

# Epigenetic Regulation: A Primer

## Lecture 15

# Outline

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

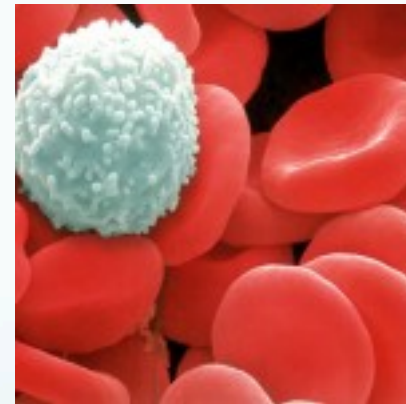
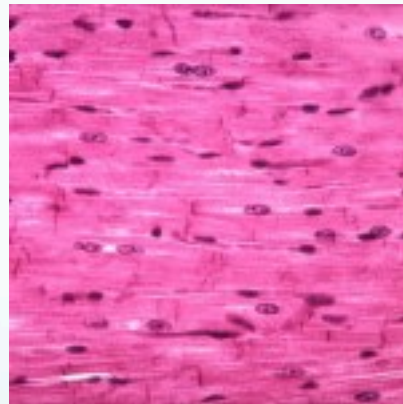
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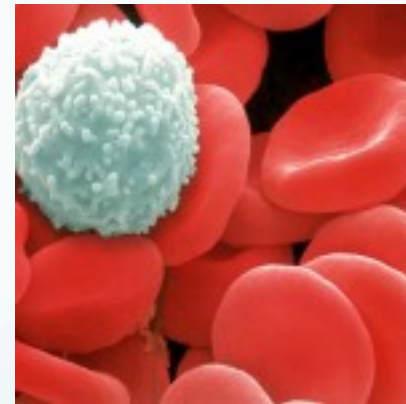
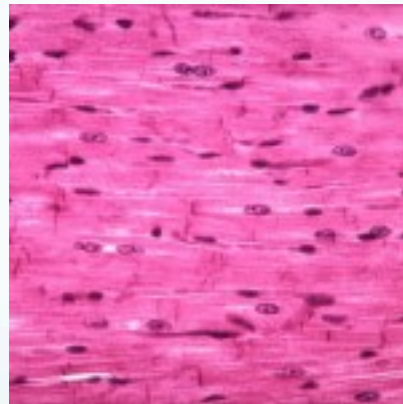
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# Epigenetics

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- Epigenome provides instructions and regulates the functional aspects of genes

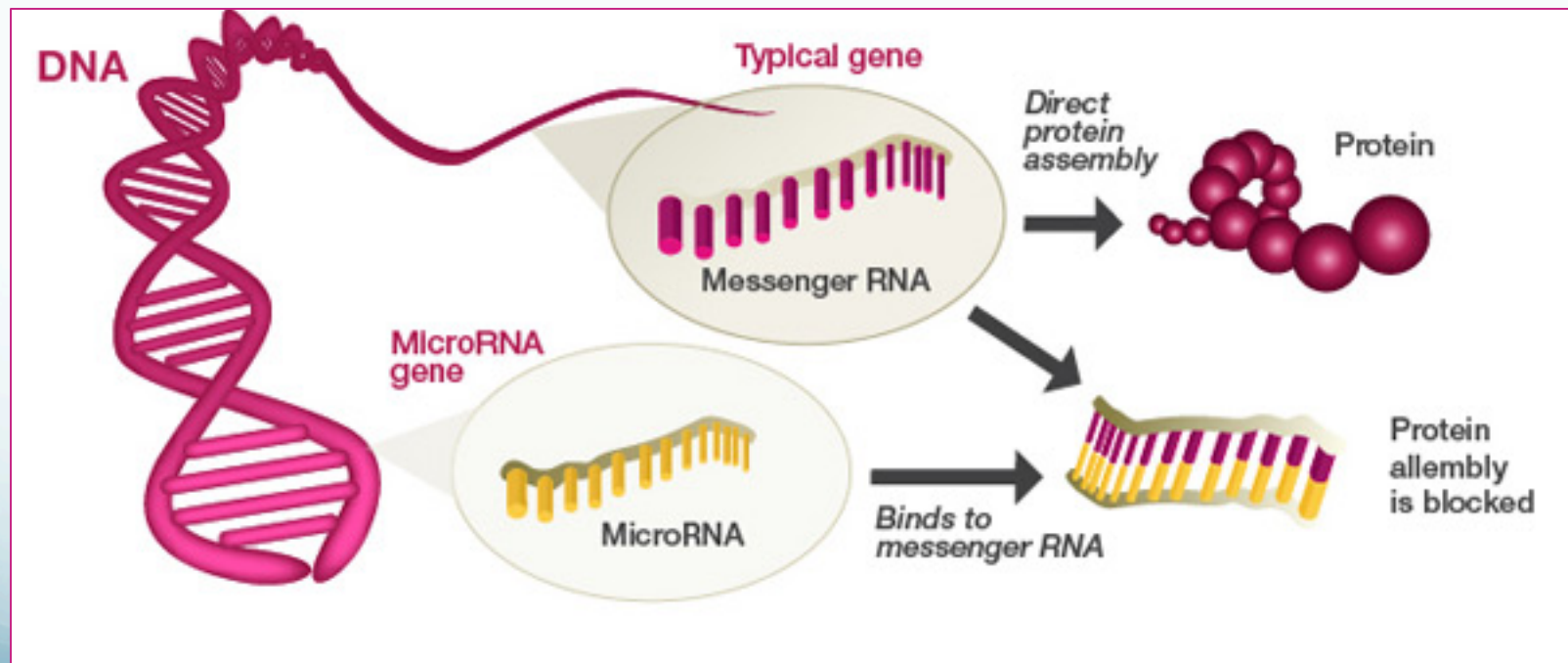
# Epigenetic Marks

- Histone modifications
  - Acetylation
  - Methylation
- DNA methylation



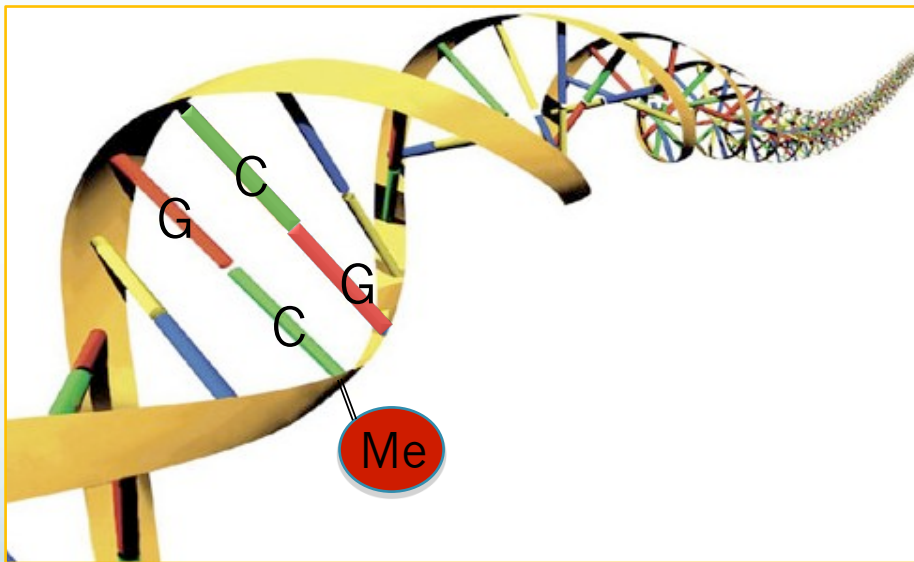
# Epigenetic Marks

- Non-coding RNAs
  - micro RNA (miRNA)



# DNA Methylation

- Most well understood epigenetic mechanism is **DNA methylation**

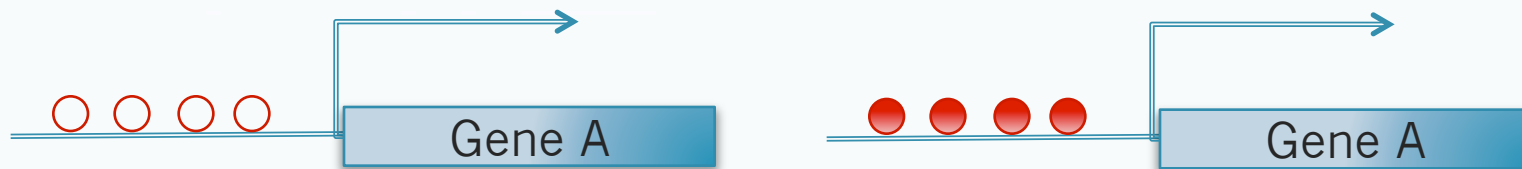


- Occurs in most plants and animals
- Most of what is known from mammals & plants, less in invertebrates
- Typically\* associated with gene silencing



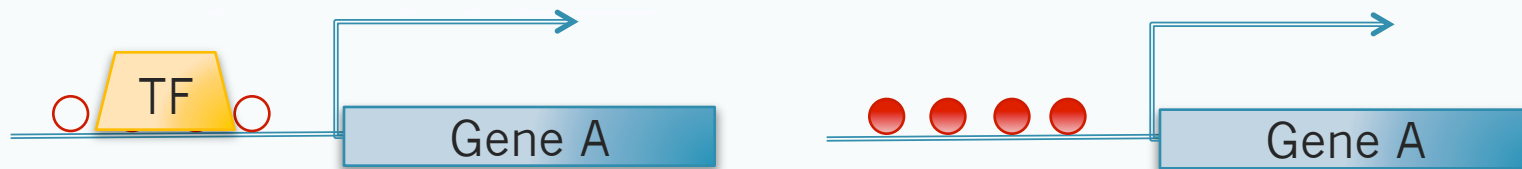
# DNA Methylation

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



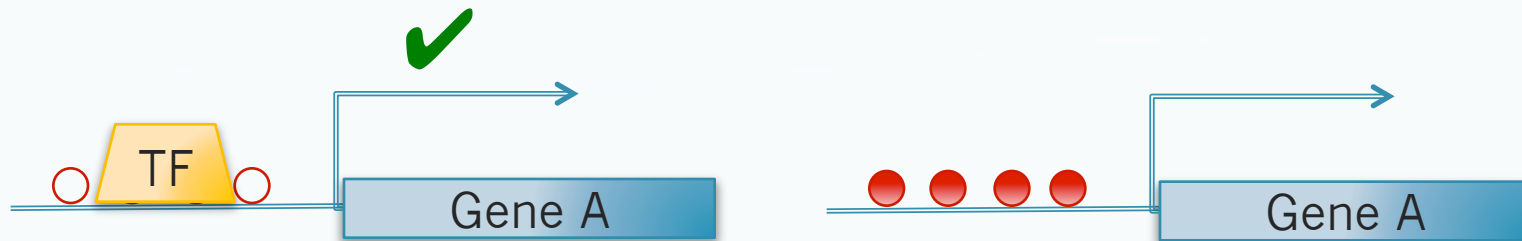
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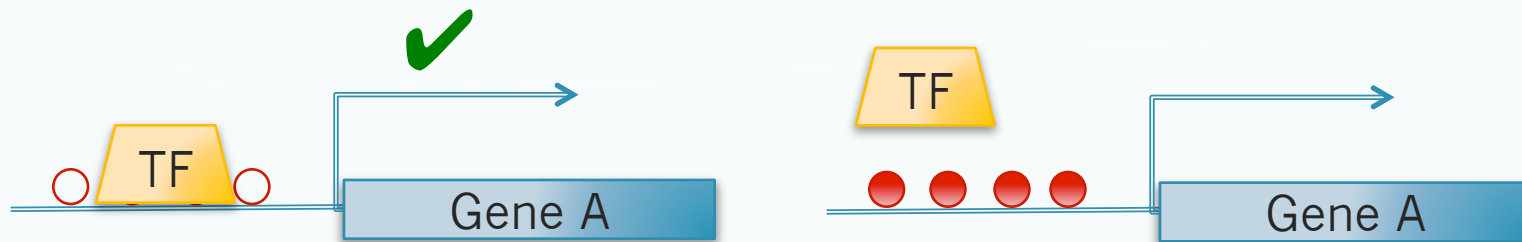
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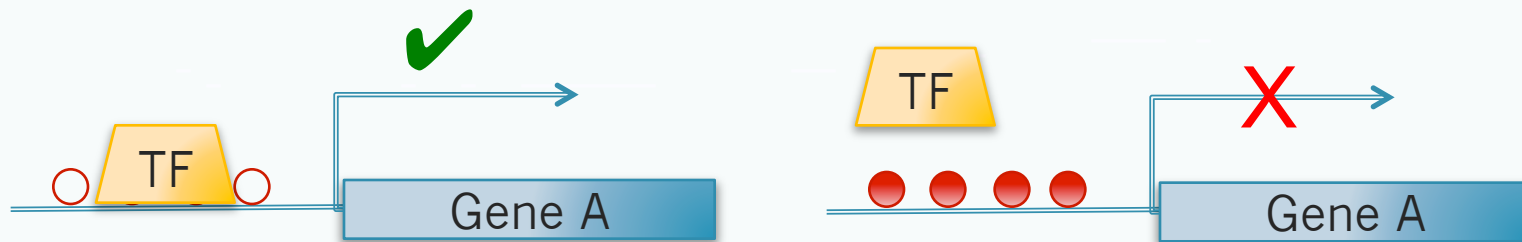
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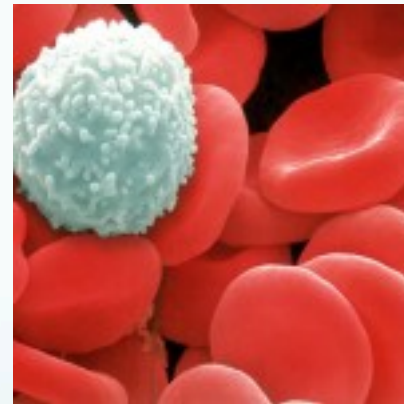
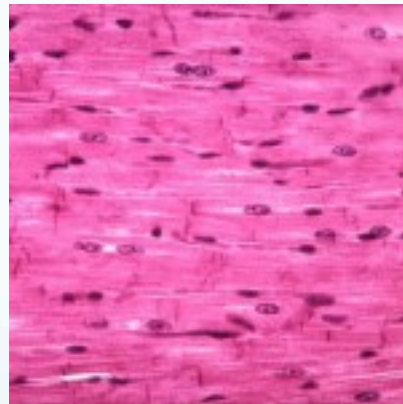
- Functions
- Epigenetic inheritance
- DNA methylation & the environment
- Patterns: variation between taxa

# DNA Methylation

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- Epigenetic inheritance
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# DNA methylation

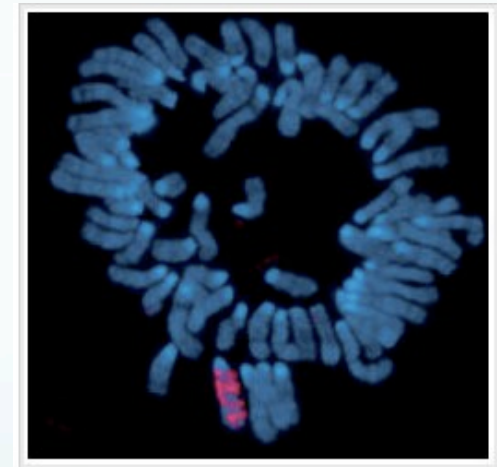
- Functions:
  - Tissue differentiation





# 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

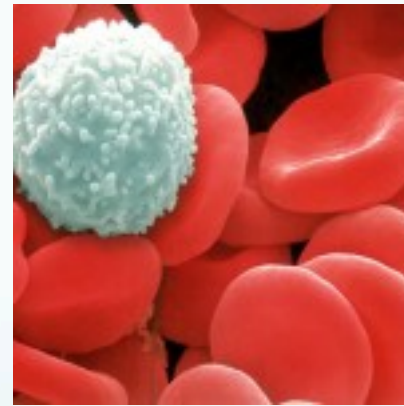
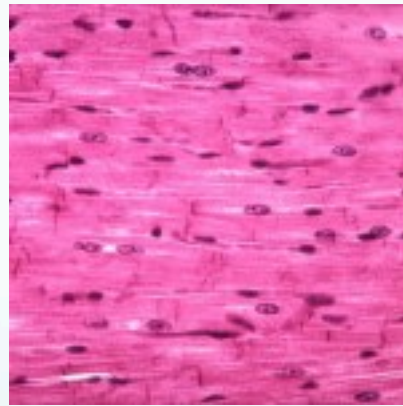


# DNA Methylation

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

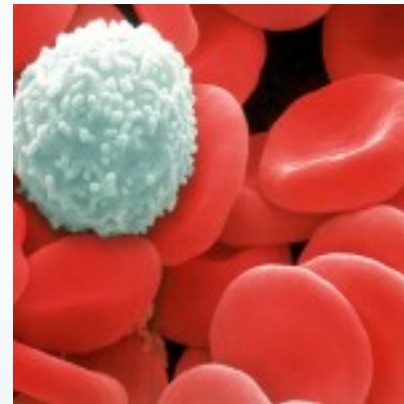
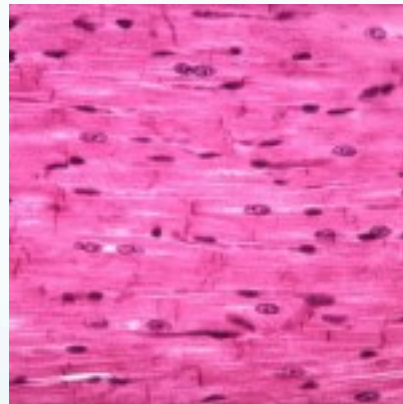
# DNA methylation

- Epigenetic inheritance:



# DNA methylation

- Epigenetic inheritance:
  - Mitotic inheritance
  - Transgenerational inheritance

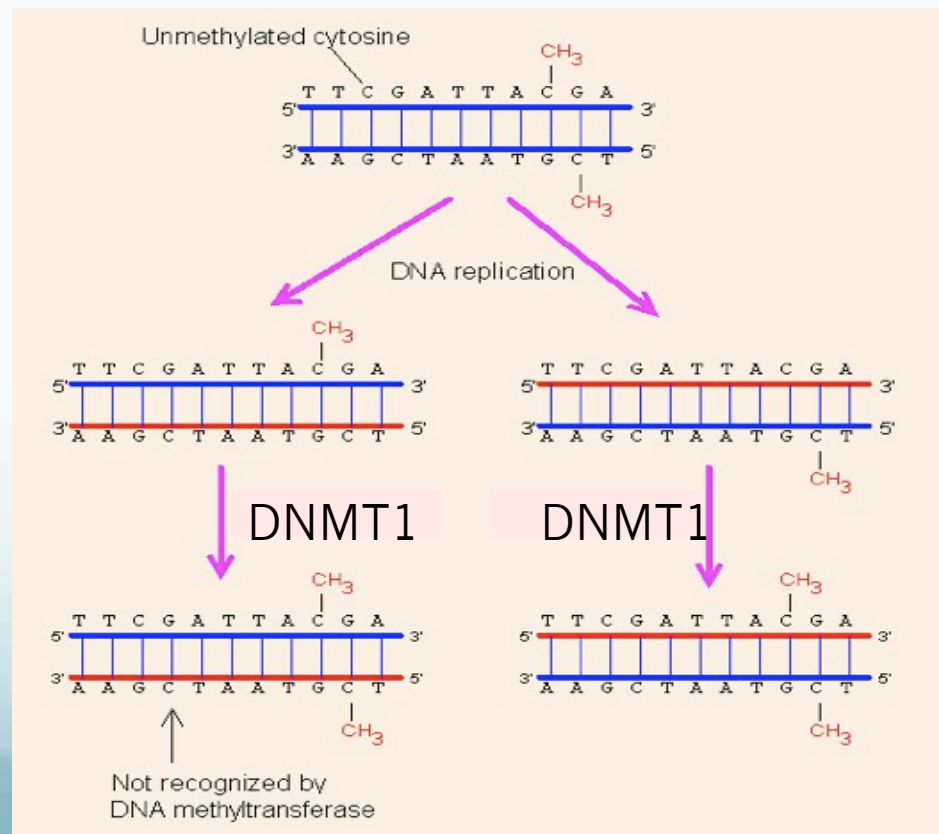


# Epigenetic Inheritance

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

# Epigenetic Inheritance

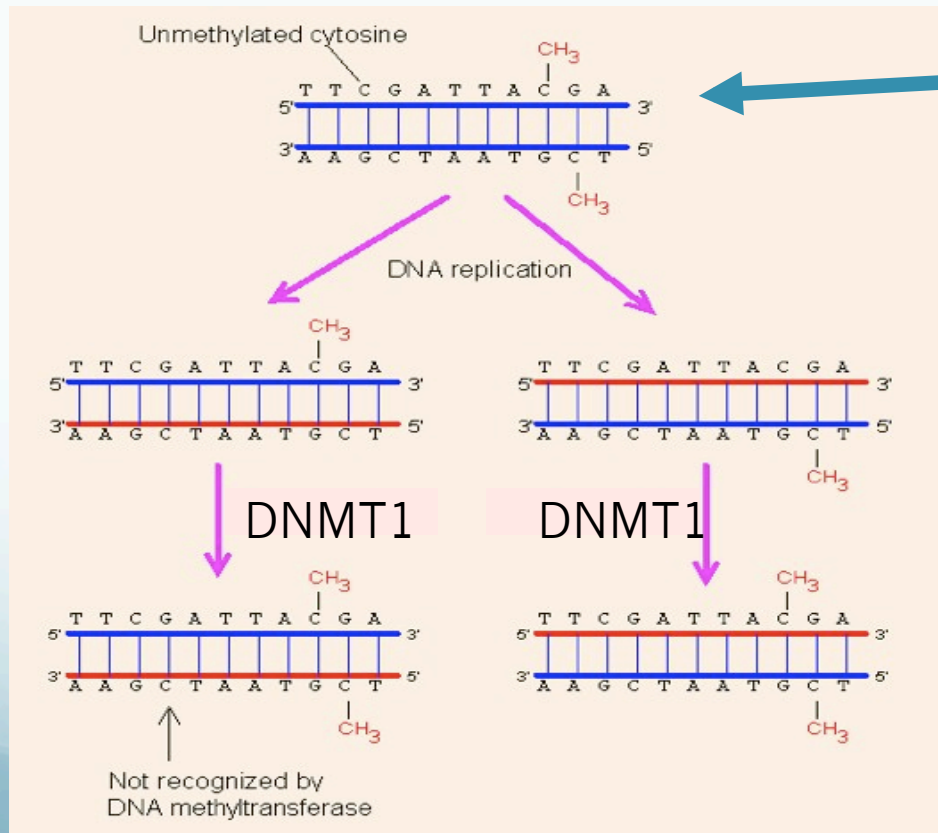
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- DNA methyltransferases (DNMTs): family of enzymes which function to methylate DNA
  - Mitotic inheritance by **DNMT1**

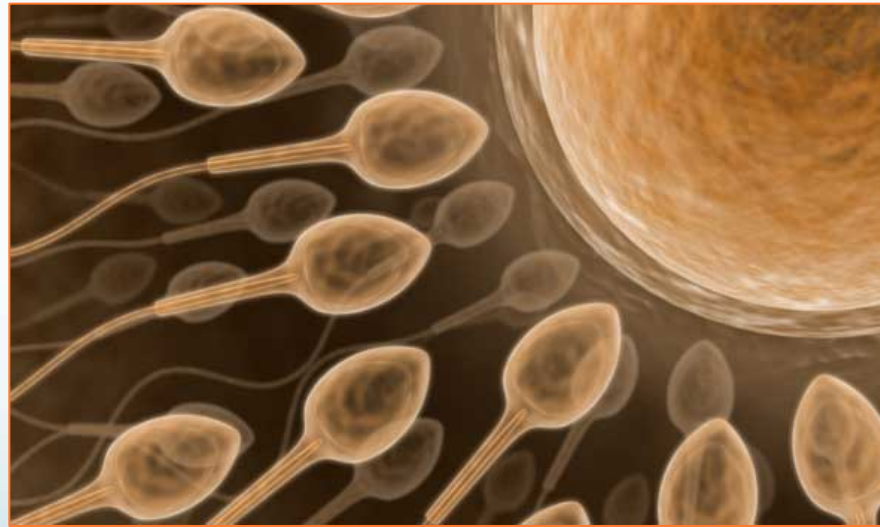


**DNMT3a**  
**DNMT3b**

- *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 as 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 of aromatase promoter



(Navarro-Martin et al, 2011)

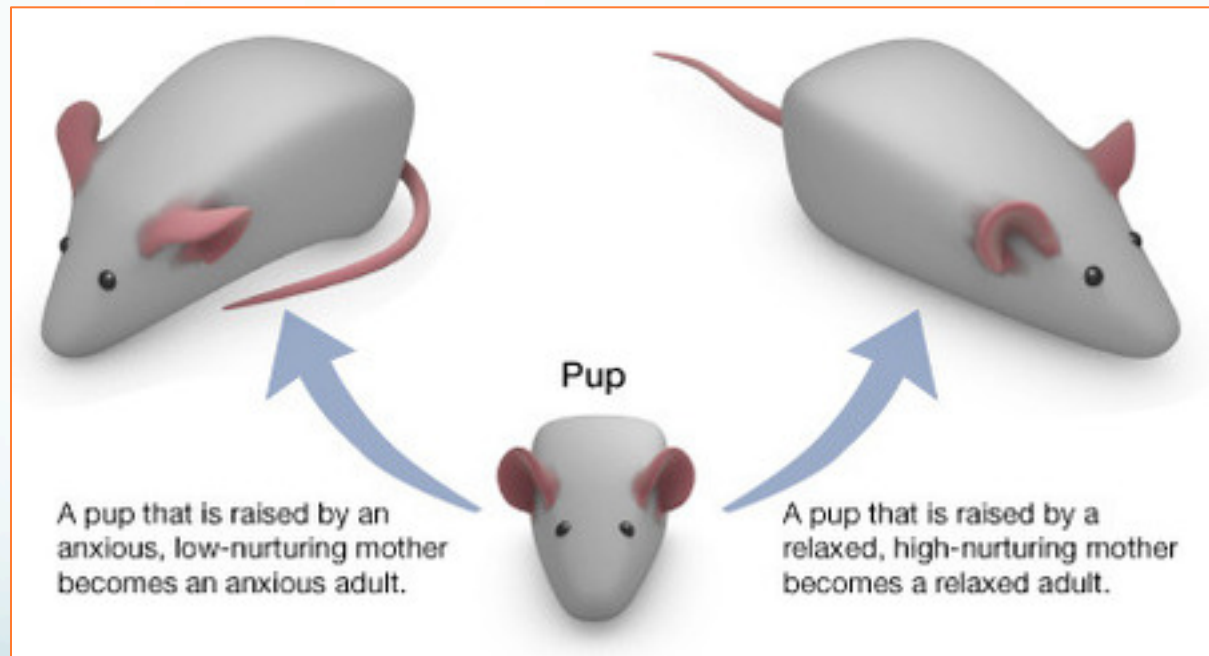
# Stress

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



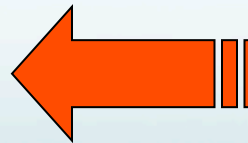
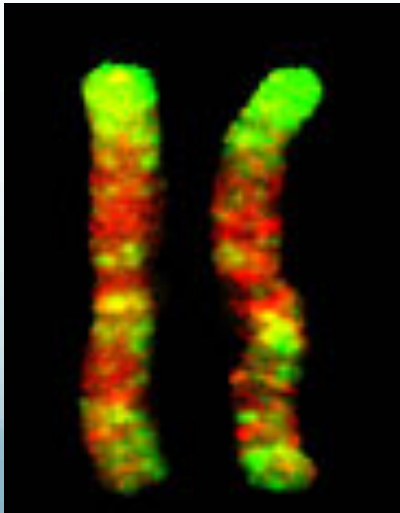
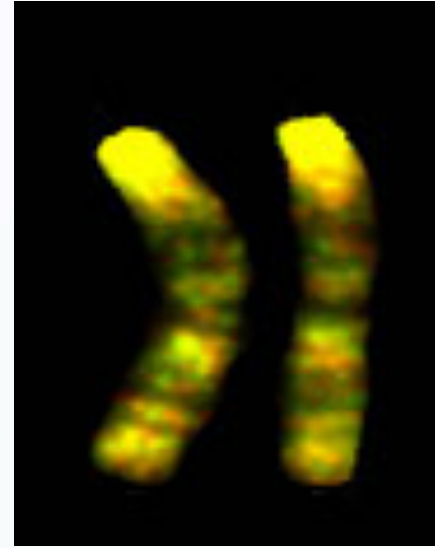
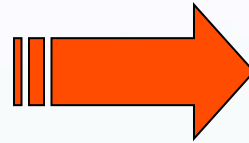
# Behavior

- 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