

Introduction to Cancer Epigenetics

Nov 02 2025

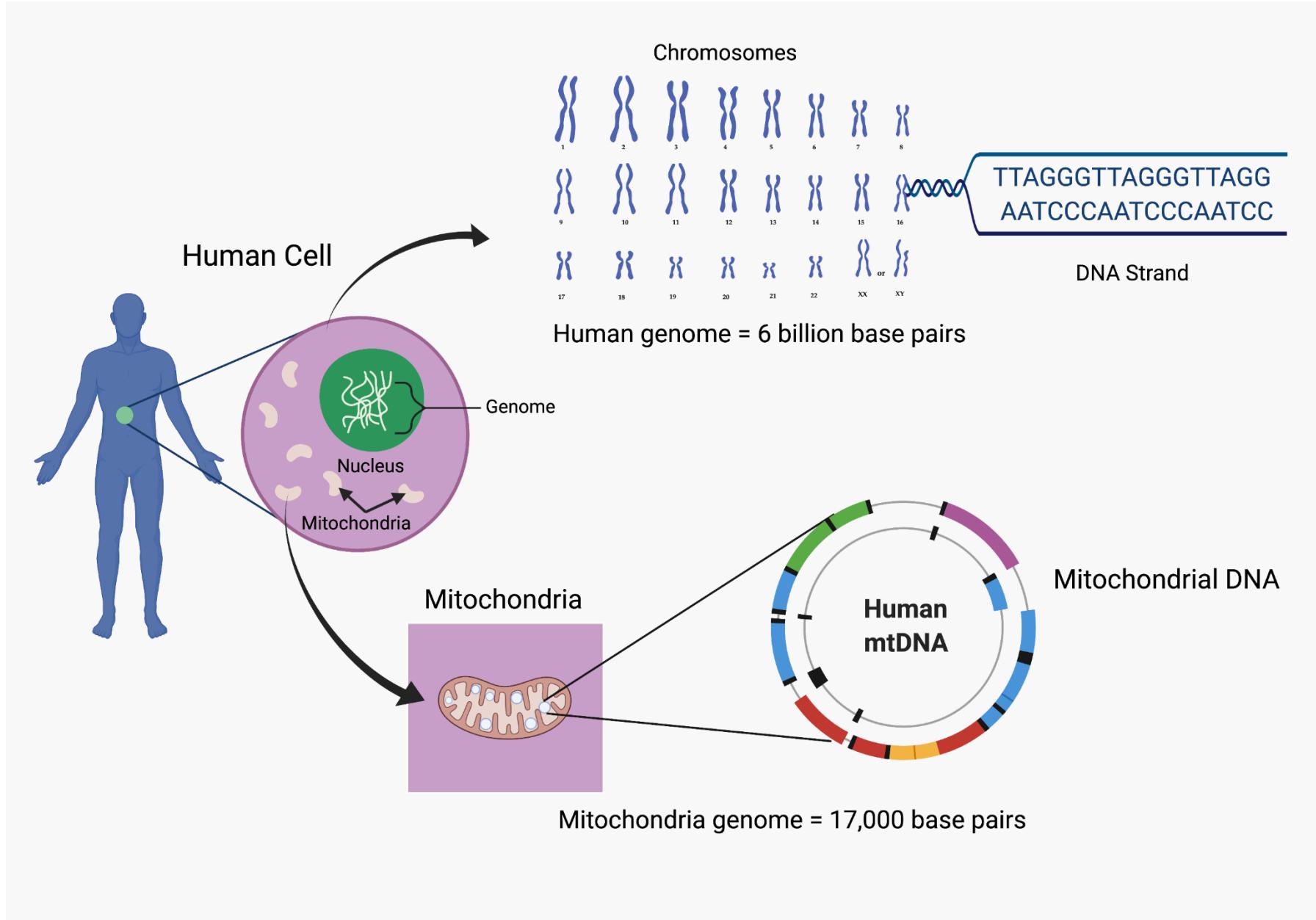
Phuc Loi Luu, PhD

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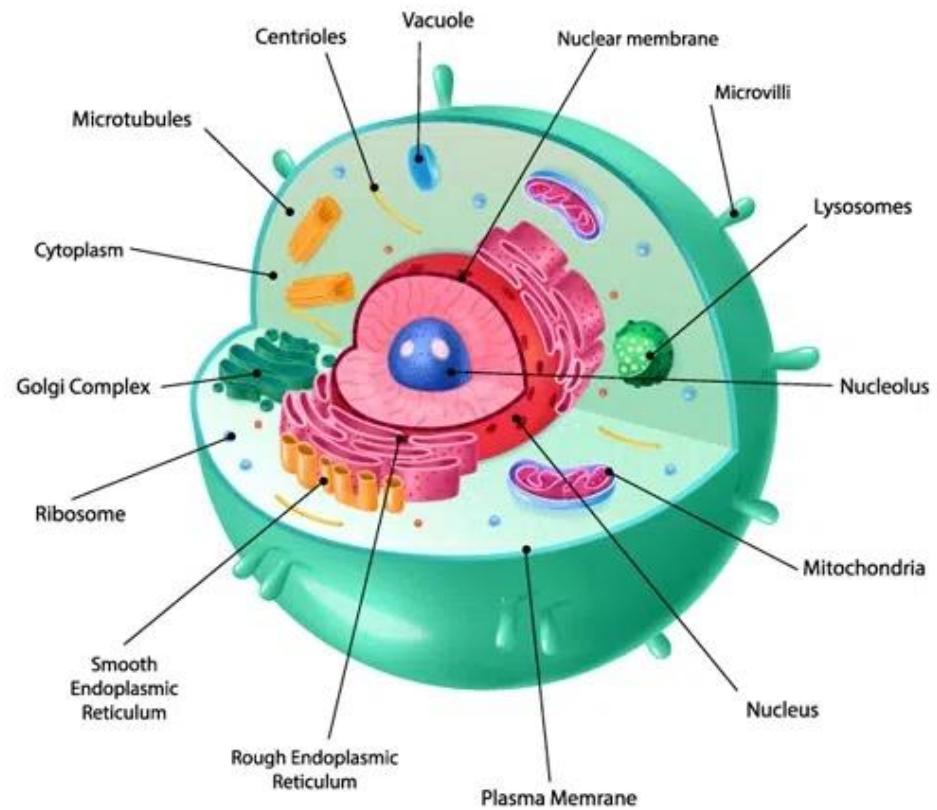
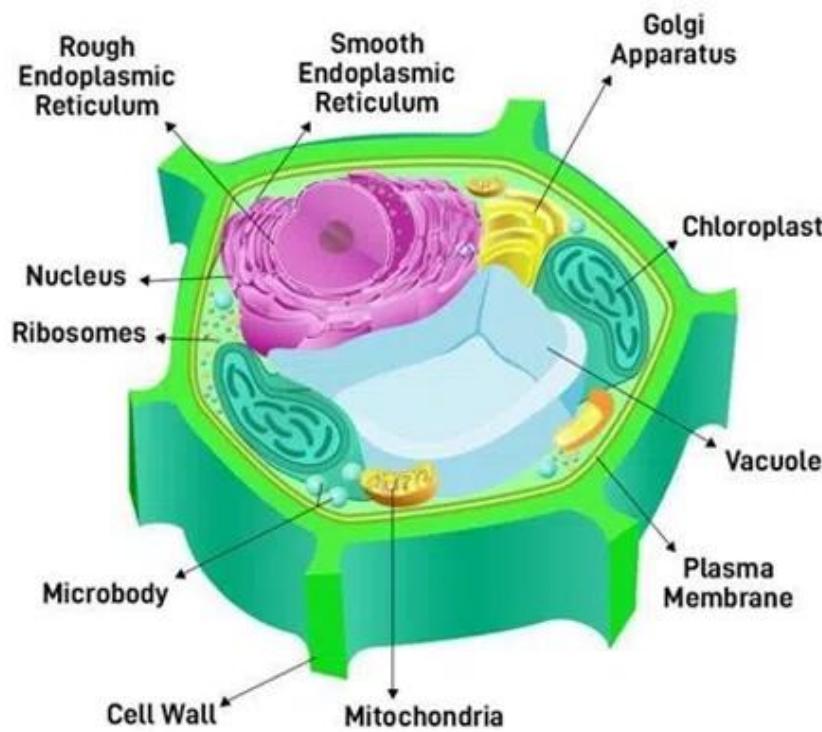
Outline

- Human genome
- Cell structure and function, Eukaryotic vs Prokaryotic
- Chromatin organization
- Central Dogma
- Germline development?
- What is Epigenetics?
- Genomics vs Epigenetics
- How does Epigenome regulate transcription?
- Epigenetic Mechanisms in Gene Regulation
- Some examples of epigenetic applications in clinical



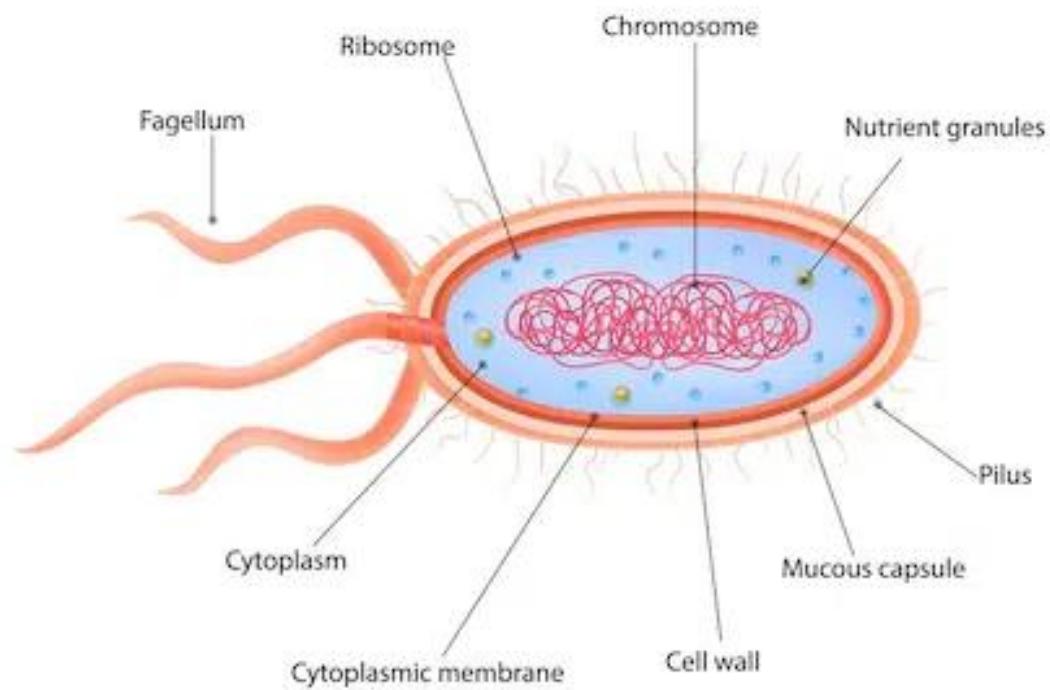
Cell structure and function

Plant Cell & Animal Cell Diagram

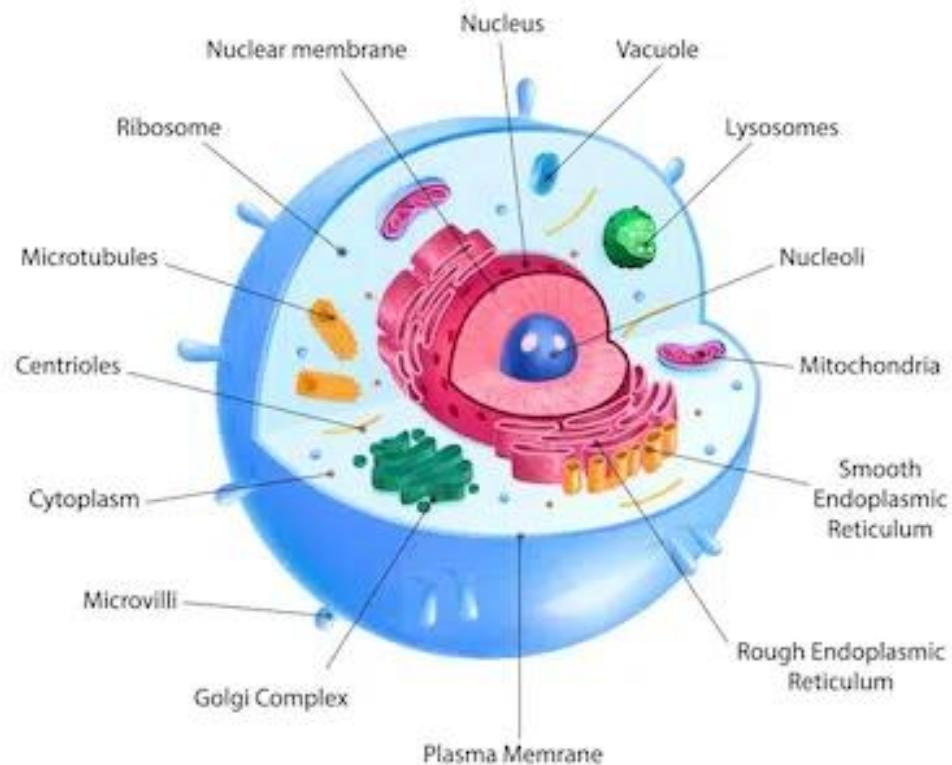


Eukaryotic vs Prokaryotic

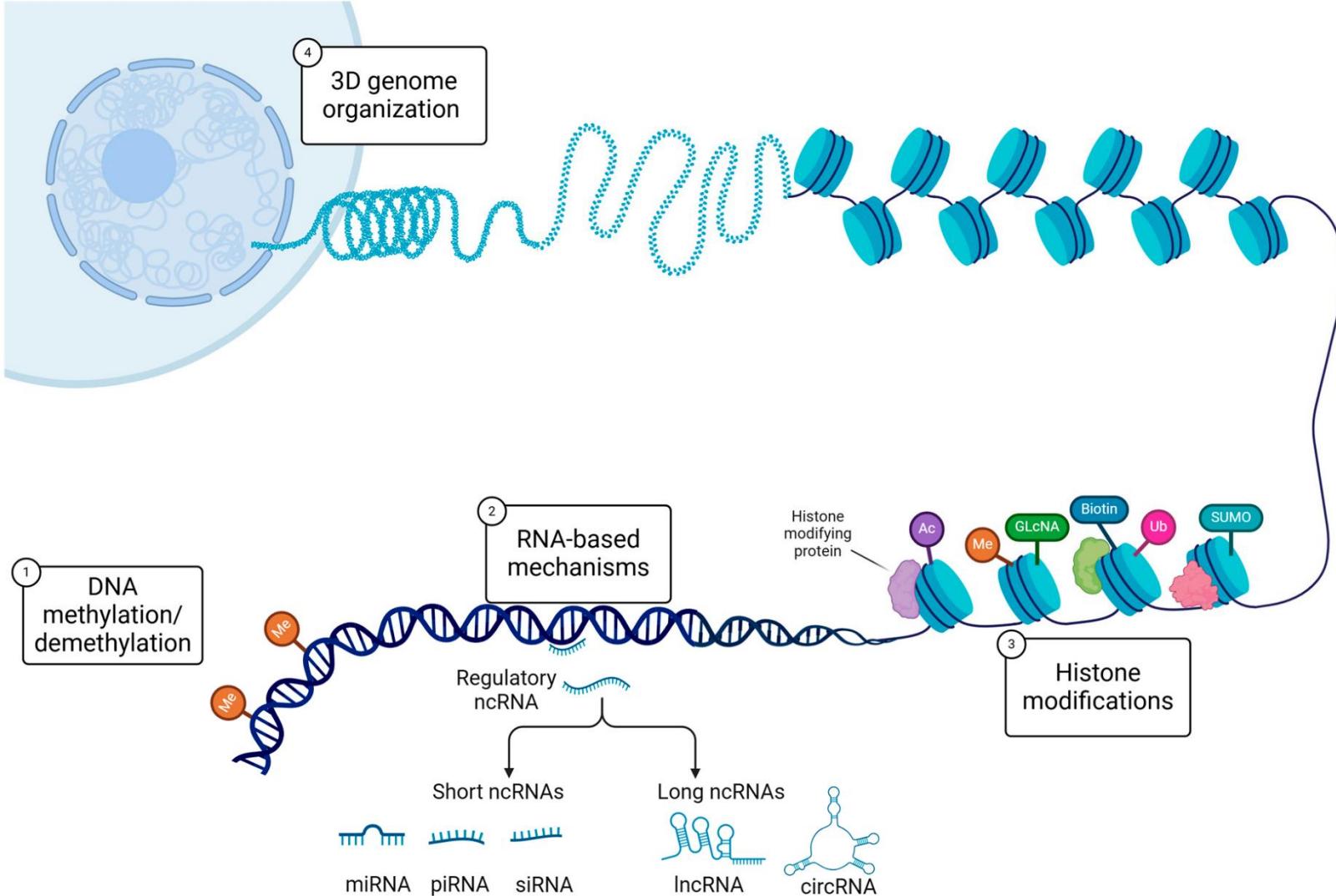
PROKARYOTIC CELL



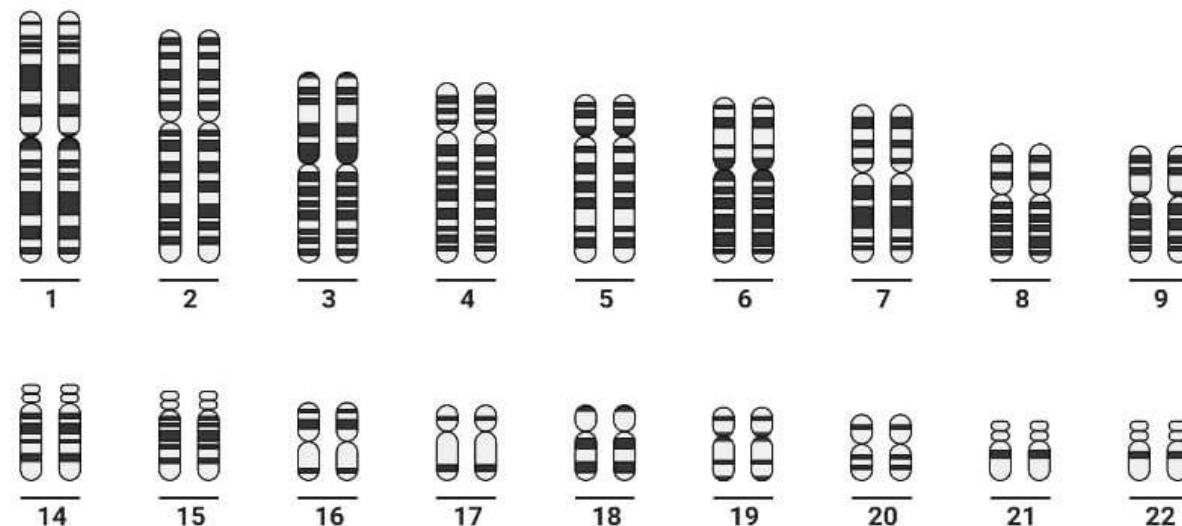
EUKARYOTIC CELL



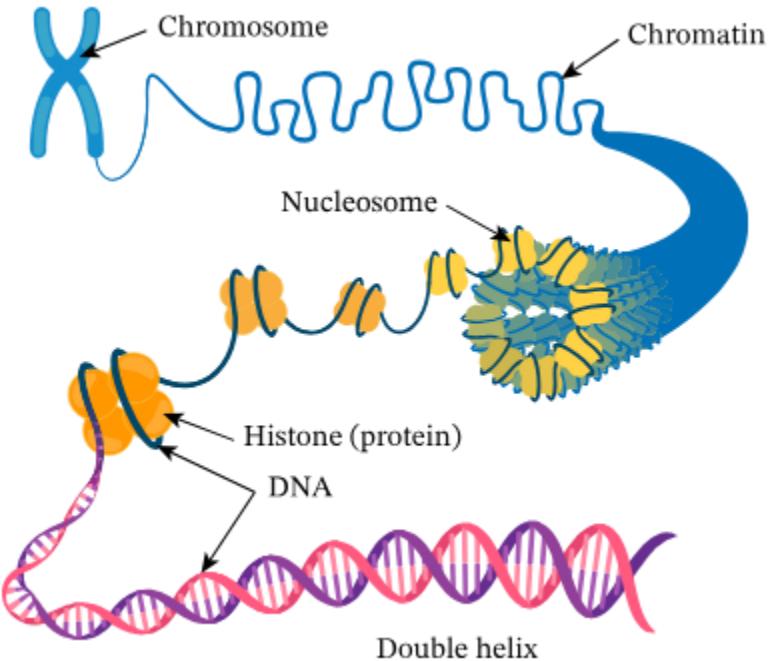
Chromatin organization



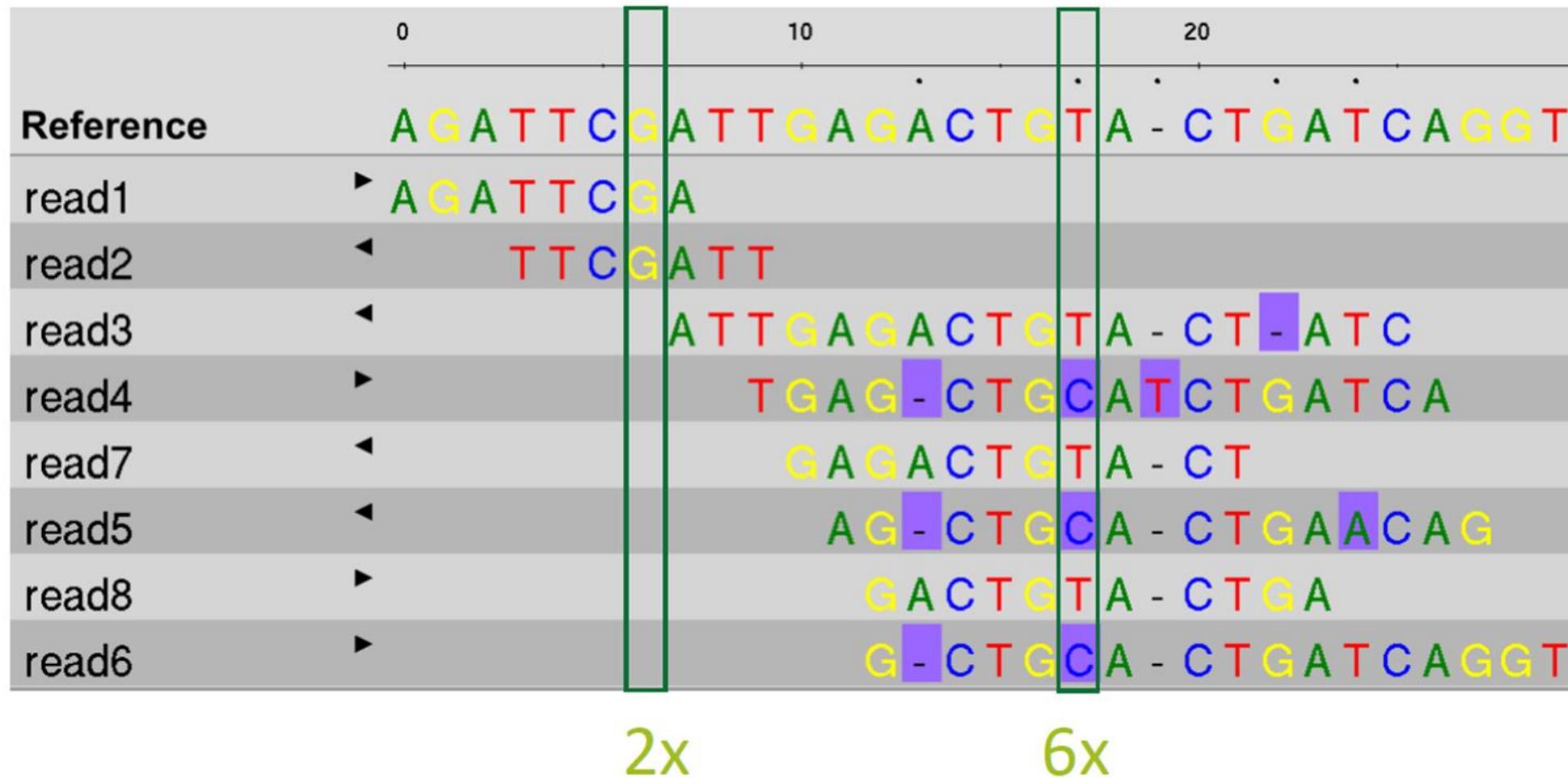
Human Karyotype



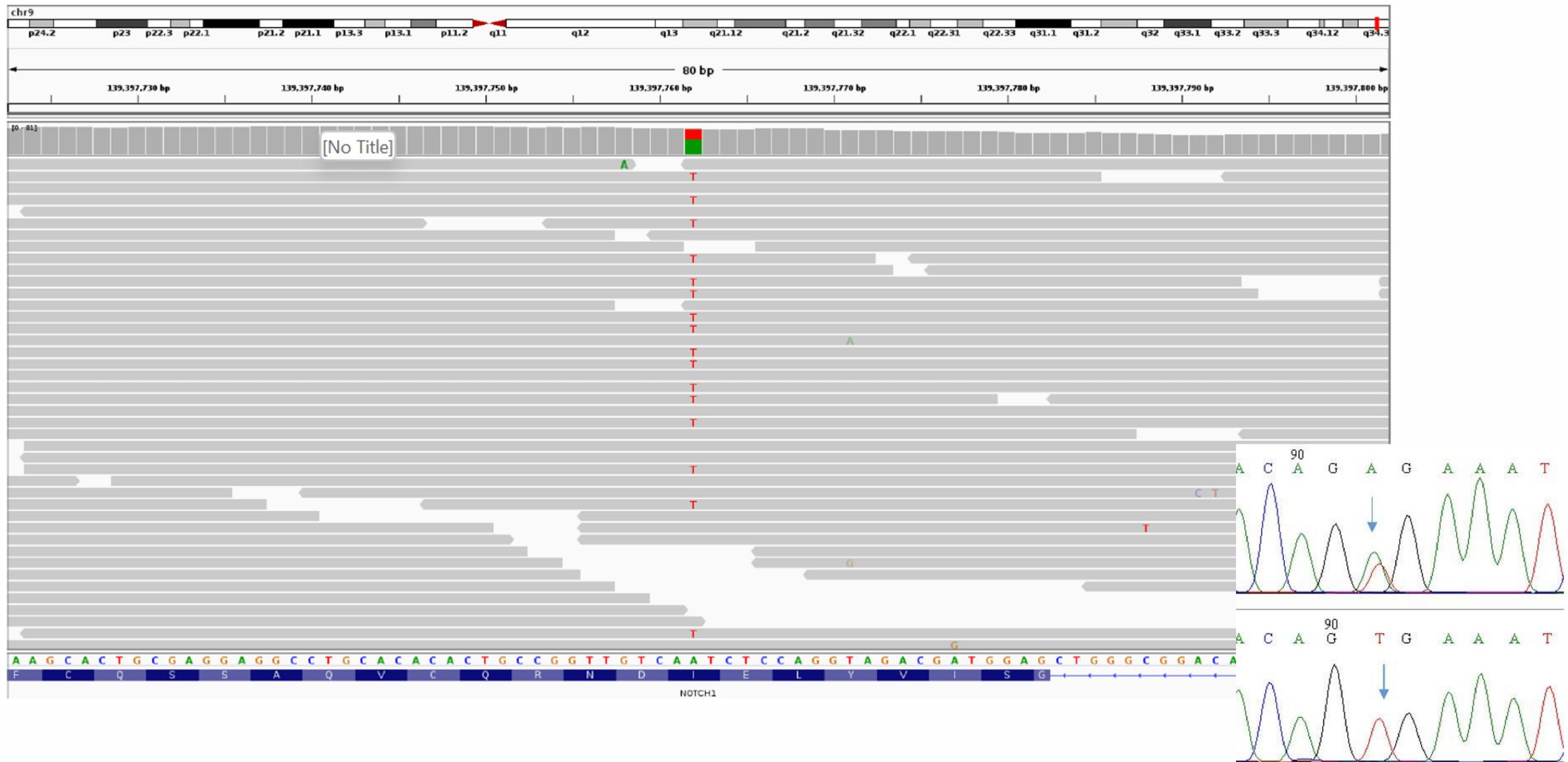
23
X Y or X X



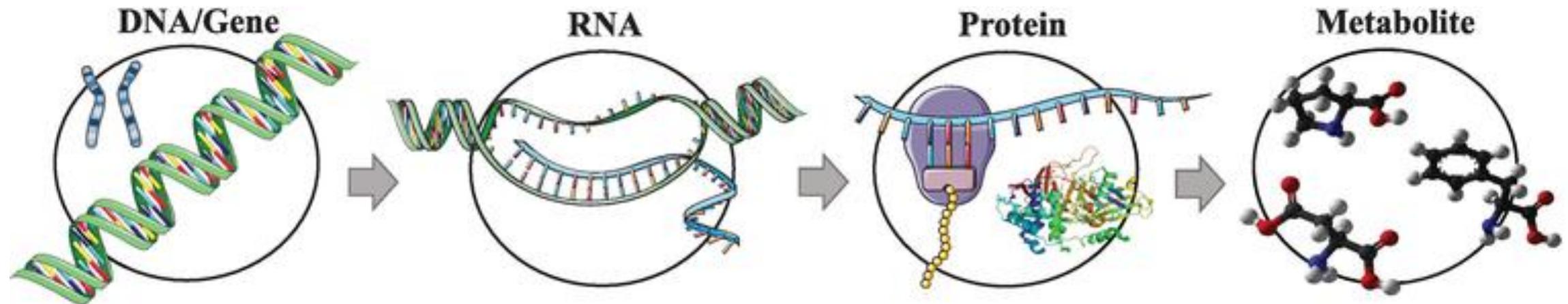
Kết quả của mapping



DNA Mutation



Central Dogma



Genomics

PAH gene
Ref ...ATCGAT...
P1 ...AACGAT...

NM_000277.3(PAH):c.971T>A

Transcriptomics

PAH mRNA
Ref ...AUCGAU...
P1 ...AACGAU...

NM_000277.3(PAH):c.971T>A

Proteomics

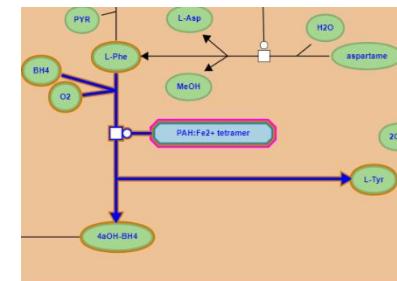
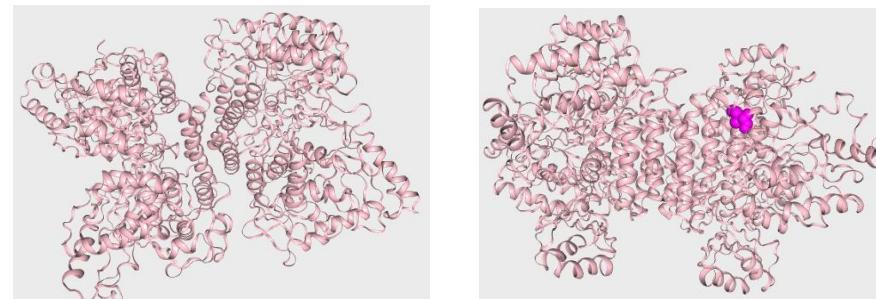
PAH protein
Ref ...Ile-Asp...
P1 ...Asn-Asp...

NM_000277.3(PAH):p.Ile324Asn

Metabolomics

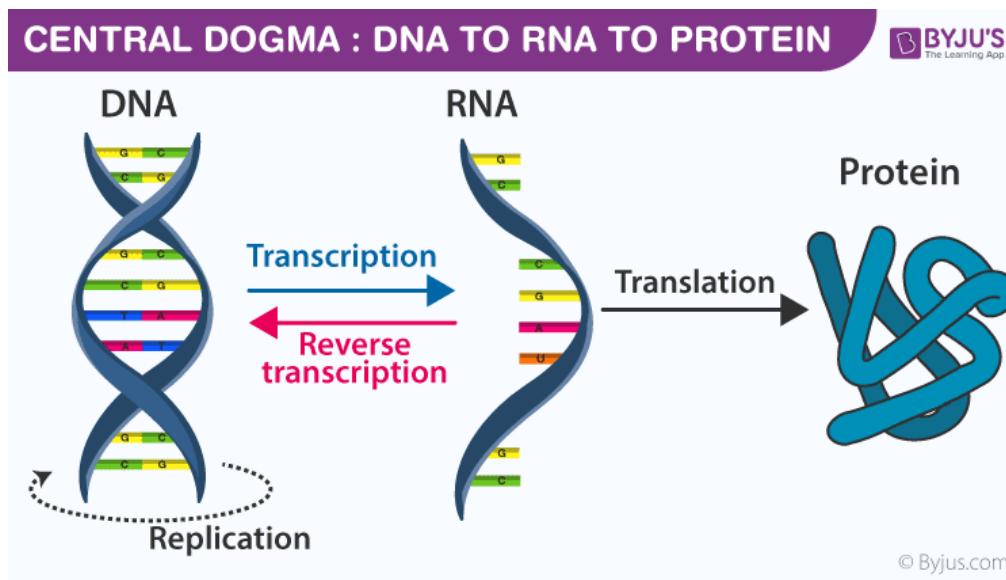
PAH
Ref Phe → Tyr

PAH
P1 Phe ~~→~~ Tyr

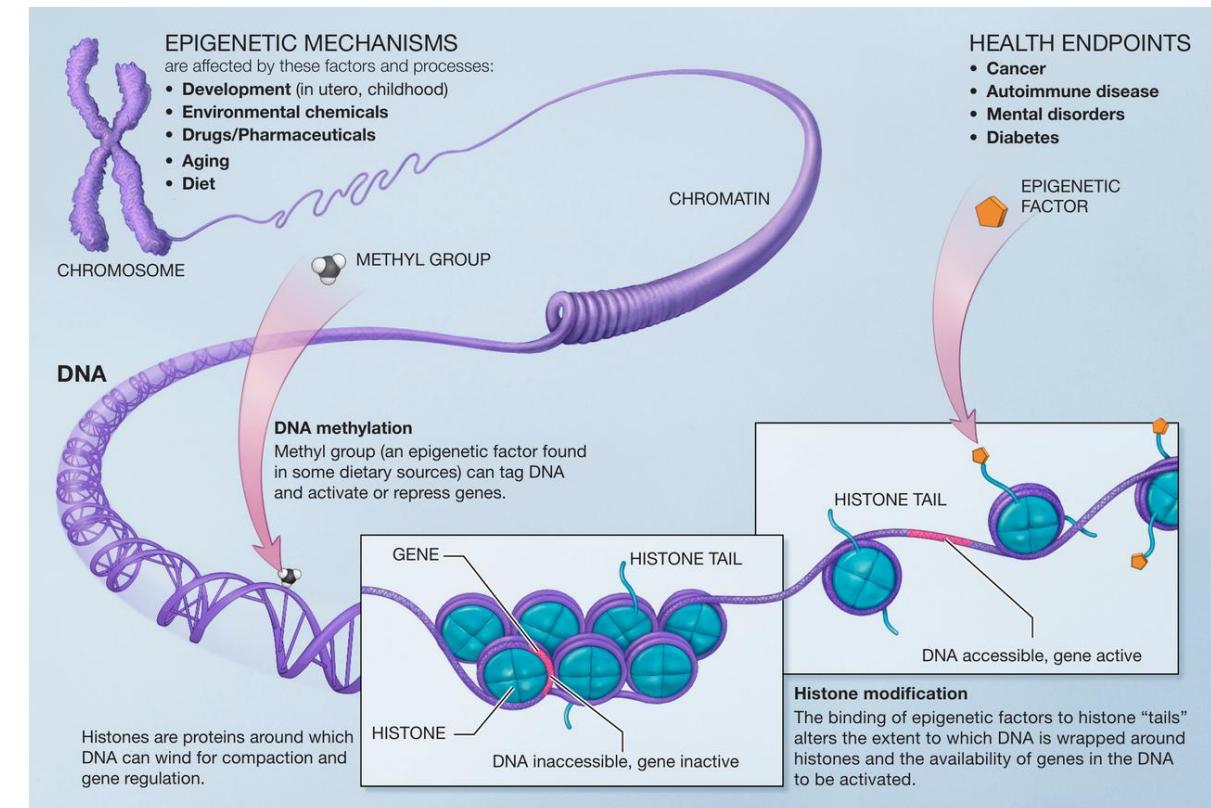


What is Epigenetics?

Your genes play an important role in your health



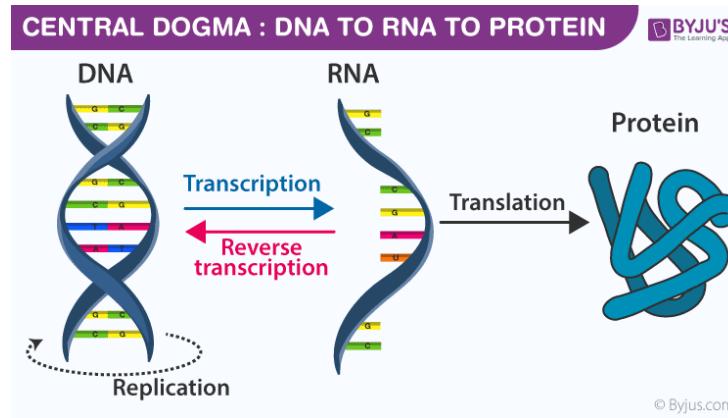
Your behaviors and environment can cause changes that affect the way your genes work



[Epigenetics - Wikipedia](#)

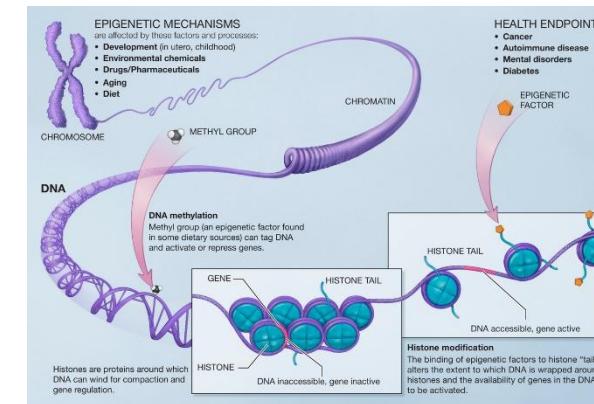
Genetics

Your genes play an important role in your health



Epigenetics

Your behaviors and environment can cause changes that affect the way your genes work



A woman without her man is nothing

A woman, without her man, is nothing
A woman: without her, man is nothing

Genetics

“Reading the book of life”

EPIGENETIC REGULATION OF NORMAL CELLULAR PROCESSES IS TYPICALLY DRIVEN IN A CELL TYPE DEPENDENT MANNER. THIS REQUIRES AN EXQUISITE LEVEL OF INTERPLAY BETWEEN EPIGENETIC LAYERS INCLUDING DNA METHYLATION, NUCLEOSOME POSITIONS AND HISTONE MODIFICATIONS AMONGST OTHERS. TOGETHER, THESE MECHANISMS ESTABLISH THE CORRECT GENE EXPRESSION PATTERNS AND HIGHER ORDER CHROMATIN STRUCTURES. THUS, THE IDENTITY OF EACH CELL IS DETERMINED BY THE PATTERN OF DNA METHYLATION.

Epigenetics

“Translating the book of life”

EPIGENETIC REGULATION OF NORMAL CELLULAR PROCESSES IS TYPICALLY DRIVEN IN A CELL TYPE DEPENDENT MANNER. THIS REQUIRES AN EXQUISITE LEVEL OF INTERPLAY BETWEEN EPIGENETIC LAYERS, INCLUDING DNA METHYLATION, NUCLEOSOME POSITIONS AND HISTONE MODIFICATIONS, AMONGST OTHERS.

TOGETHER, EPIGENETIC MECHANISMS ESTABLISH THE CORRECT GENE EXPRESSION PATTERNS AND HIGHER ORDER CHROMATIN STRUCTURES; THUS, THE IDENTITY OF EACH CELL. OF THESE, DNA METHYLATION IS THE BEST-STUDIED EPIGENETIC MODIFICATION. PRECISE DNA METHYLATION PATTERNS ARE ESTABLISHED DURING EMBRYONIC DEVELOPMENT AND ARE MITOTICALLY HERITABLE THROUGH MULTIPLE CELLULAR DIVISIONS.



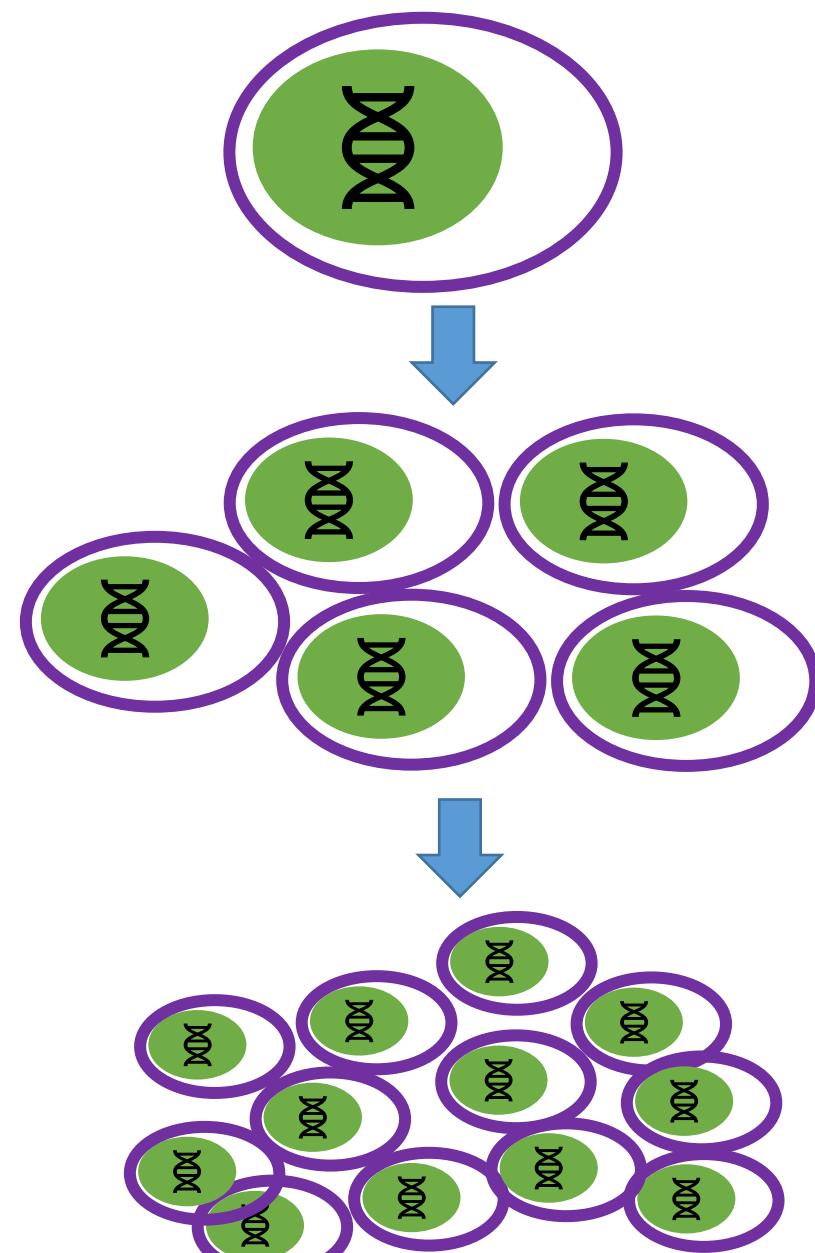
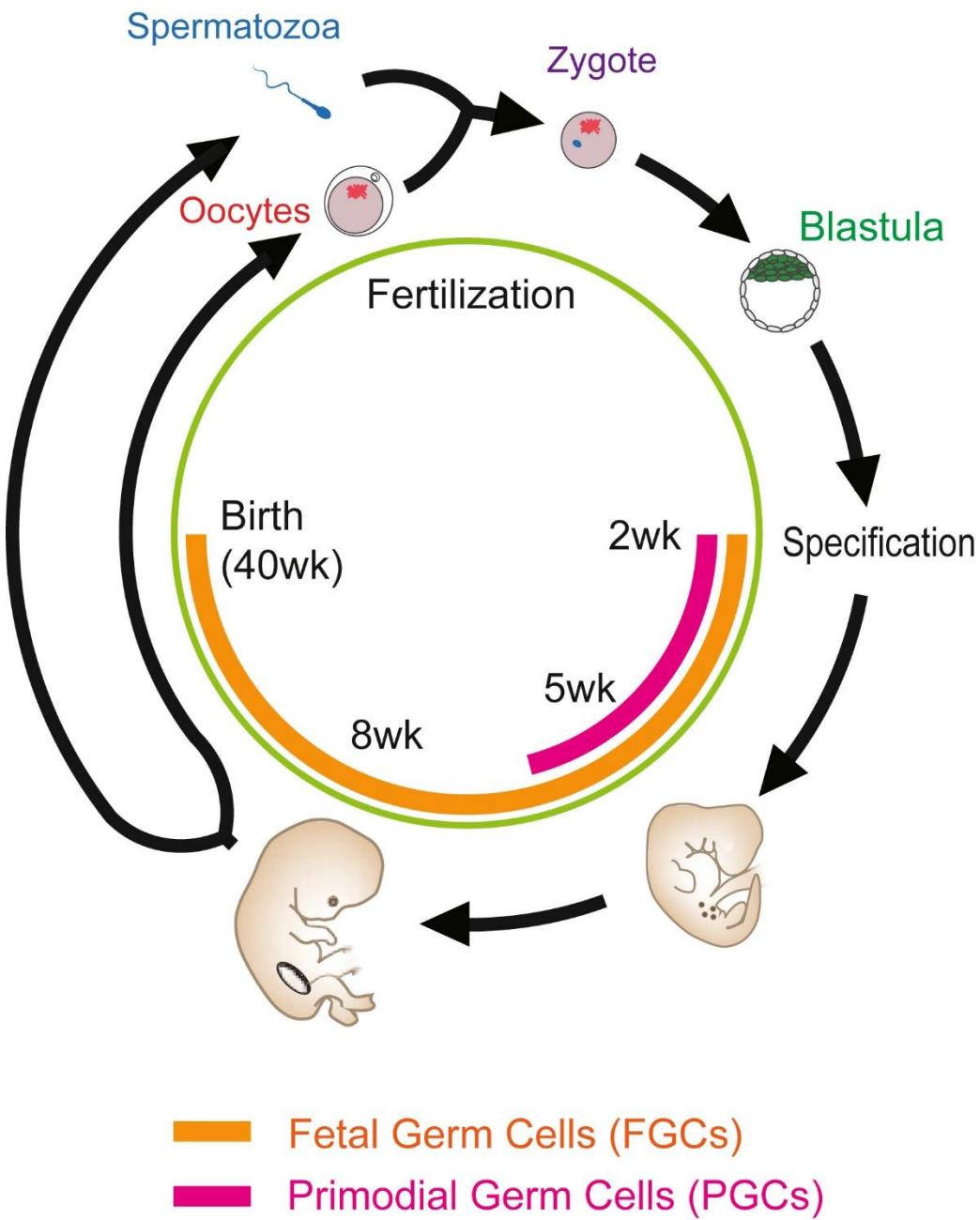
Genetics



The structure of DNA was discovered in 1953

```
GTAAGGCAGTCGATATAGGTT  
CACCGGTCTTAGGCACGTTGAG  
CTGACCAGTGCTAACGTCCAA  
TGGCATTGCAGCTGGGGTACAC  
AGTCTTGTGTCACAGTCAGGTC  
TATCTGTACTAGTCTTACGTAGT  
CGGTACCCCATGACATCGACTT  
GTGTCGGATCGATCATC
```

DNA code was mapped in 2001 – 3 billion letters (GATC)



<https://doi.org/10.1016/j.molcel.2019.08.025>

Genetics



How does each cell know what it is supposed to be?

```
GTAAGGCAGTCGATATAGGTT  
CACCGGTCTTAGGCACGTTGAG  
CTGACCAGTGCTAACGTCAA  
TGGCATTGCAGCTGGGGTACAC  
AGTCTTGTGTCACAGTCAGGTC  
TATCTGTACTAGTCTTACGTAGT  
CGGTACCCCATGACATCGACTT  
GTGTCGGATCGATCATC
```

DNA code was mapped in 2001
– 3 billion letters (GATC)

Genetics



How does each cell know what it is supposed to be?

COL1A1 gene expressed in hair cells, but not brain cells

Epigenetics



```
GTAAGGCAGTCGATATAGGTT  
TTGAG  
CTGACCAGTGCTAACGTCCAA  
TGGCATTGCAGCTGGGGTACAC  
AGTCTTGTGT  
  
CGGTACCCCATGACATCGACTT  
GTGTCGGATCGATCATC
```

Only parts of the genome are active at any one time

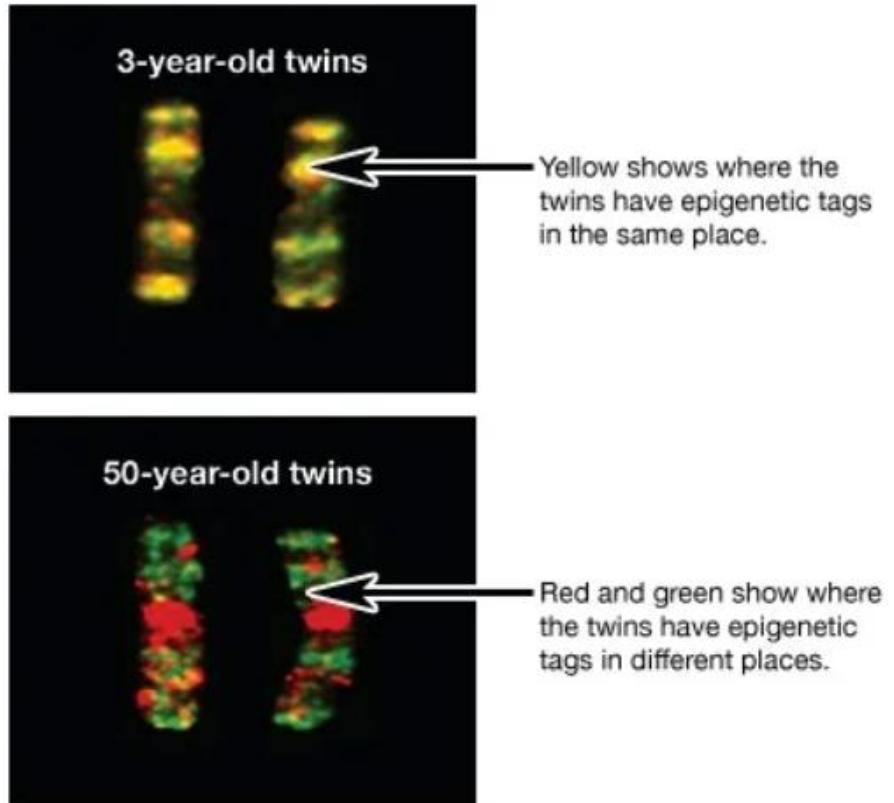
Example 1: Identical twins

Identical twins come from the same fertilized egg
→ share identical genetic profiles (genome)



→ Your behaviors and environment can cause changes that affect the way your genes work

Chromosome 3 Pairs
3-year old twins vs. 50-year-old twins



Chromosome 3 pairs in each set of twins are digitally superimposed. One twin's epigenetic tags are dyed red and the other twin's tags are dyed green. When red and green overlap, that region shows up as yellow. The 50-year old twins have more epigenetic tags in different places than do 3-year-old twins.

Example 2: Identical twins 2

Identical twins come from the same fertilized egg → share identical genetic profiles (genome)

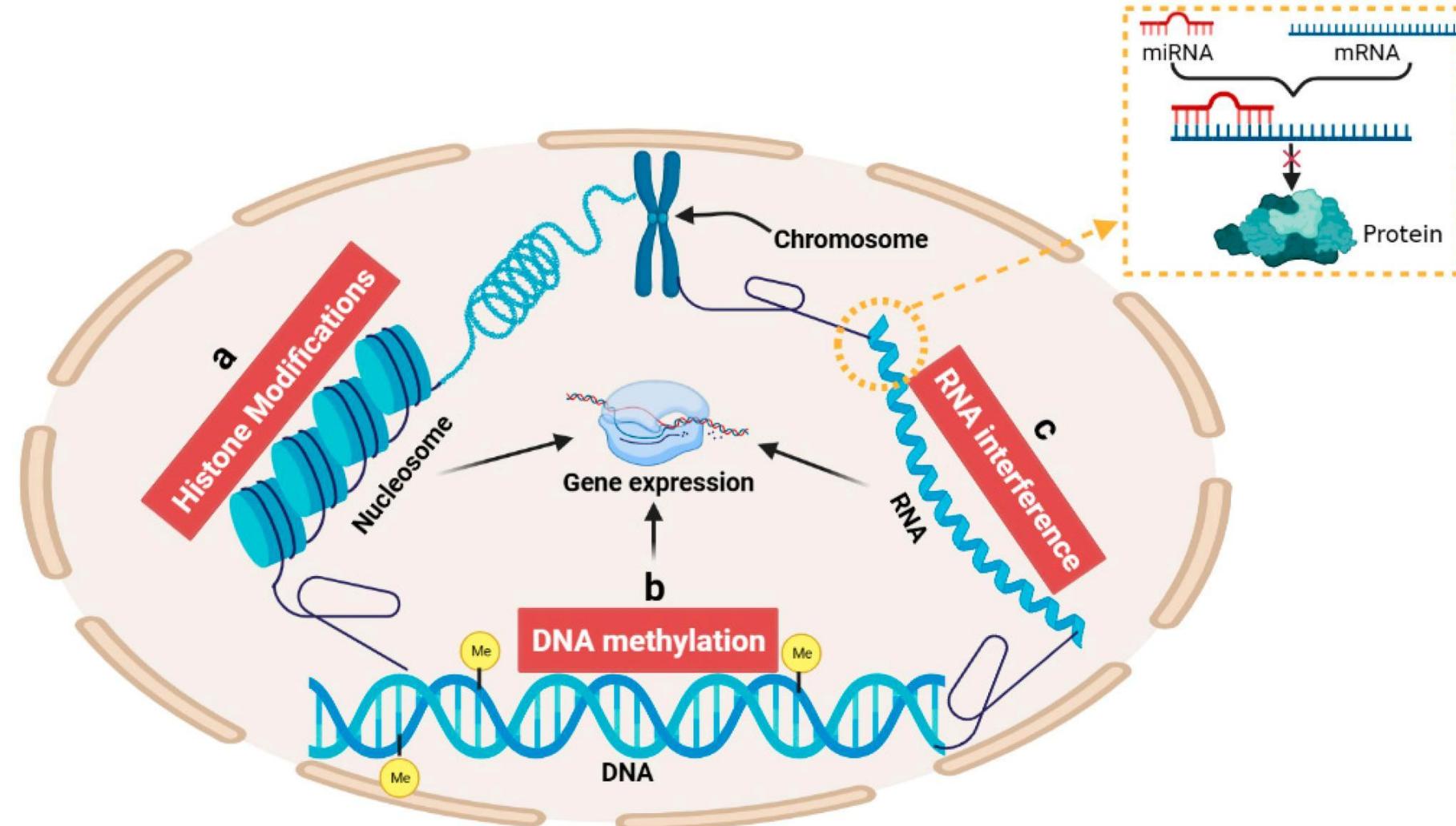


Leora Eisen

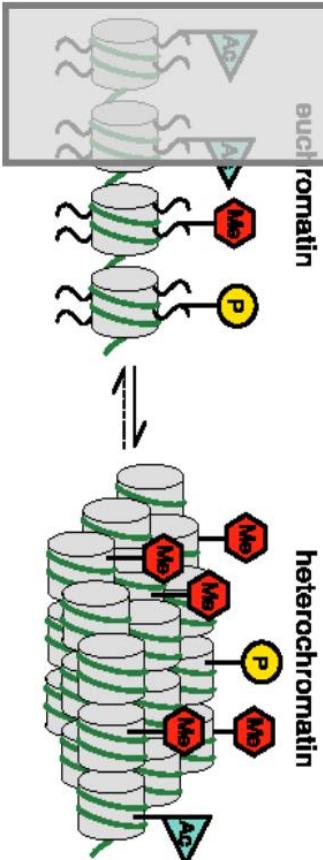
Linda Lewis
(leukemia)

→ Your behaviors and environment can cause changes that affect the way your genes work

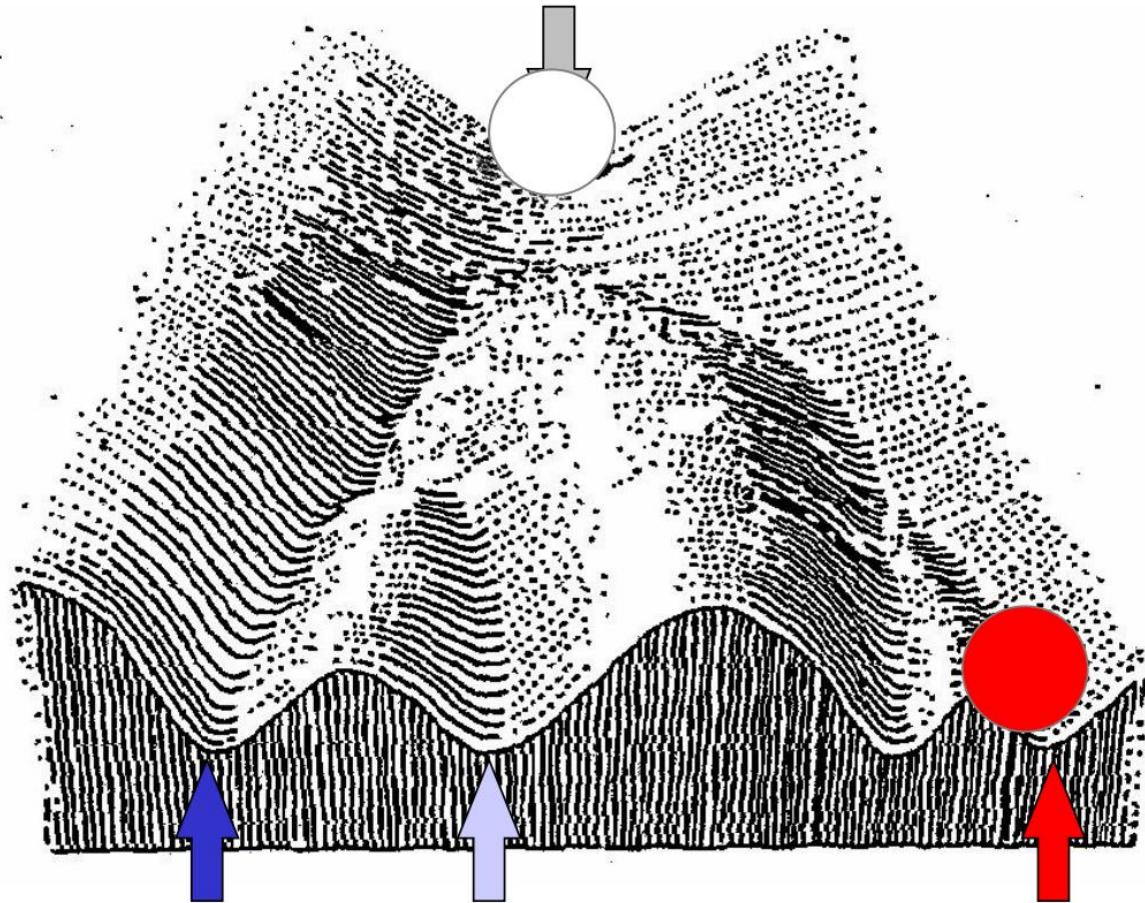
Epigenetic Mechanisms in Gene Regulation



Epigenetics and „Epigenesis“



Pluripotency



Following differentiation cells adopt different epigenomic states – reprogramming allows to revert this process

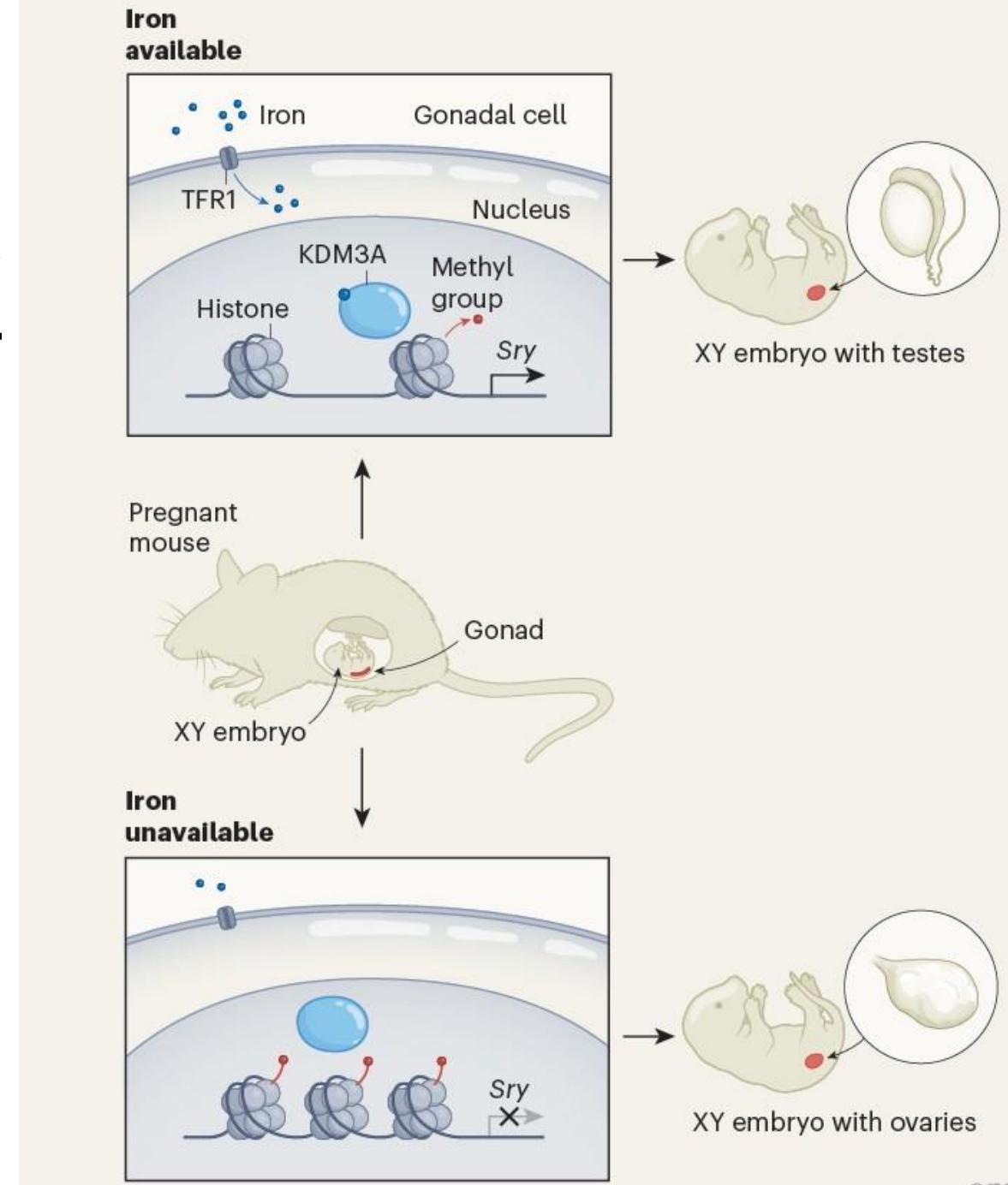
Conrad Waddington: Epigenetic landscape & "Canalization"
Modified: Timo C. Dinger & Albrecht Müller

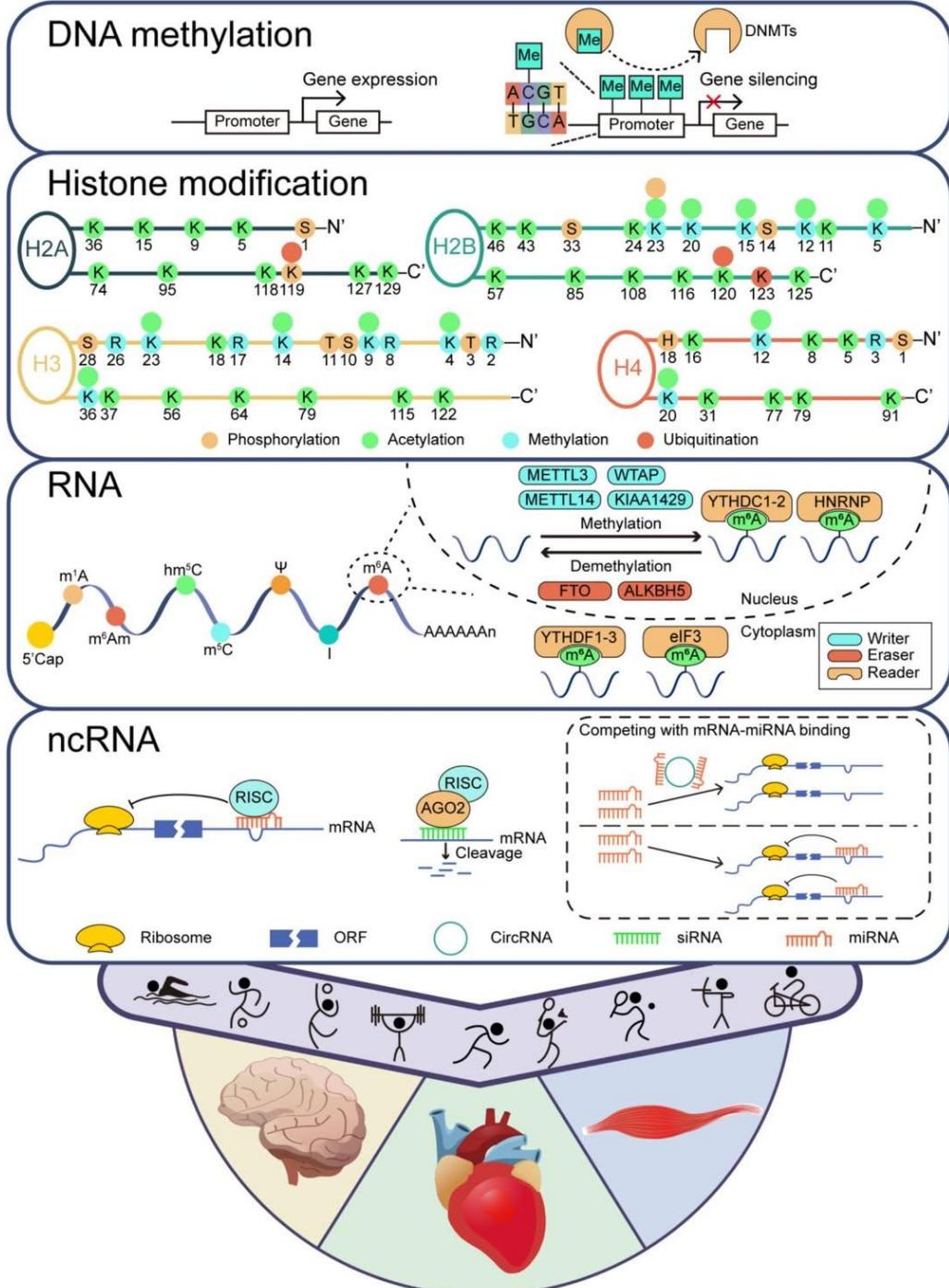
NEWS AND VIEWS | 04 June 2025

Iron deficiency in pregnant mice causes XY embryos to develop with female characteristics

In mice, a lack of maternal iron impairs an iron-dependent enzyme that activates the male sex-determining gene, causing some XY embryos to develop ovaries.

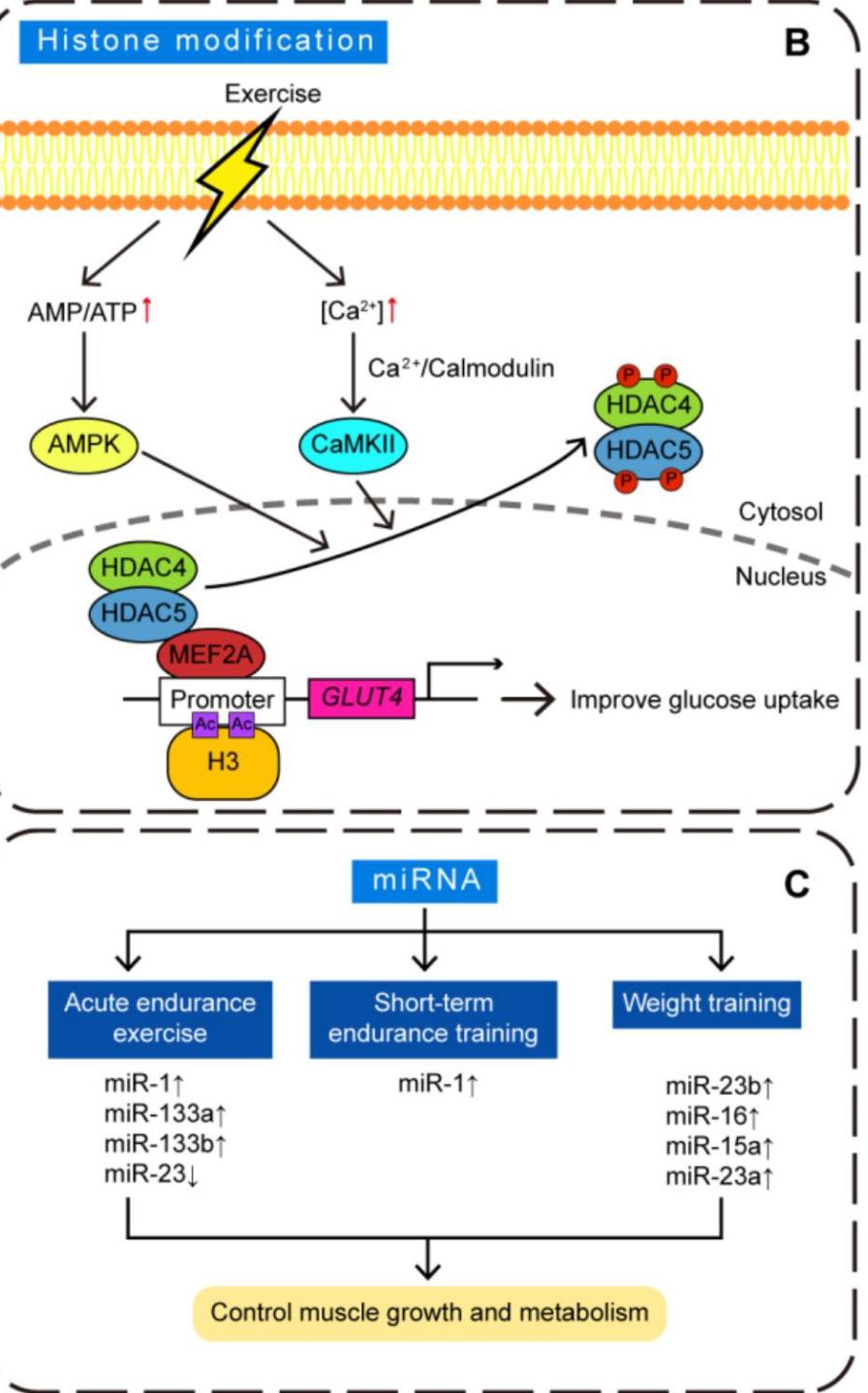
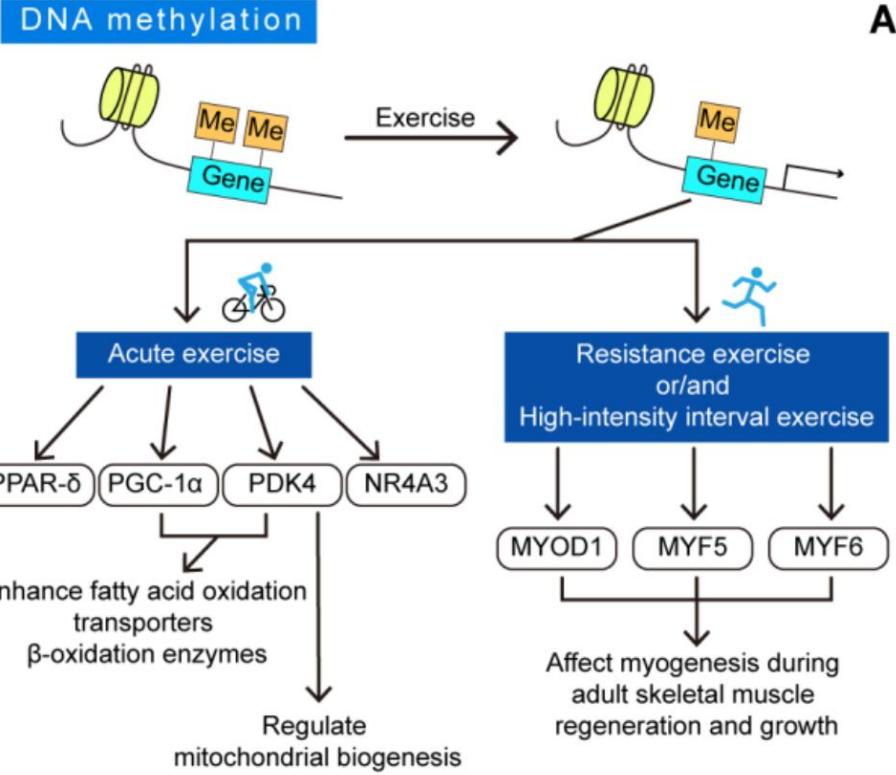
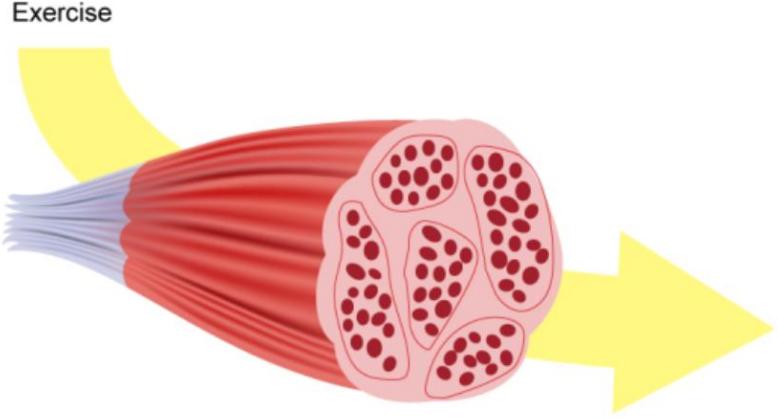
By [Shannon Dupont](#) & [Blanche Capel](#) 





Exercise induces epigenetic modifications in skeletal muscle, brain and heart. DNA methylation, catalyzed by DNMTs, modulates gene expression through the addition and removal of methyl groups. Histone modifications, including phosphorylation, acetylation, methylation, and ubiquitination on histone tails adjust chromatin compaction, thereby regulating gene accessibility. RNA modifications, particularly m⁶A methylation, mediated by ‘writer’ enzymes like METTL3, reversed by ‘eraser’ enzymes such as FTO, and recognized by ‘reader’ proteins like YTHDC1-2, critically modulates mRNA stability, translation, and decay. Non-coding RNAs, such as circRNA, miRNA, and siRNA, interact with the RISC complex involving AGO2, to modulate mRNA stability and gene silencing. The nuclear and cytoplasmic distribution of these processes suggests a spatial regulation in response to exercise, collectively contributing to the enhancement of muscle performance, cognitive function, and cardiac health by precisely tuning gene expression.

ME = methyl group; DNMTs = DNA Methyltransferases; RISC = RNA-induced silencing complex; AGO2 = Argonaute 2; ORF = Open reading frame

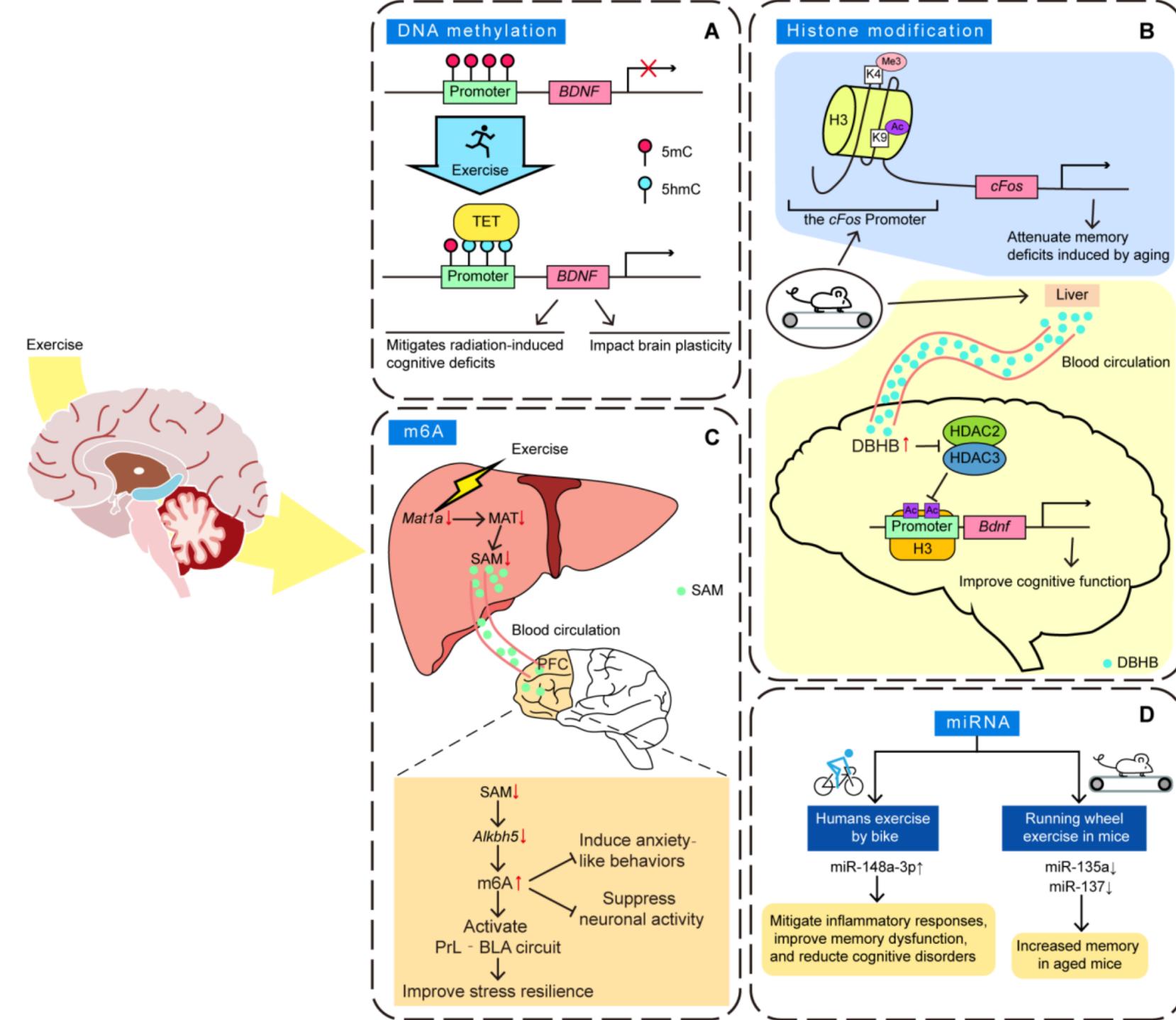


Exercise-induced epigenetic changes in skeletal muscle.

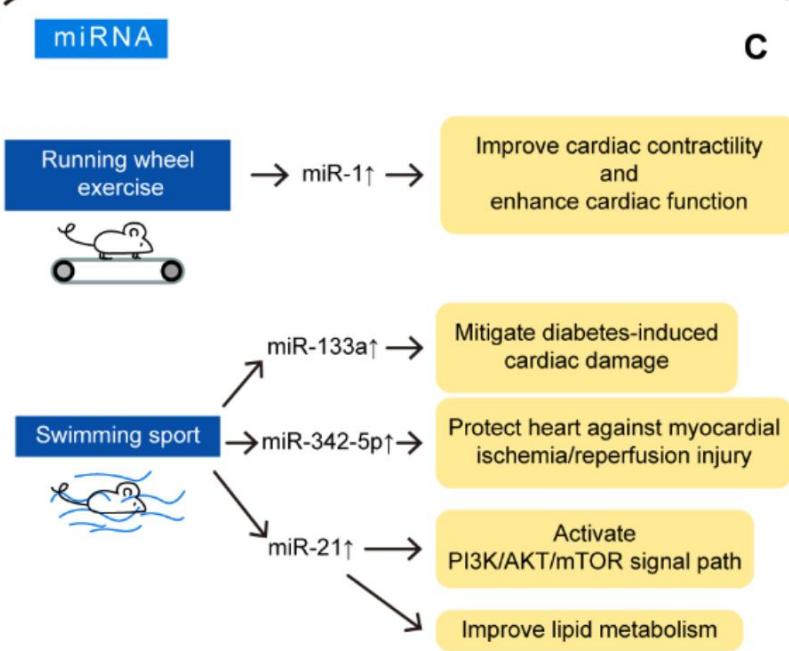
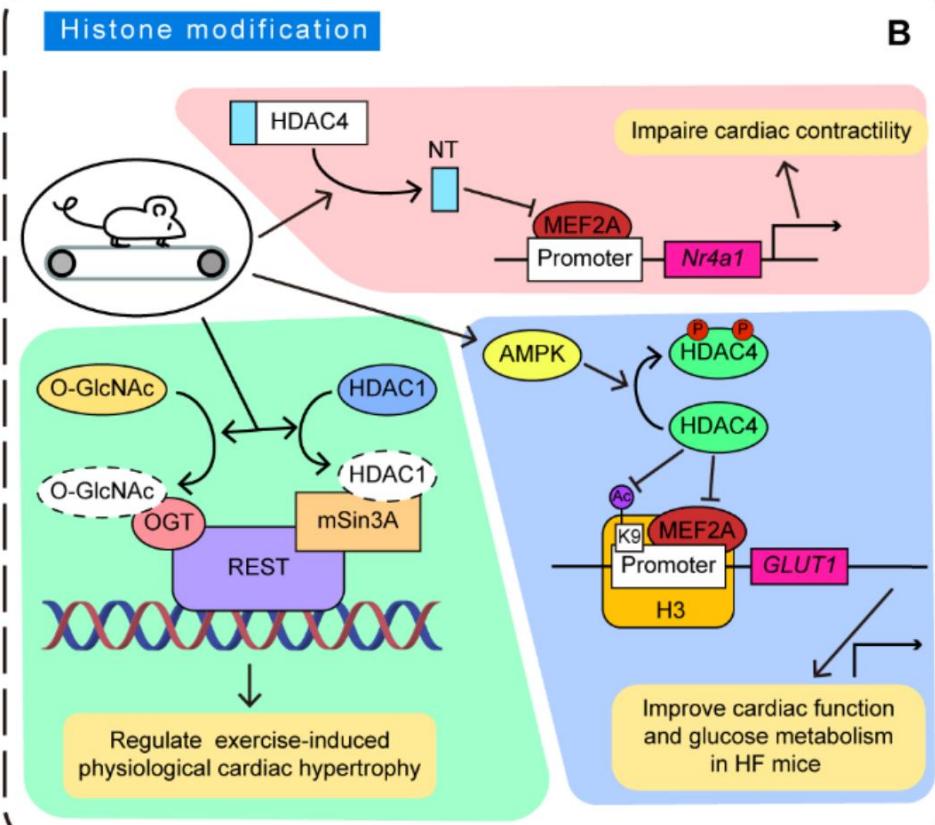
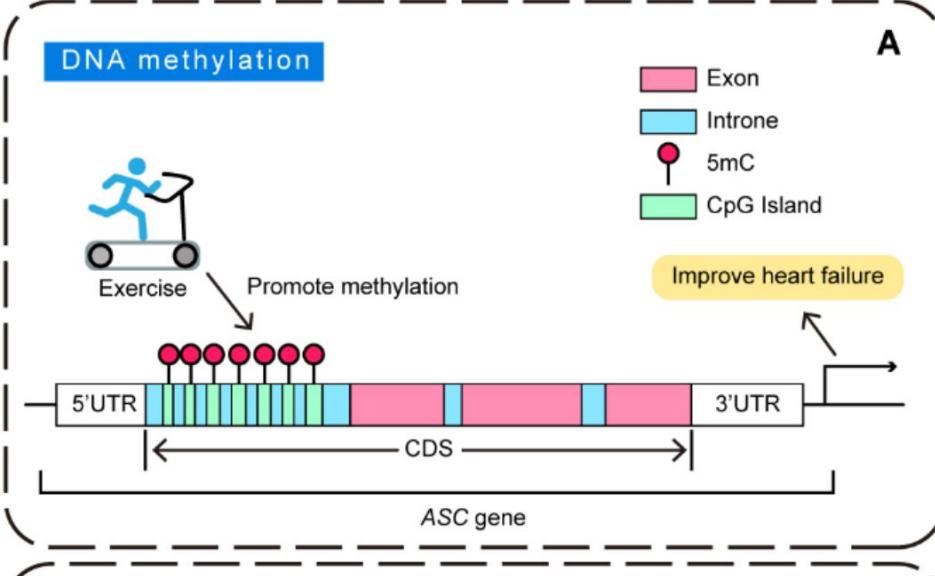
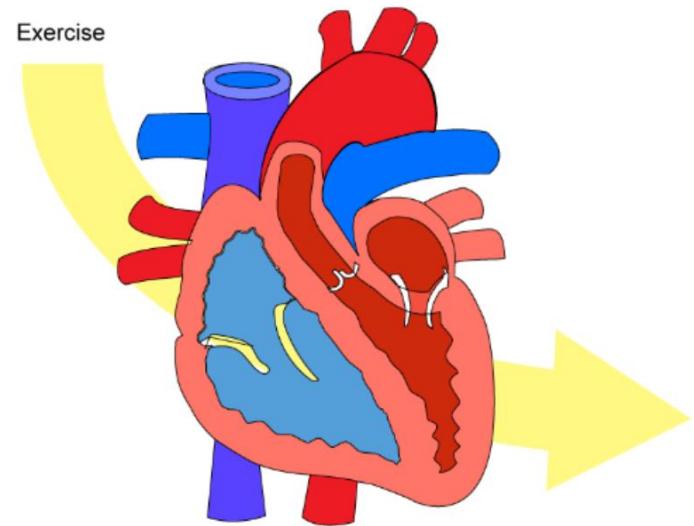
(A) DNA Methylation: Exercise induces changes in DNA methylation patterns that regulate gene expression.

(B) Histone Modification: Exercise increases AMPK activation through AMP/ATP ratio changes and calcium signaling via CaMKII. These pathways lead to the phosphorylation of HDAC4 and HDAC5, which promote MEF2A-dependent activation of the GLUT4 promoter, improving glucose uptake and enhancing metabolic adaptations.

(C) miRNA Regulation: Different types of exercise, such as acute endurance exercise, short-term endurance training, and weight training, influence the expression of specific miRNAs, which play crucial roles in regulating muscle growth and metabolism.

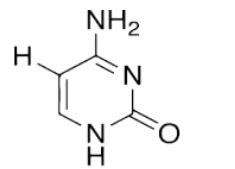


Exercise-induced epigenetic changes in the brain. **(A) DNA Methylation:** Exercise induces changes in DNA methylation that regulate gene expression, such as in the *BDNF* promoter. **(B) Histone Modification:** Exercise influences histone modifications in various brain regions, such as the *cFos* promoter in the hippocampus, which attenuates memory deficits induced by aging. Additionally, HDAC2 and HDAC3 are involved in promoting *BDNF* expression, enhancing cognitive function via circulating molecules like DBHB. **(C) m6A RNA Methylation:** Exercise affects brain m6A levels through hepatic biosynthesis of SAM, influencing anxiety-like behaviors and neural activity, improving stress resilience. **(D) miRNA Regulation:** Exercise alters the expression of specific miRNAs in the brain

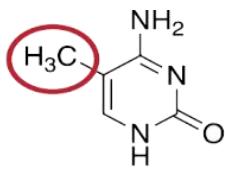


Exercise-induced epigenetic changes in the heart. (A) DNA Methylation: Exercise influences methylation status of the *ASC* gene, thereby regulating its expression and improving heart failure. (B) Histone Modification: Exercise triggers histone modifications that affect cardiac function. (C) miRNA Regulation: Specific types of exercise, such as running wheel and swimming, modulate the expression of certain miRNAs that play crucial roles in cardiac health

What are DNA Methylation and genome-wide DNA methylation (Epigenome)?

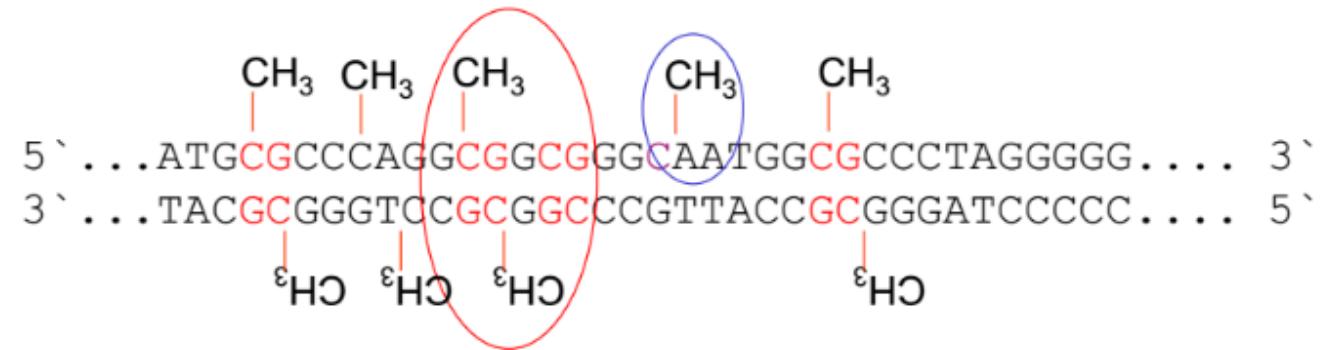
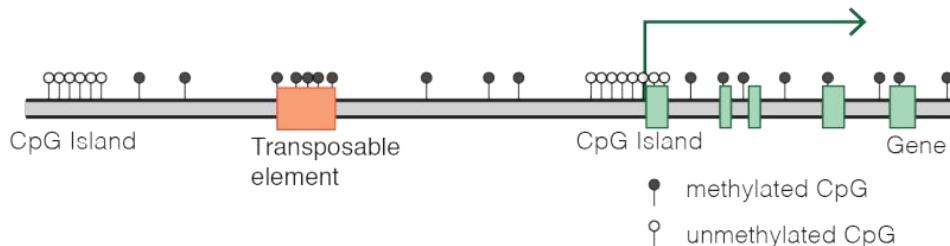


Cytosine

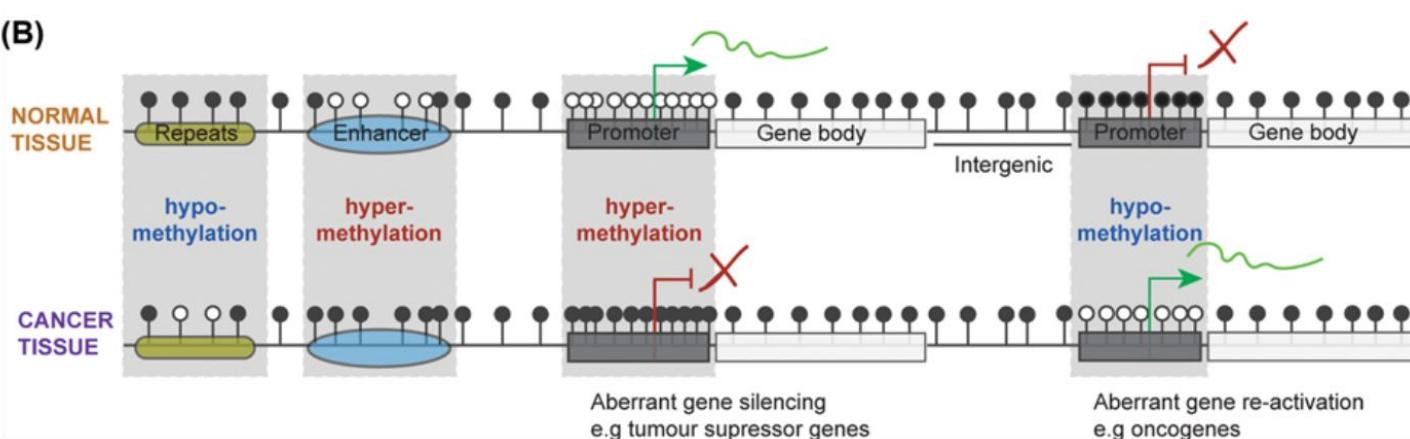


methylated Cytosine

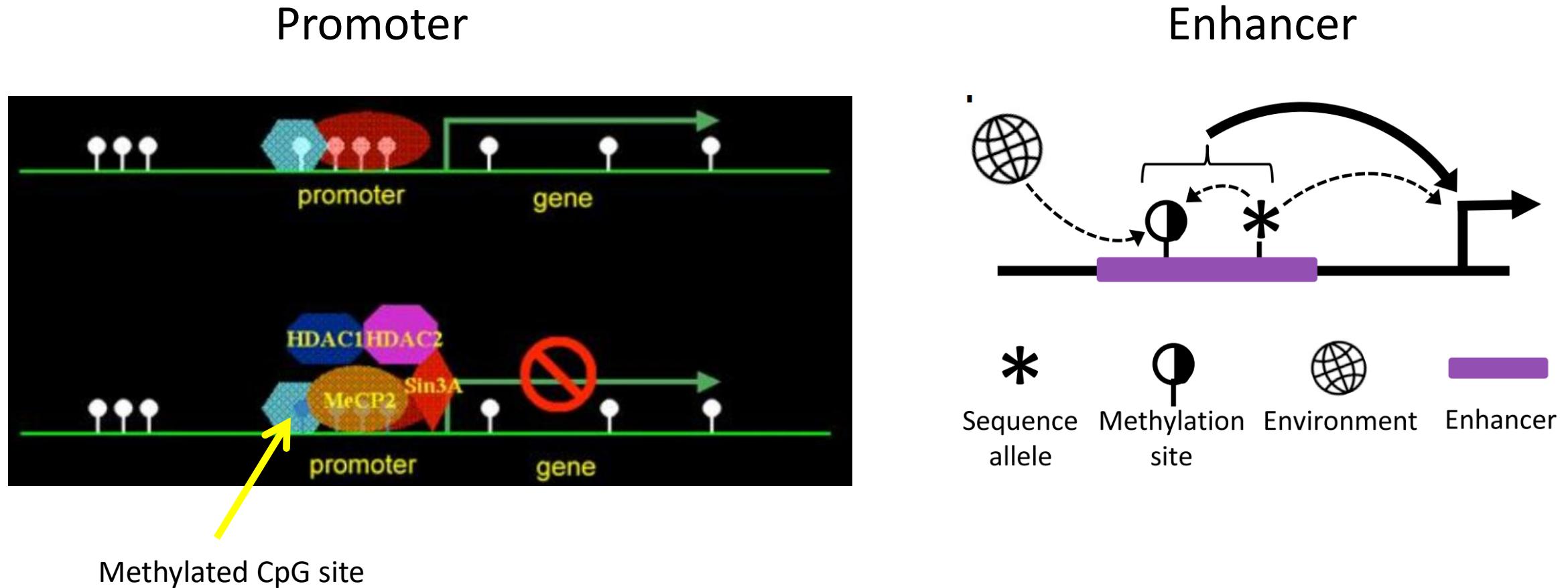
Typical mammalian DNA methylation landscape



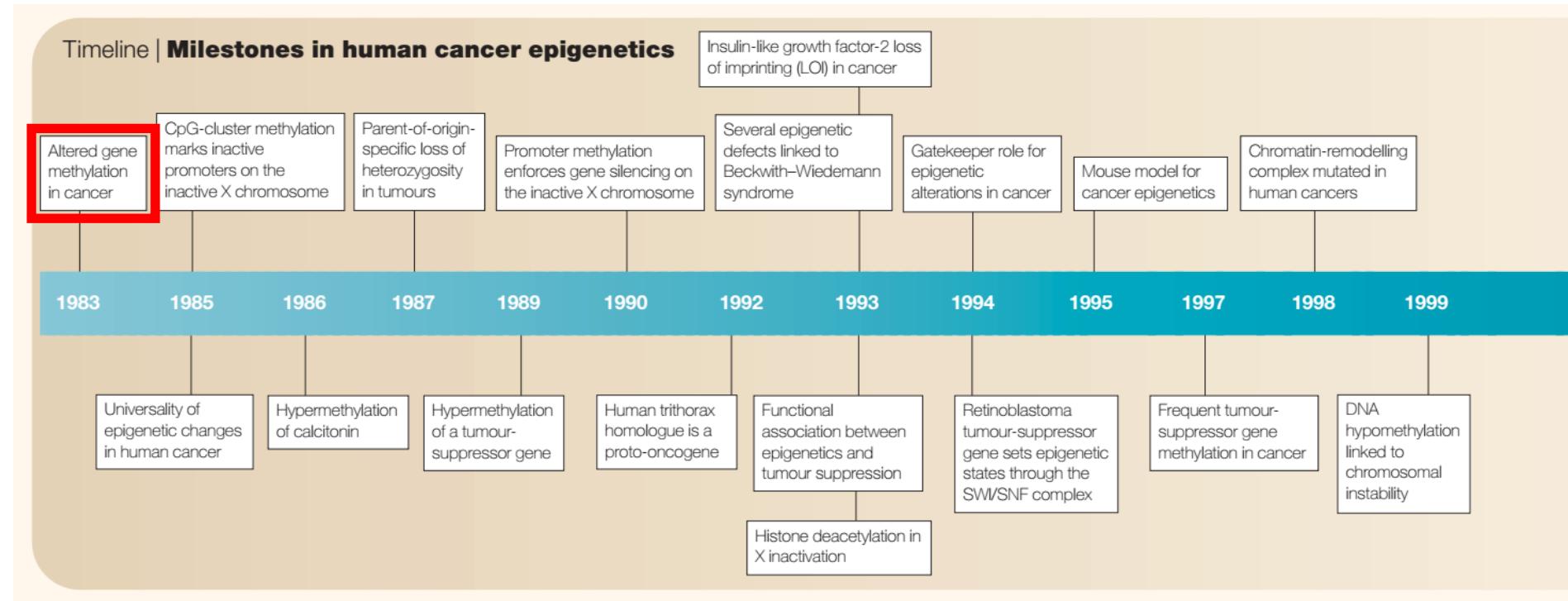
(B)



DNA methylation regulates gene expression

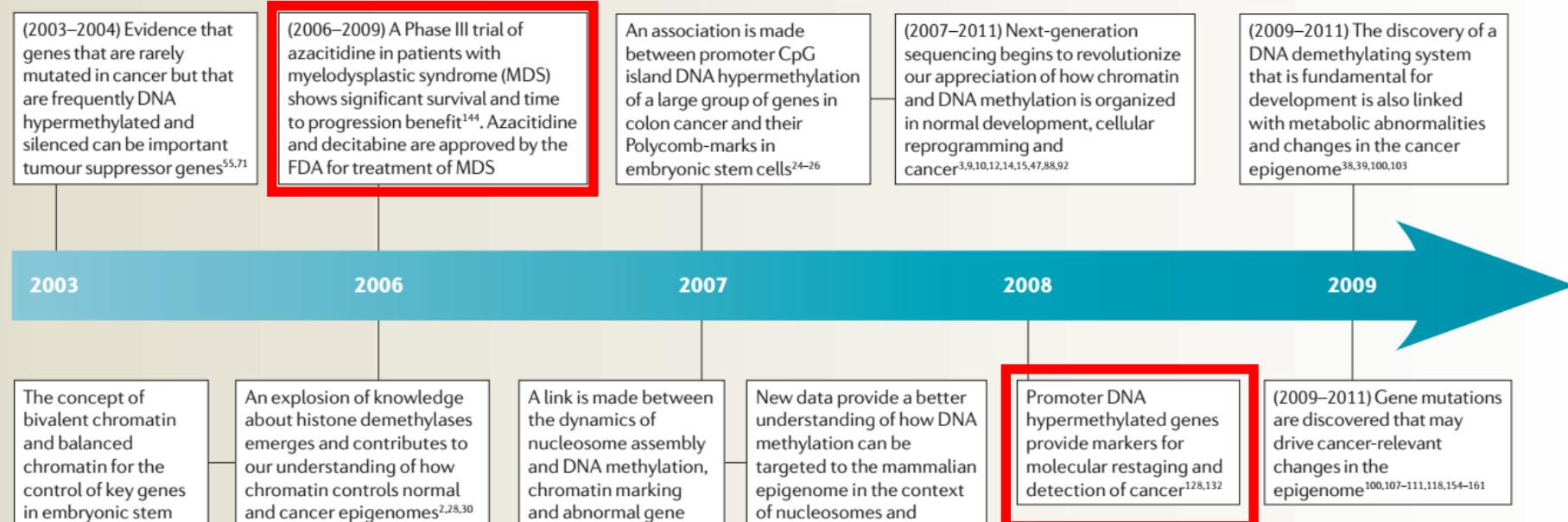


DNA methylation regulate gene expression in cancer



DNA methylation regulate gene expression in cancer

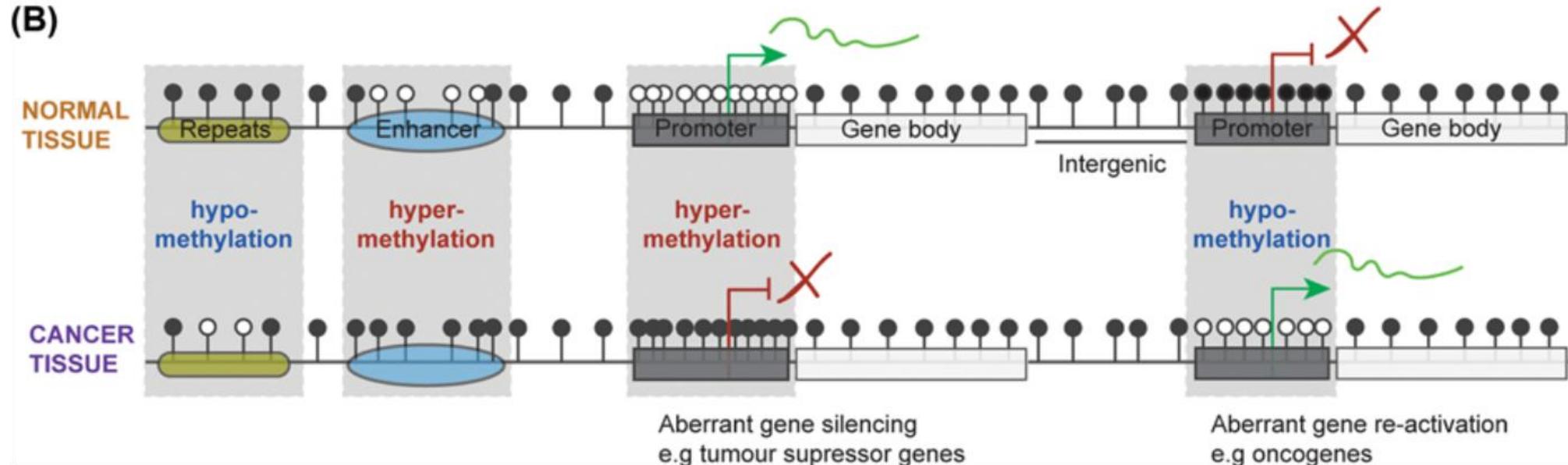
Timeline | Examples of key advances in epigenetics and cancer over the past decade



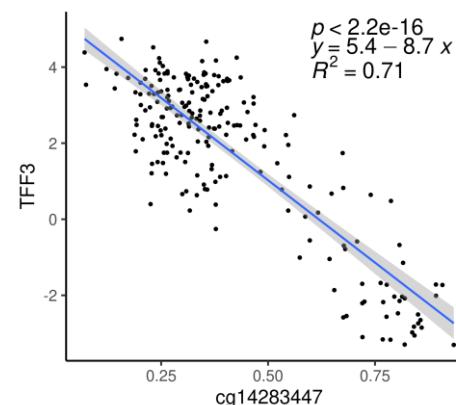
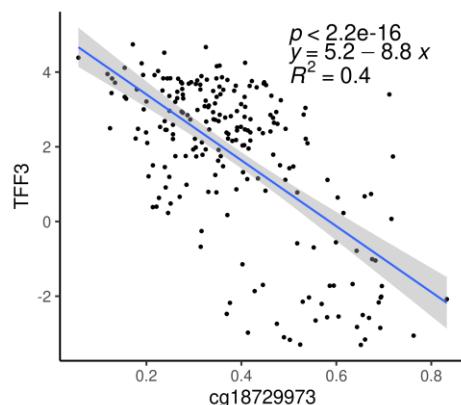
FDA, US Food and Drug Administration.

DNA methylation regulate gene expression in cancer

(B)



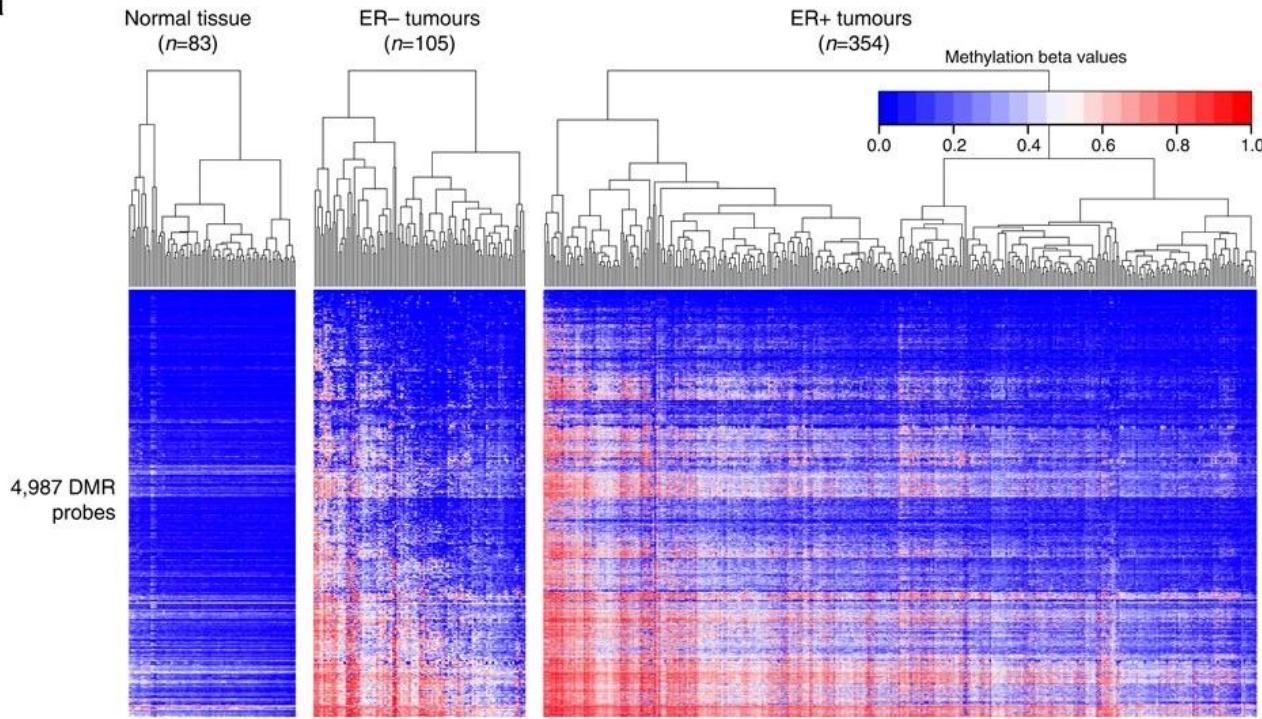
Expression



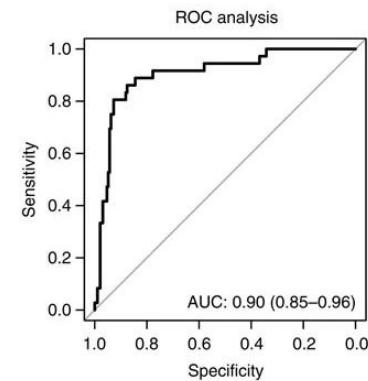
DNA methylation

DNA methylation regulate gene expression in breast cancer

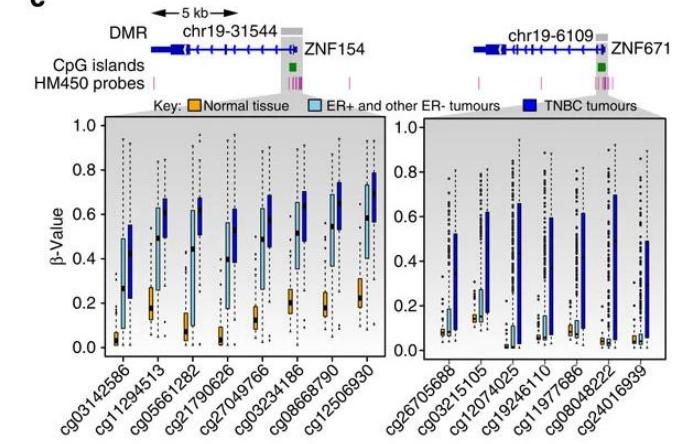
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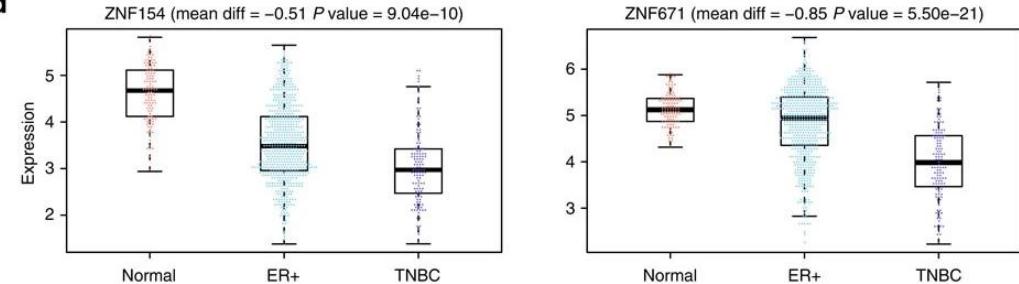
b



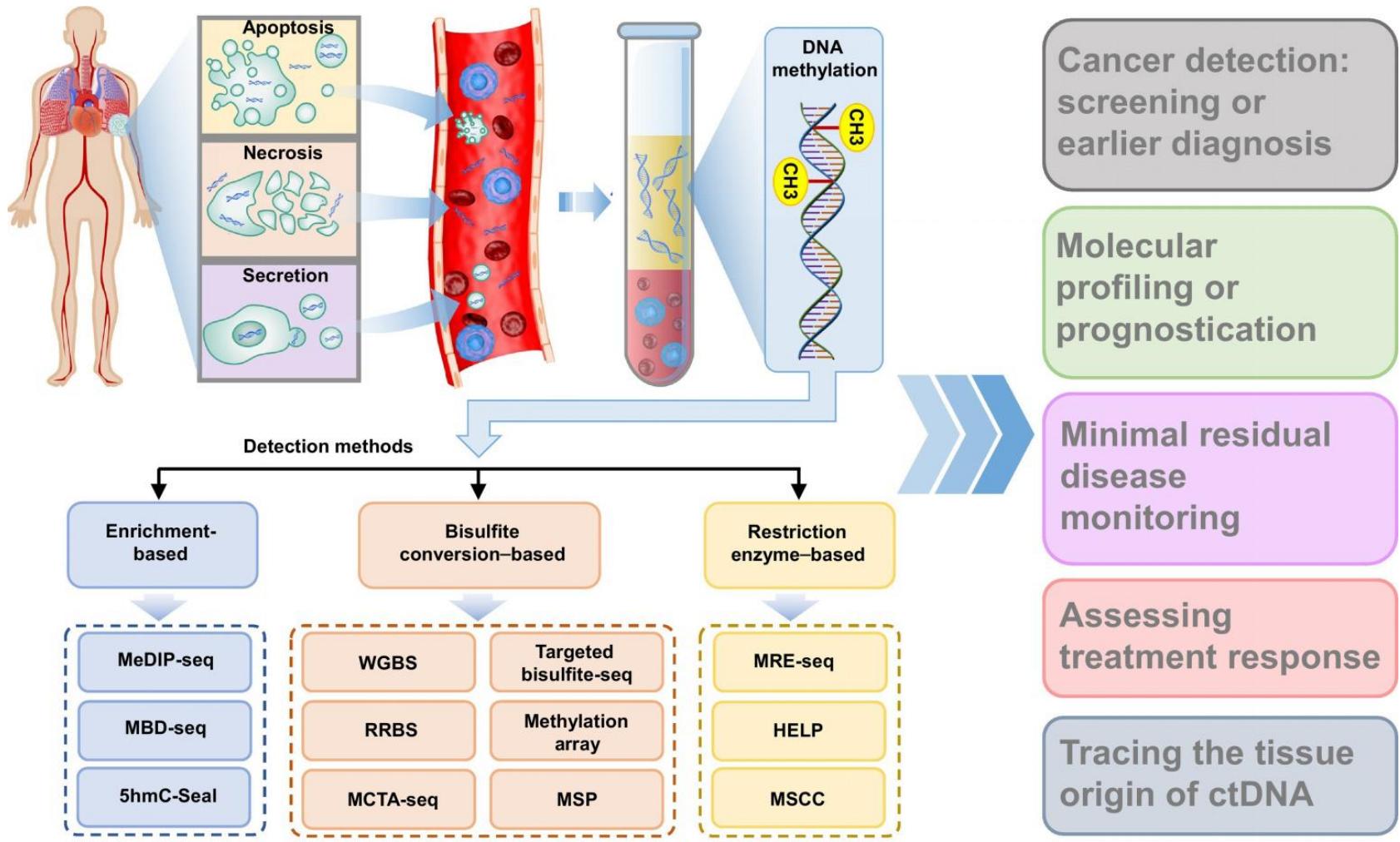
c



d



cfDNA and ctDNA



Trends in Molecular Medicine

Prognostic epigenetic biomarkers for prostate cancer mortality

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RESEARCH ARTICLE

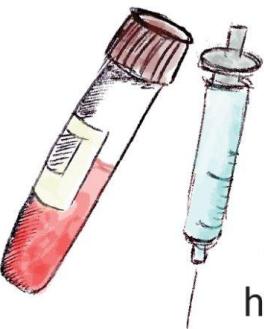


WILEY

Comprehensive methylome sequencing reveals prognostic epigenetic biomarkers for prostate cancer mortality

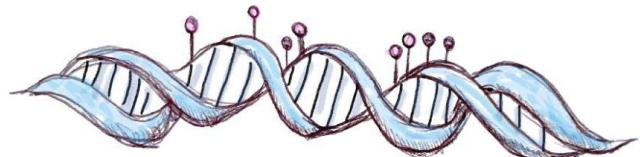
Ruth Pidsley^{1,2} | Dilys Lam¹ | Wenjia Qu¹ | Timothy J. Peters^{1,2} |
Phuc-Loi Luu^{1,2} | Darren Korbie³ | Clare Stirzaker^{1,2} | Roger J. Daly⁴ |
Phillip Stricker^{1,2,5} | James G. Kench^{1,6} | Lisa G. Horvath^{1,2,7,8} | Susan J. Clark^{1,2} 

Prostate cancer
is the second most
common cancer
diagnosed in men

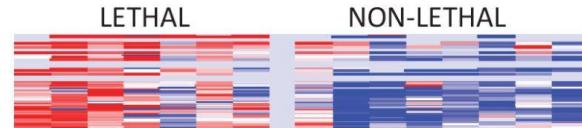


There is a critical need
for more biomarkers to
help guide management

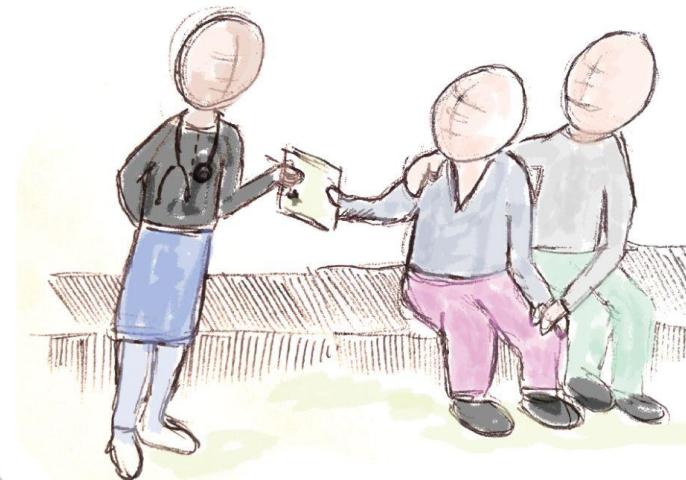
We know that **methylation markers**
on DNA are altered in prostate cancer



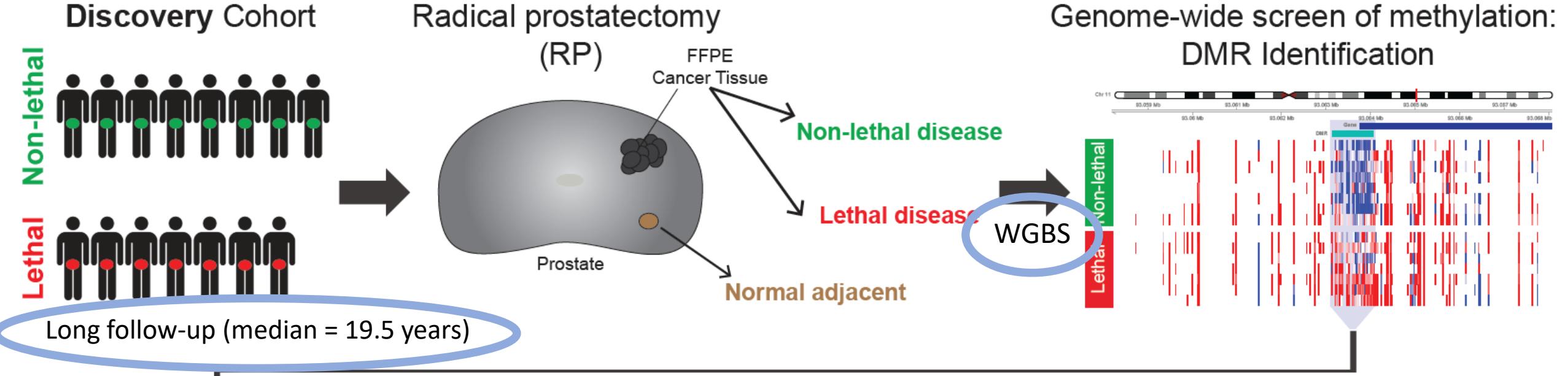
We compared lethal and non-lethal
prostate cancers and found prognostic
methylation markers on DNA



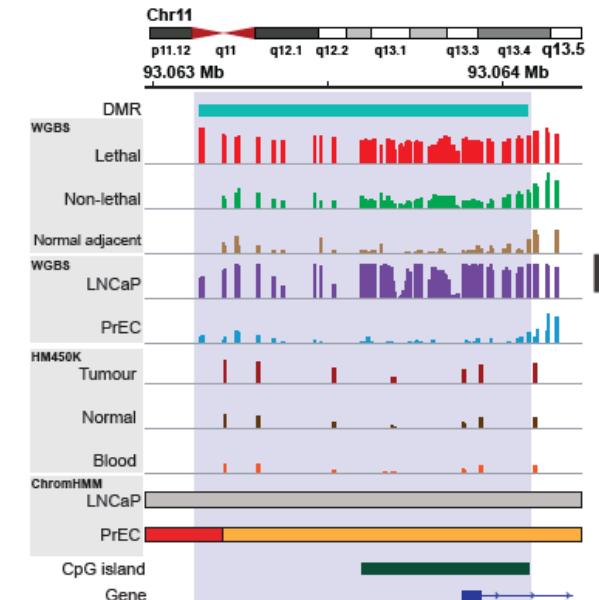
This **prognostic information** could
guide clinical decisions following a
diagnosis of prostate cancer



Credit to Dr Kate



Biomarker selection

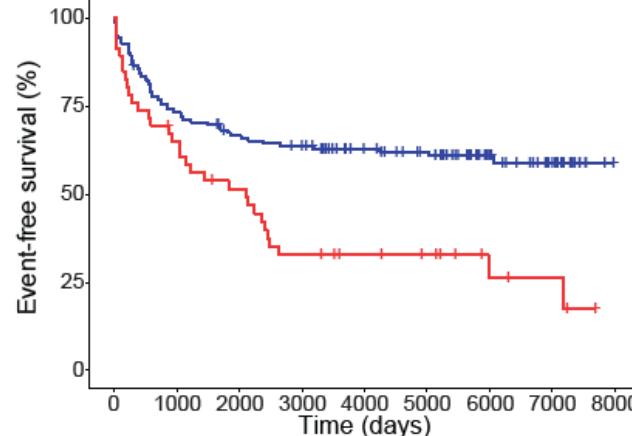


Comparison with in-house and public datasets

Targeted multiplex panel: 18 regions



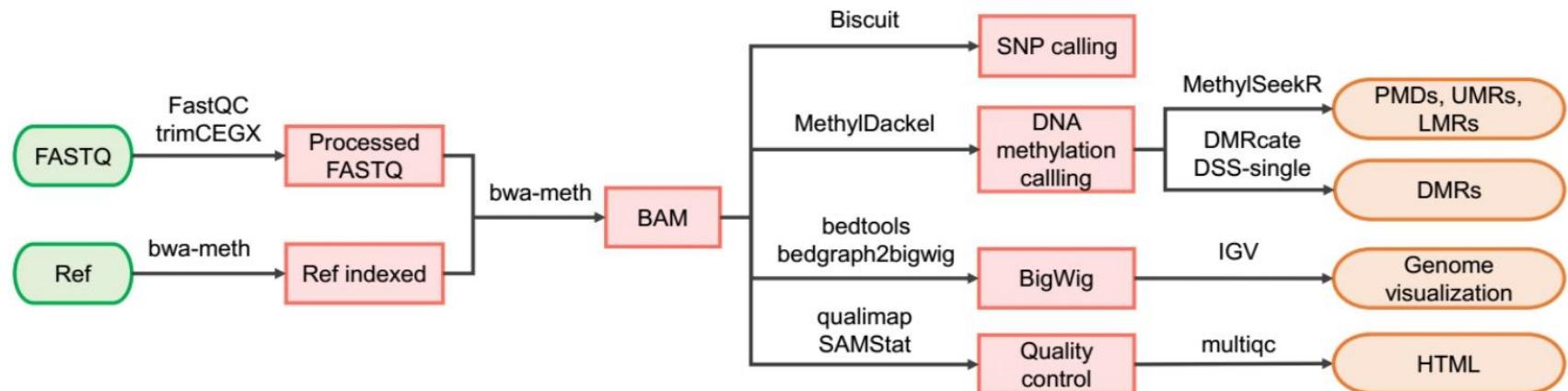
Independent Validation RP Cohort (n = 185): Long follow-up (median = 15 years)



Survival analysis

- Biochemical Recurrence
- Metastatic Relapse
- Prostate Cancer Death

Whole Genome Bisulphite Sequencing pipeline



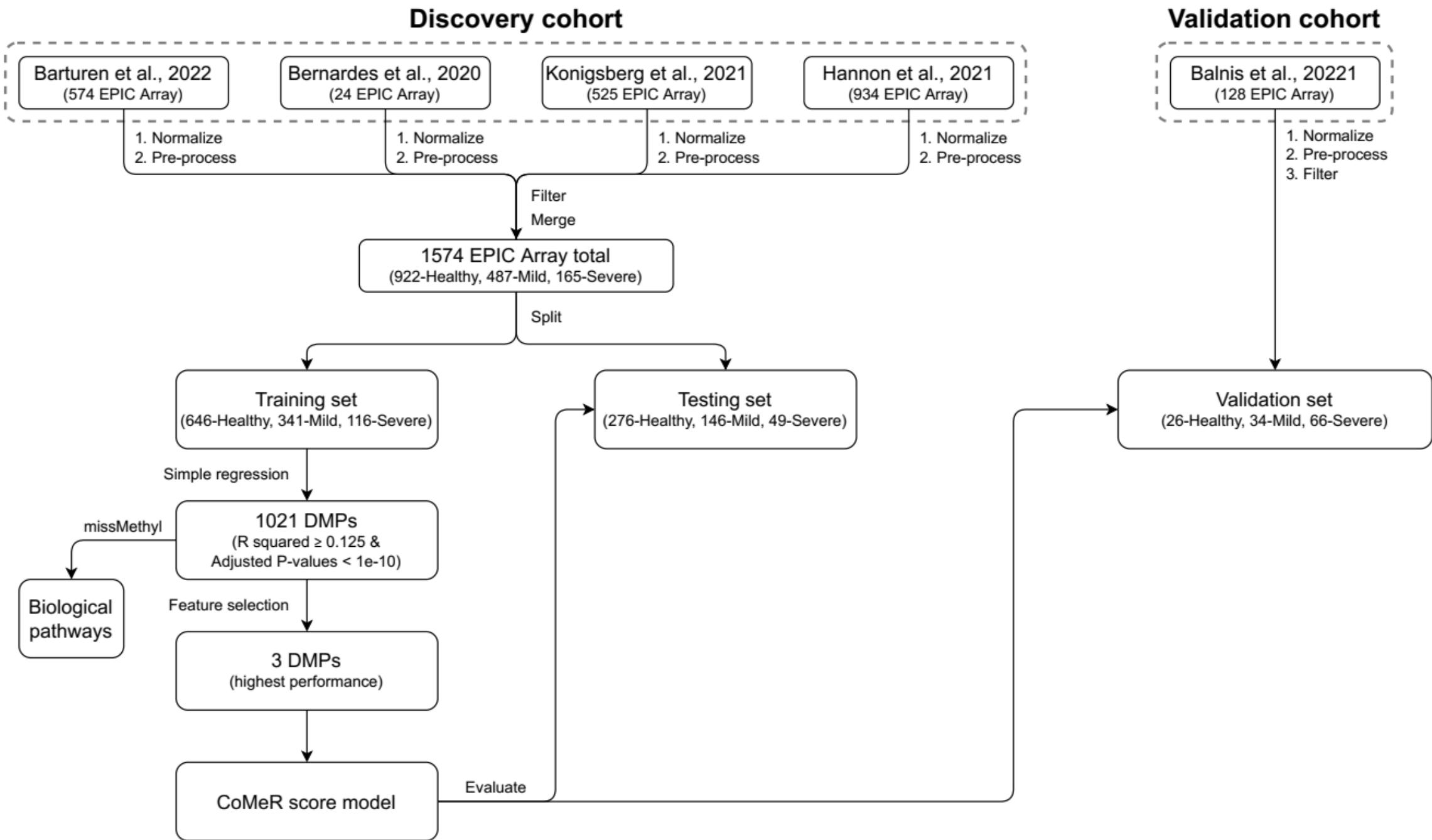
| Package | Version | Link |
|---------------------|---------|---|
| FastQC | 0.11.9 | https://www.bioinformatics.babraham.ac.uk/projects/fastqc/ |
| trimCEGX | 1.0 | https://github.com/luuloi/trim.paired.read |
| bwa-meth | 0.10 | https://github.com/brentp/bwa-meth |
| Biscuit | 0.2.0 | https://github.com/zwdzwd/biscuit |
| MethylDackel | 0.2.0 | https://github.com/dpryan79/MethylDackel |
| qualimap | 2.2.1 | http://qualimap.bioinfo.cipf.es/ |
| SAMStat | 1.08 | http://samstat.sourceforge.net/ |
| MethylSeekR | 1.0 | https://github.com/Bioconductor-mirror/MethylSeekR |
| DMRcate | 2.2.3 | https://bioconductor.org/packages/release/bioc/html/DMRcate.html |
| DSS-single | 2.36.0 | https://bioconductor.org/packages/release/bioc/html/DSS.html |
| multiqc | 1.8 | https://multiqc.info/ |

Figure 4. The WGBS pipeline and software.

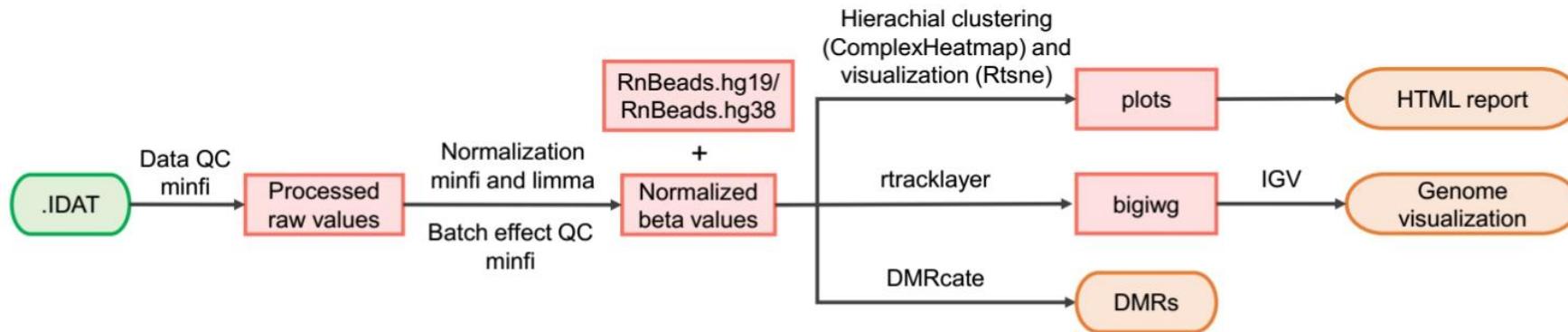
COVID19 DNA methylation risk (COMER) score for severity classification

Aims

1. Development of COVID-19 Methylation risk (CoMeR) score for Severity
2. Validation and Characterization of CoMeR score
3. ShinyApp for prediction of CoMeR

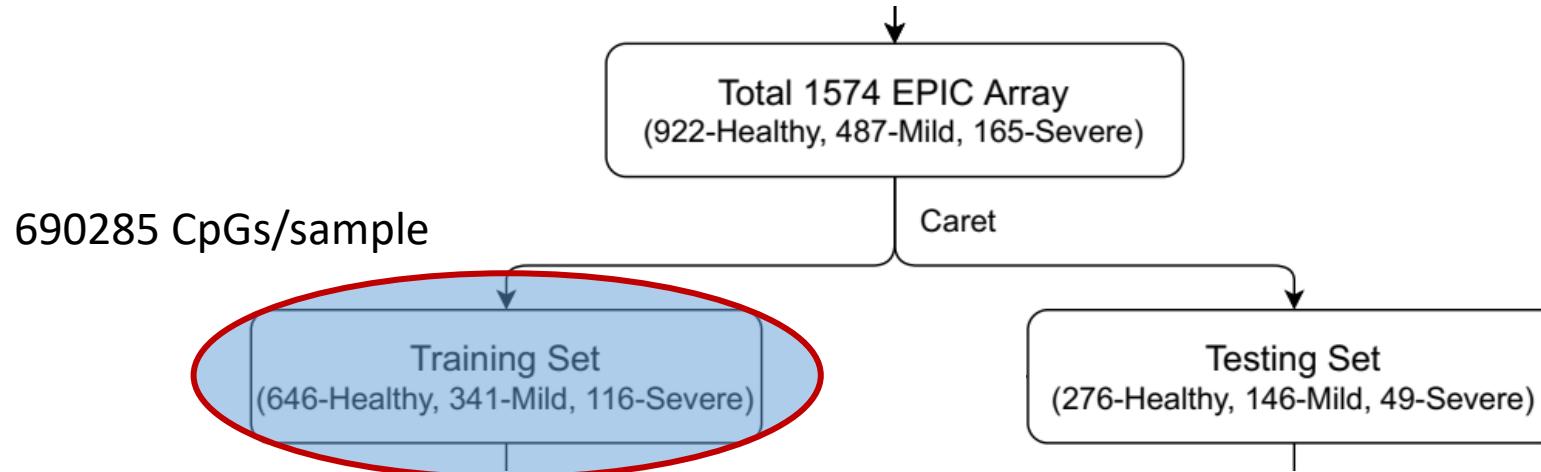


DNA Methylation Array (450K and EPIC/850K) pipeline

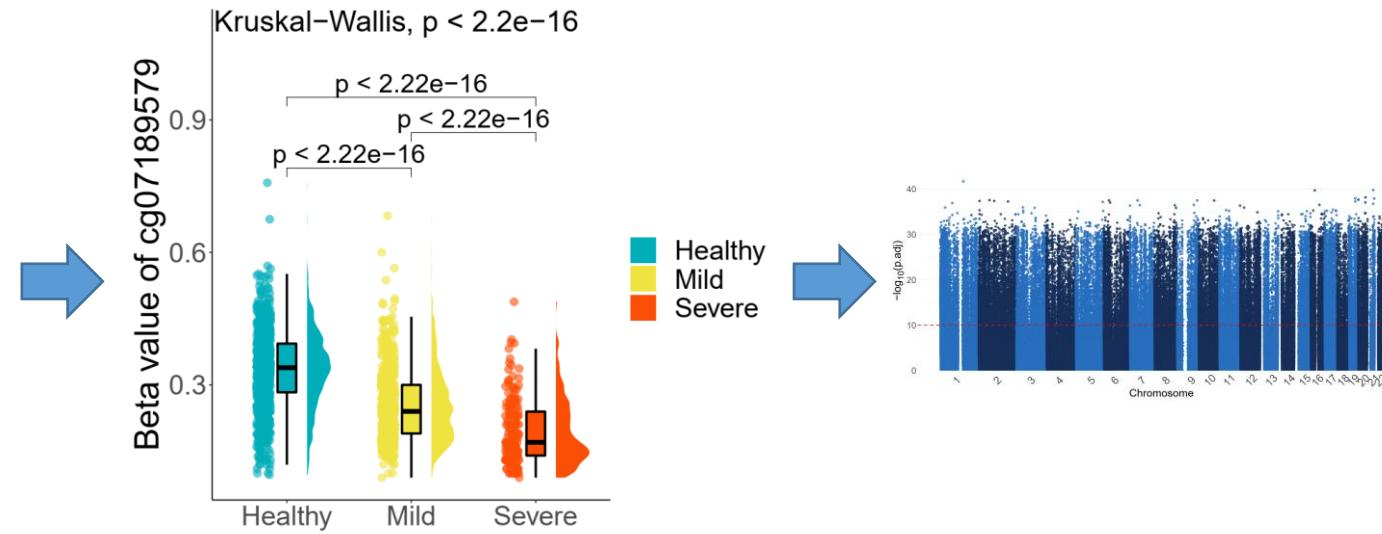


| Package | Version | Link |
|------------------------|---------|---|
| minfi | 1.34.0 | http://bioconductor.org/packages/release/bioc/html/minfi.html |
| limma | 3.44.3 | https://bioconductor.org/packages/release/bioc/html/limma.html |
| RnBeads.hg19 | 1.20.0 | https://bioconductor.org/packages/release/data/experiment/html/RnBeads.hg19.html |
| RnBeads.hg38 | 1.20.0 | https://bioconductor.org/packages/release/data/experiment/html/RnBeads.hg38.html |
| Complex-Heatmap | 2.4.3 | https://www.bioconductor.org/packages/release/bioc/html/ComplexHeatmap.html |
| Rtsne | 0.15 | https://cran.r-project.org/web/packages/Rtsne/index.html |
| rtracklayer | 1.48.0 | https://bioconductor.org/packages/release/bioc/html/rtracklayer.html |
| DMRcate | 2.2.3 | https://bioconductor.org/packages/release/bioc/html/DMRcate.html |

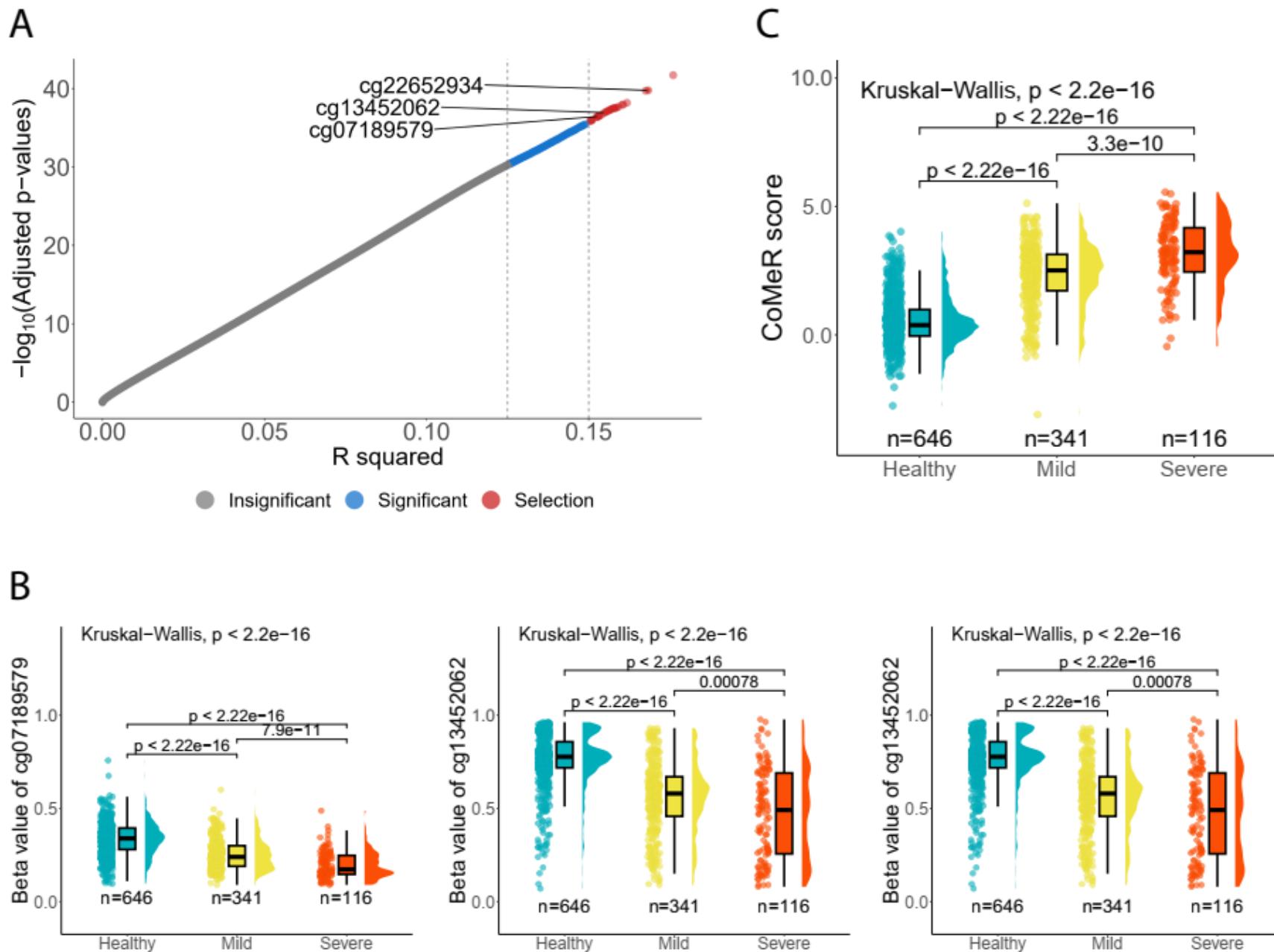
Figure 5. The DNA methylation array (Illumina Methylation 450K and 850K) pipeline and software.



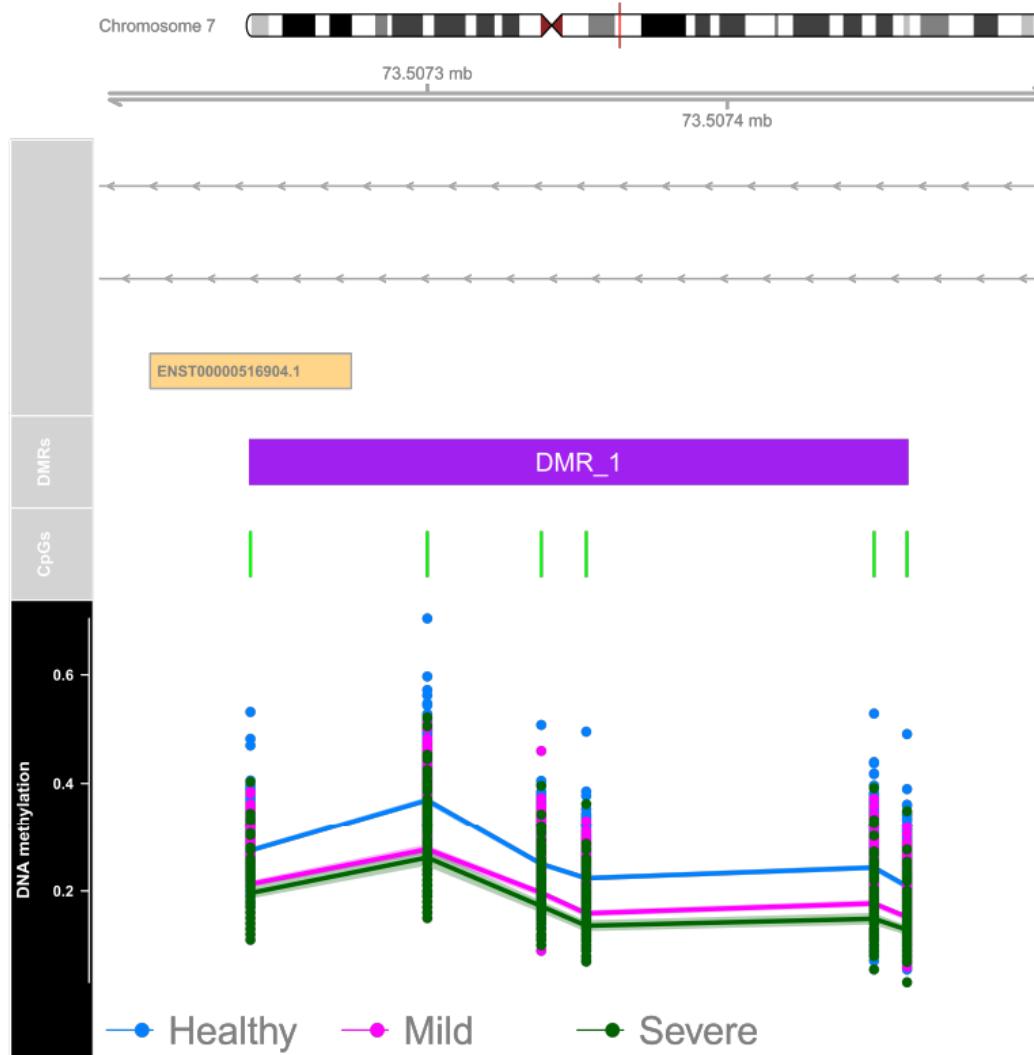
| | sample1 | sample2 | ... |
|-----|---------|---------|-----|
| cg1 | | | |
| cg2 | | | |
| ... | | | |



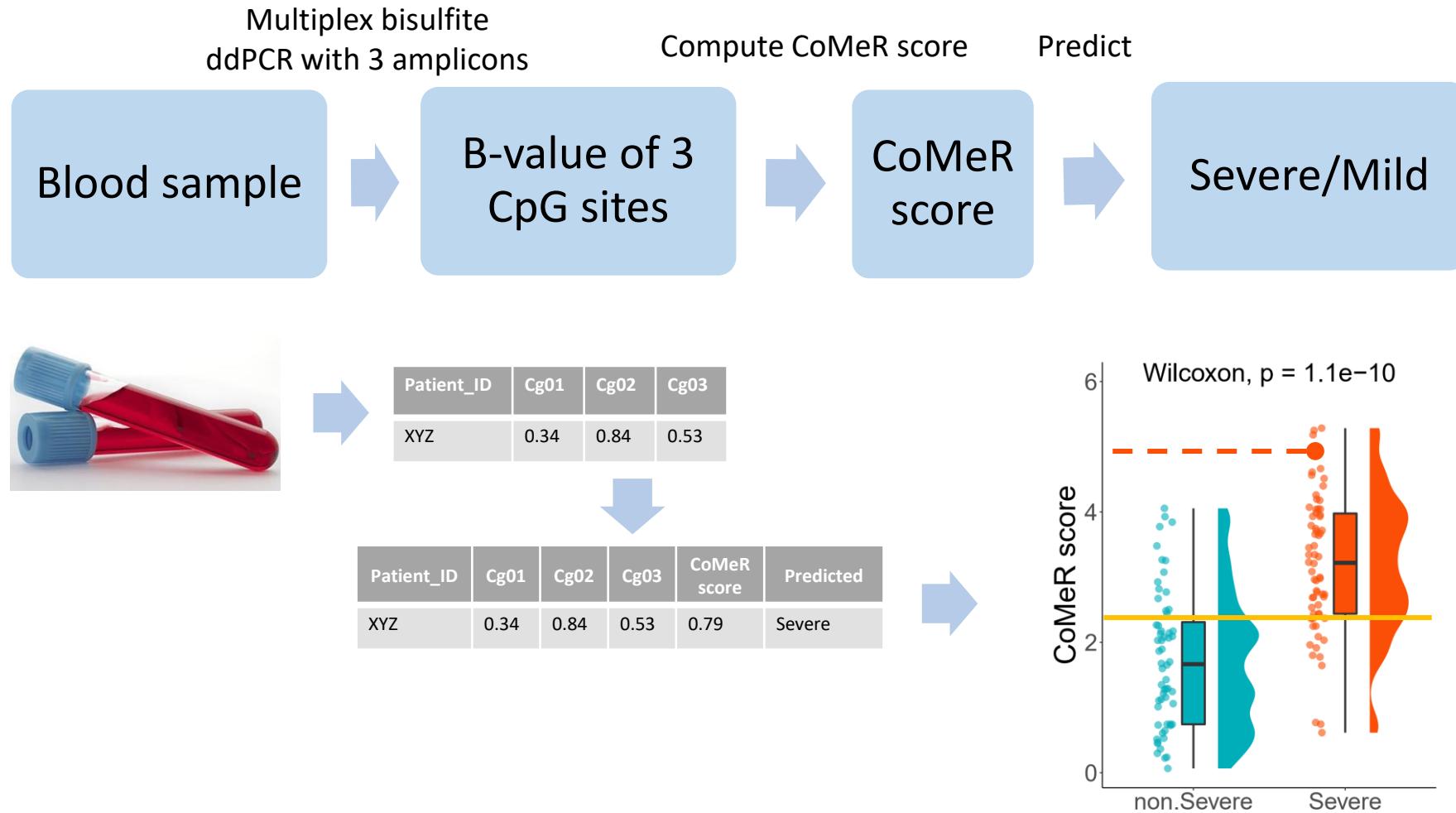
Differentially Methylated Probe (DMP)



Differential Methylation Region (DMR) ~ 500



CoMeR score for diagnosis of COVID-19 patient severity in clinic



Published: 14 March 2018

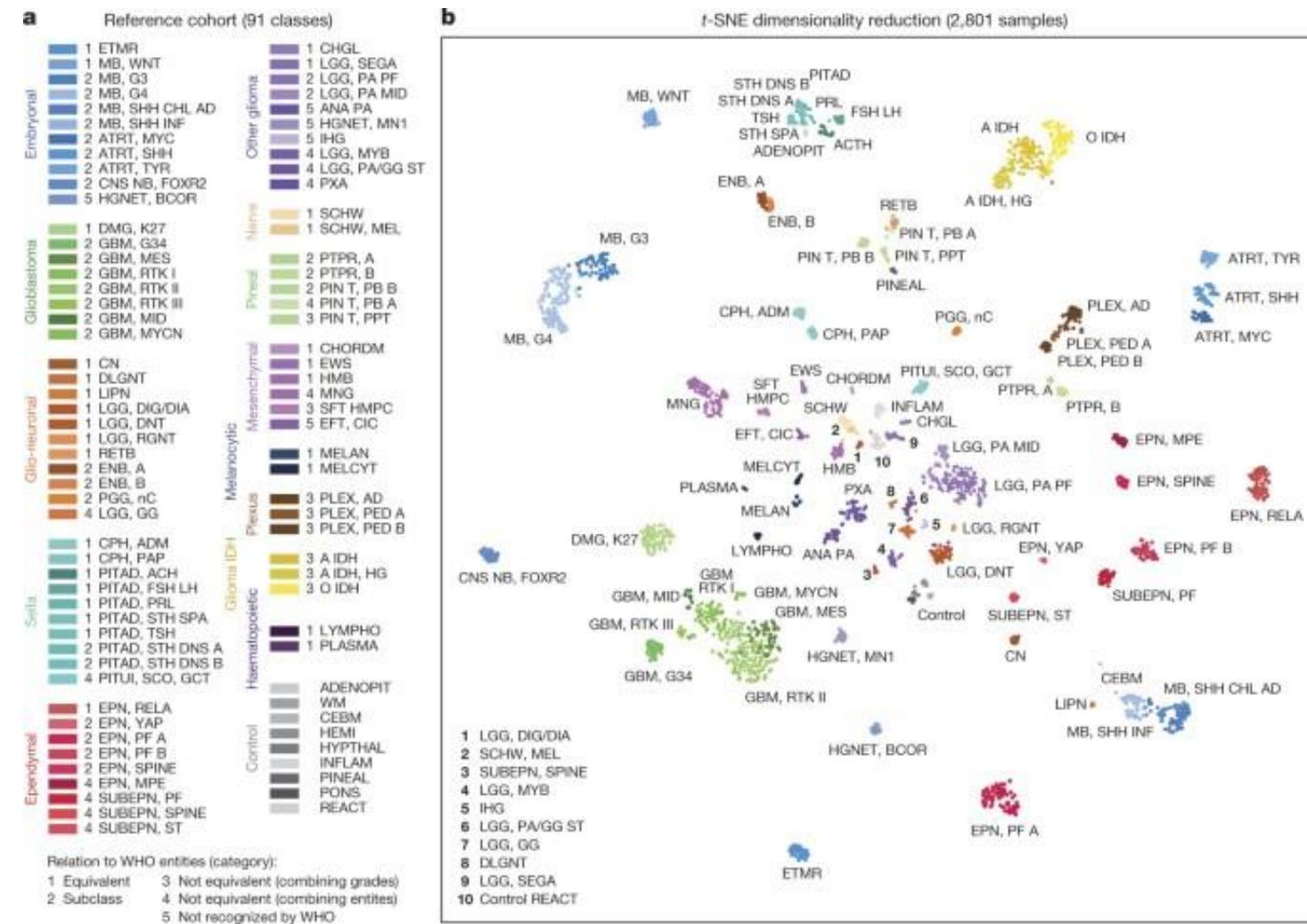
DNA methylation-based classification of central nervous system tumours

[David Capper](#), [David T. W. Jones](#), [Martin Sill](#), [Volker Hovestadt](#), [Daniel Schrimpf](#), [Dominik Sturm](#),
[Christian Koelsche](#), [Felix Sahm](#), [Lukas Chavez](#), [David E. Reuss](#), [Annekathrin Kratz](#), [Annika K. Wefers](#),
[Kristin Huang](#), [Kristian W. Pajtler](#), [Leonille Schweizer](#), [Damian Stichel](#), [Adriana Olar](#), [Nils W. Engel](#),
[Kerstin Lindenberg](#), [Patrick N. Harter](#), [Anne K. Braczynski](#), [Karl H. Plate](#), [Hildegard Dohmen](#), [Boyan K.](#)
[Garvalov](#), ... [Stefan M. Pfister](#)  + Show authors

[Nature](#) **555**, 469–474 (2018) | [Cite this article](#)

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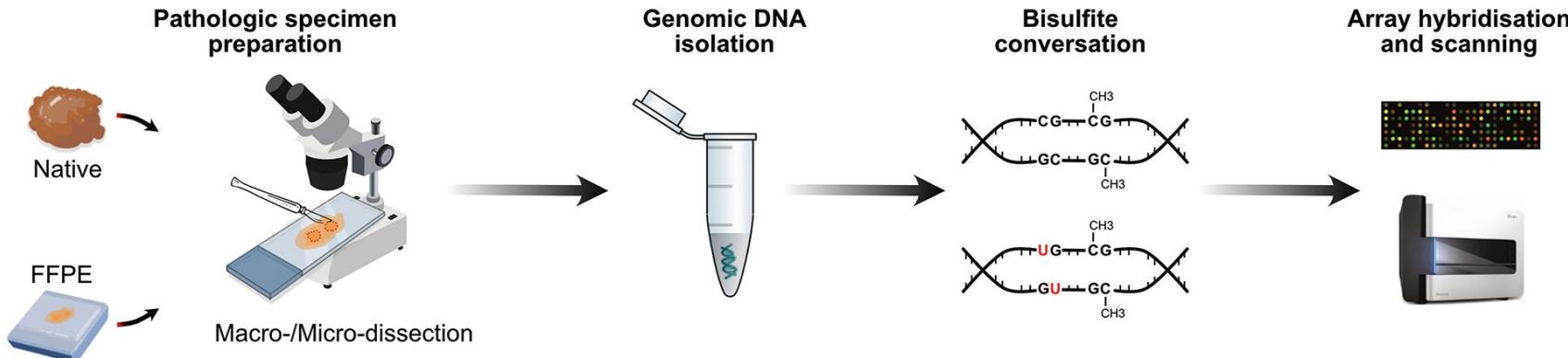
The other clinical application of DNA methylation in brain tumors



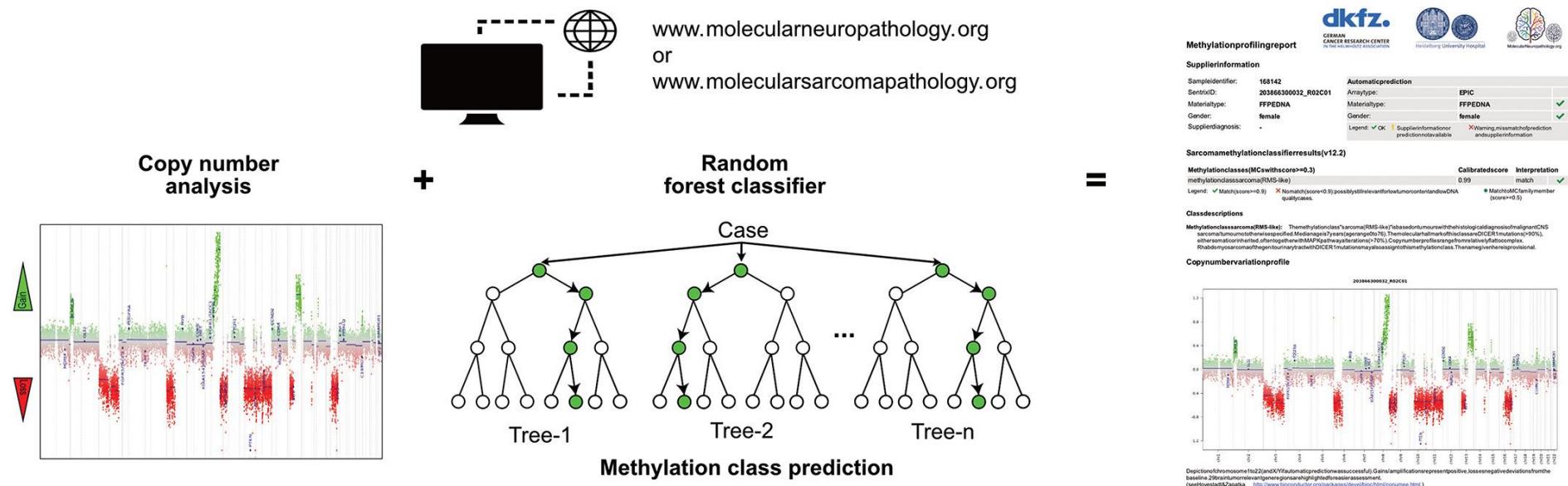
Methylation classifiers: Brain tumors, sarcomas, and what's next

- Koelsche - 2022 - Genes, Chromosomes and Cancer - Wiley Online Library

Data generation



Data visualization and classification



THANK YOU FOR YOUR ATTENTION!

Please contact:

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Zalo: 0901802182

For further information!