Epigenetics

Understanding Non-genetic Inheritance

Non-genetic Inheritance

Over the past decade it has become increasingly clear that environmental factors, such as diet or stress, can have biological consequences that are transmitted to offspring without a single change to gene sequences taking place.

What is the Epigenome?

The epigenome is a multitude of chemical compounds that can tell the genome (DNA) what to do. These compounds are able to attach to the DNA and turn genes on and off. These changes may be short-lived or they may “mark” the DNA in such a way as to be inherited with the gene.

What Does The Epigenome Do?

The epigenome is part of the system that creates genetic specialization by telling DNA to build some proteins rather than others. This has the potential to dramatically change the gene and its effect on the body or behavior.

Which Chemical Compounds?

Many chemical compounds can indirectly alter DNA. Chemicals containing methyl groups can directly affect gene activity. Nicotine is one of the most potent.

Basic Genetics

Three Types of Genetics

- Mendelian Genetics
- Molecular Genetics
- Mitochondrial Genetics

Charles Darwin

Developed the concept of Natural Selection
Delayed publication for 35 years because he knew it would create controversy
Also established the universality of emotions

Gregor Mendel

Experimented with plants to show that traits could “skip a generation” implying that some type of information was being passed from generation to generation.
- Genes were unknown at this time

Mendel’s Peas

Data implied inheritance of information somehow hidden in the individual

Darwin’s Natural Selection

- Traits that promote for survival remain and reproduce
- Traits that lead to death are removed
- However, traits that do not develop until after the age of reproduction will remain even if those traits cause fatal disease

Mathematical models show that investing resources in the building of an organism that would survive longer than its expected survival in the wild would be useless in terms of evolutionary advantage

Natural Selection

Natural selection can occur much more quickly than previously understood
Sometimes natural selection is slow but sometimes it is very fast

What About Behavior?

Tame vs Aggressive

Genetic changes can occur quickly

Domestic Dog

Mechanisms of Heritability

Genes & Gemmules
Darwin, Mendel and others were convinced that some something was being passed through sexual reproduction
Darwin’s term was “gemmales” (Didn’t take)
In 1902 Walter Sutton was investigating chromosomes and realized that Mendel’s factors must be there

21 Wilhelm Johansson
- Danish botanist
- Introduced the terms
type
- gene
- genotype
- phenotype

22 Genotype & Phenotype
- What something looks like
- versus
- the underlying genetic code

23 Mendel’s Peas
- Phenotype and genotype can coincide or differ

24 Chromatin & Chromosomes
- Chromatin is named because it can be stained
- Chromosomes were seen to be made of chromatin

25 Crick & Watson in 1953

26 James Watson Creates the Double Helix

27 The Double Helix
- Chromosomes are made of chromatin
- Chromatin is DNA and proteins called histones
- In 1953, Watson & Crick stated that DNA was a double helix with four nucleotides

28 Base-pairs
- To make long strings of molecule, chemicals have to bond together
- Nucleotides are short beads of chemicals that line up to form the long molecule of DNA
- These line up with other nucleotides and form base-pairs
- All genetic information is stored in complex strings of these paired chemicals

29 What Is The Relationship Between Genes Chromosomes and DNA?

30 DNA, Genes & Chromosomes
- Chromosomes are comprised of long strings of DNA wrapped around histones
- Genes are loops of DNA plus the histones
- Histones can be altered by environmental factors

31 DNA, Genes & Chromosomes
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32 Genes & Junk DNA

33 Alterations to Chromosomes
- Alterations to chromosomes are usually less damaging when compared to alterations at the base-pair level

34 Chromosomal Recombination

35 Gender Determination
- Many genes on the X & Y chromosomes effect our gender development
- One of the most important is the SRY gene that makes testes
- Individuals with the SRY gene will develop testes
- Regardless of their pattern of sex chromosome

36 The Creation of Gender

37 Differences in Gender Determination
- The creation of
- “trans–gendered” individuals

38 Epigenetics

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- The epigenome is a multitude of chemical compounds that can tell the genome (DNA) what to do.
- These compounds are able to attach to the DNA and turn genes on and off.
- These changes may be short-lived or they may “mark” the DNA in such a way as to be inherited with the gene.

Which Chemical Compounds?
- Many chemical compounds can indirectly alter DNA.
- Chemicals containing methyl groups can directly affect gene activity.
- Nicotine is one of the most potent.

C H Waddington
- Created the term epigenetics.
- Stated that the social world and the chemical world are interconnected through epigenetic effects on DNA.

Methyl Groups
- Methyl is an alkaloid derived from methane; a hydrocarbon related to methane.

Methylation
- All cells contain a full copy of DNA with data on every type of cell.
- Cells must differentiate into blood cells, bone cells, brain cells.
- DNA requires “something extra” to tell it to form specific types of cells.
- To get a brain cell, DNA for bone and muscle must be turned off while brain cell DNA is turned on.
- Molecules containing methyl trigger these changes.

Fetal Development
- Historically, methyl alteration of DNA was thought to occur only in fetal development.
- This process changes stem cells into differentiated body cells.

Methyl Groups
- Methyl groups are now known to alter genes throughout the lifespan.
- As identical twins age they become different as epigenetic changes alter their gene expression.

Post-natal Inheritance
- Without any mutation to the DNA the methyl groups can cause long-term heritable changes in gene function.

Genetic Assimilation
- Described by Waddington as a Darwinian mechanism that allows certain acquired characteristics to become heritable.
- This includes behavior and would allow an animal’s response to environmental stress to become a fixed part of its developmental repertoire and inherited by offspring.

Genetic Differences in Identical Twins
- Your genes change with time.
- Even the genes of identical twins will diverge across time.
- As they age, twins grow more genetically distinct.
- Epigenetics is the study of environmental impact on genes.

Gene Expression Across Time
- Epigenetic tags alter the expression of genes even though the genome of the twins is identical.

Genes Change Across Time
- Epigenetic tags alter the expression of genes.
- Various environmental factors influence this process.

Epigenetic Changes

Epigenetic Tags

Silencing A Gene

Silent Gene
60 Genes Turn On & Off
61 Medications Can Alter Tags
   ● Alcohol
   ● Nicotine
   ● Depakote
62 Food Can Alter Tags
63
64 Inherited Dietary Effects
65 Inheritance of Experience
66 Epigenetic Issues In Cloning
   ● The kitten Carbon Copy is the first cloned cat
   ● Carbon Copy does not look like Mom
   ● Animal fur is affected by several epigenetic factors in utero including maternal diet and climate
67 Environmental Control of Size
   ● Some animals vary in size by where they find themselves
   ● Ants and goldfish will grow to a size to match their environment
68 Goldfish
   ● GABA & somatostatin modify the genes to limit or trigger growth in the common goldfish
69 Queen Bee Mystery
   ● Worker bees and queens are genetically identical
   ● The “Royal Jelly” given to one larvae contains Methyl groups that create tags on the genes creating a large and fertile queen
70 Epigenetics & Mothering
   ● Experiments with rats show that poor mothering prevented glucotroid receptors from being transcribed into the baby’s hippocampus creating another generation of poor mothers
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72
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74 Moshe Szfy
   ● Dr. Szfy is a geneticist at McGill University and a world expert in epigenetics
   ● He has performed experiments showing that parental care can modify the genome
75 Moshe Szfy
76 Mothering & Methylation
77 Epigenetics & Alcoholism
78 Moshe Szfy
   ● “We certainly know that human experiences affect how our genes are expressed”
79 Moshe Szfy
   ● Extreme experiences have more extreme effects
80 Orphanages
81 Generational Changes
   ● Once changed the altered DNA can be inherited like a mutation
   ● The DNA itself is not changed but it’s on-off status may survive conception and effect the next generation
82 Epigenopathy
   ● Disorders such as autism, Rett syndrome, fragile X show decreased methylation on some genes and hyper methylation on others
83 Genetic Determinism?
   ● As information regarding epigenetic factors develops researchers are looking for new interventions to de-methylate DNA and reverse negative epigenetic conditions
   ● Will these drugs also remove beneficial changes as well?
84 Epigenetic Therapy
85 Epigenetic Treatment for Cancer
   ● Many cancers are caused by runaway cells which have been silenced by epigenomic alterations
   ● Altering the epigenome by removing methyl tags may treat this class of cancer
86 Myelodysplastic Syndrome
Now successfully treated with decitabine
Decitabine alters the epigenome by removing methyl tags
Treatment has fewer side effects than either radiation or chemotherapy

Dr. James Fallon
A neuroscientist who studies murderers
Murderers often have deficits in the orbital cortex & temporal lobes
He discovered that his paternal line was full of murderers
His own PET scan shows deficits in the orbital cortex and temporal lobes

James Fallon & Lizzie Borden
Neurobiology of Murder
Epigenetic Changes?
All You Need Is Love ...
Not quite true but it is very clear that a nurturing environment can go a long way to remediating symptoms of many psychiatric disorders
Loving kindness can actually alter gene expression and silence the genes for affective disruption

Summary