Epigenetic Regulation: A Primer

Mackenzie Gavery
University of Washington
School of Aquatic and Fishery Sciences
Outline

- Epigenetics Basics
  - Definitions
  - DNA methylation
    - Functions
    - Epigenetic inheritance
  - Environment
  - Variation between taxa
Epigenetics

- Heritable changes in trait or phenotype, caused by a mechanism other than mutation to the DNA sequence
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All of these cell types contain the same DNA.. so why do they look so different?
**Epigenetics**

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All of these cell types contain the same DNA... so why do they look so different?

- Epigenome provides instructions and regulates the functional aspects of genes.
Epigenetic Marks

- Histone modifications
  - Acetylation
  - Methylation
- DNA methylation

CHROMATIN PACKAGING
Epigenetic Marks

- Non-coding RNAs
  - micro RNA (miRNA)
DNA Methylation

- Most well understood epigenetic mechanism is DNA methylation

- Occurs in most plants and animals

- Most of what is known from mammals & plants, less in invertebrates

- Typically* associated with gene silencing
DNA Methylation

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- Functions
- Epigenetic inheritance
- DNA methylation & the environment
- Patterns: variation between taxa
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DNA methylation

- Functions:
  - Tissue differentiation
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  - Imprinting & x-inactivation
DNA methylation

- Functions:
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  - Development
DNA methylation

- Functions:
  - Tissue differentiation
  - Imprinting & x-inactivation
  - Development
  - Genome stability – transposable element silencing
DNA Methylation

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DNA methylation

- Epigenetic inheritance:
DNA methylation

- Epigenetic inheritance:
  - Mitotic inheritance
  - Transgenerational inheritance
Epigenetic Inheritance

- DNA methyltransferases (DNMTs): family of enzymes which function to methylate DNA
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- Mitotic inheritance by DNMT1
Epigenetic Inheritance

- DNA methyltransferases (DNMTs): family of enzymes which function to methylate DNA
  - Mitotic inheritance by **DNMT1**
  - *de novo* methylation by DNMT3

![Diagram showing DNA replication and methylation processes](image)
Epigenetic Inheritance

- Transgenerational inheritance

- You inherit more from your parents than just DNA.
DNA Methylation

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DNA Methylation

- Many environmental factors have been shown to affect epigenetic marks such as DNA methylation.
Toxins and Nutrition

- Genetically identical female mice
- Different DNA methylation status of the Agouti gene
- Affected by toxins/diet
Temperature

- sex determination in European sea bass is temperature dependent

- High temp early in development = more males

- Mechanism: methylation status of aromatase promoter

(Navarro-Martín et al, 2011)
Stress

- Plants show dynamic DNA methylation changes in response to various abiotic factors
  - Salinity
  - Drought
  - Temperature
  - Frost
Behavior

- Licking/grooming behavior by rat mothers influences the DNA methylation status of the glucocorticoid receptor in juvenile rats.
Aging
Disease

- Virus/host interactions
- Cancer
- Diabetes
- Asthma
DNA methylation & the environment

- What we know:
  - Important functions
  - Affected by environment
  - Can be inherited

- If DNA methylation can be passed on to future generations
  - Could this have negative effects?
  - What about positive effects?
DNA Methylation

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DNA methylation: non-models

- Primarily studied in mammalian systems
- Variation in eukaryotes
  - Density
  - Distribution
  - Context
- Methods - Limited genomic information
  - Many approaches rely on sequence information
  - Molecular pathways may not be clear
DNA methylation: invertebrates

- Only a handful of species have been evaluated
- Model invertebrates lack DNA methylation
- Most: 30 – 60 % methylation
- Primarily in exons
- Important regulatory functions – honey bee
  (e.g. Kucharski et al., 2008; Elango et al., 2009; Lyko et al., 2010)
Summary: DNA Methylation

- Functions
- Epigenetic inheritance
- DNA methylation & the environment
- Patterns: variation between taxa
Thinking about lab..

- How could you measure epigenetic changes for your projects in lab?