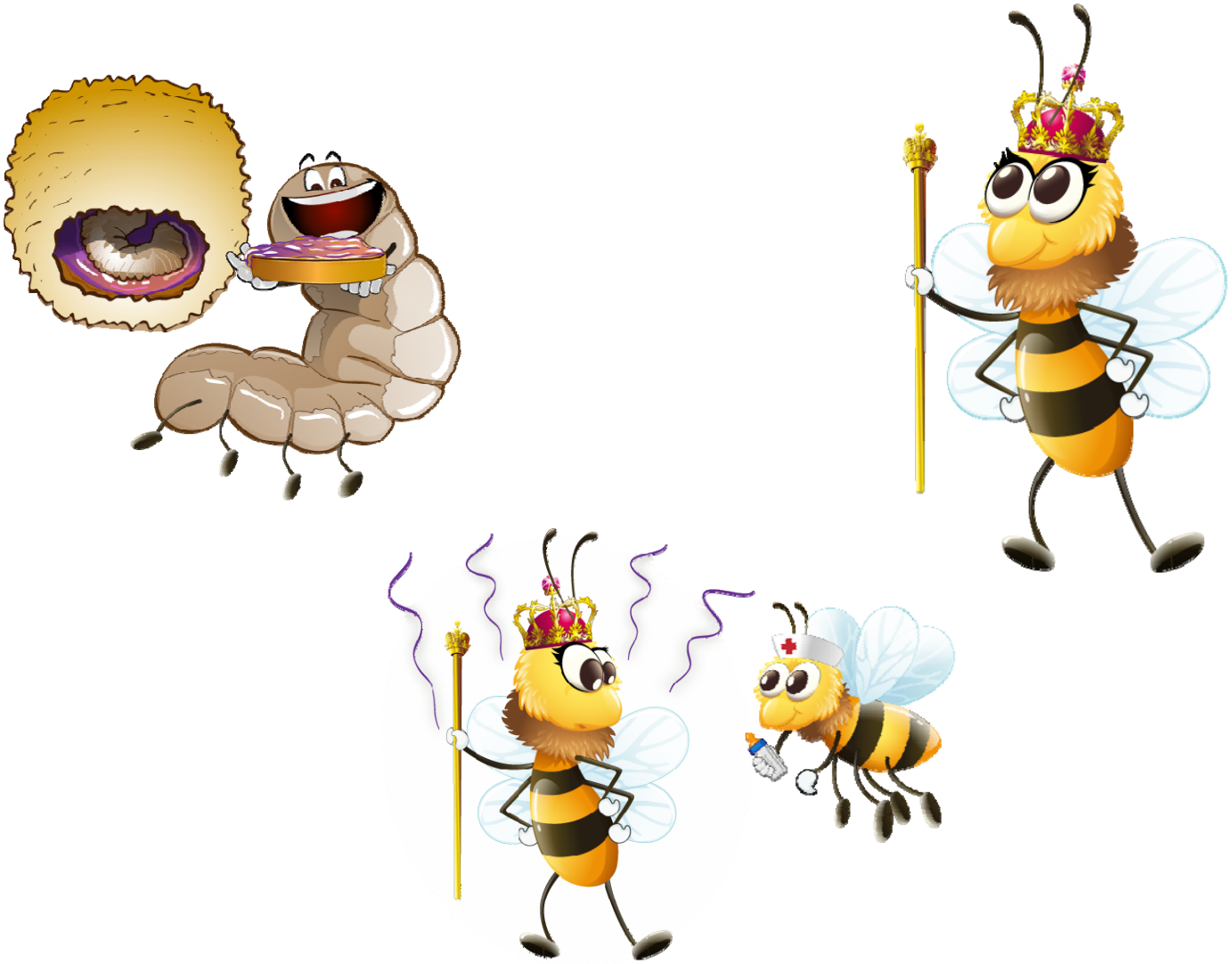
Role in the hive:

ATCGGGATTCACG
ATCGGGATTCACG

Birth 2-3 weeks

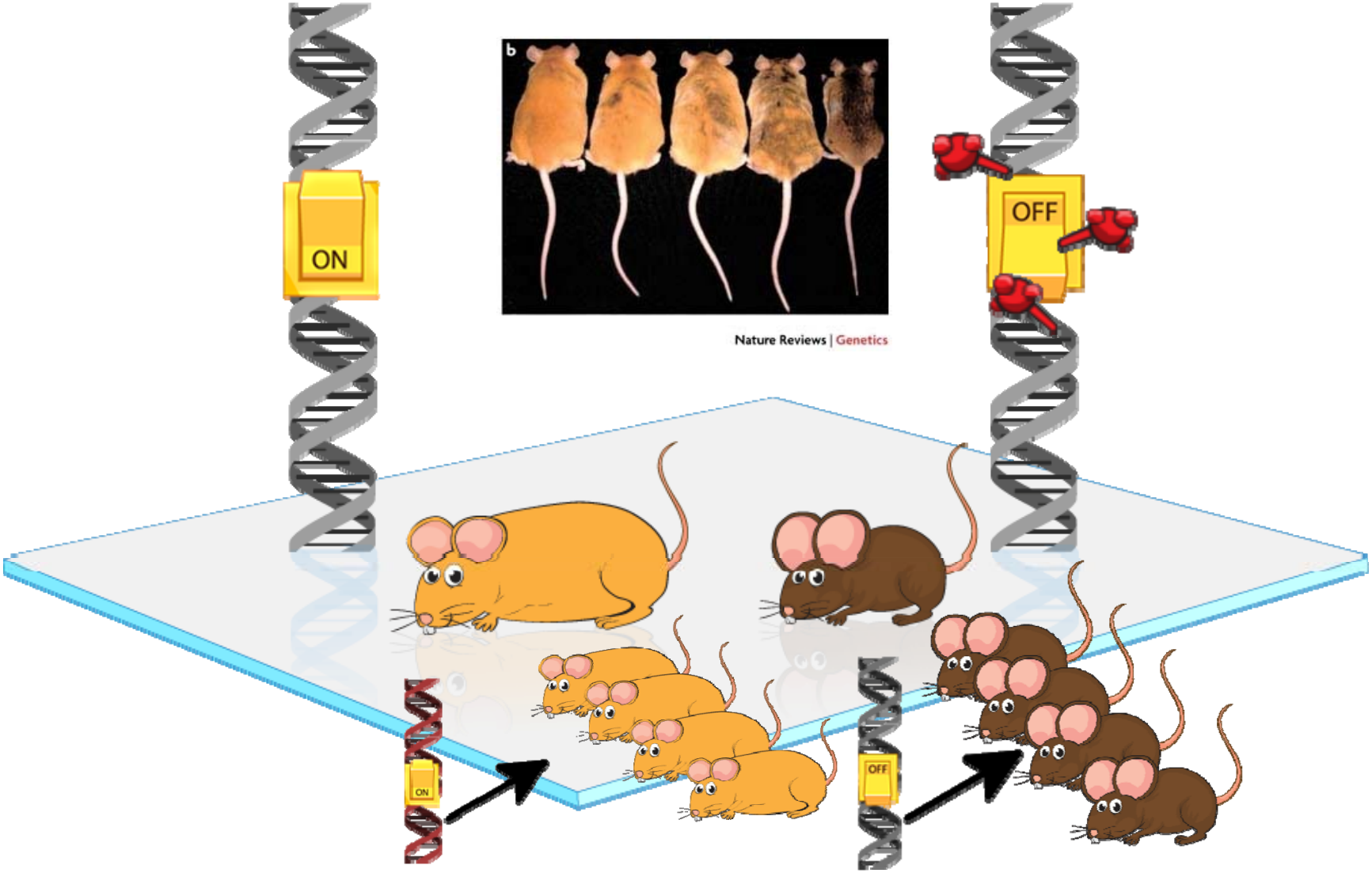
Science from Herb et al.(2012). Nature Neuroscience, 15,1371-1373. Graphics from Let's Get Healthy! "Nurture Your Nature"

Epigenetics and Diet



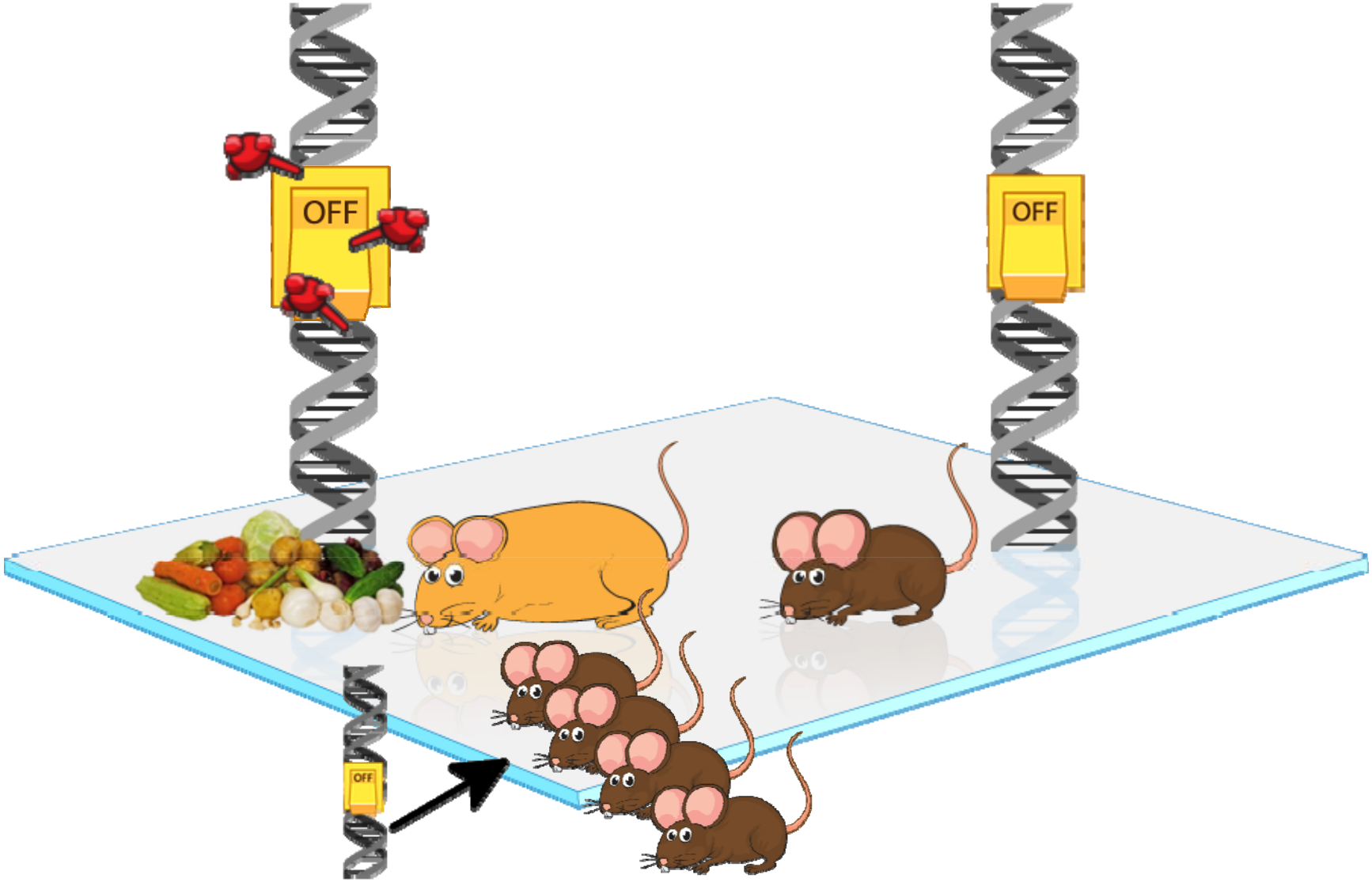
Science from Herb et al.(2012). Nature Neuroscience, 15,1371-1373. Graphics from Let's Get Healthy! "Nurture Your Nature"

Agouti Epigenetics and Diet



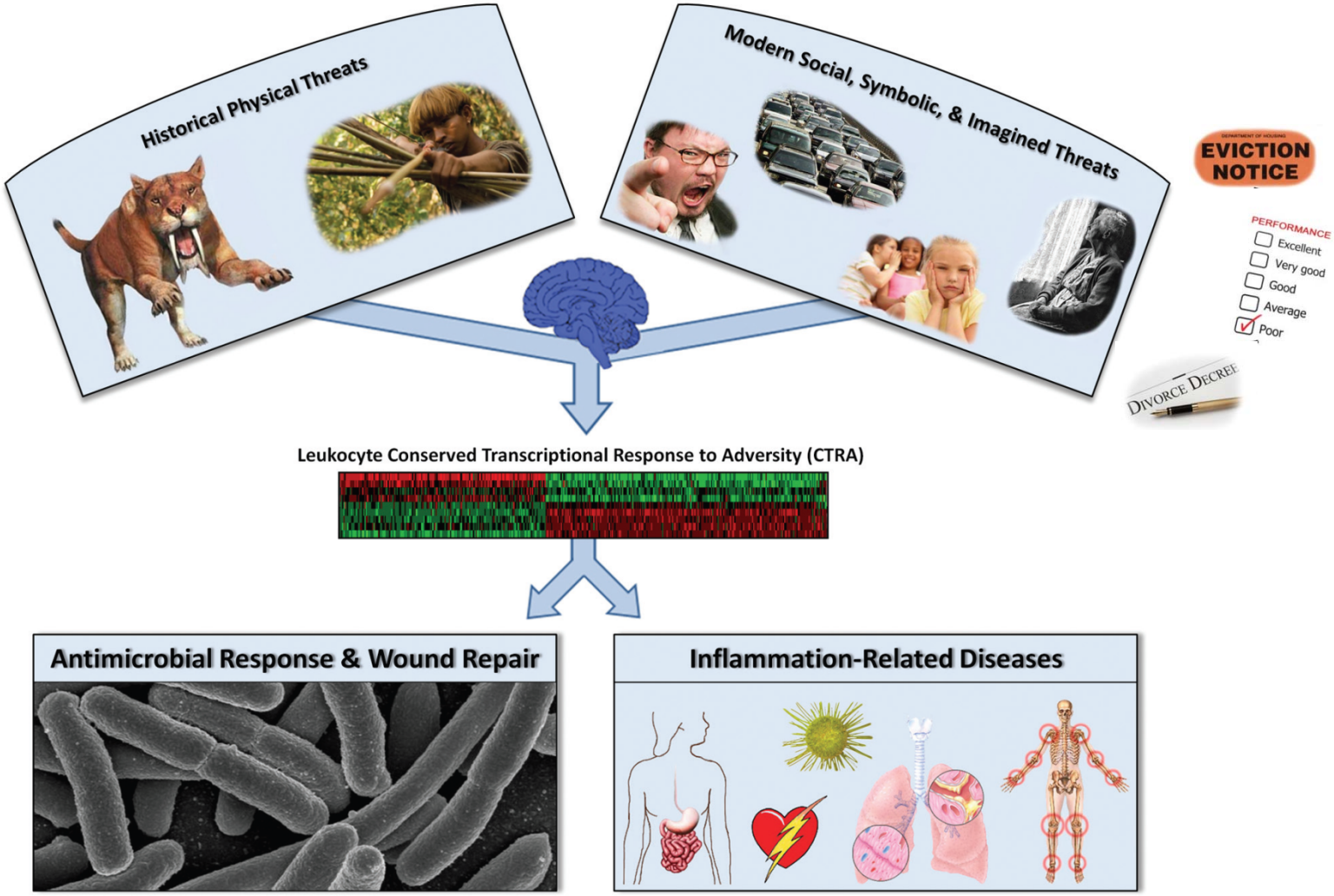
Science from Dolinoy (2008), Nutr Rev; Wolff et al. (1998), FASEBJ. Graphics from Let's Get Healthy! "Nurture Your Nature"

Agouti Epigenetics and Diet



Science from Dolinoy (2008) , Nutr Rev. ; Wolff et al. (1998), FASEBJ. Graphics from Let's Get Healthy! "Nurture Your Nature"

Social Interactions

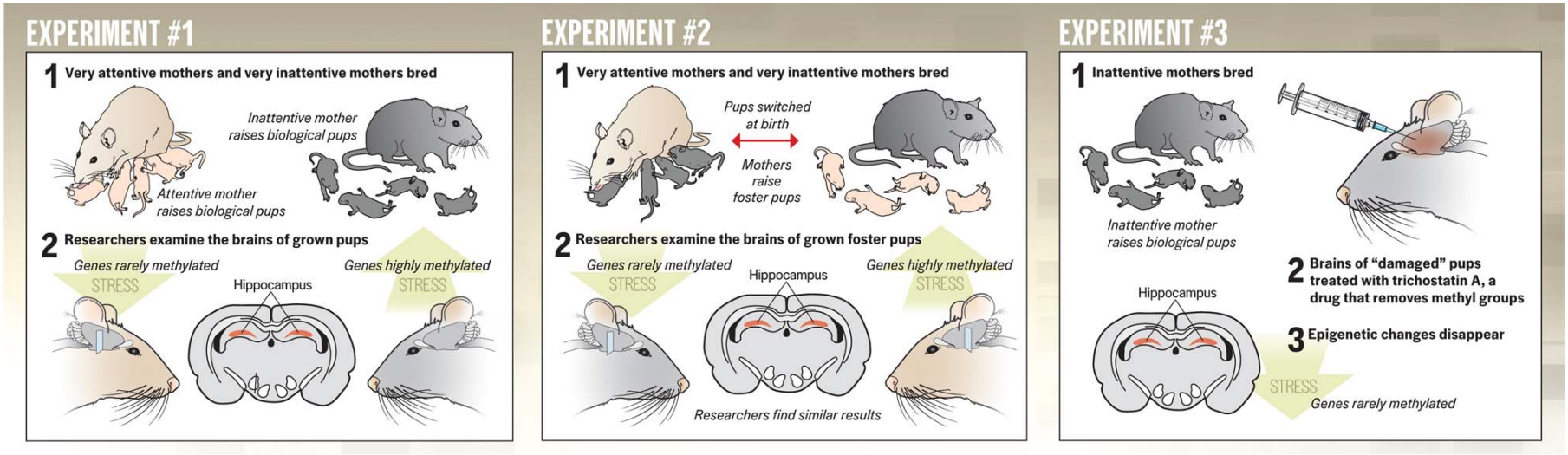


Slavich & Cole, 2013. The emerging field of human social genomics. Clinical Psychological Science, 1(3), 331-348. Thanks Sheldon!
Stankiewicz et al., (2013) Epigenetics of stress adaptations in the brain. Brain Research Bulletin, 98, 76-92.

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…

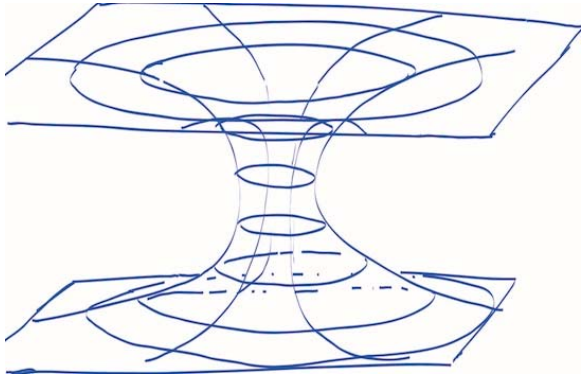


Hurley (2013). Grandma's experiences leave a mark on your genes. Discover, May issue. (History of how they discovered it and image above)
Gudsnuk and Champagne (2012). Epigenetic influence of stress and the social environment. ILAR Journal, 53, 3-4 (detailed science)

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



Rozek LS, Dolinoy DC, Sartor MA, Omenn GS. (2014). Epigenetics: relevance and implications for public health. Annu Rev Public Health. 35, 105-22.

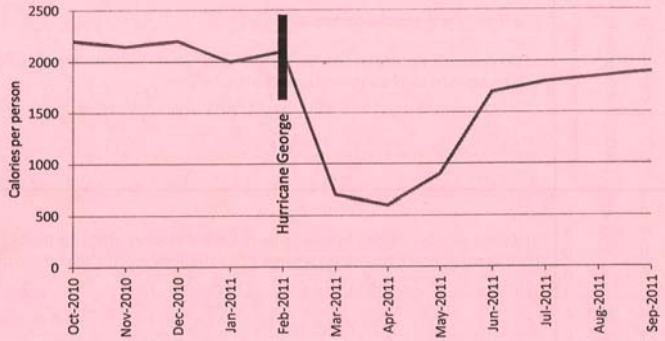
From Students' Perspectives

Name: Group #

Hurricane George and Costa Blanca

Hurricane George strikes the (fictional) island of Costa Blanca in early February of 2011. The typical food supply was mostly wiped out and, due to its remoteness and debris in surrounding waters, it takes a few months for relief supplies to restore the food supply for the residents. Here is a graph of the number of calories per person per day consumed over that period of time.

Calorie Intake 2010-2011



1. Use what you have learned to explain what we might expect 50 years after Hurricane George and the resulting famine in Costa Blanca . Who might you expect to show heart disease in later life?

The mothers that were pregnant during Hurricane George had little access to food and water. These kids will likely have heart disease. do to little calorie intake.

2. Explain how environmental stressors experienced by a person in the womb could cause a health effect in an adult?

An environmental stressor can cause shortages in food, water and shelter. The babies organs will not grow like it normaly would and can cause health issues later in life.

3. What other natural or human-made events might impact the health of a population?

- tornadoes - pollution - earthquake
- temperature rises/lowers - government shutdown
- Tidal wave - prices of food skyrocket -

Name: Caleb Habel Group # Period 2

Bees and Berries

A group of students noticed bees around new berry plants growing in their school garden. They decide to study whether bees may be pollinating the flowers on berry plant. They count ten plants in the school's garden. Each week, starting in March, they recorded the number of flowers in bloom on the plants, the number of bees visiting the plants, and the number of ripe fruit on the plants. Of course, at first there was no ripe fruit and later there were no flowers in bloom. Two students continued their work over the summer. Here is a table of their results:

	Week Number	Number of plant flowers	Number of bees present	Number of berries ripe
3/1	1	0	0	0
3/8	2	0	0	0
3/15	3	0	0	0
3/22	4	0	0	0
3/29	5	0	0	0
4/5	6	0	0	0
4/12	7	7	2	0
4/19	8	14	4	0
4/26	9	21	6	0
5/3	10	35	11	0
5/10	11	49	15	0
5/17	12	70	21	0
5/24	13	75	23	0
5/31	14	65	20	0
6/7	15	53	16	2
6/14	16	31	9	7
6/21	17	7	2	15
6/28	18	0	0	29
7/5	19	0	0	45
7/12	20	0	0	36
7/19	21	0	0	19
7/26	22	0	0	12
8/2	23	0	0	7
8/9	24	0	0	4
8/16	25	0	0	0
8/23	26	0	0	0
8/30	27	0	0	0

Use their data to answer the following questions:

1) How many weeks does it take for the fruit of this plant to go from flower to ripe fruit? Explain how you used the data to estimate this.

9 weeks, I used the Graph by going from when it started flowering to when it started producing berries.

2) If warm weather triggers bees to come earlier but does not affect the flowering of the plant as much, how might climate change affect the berry production of these plants?

If it is really cold and the bees don't come the plant might not survive.

3) Bees are responsible for pollinating 15-30% of all food that United States consumers eat (Roach, 2004). Their numbers have dropped by half in the last 60 years. If their numbers continue to decline, what would you expect to happen to the United States food supply?

We will have less food and food will decline like bees.

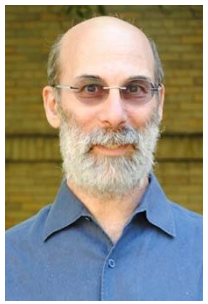
4) For a family who got *all* of their food from bee-pollinated crops, how might a large decline in bees affect their family's health now and in 50 years?

The family might be starving and some of the people generations to come might get heart disease.

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



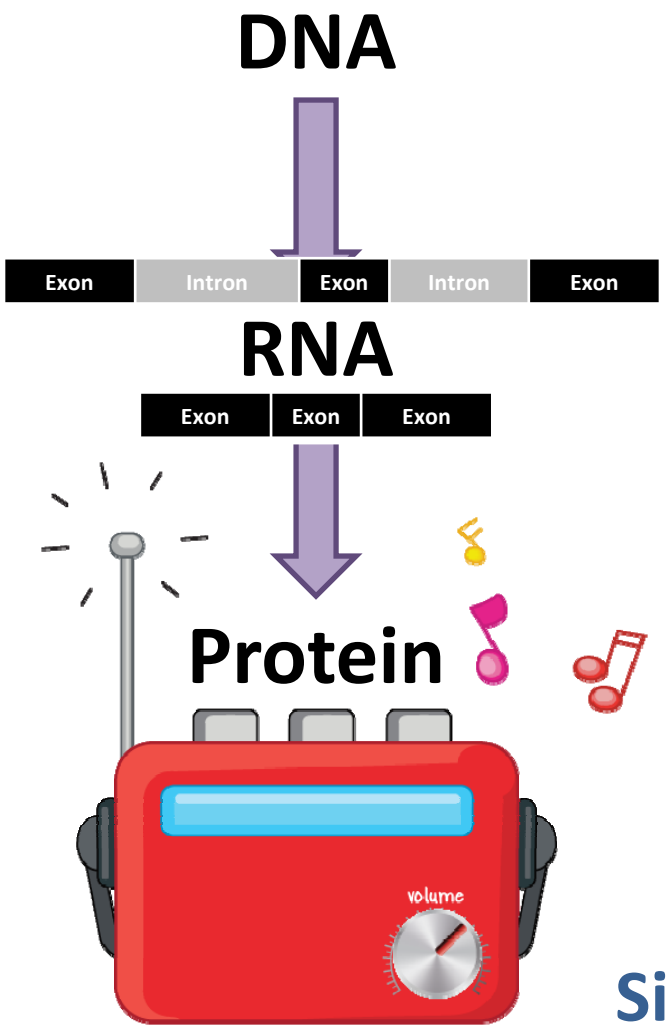
Mitch Turker, PhD JD (OHSU)
Epigenetics Researcher

Lisa Weasel, PhD (PSU)
Ethics and Education Researcher, ICESS

Cathy Klein, PhD (NYU)
Epigenetics Researcher with focus on environmental exposures

Molly Malone (U Utah)
Teacher and Curriculum Developer, Genetic Science Learning Center

Don’t Get Bogged Down in the Details



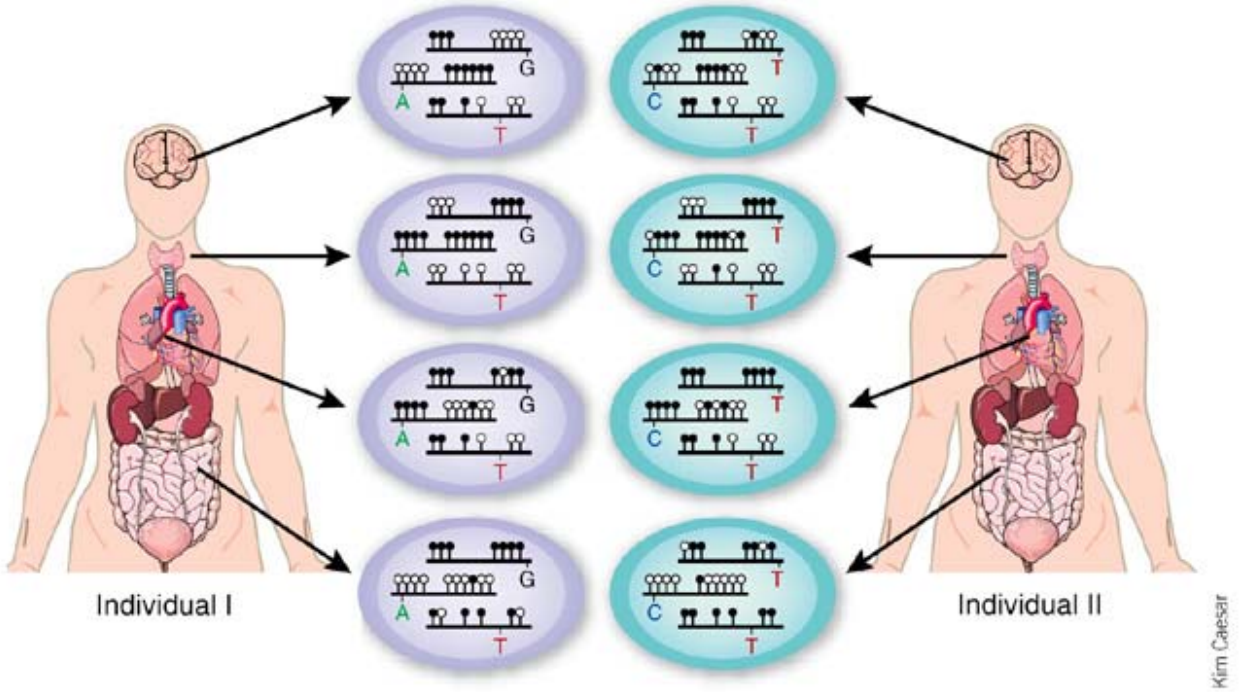
Your job is not to teach the public the mechanisms, it’s to teach them the **concept**

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

1988

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

Marriott, L.K., Charbonneau, A., Moss, G.B., Shannon, J., Thornburg, K.L., and M.S. Turker (2015). "Epigenetics: A new science for middle school – and why you should teach it. *Science Scope*, in review.

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

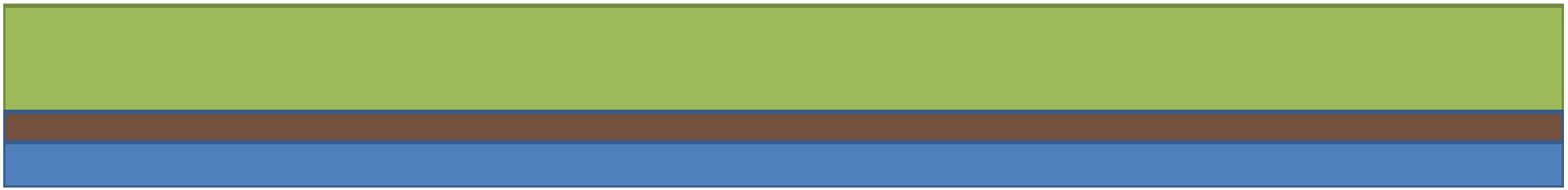
Scientists' and Teachers' Agreed upon Learning Goals for Teaching Epigenetics

1) Students will be able to **recognize the term**

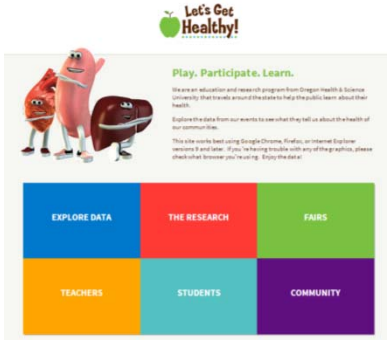
2) Students will understand that epigenetics can **modify health outcomes** in both directions – "good" and "bad"

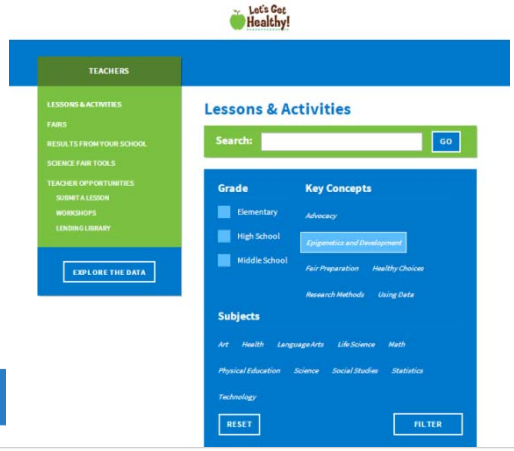
3) Students will understand that the **process of science** (epigenetics) is more applicable than learning the specific mechanisms.

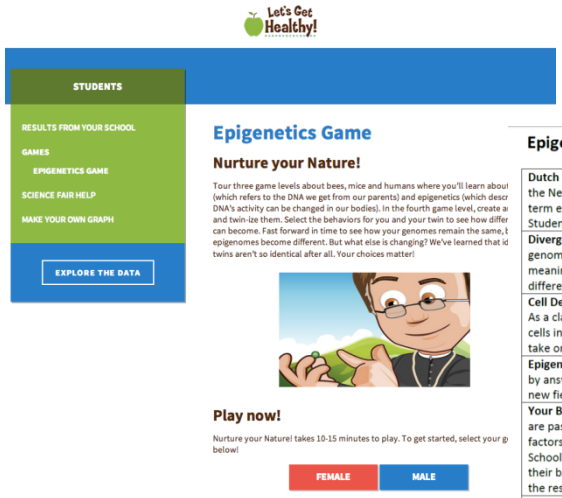
Resources to help you….



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







Epigenetics and Cell Development Lessons

Dutch Hunger Winter (45-55 min) – The Dutch Hunger Winter is a famine that took place in the Netherlands at the end of World War II. Students learn about the immediate and long-term effects of the famine. Students will read and create an epigenetic pedigree chart. Students will learn how healthy and unhealthy choices can affect the epigenome.	Sci SSt ELA Hlth	MS HS
Diverging Twins (45 min) – Introduce students to epigenetics and how an individual's genome responds to his or her environment. Identical twins are genetic carbon copies, meaning their DNA sequencing is the same. Yet physically they become increasingly different over time. Why is this so?	Sci Hlth	MS HS
Cell Development Pathways (30 min) – Introduce how epigenetics leads to specialized cells. As a class, students role-play as individual developing cells in an embryo to understand how cells in a human body have the same DNA, yet through epigenetics become specialized and take on a unique profile.	Sci Hlth	MS
Epigenetics IQ (15 min) – Students test their knowledge and understanding of epigenetics by answering 18 true and false questions. All answers are true, prompting discussion of this new field of science.	Sci Hlth	MS HS
Your Baby's Genome, Epigenome and More (2-3 class periods) – Students learn how genes are passed down from parents to child; how genes determine traits, and how environmental factors affect the expression of the genome. This lesson begins with the Desert Vista High School Genotype to Phenotype Simulation Booklet and, once the students have selected their baby's genome, they will add a layer of epigenetics onto their baby's DNA and draw the resulting adult. Includes ELA extension activities.	Sci ELA	MS
Trans-generational Nutrition (1 or 2 class periods) – Did you know that what you're eating not only affects your kids, but your grandkids? Students play a modified game of go-fish to learn how our history affects our future. Students conduct interviews of their family members to begin investigating the effects of nutrition within their own family and write a letter to their future children to reflect on their lifestyle choices today.	Sci Hlth SSt ELA	MS

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.

Description	Download as
About Epigenetics! One page description about what it is, why it matters and how it works	.docx .pdf
Timeline — From Genetics to Epigenetics DNA has come a long way over the millenia. Check out this quick time-travelling tour of DNA through history	.doc .pdf
Nutrition and your Epigenome One page flyer about how our diets can affect our epigenomes; diet content by Univ. of Utah's Genetic Science Learning Center	.docx .pdf
Epigenetics Flip Board Create your own question and answer flip board using this easy template!	.pptx .pdf
Ideas for Epigenetic Manipulatives Here are some of the ways we explain epigenetics at our fairs. Feel free to adapt these ideas to create your own manipulatives!	.docx .pdf
Epigenetics Glossary of Terms Brief glossary of terms created by Oregon teachers to help explain epigenetics to students	.docx .pdf
Briefing Sheet for Students One page epigenetics briefing sheet for students created by Oregon teachers	.docx .pdf
Briefing Sheet for Parents One page briefing sheet for parents whose students are learning about epigentics; created by Oregon teachers	.docx .pdf
Briefing Sheet for Teachers Created by Oregon teachers, this background information is great for teachers who are new to epigenetics	.docx .pdf
Briefing Sheet for Principals At a glance information for principals whose teachers are discussing epigenetics in the classroom	.docx .pdf
Online Resources for Epigenetics Resources for teachers discussing epigenetics in the classroom; compiled by Oregon teachers	.docx .pdf

http://www.letsgethealthy.org

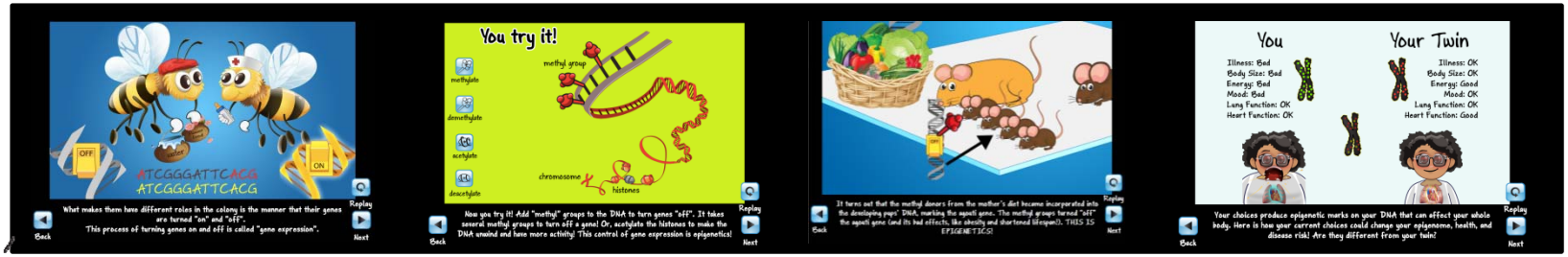
DOHAD Lesson: Password is NSTA

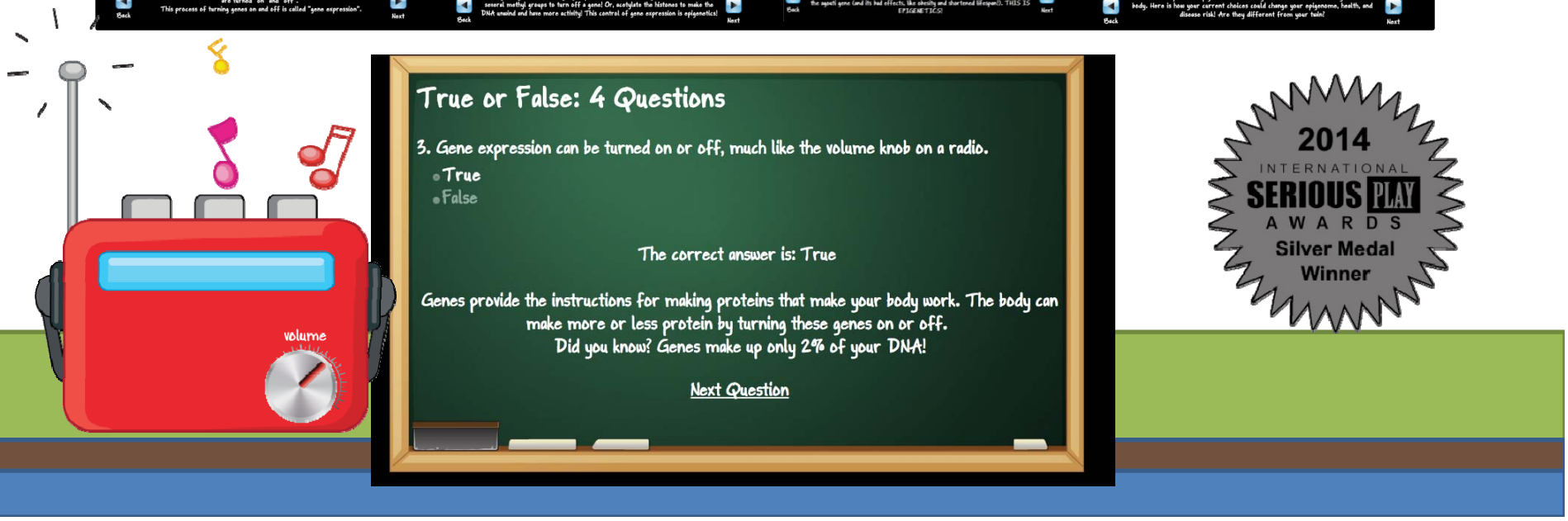
http://www.letsgethealthy.org/about-the-research/station-descriptions/epigenetics/

Epigenetics Game

Level 1 | Level 2 | Level 3 | Level 4

Pre-game questions → Post-game questions

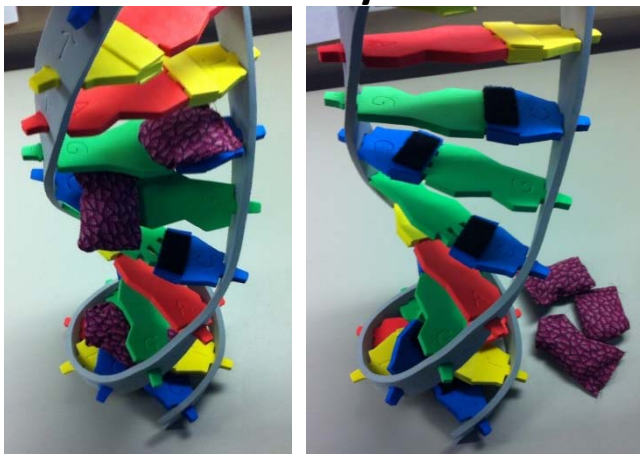




2014 INTERNATIONAL SERIOUS PLAY AWARDS
Silver Medal Winner

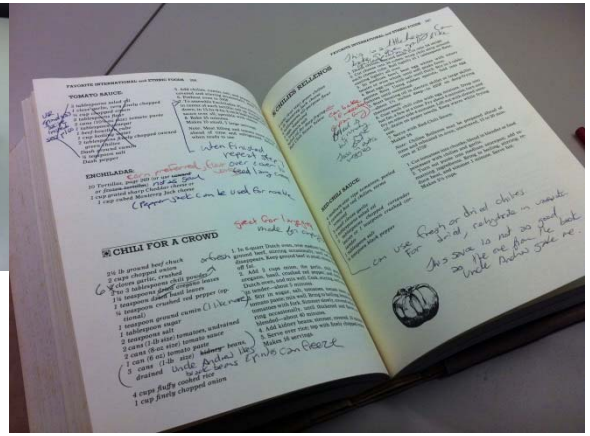
Additional Manipulatives

DNA methylation

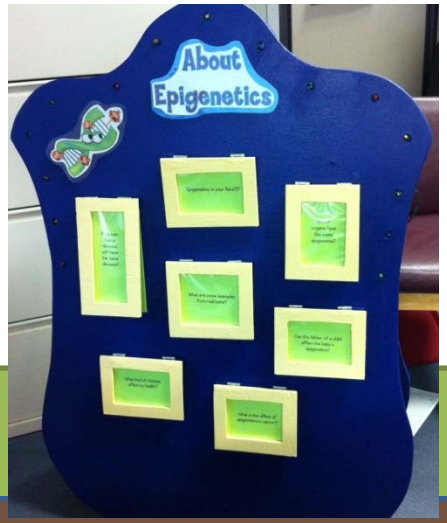


Analogy to your grandmother's cookbook

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

- Dobbs, D. (2013). The Social Life of Genes. Pacific Standard, September 3, 2013. Retrieve from: http://www.psmag.com/books-and-culture/the-social-life-of-genes-64616

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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)

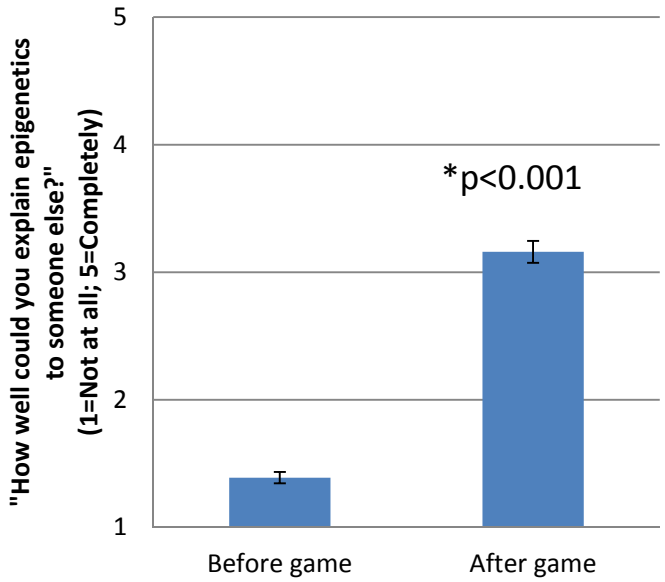
Game Development

- 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 ($p=0.44$).

Ongoing Results (n=1000)