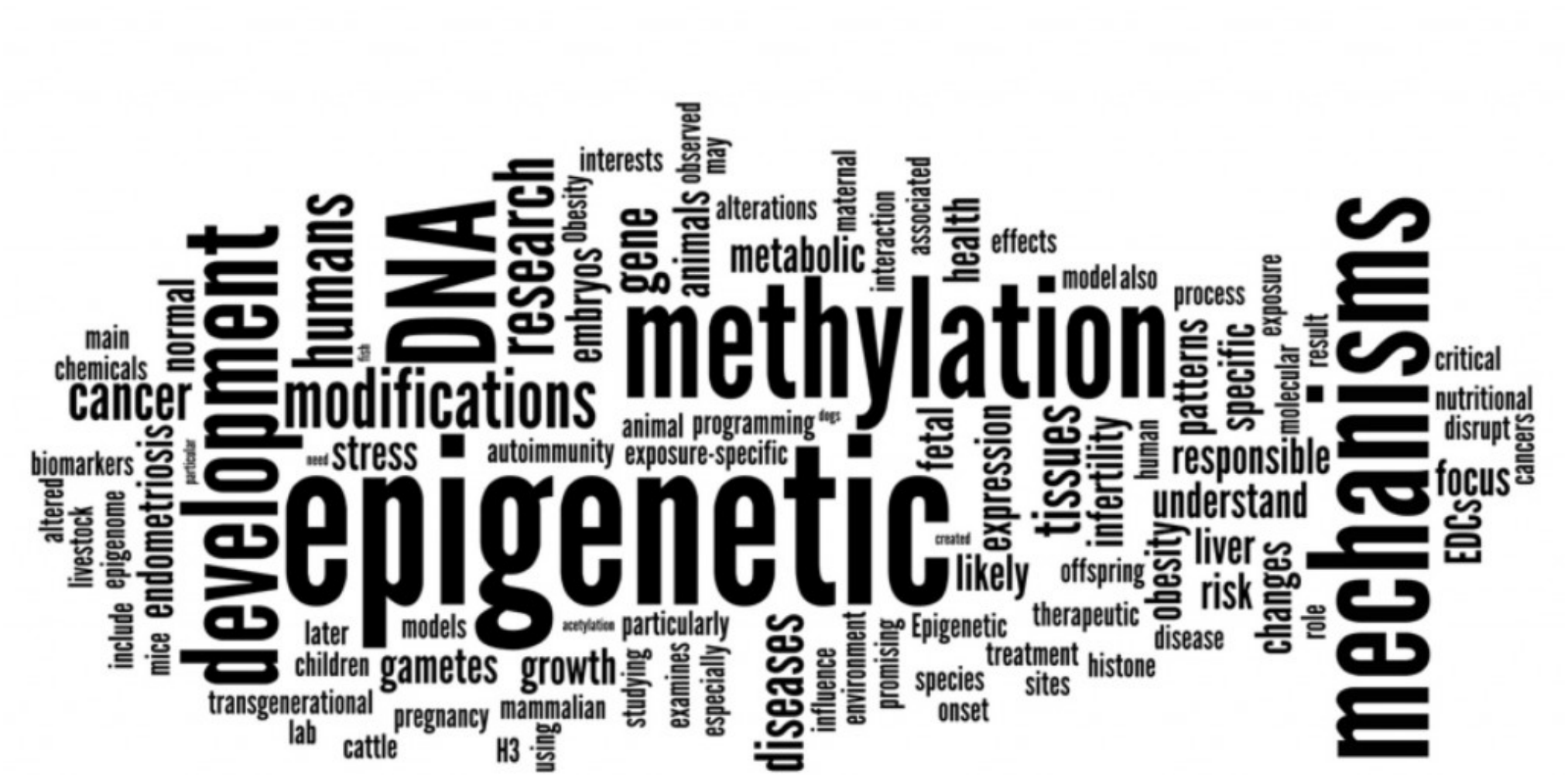
EPIGENTICS


epigenetic
methylation
mechanisms
development
DNA
modifications
research
humans
cancer
gene
metabolic
tissues
responsible
understand
diseases
gametes
growth
stress
autoimmunity
exposure-specific
animal programming
fetal
expression
infertility
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Epigenetic
treatment
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mammalian
transgenerational
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models
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biomarkers
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Obesity
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also
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molecular
result
specific
patterns
critical
nutritional
disrupt
cancers
focus
EDCs
human
created
dogs
fish
particular
need

MATERIALE DIDATTICO

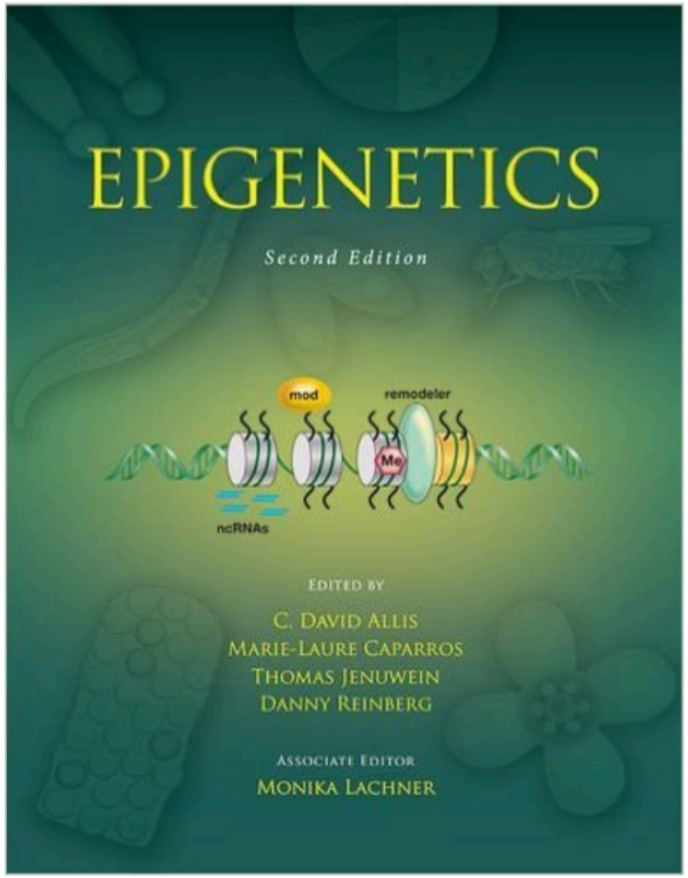
UNIVERSITÀ
DEGLI STUDI DI TRIESTE

MOODLE FEDERATO

1. PPT SLIDES – Moodle Federato

Lezione: Epigentica

Password: LezioneEpigenetica
http://moodle2.units.it/



2. TEXTBOOK:

“Epigenetics”, Second Edition, CSH Press
Prezzo: Euro 150,--
Bibliotheca Uni TS (ordinato)

PROGRAM EPIGENTICS

Prof. Schoeftner – 6 CFU

TEXTBOOK: "Epigentics", Second Edition, CSH Press

1. Overview and Concepts
2. Writers and Readers of Histone Acetylation
3. Erasers of Histone Acetylation
4. Structural and Functional Coordination of DNA and Histone methylation
5. Position Effect Variegation, Heterochromatin Formation and Gene Silencing In Drosophila
6. RNAi and Heterochromatin assembly
7. Polycomb group and Trithorax group proteins
8. Histone Variants and Epigenetics
9. Maintenance of Epigenetic Information
10. Genomic Imprinting in Mammals
11. Induced Pluripotency and Epigenetic Reprogramming
12. Epigenetics and Human Disease
13. Epigenetic Determinants of Cancer
14. Histone modifications and Cancer

1. MODALITY OF THE EXAM:

The exam comprises a WRITTEN test that comprises two parts:

Short answer part:

11 Questions; 1 point/question

This part of the exam can consist: questions with multiple choice or questions with short written answers or questions that require a simple, schematic drawing/diagram as answer.

Detailed answer part:

4 Questions, 5 points/question

Questions of this part of the exam will address a general concept of molecular biology or central processes in molecular biology. Students are asked to give a detailed and focused answer (max. 1 page). A focus will be given on the use of specific scientific terms that relate to the respective topic of the question. The question can also be formulated in a manner that evaluates the logic understanding of topics addressed during the lecture.

Duration of the exam:

2 hours

What to bring:

Carta d'Identità

2 pens with different colors (useful for answers that require simple drawings)

Max. Points:

11+20 → **30** (31)

2. RESULTS OF THE EXAM:

Students that participated in a call/appello will be informed via e-mail when the results of the exam have been published. Results will be published on the **Moodle federale (Moodle 2)** webpage, where also the material for the lecture "Epigenetica" is available. Students are asked to open the folder "**RESULTS EXAM**" and check the results of the respective appello/call.

3. REGISTRAZIONE VOTI

After publishing the results of the exam, students have 7 days time to decide whether they refute the vote.

If a student desires to refute a voto, the student needs to use **ESSE 3 – EPIGENTICA** and make an inscription to an appello named **"RIFIUTO VOTO – DATA APPELLO**". As a consequence the result of the respective appello will not be considered.
If a student doe not make an inscription to this list, the voto will be automatically registered.

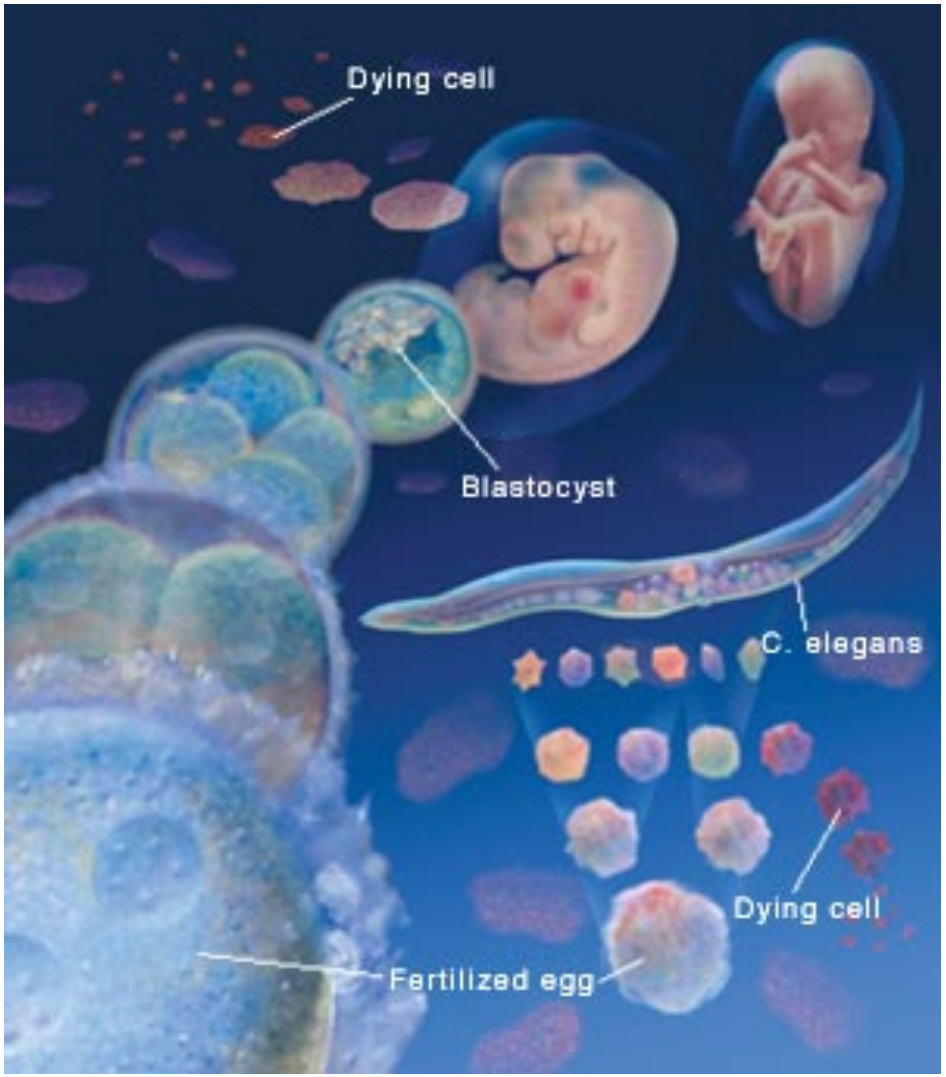
IMPORTANT: 8 days after the publication of the voti in Moodele federale, it is no longer possible to refute the voto. At this point all voti will be registered (see below). NO EXCEPTIONS WILL BE MADE.

In a last step, the "accepted" volti will be published in a separate list in Moodle federale in the folder "**REGISTRAZIONE VOTI**".
Students have 3 days time to check the correctness of voto before final registration. Note: At this point it is only possible to check the numeric correctness of the voto, it is no longer possible to refute the voto.

What is Epigentics?
….a scientific term in evolution

Waddington 1950

…Epigenetics is the study of processes that categorize all of the developmental events leading from the fertilized oozyte to the mature organism – that is, all of the regulated processes that, beginning with the genetic material, shape the final product



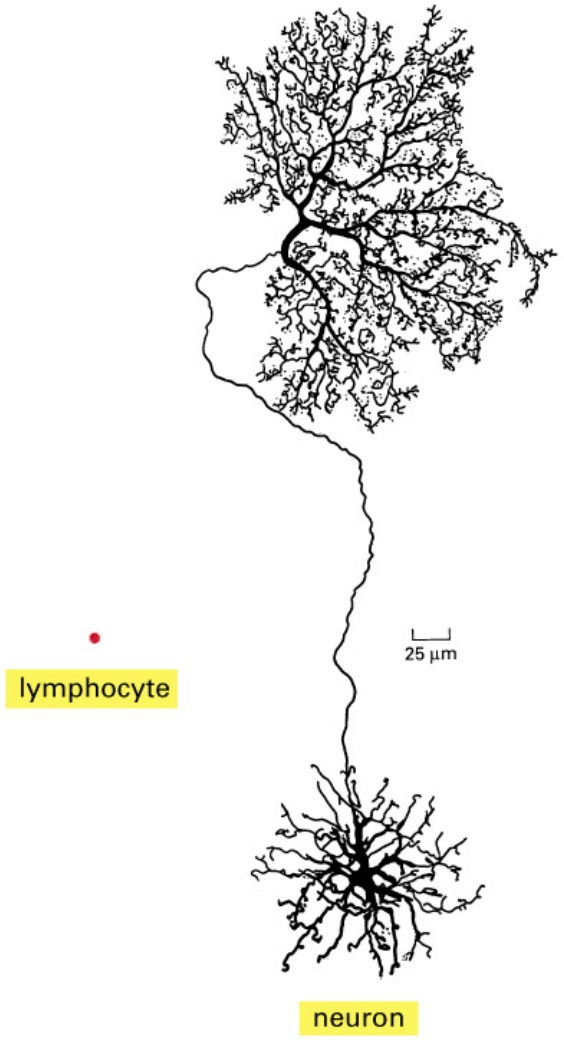
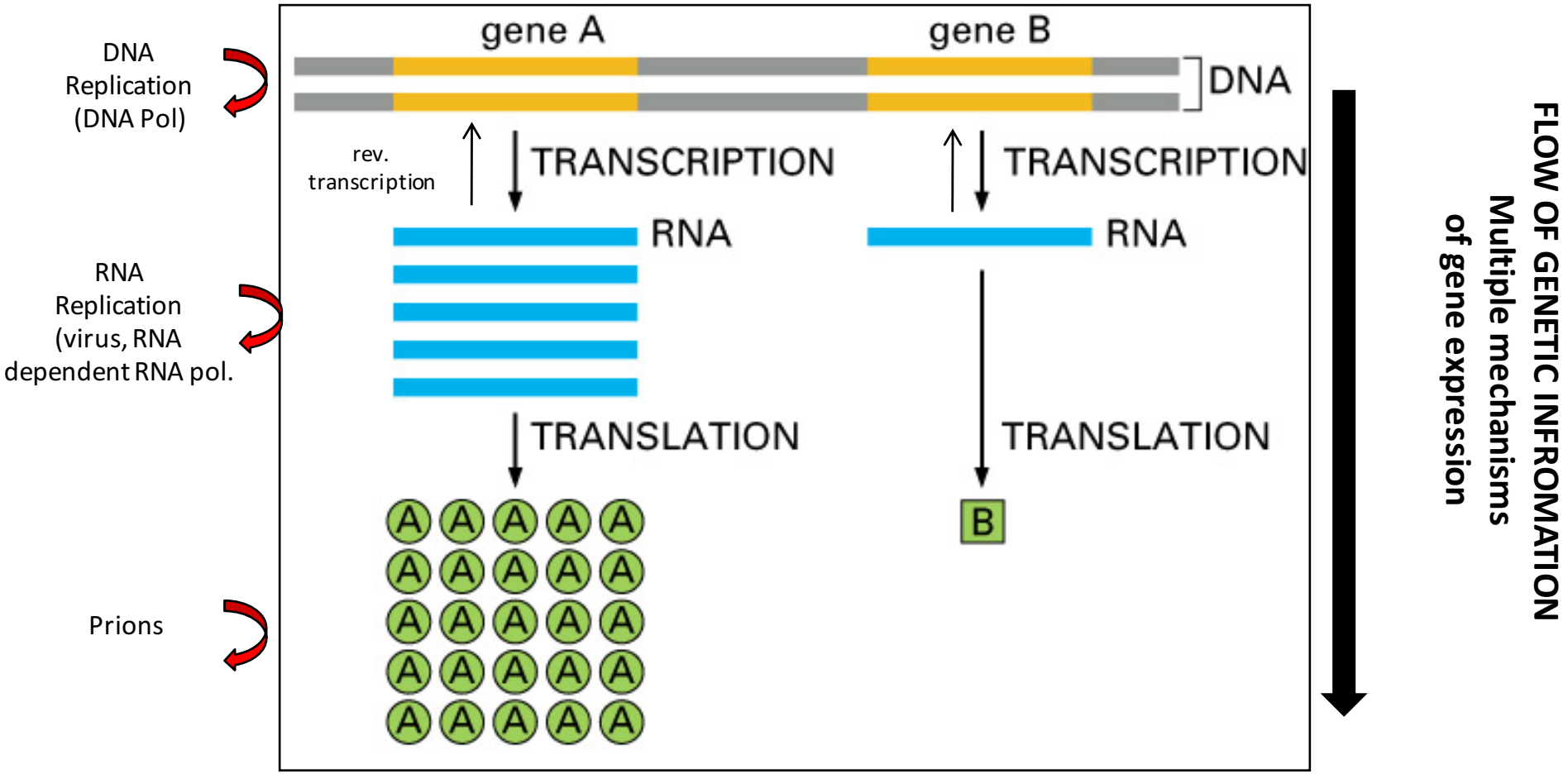


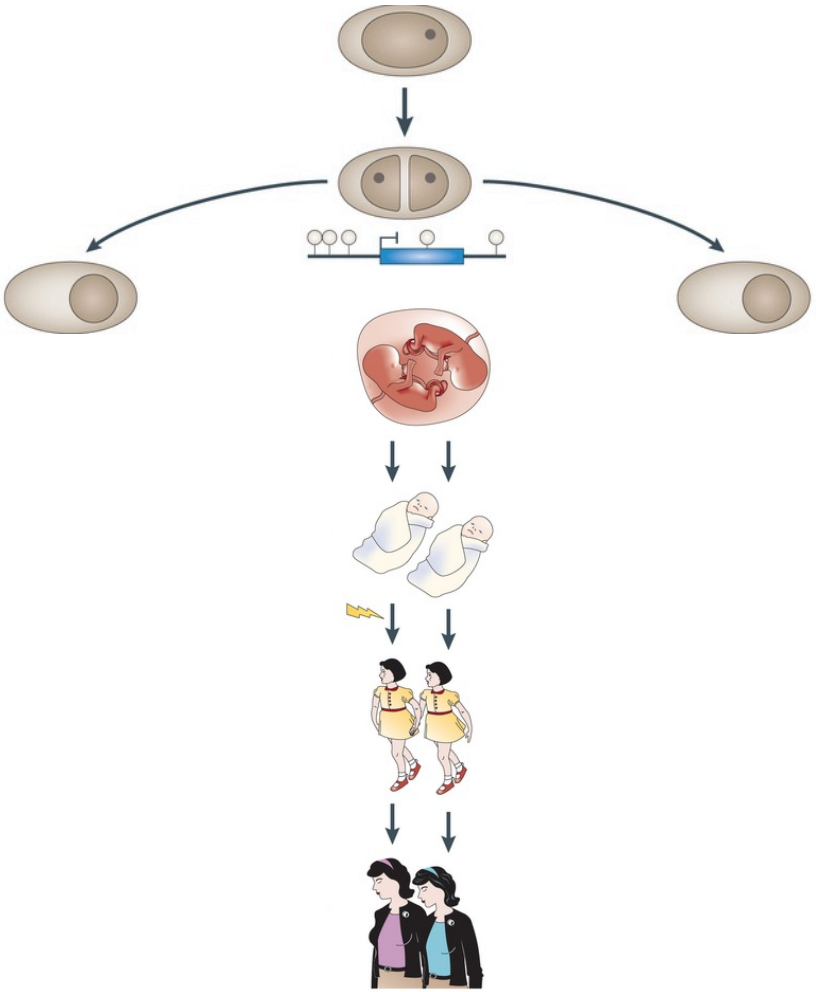
Figure 7–1. Molecular Biology of the Cell, 4th Edition.

The central dogma

Crick, F (1970). "Central dogma of molecular biology.". Nature 227 (5258): The central dogma of de molecular biology deals with the detailed residue-by-residue transfer of sequential information. It states that such information cannot be transferred back from protein to either protein or nucleic acid.



Observations that cannot be explained by genetics…..



Monozygotic twins have 100% identical DNA

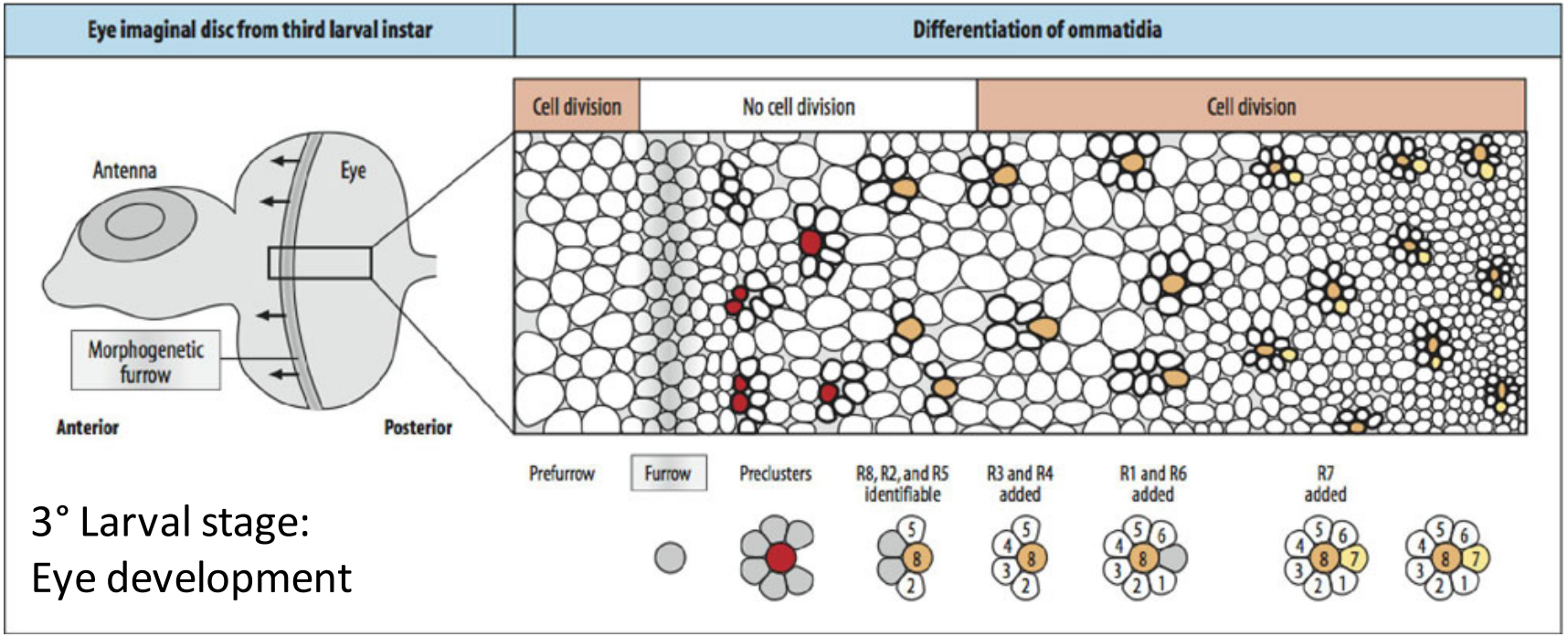
…but disease (multiple sclerosis) only in one of the two twins

…. There must be a special type of genetic information other than that of DNA

Observations that cannot be explained by genetics…..
Muller 1950

W = white gene:wncodes a red pigment that is incorporated into ommatides of the Drosphila melanogaster

Position effect variegation: Drosophila melanogaster



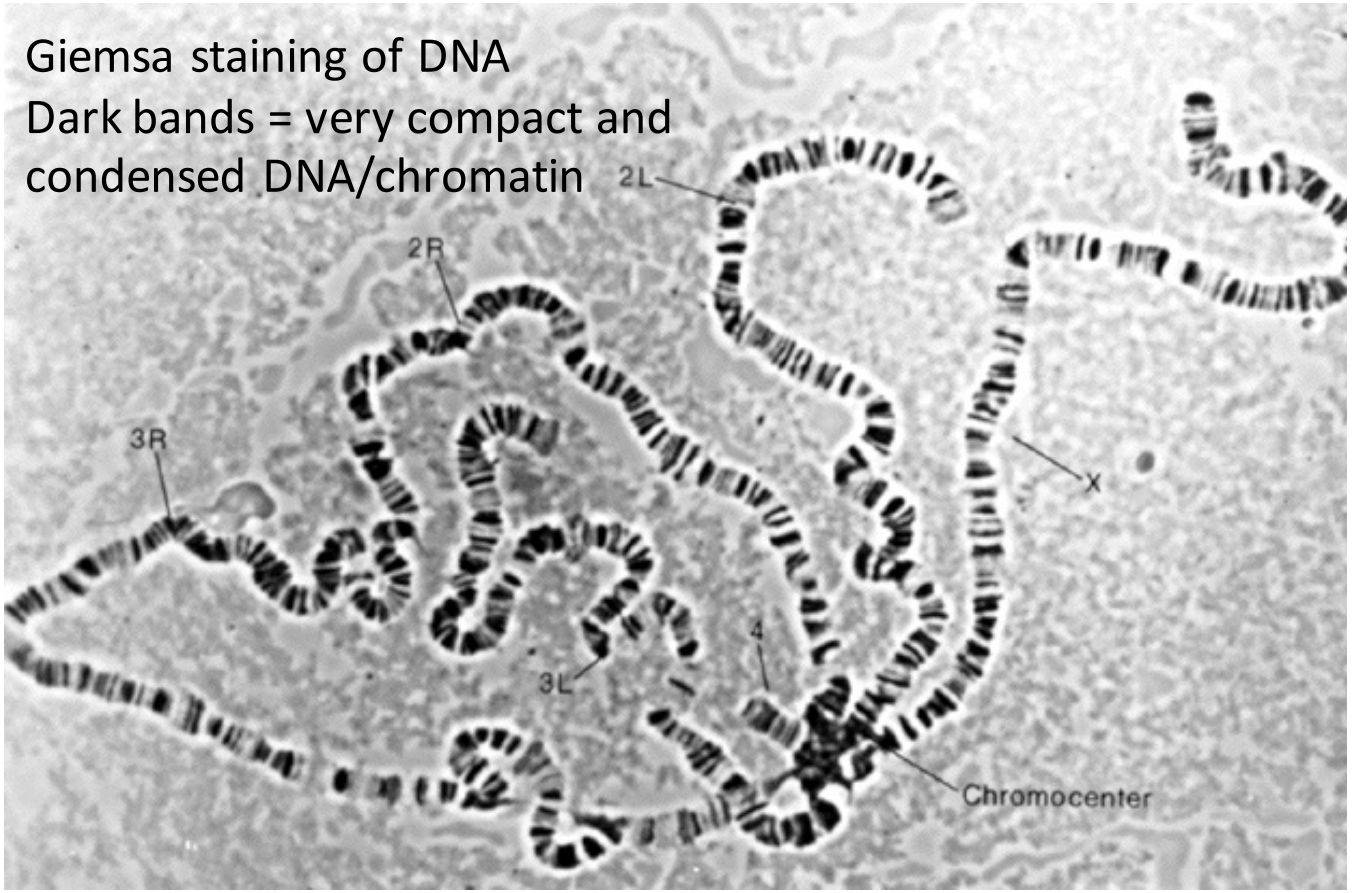
The Drosophila compound eye has 800 ommatidia (the photoreceptor organ), each which has 8 photreceptor neurons (R1-8), 4 cone cells (lens secretion) and **pigment cells**. Great model system to study a small group of cells. The eye develops as a single cell epithelial layer. During 3rd larva instar, posterior part of the eye begins to develop. Over two days the patterning moves towards the anterior while the disc grows 8 fold in size. Th morphogenetic furrow forms early in the posterior eye disc and sweeps across the disc (P->A) to leave clusters of cells spaced in a hexagonal array in its wake. The morphogenetic furrow moves at a rate of 2 hours per row of ommatidial clusters (2 days for the eye). Behind the furrow, cells differentiate to become regularly spaced ommatidia, each row out 1/2 register from the next to give the hexagonal arrangement. The R8 photoreceptor neurons differentiate first separated by ~8 cells. Each R8 starts a series of signals that recruit a cluster of 20 cells. R2 &R5 form two identical neurons on either side of the R8, then R3 & R4 (different photreceptor types), then R1 & R6 abd finally R7 to surround the R8 cell.

Observations that cannot be explained by genetics…..
Muller 1950

W = white gene:wncodes a red pigment that is incorporated into ommatides of the Drosphila melanogaster
when mutated, eyes become white

Position effect variegation: Drosophila melanogaster

Polythen chromosomes are generated by endoduplication
Polytene chromosomes are large chromosomes which have thousands of DNA strands. They provide a high level of function in certain tissues such as salivary glands. They are produced when repeated rounds of DNA replication without cell division forms a giant chromosome. Thus polytene chromosomes form when multiple rounds of replication produce many sister chromatids which stay fused together.Polytene chromosomes, at interphase, are seen to have distinct thick and thin banding patterns. These patterns were originally used to help map chromosomes, identify small chromosome mutations, and in taxonomic identification. Now they are used to study the function of genes in transcription.
In insects, polytene chromosomes are commonly found in the salivary glands; they are also referred to as "salivary gland chromosomes".



Observations that cannot be explained by genetics…..
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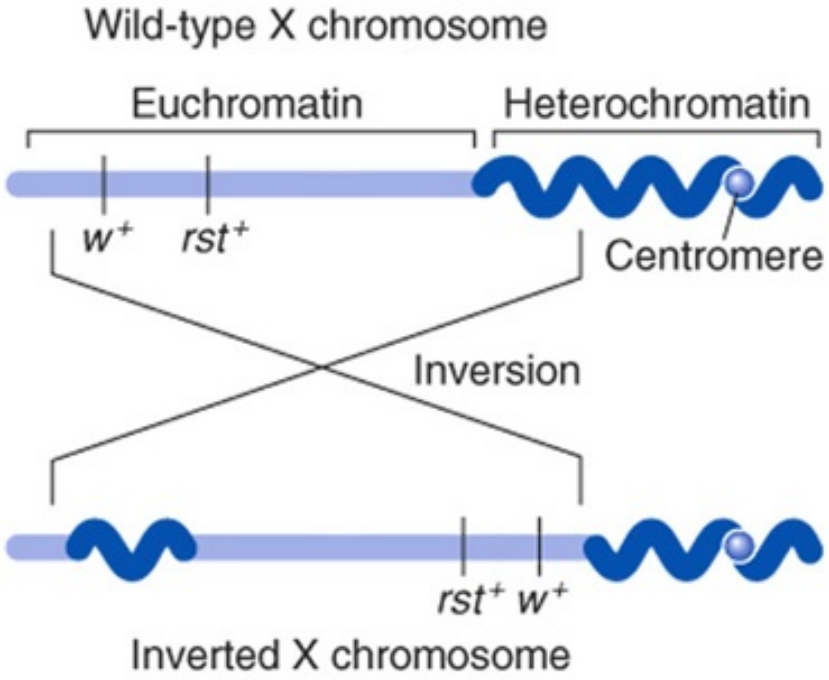
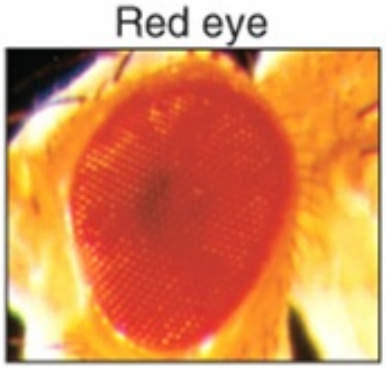
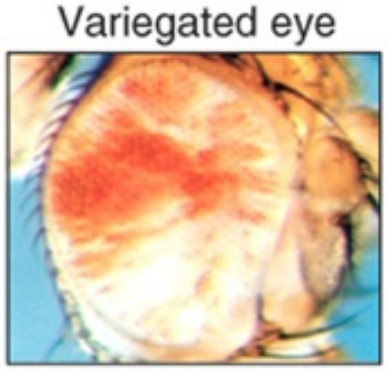
Position-effect variegation Drosophila melanogaster





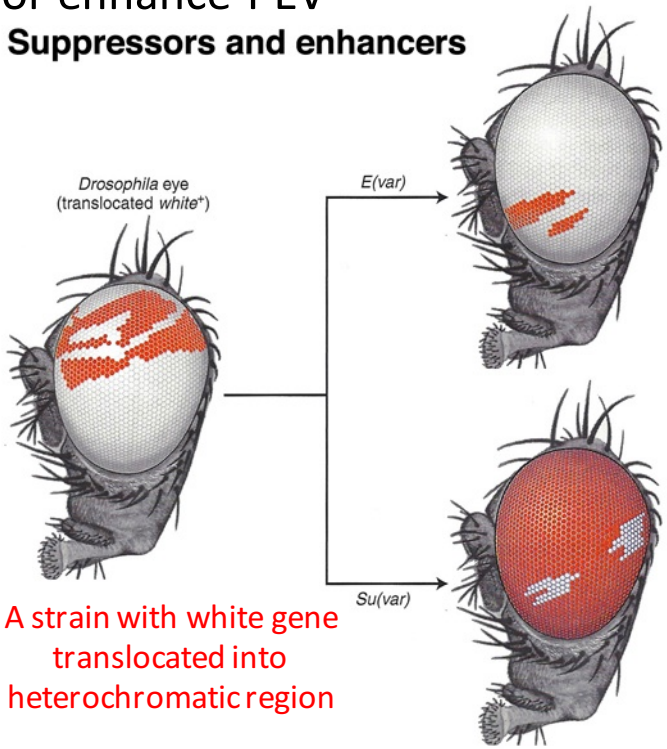
Normal fly:
w^+: red pigment expressed



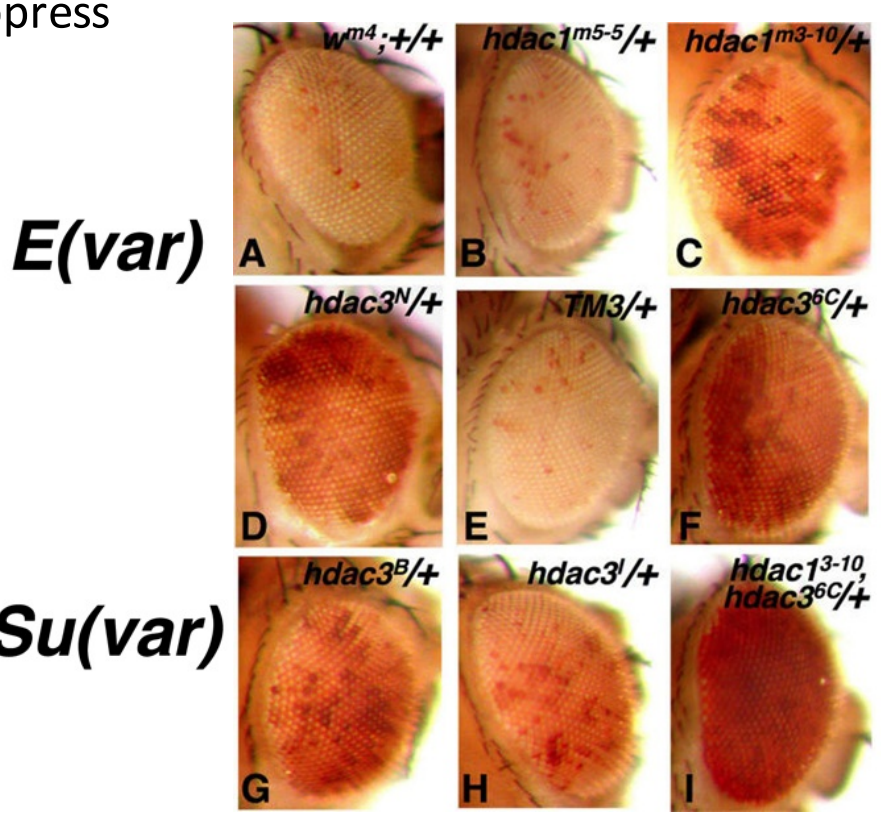
Genome rearrangement:
DNA sequence has not Changed; but white gene is close to the centromere
White gene is still wild type but no longer expressed

Observations that cannot be explained by genetics…..

Mutations in certain genes can suppress or enhance PEV



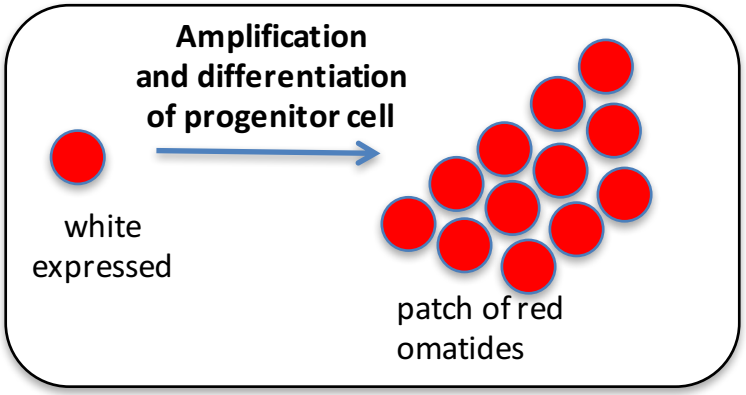
A strain with white gene translocated into heterochromatic region

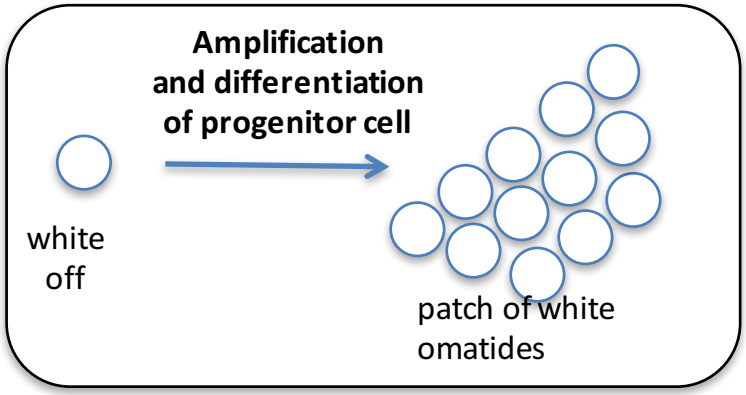


Additive effects of two *Su(var)* mutations

Su(var) = hdac

***hdac* = histone deacetylase**

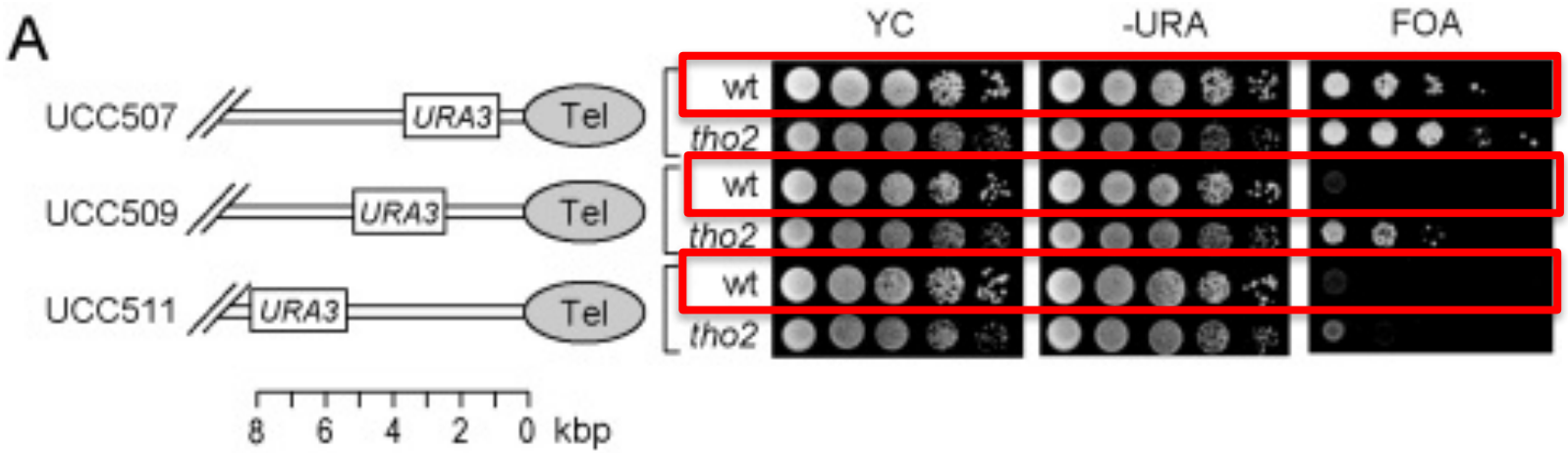




Variegated Phenotype is Stably during Cell division →Is propagated to daughter cells =a sort of inheritance

Observations that cannot be explained by genetics…..

Telomere position effect: yeast, human, drosophila



URA3 marker (=promoter+cDNA constrct) is inserted at different distances to telomere
If the URA3 marker is close to the telomere → FAO resistance is good
If the URA3 marker is far away from the telomere → FAO resistance is low

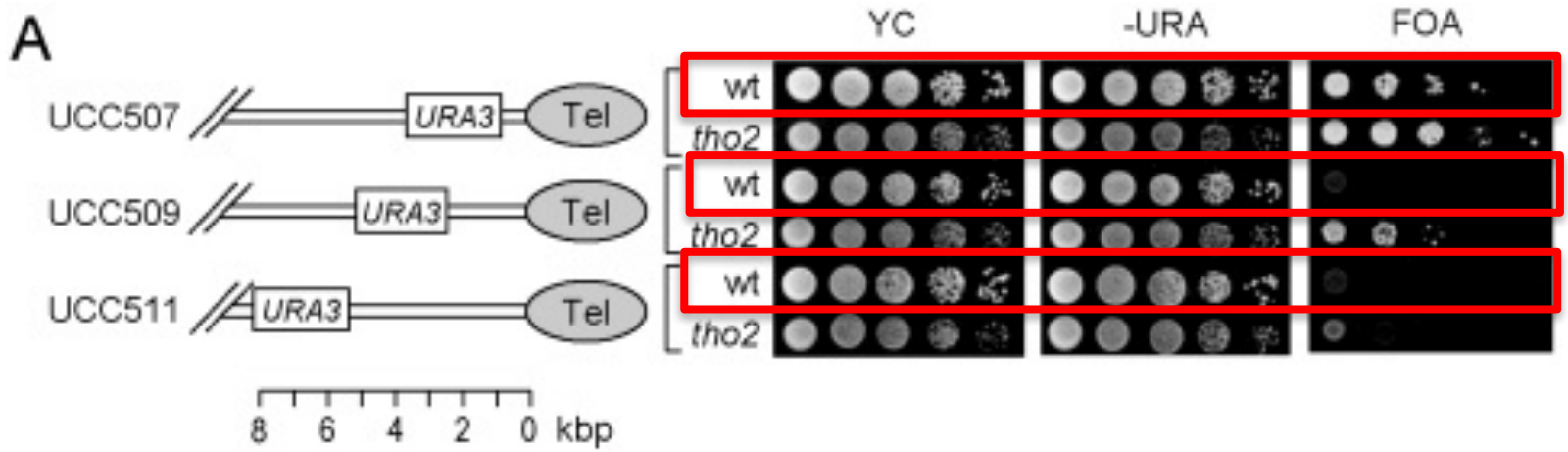
= TELOMERE POSITION EFFECT

URA3 is a gene on chromosome V in Saccharomyces cerevisiae (yeast). URA3 is often used in yeast research as a "marker gene", that is, a gene to label chromosomes or plasmids. URA3 encodes Orotidine 5'-phosphate decarboxylase (ODCase), which is an enzyme that catalyzes one reaction in the synthesis of pyrimidine ribonucleotides (a component of RNA)

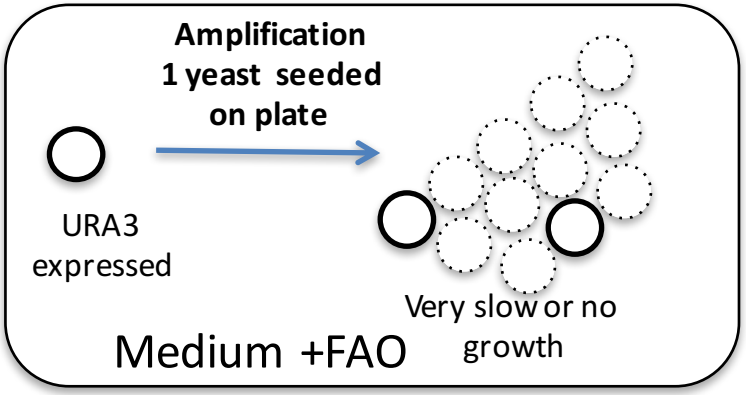
Loss of ODCase activity leads to a lack of cell growth unless uracil or uridine is added to the media. The presence of the URA3 gene in yeast restores ODCase activity, facilitating growth on media not supplemented with uracil or uridine, thereby allowing selection for yeast carrying the gene. In contrast, if 5-FOA (5-Fluoroorotic acid) is added to the media, the active ODCase will convert 5-FOA into the toxic compound (a suicide inhibitor) 5-fluorouracil causing cell death, which allows for selection against yeast carrying the gene.

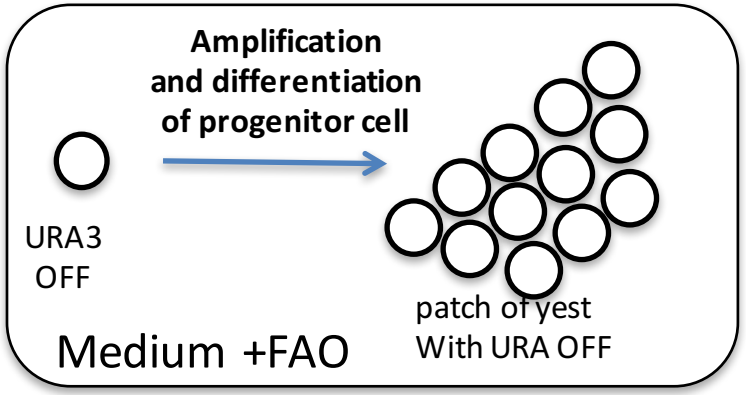
Observations that cannot be explained by genetics…..

Telomere position effect: yeast, human, drosophila



URA3 far from telomere





URA3 close to telomere

Phenotype is stably during Cell division

→Status is propagated to daughter cells =a sort of inheritance

WHAT IS EPIGENTICS - 1996 ??

Waddington 1950

…Epigenetics is the study of processes that categorize all of the developmental events leading from the fertilized oozyte to the mature organism – that is, all of the regulated processes that, beginning with the genetic material, shape the final product

Riggs,1996; Riggs and Porter 1996:

…the study of meiotically/mitotically heritable changes changes in gene function that cannot be explained by changes in in DNA seqeunce"

Berger 2009

…the initiation of a new epigenetic state involve a transient mechanism Separate from the one required to maintain it

WHAT IS EPIGENTICS - 2009 ??

Berger 2009

…the initiation of a new epigenetic state involve a transient mechanism, separate from the one required to maintain it

- ***Molecule that initiate regulation***
- ***Molecules that maintain regulation***

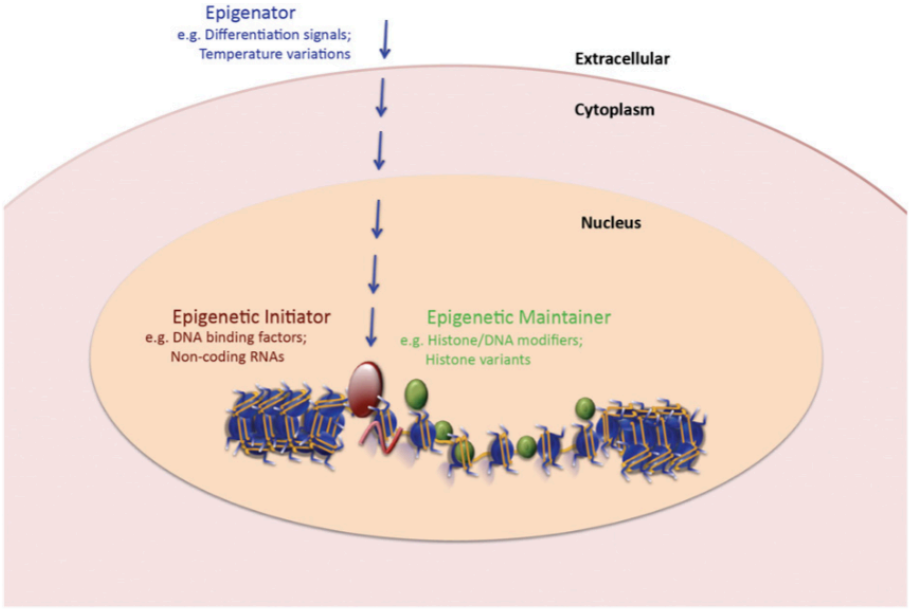


Figure 1. The epigenetic pathway. Three categories of signals are proposed to operate in the establishment of a stably heritable epigenetic state. An extracellular signal referred to as the "Epigenator" (shown in blue) originates from the environment and can trigger the start of the epigenetic pathway. The "Epigenetic Initiator" (shown in red) receives the signal from the "Epigenator" and is capable of determining the precise chromatin location and/or DNA environment for the establishment of the epigenetic pathway. The "Epigenetic Maintainer" (shown in green) functions to sustain the chromatin environment in the initial and succeeding generations. Persistence of the chromatin milieu may require cooperation between the Initiator and the Maintainer. Examples for each category are shown *below* each heading. Chromatin is depicted in blue.

PERSPECTIVE

An operational definition of epigenetics

Shelley L. Berger,[1,5] Tony Kouzarides,[2,5] Ramin Shiekhattar,[3,5] and Ali Shilatifard[4,5]

[1]Department of Cell and Developmental Biology, University of Pennsylvania, Philadelphia, Pennsylvania 19104, USA; [2]Gurdon Institute and Department of Pathology, Cambridge CB2 1QN, United Kingdom; [3]Wistar Institute, Philadelphia, Pennsylvania 19104, USA; [4]Stowers Institute for Medical Research, Kansas City, Missouri 64110, USA

A recent meeting (December 2008) regarding chromatin-based epigenetics was hosted by the Banbury Conference Center and Cold Spring Harbor Laboratory. The intent was to discuss aspects of epigenetic control of genomic function, and to arrive at a consensus definition of "epigenetics" to be considered by the broader community. It was evident that multiple mechanistic steps lead to the stable heritance of the epigenetic phenotype. Below we provide our view and interpretation of the proceedings at the meeting.

and subsequent generations. These classes are depicted in Figure 1 and are explained below.

Epigenator

The epigenetic phenotype is likely triggered by changes in the environment of the cell. Everything occurring upstream of the first event on the chromosome would be part of the Epigenator signal, including an environmental cue or niche and the subsequent signaling pathways leading to the

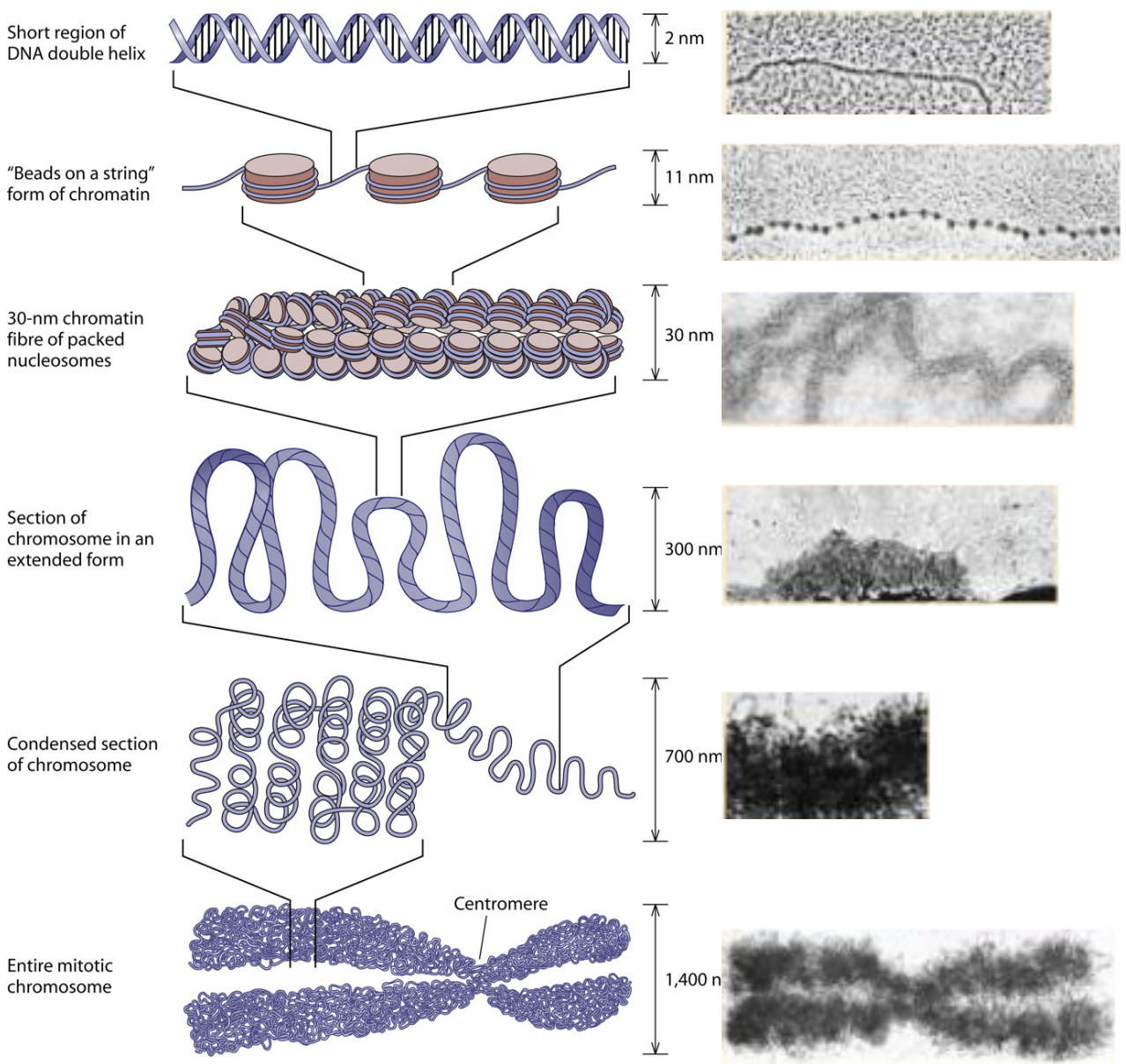
The "packaging" of genetic information is essential for gene expression

The DNA is not a naked Molecule In the nucleus.

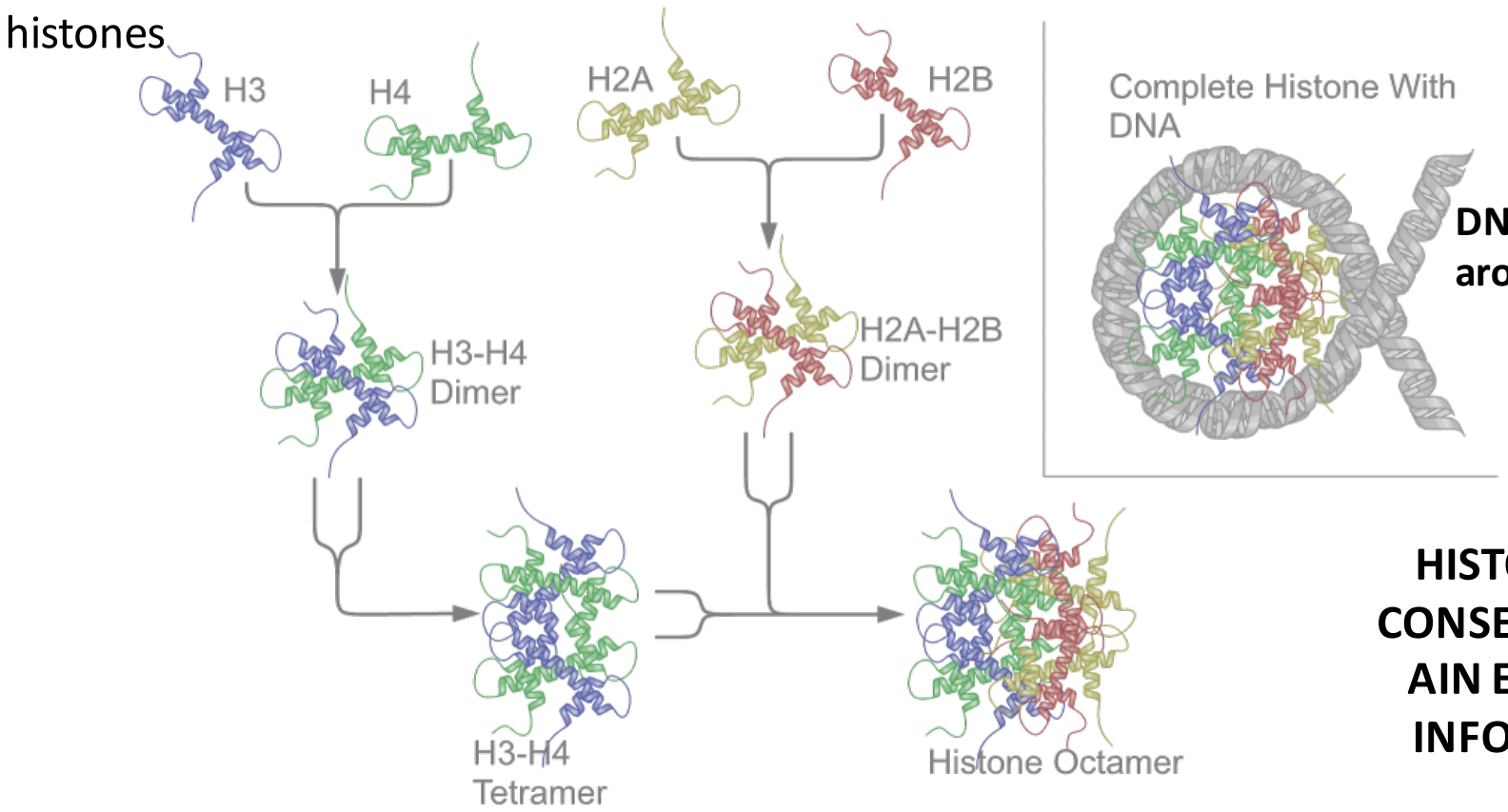
DNA is bound to proteins

DNA+DNA-bound proteins = CHROMATIN

Chromatin is organized at different levels



The "packaging" of genetic information is essential for gene expression



HISTONES CAN CONSERVE/MAINT AIN EPIGENETIC INFORAMTION

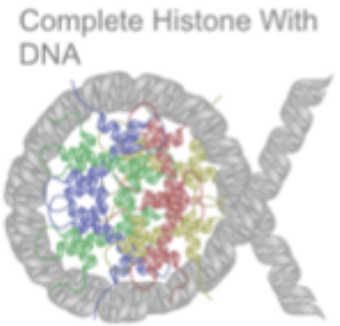
1950 Stedman and Stedman: all cells contain the same DNA information. It must have different histones that bind to DNA that allow the differentiation in to all different cell types of an organism

The general imagination was that histones act as repressor of gene expression. Only a small part of the chromatin was accessible to probes or digestion. That
Means stripping off an histone is required to turn on the expression of a gene.

Histone tails are essential for epigenetic information

Cell, Vol. 65, 1023–1031, June 14, 1991, Copyright © 1991 by Cell Press

Yeast Histone H4 N-Terminal Sequence Is Required for Promoter Activation In Vivo



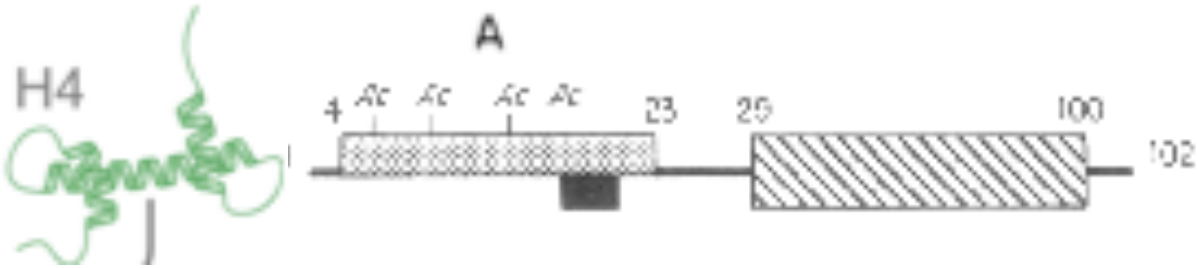
Model system:

CONCEPT: Yeast strain with a deletion of both histone H4 genes; contemporarily the yeast strain contains an extra copy of histone H4 (was introduced) that is controlled by the Galactose-inducible GAL promoter. That means, that upon addition of Galactose to the medium histone H4 is expressed and yeast survives

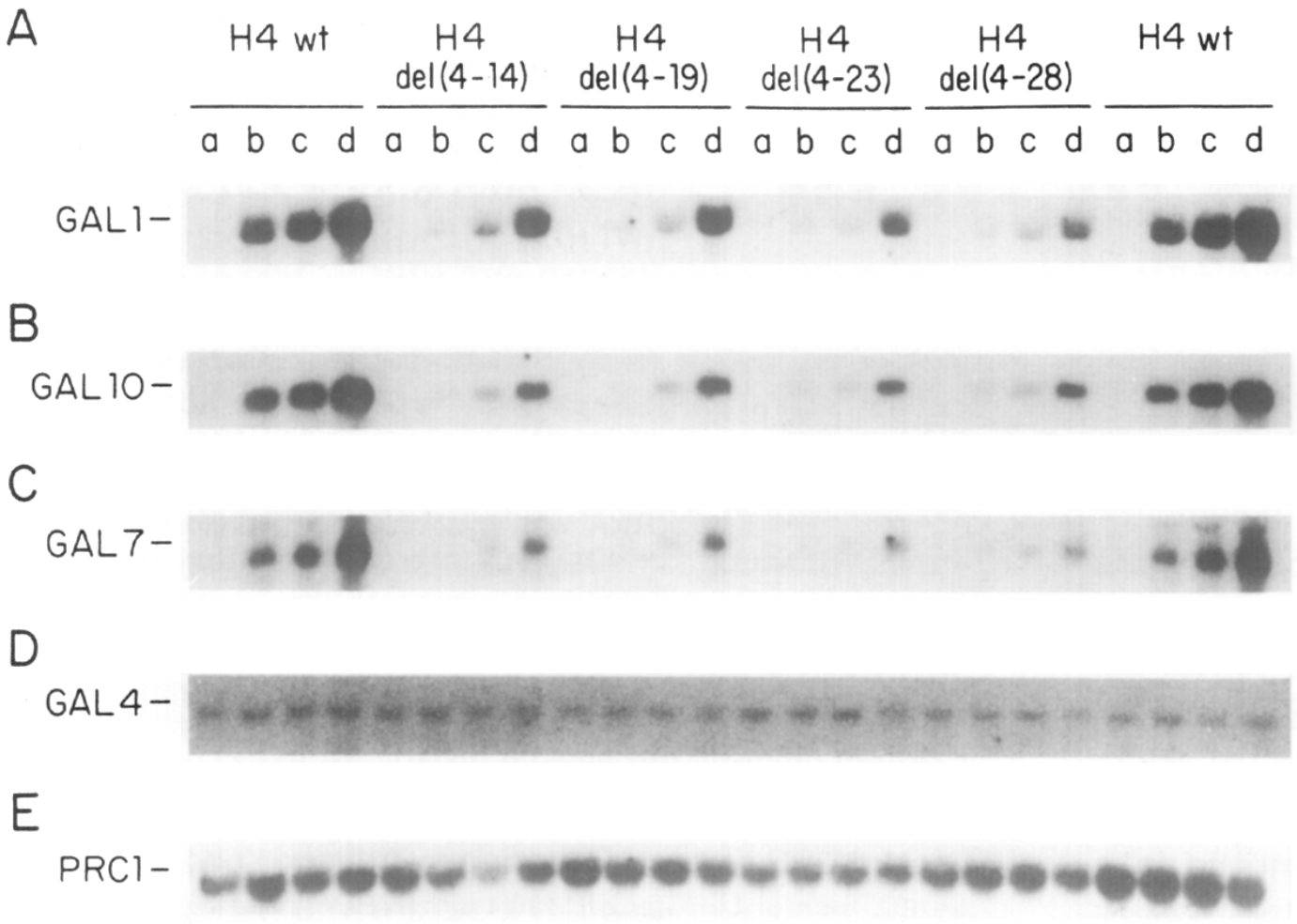
Galactose also activates genes
GAL1, GAL10, GAL7
and GAL4 that are necessary to process galactose

Model system for the study:

CONCEPT: Yeast strain where previously Both histone H4 genes were deleted.
In addition, GAL inducible histone H4 genes that contain the wild-type or different deletion in the N-terminal domain of H4 were
introduced

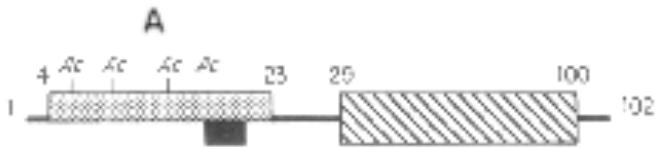


Histone tails are essential to control gene expression



Then Yeast cells were treated with Galactose to induce H4 (wt or mutant) expression and to activate the galactosidase inducible genes GAL1, GAL10, GAL7 and GAL4 genes. PRC1 gene is not inducible by Galactosidase
THEN:
NORTHERN BLOT

Cells with mutant H4 tails only inefficiently activate Gal1, 10, 4, 4 expression



H4 TAIL CONTAINS INFORMATION TO ACTIVATE GENE EXPRESSION

Histones can be chemically modified

Proc. Natl. Acad. Sci. USA
Vol. 92, pp. 6364–6368, July 1995
Cell Biology

An activity gel assay detects a single, catalytically active histone acetyltransferase subunit in *Tetrahymena* macronuclei

(acetylation/chromatin)

JAMES E. BROWNELL AND C. DAVID ALLIS*
Department of Biology, Syracuse University, Syracuse, NY 13244

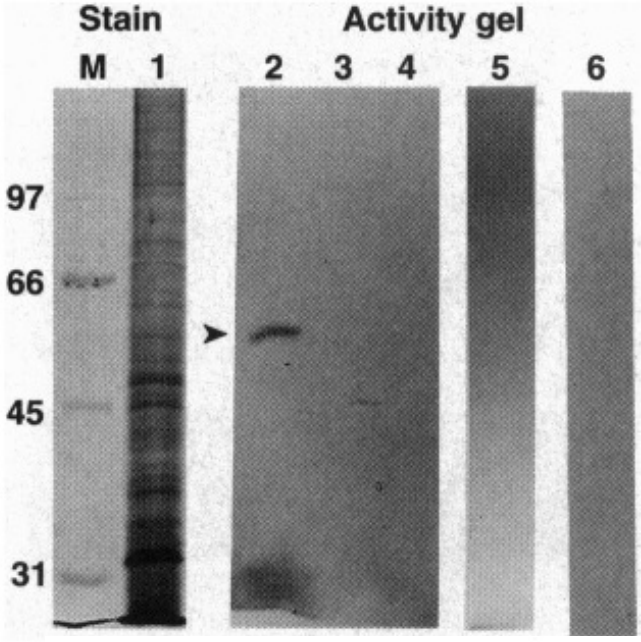
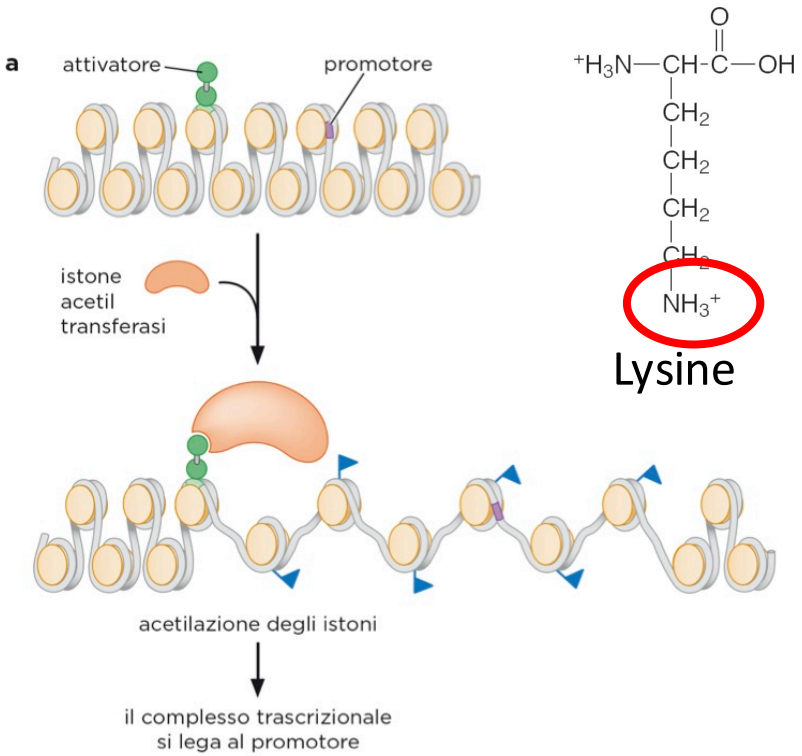
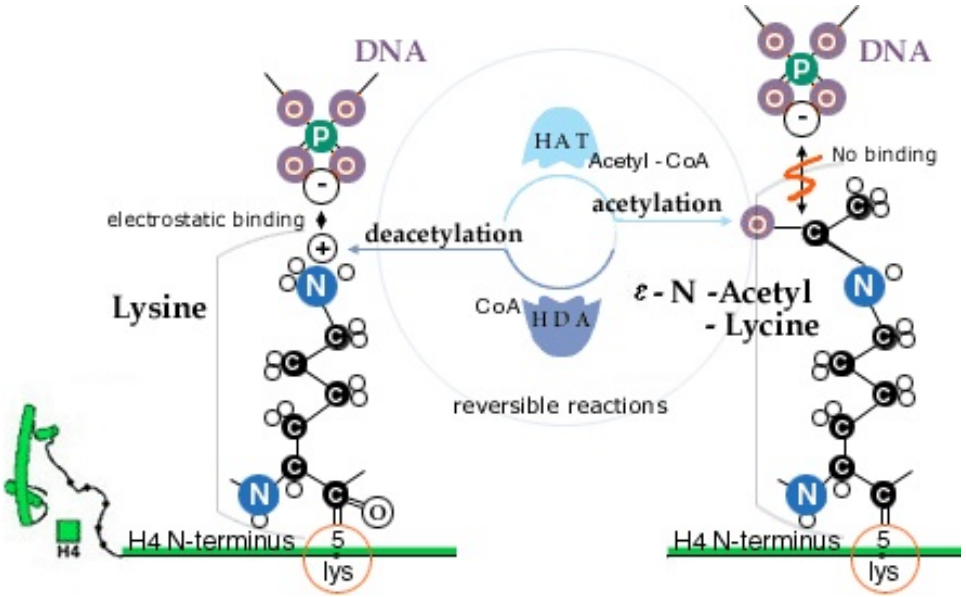


FIG. 1. A 55-kDa polypeptide specifically labels histones in an acetyltransferase activity gel assay. Crude macronuclear histone acetyltransferase activity was subjected to electrophoresis in SDS/8% polyacrylamide gels in which histones (lanes 2, 3, and 4), bovine serum albumin (lane 5), or no protein substrates (lanes 1 and 6) were incorporated prior to polymerization. Following electrophoresis, the gels were prepared for the activity gel assay and processed for fluorography (lanes 2–6) or silver stained (lane 1); M, molecular weight markers. In some cases, the enzyme was inactivated prior to loading the gel either by boiling for 5 min in sample buffer (lane 3) or by incubation with 10 mM *N*-ethylmaleimide (lane 4). [^{3}H]Acetate was incorporated into histones in a single region of the gel corresponding to a molecular mass of 55 kDa (arrowhead, lane 2). The gel was exposed for 1 week.

1. Make Polyaclylamide gel with incorporated, purified histones (lanes 2, 3, 4) or BSA (lane 5)
2. Take protein extract from Tetrahymena Macronuclei and load run on gel.
3. After stop of the gel the enzymatic assay will be performed: radioactive [^{3}H]-Acetyl-CoA (contains acetyl group – is a major enzymatic cofactor in cells) on top of gel.
4. After autoradiography, a band appears that marks acetylated histones that co-lolocalize with a “histone acetyltransferase” present in the Tetrahymena extract

Post-translational modifications can change the topology of chromatin

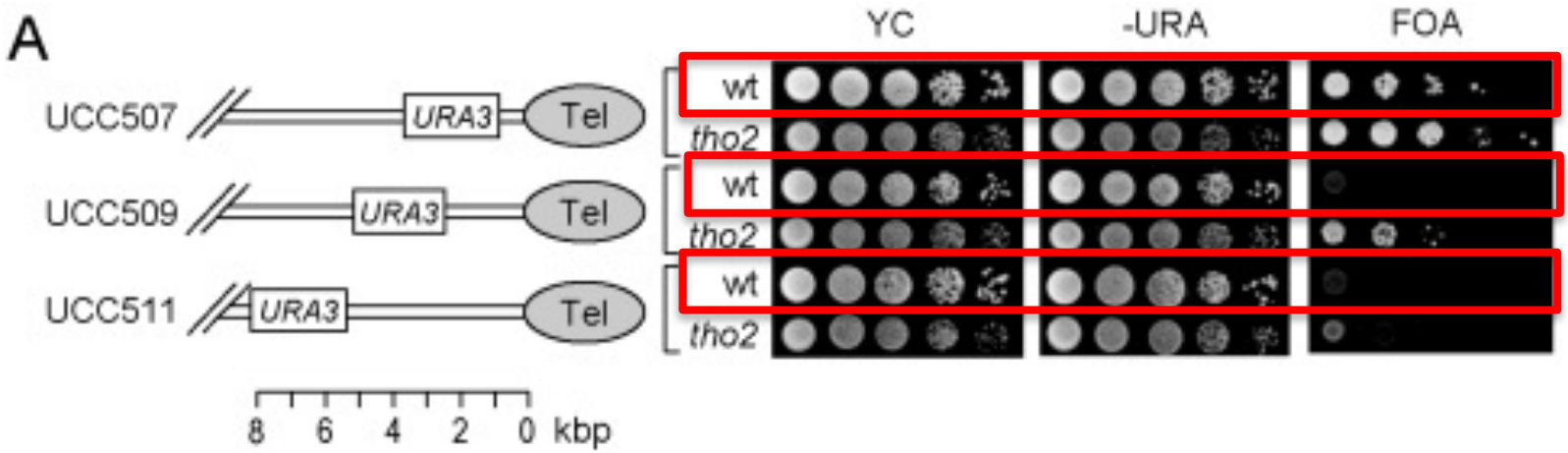


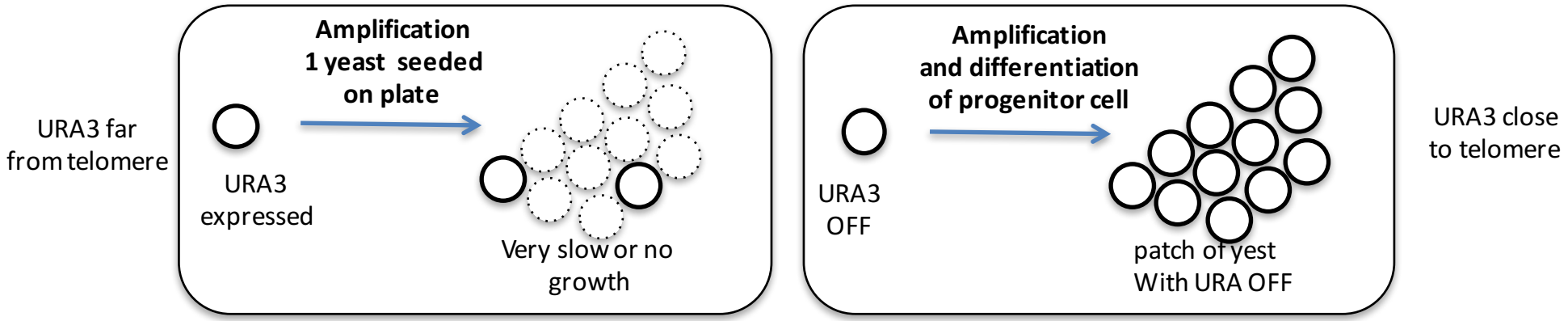


“EPIGENETIC GENE REGULATION” IS MAINLY BASED ON CHEMICAL MODIFICATIONS OF HISTONES AND DNA

Observations that cannot be explained by genetics…..

Telomere position effect: yeast, human, drosophila

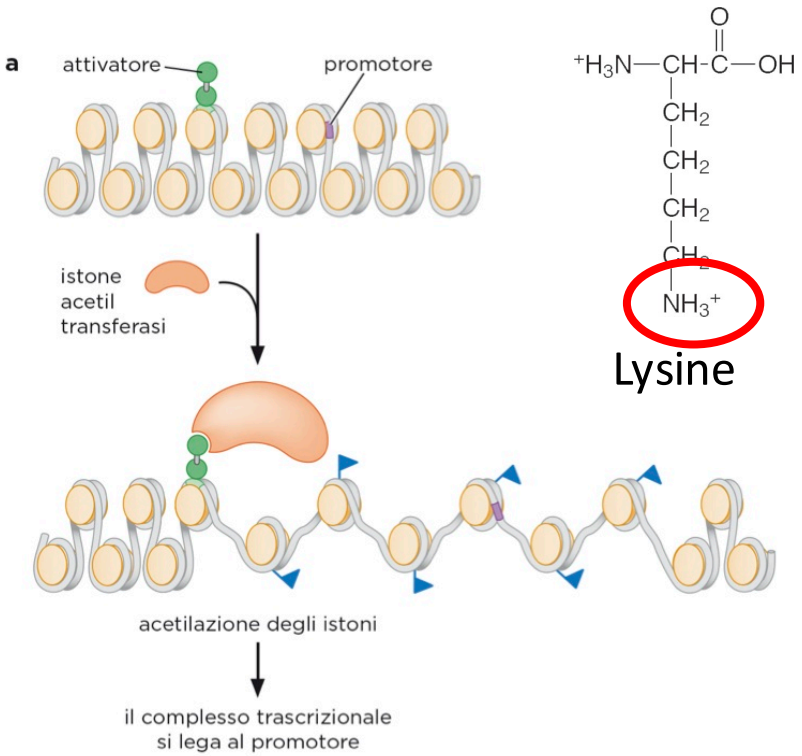


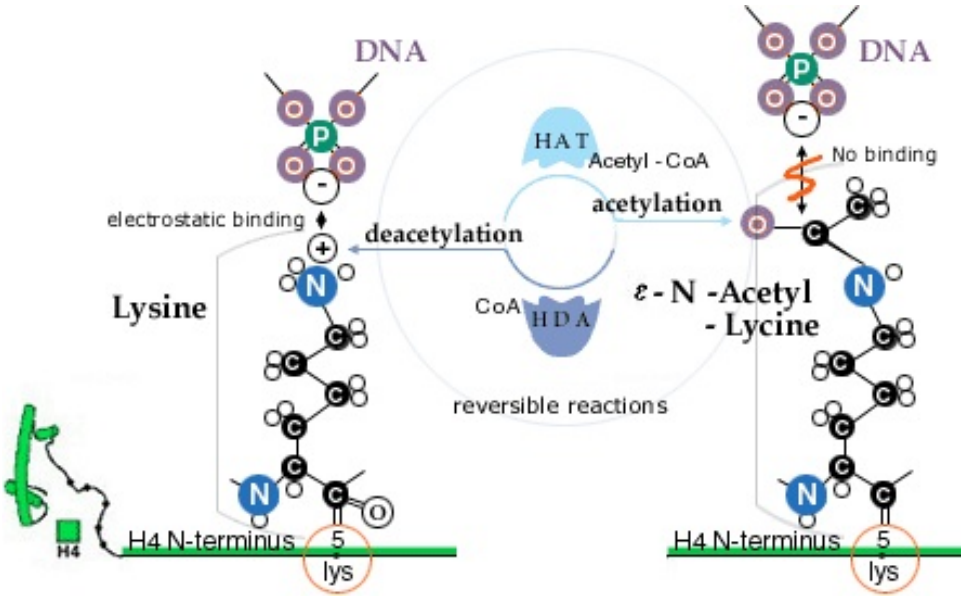


Phenotype is stably during Cell division

→Status is propagated to daughter cells =a sort of inheritance

Post-translational modifications can change the topology of chromatin

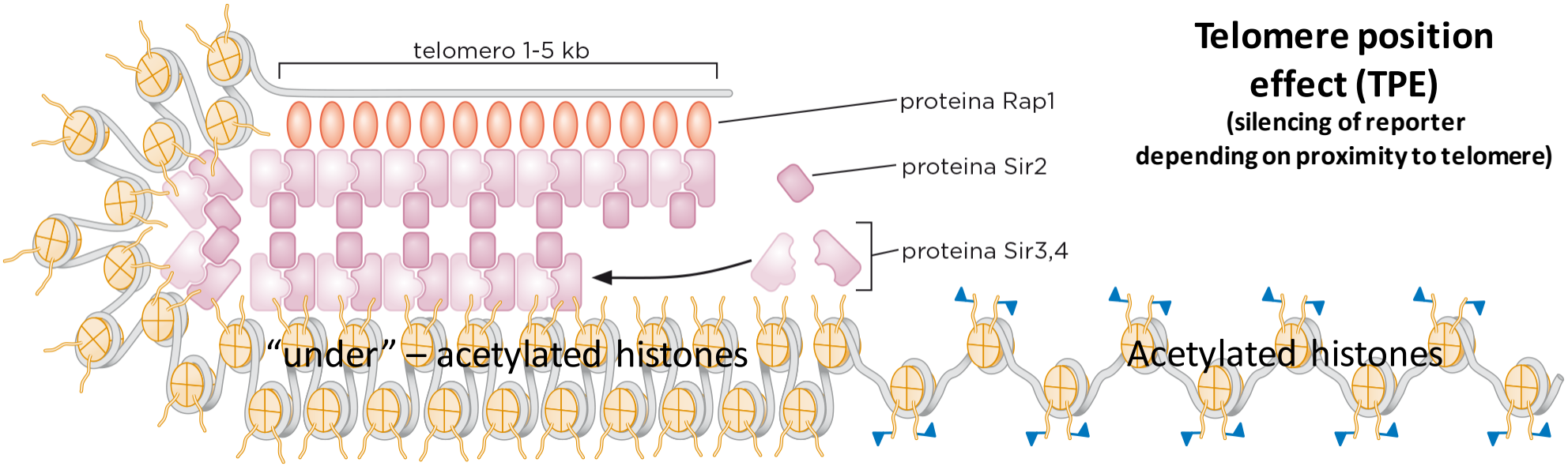




“EPIGENETIC GENE REGULATION” IS MAINLY BASED ON CHEMICAL MODIFICATIONS OF HISTONES AND DNA

Post-translational modifications decide on gene expression
TELOMERE POSITION EFFECT AND ACETYLATION

Observation: URA3 Reporter gene inserted into central position in chromosome: EXPRESSED
→ URA 3 Reporter gene inserted in proximity to chromsome ends: SILENT
→ make mutatant S. cerevisiae that release reporter from silencing
→ identify genes that are mutated
= SILENT INFORMATION REGUALTORS (SIR) GENES



Telomere position effect (TPE)
(silencing of reporter depending on proximity to telomere)

1. Rap1 specifically binds to telomeric repeat sequences $(G_{(2-3)}(TG)_{(1-6)}T$ consensus)
2. **Rap1 recruits the SIR complex (SIR2,3,4) SIR2 is a HDAC → silencing of chromatin by histone deacetylation**
3. SIR complex spreads towards the centromere

Post-translational modifications decide on gene expression
TELOMERE POSITION EFFECT AND ACETYLATION

HOW IS SPREADING REGUALTED??

Silencing complex spreads until meets gene-rich regions that contain H2A variant H2AZ = **barrier**

(S. cerevisiae name: Htz1 and H4K16-acetylation (active regions)

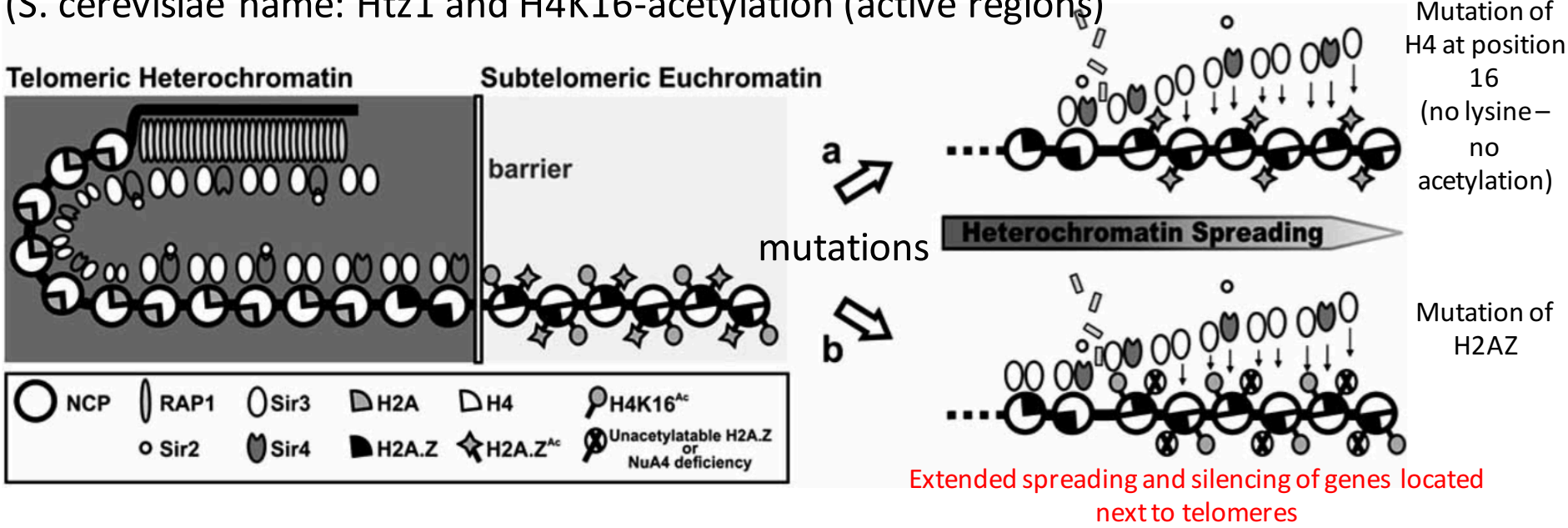
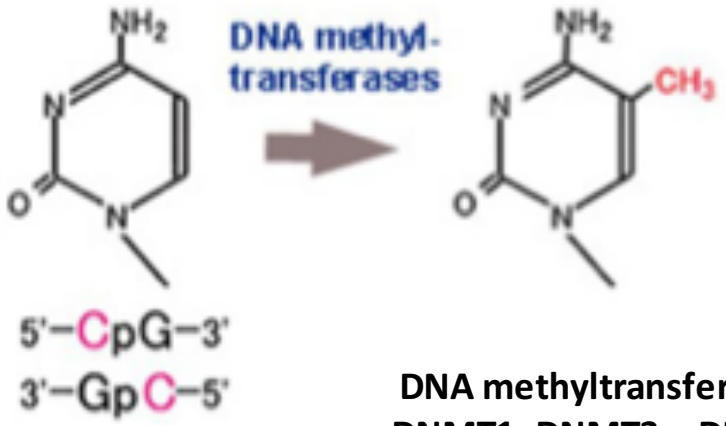
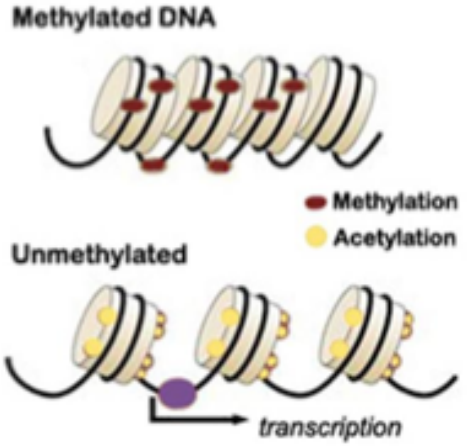


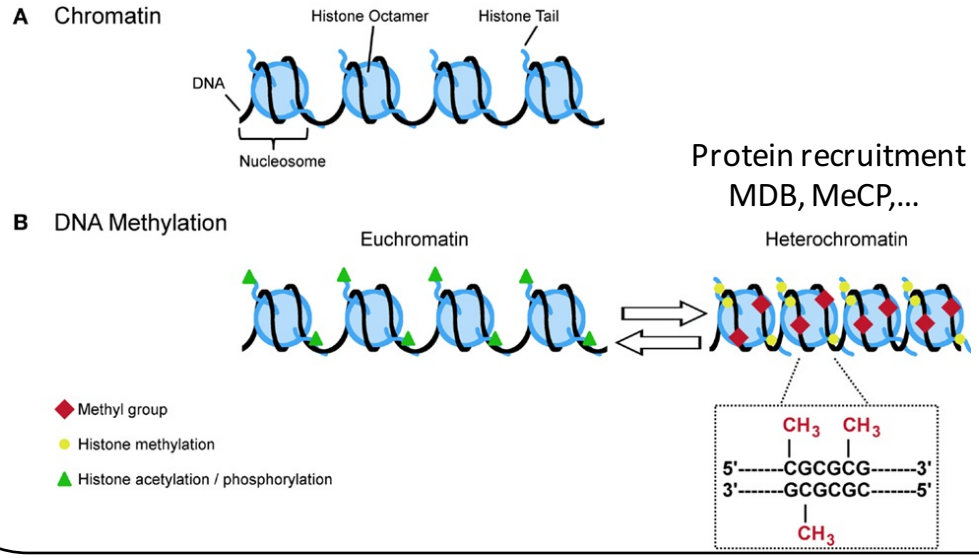
Fig. (2). A model for yeast telomeric heterochromatin adapted from [39]. Heterochromatin formation and maintenance involve the RAP-1 containing telosome, different Sir proteins and the interaction of these elements with histone H4. H2A.Z participates in preventing the spread of telomeric heterochromatin to subtelomeric euchromatin regions by creating a barrier effect, and this boundary function is highly dependent on acetylation. For instance, the absence of H4-K16^{Ac} results in the disruption of this barrier even in the presence of acetylated H2A.Z (pathway a [7, 8, 17**]). Furthermore, absence of H2A.Z acetylation or NuA4 deficiency (pathway b) also break this barrier even in the presence of H4-K16^{Ac} [11**, 27**]. Thus, the boundary function played by H2A.Z and H4 histones is mainly regulated by their acetylation rather than by their mislocalization at subtelomeric regions.

DNA can carry information that prevent the activation of genes
DNA methylation



DNA methyltransfererases
DNMT1, DNMT3a, DNMT3b
act only on CpG di-nuceotides



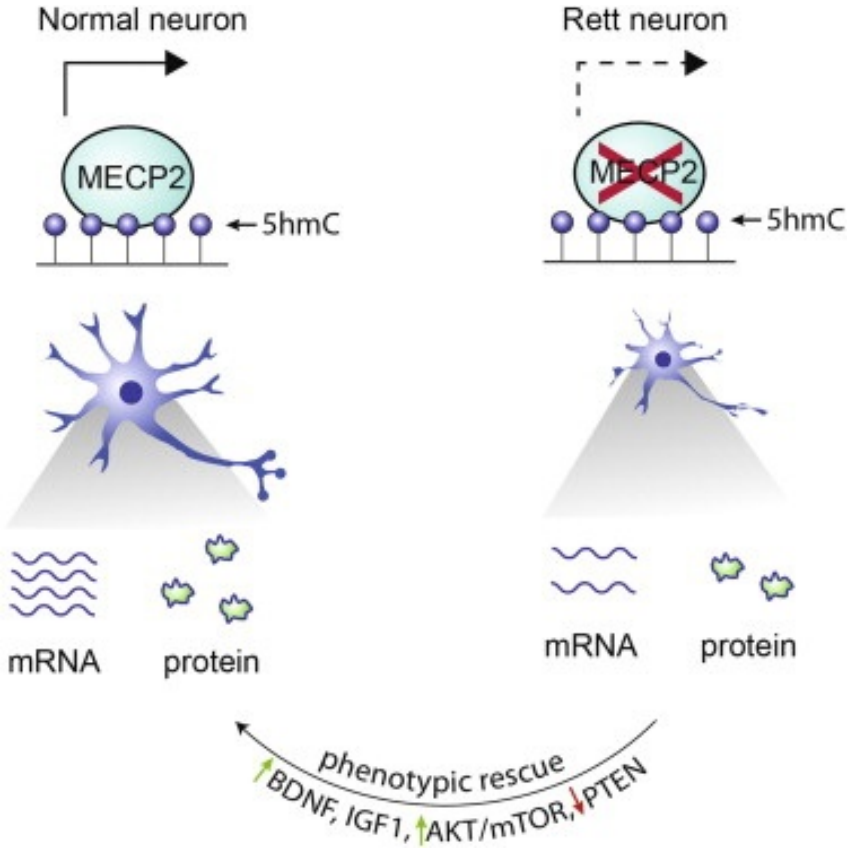


DNA methylation
Is co-ordinated
with repressive
histone modifications

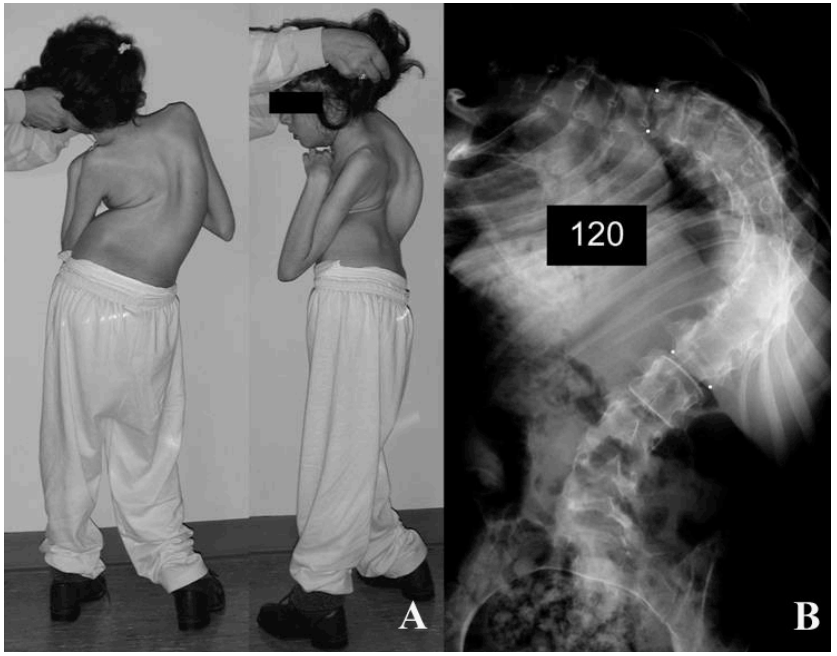
= FUNCTIONAL REDUNDANCY TO ENSURE REPRESSION

DNA can carry information that prevent the activation of genes
DNA methylation

methylated DNA is bound
By MeCP2 (and other methyl-DNA
Specific proteins such as MBD1, MBD2,
MBD4 and BAZ2)



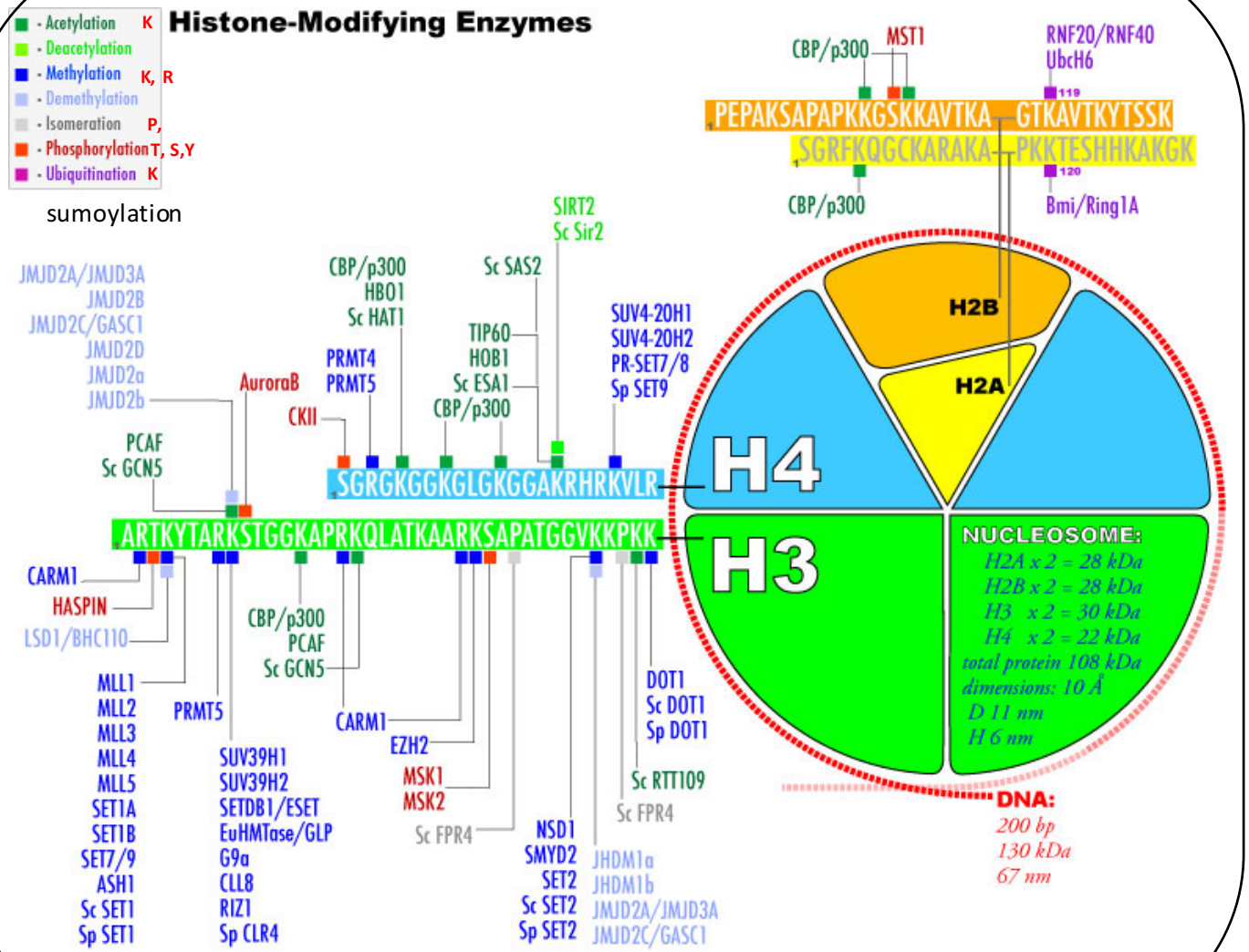
Rett syndrome is caused by mutations in MeCP2



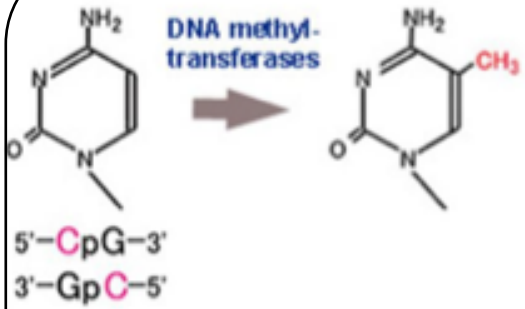
Rett syndrome (RTT), originally termed cerebroatrophic hyperammonemia is a rare genetic postnatal neurological disorder of the grey matter of the brain that almost exclusively affects females but has also been found in male patients. The clinical features include small hands and feet and a deceleration of the rate of head growth (including microcephaly in some). Repetitive stereotyped hand movements, such as wringing and/or repeatedly putting hands into the mouth, are also noted. People with Rett syndrome are prone to gastrointestinal disorders and up to 80% have seizures. They typically have no verbal skills, and about 50% of affected individuals do not walk. Scoliosis, growth failure, and constipation are very common and can be problematic.

"EPIGENETIC GENE REGULATION" COMPRISES THE FORMATION OF LARGE DNA:PROTEIN CHROMATIN STRUCTURES (epigenetic writer – chemical modification - epigenetic reader)

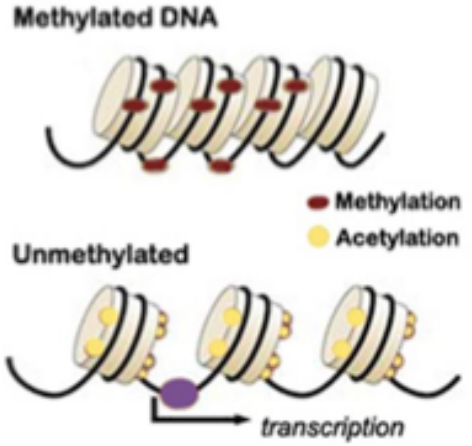
Histones carry multiple chemical modifications
=POST TRANSLATIONAL HISTONE MODIFICATIONS



THE "HISTONE CODE"

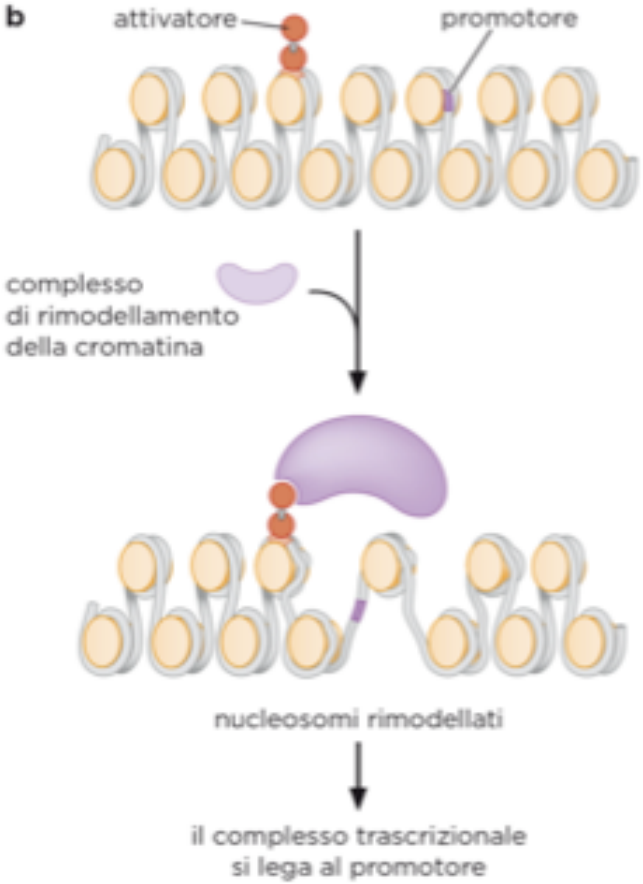


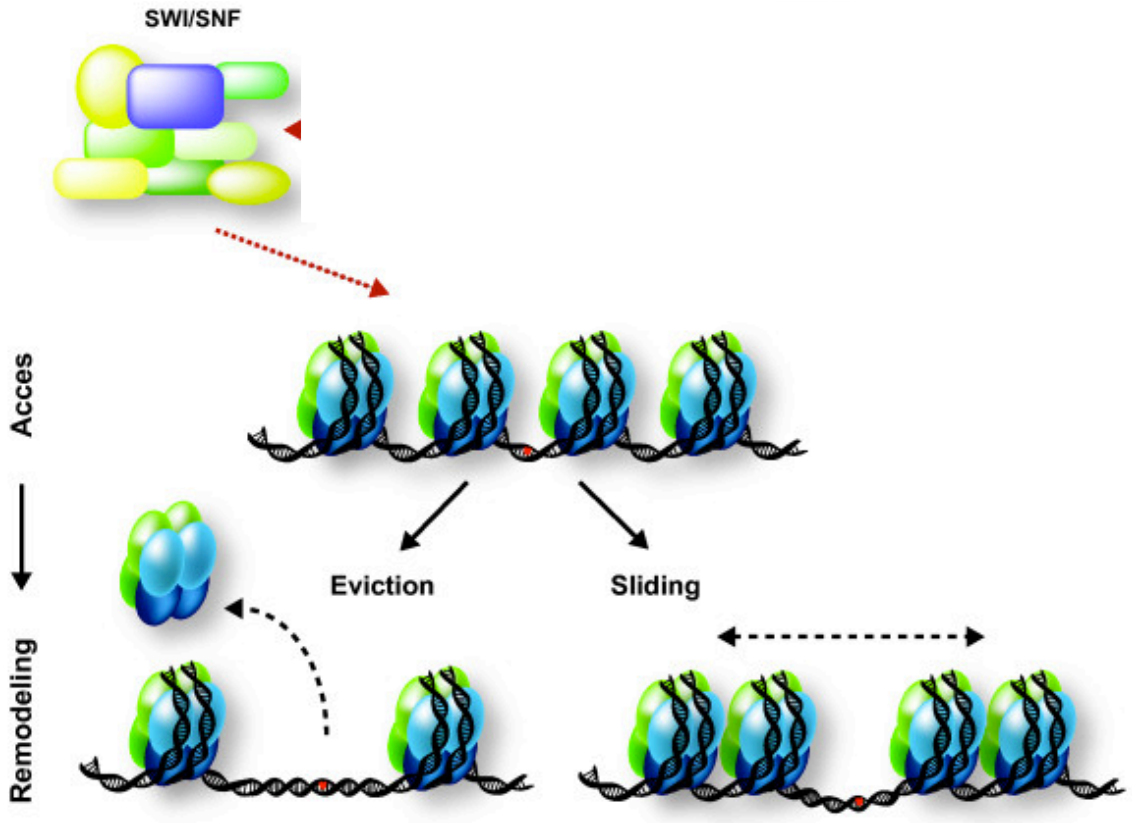
DNA methyltransfererases DNMT1, DNMT3a, DNMT3b act only on CpG di-nuceotides



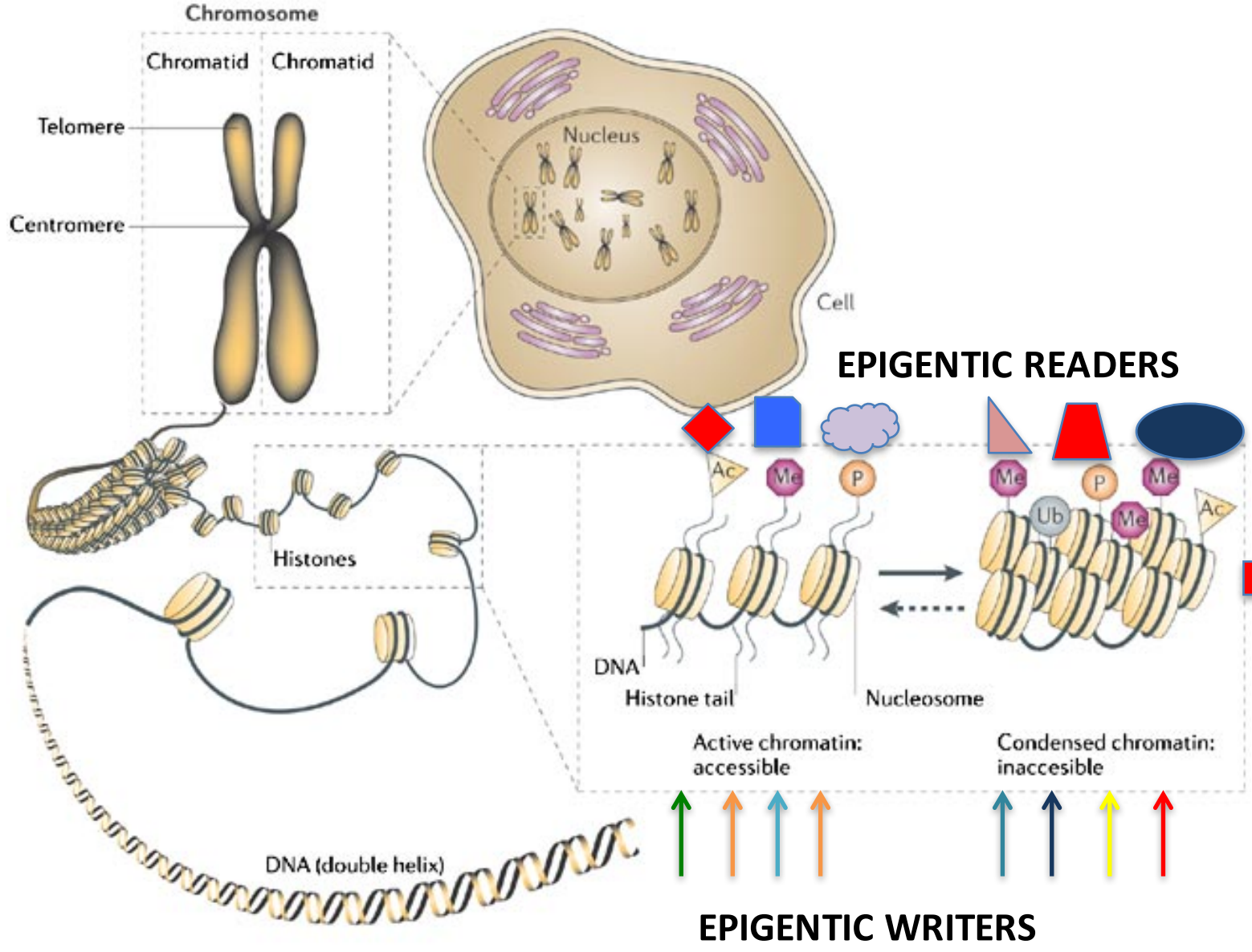
Core histones can be moved or eliminated = chromatin remodelling complexes

-Activator can recruit a **chromatin remodelling complex** → SWI/SNF complex, moves nucleosomes to make promoter/response elements accessible (ATP dependent!)
-Activator can recruit a **histone acetyl transferase** → add acetyl groups to lysine histone tails (p300,, GCN5, MOF, etc)
→arrangement of nucleosomes change at response elements
→acetylated tails serve as a binding site for bromo-domain proteins (TFIIH contains such protein)





Histones can carry multiple chemical modifications =POST TRANSLATIONAL HISTONE MODIFICATIONS



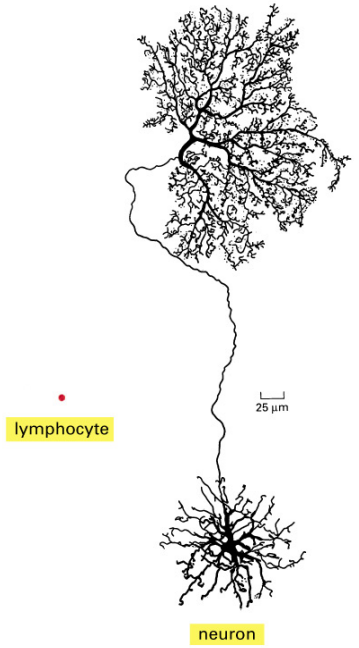


Figure 7–1. Molecular Biology of the Cell, 4th Edition.

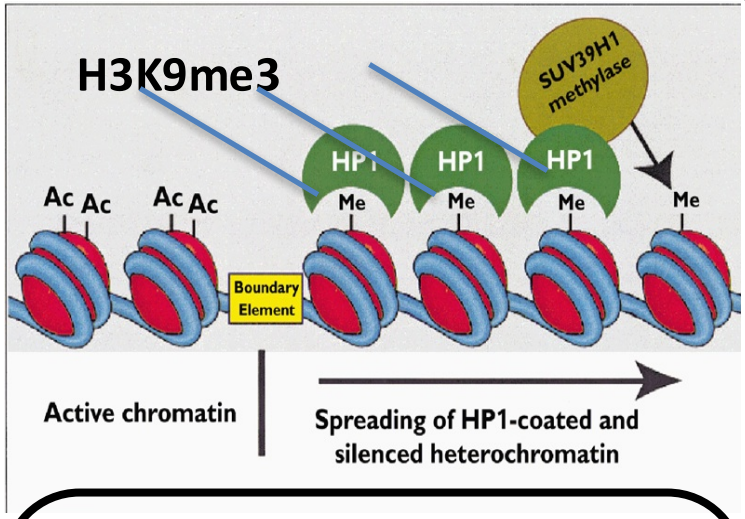
GENE EXPRESSION PROGRAMS:
→CELL TYPE SPECIFIC

→NORMAL/ CANCER

EPIGENTIC WRITERS AND READERS

HMTase generates post-translational histone modifications can recruit specialized proteins

Example: SUV39H1 and HP1 form heterochromatin at centromeric and telomeric Heterochromatin in flies and vertebrates



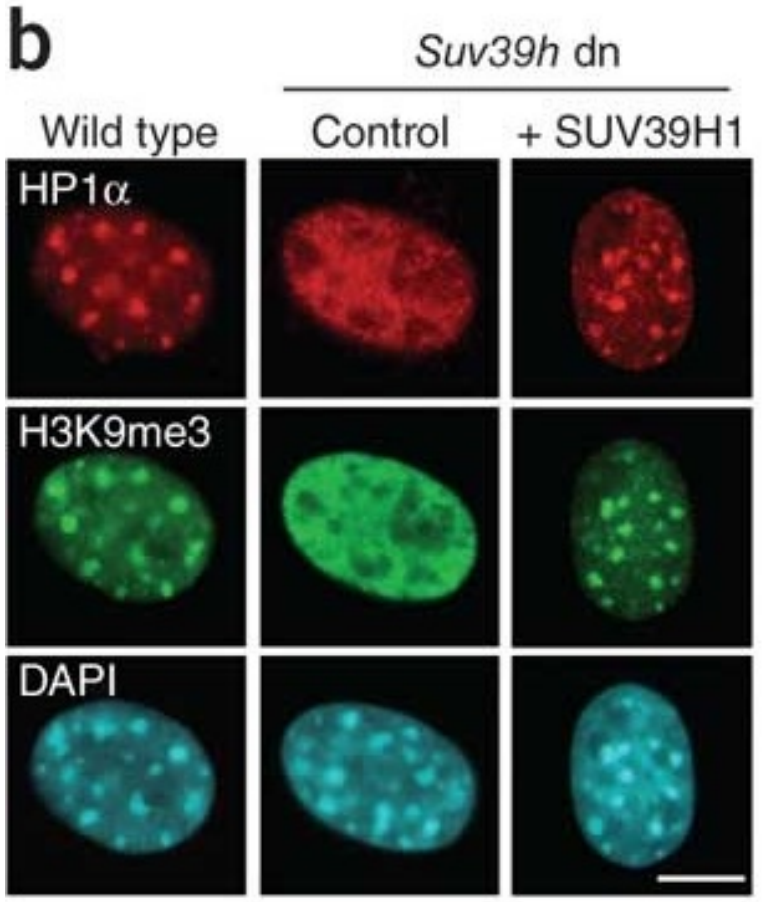
Suv39h1/2 tri-methylate
Lysine 9 on histone H3

↓

tri-methylated Lysine 9 on histone H3 recruits HP1

↓

heterochromatin

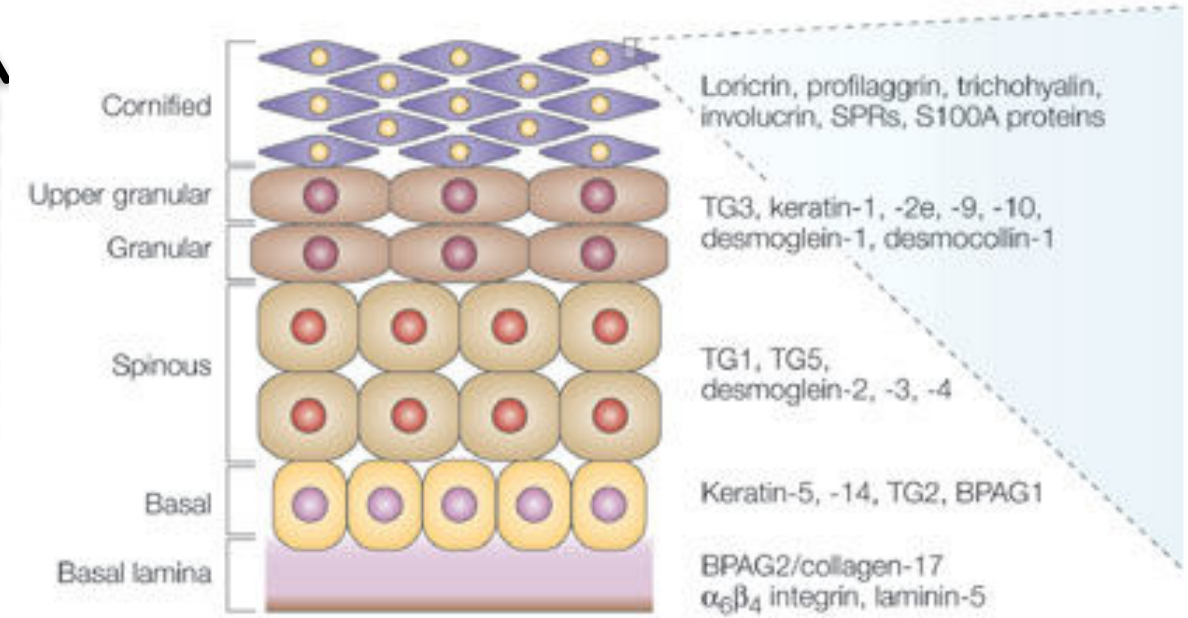


histone modifications can reach high levels in cells and can be visualized by immunofluorescence

CAN EPIGENTIC INFORMATION BE CONSERVED AFTER DNA REPLICATION??

EPIGENETIC PROGRAM ENSURES CELL IDENTITY

EPIGENETIC REGUALTION
DIFFERNETIATION



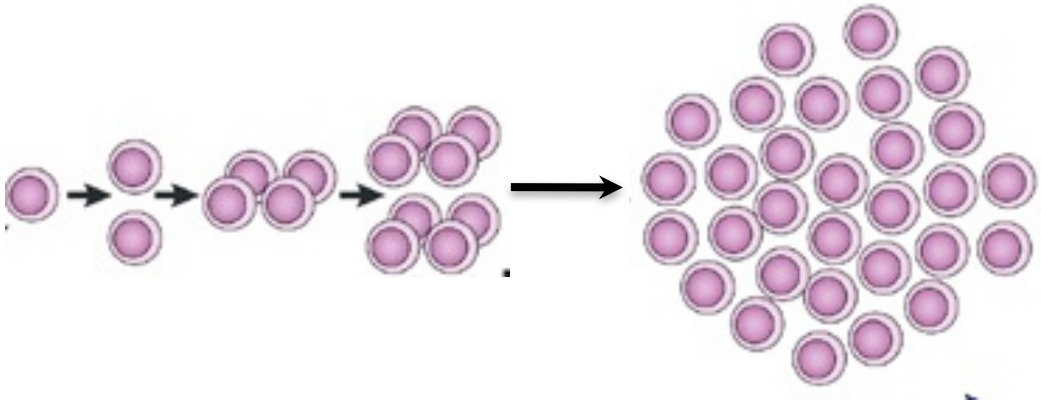
PROLIFERATION OF IDENTICAL CELLS

STEM CELLS – SLOW PROLIFERATION

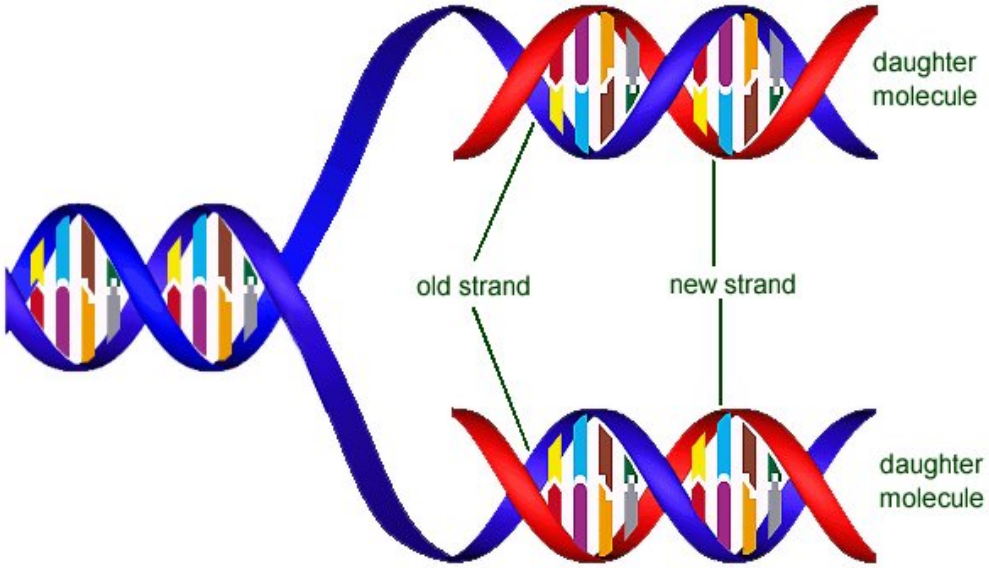
Nature Reviews | Molecular Cell Biology

CAN EPIGENTIC INFORMATION BE CONSERVED AFTER DNA REPLICATION??

Cell proliferation



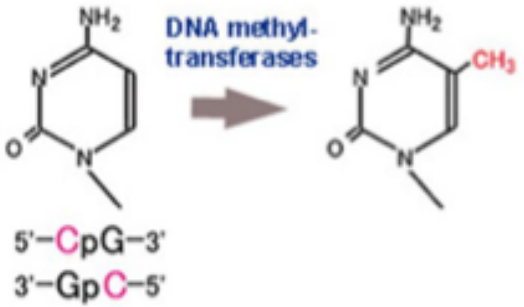
SEMICONSERVATIVE DNA REPLICATION



WHAT IS HAPPENING WITH EPIGENTIC INFORMATION DURING DNA REPLICATION

HOW CAN IT BE MAINTANED DURING SEMICONSERVATIVE REPLICATION??

CAN EPIGENTIC INFORMATION BE CONSERVED AFTER DNA REPLICATION??



DNA methyl transfererases
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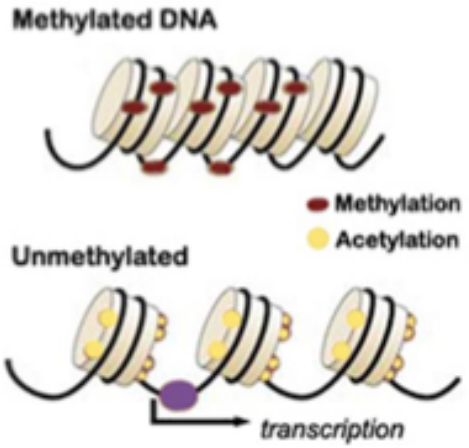
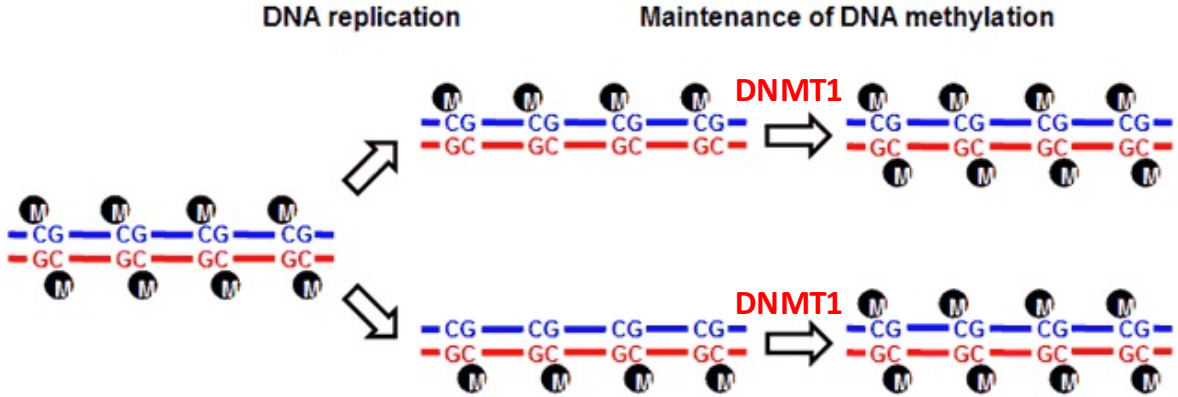
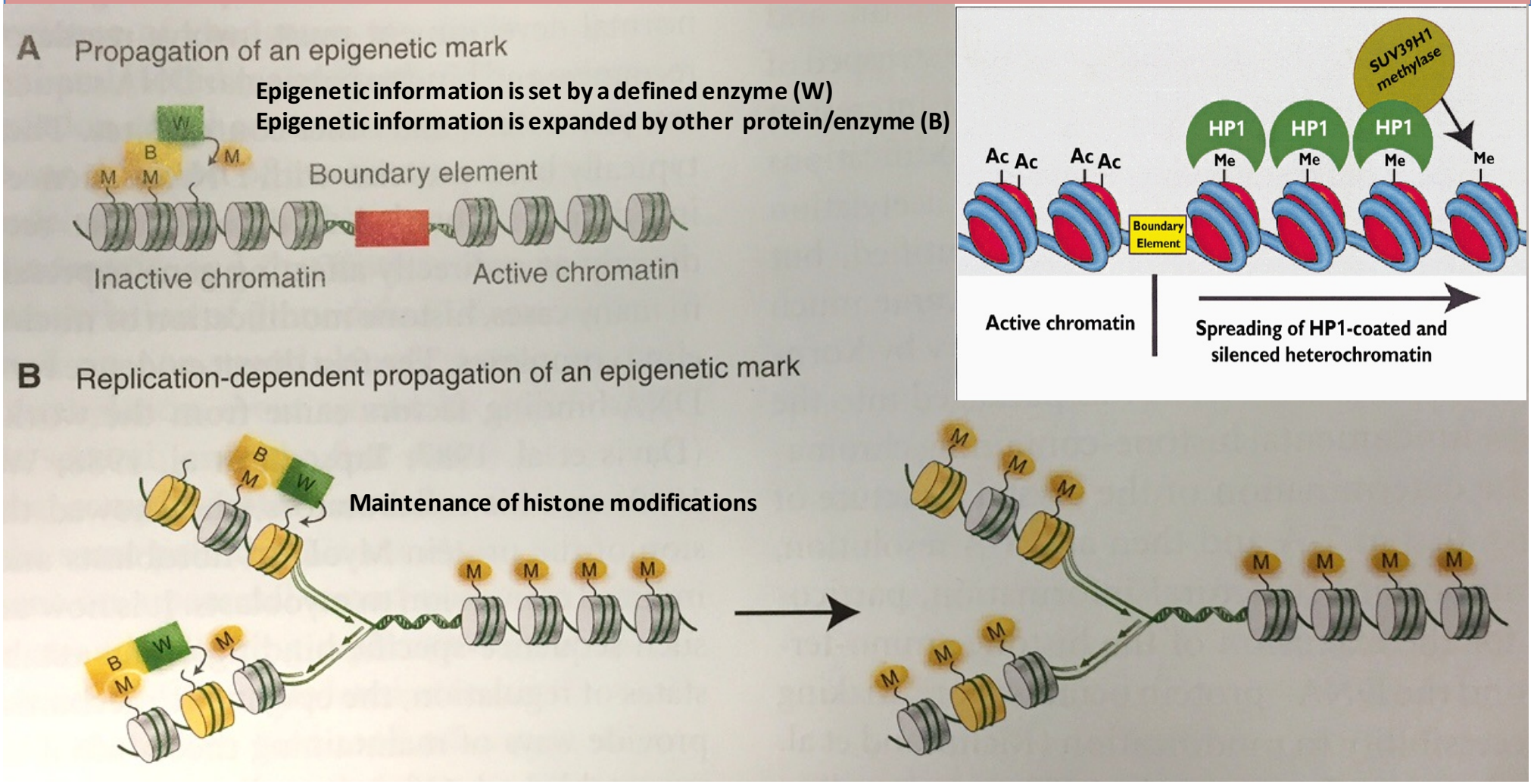




Newly synthesized DNA is without DNA methylation. DNMT1 specifically, reads hemi-methylated DNA and methylates the opposite C on the the newly synthesized, unmethylated DNA filament. Both Daughter cells contain the same DNA methylation pattern like the patental cell

The propagation of epigenetic marks



S-Phase: New, randomly deposited histones octameres without histone modifications are inserted during DNA replication. Epigenetic writers associated with the parental DNA now Impose the parental histone code to newly incorporated histones. Epigenetic code is maintained in both daughter cells

WHAT IS EPIGENTICS ??

Waddington 1950

…Epigenetics is the study of processes that categorize all of the developmental events leading from the fertilized oozyte to the mature organism – that is, all of the regulated processes that, beginning with the genetic material, shape the final product

↓

Riggs,1996; Riggs and Porter 1996:

…the study of meiotically/mitotically heritable changes changes in gene function that cannot be explained by changes in in DNA sequence"

+

Berger 2009

…the initiation of a new epigenetic state involve a transient mechanism that is separate from the one required to maintain it

DEFINING EPIGENTICS

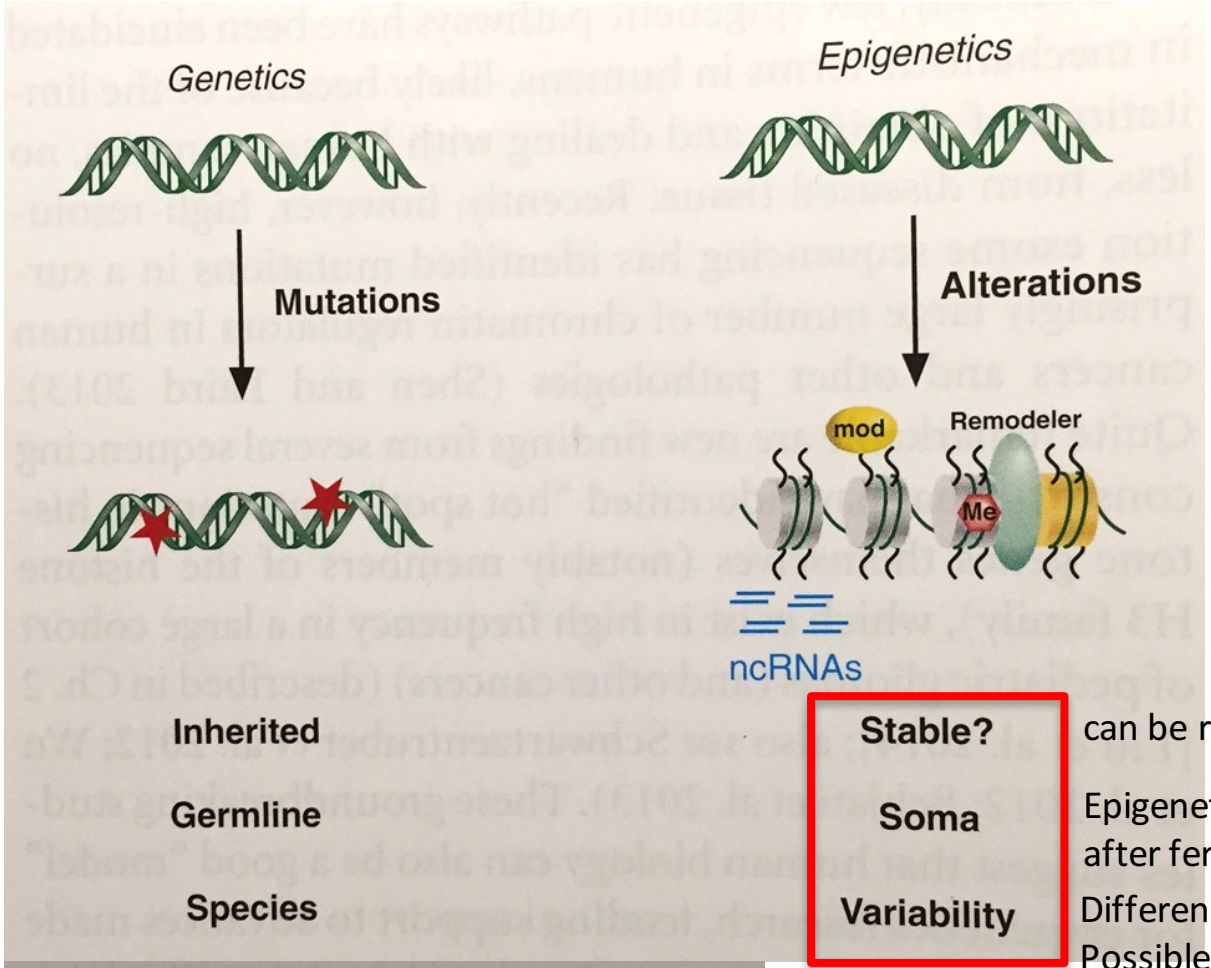


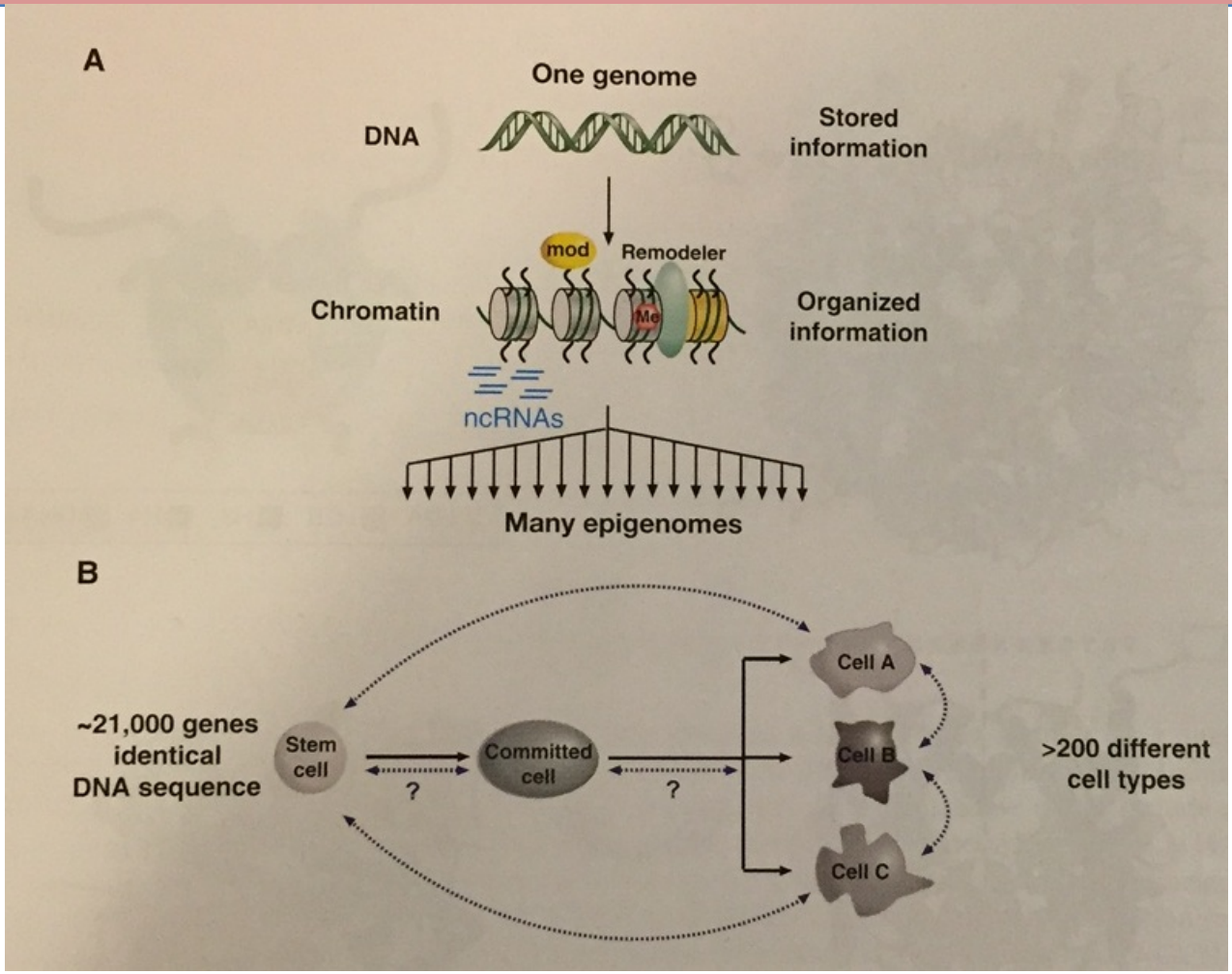
Figure 3. Genetics versus epigenetics. Genetics: Mutations (red stars) of the DNA template (green helix) are heritable somatically and through the germline. Epigenetics: Variations in chromatin structure modulate the use of the genome by (1) histone modifications (mod), (2) chromatin remodeling (remodeler), (3) histone variant composition (yellow nucleosome), (4) DNA methylation (Me), and (5) noncoding RNAs (ncRNAs). Marks on the chromatin template may be heritable through cell division and collectively contribute to determining cellular phenotype.

can be reversed

Epigenetic code is erased after fertilization (DNA methylation)

Differences between individuals Possible (life-style, nutrition, external Effects)

DEFINING EPIGENTICS



Epigenetics controls the use of our DNA

Alterations of the Epigenetic code change Gene expression and change the identity of the cell
→Such changes can come from the Developmental programs, disease, environment, metabolism, mutations in epigenetic regulators, etc

The human body contains more Than 200 different cell types That share the same information (exception: B and T cells)
Each cell type has a characteristic Gene expression profile that is controlled and maintained (inherited or epigenetic memory) by an defined epigenetic profile

Holliday 1994: Epigenetics is the nuclear inheritance which is not based on differences in DNA sequence

More mechanistically: Epigenetics is the sum of the alterations to the chromatin template that collectively establish and propagate different patters of gene expression (transcription) and silencing from the same genome

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