BHARATHIDASAN UNIVERSITY

Tiruchirappalli- 620 024
Tamil Nadu, India

Programme: M.Sc. Biochemistry

Course Title : Chromatin and Epigenetics
Course Code : BC205DCE

Unit-4
Epigenetic Control of Chromatin

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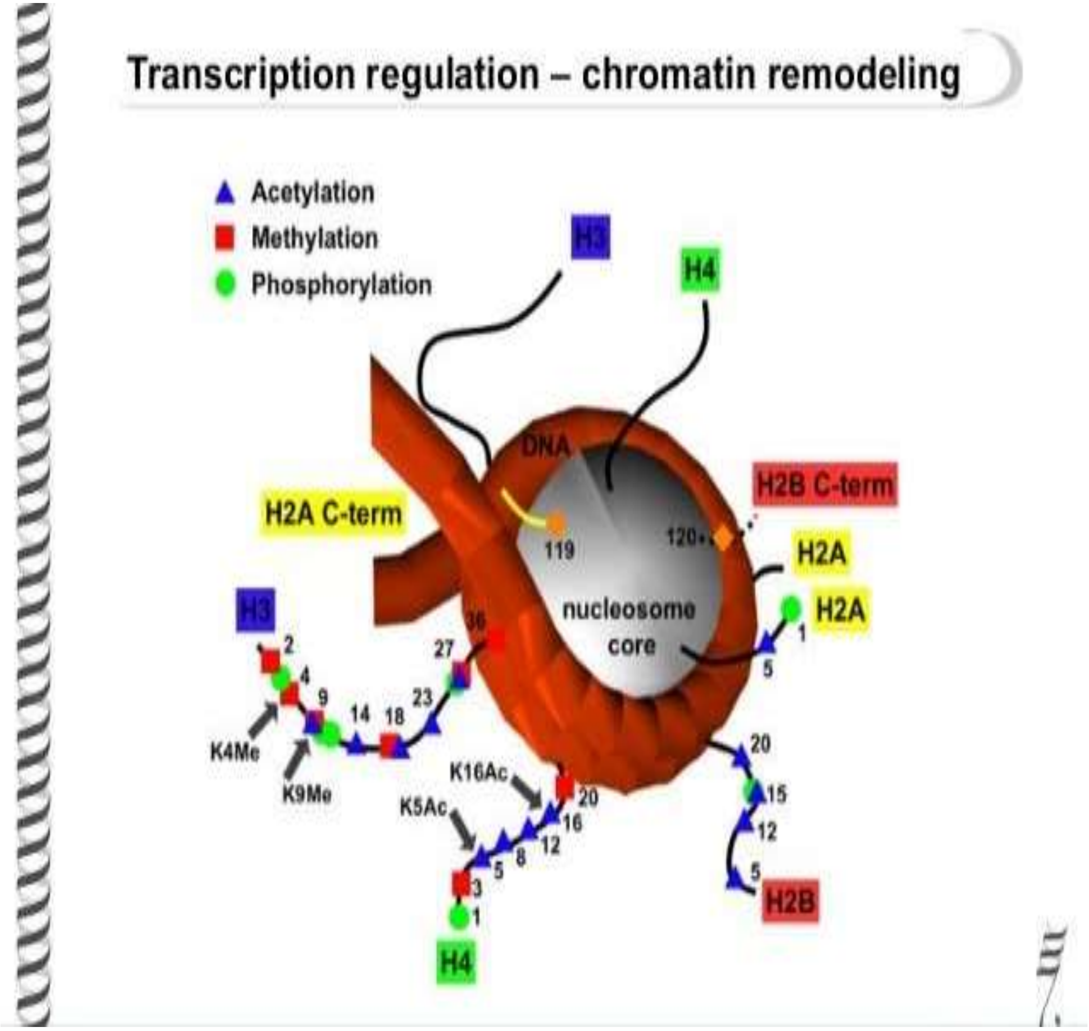
Unit-4 Overview

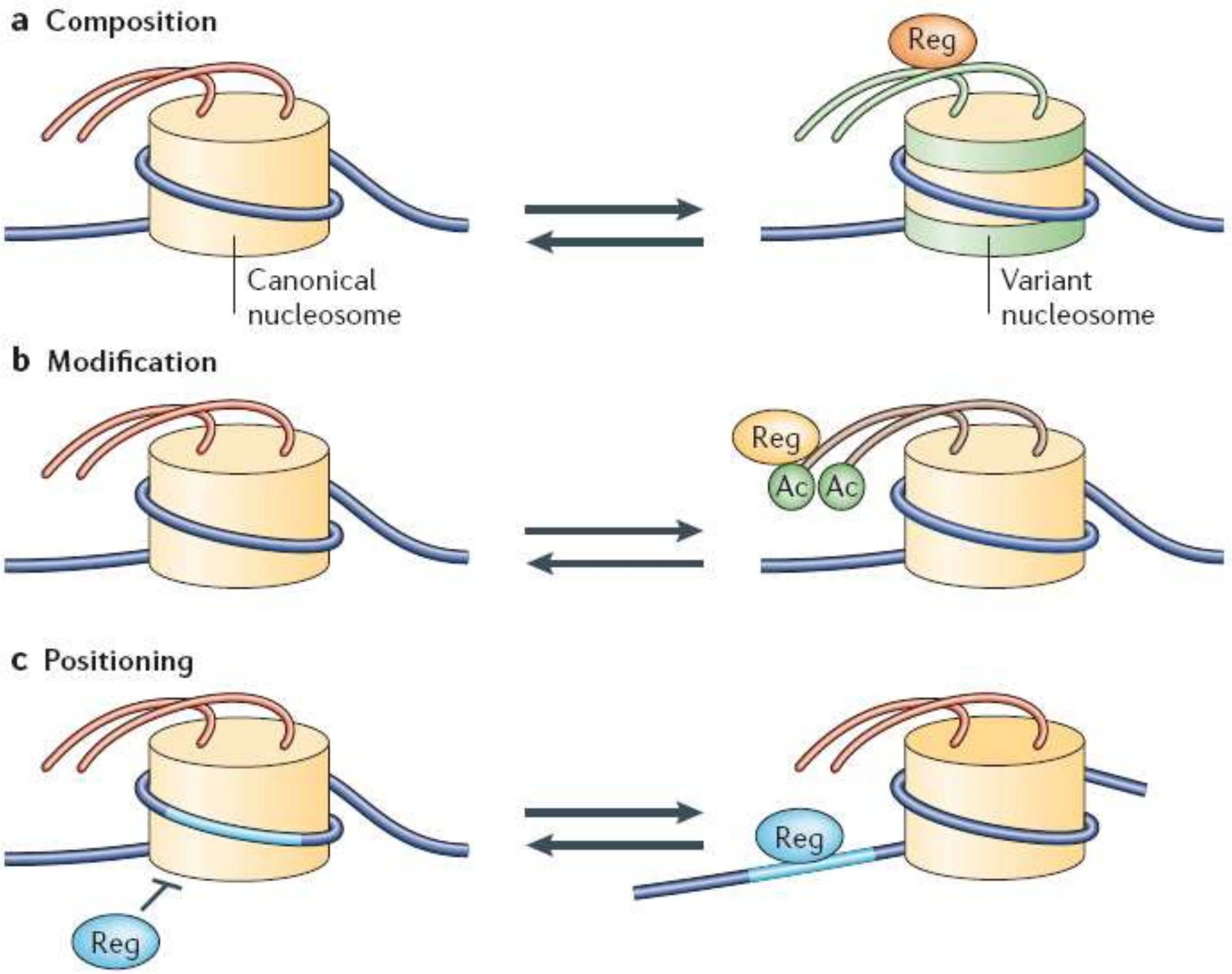
- Locus specific control
- NuRD, SIN3A, methyl transferase and kinase complexes
- Coordination among chromatin modifying complexes
- Epigenetic control of cell specific gene expression
- Mitotic cell cycle
- Gene imprinting
- Cellular differentiation
- Reversibility of epigenetic modifications
- Reprogramming epigenome by somatic cell nuclear transfer, cell fusion and by cell extracts

Chromatin remodelling and Transcription

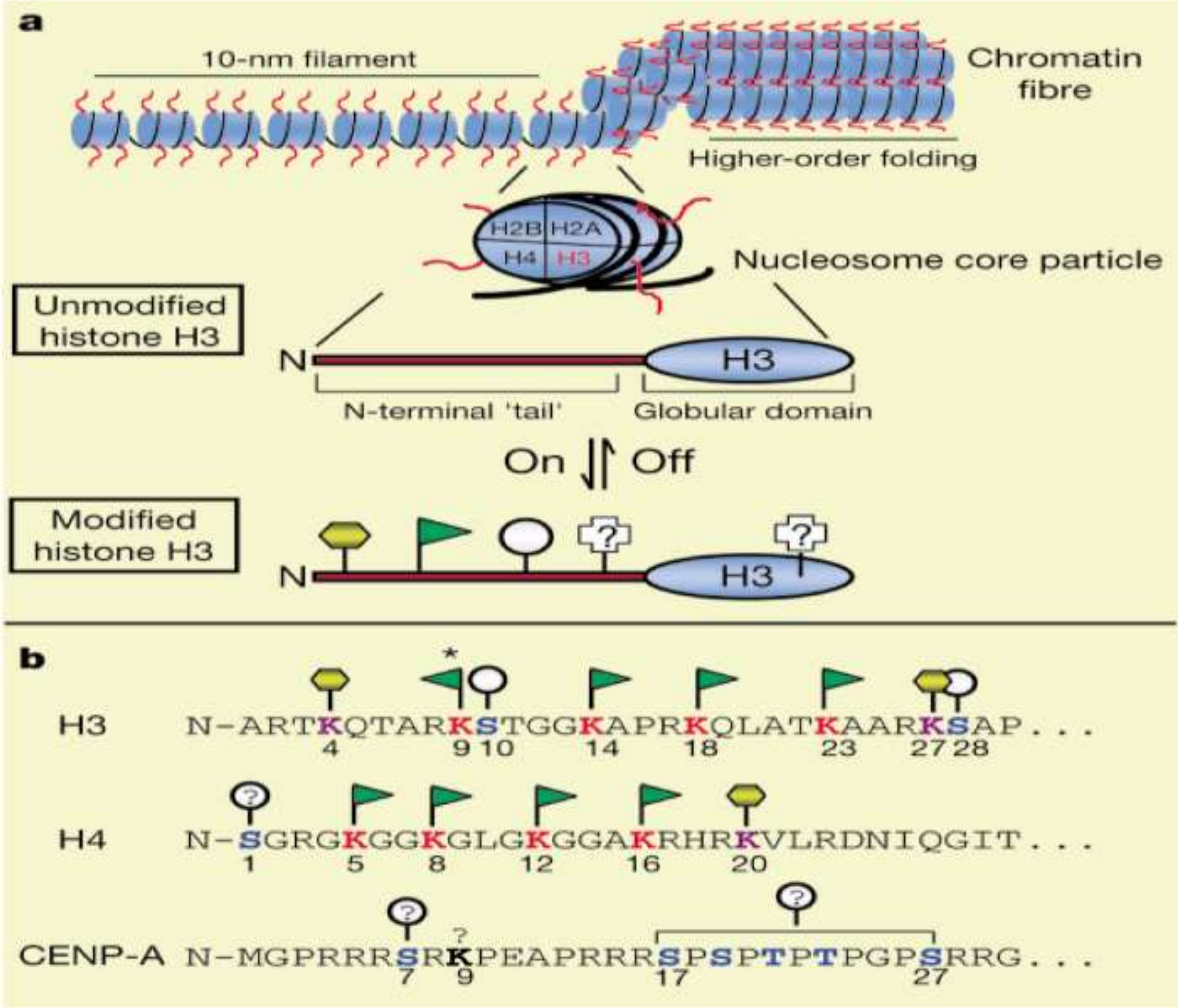


Transcription regulation – chromatin remodeling

Nucleosome

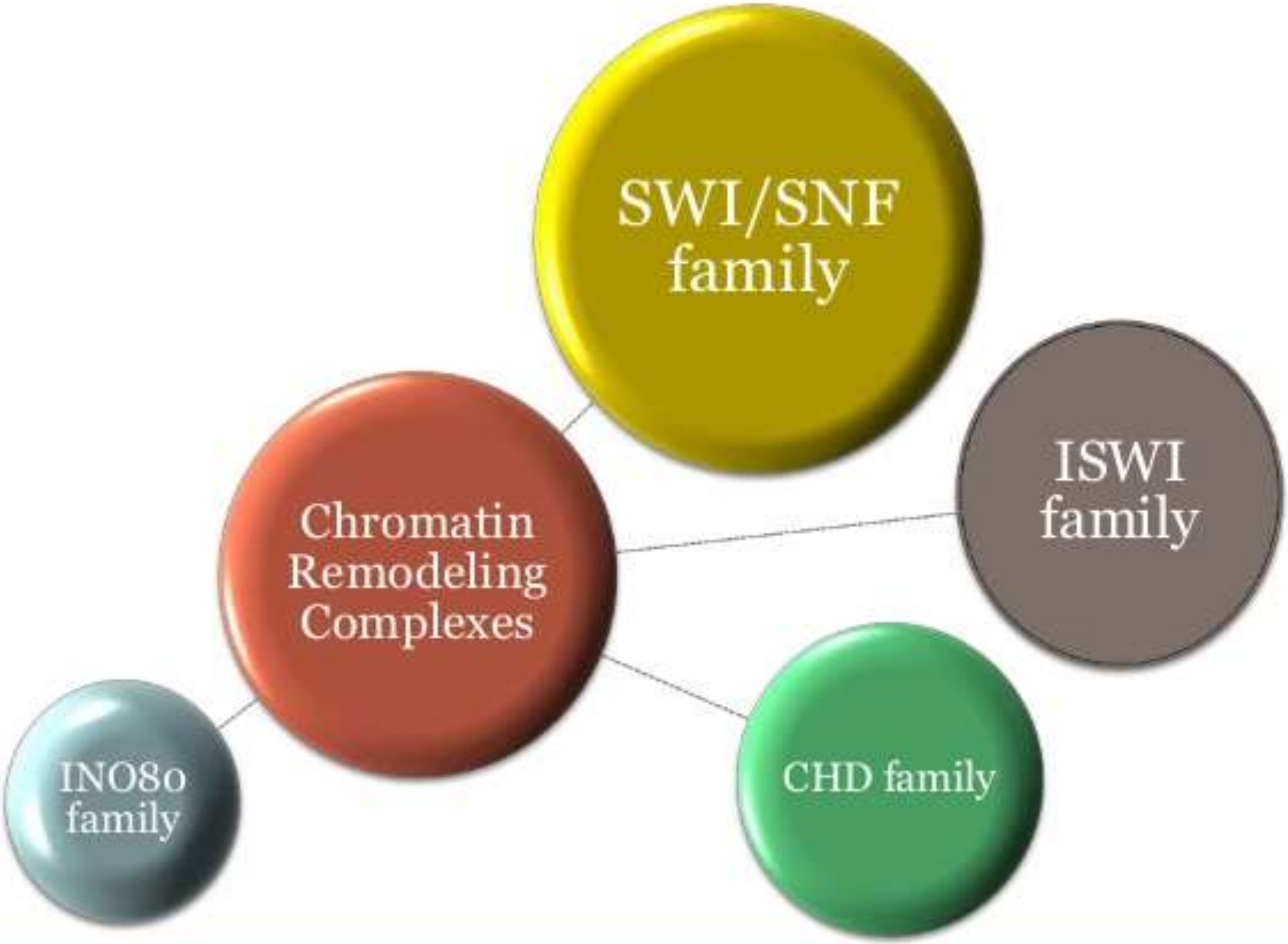

a Composition
Reg
Canonical nucleosome
Variant nucleosome
b Modification
Reg
Ac
Ac
c Positioning
Reg
Reg

Histone


a
10-nm filament
Chromatin fibre
Higher-order folding
H2B
H2A
H4
H3
Nucleosome core particle
Unmodified histone H3
N
H3
N-terminal 'tail'
Globular domain
On
Off
Modified histone H3
N
?
?
H3
b
*
H3
N-ARTKQTARKSTGGKAPRKQLATKAARKSAP...
4
9 10
14
18
23
27 28
H4
?
N-SGRGKGGKGLGKGGAKRHRKVLRDNIQGIT...
1
5
8
12
16
20
CENP-A
?
?
?
N-MGPRRRSRKPEAPRRRSPSPTPTPGPSRRG...
7
9
17
27

2. ATP dependent chromatin remodeling

- ATP dependent chromatin remodeling complexes regulate gene expression by either moving, ejecting or restructuring nucleosomes.
- These protein complexes have a common ATPase domain and energy from the hydrolysis of ATP allows these remodeling complexes to reposition (slide, twist or loop) nucleosomes along the DNA, expel histones away from DNA or facilitate exchange of histone variants thus creating nucleosome free regions of DNA for gene activation.



Chromatin Remodeling Complexes

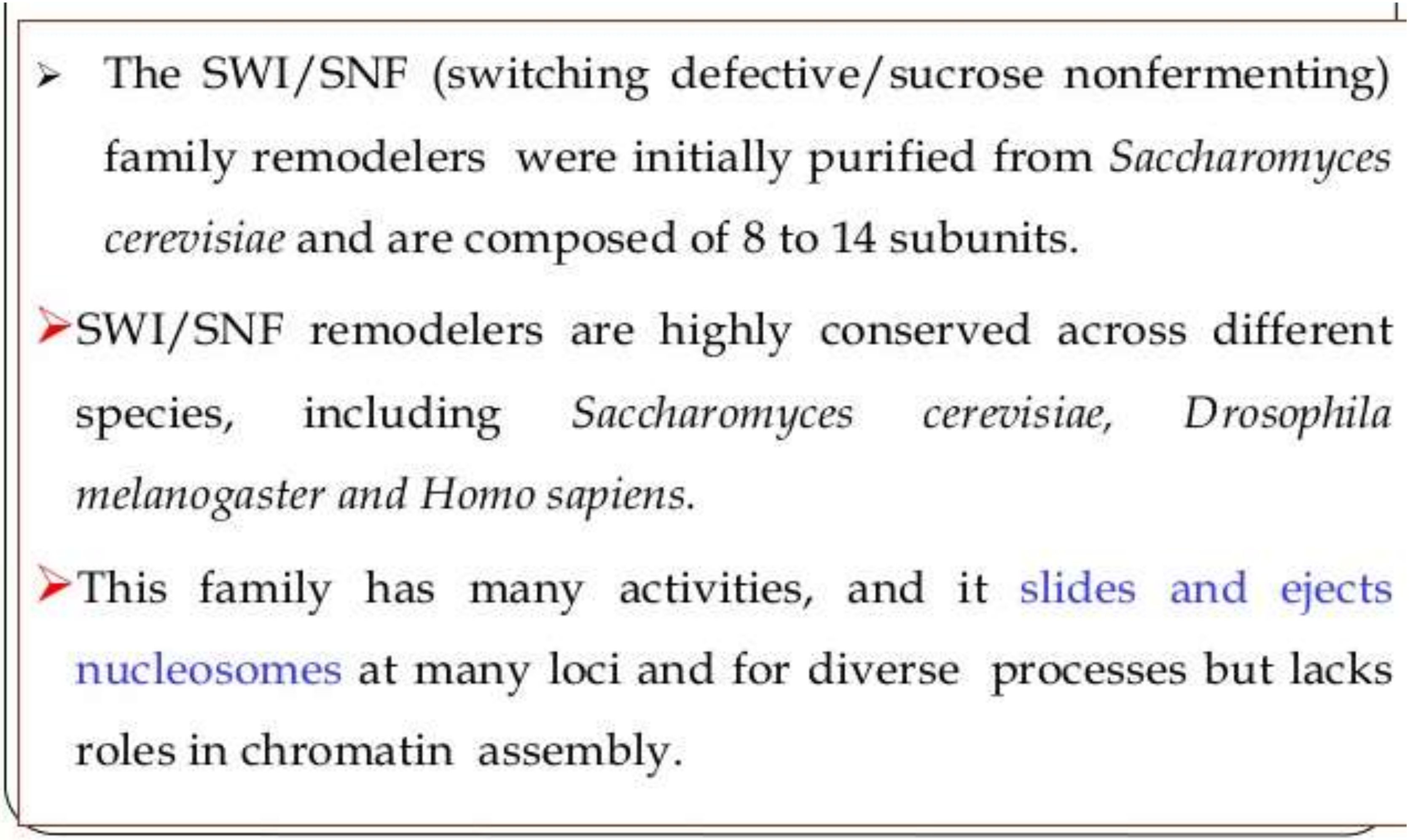
SWI/SNF family

ISWI family

CHD family

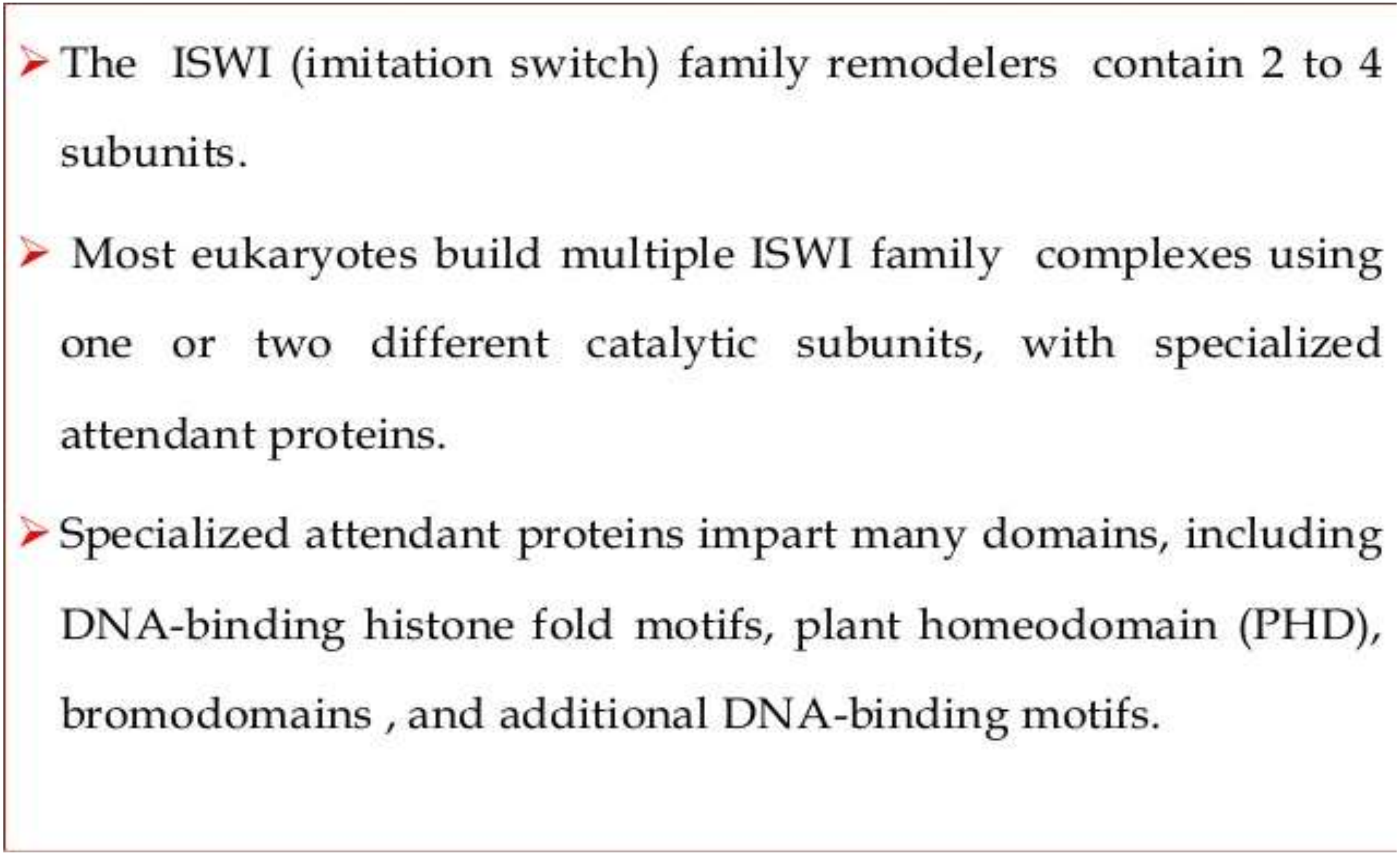
INO80 family

SWI/SNF Family Remodelers



- The SWI/SNF (switching defective/sucrose nonfermenting) family remodelers were initially purified from *Saccharomyces cerevisiae* and are composed of 8 to 14 subunits.
- SWI/SNF remodelers are highly conserved across different species, including *Saccharomyces cerevisiae, Drosophila melanogaster and Homo sapiens.*
- This family has many activities, and it slides and ejects nucleosomes at many loci and for diverse processes but lacks roles in chromatin assembly.

ISWI Family Remodelers



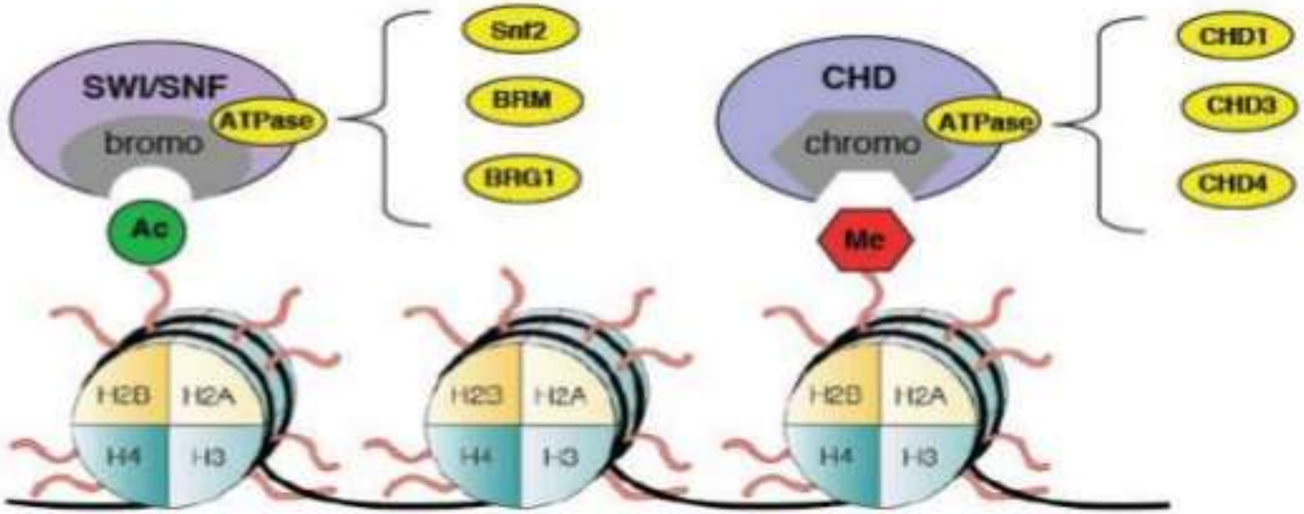
- The ISWI (imitation switch) family remodelers contain 2 to 4 subunits.
- Most eukaryotes build multiple ISWI family complexes using one or two different catalytic subunits, with specialized attendant proteins.
- Specialized attendant proteins impart many domains, including DNA-binding histone fold motifs, plant homeodomain (PHD), bromodomains , and additional DNA-binding motifs.

ATP-dependent chromatin remodeling complexes

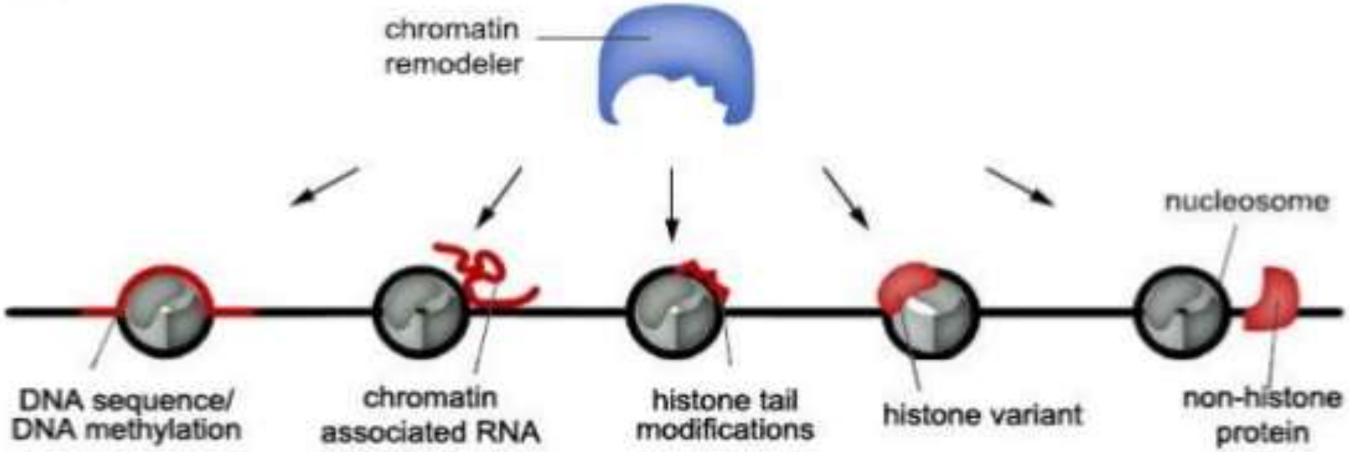
main families:

→ SWI/SNF: enzyme contains bromo-domain that binds to acetylated histone

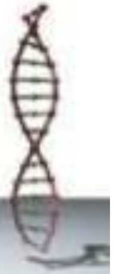
→ CHD: enzyme contains chromo-domain that binds to methylated histone



Target location signals and translocation reaction scheme for chromatin remodelers.



Mechanisms of Chromatin Remodeling



One

- Nucleosome Sliding

Two

- eject histone octamers

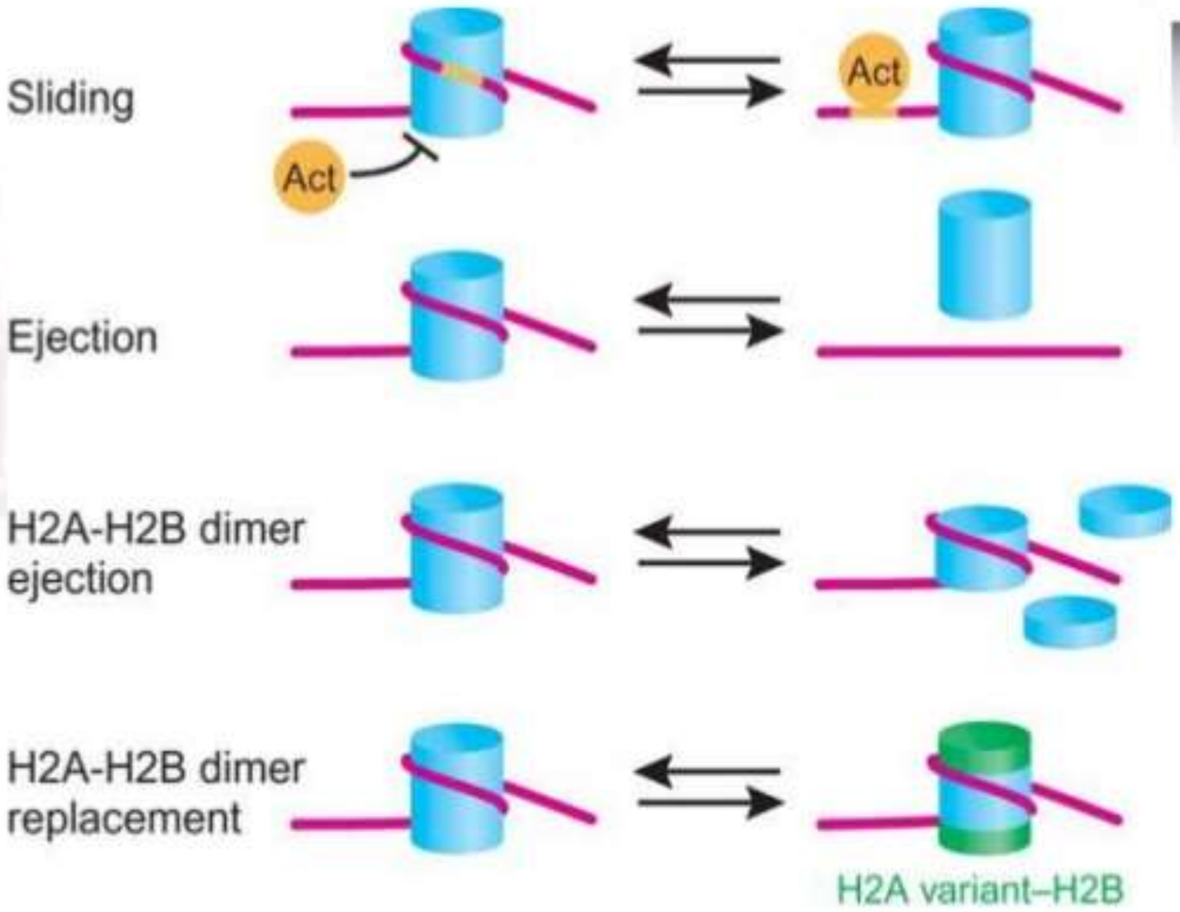
Three

- Remove H2A-H2B dimers

Four

- replace dimers

Mechanisms of Chromatin Remodeling



Sliding

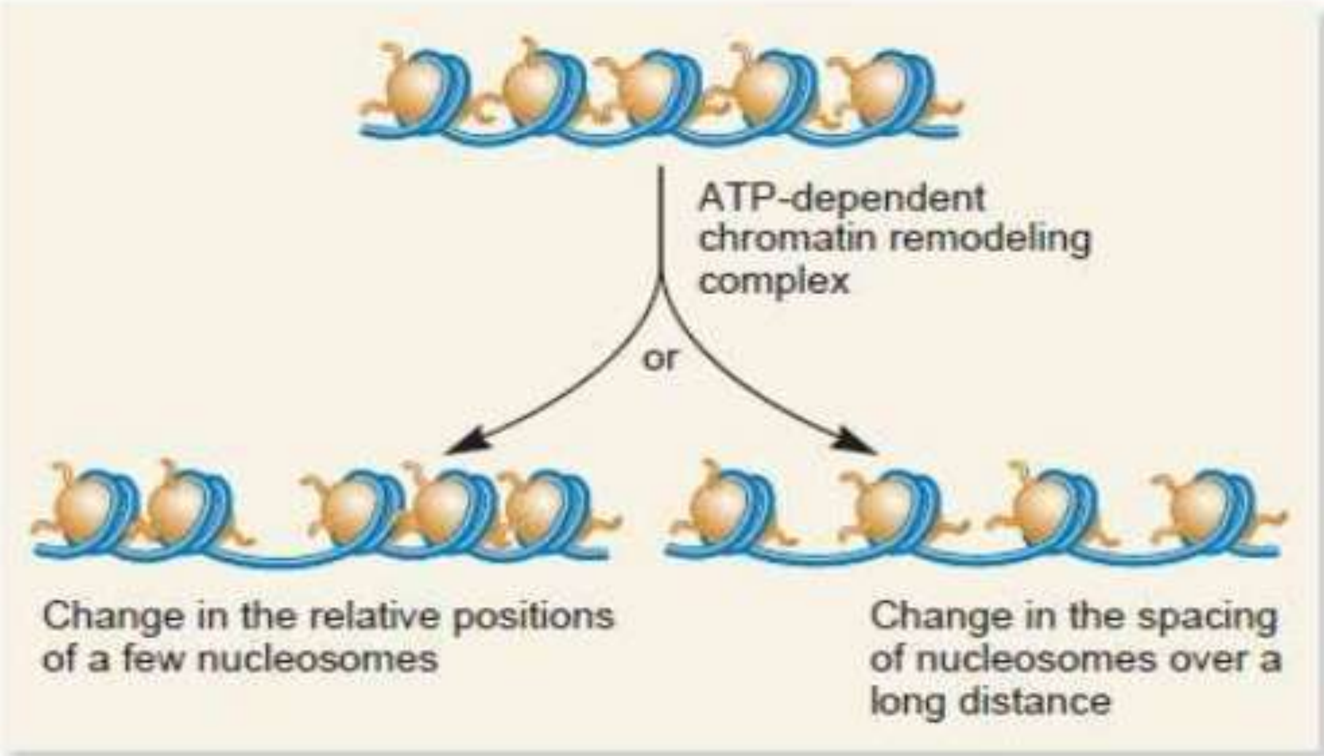
Ejection

H2A-H2B dimer ejection

H2A-H2B dimer replacement

ATP-dependent chromatin remodeling.

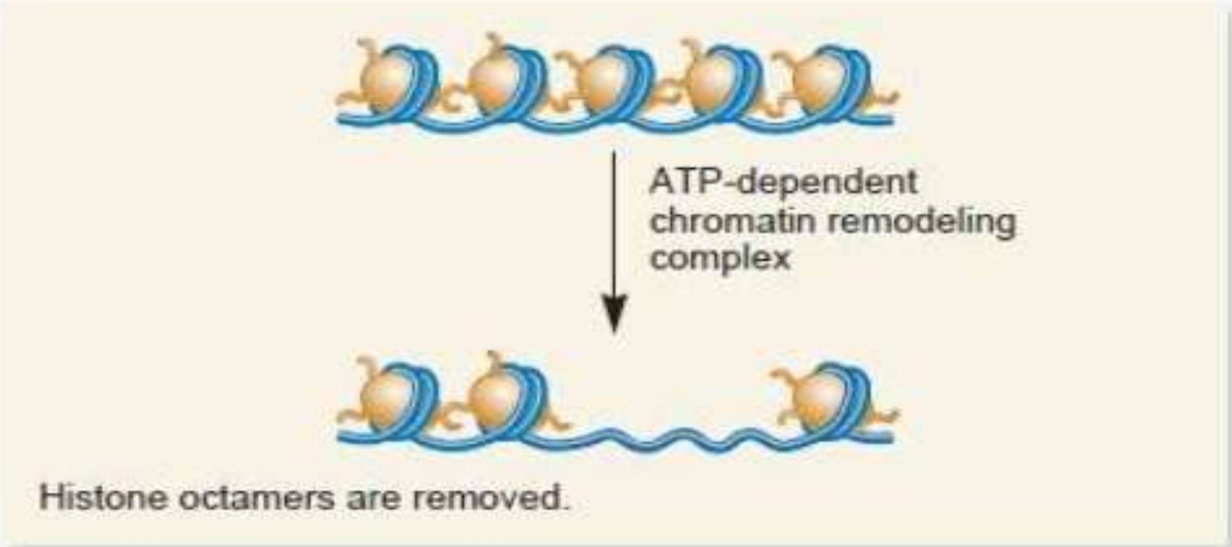
(a) change the locations of nucleosomes



(a) Change in nucleosome position

ATP-dependent chromatin remodeling.

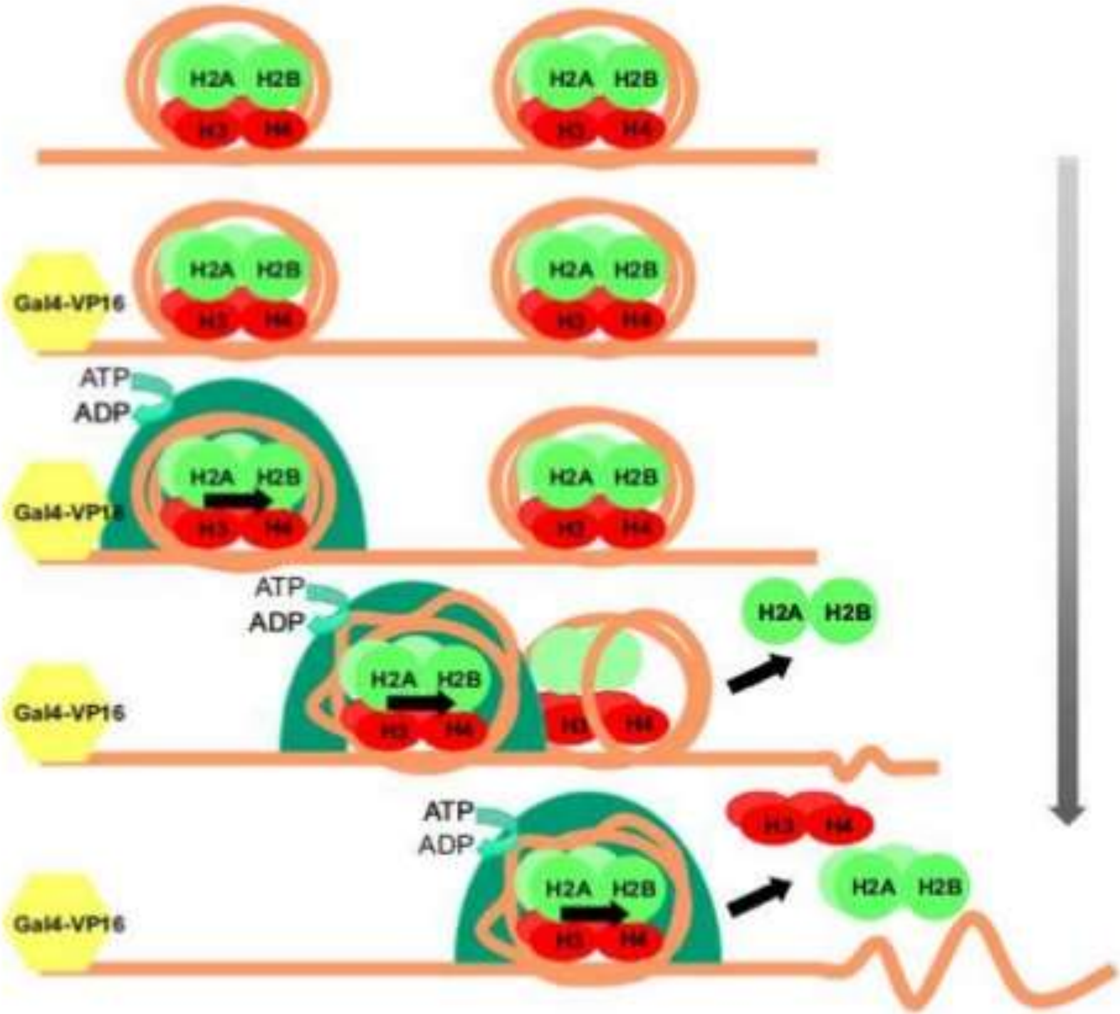
(b) remove histones from the DNA



Histone octamers are removed.

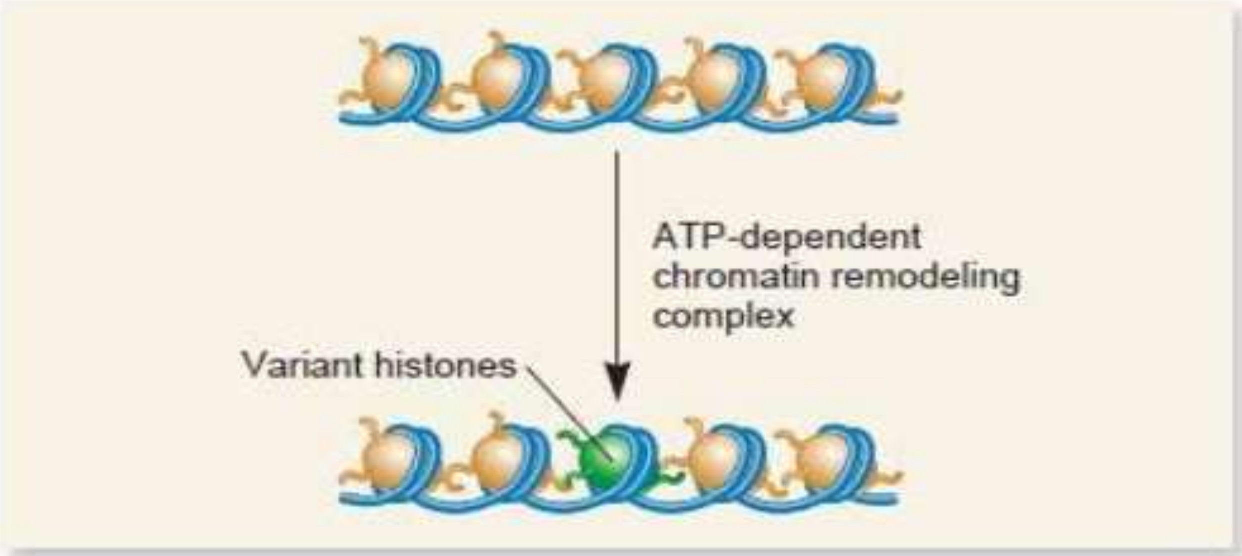
(b) Histone eviction

Proposed Mechanism of SWI/SNF Nucleosome Eviction



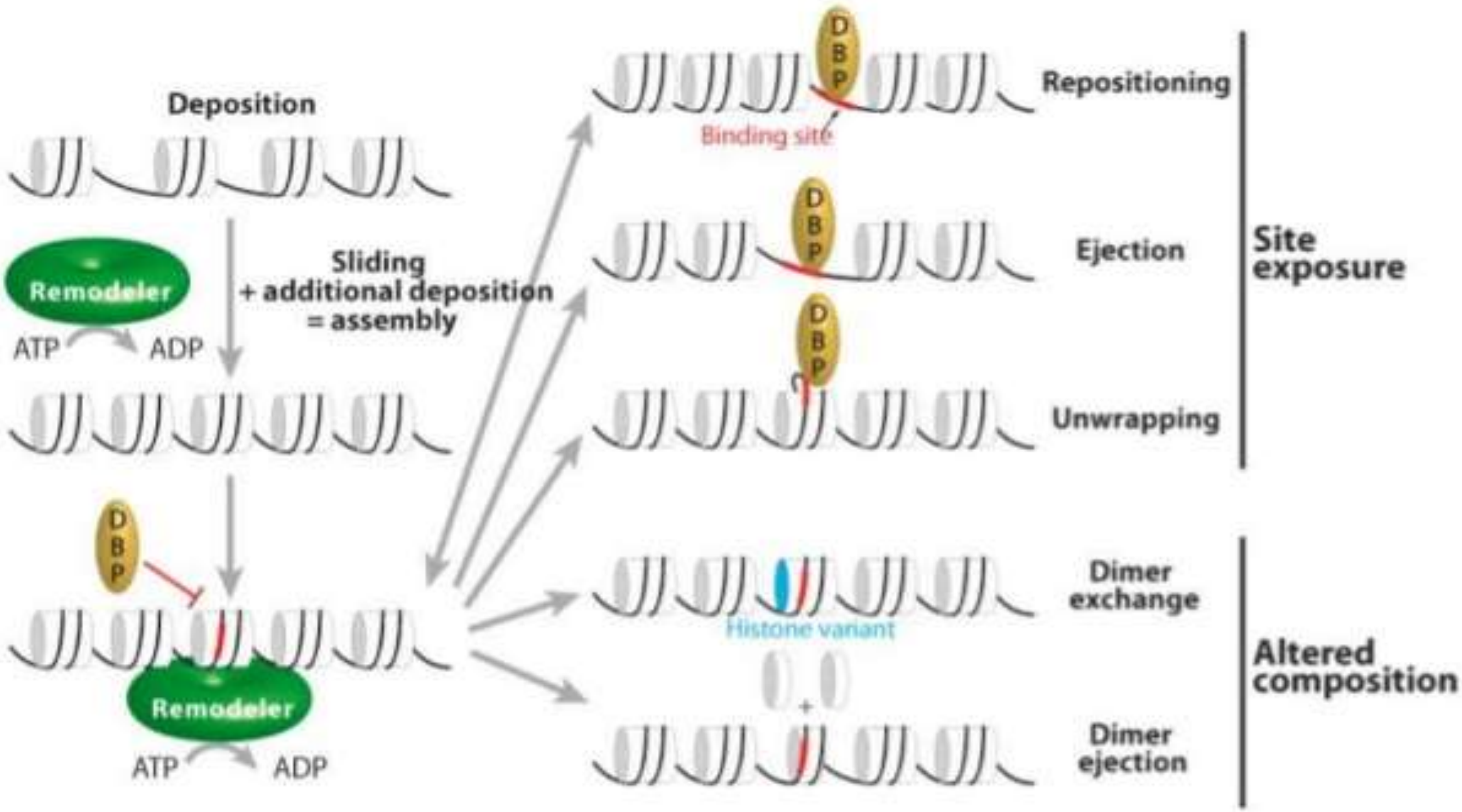
ATP-dependent chromatin remodeling.

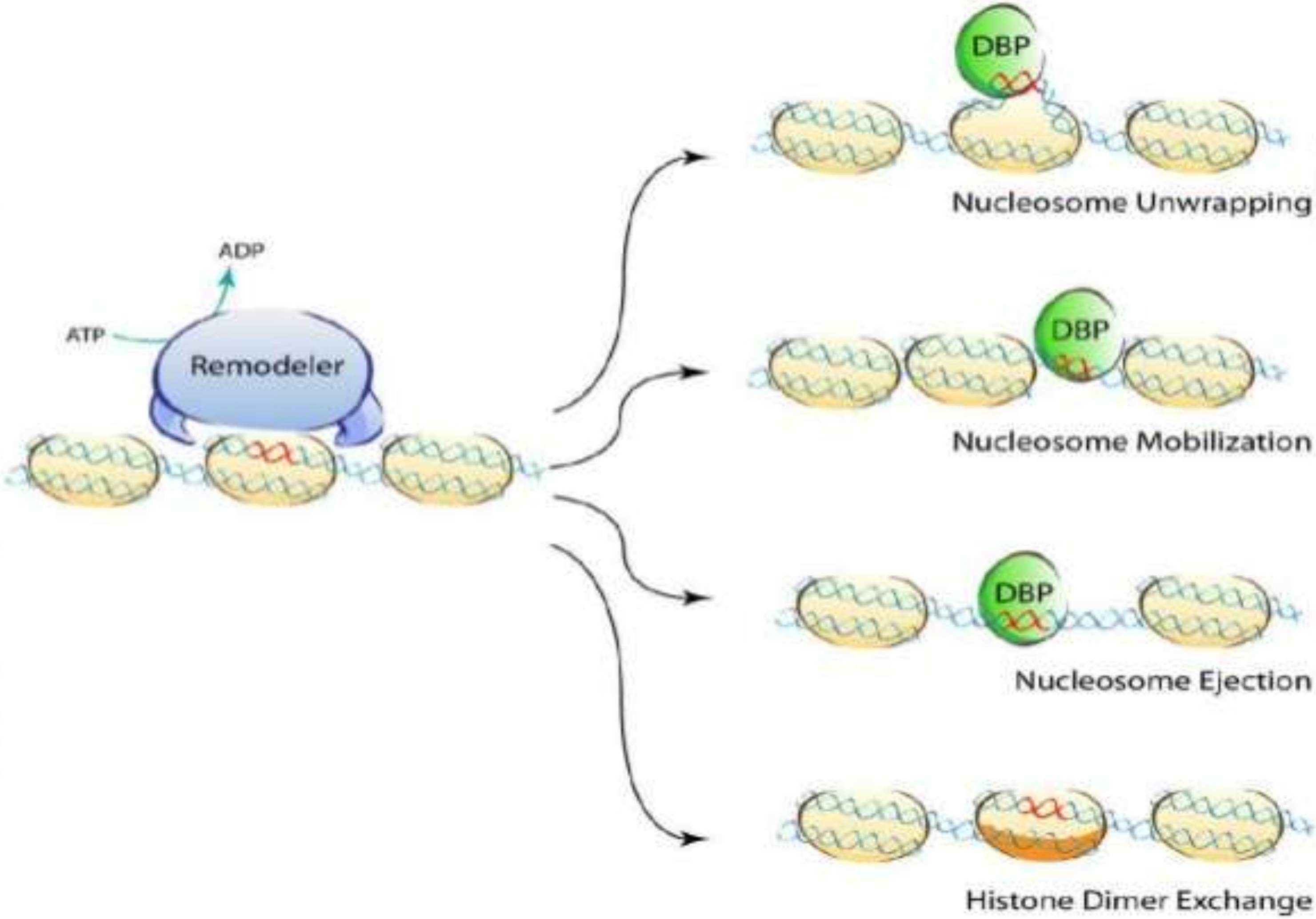
(c) replace core histones with variant histones.



(c) Replacement with variant histones

Reactions catalyzed by ATP-dependent chromatin remodeling factors




ADP
ATP
Remodeler
DBP
Nucleosome Unwrapping
DBP
Nucleosome Mobilization
DBP
Nucleosome Ejection
Histone Dimer Exchange