

Epigenetic Regulation: A Primer

Lecture 15

Outline

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

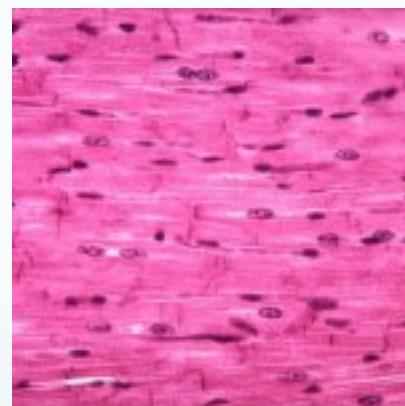
Epigenetics

- Heritable changes in trait or phenotype, caused by a mechanism other than mutation to the DNA sequence

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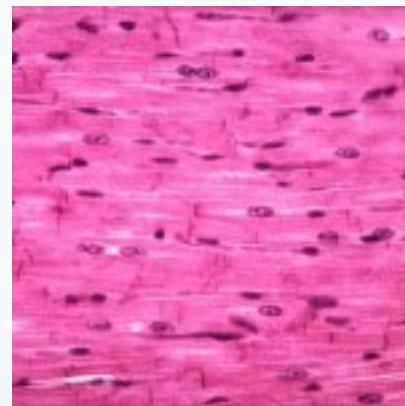
All of these cell types contain the same DNA.. so why do they look so different?



Epigenetics

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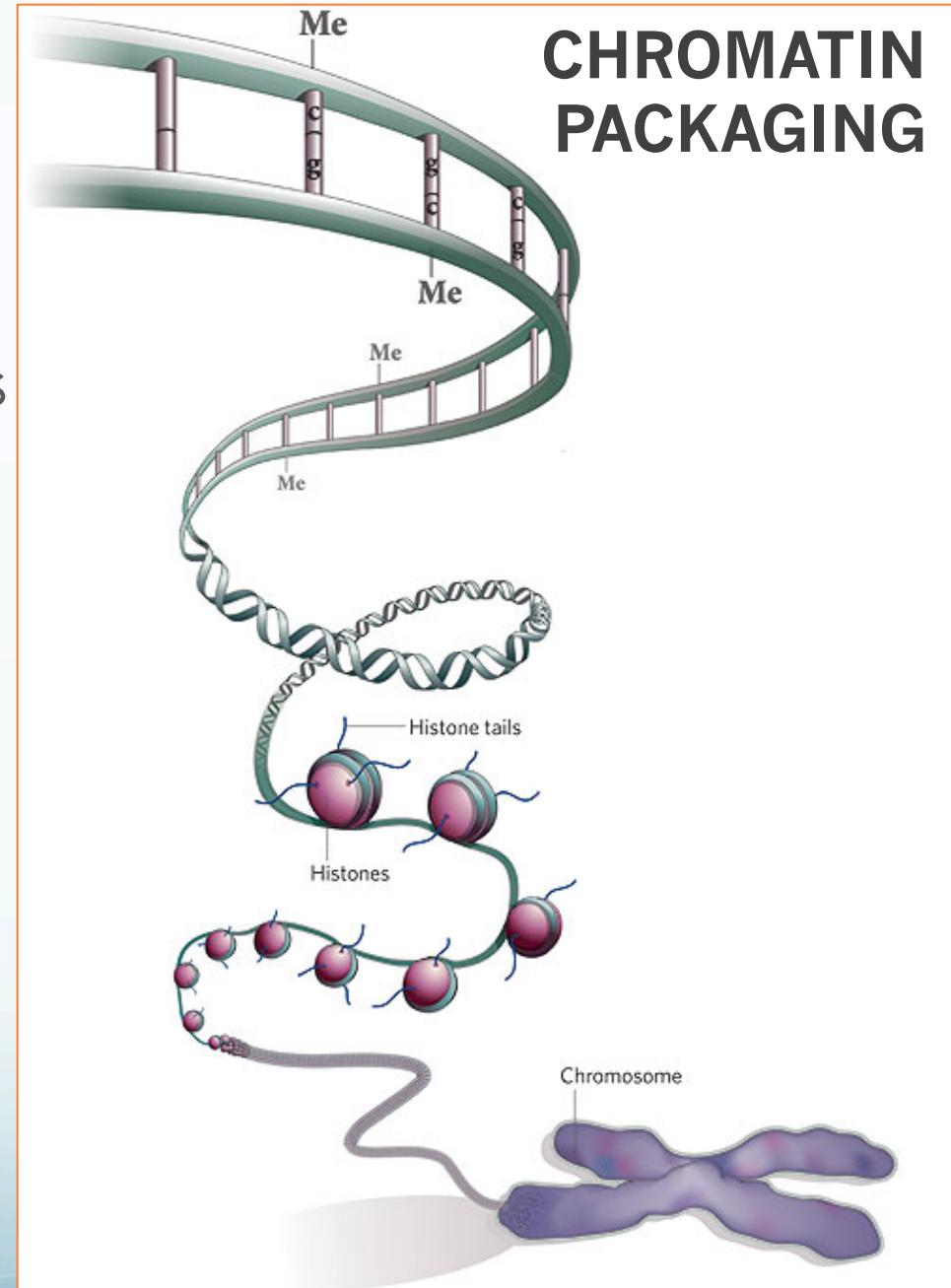
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- Epigenome provides instructions and regulates the functional aspects of genes

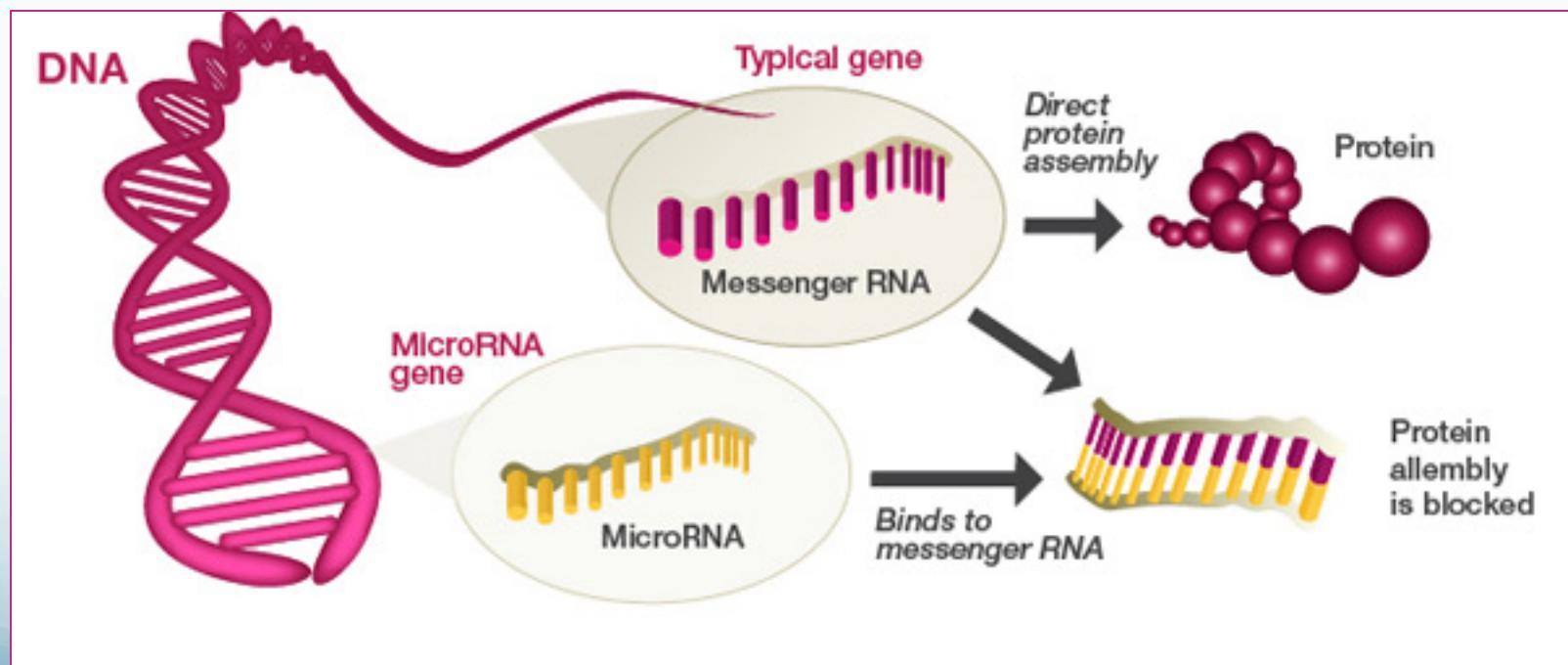
Epigenetic Marks

- Histone modifications
 - Acetylation
 - Methylation
- DNA methylation



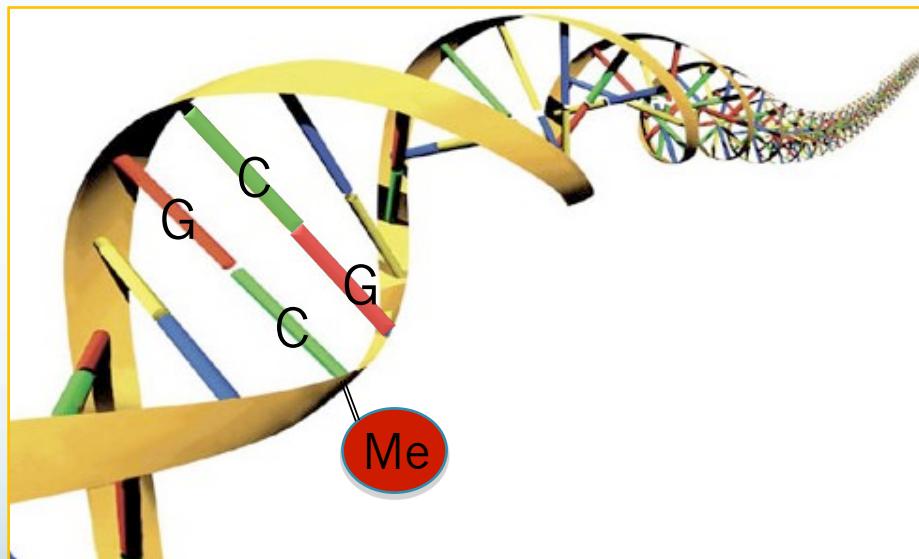
Epigenetic Marks

- 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

- DNA methylation in a promoter can inhibit transcription by blocking access to transcription factors



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DNA Methylation

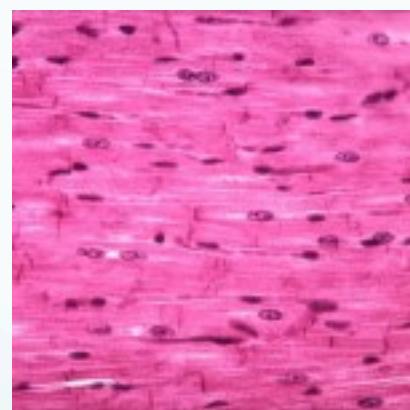
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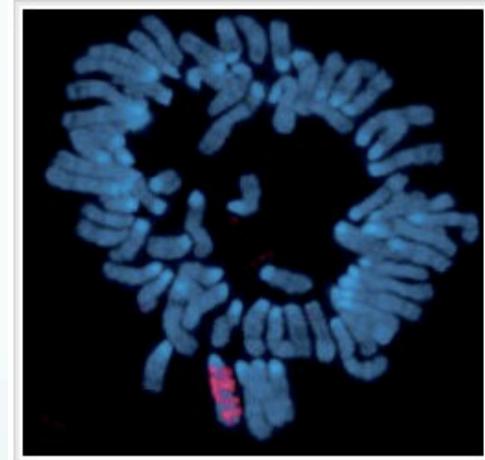
DNA methylation

- Functions:
 - Tissue differentiation



DNA methylation

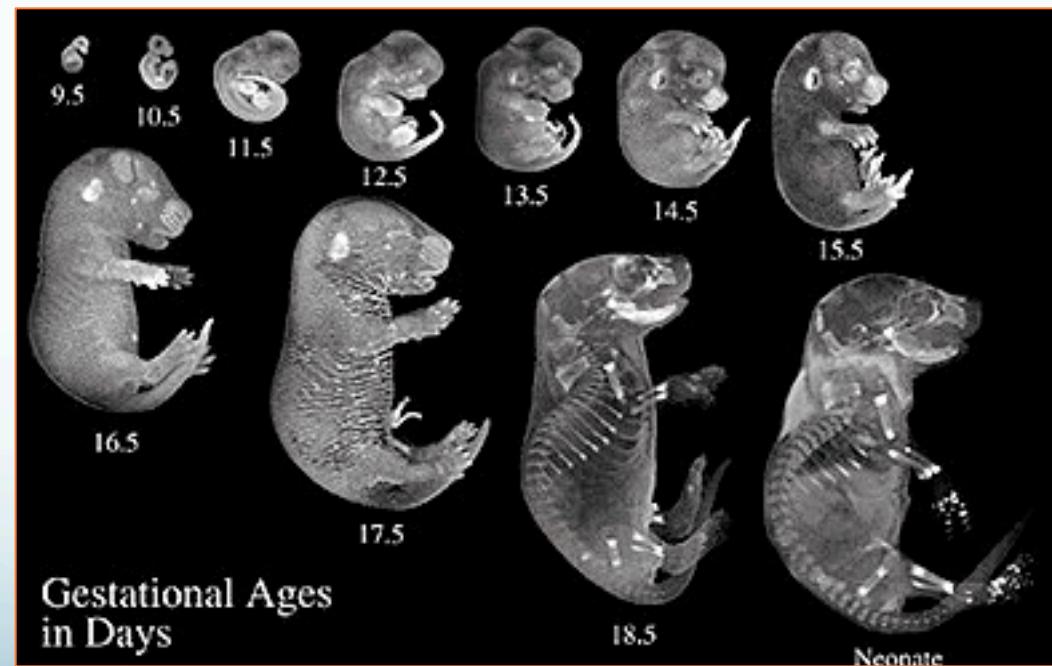
- Functions:
 - Tissue differentiation
 - Imprinting & x-inactivation



x chromosome
inactivation

DNA methylation

- Functions:
 - Tissue differentiation
 - Imprinting & x-inactivation
 - Development



DNA methylation

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

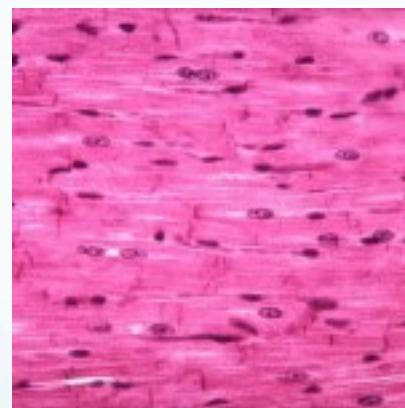


DNA Methylation

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

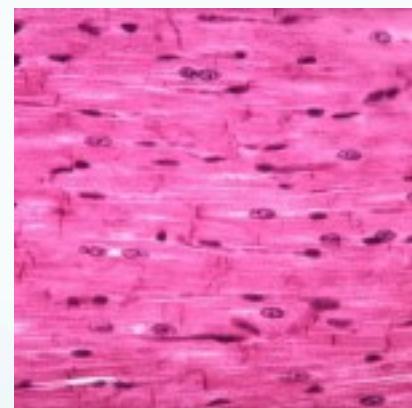
DNA methylation

- Epigenetic inheritance:



DNA methylation

- Epigenetic inheritance:
 - Mitotic inheritance
 - Transgenerational inheritance

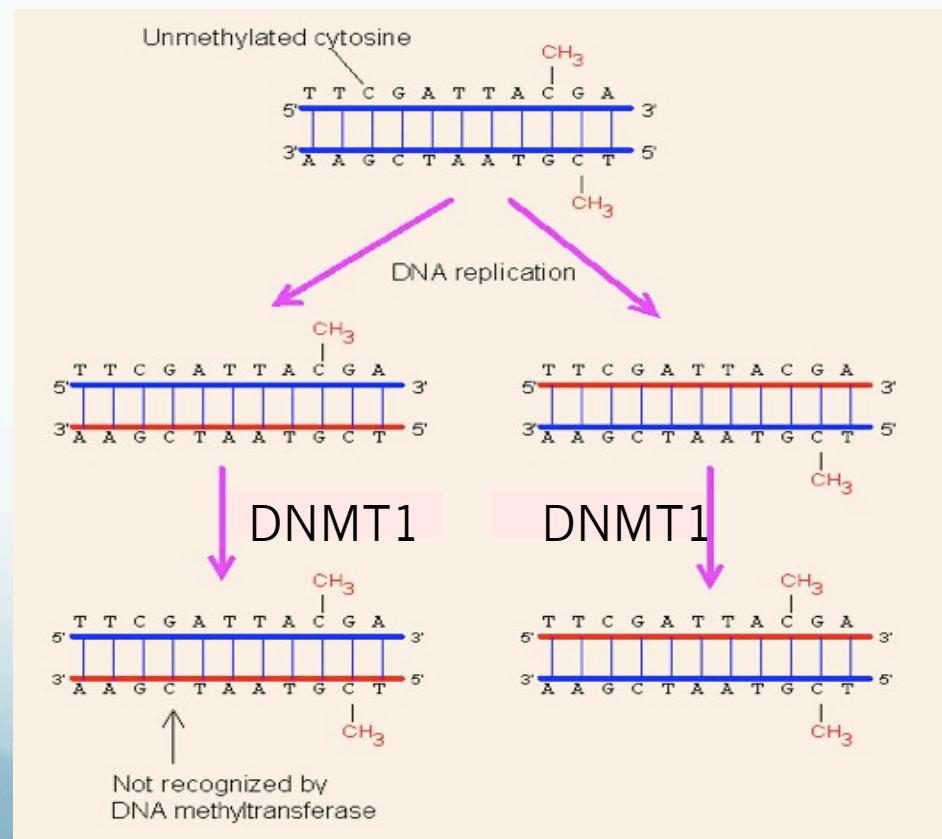


Epigenetic Inheritance

- DNA methyltransferases (DNMTs): family of enzymes which function to methylate DNA

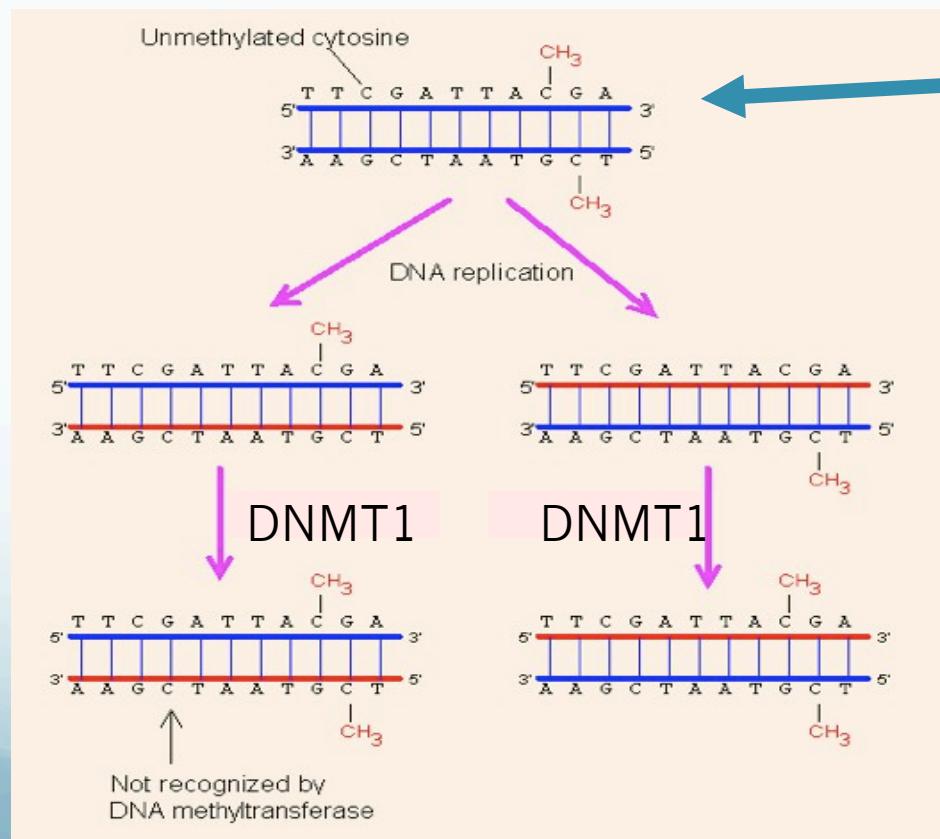
Epigenetic Inheritance

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 - Mitotic inheritance by **DNMT1**



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DNMT3a
DNMT3b

- *de novo* methylation by DNMT3

Epigenetic Inheritance

- Transgenerational inheritance
- You inherit more from your parents than just DNA..



DNA Methylation

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

DNA Methylation

- Many environmental factors have been shown to affect epigenetic marks such DNA methylation



Toxins and Nutrition

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



Source: Randy Jirtle

Temperature

- sex determination in European sea bass is temperature dependent
- High temp early in development = more males
- Mechanism: methylation status the of aromatase promoter



(Navarro-Martin et al, 2011)

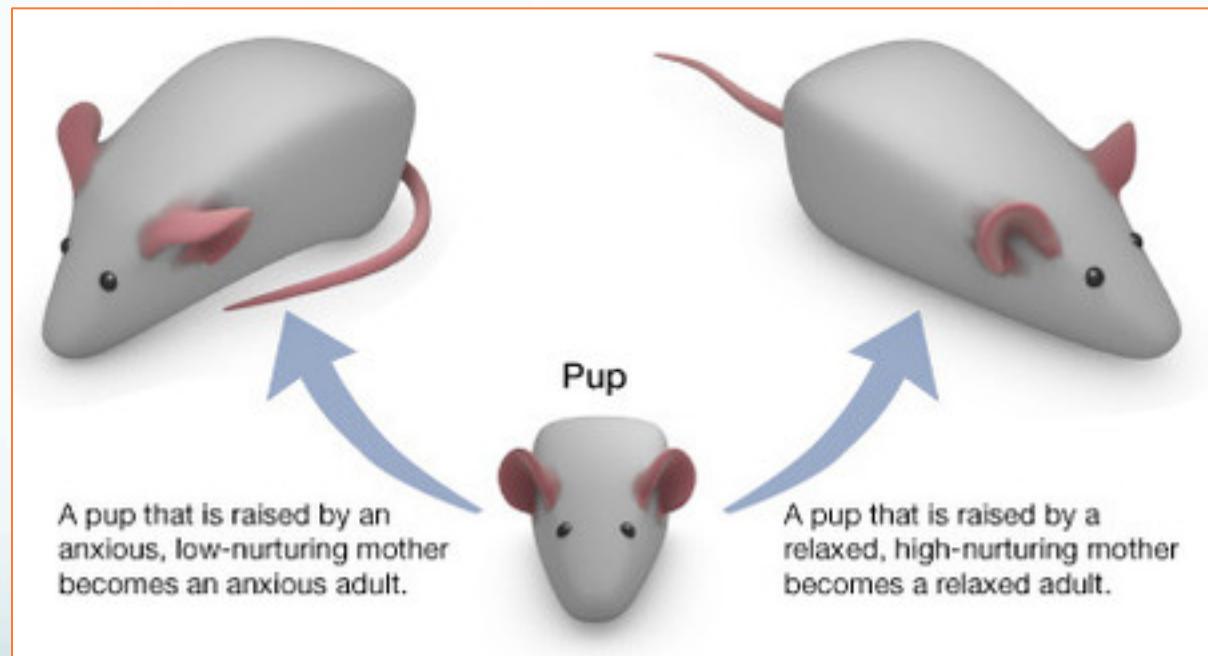
Stress

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

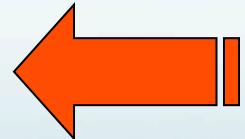
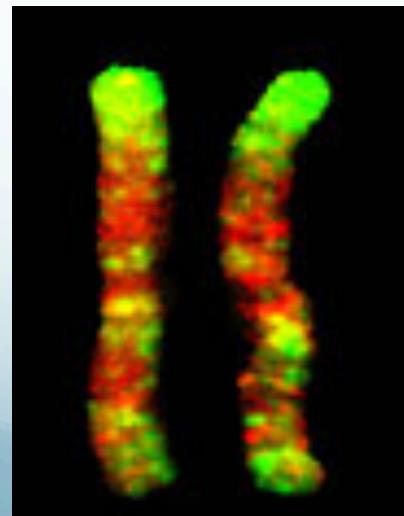
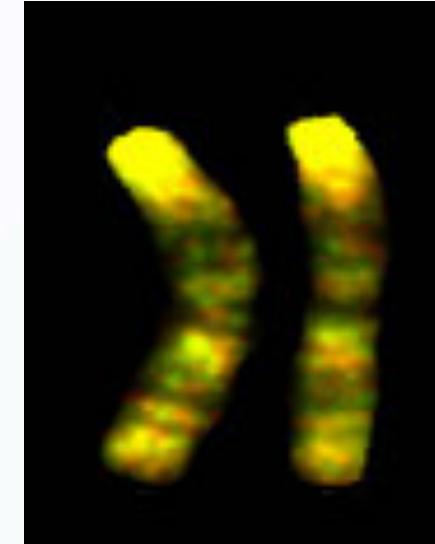
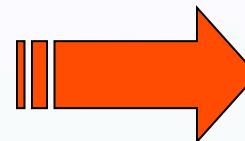


Behavior

- 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

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

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