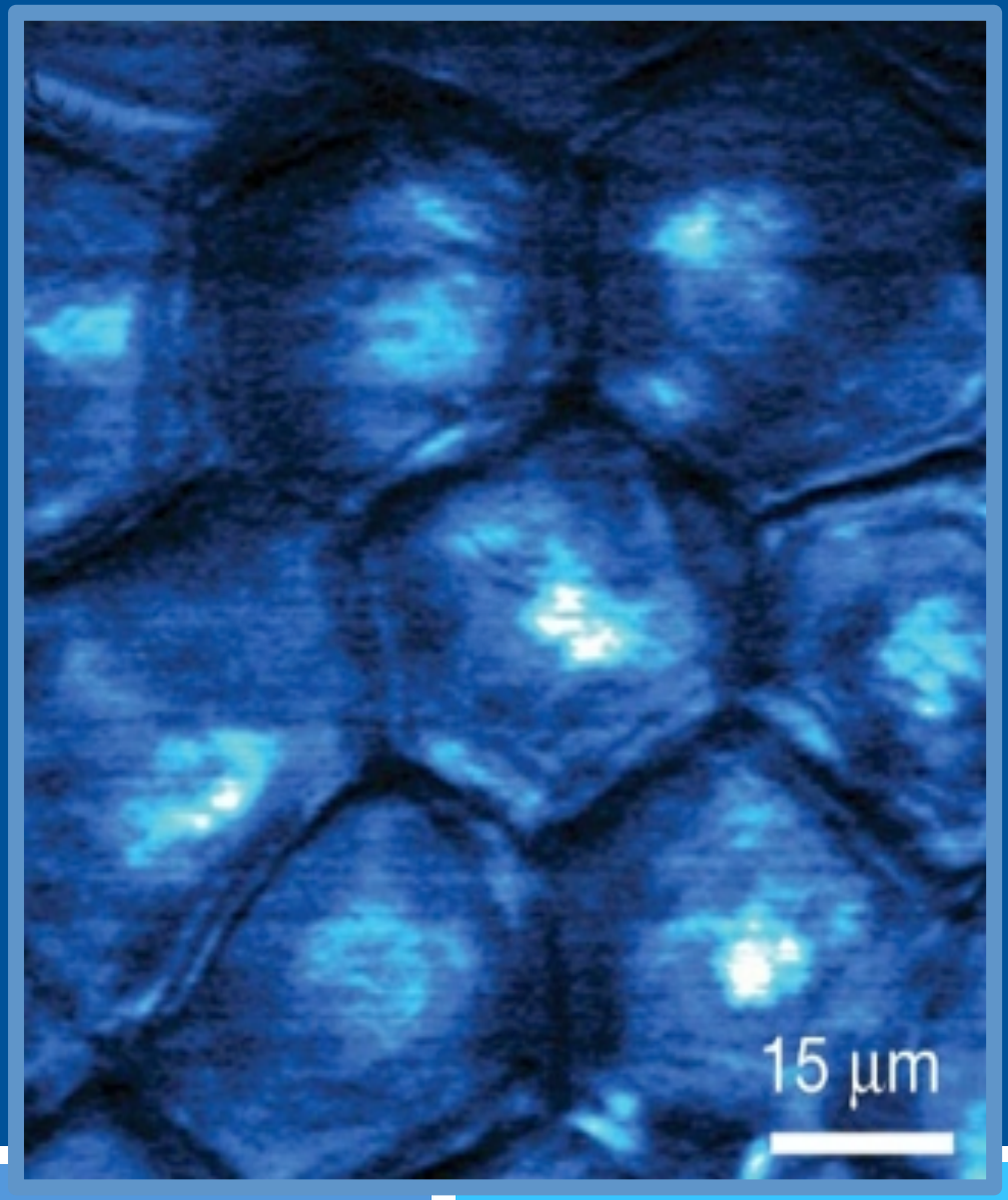


GENES AND CHROMOSOMES IV

Lecture 6

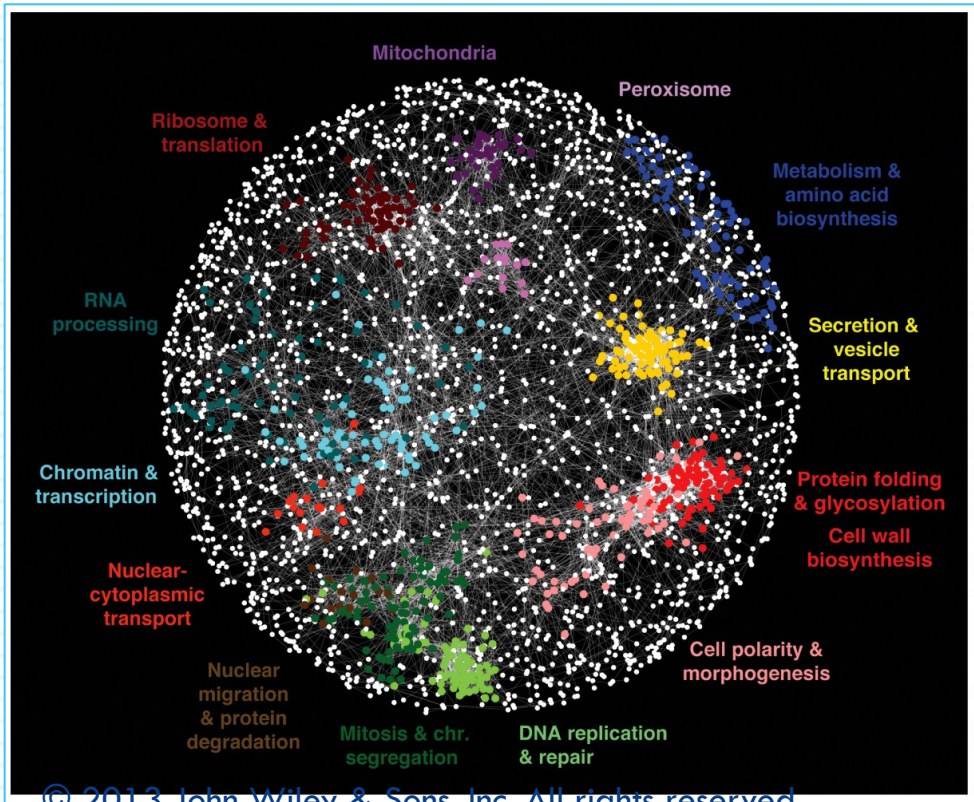
BIOL 266/4

2014-15

Dr. S. Azam

Biology Department
Concordia University

CELL NUCLEUS AND THE CONTROL OF GENE EXPRESSION

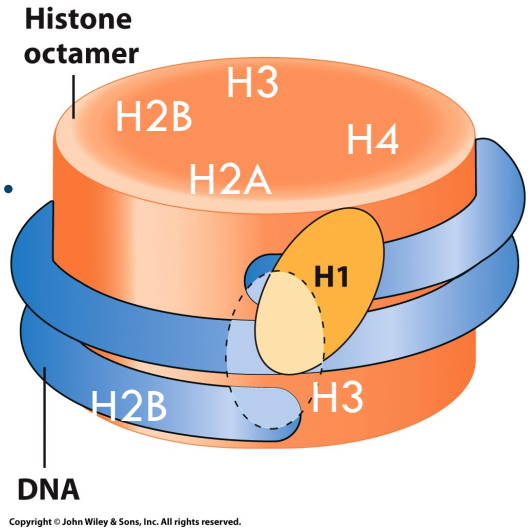


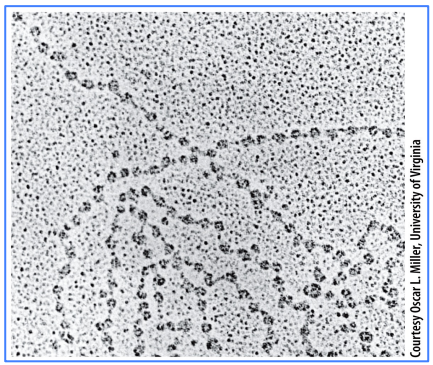
From Michael Costanzo, et al., Science 327425, © 2010, reprinted with permission from AAAS. Courtesy of Charles Boone, University of Toronto.

Control of Gene Expression in Eukaryotes

Chromosomes and Chromatin

- DNA and histones are organized into repeating subunits called **nucleosomes**.
- Each nucleosome includes a *core particle* of supercoiled DNA and histone H1 serving as a *linker*.
- DNA is wrapped around the core complex.
- The histone core complex consists of two molecules each of H2A, H2B, H3, and H4 forming an octamer.

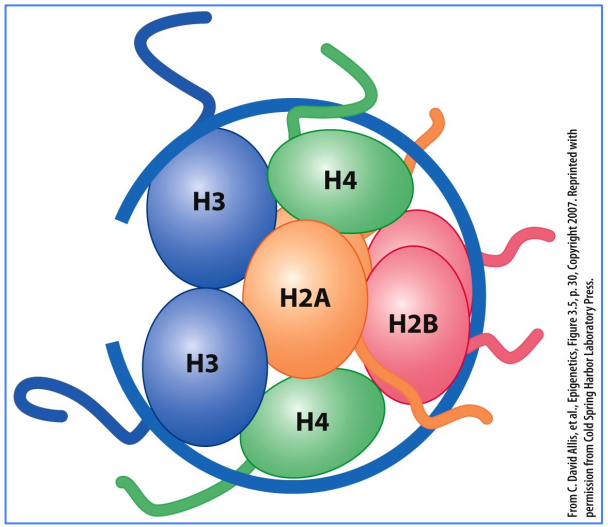


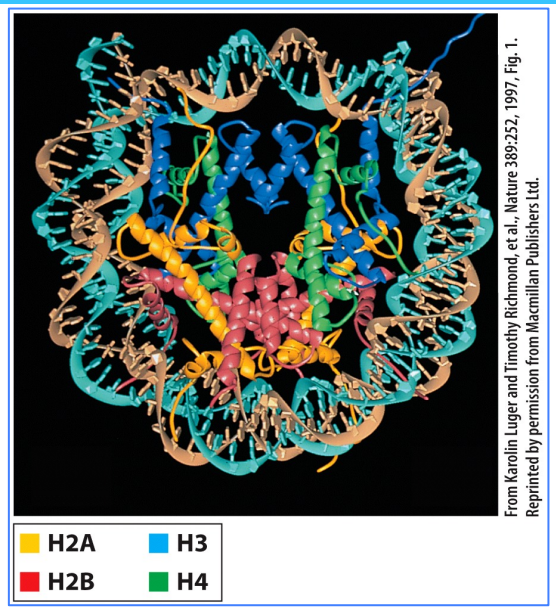


Nucleosomal organization of chromatin: Schematic diagram (top) and EM of *Drosophila* cell nucleus with nucleosomes along DNA strand (bottom)

Control of Gene Expression in Eukaryotes

Chromosomes and Chromatin



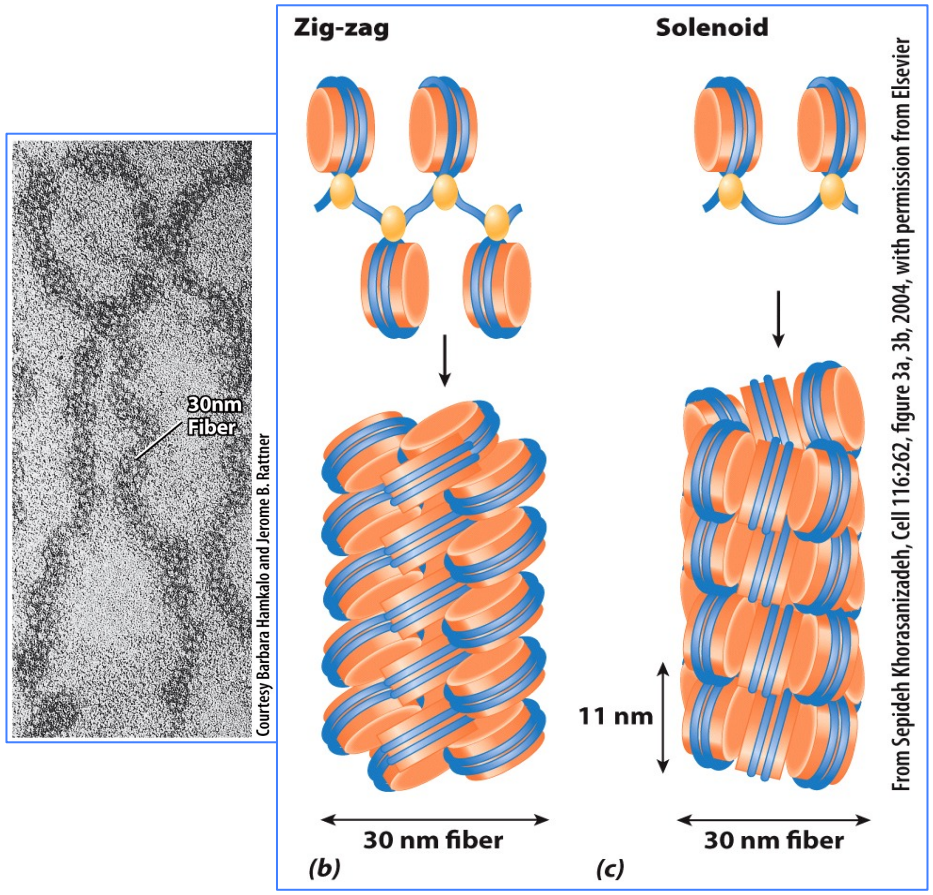


3D structure of a nucleosome from X-ray crystallography. Core particle at two views (top) and schematic of half of a core particle (side)

Control of Gene Expression in Eukaryotes

Higher Levels of Chromatin Structure

- A 30-nm filament is another level of chromatin packaging, maintained by histone H1.
- Chromatin filaments are organized into large supercoiled loops.

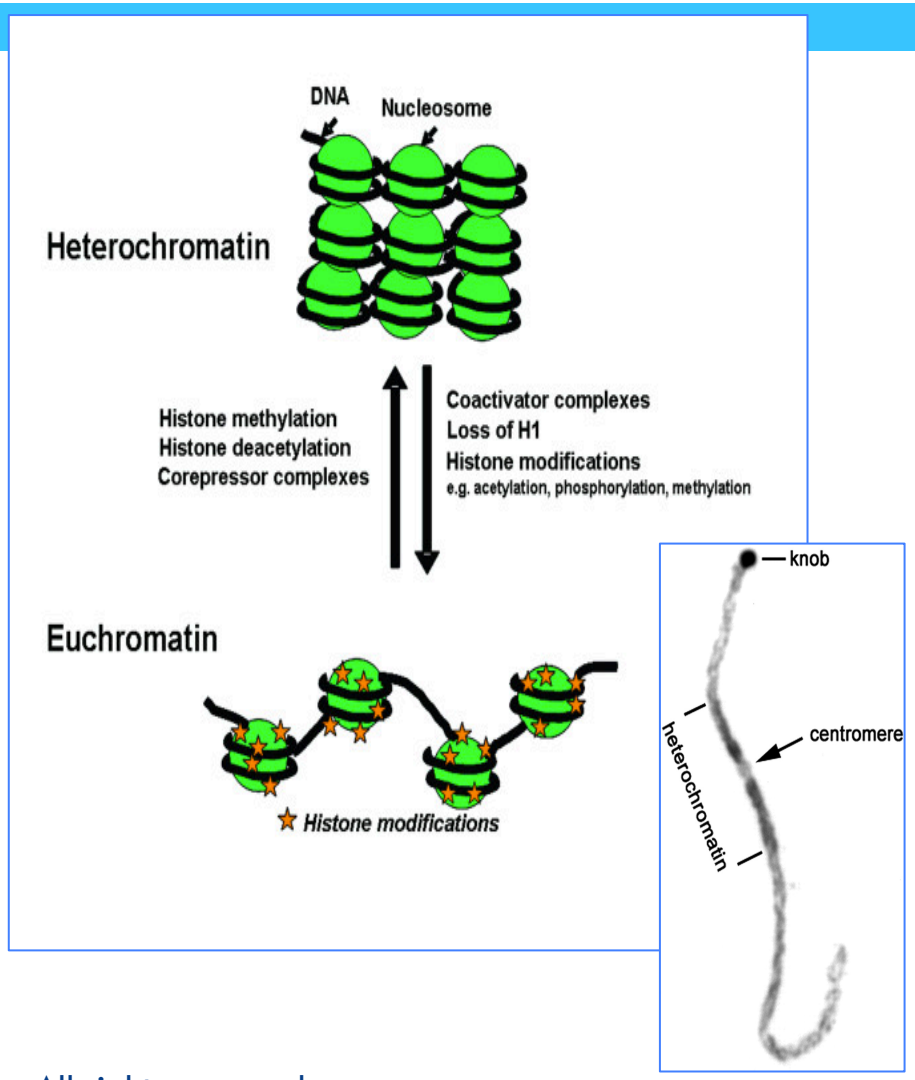


30-nm fiber: EM of a fiber (left) and two packaging models (middle, right).

Control of Gene Expression in Eukaryotes

Heterochromatin and Euchromatin

1. **Euchromatin (active)** returns to a dispersed state after mitosis.
2. **Heterochromatin (inactive)** is condensed during interphase.
   - ***Constitutive heterochromatin*** remains condensed all the time.
     - Found mostly around centromeres and telomeres.
     - Consists of highly repeated sequences and few genes.
   - ***Facultative heterochromatin*** is inactivated during certain phases of the organism's life.



Control of Gene Expression in Eukaryotes

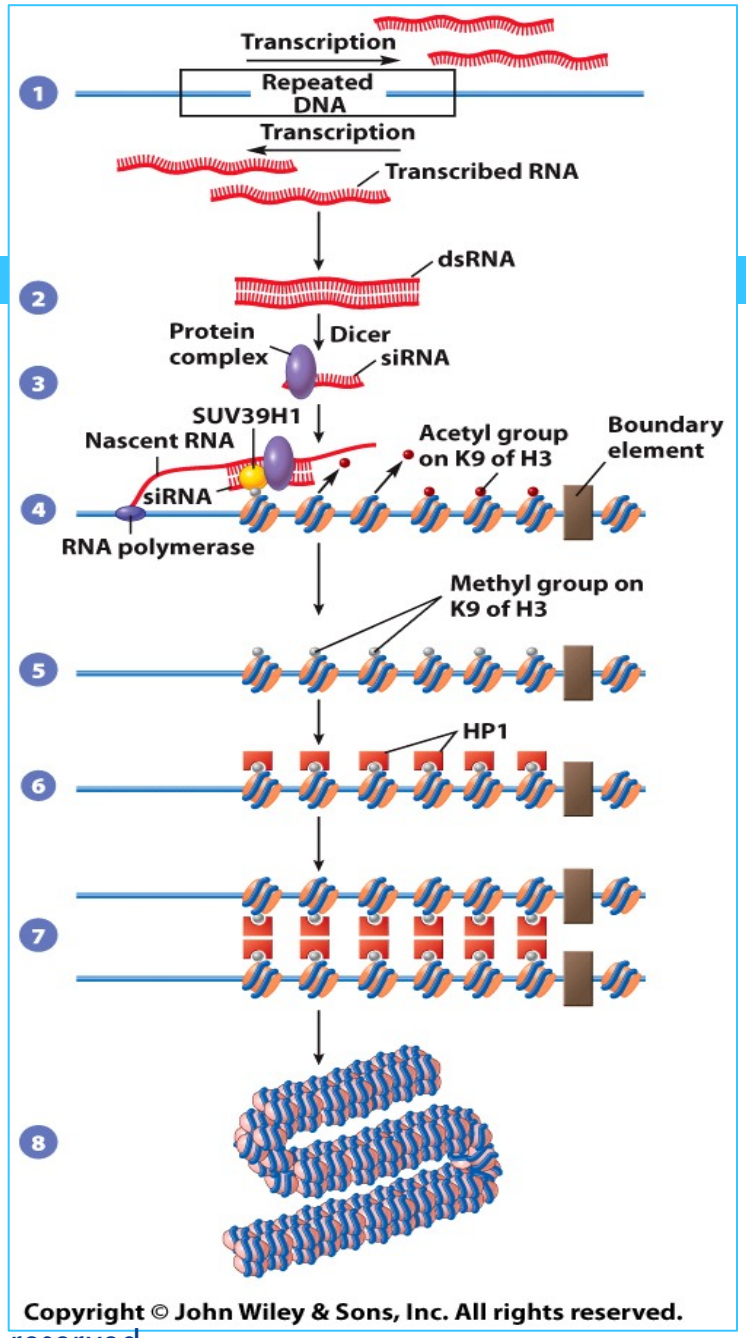
Histone Modification

- Removal of the acetyl groups from H3 and H4 histones is among the initial steps in conversion of euchromatin → heterochromatin.
- Histone deacetylation is accompanied by methylation of H3K9 by *histone methyltransferase* in humans.
- Methylated H3K9 binds to proteins with a *chromodomain*, for example *heterochromatic protein 1 (HP1)*
- Once HP1 is bound to the histone tails, HP1-HP1 interactions facilitate chromatin packaging into a heterochromatin state

Control of Gene Expression in Eukaryotes

Histone Modification

Histone deacetylase
Histone methyltransferase

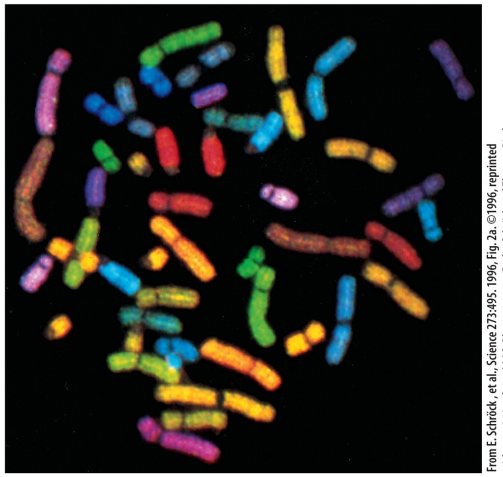


Model of possible events during the formation of heterochromatin

Control of Gene Expression in Eukaryotes

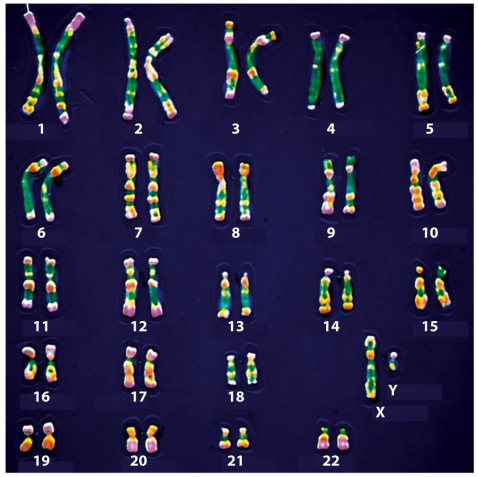
The Structure of a Mitotic Chromosome

- Chromatin of a mitotic cell exists in its most highly condensed state.
- Staining mitotic chromosomes can provide useful information.
- A **karyotype** is a preparation of homologous pairs ordered according to size.
- The pattern on a karyotype may be used to screen chromosomal abnormalities.



From E. Schröck, et al., Science 273:495, 1996, Fig. 2a. ©1996, reprinted with permission from AAAS. Photo courtesy Evelin Schröck and Thomas Ried.

Human mitotic chromosomes labeled with different specific fluorescent dyes.



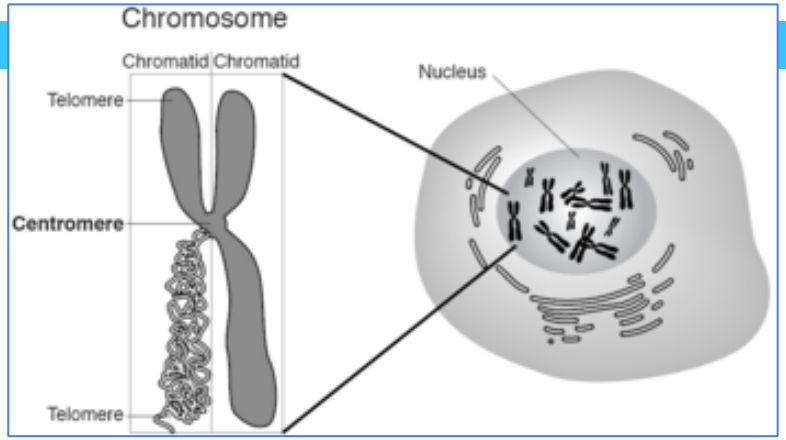
CNRI/Science Photo Library/Photo Researchers, Inc.

The stained chromosomes of a human male arranged in a karyotype

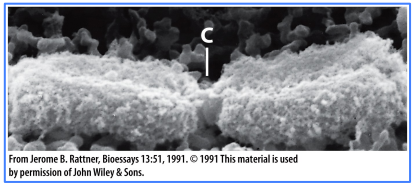
Control of Gene Expression in Eukaryotes

Centromeres

- **Centromere** is located at the site markedly indented on a chromosome.
- Centromeres contain constitutive heterochromatin.
- Centromeric DNA is the site of microtubule attachment during mitosis.



Centromere location	Designation	Metaphase shape	Anaphase shape
Middle	Metacentric	p arm, Centromere, q arm	Migration
Between middle and end	Submetacentric		
Close to end	Acrocentric		
At end	Telocentric		



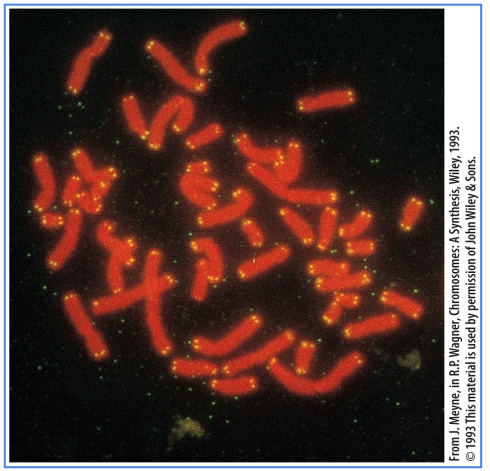
From Jerome B. Rattner, Bioessays 13:51, 1991. © 1991 This material is used by permission of John Wiley & Sons.

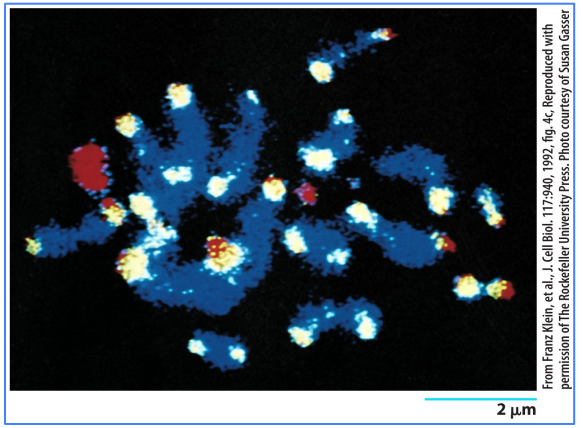
TELOMERE

Control of Gene Expression in Eukaryotes

Telomeres

- The end of each chromosome is called a **telomere** and is distinguished by a set of repeated sequences.
- New repeats are added by a **telomerase**, a reverse transcriptase that synthesizes DNA from a RNA template.
- Telomeres are required for the complete replication of the chromosome because they protect the ends from being degraded.

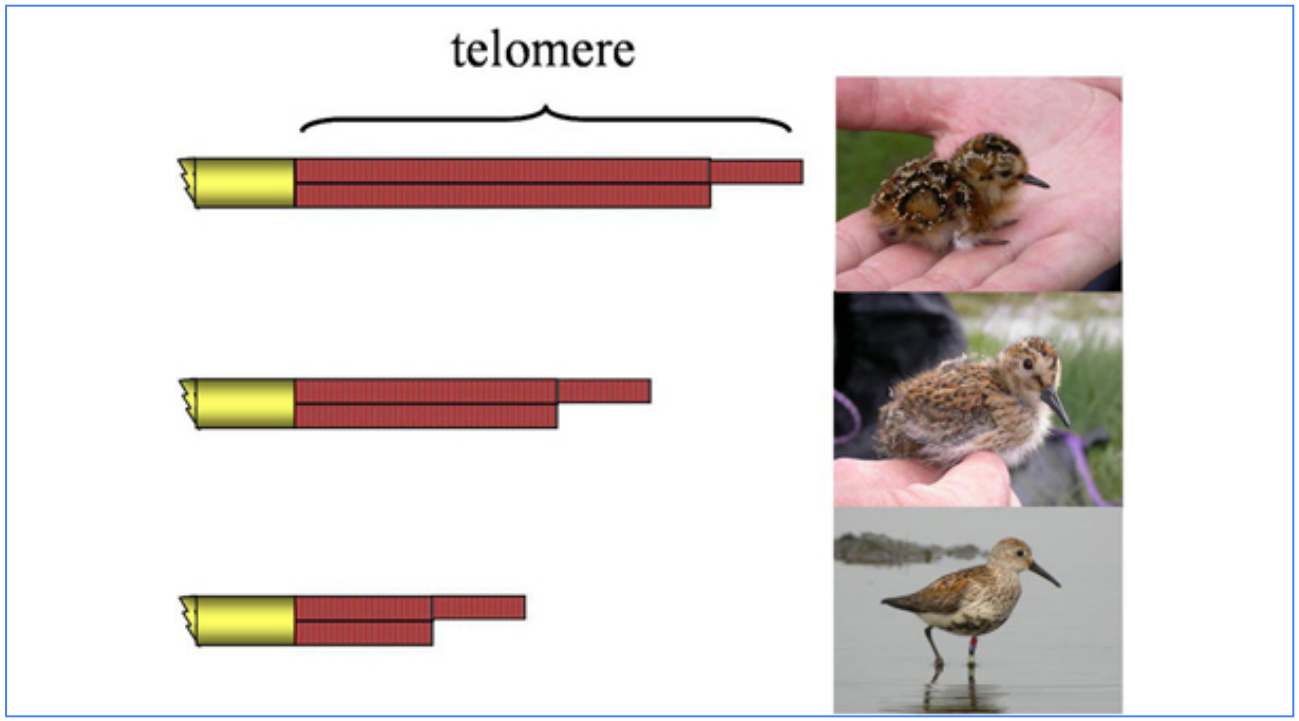




Control of Gene Expression in Eukaryotes

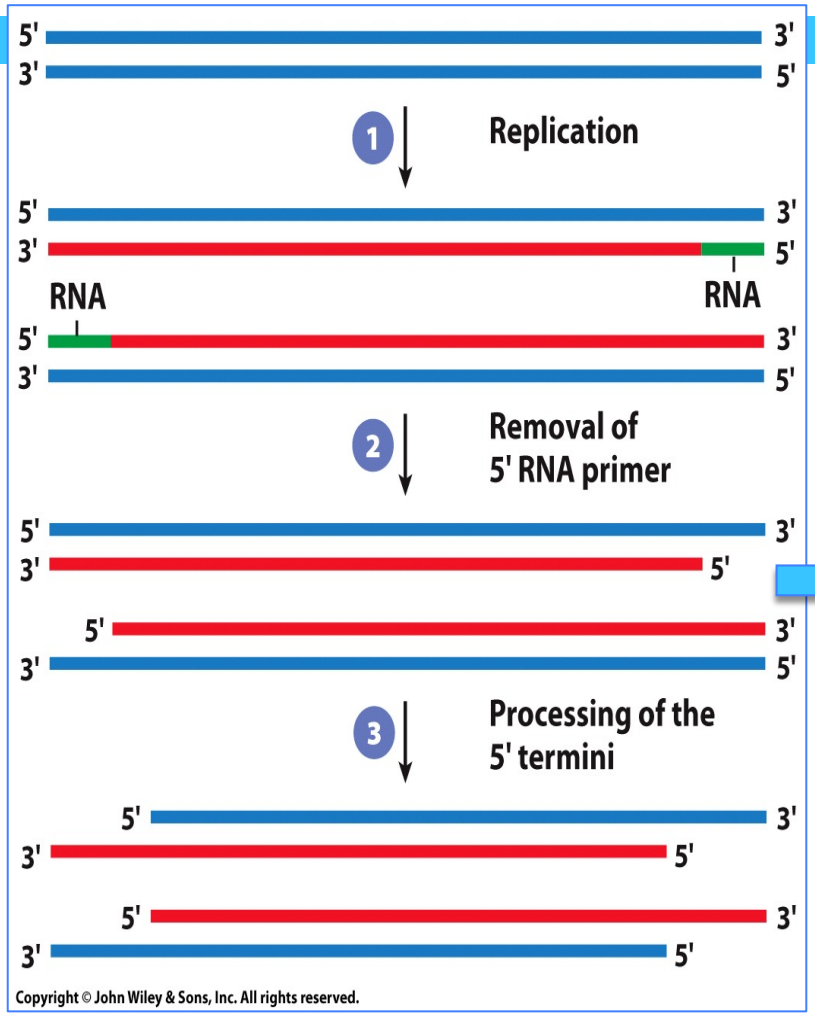
Telomeres

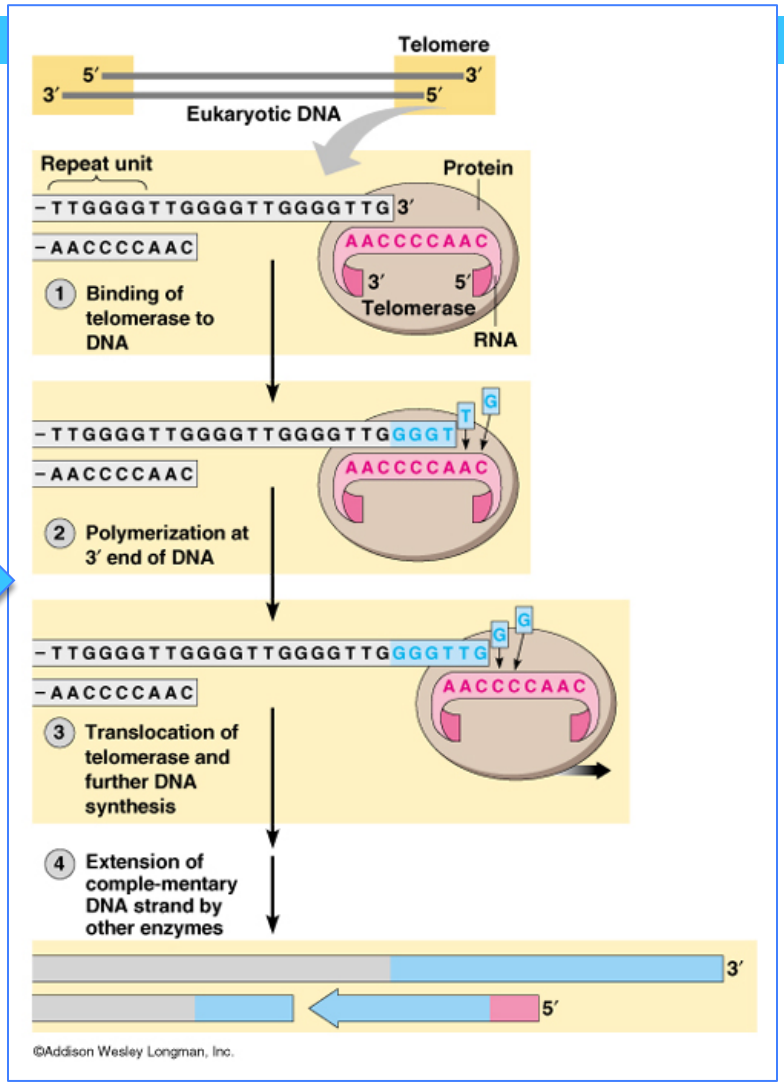
Telomerase activity is thought to have major effects on cell life



Control of Gene Expression in Eukaryotes

Telomeres



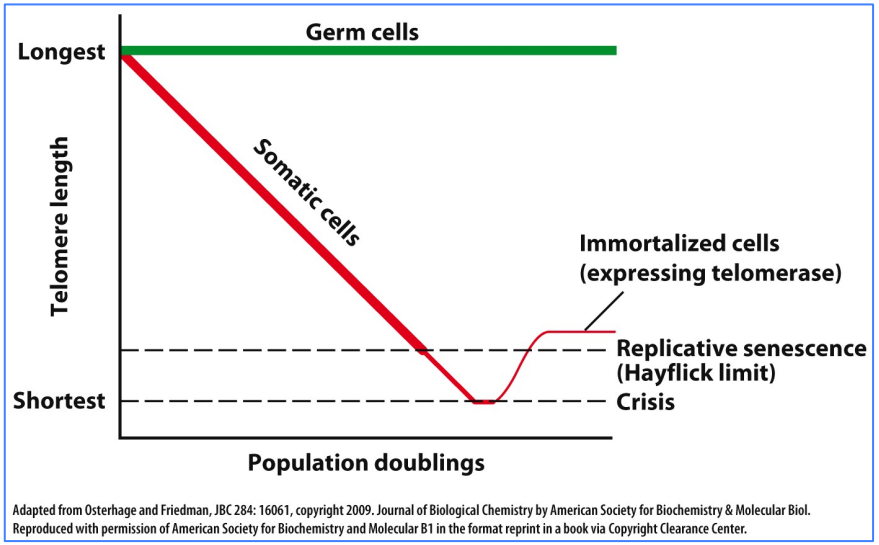


Control of Gene Expression in Eukaryotes

Telomeres

- In somatic cells, telomere lengths are reduced after every cell division to limit cell doublings.
- A critical point occurs from telomere shortening when cells stop their growth and division.
- In contrast, cells that are able to resume telomerase expression continue to proliferate.
- These cells continue to divide and do not shown normal signs of aging.

What do you think happens in tumor cells?



Adapted from Osterhage and Friedman, JBC 284: 16061, copyright 2009. Journal of Biological Chemistry by American Society for Biochemistry & Molecular Biol.
Reproduced with permission of American Society for Biochemistry and Molecular B1 in the format reprint in a book via Copyright Clearance Center.

Telomerase dynamics during normal and abnormal growth. Limited telomerase levels in somatic cells reduces the amount of cell doublings compared to germ cells, unless telomerase is reactivated.

An Overview of Gene Regulation in Eukaryotes

Cells of a complex eukaryote exist in many differentiated states.

- Differentiated cells retain a full set of genes.
- Nuclei from cells of adult animals are capable of supporting the development of a new individual, as demonstrated in experiments.

Cloning of animals demonstrates that nuclei retain a complete set of genetic information