# An introduction to the epigenome

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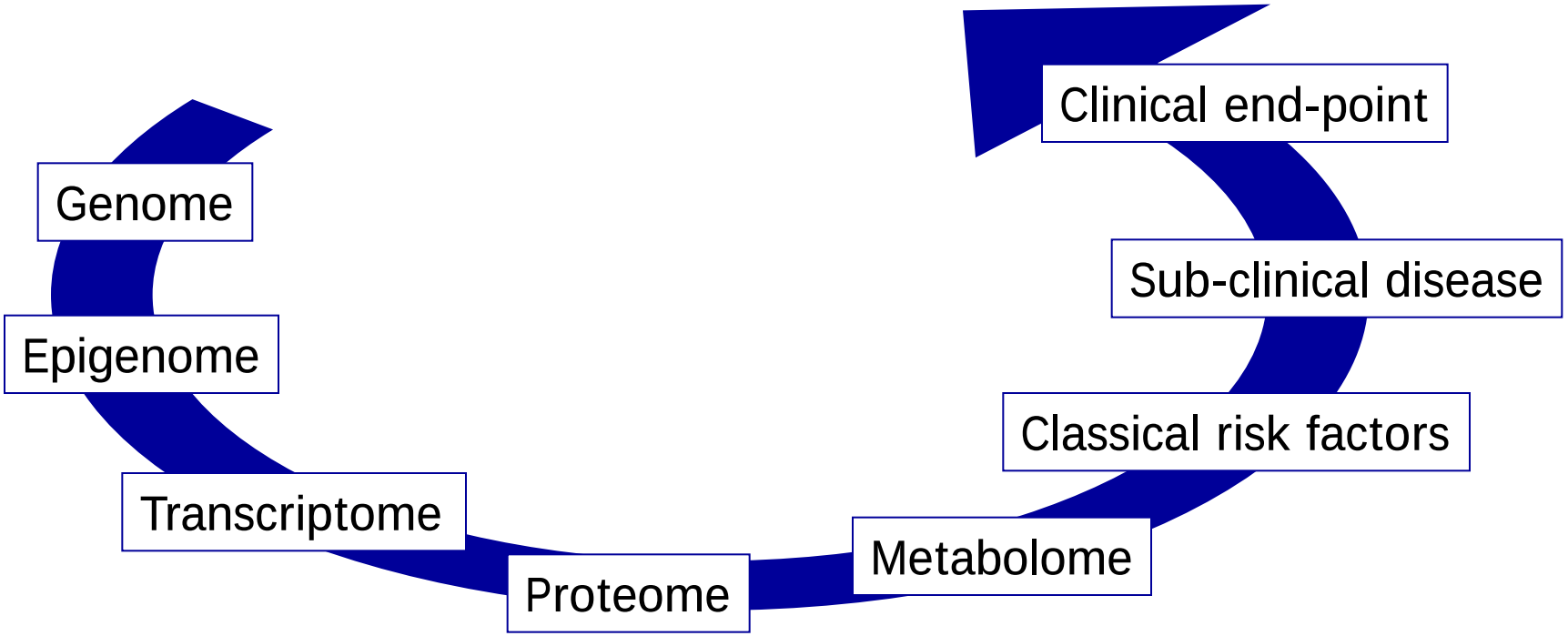
Clinical end-point
Sub-clinical disease
Classical risk factors
Metabolome
Proteome
Transcriptome
Epigenome
Genome

# On offer for today

- The molecular basis of epigenetics
- The role of epigenetics in fundamental biology
- Epigenetics as integrator of environmental signals
- Epigenetics in disease mechanisms

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# The genetic code is not enough

AGTGCCGGGAAGTGGGGCTTGGC
CCAGGGCCCCCAAGACACACAGA
CGGCACAGCAGGGCTGGTTCAAG
GGCTTTATTCCATCTCTCTCGGT
GCAGGAGGCGGCGGGTGTGGGGC
TGCCTGCGGGCTGCGTCTAGTTG
CAGTAGTTCTCCAGCTGGTAGAG

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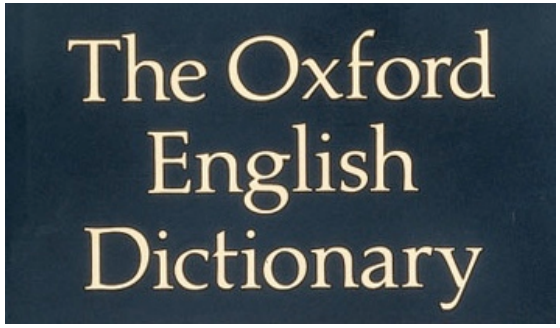


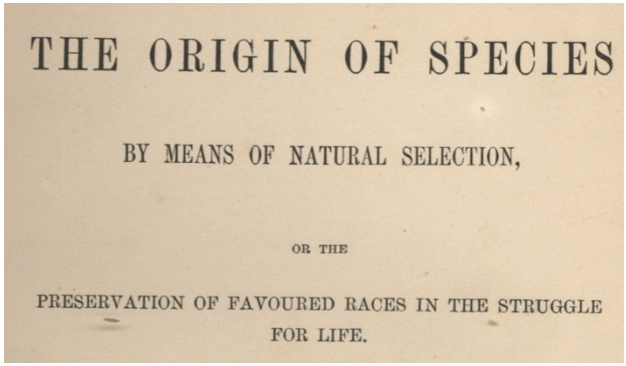

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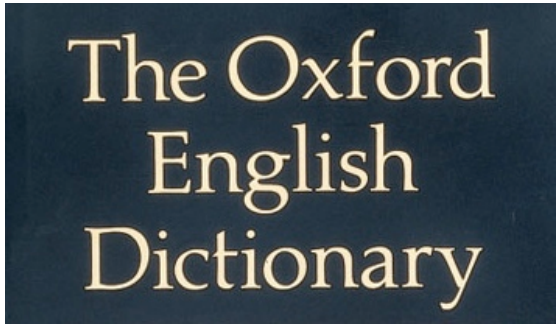


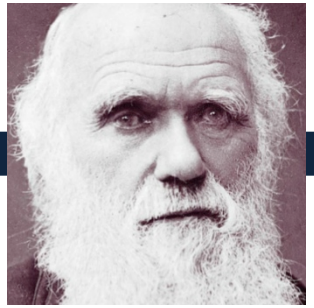

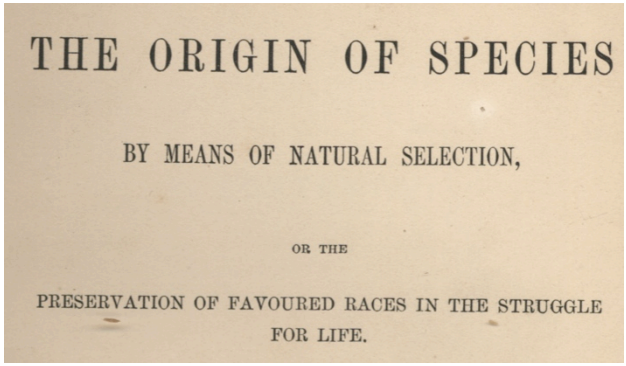

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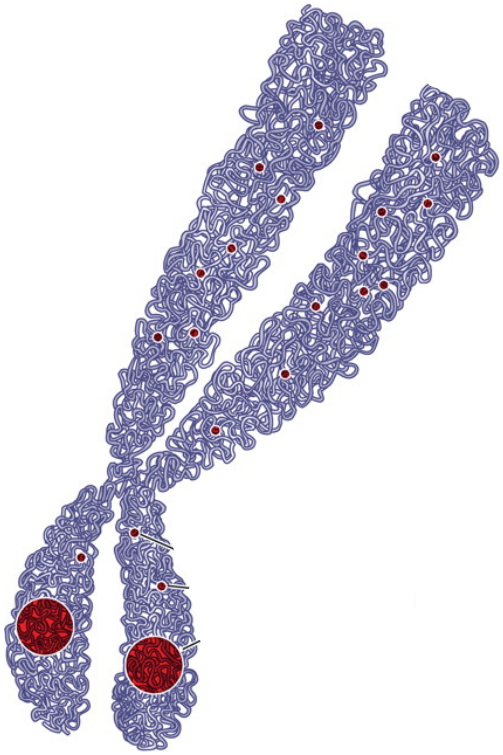
- Instructing the DNA where, when and how much to express a gene

# Molecular dimmers on the DNA

# Molecular dimmers on the DNA



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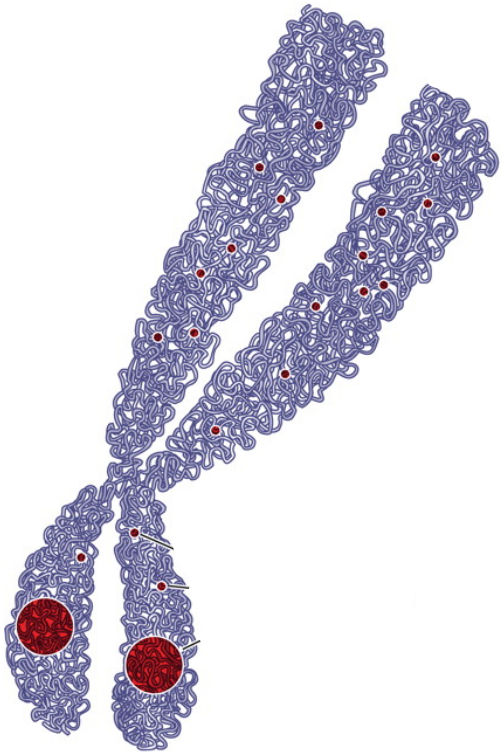

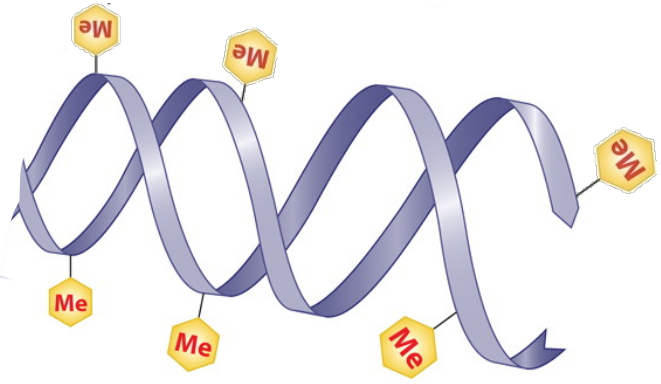

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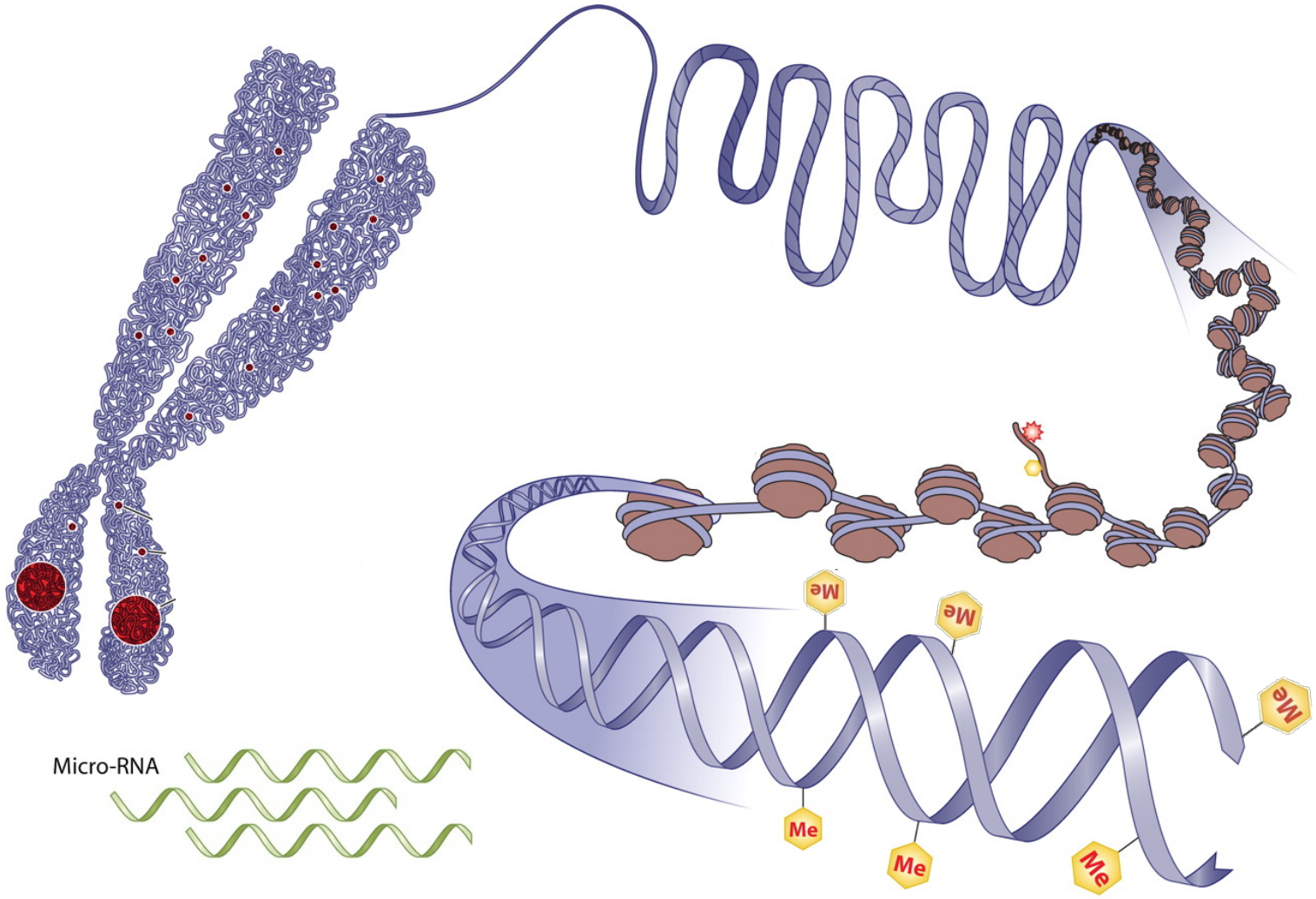
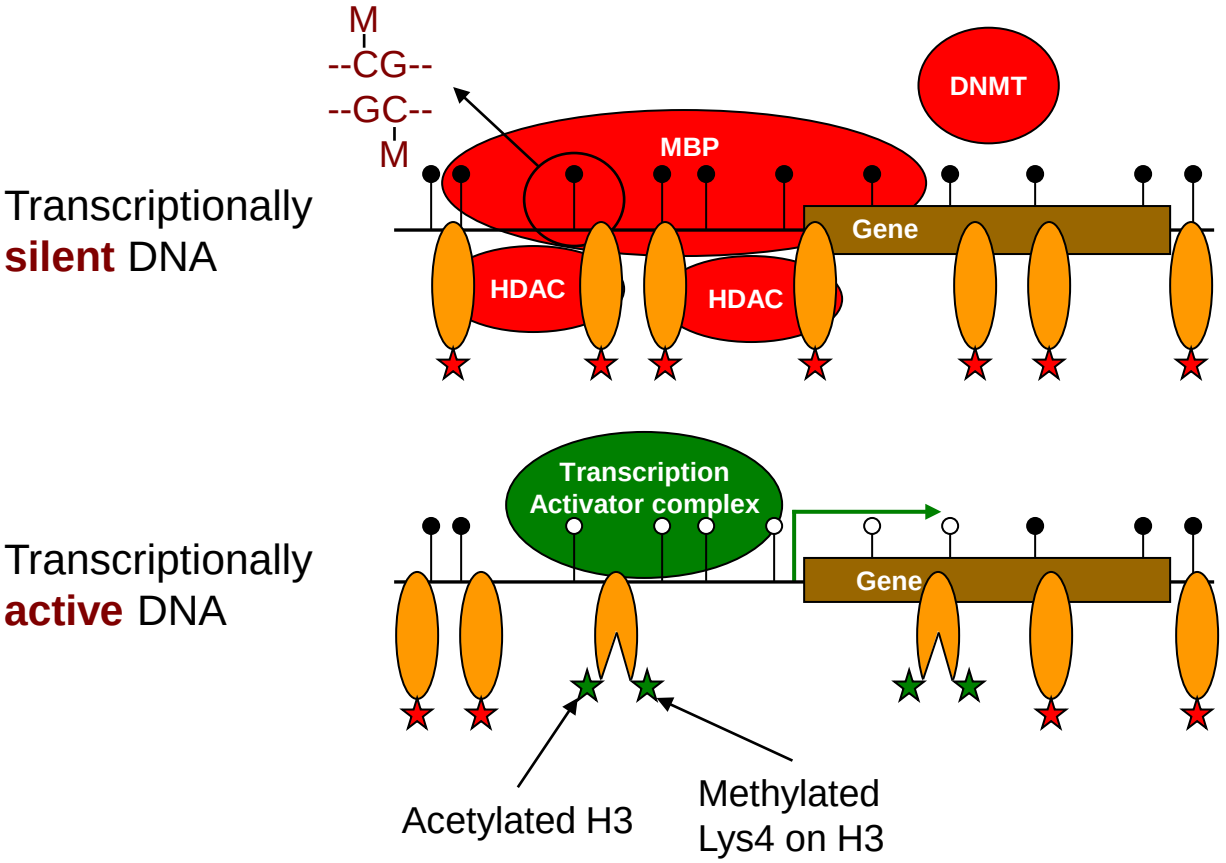


# Roles for epigenetic mechanisms

- Controls gene expression by regulating accessibility and recruiting chromatin modifiers

The simplified (and outdated) text book view



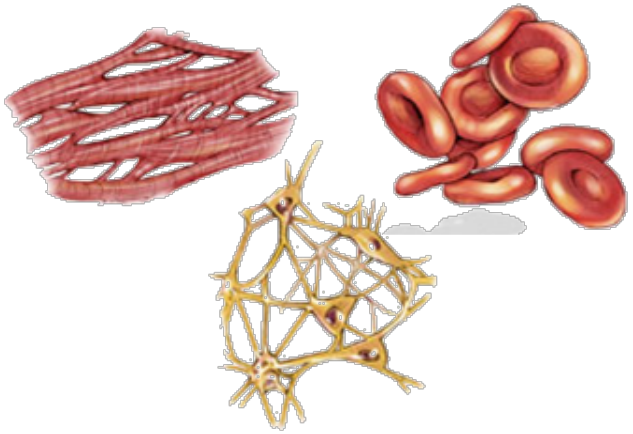

Note: The order of events (cause and consequence) is not known

# Epigenetic mechanisms

## Memory and variation

1. Controls gene expression by regulating accessibility and recruiting chromatin modifiers in interaction with transcription factors.
2. Stable, long-term, but in principle reversible.
3. Transmitted during cell division, particularly mitosis (‘genetic’).

Epigenome: the whole of epigenetics marks in a cell.



# Human Epigenome Projects

IHEC

International Human Epigenome Consortium

Home | Areas of focus | Standard Operating Procedures | Tools / Useful Information | Policies and Guidelines | IHEC Structure | Outreach and Training | Feedback | Intranet

**Links**

The EPIGENOME Network of Excellence

The focal point for the European epigenetics research community

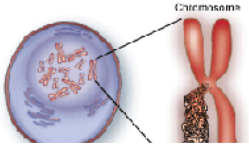
Centre for Epigenetics

Centre of Excellence funded by The Danish National Research Foundation.

**Overview**

**What is the International Human Epigenome Consortium?**

The deciphering of the human genome sequence has helped our understanding of biological processes in health and diseases. However, the way in which the genomic information is organized within the cell, through epigenetic processes, is known to play a major role in regulating gene expression and in controlling specific cellular functions. Epigenetic processes

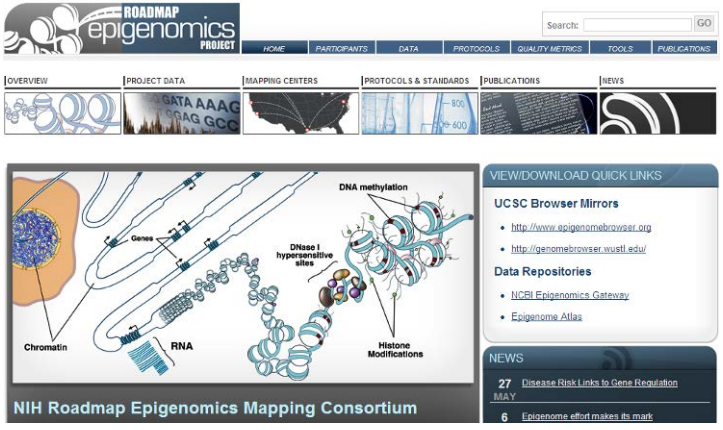


**Consortium goals**

**Primary Goals**

1. Coordinate the production of reference maps of human epigenomes for key cellular states relevant to health and diseases. To have a substantial coverage of the human epigenome, the IHEC sets the ambitious goal to decipher at least 1000 epigenomes within the next 7-10 years. To reach this goal, the consortium will use robust and validated technologies to generate:

There is one human (reference) genome. How many epigenomes?



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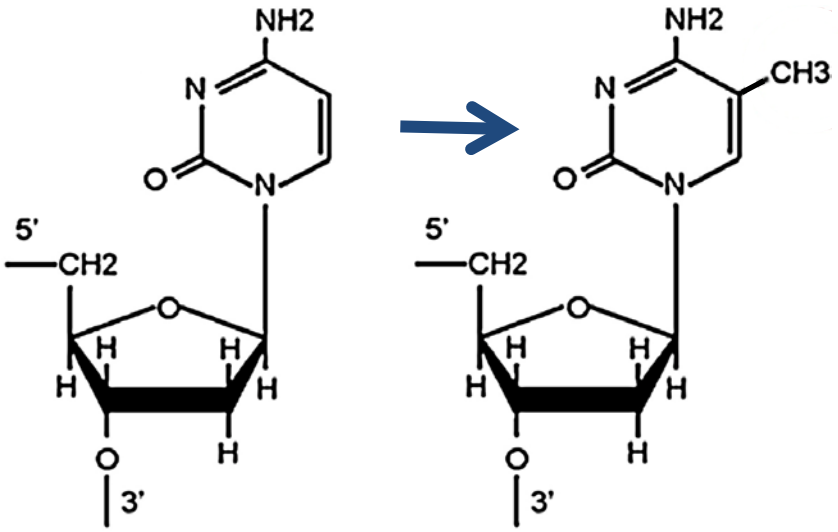
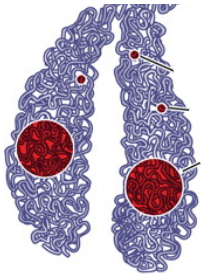
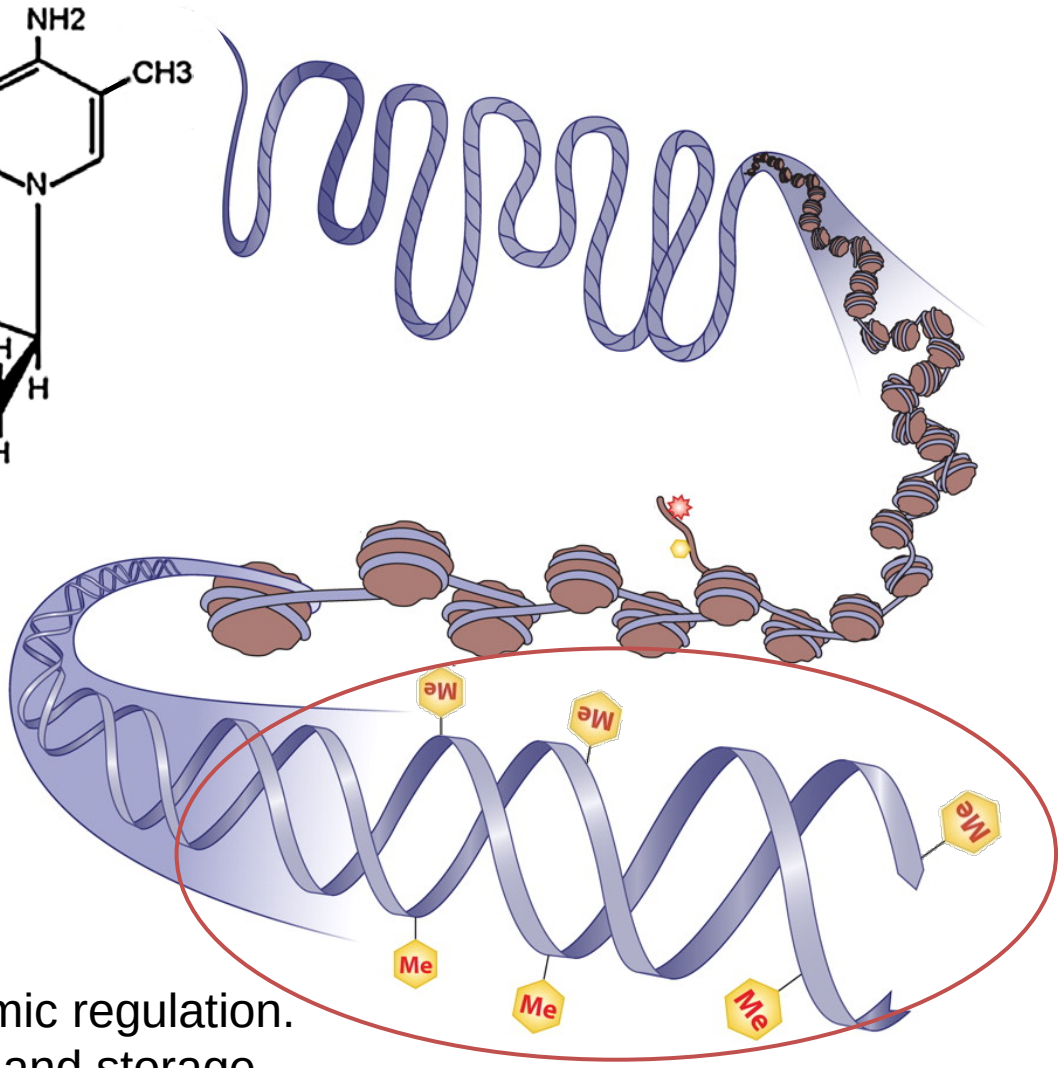
# Focus on DNA methylation

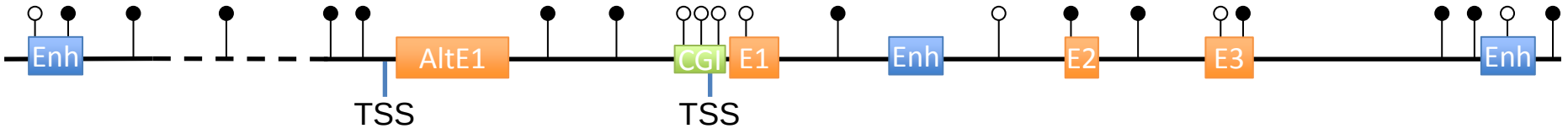





- Signals altered genomic regulation.
- Standard biomaterial and storage.
- High-throughput profiling.

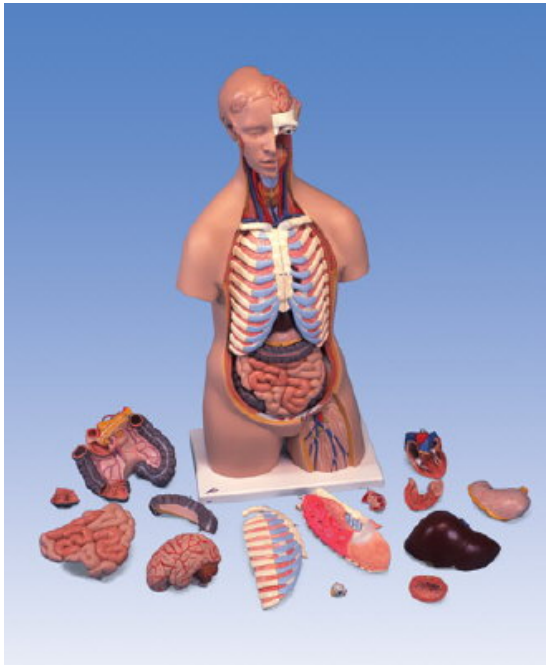
# Effect methylation depends on genomic context




→ Genomic annotation is essential when interpreting DNA methylation data

# First practical

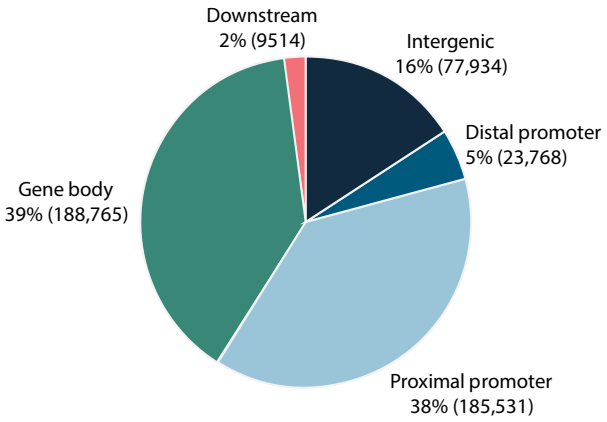
- Characterizing DNA methylation differences between tissues.
- Genome-wide methylation of close to 500 thousand CpG sites.



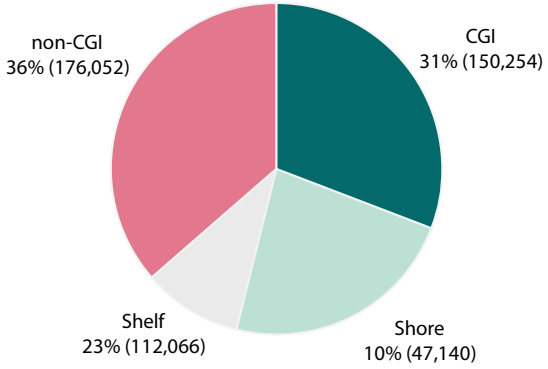
# Illumina 450k DNA methylation array

- Informative: ~482,000 CpGs (<2%) but many annotations
- Affordable: ~200 euro per sample
- Fast: >1000 samples a week
- Data: easy to manage (amount and complexity)

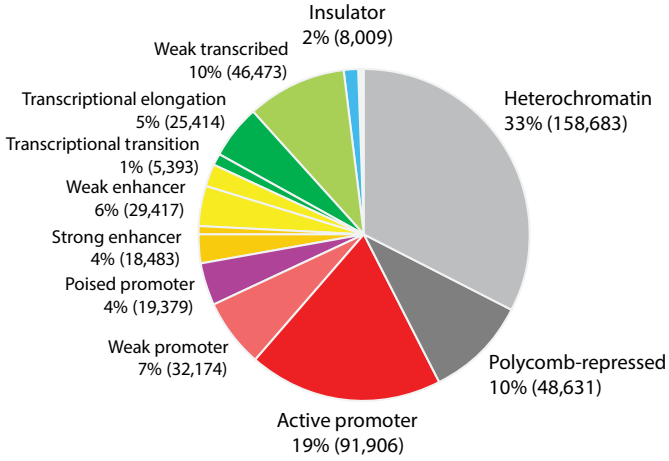
## Genic




## CpG island




## Chromatin



# Principle methylation array

M? M? M? M? x 485,000 (out of 28M)

…CCTGGTACGTCTAGCCGTAATTAGCTCGATTCCGGT…

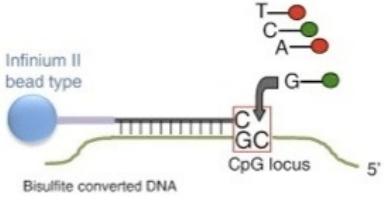
Bisulfite conversion

unmethylated methylated

…UUTGGTUGTUTAG… …UUTGGTCGTUTAG…

unmeth signal meth signal

β-value = meth / (meth + unmeth)



# DNA methylation levels

M?

…CCTGGTACGTCTAG…

β-value = meth / (meth + unmeth)

- A DNA molecule?
- A cell?
- A population of cells?
- An organ?

Amazing
DISCOVERIES