2 - Chromosome Compaction

Part 2 is divided into two sections. The first section discusses how large DNA molecules are compacted to fit inside virus particles, prokaryotic cells, and eukaryotic cells. This process of packaging DNA is called **chromosome compaction**. Chromosome compaction overcomes a significant problem for all organisms. For example, a virus called bacteriophage lambda can package a 17 micrometer (μm) long nucleic acid molecule into a virus particle less than 0.1 μm in diameter (~200 times compaction); the intestinal bacterium *E. coli* can package a chromosome 1.2 millimeters (mm) in length in a cell that is only 0.002 mm long (~1000 times compaction). Human cells package a genome that is 200,000 times longer than the diameter of the nucleus!

The second section within Part 2 explores the process of **X chromosome inactivation (XCI)**. X chromosome inactivation involves compacting one of the two X chromosomes found in the cells of female mammals to produce a condensed **Barr body** structure. This compaction of the X chromosome effectively silences one copy of every X-linked gene in the cell.

A. Chromosome Compaction Strategies

Bacterial Chromosome Compaction

The bacterial chromosome must be compacted approximately 1000 times to fit into the nucleoid region within a bacterial cell. To compact the DNA tenfold, the bacterial cell forms **microdomains** within the chromosome (see **Figure 2.1**). Each microdomain is a loop connected to a centralized core structure composed of DNA binding proteins. The *E. coli* chromosome forms 400 to 500 microdomains, each of which contains approximately 10,000 base pairs (bp) of DNA. Adjacent microdomains are further bundled together to create **macrodomain** regions (not shown in **Figure 2.1**). Each macrodomain contains 80–100 bundled microdomains. Microdomains and macrodomains are formed when the repetitive DNA sequences (see Part 1) within the bacterial chromosome bind to **nucleoid-associated proteins (NAPs)**.

To compact the bacterial chromosome even further, the microdomains are **supercoiled** (i.e., twists are introduced into the microdomains; see **Figure 2.1)**. **Topoisomerases** (see below) are the enzymes that direct the supercoiling of *E. coli* DNA.

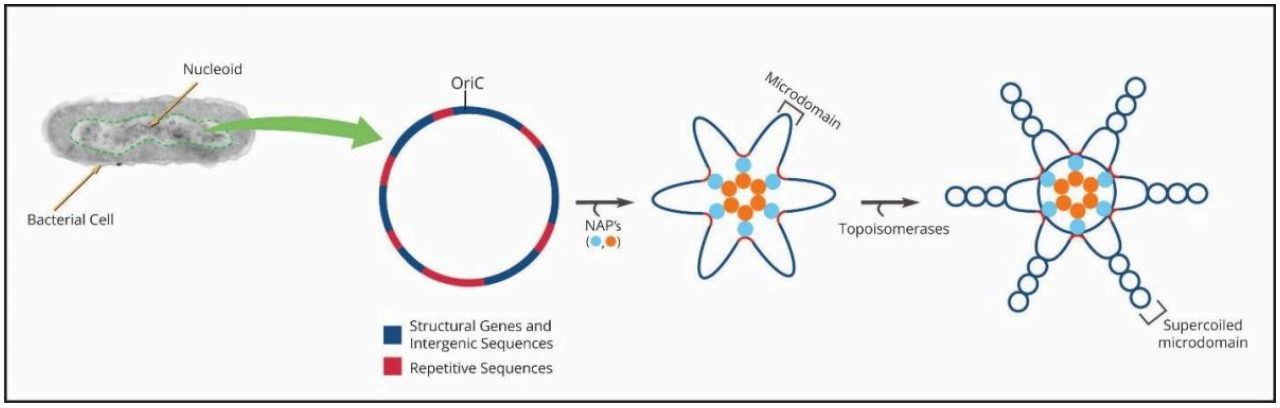

Figure 2.1 ***Bacterial Chromosome Compaction ---*** *Bacterial chromosome compaction involves the formation of microdomains (middle), followed by supercoiling (right). For the sake of simplicity, macrodomains are not included in this diagram. Prokaryote Cell pictured left adapted from OpenStax (access for free at https://openstax.org/books/biology-2e/pages/1-introduction) --- Image created by SL*

Key Questions

- What are the three levels of chromosome compaction in prokaryotic cells?
- How are microdomains formed?
- What are macrodomains?
- What is meant by supercoiling?

Supercoiling

Suppose a piece of linear double-stranded DNA is connected to two supports, one on each end of the molecule. Also suppose that the bottom support is held firmly in place, while the top support is twisted in the left-handed (counterclockwise) direction. DNA is naturally a right-handed double helix, meaning that the two DNA strands interact by hydrogen bonding to produce a double helix that rotates clockwise. Introducing counterclockwise twists into a right-handed double helix produces **underwinding**.

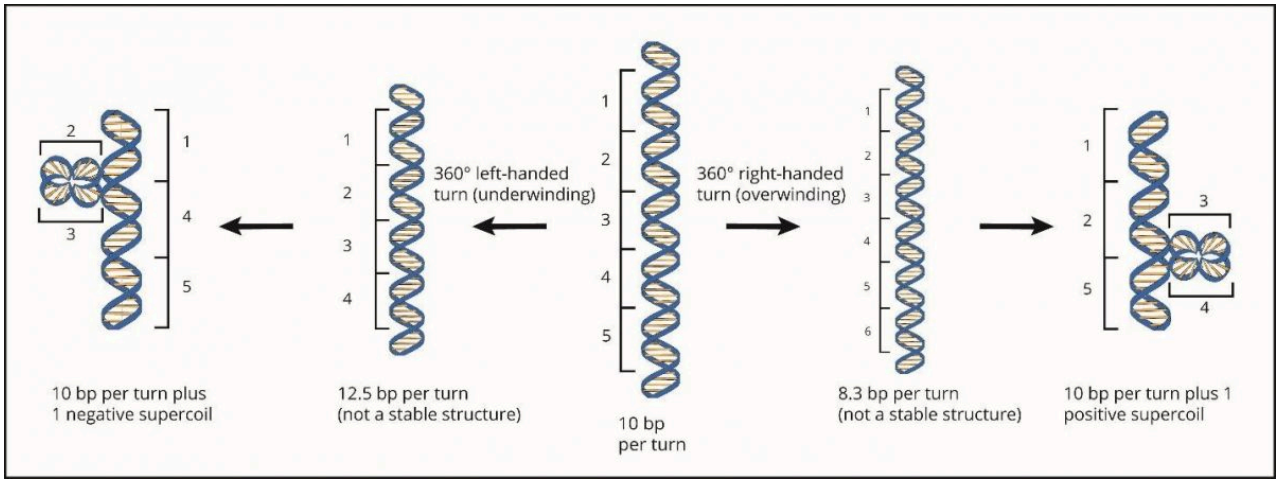

Figure 2.2 ***Negative and Positive Supercoiling –*** *The molecule in the center of the image contains five turns, with each turn containing 10 base pairs (bp). Underwinding by one turn produces an unstable structure with four turns, while overwinding by one turn produces an unstable structure with six turns. In both cases, the DNA double helix is stabilized by supercoiling --- Image created by SL*

Underwinding of the DNA produces fewer turns in the double helix. For example, a linear 50 base pair (bp) DNA molecule with five turns in the double helix (10 bp per turn) would have 12.5 bp per turn if it is underwound by one turn (50 bp/4 turns = 12.5 bp/turn) (see the left-hand side of **Figure 2.2**). This linear form of DNA with 12.5 bp per turn is an unstable structure that does not naturally occur in cells. Instead, the underwound DNA molecule produces a negative supercoil, an attempt by the DNA double helix to stabilize itself. This negative supercoil causes the distance between the ends of the DNA molecule to decrease (i.e. compaction). Negative supercoils are observed within bacterial chromosomes and function to compact the bacterial DNA into the nucleoid.

Overwinding, twisting the DNA double helix in the right-handed direction, increases the number of turns in the double helix. For example, a 50 base pair (bp) DNA molecule with five turns in the double helix (10 bp per turn) would have 8.3 bp per turn if it is overwound by one turn (50 bp/6 turns = 8.3 bp/turn) (see the right-hand side of **Figure 2.2**). This linear form of DNA with 8.3 bp per turn is an unstable structure that does not naturally occur in cells. The DNA molecule attempts to stabilize itself by producing a supercoil. This time, the supercoil is a **positive supercoil** that causes the distance between the ends of the DNA molecule to decrease (i.e. compaction).

A DNA molecule that lacks supercoils, has a single negative supercoil, or has a single positive supercoil can be converted into each other using **topoisomerase** enzymes (see below). These DNA molecules have the same base pair sequence and only differ in the degree of supercoiling. As a result, these three DNA molecules are considered to be **topoisomers** of each other.

Key Questions

- What is meant by positive and negative supercoiling?

Negative Supercoiling

Bacteria prefer negative supercoiling to positive supercoiling. In fact, typical bacterial chromosomes contain approximately one negative supercoil per 400 base pairs (bp) of DNA. Negative supercoiling is preferred because negative supercoiling:

- **Compacts the chromosomal DNA into the nucleoid of the cell**.
- **Promotes DNA strand separation**. Separation of the DNA strands is required for DNA replication prior to cell division and transcription to activate a gene.

Note that positive supercoiling compacts the chromosomal DNA to the same extent as negative supercoiling; however, positive supercoiling is inhibitory to DNA replication and transcription.

Key Questions

- What impact does supercoiling have on chromosome structure and function?
- Why is negative supercoiling preferred to positive supercoiling?

Topoisomerases

Topoisomerases are enzymes that supercoil DNA. There are two general classes of topoisomerases: **topoisomerase I** and **topoisomerase II**. Topoisomerase I enzymes are thought to mainly generate positive supercoils but can generate negative supercoils under certain conditions. Unlike topoisomerase II enzymes (see below), topoisomerase I enzymes are composed of a single protein subunit, do not cleave ATP during supercoiling, and only cut one of the two DNA strands during supercoil formation.

DNA gyrase from the bacterium *E. coli* is the best characterized example of a **topoisomerase II** enzyme**.** DNA gyrase cleaves ATP and uses the released energy to introduce negative supercoils into chromosomes. Further, DNA gyrase is composed of four protein subunits, two **A subunits** and two **B subunits**. Negative supercoils are generated by DNA gyrase using the following mechanism:

1. The A subunits of DNA gyrase bind to the DNA.
2. The A subunits function as an endonuclease to cut both strands of the DNA.
3. The B subunits pass another portion of the DNA molecule through the break using the energy released by cleaving ATP.
4. The DNA break is repaired producing an intact DNA double helix.

DNA gyrase generates two negative supercoils in the bacterial DNA per catalytic cycle; the production of each negative supercoil requires the cleavage of a single ATP molecule. For example, if the original bacterial DNA molecule had no supercoils, the same molecule would have two negative supercoils after DNA gyrase action (two ATP molecules cleaved). In bacteria, topoisomerase I and topoisomerase II compete to determine the overall level of supercoiling within the chromosome. Topoisomerase I and topoisomerase II enzymes also function in eukaryotic cells, as well.

The ability to produce negative supercoils in the DNA is required for bacterial survival. For example, a group of antibiotics called **quinolones** inhibit DNA gyrase. Since DNA gyrase is involved in both negative supercoiling and DNA replication (see Part 6), the bacterial cells are killed. One example quinolone antibiotic, **ciprofloxacin**, is used to treat patients infected with serious bacterial infections, including anthrax and typhoid fever.

Key Questions

- Describe how DNA gyrase introduces negative supercoils.
- What are some differences between the structure and function of topoisomerase I and DNA gyrase?

Eukaryotic Chromosome Compaction

Let us now consider how the human genome, which is over six feet in length, can be packaged into the nucleus within a cell. An important aspect of chromosome compaction in eukaryotes involves the association of the DNA double helix with proteins (both **histone** and **nonhistone proteins**) to form **chromatin**.

The basic structure of chromatin consists of chains of **nucleosomes** that resemble beads on a string (see Figure 2.3). A nucleosome consists of 146 or 147 base pairs (bp) of DNA negatively supercoiled around eight **histone** proteins. There are four types of histone proteins within a nucleosome; each histone protein is present in two copies. These histone proteins are called **H2A, H2B, H3**, and **H4**. Each histone protein consists of a **globular domain** and an extended, flexible region called a **histone tail**. The globular domain allows the individual histone proteins to bind to each other to form the nucleosome core, while the histone tails are enriched in positively charged amino acids, such as arginine and lysine. Recall that the backbone portion of the DNA double helix is negatively charged; thus, the histone tail and DNA backbone bind through electrostatic interactions.

Nucleosomes are connected by a **linker** DNA sequence that is approximately 50 bp long. Histone **H1**, also called the **linker histone**, as well as other nonhistone proteins bind to the linker region DNA. H1 and these nonhistone proteins play a role in further compaction of eukaryotic DNA into 30-nm fibers (see below).

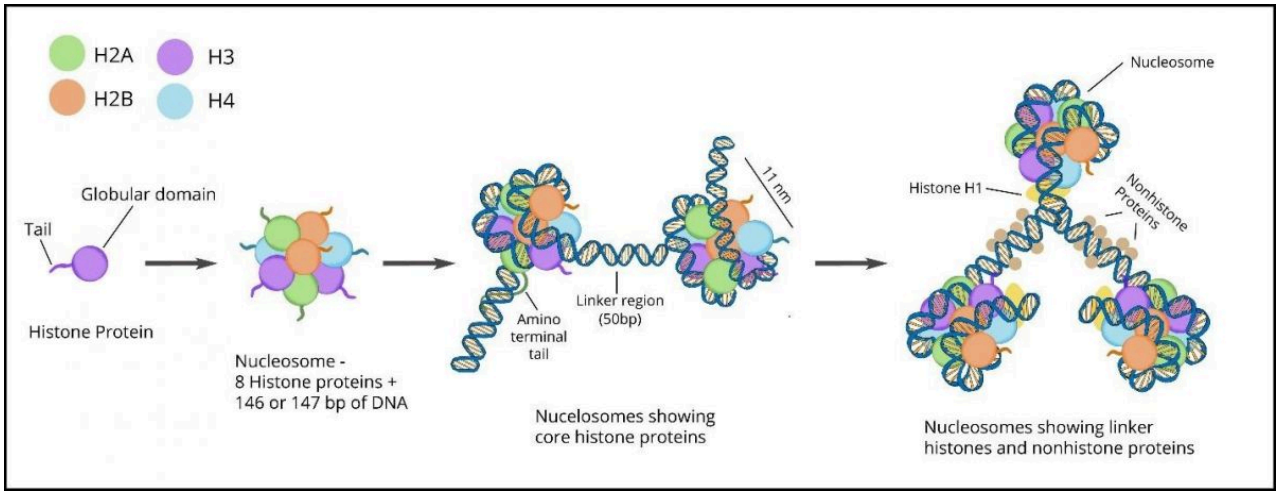

Figure 2.3 Nucleosomes are the first level of chromosome compaction. *Histone proteins contain a globular region and a positively charged histone tail. Eight histone proteins (two copies each of the H2A, H2B, H3, and H4 proteins) form the nucleosome core. The eight histones bind to 146 or 147 base pairs of DNA to form nucleosomes, which resemble beads on a string. The linker histone H1 and nonhistone proteins bind to the 50 base pair linker sequence between nucleosomes.* ***---*** *Image created by SL*

Key Questions

- What is a nucleosome?
- What are the names of the protein components within a nucleosome?
- Explain how the DNA and histone proteins assemble to make a nucleosome.
- What is a linker region?

30-nm Fiber

The second level of chromosome compaction in eukaryotes involves the association of a string of nucleosomes into a fiber that is 30 nanometers (nm) wide (**30-nm fiber**). The formation of the 30-nm fiber depends on the linker histone protein H1 and nonhistone proteins. Two 30-nm fiber structures have been proposed (see **Figure 2.4**):

- **Solenoid**. The solenoid involves tight interactions between nucleosomes to form a compact, symmetrical structure that resembles a cylinder. The solenoid form of the 30-nm fiber is advantageous because it allows a high degree of chromosome compaction; however, structural genes within the solenoid are difficult to activate by transcription.
- **Zigzag**. In the zigzag, nucleosome interaction is minimal and the linker regions are free to bend and twist. As a result, the overall structure of the zigzag 30-nm fiber is irregular. The zigzag form of the 30-nm fiber is advantageous because it promotes the transcription of structural genes, but the degree of chromosome compaction is not as great as with the solenoid form.

Recent evidence suggests that the zigzag form of the 30-nm fiber is found predominantly in cells; however, some scientists believe that the two forms of the 30-nm fiber can convert into each other depending on whether a region of DNA needs a high degree of chromosome compaction or gene activation.

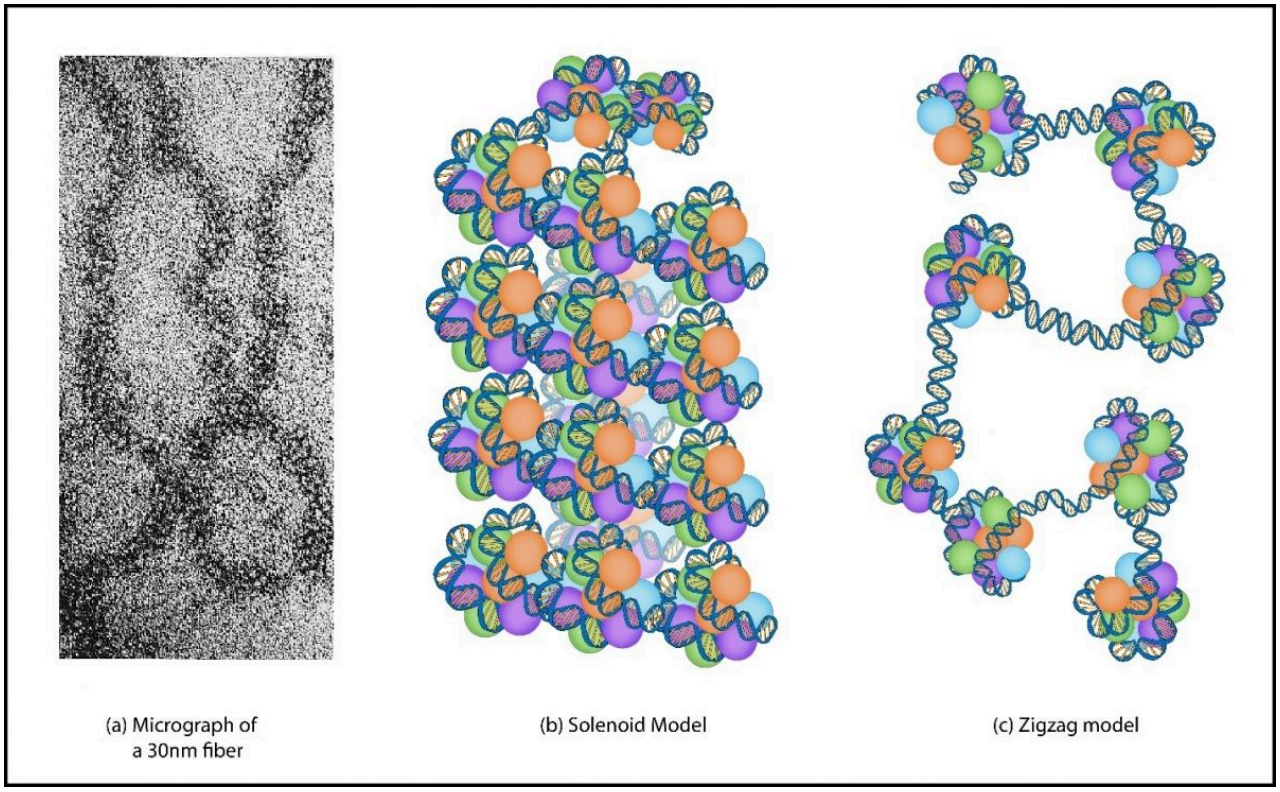

Figure 2.4 ***30-nm Fiber*** *–(a)* Photo courtesy of Dr. Barbara Hamkalo (b) Solenoid model (c) Zigzag model --- Image created by SL

Key Questions

- What are the advantages and disadvantages of the solenoid and zigzag 30-nm fiber models?

Radial Loop Domains

The third level of DNA compaction in eukaryotes involves the interaction of the 30-nm fibers with **nuclear matrix proteins** to form **radial loop domains** (see **Figure 2.5**). The eukaryotic radial loop domain is somewhat similar to the prokaryotic microdomain, with each radial loop consisting of 25,000–200,000 base pairs (bp) of DNA.

The nuclear matrix consists of two parts, the **nuclear lamina** and the **internal nuclear matrix**. The nuclear lamina portion of the nuclear matrix is composed of cytoskeletal proteins and lies adjacent to the inner surface of the nuclear membrane. The internal nuclear matrix, which likely includes hundreds of different protein types, forms a fine meshwork of filaments throughout the interior of the nucleus. DNA sequences called **matrix-attachment regions (MARs)** link the 30-nm fiber to the internal nuclear matrix. Anchoring the 30-nm fiber to the internal nuclear matrix results in the formation of radial loop domains.

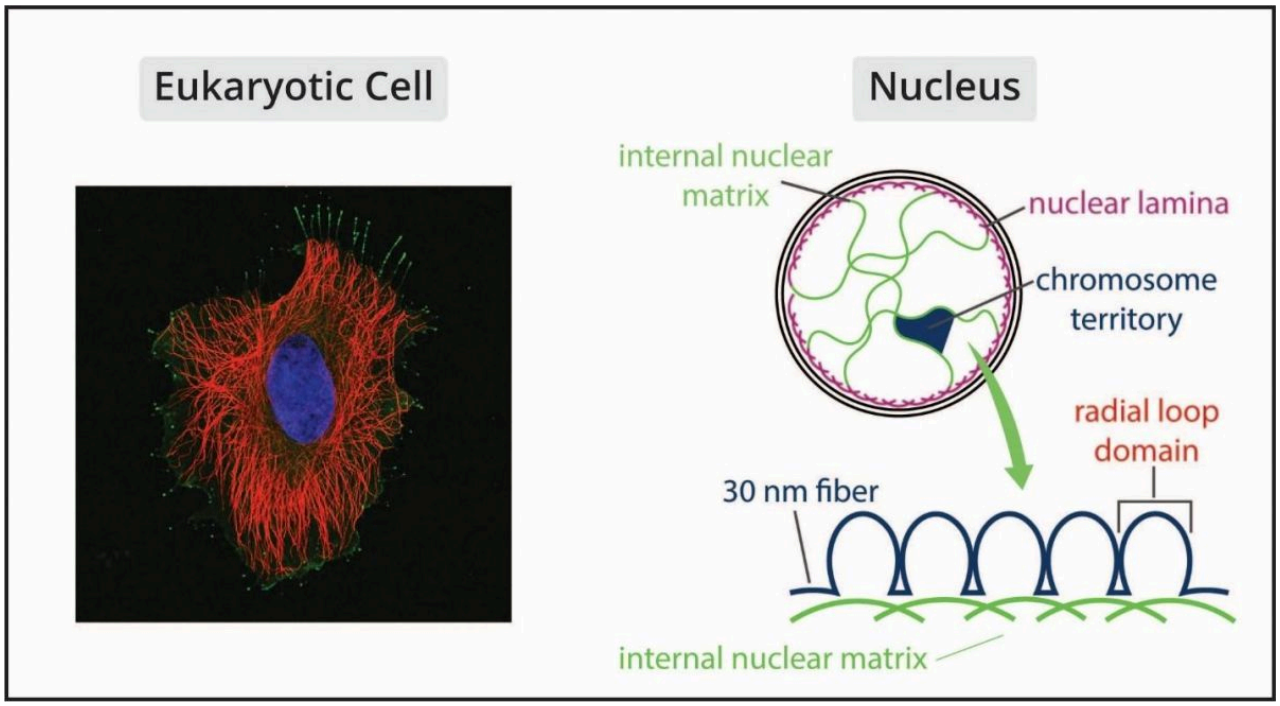

Figure 2.5 ***Radial Loop Domains.*** *Fluorescence micrograph of a eukaryotic cell (left). The DNA is shown in blue, the microtubule cytoskeleton is shown in red, while the actin cytoskeleton is shown in green. The nucleus of a eukaryotic cell (right) contains nuclear lamina and internal nuclear matrix protein fibers. The chromatin 30-nm fibers bind to internal nuclear matrix proteins to form radial loop domains.--- Image created by SL*

Key Questions

- What is a radial loop domain?
- How do the MARs and the internal nuclear matrix contribute to the formation of radial loop domains?

Chromosome Territories

The internal nuclear matrix bound to radial loop domains also functions to localize each chromosome within a unique region of the nucleus called a **chromosome territory**. These chromosome territories within the nucleus can be visualized when the individual chromosomes are stained with uniquely colored fluorescent dyes (see **Figures 2.5** and **2.6**).

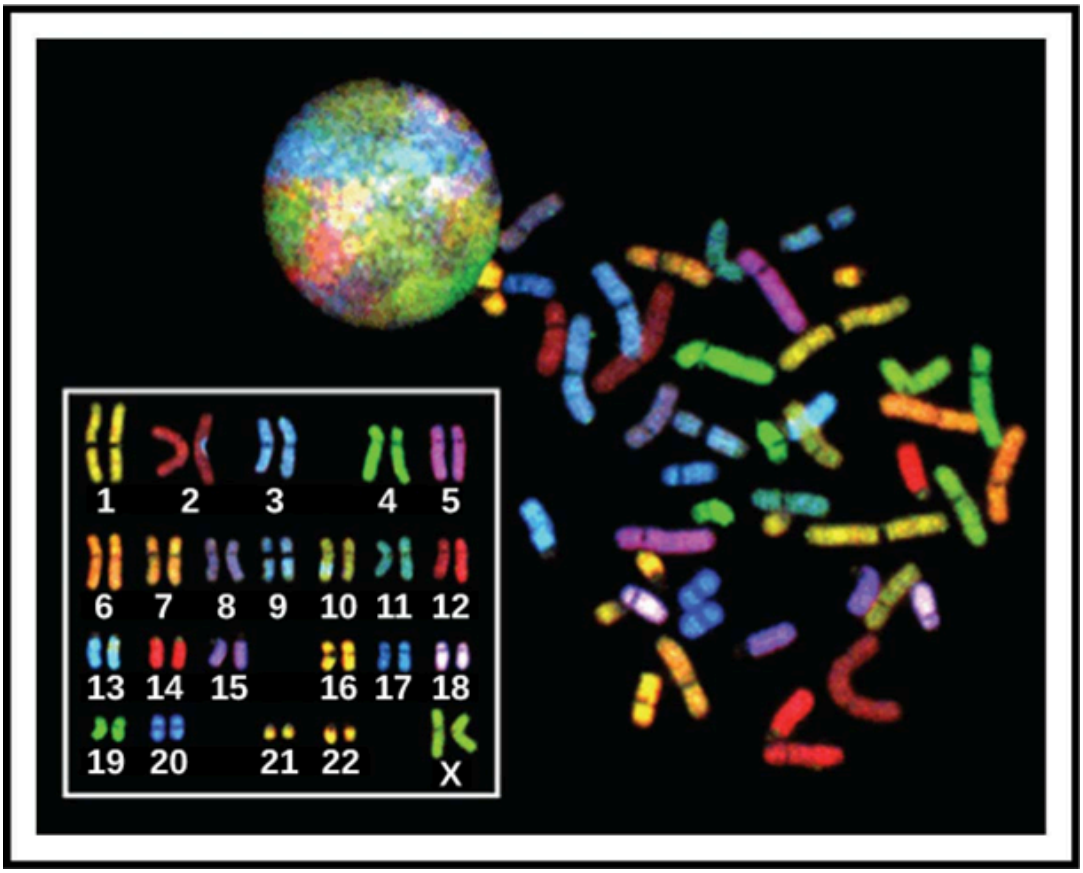

Figure 2.6 ***Chromosome Territories*** *--- Chromosome Territories was used from OpenStax (access for free at* https://openstax.org/books/biology-2e/pages/1-introduction

Key Questions

- What is a chromosome territory?

Heterochromatin and Euchromatin

The radial loop domains can assume two different structural conformations (see **Figure 2.7**):

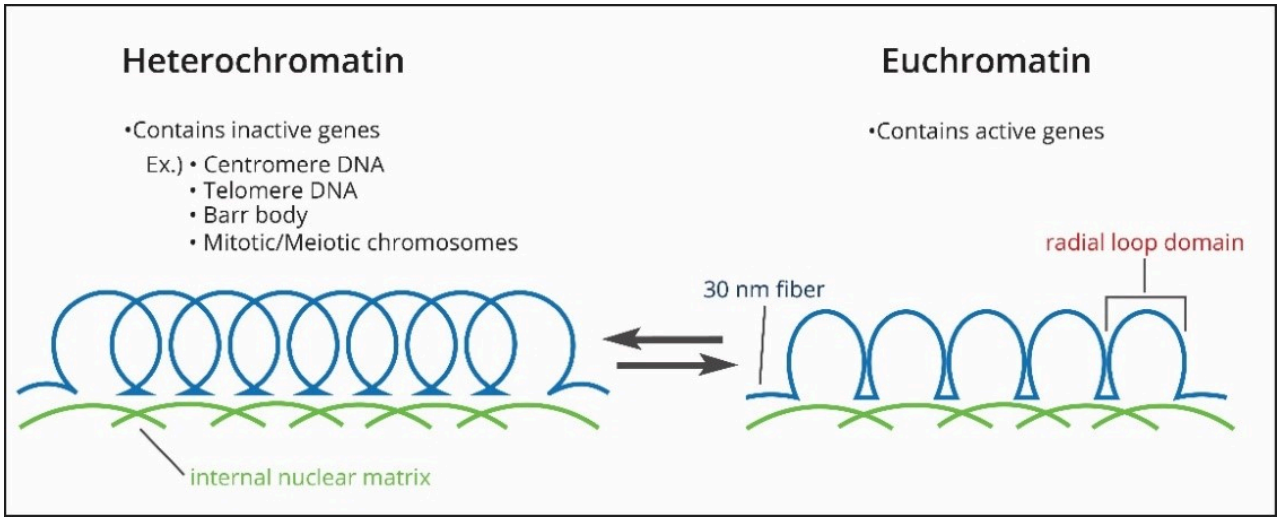

Figure 2.7 ***Heterochromatin and Euchromatin*** *--- Image created by SL*

- **Euchromatin.** Euchromatin is a region of chromatin in which the radial loops are not tightly compacted. Transcibed structural genes are typically found in euchromatin.
- **Heterochromatin.** Heterochromatin is defined as regions of the chromosome where the radial loops are tightly compacted. Most areas of heterochromatin either do not contain structural genes or the structural genes within these regions are not transcribed. There are two forms of heterochromatin:
    - **Constitutive heterochromatin.** The centromere and the telomeres regions of chromosomes always assume the heterochromatin conformation and, are therefore, considered to be constitutive heterochromatin. Constitutive heterochromatin often contains either moderately or highly repetitive DNA sequences (see Part 1).
    - **Facultative heterochromatin.** Facultative heterochromatin is a dynamic structure that can convert between the heterochromatin and euchromatin states. For example, when one of the two X chromosomes in female mammals is chosen to be inactivated during early embryogenesis, the X chromosome is converted from euchromatin to heterochromatin (see below). The heterochromatin form of the X chromosome is the **Barr body**. Further, each cell type in the body contains a unique pattern of facultative heterochromatin, meaning the distribution of facultative heterochromatin in a white blood cell is different from an epithelial cell. These differences in facultative heterochromatin ensure that each cell type transcribes a unique subset of structural genes. We will examine how changes in facultative heterochromatin influences gene activation in Parts 14 and 15.

Key Questions

- What is the difference between euchromatin and heterochromatin?
- How do the two types of heterochromatin differ from one another?

Scaffold

Nucleosomes, 30nm fibers, and radial loop domains are found in the chromatin of interphase cells. In contrast, during mitosis and meiosis, the chromosomes become even more compacted—10,000 times more compact than what is observed during interphase. In fact, the characteristic X-shaped chromosomes observed in mitosis and meiosis are so compact that scientists think that they are composed mainly of facultative heterochromatin. As a result, few structural genes are active during mitosis and meiosis.

To form highly compacted mitotic and meiotic chromosomes, the radial loops interact with a **scaffold** (see **figure 2.8**). The scaffold is a protein structure that ensures the radial loops throughout the chromosome are in the heterochromatin state. The structure of the scaffold is poorly understood; however, scientists believe the scaffold is composed of nonhistone proteins, including condensin (see below), and nuclear matrix proteins. The X-shaped metaphase chromosomes are produced by radial loop domains binding to the scaffold.

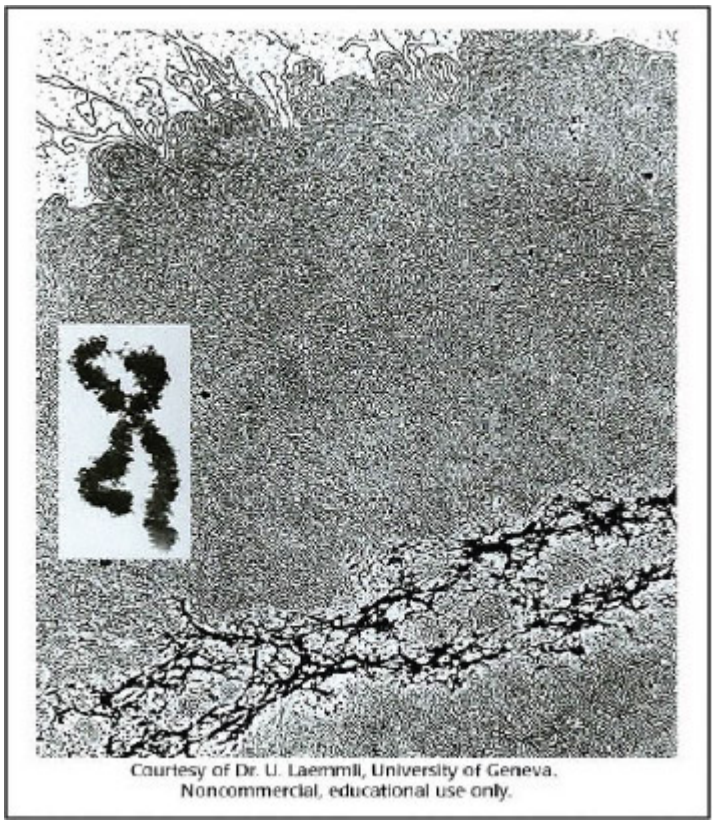

Figure 2.8 ***The Scaffold*** *– A mitotic chromosome was experimentally treated to release the DNA double helix (seen most clearly at the top of the image), while preserving the scaffold structure (darker area near the bottom of the image). --- Photo courtesy of Dr. U. Laemmli*

Key Questions

- What are the four levels of chromosome compaction in eukaryotes?
- Which levels are compaction are observed during interphase?
- Which levels of compaction are observed during mitosis and meiosis?

Condensin

The **condensin** protein plays an important role in the formation of mitotic and meiotic chromosomes. When a eukaryotic cell is in interphase, condensin is found in the cytoplasm of the cell. However, during mitosis and meiosis, the nuclear envelope breaks down and condensin can then bind to the chromosomes. Condensin is thought to link radial loop domains together and hold them in place, forming the dense heterochromatin observed in mitosis and meiosis. Condensin is a member of a group of proteins called **structural maintenance of chromosome (SMC)** proteins. Other members of the SMC family include the NAPs that play a role in bacterial chromosome compaction (see above). All SMC proteins cleave ATP and use the released energy to promote changes in chromatin structure.

Key Questions

- How does condensin contribute to chromosome compaction?

B. X Chromosome Inactivation (XCI)

Dosage Compensation

Because female animals have two X chromosomes and males have a single X chromosome, females can potentially produce twice as much of the protein products from X-linked structural genes as their male counterparts. However, we know that the level of X-linked protein production is similar males and females. This **dosage compensation** between males and females can be accomplished in several different ways. In mammals, one of the two X chromosomes is inactivated in females. For example, placental mammals randomly inactivate either the paternally-inherited or the maternally-inherited X chromosome in somatic cells. On the other hand, female marsupials inactivate the X chromosome they inherited from their father. Fruit flies conduct dosage compensation by increasing X-linked gene expression in males twofold. Finally, female nematode worms reduce gene expression on each X chromosome by 50% to accomplish dosage compensation.

Key Questions

- Why is dosage compensation important?
- How do humans accomplish dosage compensation?

Evidence for X Chromosome Inactivation (XCI)

In mammals, one of the X chromosomes experiences **X chromosome inactivation (XCI)**. XCI was first suggested by two lines of experimental evidence:

- **The studies of Murray Barr and Ewart Bertram**. Barr and Bertram found that somatic cells (i.e., non-gamete cells) from female cats contained a nuclear structure (**Barr body**), not found in the males (see **Figure 2.9**). The Barr body is a highly condensed, inactive X chromosome; few structural genes present within a Barr body are expressed.
- **The studies of Mary Lyon**. Female tortoiseshell (black and orange) and calico (black, orange, and white) cats have a distinctive coat pattern, containing patches of orange and black fur (**mosaics**). The mosaic phenotype occurs in female cats that are heterozygous for X-linked coat color alleles (X^bX^o). The X^b allele is expressed in black patches, while the X^o allele is silenced. In contrast, the X^o allele is expressed in orange patches, while the X^b allele is silenced. Mary Lyon suggested that the mosaic tortoiseshell and calico patterns are due to XCI.

Key Questions

- How did the experiments by Barr, Bertram, and Lyon demonstrate that XCI occurs?

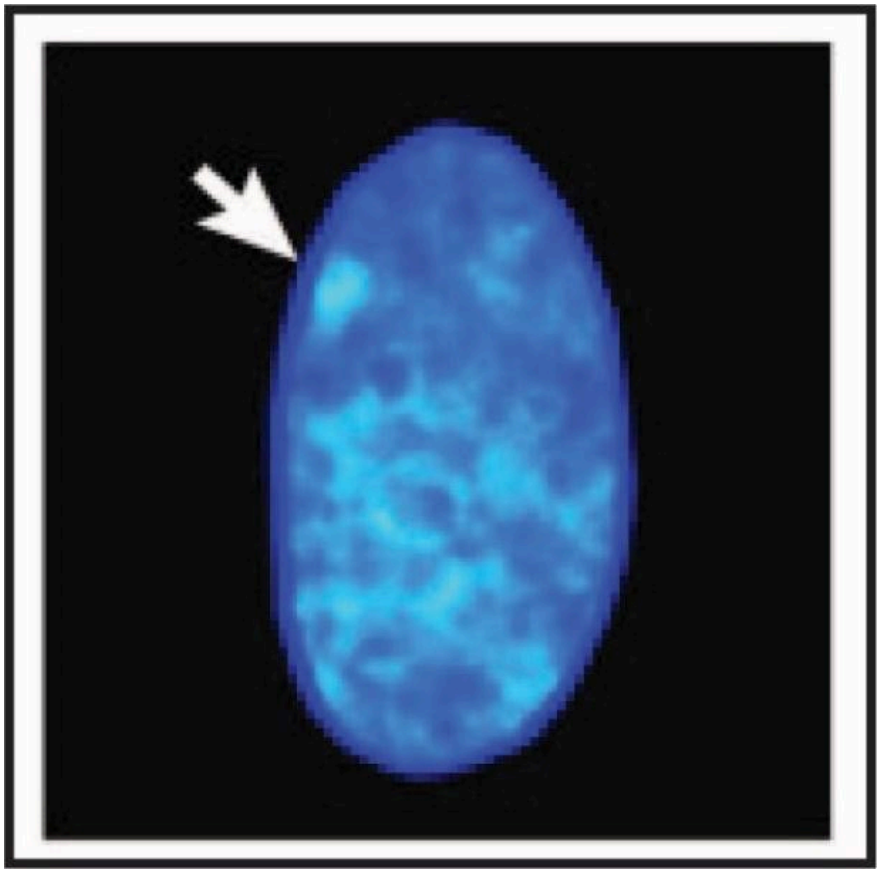

Figure 2.9 ***Evidence for X Chromosome Inactivation –*** *A) The arrow in the image indicates a Barr Body within the nucleus of a cell. --- Barr Body BMC by Stanley Gartler is used under CC BY 2.0) B) A calico cat displaying the mosaic orange and black phenotype.--- Tortoiseshell Cat by James Petts is used under CC BY-SA 2.0*

The Lyon Hypothesis

The **Lyon Hypothesis**, first proposed by Mary Lyon, provided a deeper understanding of X chromosome inactivation (XCI). In mice, fur color is controlled by two X-linked alleles: The X^B allele produces black fur color, while the X^b produces white fur. Consider a heterozygous female mouse (X^BX^b), with a mosaic phenotype, similar to the tortoiseshell and calico cat coat patterns discussed above. The Lyon hypothesis states that during embryonic development in mice, both of the X chromosomes are active in each embryonic cell. However, one of the X chromosomes in each embryonic cell is soon inactivated and becomes a Barr body. This inactivation process is random in each embryonic cell, one cell may inactivate X^B; a neighboring cell may inactivate X^b. The embryonic cell containing an active X^b (silenced X^B) divides to produce a white fur patch (see **Figure 2.10**). The embryoinc cell with an active X^B (silenced X^b) divides to produce a black patch. Collectively, these events produce the mosaic phenotype of the heterozygous mouse.

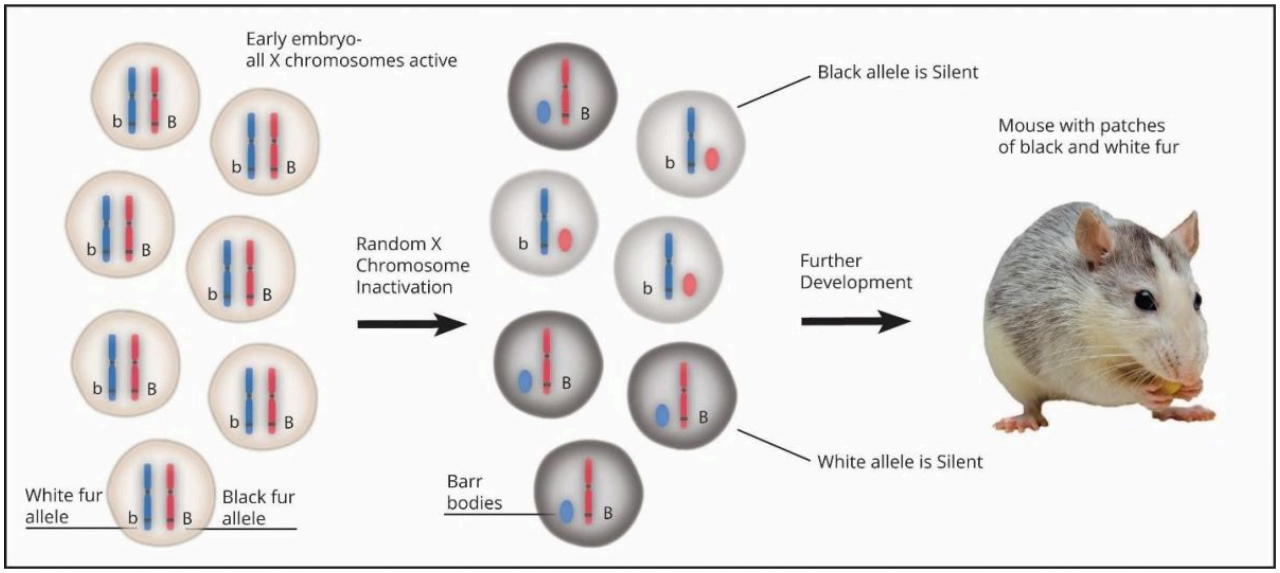

Figure 2.10 ***The Lyon Hypothesis*** *--- Image created by SL (mouse image by Pexels and is under CC0)*

One consequence of the Lyon hypothesis is that all female mammals (including humans) are thought to be mosaics. That means that in some areas of the body one X-linked allele is expressed; other areas of the body express the other X-linked allele. **Anhidrotic ectodermal dysplasia** provides evidence for human mosaicism. Anhidrotic ectodermal dysplasia is a human genetic disease caused by an X-linked recessive mutation. If a male possesses the recessive disease allele, he displays a variety of defects, including the absence of sweat glands. Heterozygous females are mosaics in which some areas of the body have sweat glands; other areas lack sweat glands.

Key Questions

- What is the Lyon hypothesis and how does it explain the mosaic coat phenotypes seen in mice and cats?

X-inactivation Center (*Xic*)

In females with two X chromosomes, one X chromosome is inactivated to produce a Barr body. In **Turner syndrome** females with one X chromosome, Barr bodies are not observed. In **Triplo-X syndrome** females with three X chromosomes, two Barr bodies are formed; and in **Klinefelter syndrome** males with two X chromosomes and a Y chromosome, a single Barr body is formed. Thus, it appears that mammalian cells can "count" the number of X chromosomes in a particular cell and ensure that only one X chromosome remains active.

X chromosome inactivation is controlled by a region within the X chromosome, near the centromere, called the **X-inactivation center (*Xic*)**. If the *Xic* is missing from one X chromosome and is present on the other X chromosome, then both X chromosomes remain active; two *Xics* must be present for one X chromosome to be inactivated. This result suggests that it is not the X chromosomes that are counted by the cell, *per se,* but actually the number of *Xics*. If two or more *Xics* are present in a cell, only one remains active. The additional *Xics* (and the X chromosomes) are inactivated.

Key Questions

- Why does the number of Barr bodies differ in genetic disorders of the X chromosome?

Xist and *Tsix*

The *Xic* region of the X chromosome contains two genes: ***Xist*** and ***Tsix*** (see **figure 2.11**).

- **The *Xist* gene**. The *Xist* (X-inactive specific transcript) gene is transcribed preferentially from the X chromosome that will be inactivated. The *Xist* gene produces an RNA molecule that is a **non-coding RNA (ncRNA).** Non-coding RNA molecules function directly in the cell and are not translated to make a protein product. The ***Xist* RNA** functions to recruit proteins that modify the structure of the X chromosome, converting an active X chromosome into a Barr body composed of heterochromatin.
- **The *Tsix* gene**. When the *Tsix* gene is transcribed, a ***Tsix*** ncRNA is made. The *Tsix* RNA is transcribed from both X chromosomes prior to XCI and likely allows the two X chromosomes to pair briefly during early embryonic development (see Part 15). The *Tsix* RNA is later transcribed preferentially from the active X chromosome, which in turn inhibits the production of the *Xist* RNA on the active X chromosome. Thus, the *Xist* RNA does not inactivate one X chromosome because the *Tsix* gene is transcribed. Interestingly, the *Tsix* gene overlaps the *Xist* gene but is transcribed in the opposite direction.

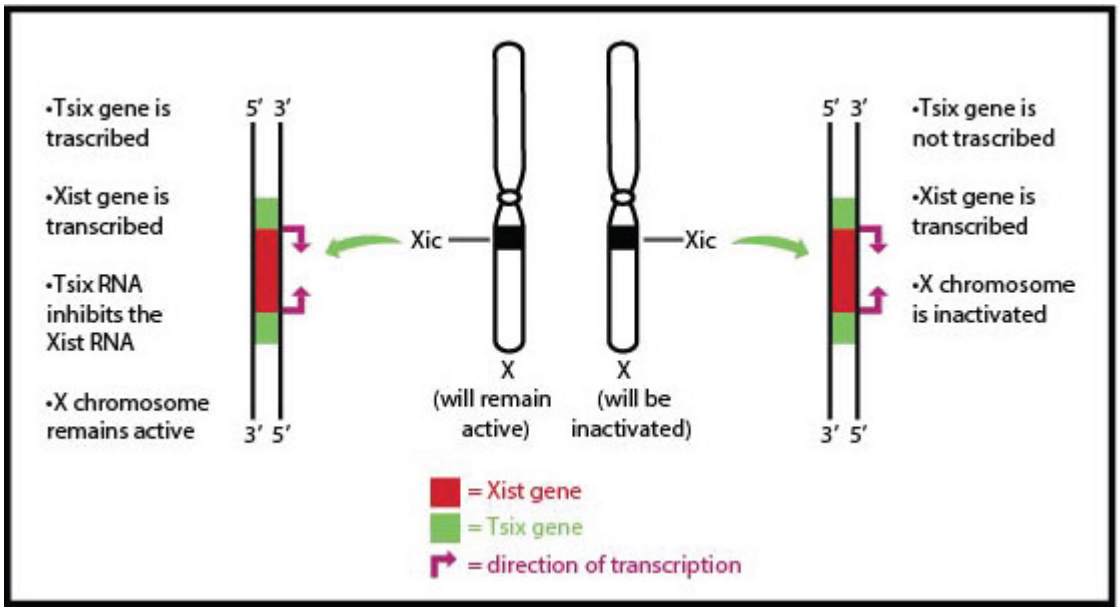

Figure 2.11 ***Mechanism of X Chromosome Inactivation*** *--- Image created by SL*

Key Questions

- How does the *Xist* gene promote the formation of a Barr body?
- How does the *Tsix* gene ensure that one X chromosome remains active?

The Three Stages of XCI

The process of XCI has three stages (see **Figure 2.12**):

1. The **initiation** stage involves a choice as to which X chromosome is inactivated. *Tsix* gene expression from the X chromosome that will remain active inhibits the production of the *Xist* RNA. The X chromosome that is inactivated does not express the *Tsix* RNA. As a result, the *Xist* RNA is produced, leading to the formation of a Barr body.
2. The **spreading** stage involves the actual inactivation of the chosen X chromosome. The *Xist* RNA participates in spreading by starting at the *Xic* and coating the X chromosome to be inactivated in both directions. This coating with *Xist* RNA allows proteins to recognize the X chromosome and compact it into heterochromatin, forming a Barr body.
3. **Maintenance** of the Barr body after cell division. Suppose a cell divides by mitosis. Prior to mitosis, this cell converts the Barr body back into euchromatin and replicates the DNA. The replicated X chromosome is then separated into the daughter cells and is silenced again by converting it back into a Barr body. Interestingly, the daughter cells have the ability to remember which X chromosome was inactivated in the parent cell prior to cell division. Thus, the two progeny cells both contain inactive copies of the same X chromosome as the parent cell.

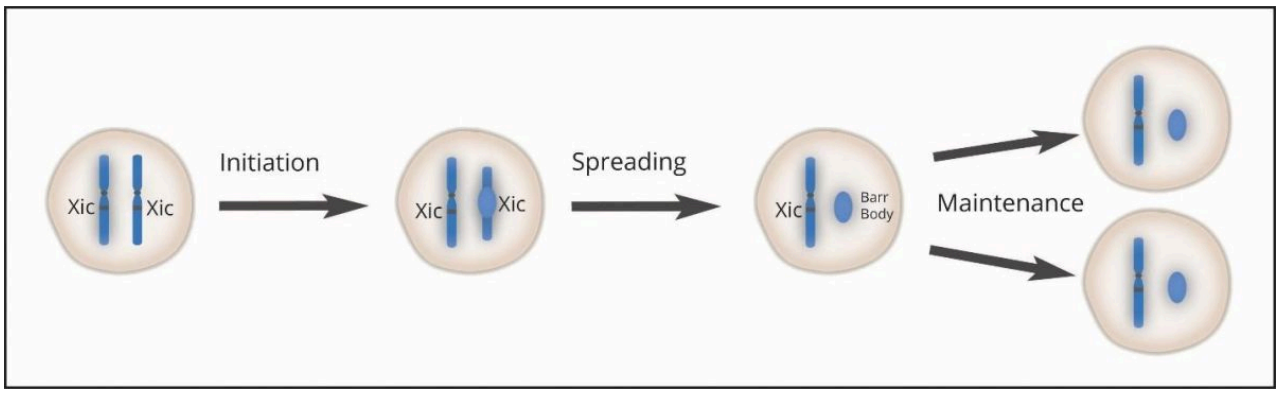

Figure 2.12 ***Stages of XCI*** *--- Image created by SL*

Key Questions

- Explain the three stages of XCI.

Review Questions

Fill in the blanks:

Chromosome Compaction Strategies in Prokaryotes and Eukaryotes

1. _____ are proteins that help compact the *E. coli* chromosome into microdomains.
2. The enzyme _____ produces both positive and negative supercoiling.
3. Topoisomerase _____ uses ATP to generate negative supercoils in bacterial chromosomes.
4. Histone _____ is also called the linker histone because it links two nucleosomes together.
5. A nucleosome contains _____ bp of DNA wrapped around _____ histone proteins.
6. Amino acids _____ and _____ are positively charged, and make up many of the amino acids in the histone tail.
7. The _____ form of the 30-nm fiber resembles a cylinder.
8. DNA sequences called _____connect the 30-nm fiber to the internal nuclear matrix.
9. _____ heterochromatin can be transcribed under certain cellular conditions.
10. A region in the nucleus where a particular chromosome is located is called a chromosome _____.
11. During interphase, condensin proteins are located in the _____ of the cell.

X Chromosome Inactivation

1. A normal female has _____ Barr body(bodies) whereas a female with Turner syndrome has _____ Barr body (bodies).
2. When the *Xist* gene is active, it transcribes an RNA molecule that attaches to the chromosome that becomes (active or inactive). Circle the correct answer.
3. When the *Tsix* gene is active, it transcribes an RNA molecule that is associated with the (active or inactive) X chromosome. Circle the correct answer.
4. The inactive X chromosome condenses into a tight nuclear structure called a _____.