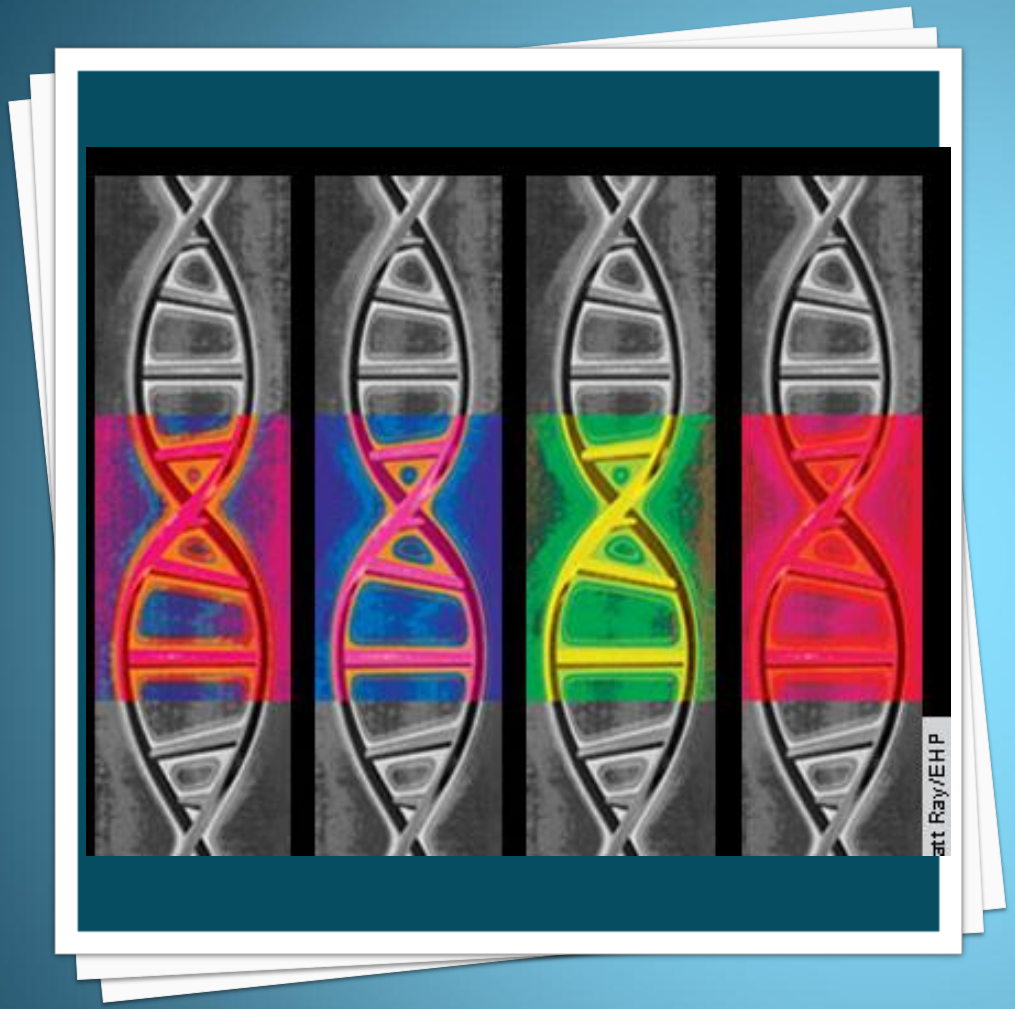
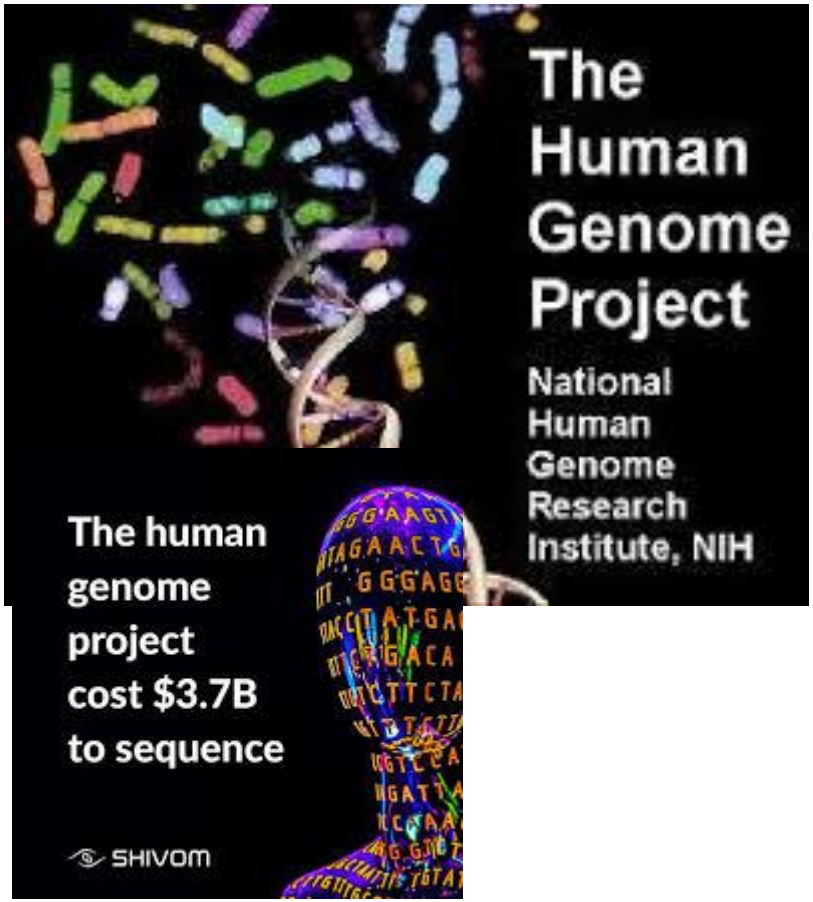
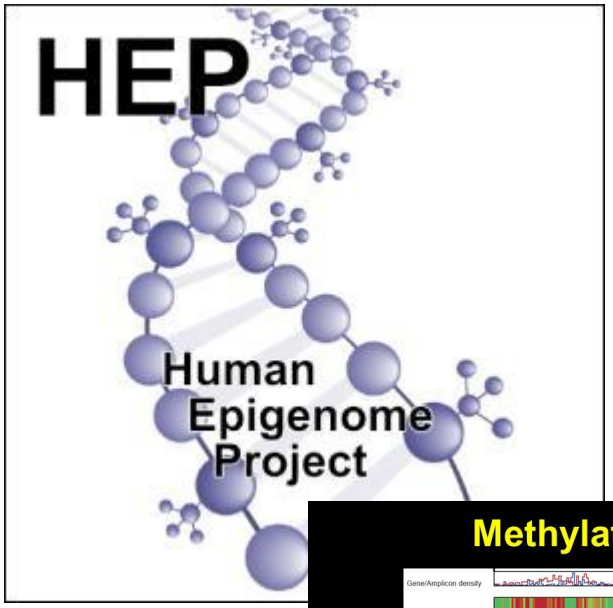
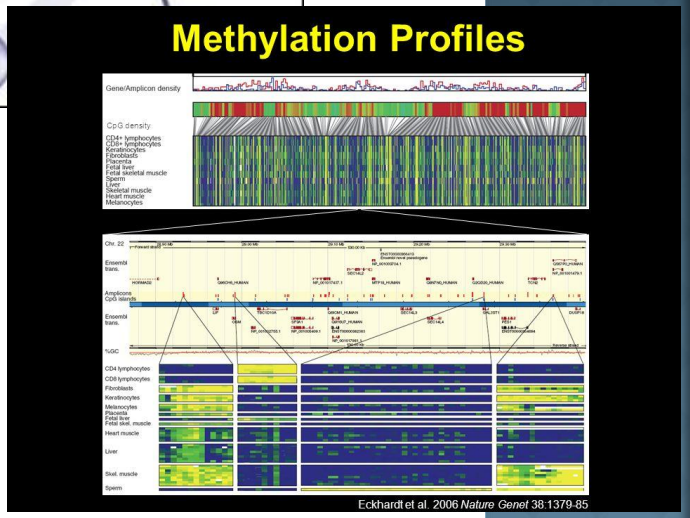


GENERAL BIOLOGY
EPIGENETICS





2008



Encyclopedia of DNA Elements called ENCODE

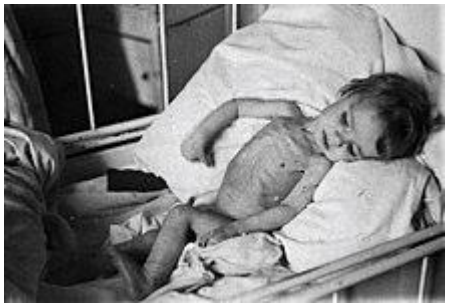
20,000 to 25,000 genes

1990-2003

A range of matters remains to be resolved, such as the relationships between the epigenetic players (the epigenetic code) and how the environment and/or aging modulate the epigenetic marks.

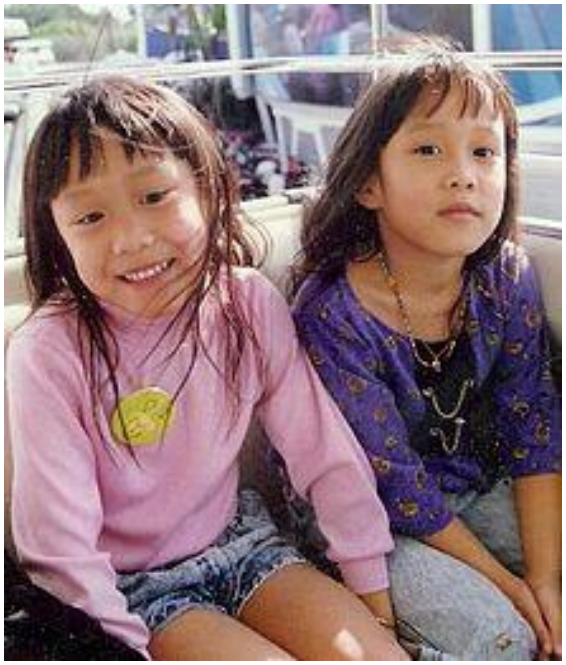
THE DUTCH FAMINE OF 1944-1945

A rare case of a famine which **took place in a modern, developed, country.**
The **well-documented experience** has helped scientists to measure the effects of famine on human health.

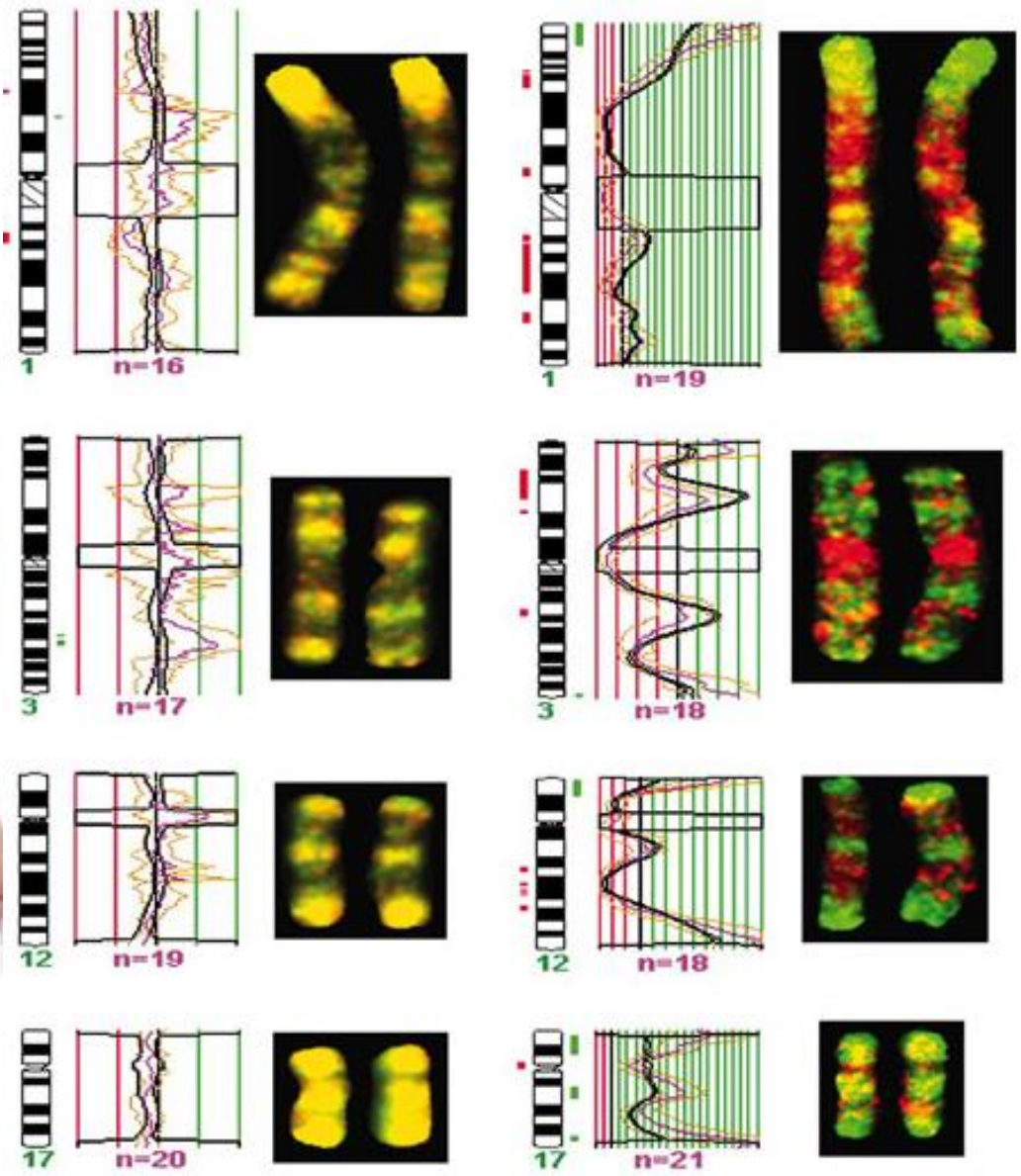


- **the children of the women** who were pregnant during the famine were smaller more susceptible to diabetes, obesity, cardiovascular disease, microalbuminuria,
- when these children grew up and had children those children were thought to *also* be smaller than average.

Genetically identical



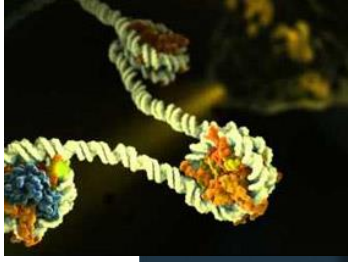
MONOZYGOTIC TWINS



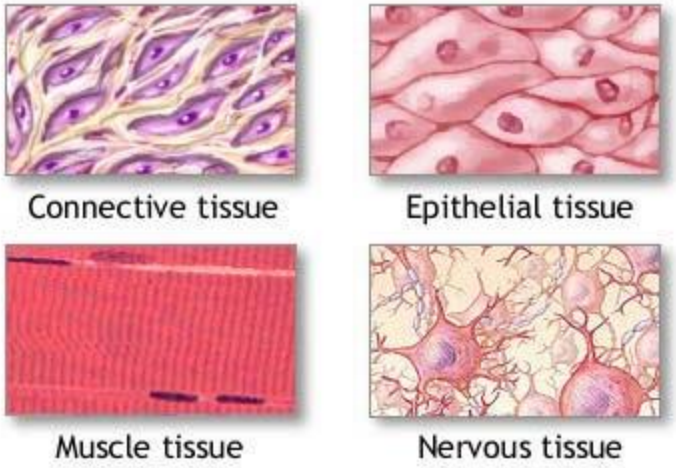
3-year-old twins

50-year-old twins

ORGANISM

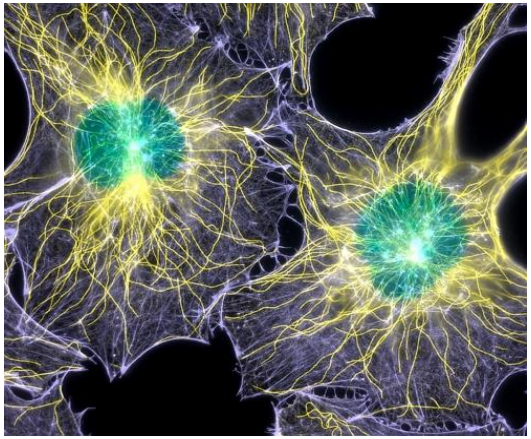


Tissue

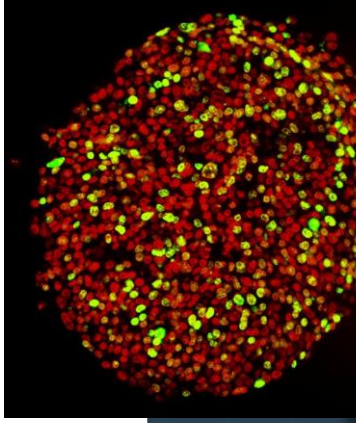


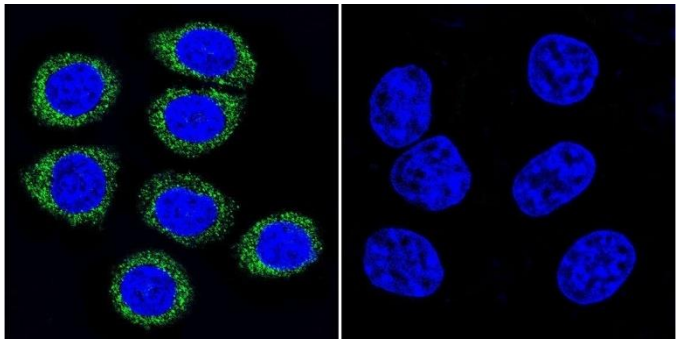
DNA

CELLS



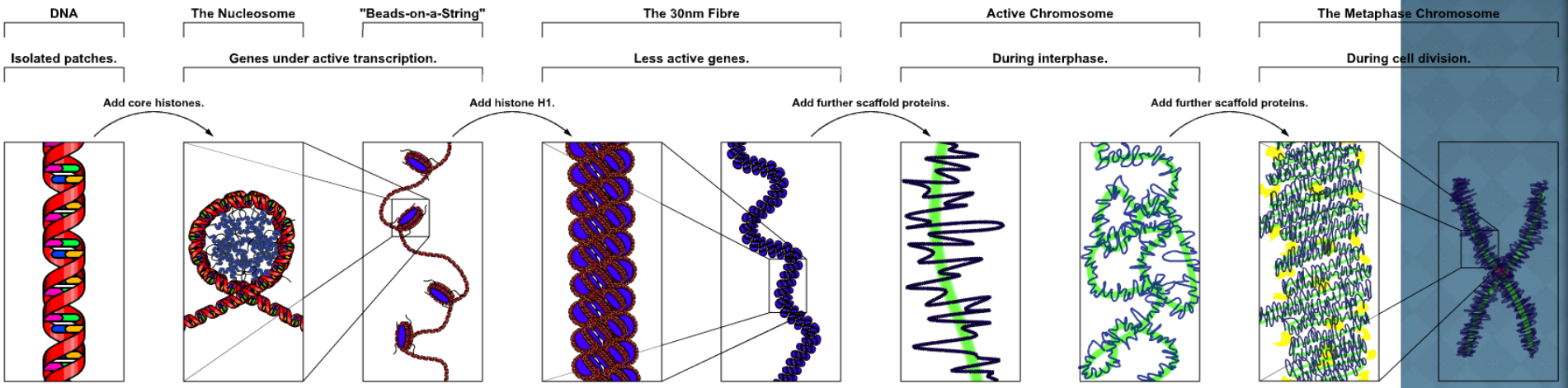
DNA: 2 m





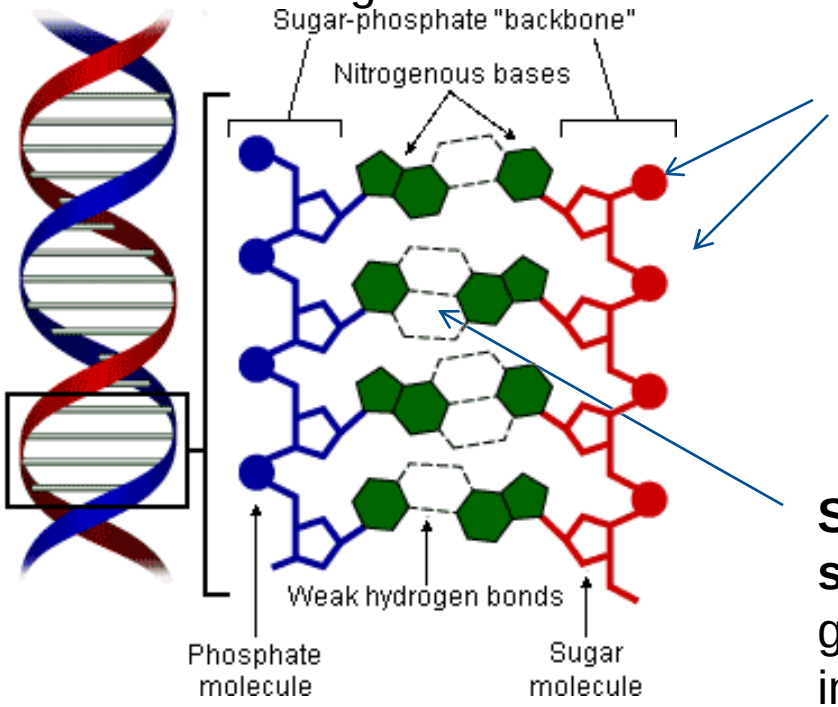
Cell nucelus: 10 µm

DNA packaging in the nucleus



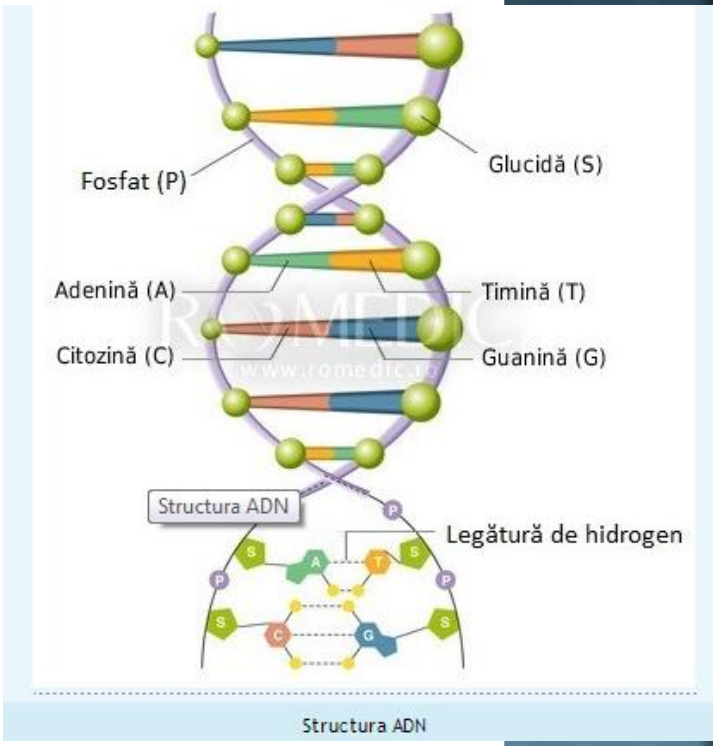
DNA STRUCTURE AND ORGANIZATION

Tertiary structure given by the three-dimensional spatial organization

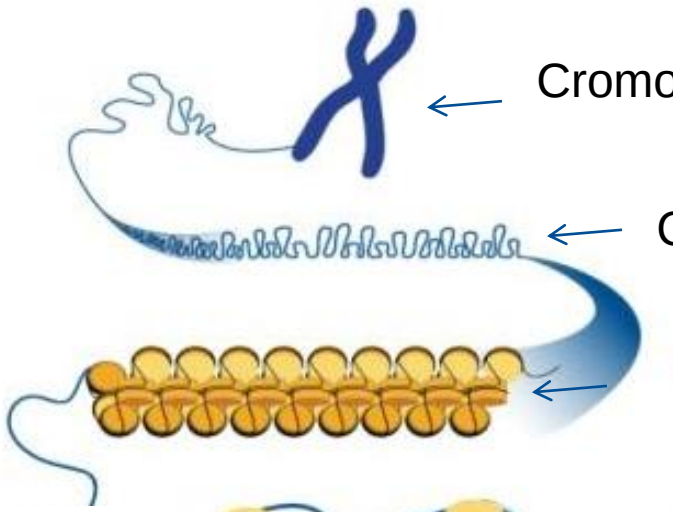


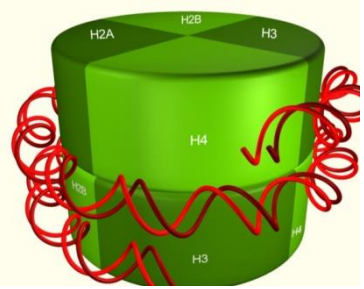
Primary structure

Secondary structure given by the interaction between the bases



DNA STRUCTURE AND ORGANIZATION





Core histone (8 histone overlapping) Around which is wound a loop of DNA (146 bp)

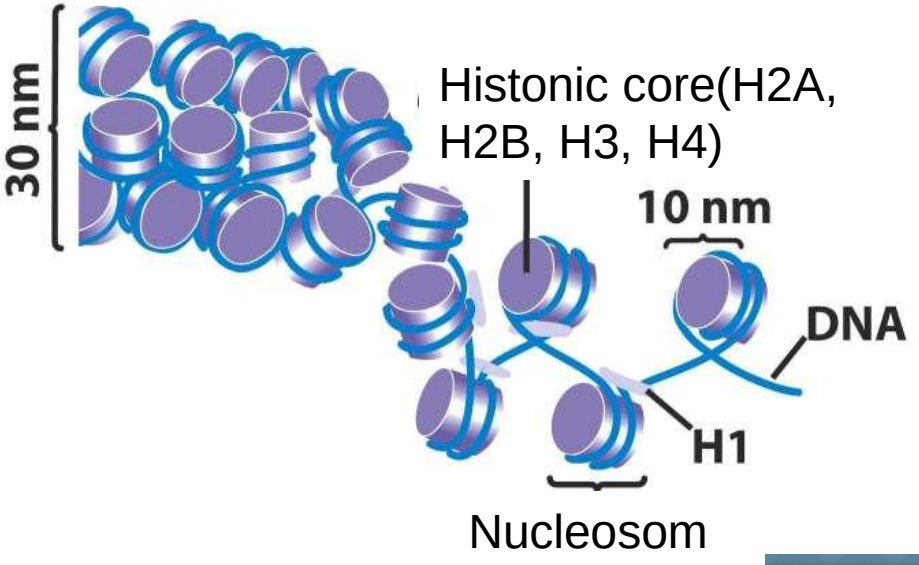
The **quaternary structure** is given by the interaction of DNA with other molecules involved in the folding and packaging of DNA in the nucleus.

HISTONE INVOLVED IN DNA PACKAGING

There are basic proteins with high affinity to DNA present in all eukaryotes.

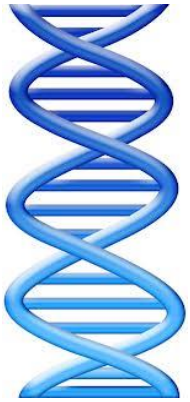
In eukaryotes five types of histones H1, H2A, H2B, H3, H4. With the exception of H1, other types (especially H3, H4) have a stable structure well conserved in evolution.

- H2A - rich in leucine
- H2B - rich in serine
- H3 - rich in arginine and cystein
- H4 - rich in arginine

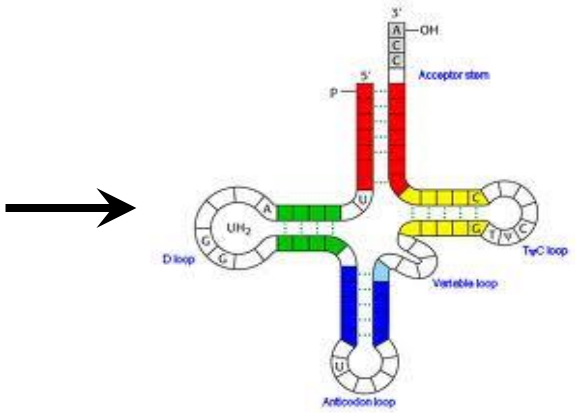


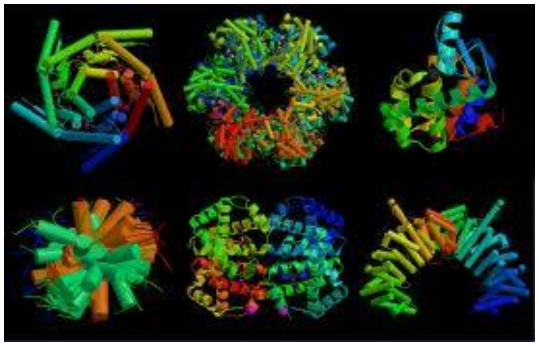
The central dogma of molecular biology, F. Crick in 1958

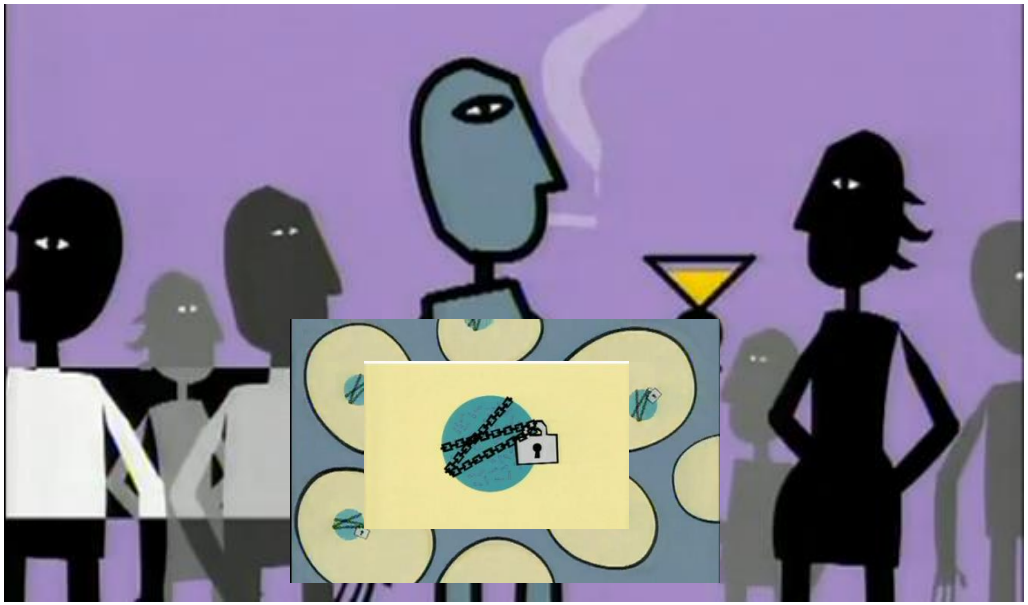
DNA



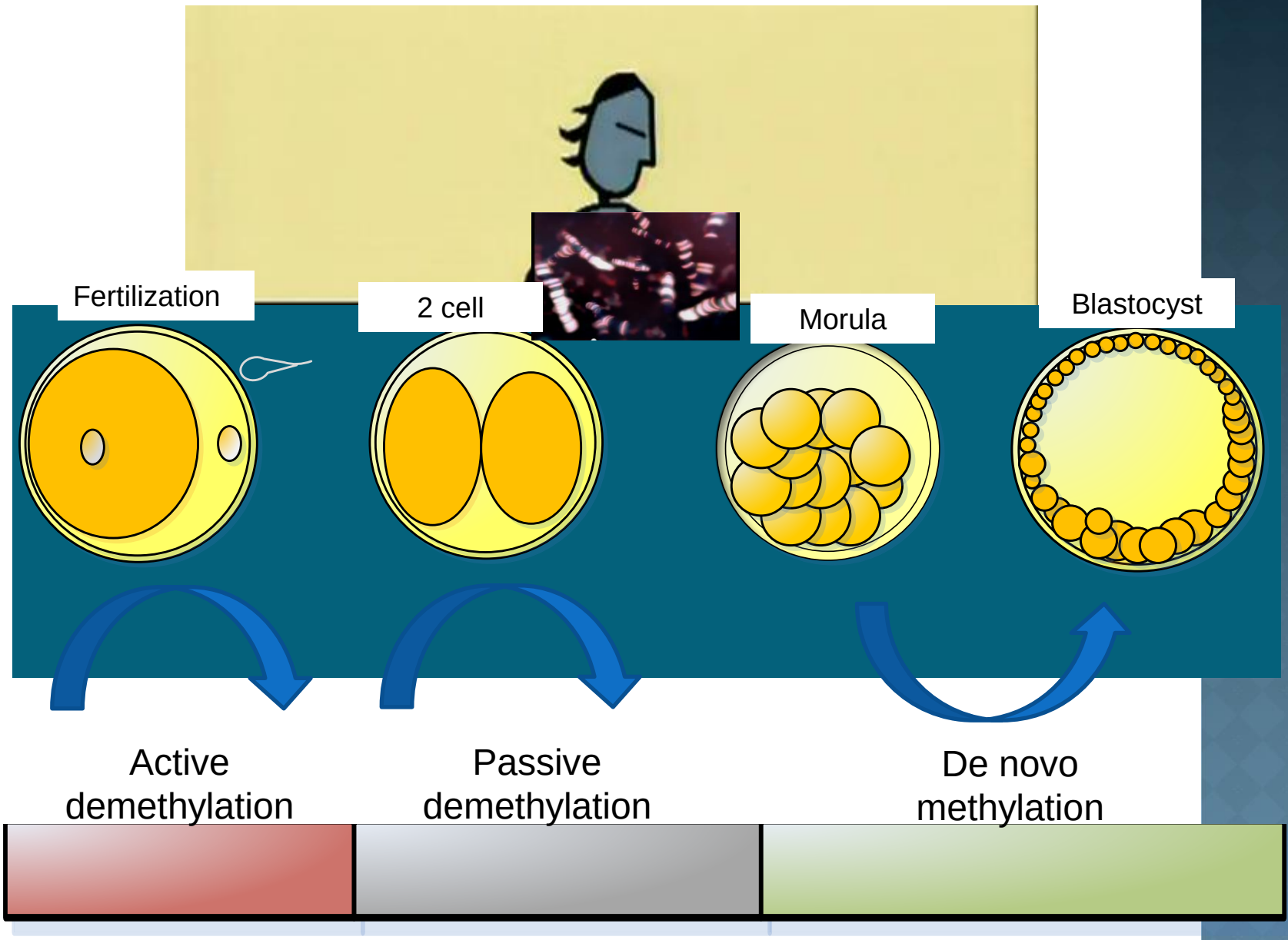
RNA

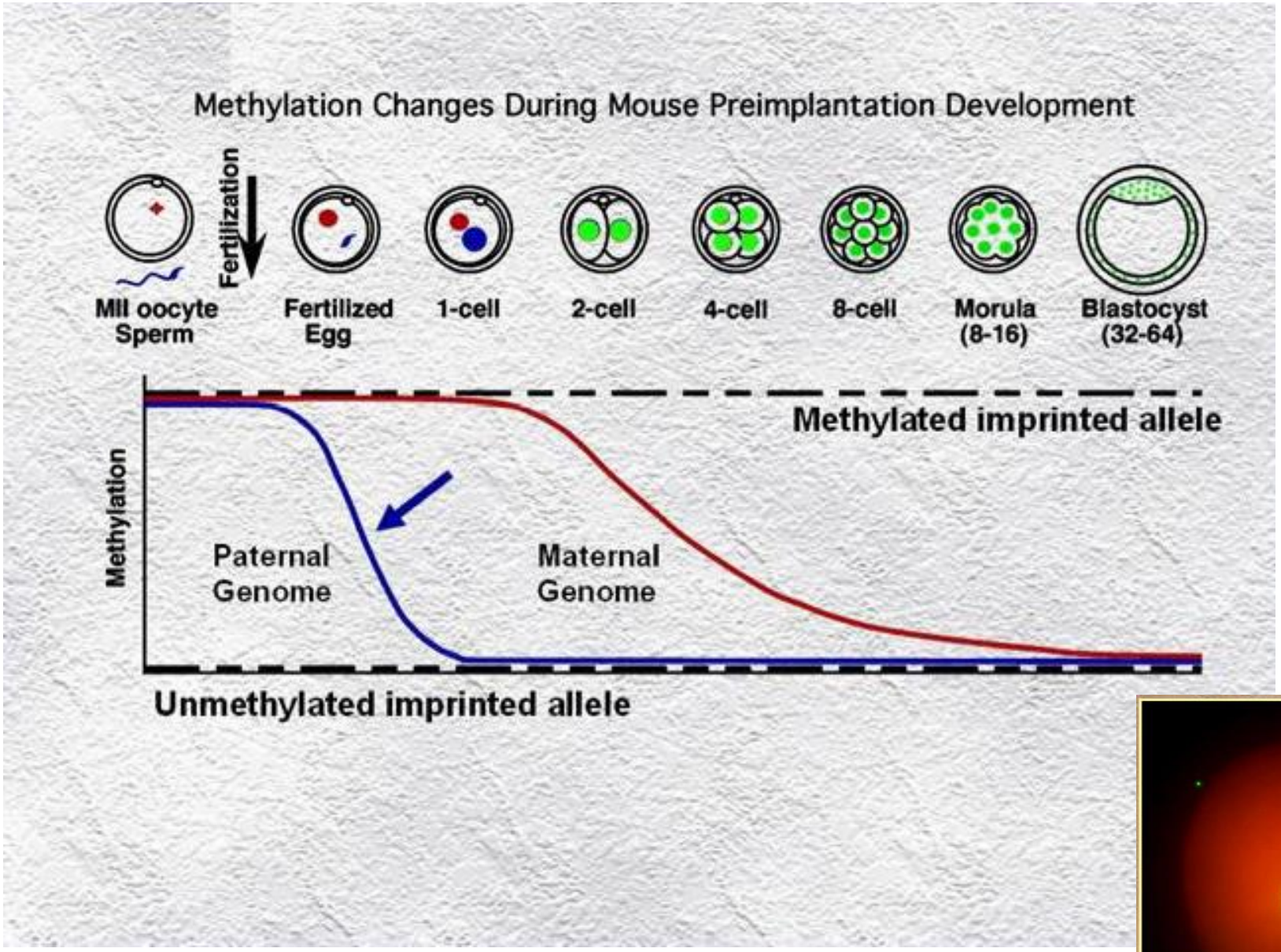


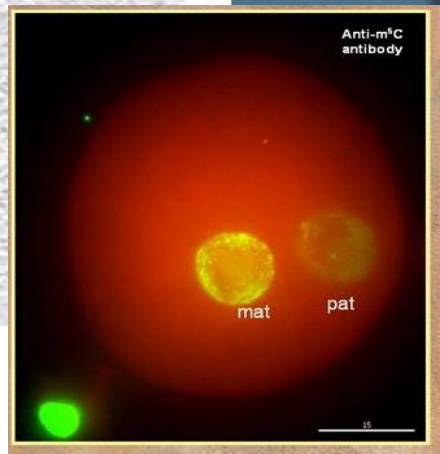




Epigenetic mechanisms and gene filtering infromation




Methylation Changes During Mouse Preimplantation Development
Fertilization
MII oocyte
Sperm
Fertilized
Egg
1-cell
2-cell
4-cell
8-cell
Morula
(8-16)
Blastocyst
(32-64)
Methylated imprinted allele
Methylation
Paternal
Genome
Maternal
Genome
Unmethylated imprinted allele


Anti-m5C
antibody
mat
pat

Zygote

ACATAGACATACACACTGTTGATTAGGGAGATAGTGACAGATCCATTACAGCACCATACCATGAT
GTTTTTATTACCAGGATGATCACCATTGGGTACCATTTACCAGGATTACACAGTTTTAGATGACC
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TTTATTACCAGGATGATCACCATTGGGTACCATTTACCAGGATTACACAGTTTTAGATGACCAGT
AGCTATTAGAGGATTTTAAATTTATTTAGGATTTTATGGGATTGATAAAGGGAGATTTTTATTAT
AGGACATAGACATACACACTGTTGATTAGGGAGATAGTGACAGATCCATTACAGCACCATACCAT
GATGTTTTTATTACCAGGATGATCACCATTGGGTACCATTTACCAGGATTACACAGTTTTAGATG
ACCAGTAGCTATTAGAGGATTTTAAATTTATTTAGGATTTTATGGGATTGATAAAGGGAGATTTA
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How is the diversity of cell types created and maintained in multi-cellular organisms?

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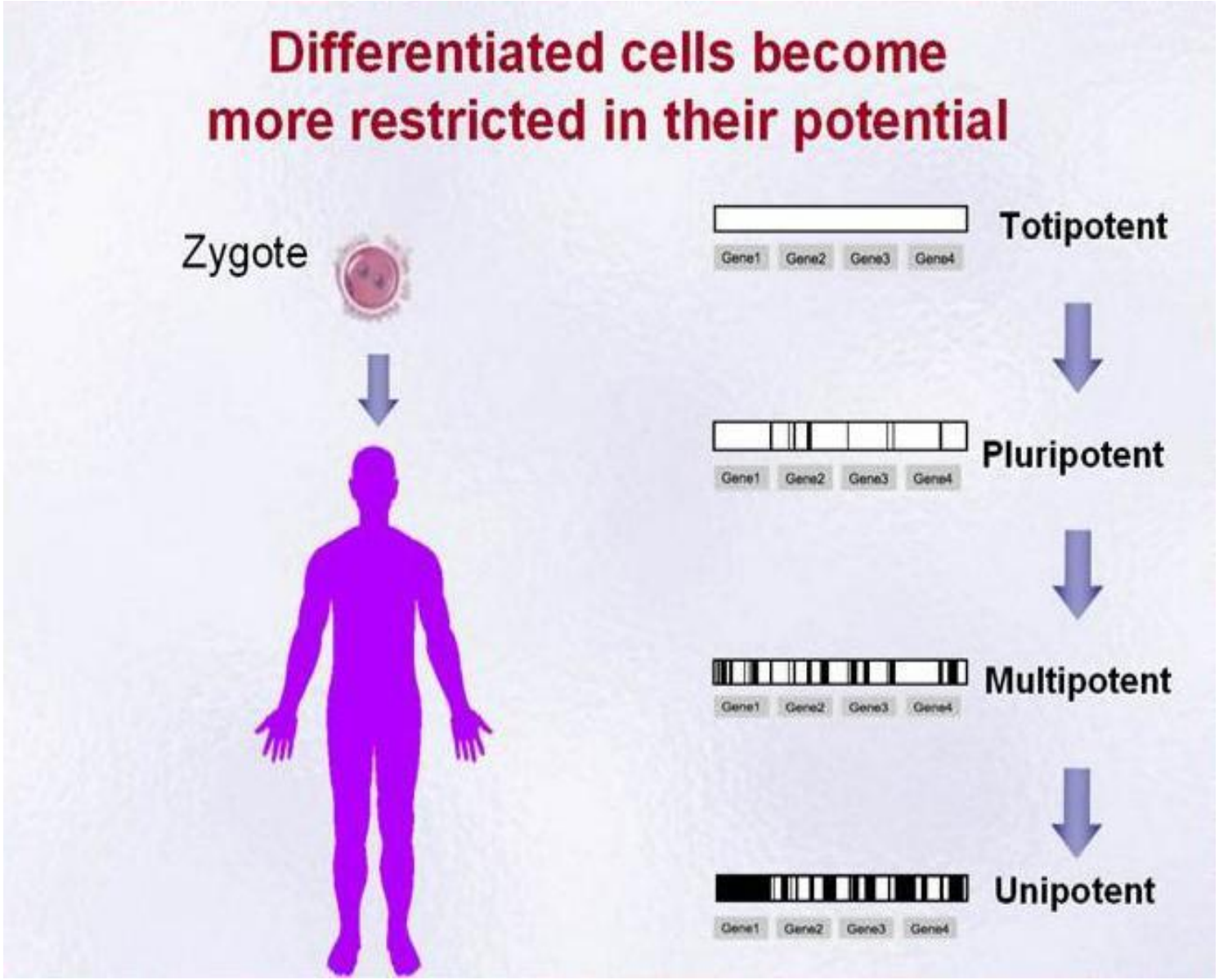
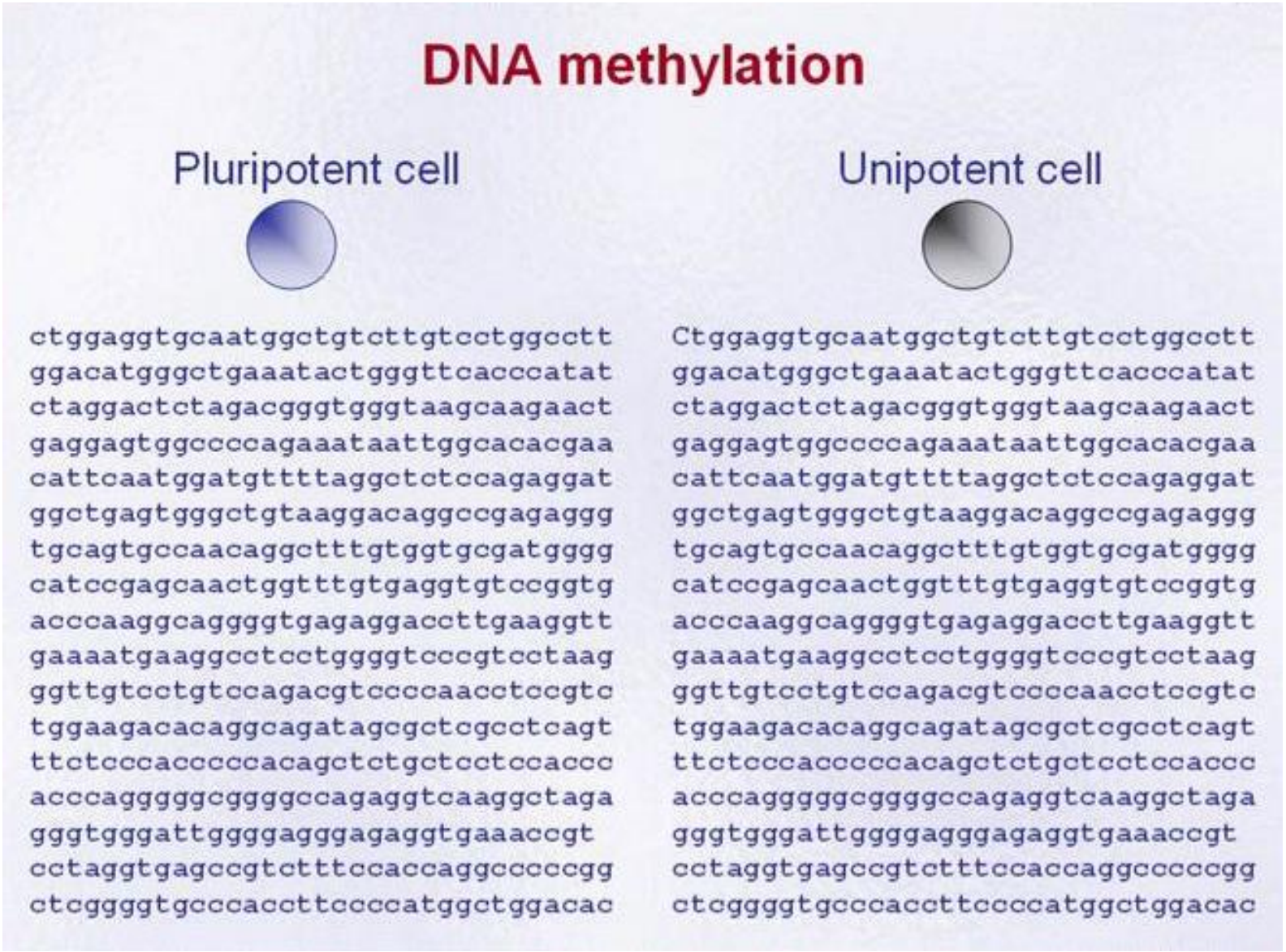
GATGTTTTTATTACCAGGATGATCACCATTGGGTACCATTTACCAGGATTACACAGTTTTAGATG
ACCAGTAGCTATTAGAGGATTTTAAATTTATTTAGGATTTTATGGGATTGATAAAGGGAGATTTA
ACATAGACATACACACTGTTGATTAGGGAGATAGTGACAGATCCATTACAGCACCATACCATGAT

Alex Meissner, Henry Stewart Talks



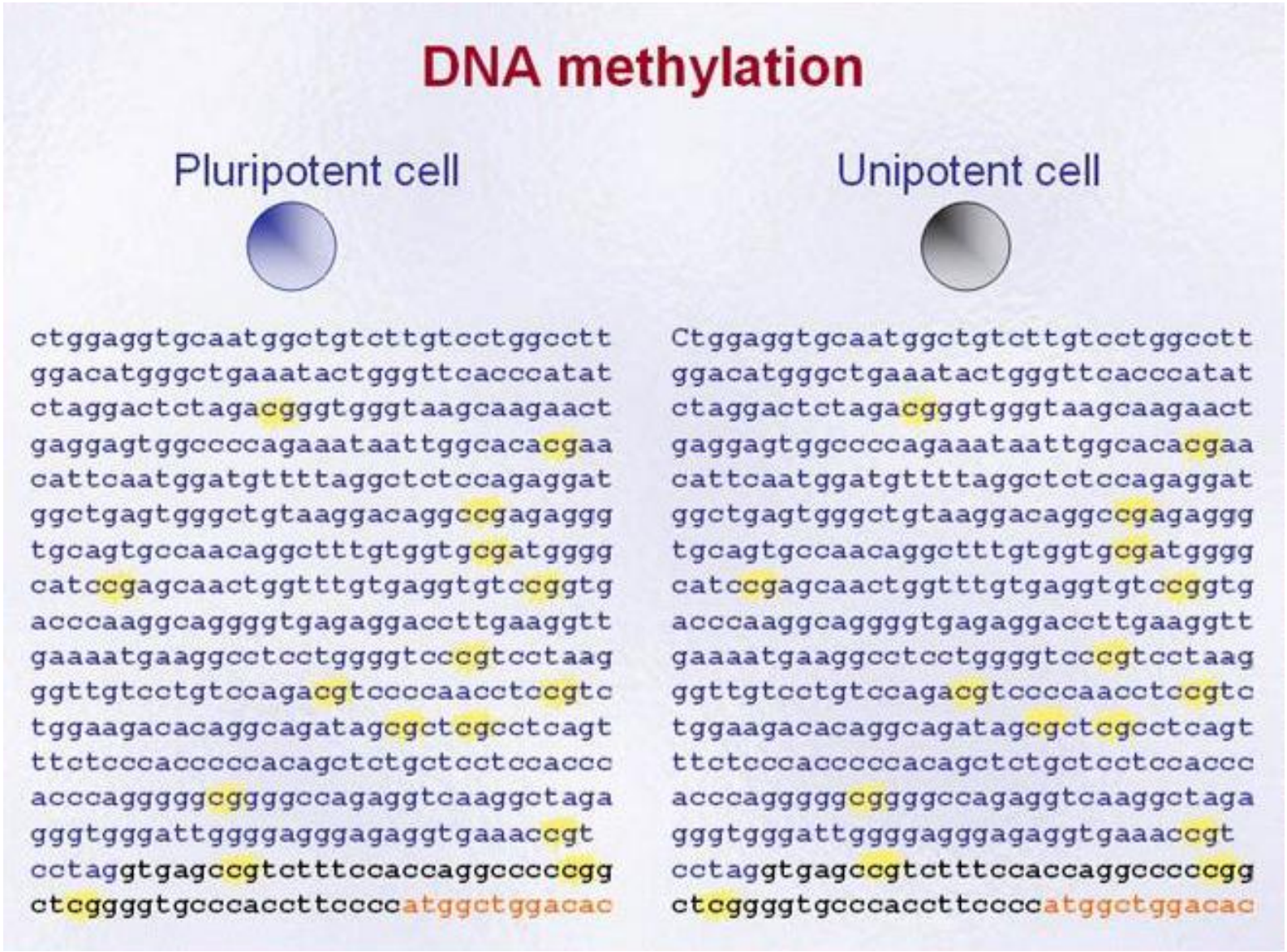
Alex Meissner, Henry Stewart Talks

DNA methylation

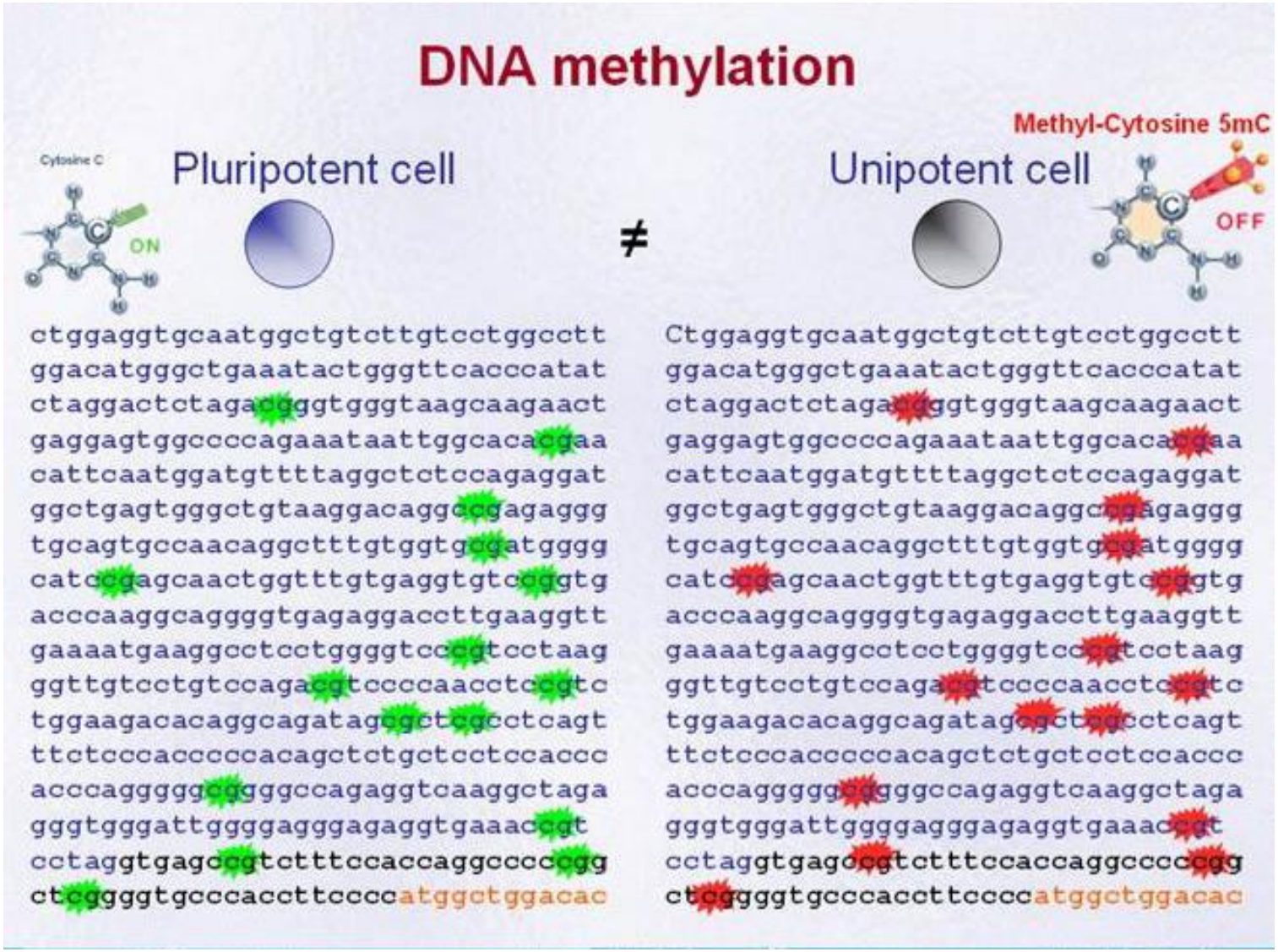


Alex Meissner, Henry Stewart Talks

DNA methylation



Alex Meissner, Henry Stewart Talks

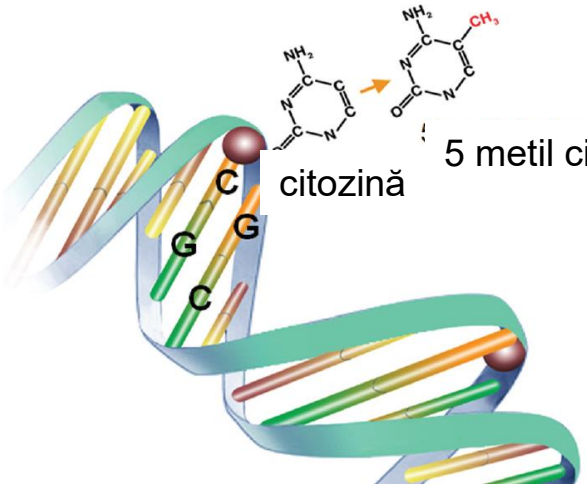


Alex Meissner, Henry Stewart Talks

DNA METHYLATION

DNA methylation

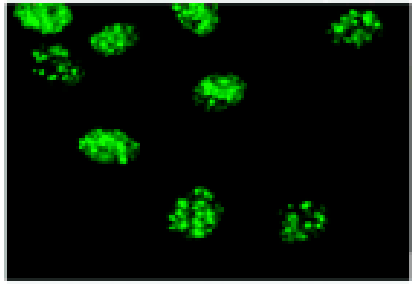
DNMT1 → DNMT3a DNMT3b

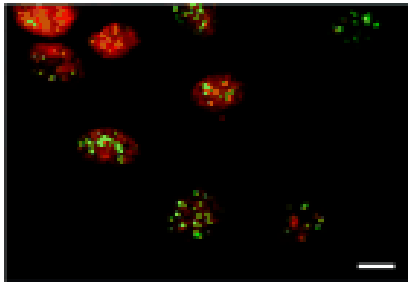


citozină

5 metil citozină

Addition of CH3 groups at C5 of cytosine within CpG islands so called

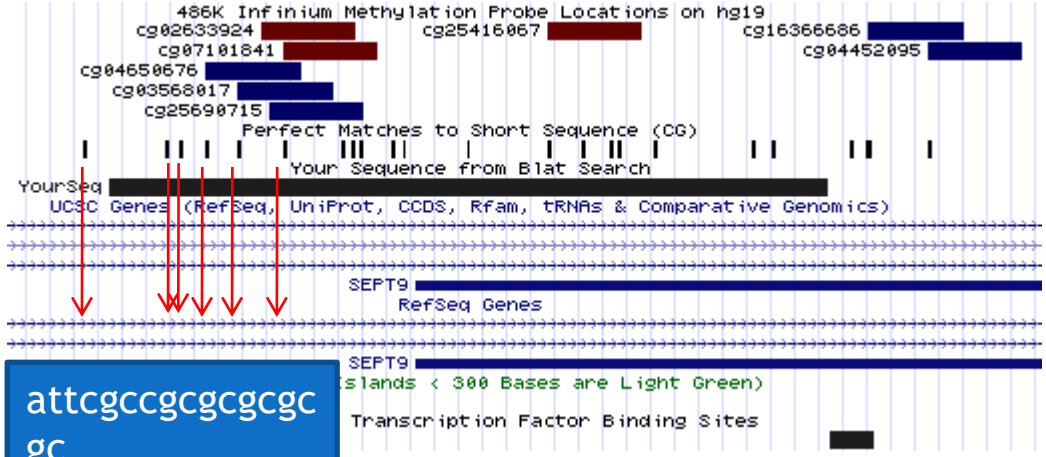




DNA methylation → Histone deacetylation → Condensation of chromatin

CPG ISLANDS

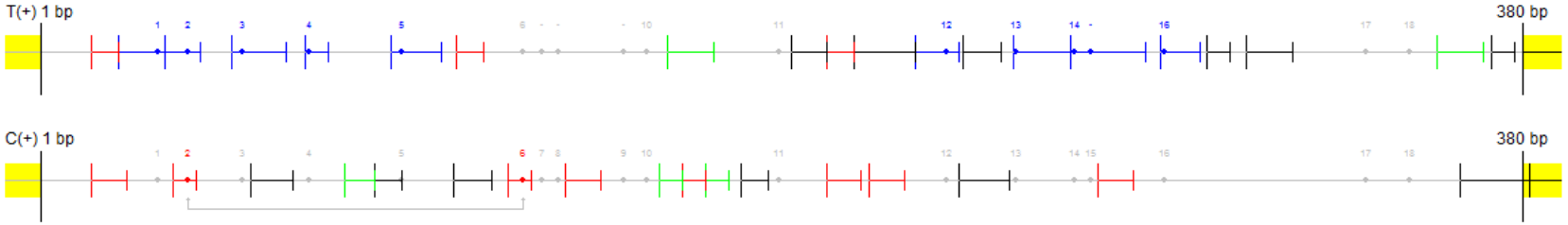
CpG islands



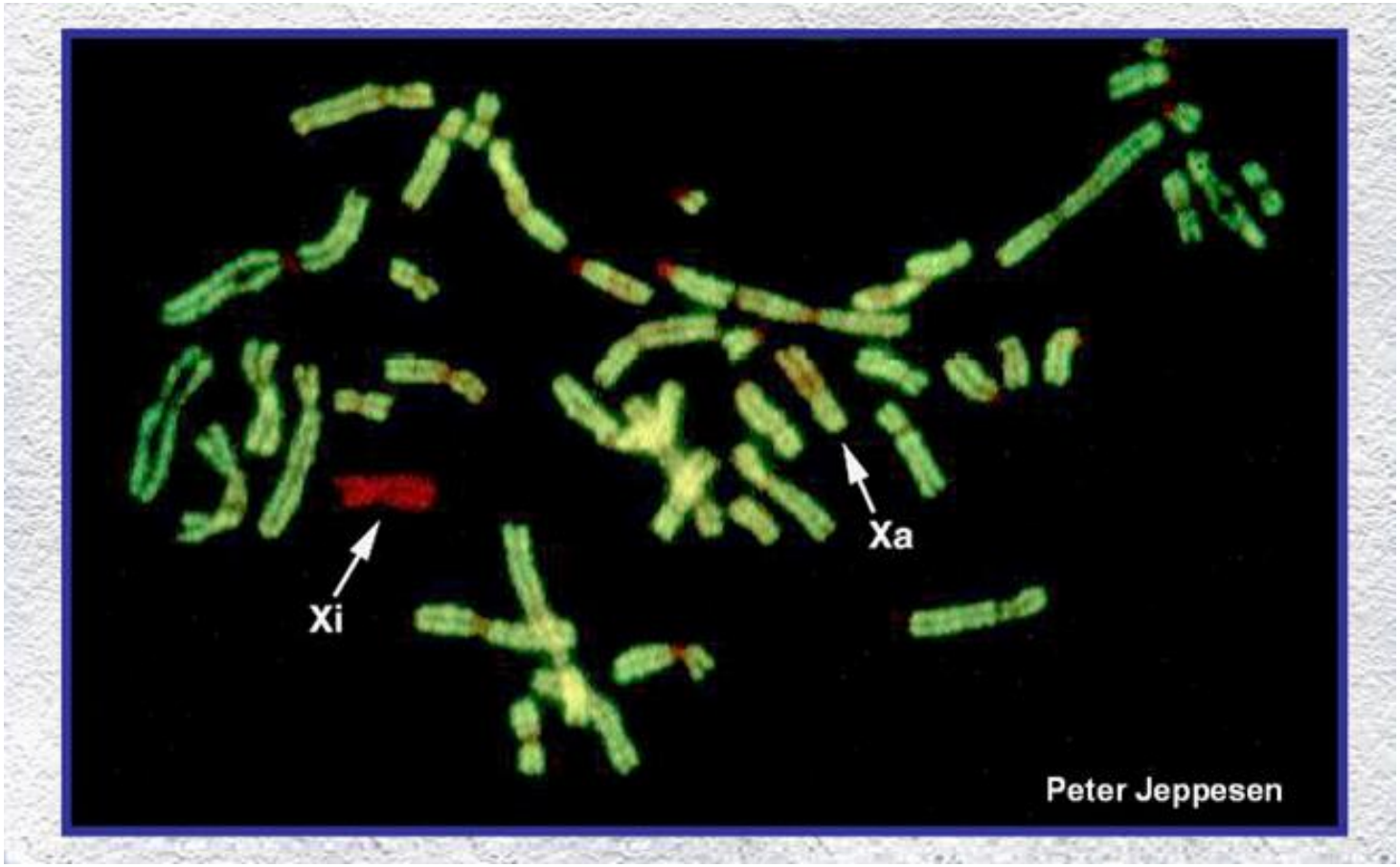
CpG islands

attcgccgcgcgcgc
gc

inSilico Assay Prediction

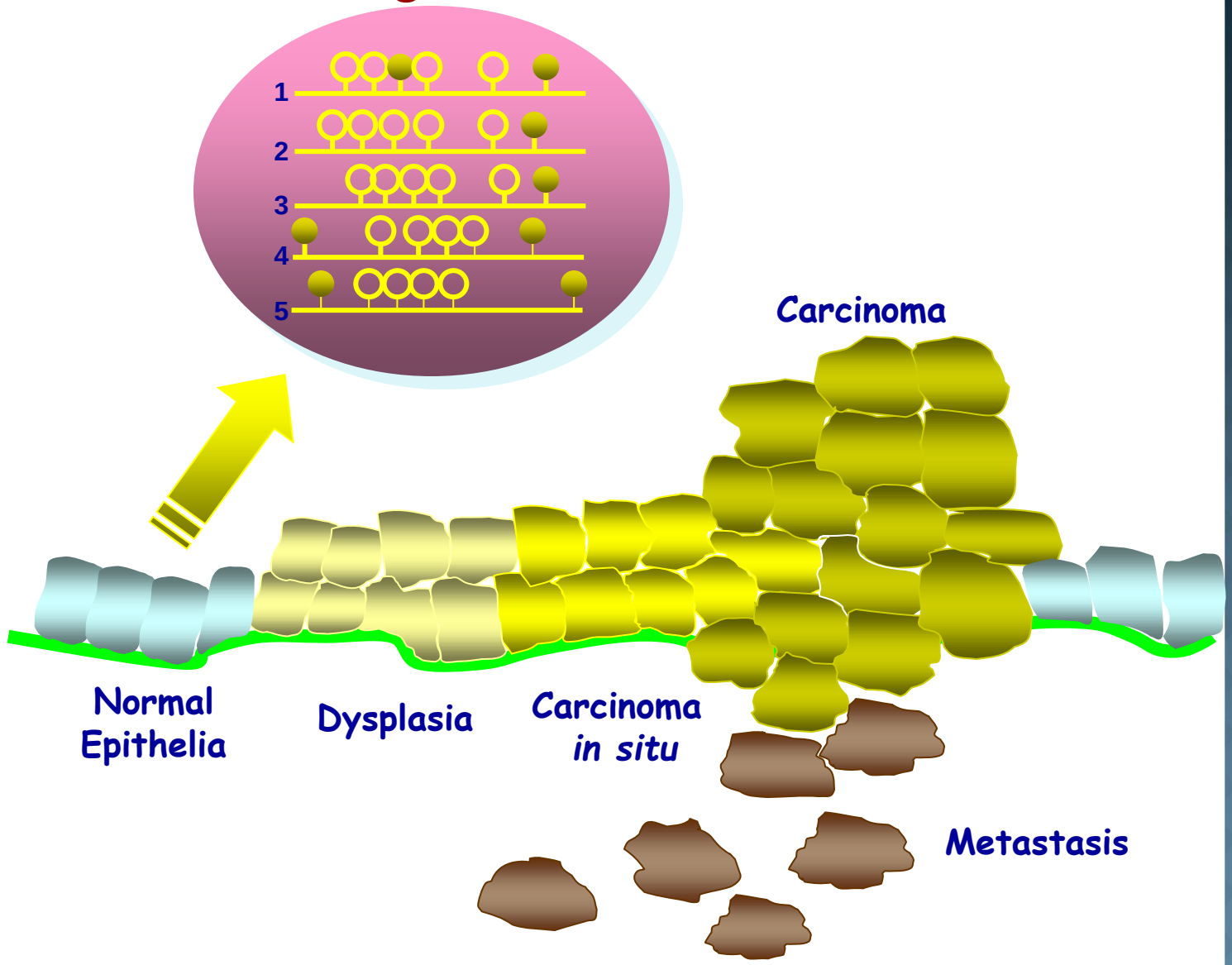


X CHROMOSOME INACTIVATION

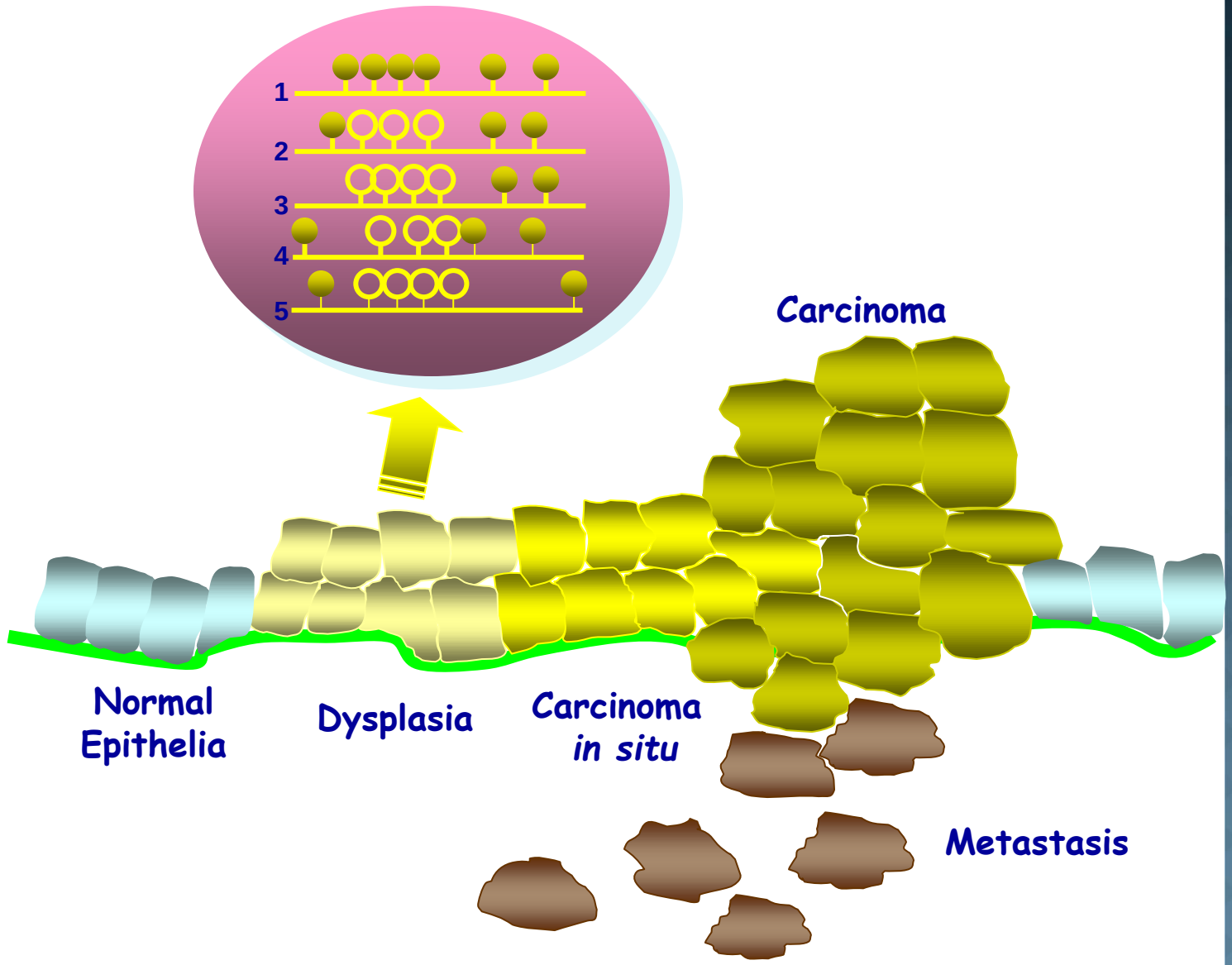


Barbara Migeon, Henry Stewart Talks

CpG island methylation: a stable and detectable signal in cancer



CpG island methylation: a stable and detectable signal in cancer



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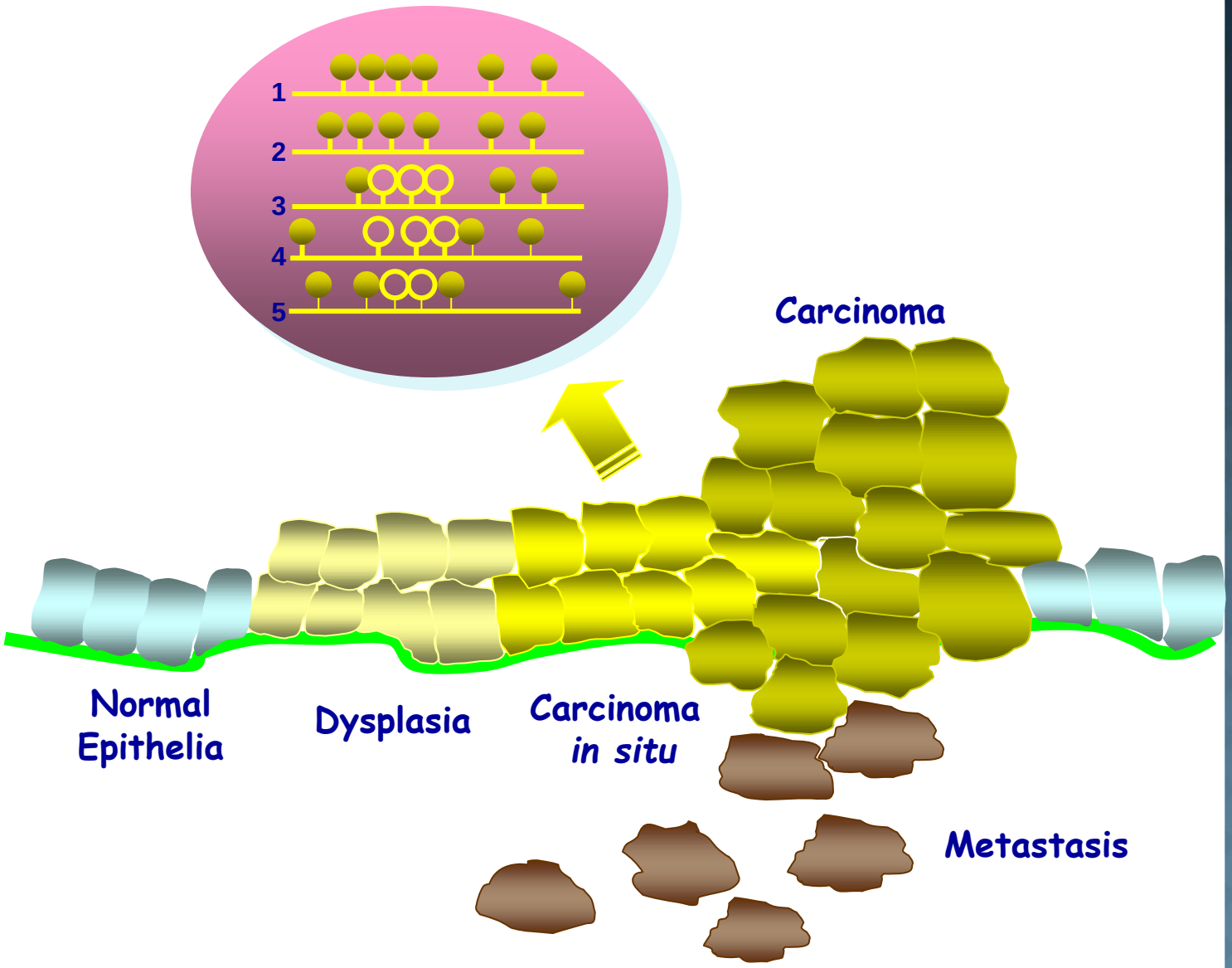
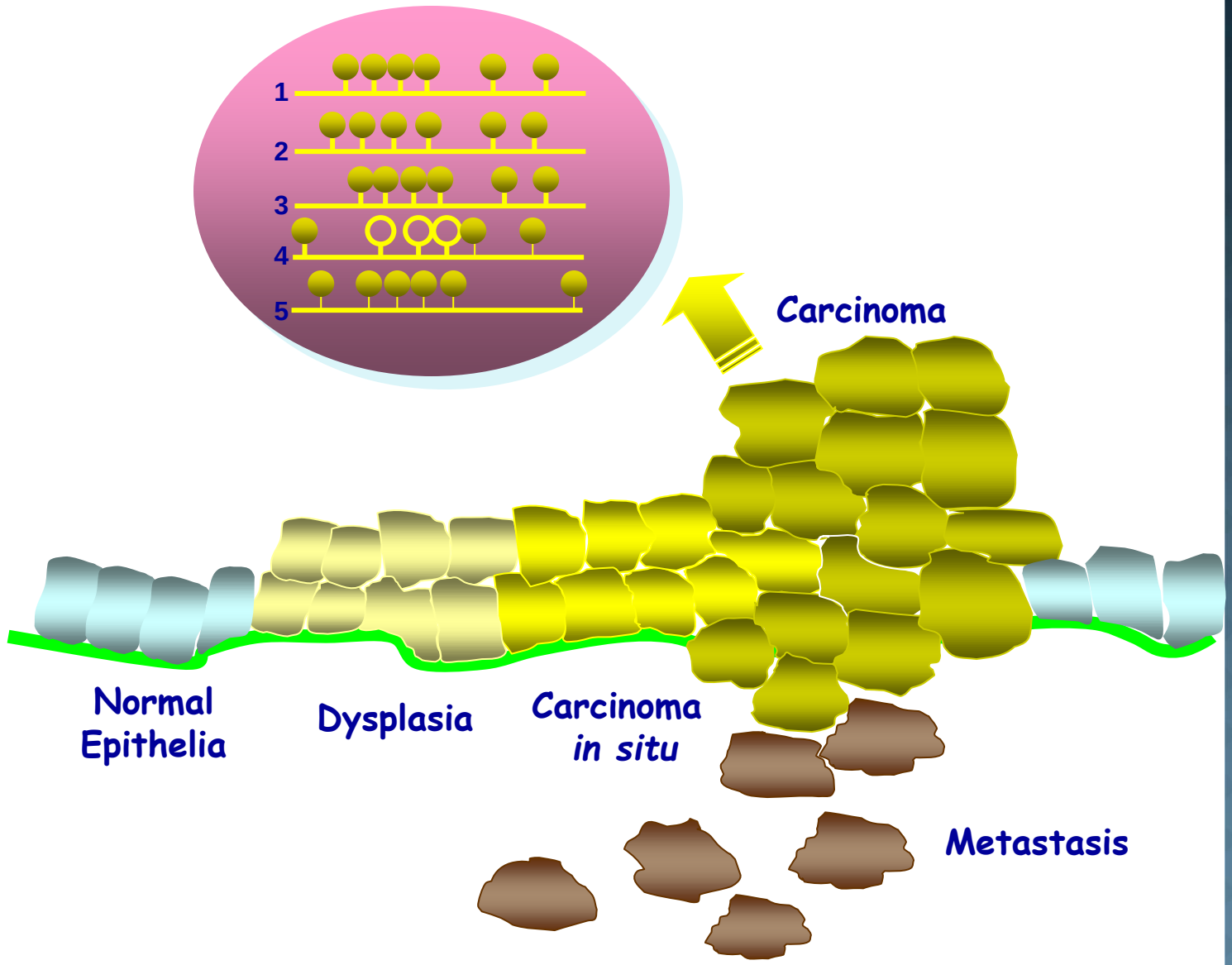
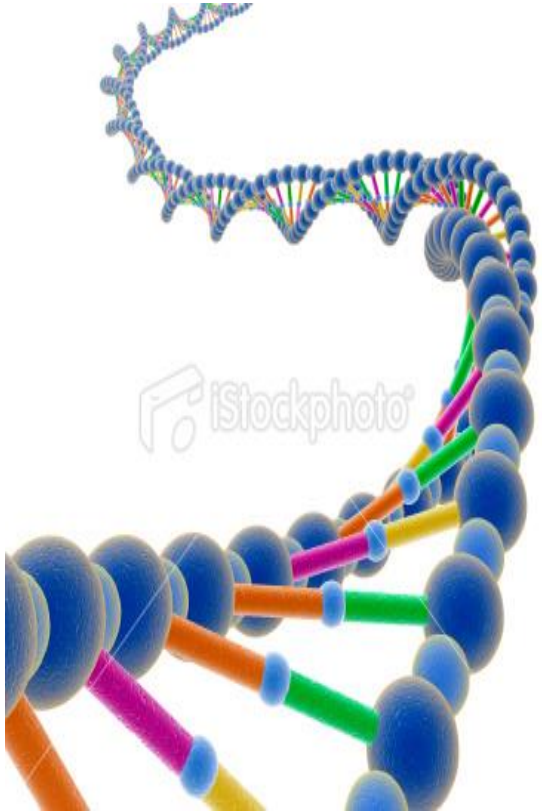


CpG island methylation: a stable and detectable signal in cancer



CHANGES IN DNA METHYLATION

- It is known that certain factors play an important role in controlling DNA methylation process. They can be divided into four categories:
- Ereditation



CHANGES IN DNA METHYLATION

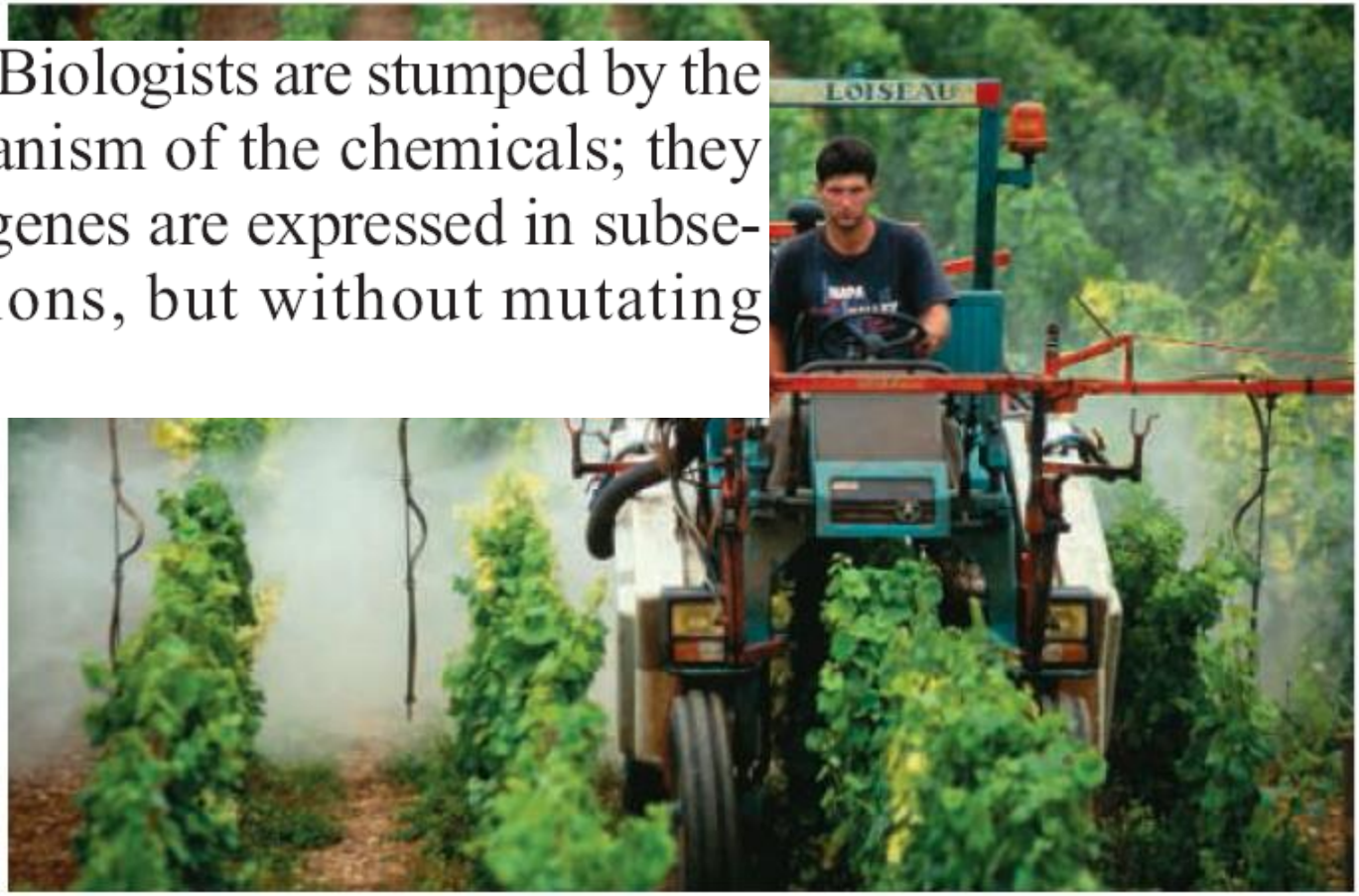
- It is known that certain factors play an important role in controlling DNA methylation process. They can be divided into four categories:

1. Ereditation
2. Environment

DEVELOPMENTAL BIOLOGY

Endocrine Disrupters Trigger Fertility Problems in Multiple Generations

Biologists are stumped by the apparent mechanism of the chemicals; they may alter how genes are expressed in subsequent generations, but without mutating DNA.

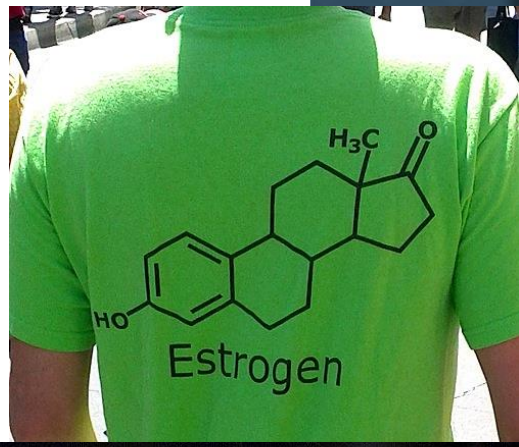


Unfertile ground. The fungicide vinclozolin, which is sprayed on vineyards like these, can cause fertility problems in male offspring of exposed rats.

CHANGES IN DNA METHYLATION

- It is known that certain factors play an important role in controlling DNA methylation process. They can be divided into four categories:

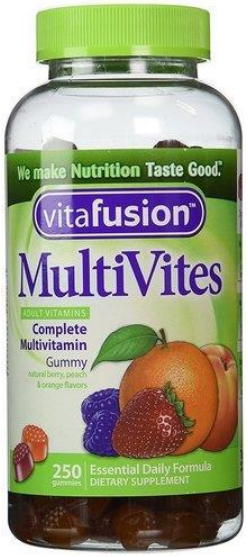
1. Ereditation
2. Environment
3. Endogens factors



CHANGES IN DNA METHYLATION

- It is known that certain factors play an important role in controlling DNA methylation process. They can be divided into four categories:

1. Ereditation
2. Environment
3. Endogens factors
4. Nutrition



PNAS

2007

Maternal nutrient supplementation counteracts bisphenol A-induced DNA hypomethylation in early development

Dana C. Dolinoy*†‡, Dale Huang*, and Randy L. Jirtle

The hypothesis of fetal origins of adult disease posits that early developmental exposures involve epigenetic modifications, such as DNA methylation, that influence adult disease susceptibility. *In utero* or neonatal exposure to bisphenol A (BPA), a high-production-volume chemical used in the manufacture of polycarbonate plastic, is associated with higher body weight, increased breast and prostate cancer, and altered reproductive function.

evidence that epigenetic patterning during early stem cell development is sensitive to BPA exposure. Moreover, maternal dietary supplementation, with either methyl donors like folic acid or the phytoestrogen genistein, negated the DNA hypomethylating effect of BPA. Thus, we present compelling evidence that early developmental exposure to BPA can change offspring phenotype by stably altering the epigenome, an effect that can be counteracted by maternal dietary supplements.

Epigenetics, meaning 'above (epi-) genetics', is the study of gene expression regulation that cannot be directly attributed to changes in the DNA sequence.

Among the 3 billion nucleotides in our genome, less than 2% are responsible for coding proteins.

Epigenetics is a management system that determines how to use the DNA.

Epigenetic effects can last for several generations