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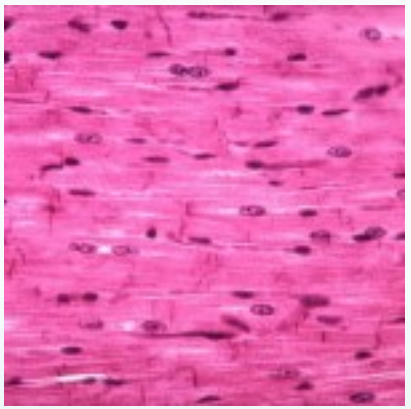
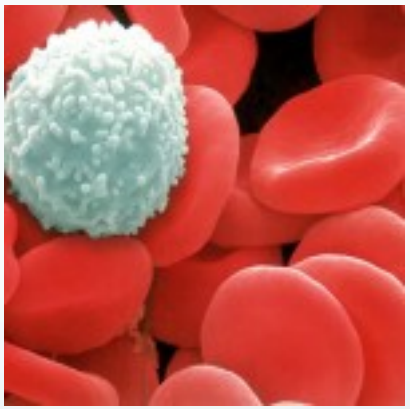
All of these cell types contain the same DNA.. so why do they look so different?

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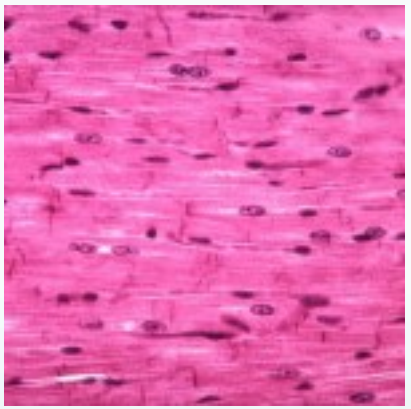
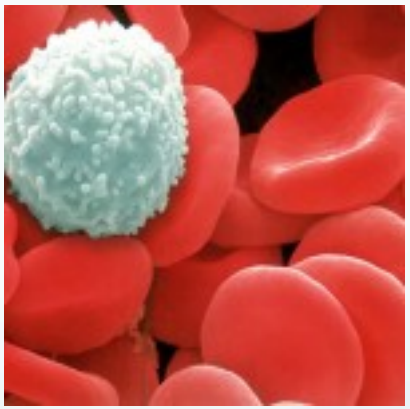
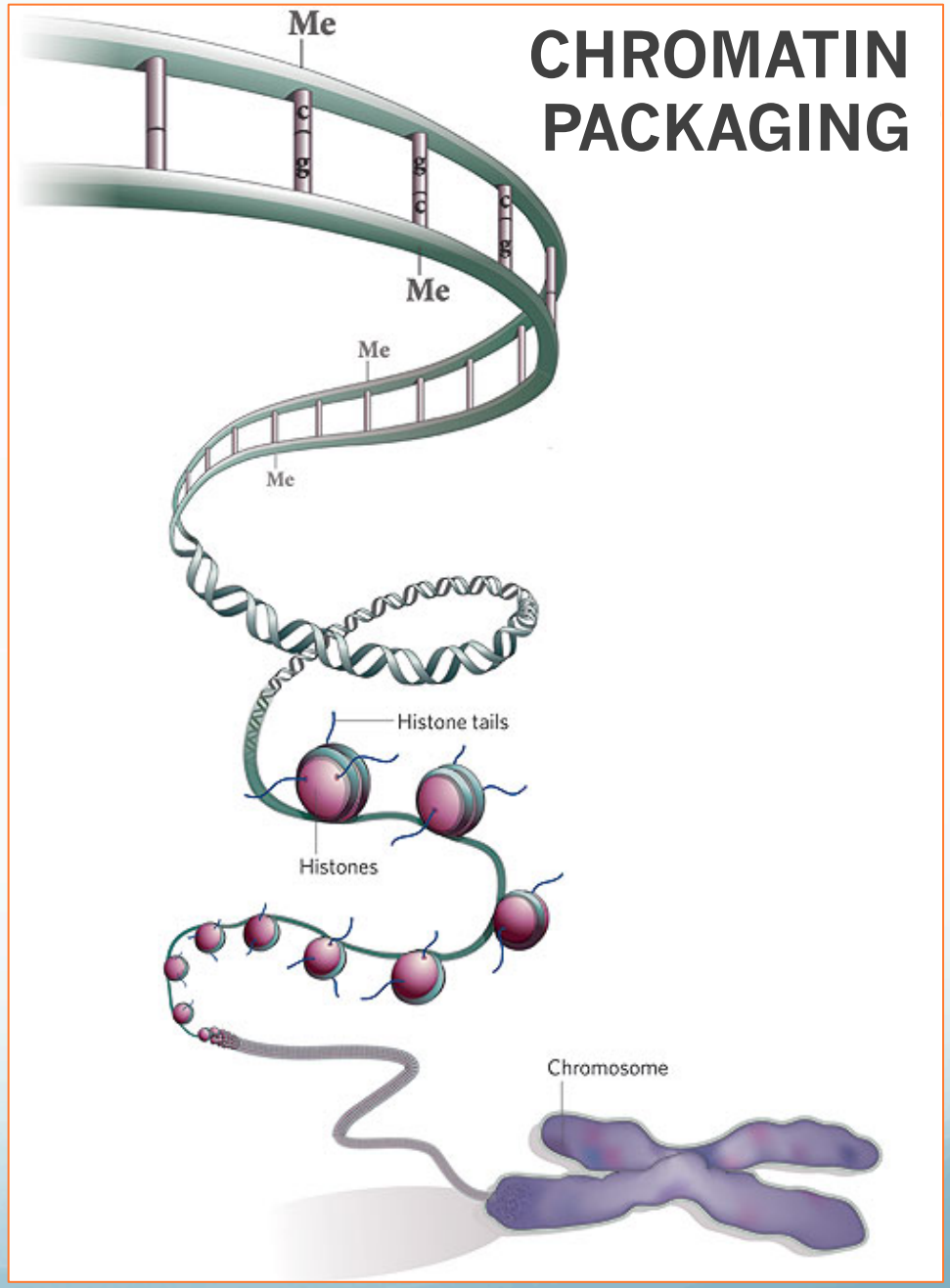



- Epigenome provides instructions and regulates the functional aspects of genes

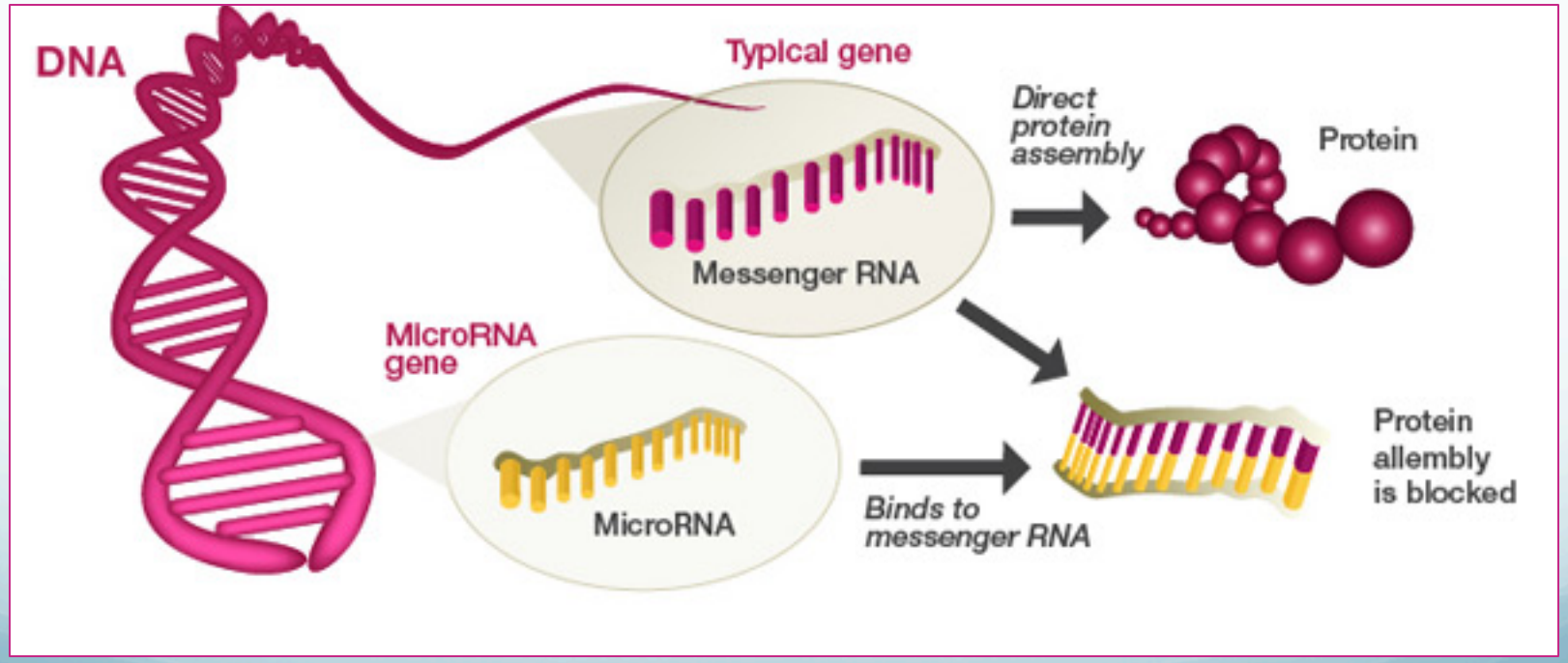
Epigenetic Marks

- Histone modifications
  - Acetylation
  - Methylation
- DNA methylation



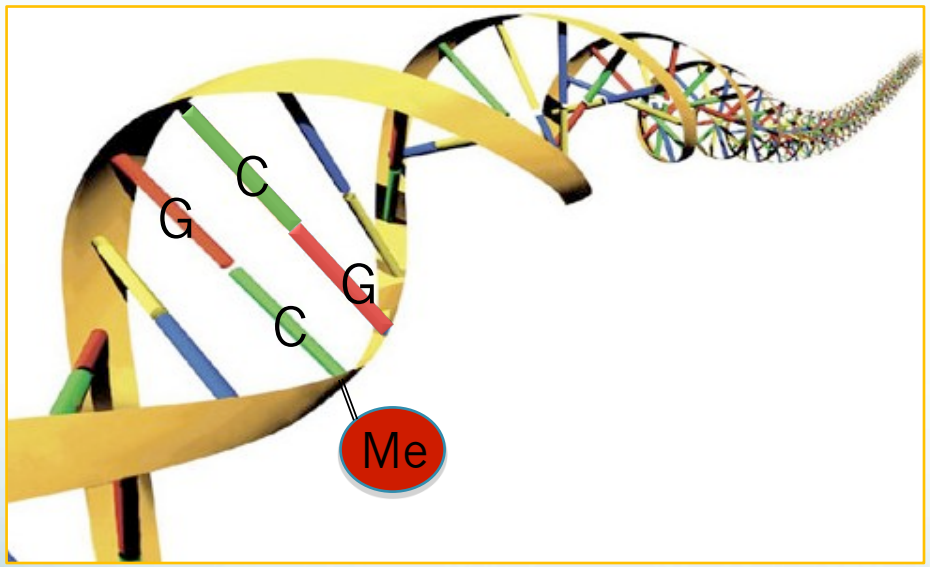
Epigenetic Marks

- 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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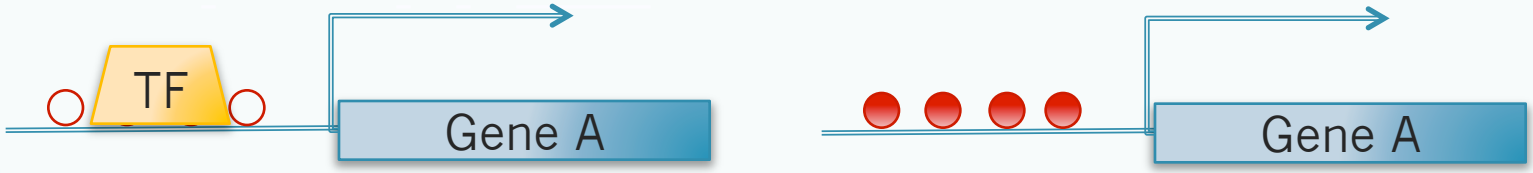

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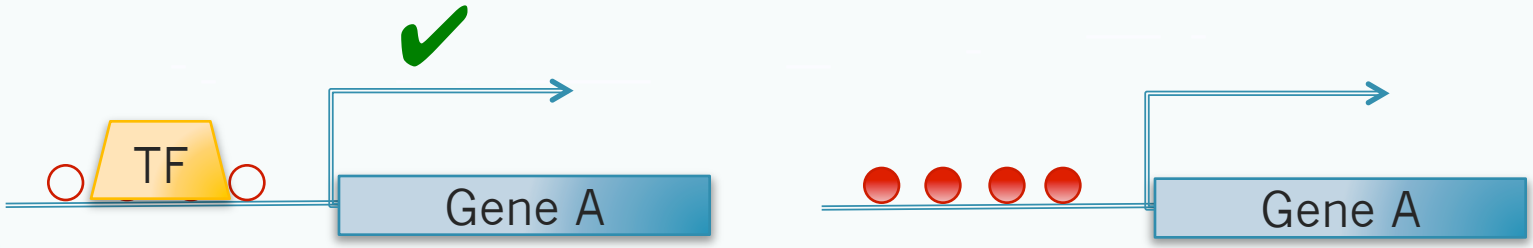

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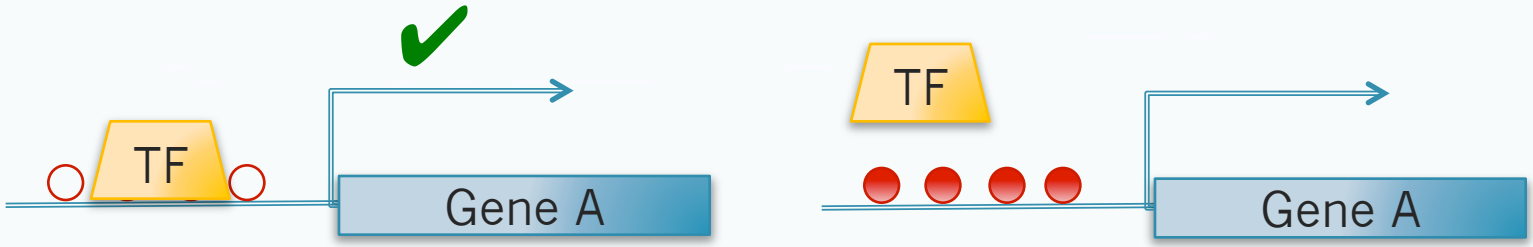

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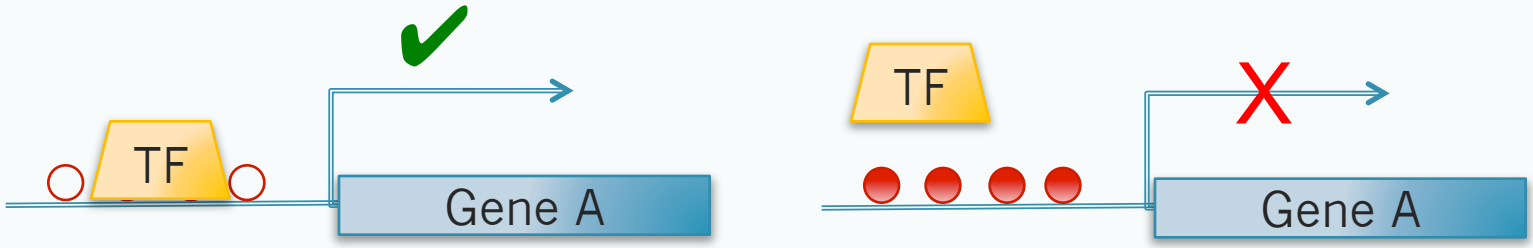

DNA Methylation

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

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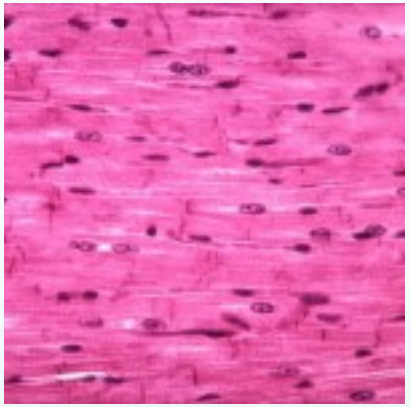
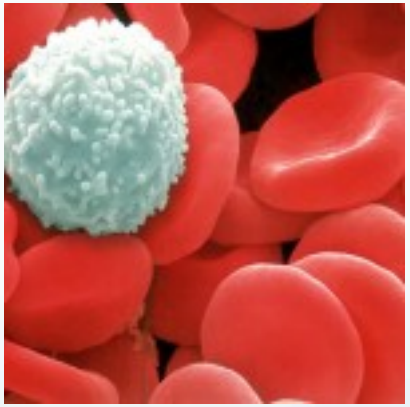
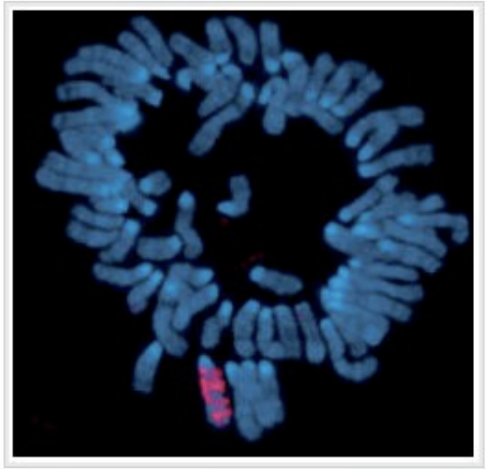
DNA methylation

- Functions:
  - Tissue differentiation

DNA methylation

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



x chromosome inactivation

DNA methylation

- Functions:
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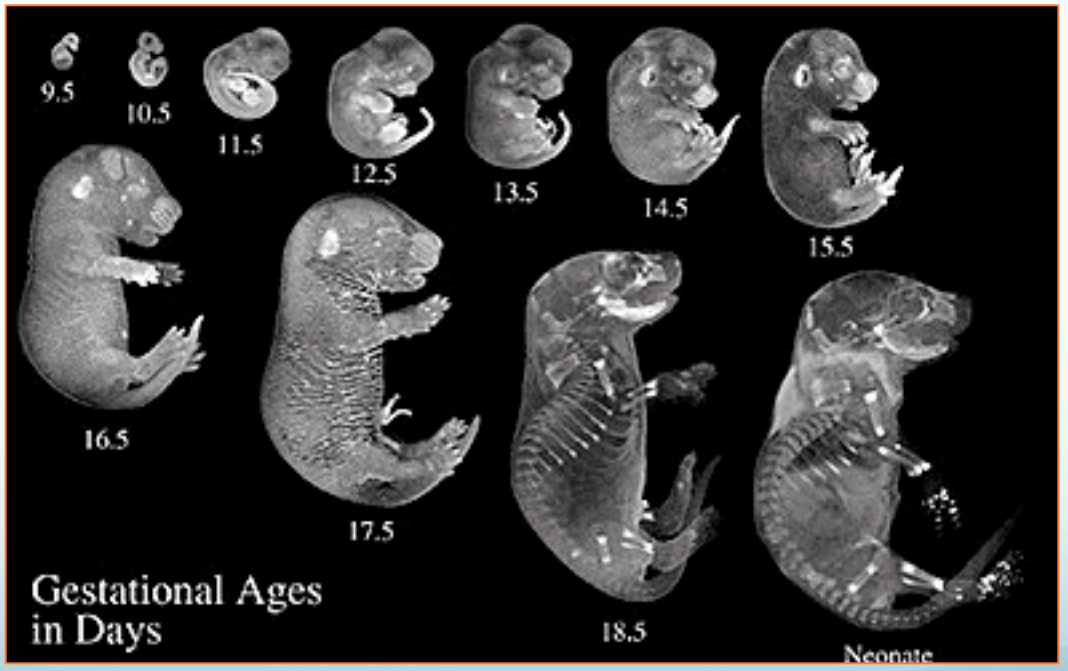
  - Imprinting & x-inactivation
  - Development



DNA methylation

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

DNA Methylation

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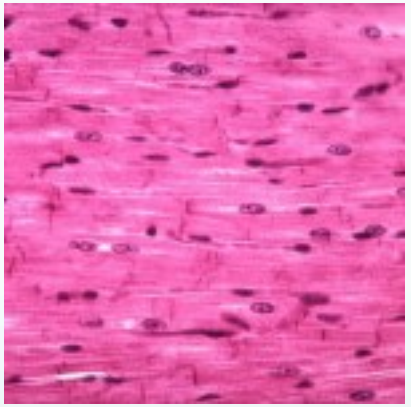
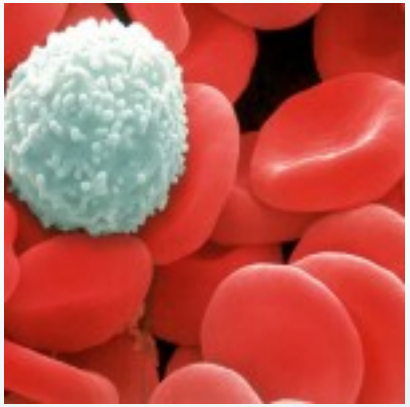
- **Epigenetic inheritance**
- DNA methylation & the environment
- Patterns: variation between taxa

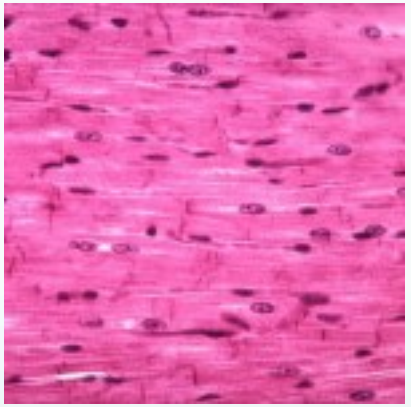
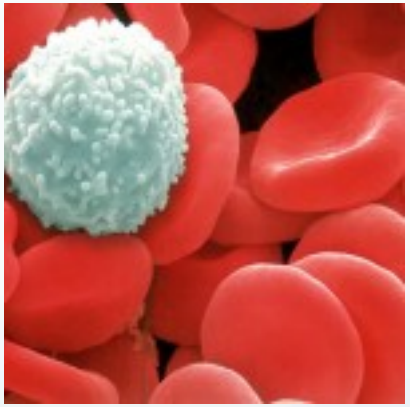
DNA methylation

- Epigenetic inheritance:

DNA methylation

- Epigenetic inheritance:
  - Mitotic inheritance
  - Transgenerational inheritance

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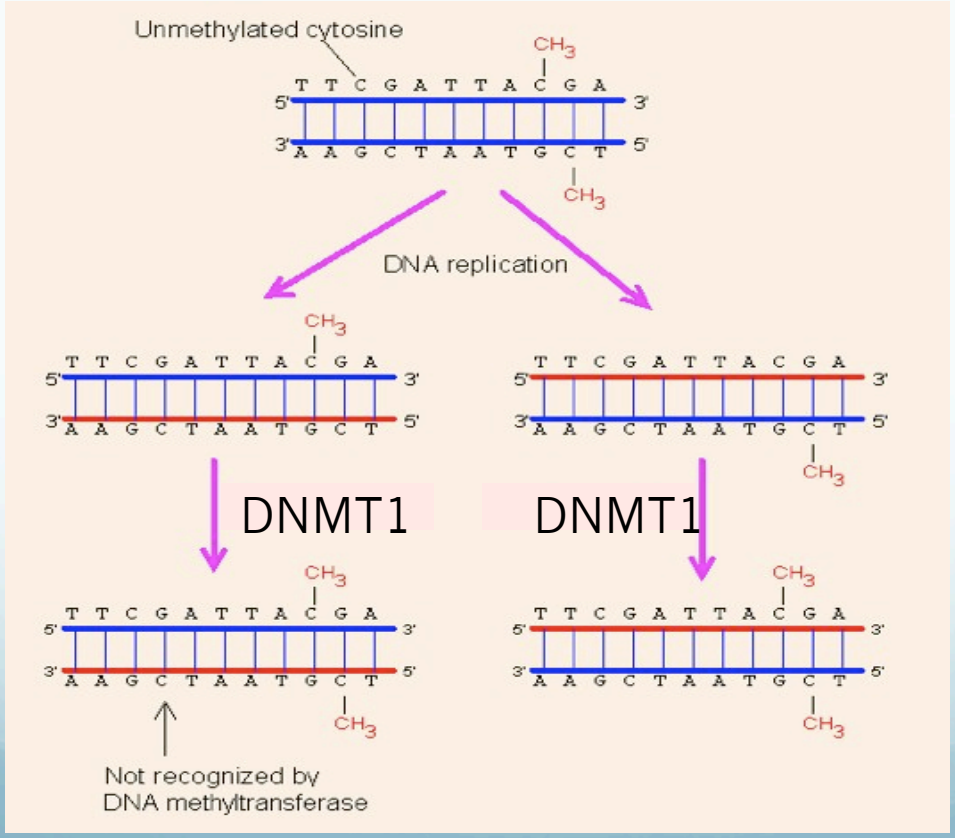

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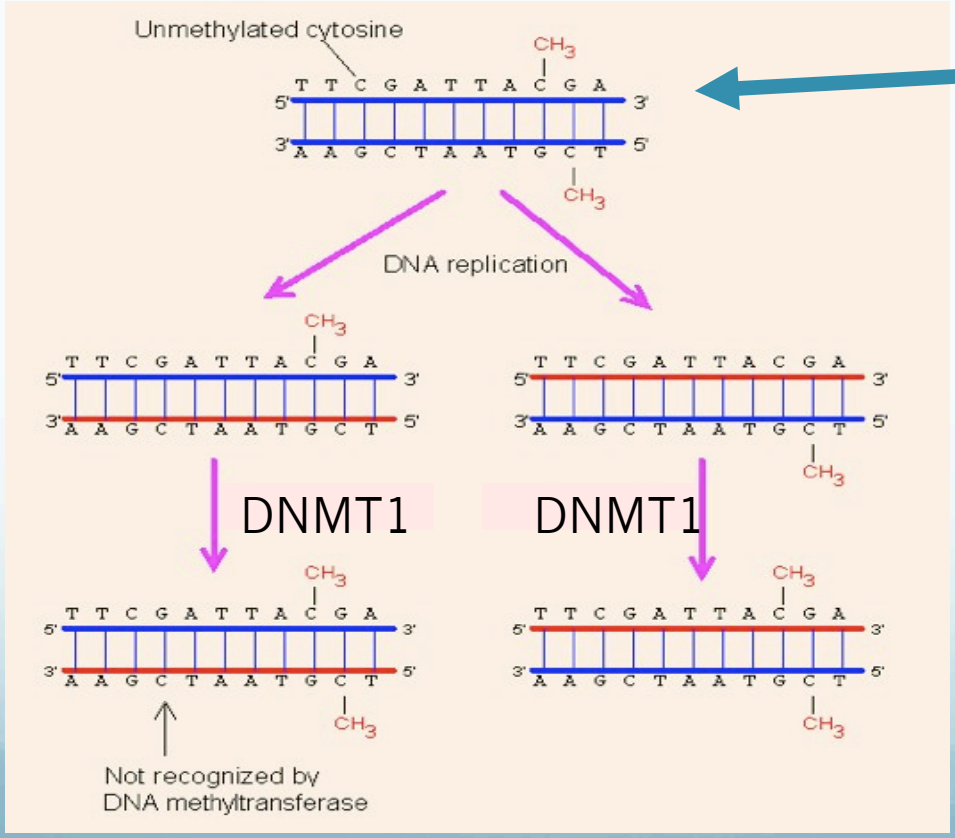
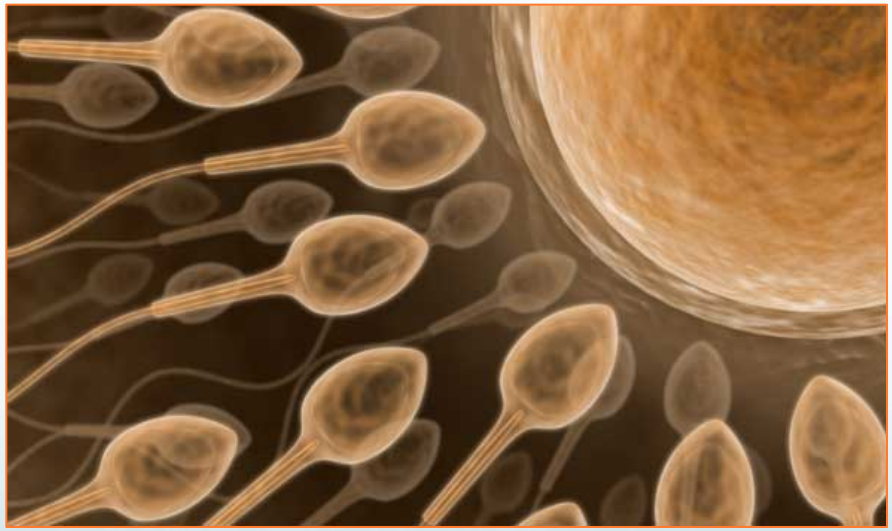


DNMT3a
DNMT3b

- *de novo* methylation by DNMT3

Epigenetic Inheritance

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



DNA Methylation

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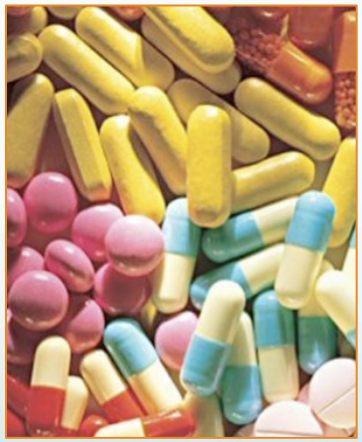
DNA Methylation

- 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

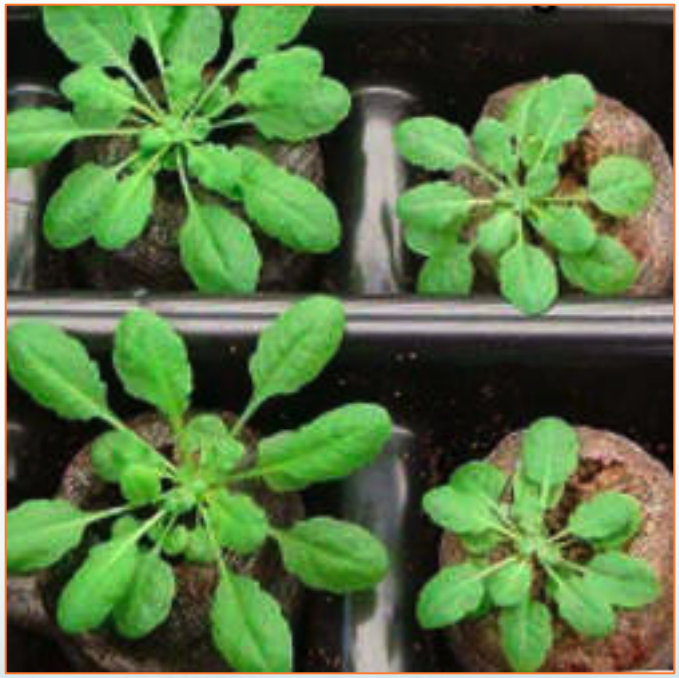
Temperature

- 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)

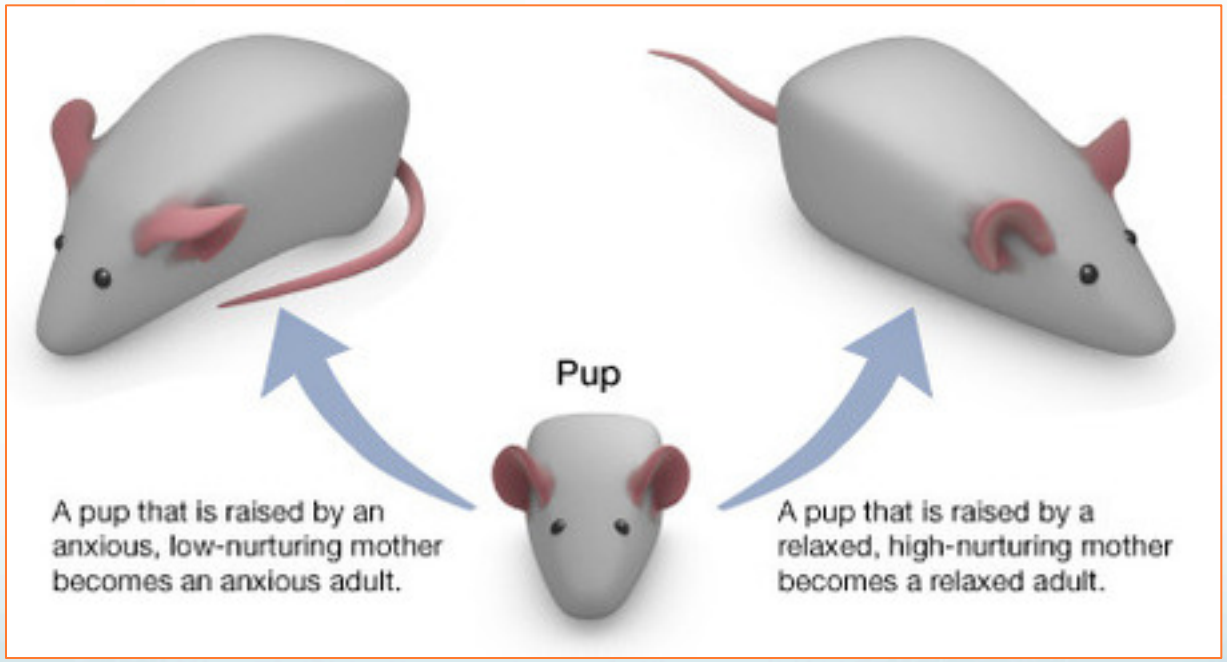
Stress

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

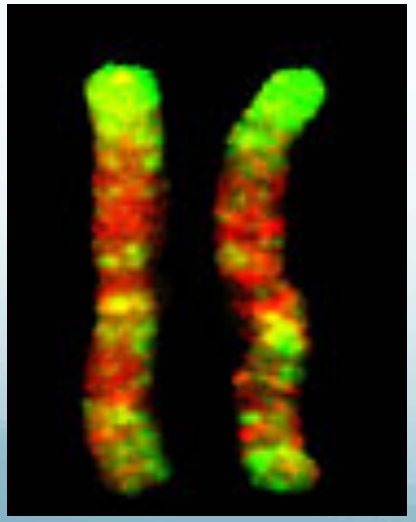


Behavior

- 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?

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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
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Thinking about lab..

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