Similarities Between Histones and Bookshelves

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Rule to Build By:

One of the rules to build by on the Living Architecture was of my own creation. It states that human-built and nature-built architectural forms regulate the accessibility of information by sort of machinery that will compact the information at different levels.

What:

To illustrate this rule-to build-by the histone proteins associated with DNA are used as a cellular structure that upholds this principle and the bookends at the Wallace Library at Wheaton College Norton, Massachusetts, is used as an example of human-built structure that upholds this principle

How:

Histones compact 1.8 meters of DNA into about 90 mm of chromatin by the DNA's "magnetic attraction" to a histone octamer (Raven, 189) (Victoria, (Wikipedia), 2010). Two histones of H2A, H2B, H3, and H4 form a complex of 8 histones, also referred to as an octamer (Webbooks, 2001). DNA is negatively charged because of its phosphate backbone and histones are positively charged because of their high proportion of positive amino acids (lysine and arginine) (Alberts, 186). The negatively charged DNA is attracted to the positively charged octamer, and so sections of DNA that are 147 nucleotide pairs long wind 1.7 left handed turns around the octamer (Raven, 189). The complex of DNA and histones is termed a nucleosome (Raven, 189). Before the nucleosomes are further compacted, the chromosome resembles "beads on a string" (Alberts, 185). This packing is the first and most fundamental level of condensing of chromatin. The chromatin is then subjected to further condensing by a linker histone that pulls the nucleosomes together and forms the 30 nm fiber, or also referred to as a solenoid (Raven, 189). 50 base pairs of DNA separate each nucleosome, and histones H1 and H5 lock that DNA into place by binding to the nucleosome and the entry and exit sites of DNA. (Raven, 189)(Victoria (Wikipedia), 2010)

When certain proteins need to access specific DNA sequences, the nucleosomes undergo alterations, which expose the needed sequences (Alberts, 193). The position of the DNA in the nucleosomes can change by protein machines that push on the nucleosomes (using energy from ATP hydrolysis) and loosen the DNA. This then exposes the DNA to binding proteins, however some sliding of nucleosomes can actually condense the chromatin further (Raven, 316).

Access to DNA is also created by reversible chemical modifications made to the nucleosomal histone's tails. Enzymes alter the tails of histones by adding or removing acetyl, phosphate or methyl groups. Specific enzymes that modify particular histones are brought to a specific region by some sort of cue. For example when a tail is methylated that region of the chromatin is inactive, and when the tail is acetylated that region is active (Raven 316). When a region of DNA is inactive the DNA is inaccessible to the transcription apparatus and when a region of DNA is active it is accessible. An example of when a region of DNA is inactive, is when histone H3's lysine residue 9 is methylated (Alberts, 190) When this modification occurs heterochromatin is induced and heterochromatin-specific proteins will "induce the same tail modifications in adjacent nucleosomes" (Alberts, 190). This results in an increase of heterochromatin and creates an extended region of heterochromatin along the DNA (Alberts, 190). Heterochromatin is considered inactive because it is inaccessible to transcription proteins, which causes the gene to be silenced. Conversely, when histone H2A is modified through acetylation

and produces this produces an active region of DNA because it makes DNA accessible. Histone H2A prevents the spread of heterochromatin regions (Victoria (Wikipedia), 2010) to promote regions of euchromatin (Alberts, 191) and therefore the transcription apparatus can access it(Raven, 316). Because specific enzymes are attracted to a specific amino acid sequence in a histone tail, it is believed that a "histone code" (analogous to the genetic code) exists (Raven, 316).

Bookends are an L shaped metal piece of equipment that typically have about a 6-inch length base and a height of about 8 inches and are positioned at the end of a sequence of books on a bookshelf. They are able to condense the books on a bookshelf by using their base to slide under the last 3-6 books (depending on the width of the books), and the height of their "wall" lines up against the last book to hold it in place. By holding the last book in place all of the books are pushed firmly against the end of the bookshelf, and this force condenses the books. In order for this method to work properly the books must be lined up vertically for maximum compaction, this leads to greater accessibility. If some of the books are lined horizontally (and they would be without the compression from the bookends), they fall and the amount of space used by the books on the bookshelves is greatly increased, which leads to less accessibility. By sliding the bookend towards the end of the bookshelf greater compaction is created and therefore less space on the shelf is used and more books can fit, and by sliding the bookends the opposite way it creates less accessibility because by less compaction more space is used up. The level of compaction (degree as to which the bookend is slid) regulates how easy it is for one to access a book.

How:

The degree as to which the DNA is compacted regulates the accessibility of it to certain proteins throughout certain events in mitosis and meiosis (Alberts, 192). The events that will be examined in which histones regulate the accessibility to DNA will be gene expression, replication, and repair. The compacting of DNA by histones regulates gene expression by two methods: in one method the cell utilizes the tightness of the DNA wound around a histone to make the DNA accessible or inaccessible to the transcription apparatus (Alberts, 190), and the second method involves using the packaged DNA to physically block the initiation of transcription (Raven,316). Depending on how tight a region of DNA is wrapped around a histone it can cause a gene to either be expressed or silenced. The cell takes advantage of this interaction by producing proteins called acetyltransferases that unwind the DNA so that the gene can be expressed, and histone deacetylation complexes that tightly wind the DNA so that the gene will be silenced (eHow, 2004). This supports the principal that histones are the cells machinery to regulate access to information because when they create a euchromatin region on DNA they allow access to that region and therefore that region is expressed, or they create a heterochromatin region that cannot be expressed (Alberts, 190). For example, it is advantageous for a female mammalian cell during interphase to fold one its X chromosome genes into heterochromatin. This condensed folding silences the gene and it does so because a "double dose of X chromosome products" would be harmful for the cell (Alberts, 190-191). The other method, in which histones are used to regulate gene expression, is by physically blocking the site of transcription. If a nucleosome is positioned over the DNA's promoter, basal transcription factors or the RNA polymerase cannot assemble on it because it is physically blocked. Inhibition of the initiation of transcription is especially important in the absence of the proper "activator proteins" (Raven, 316). It is believed that the compacting of chromatin evolved to avoid "leaky gene expression" (Raven, 316).

The next event that will be evaluated is replication, and how the principle upholds here as well. As described earlier, the structure of an interphase chromosome is established and maintained by the modifications on specific histones tails, and as a result the chromosome is composed of a mixture of heterochromatin and euchromatin (Alberts, 191). It is important that the same histone modification patterns are passed onto a daughter cell during replication so that the daughter cell will express and silence the same genes. When a chromosome is replicated its histones are divided randomly in half amongst its two daughter DNA helices, so each daughter DNA helix receives half modified histones and half virgin histones. Proteins then utilize the histone code on a parental histone and bind to a nearby virgin histone to deposit the same type of modification, which recreates the pattern of the parental chromatin structure in the newly synthesized helices. It is an evolutionary advantage that a cell is able to inherit the same pattern of chromatin structure as its parent because then it can "remember" whether a gene was expressed or not its parental cell. This is called epigenetic inheritance (Alberts, 192).

The process of DNA repair also relies on histones packaging for the regulation of accessing DNA. Modifications (usually phosphorylation or monoubuitylation) to the histone tail of H2A are crucial during DNA repair because the chromatin structure must be remodeled in order for Crb2 and other factors to be able to access and repair the lesion (Smith, 2006). Throughout the repair process the chromatin transits between different structures allowing specific repair factors to gain access to specific regions of the DNA (Downs, 2000), (Nakamura, 2004). These modifications also induce signaling that certain checkpoints depend on in order to pause the cell cycle until the DNA has been repaired (Salomons, 2006).

Through the level of compaction of books by bookends, regulation of the accessibility is achieved. This is because the amount of space utilized depends on level of compaction, which then regulates accessibility for two reasons: one because more books of a genre can be present on the bookshelf and therefore more accessibility of information of that genre, and second because decrease in compaction increases the possibility of books collapsing, which then results in the call number and title not being visible and books being dropped and lost.

Figures:

Hitsones and the bookends at the Wallace Library of Wheaton College in Norton, Massachusetts are illustrated with images from separate sources.

Figure 1a: Displayed are books on a bookshelf at the Wallace Library at Wheaton College, Norton Massachusetts. This displays a low level of compaction of a sequence of books through the use of bookends. The books on the shelf have collapsed at the end, which results in not visible call numbers and titles, greater space utilized, and books have been dropped.

Figure 1b. Displayed is the same the bookshelf image from 1a at the Wallace Library at Wheaton College Norton, Massachusetts. The books are more tightly compacted. More books of the genre can fit, their titles and call numbers are visible, and none of the books have been dropped.

Figure 2: This displays a bookend at the Wallace Library at Wheaton College, Norton Massachusetts. It is L shaped because the base slides under the books at the end of the sequence and the “wall” of the bookend supports the books at the end, creating compression against the end of the bookshelf. Bookends can be seen at the end of the sequence of books in the

background.

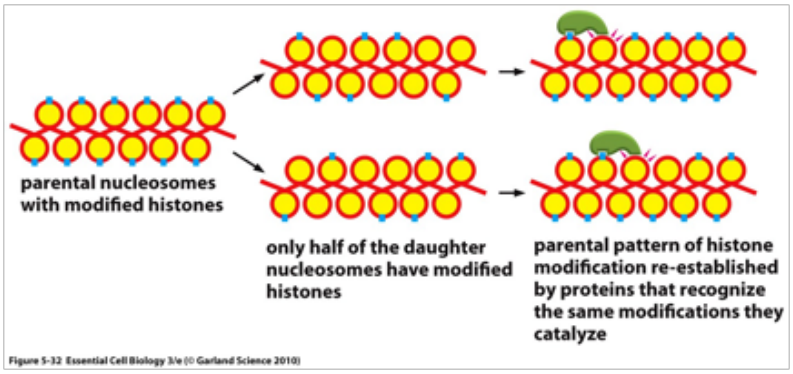

Figure 3: This is an image from Essential Cell Biology Third Addition. The figure shows epigenetic inheritance where modified histones are inherited during DNA replication. The parental nucleosomes are distributing half of their modified histones to each daughter helix. The daughter helix contains half virgin histones and half modified histones from the parent. The green structure binding to the histones without the blue square that are adjacent to the modified histones (with the blue squares) are the virgin histones. The green structure is a protein that recognizes modified histones. It first bound itself to a parental modified histone (not shown) and then bound itself to the adjacent virgin histone to deposit the modifications of the parental histone to the virgin histone. The parental pattern is reestablished in the newly synthesized helices. This figure supports the regulation of DNA replication.

Figure 4: figure 4a and 4b display the two methods in which gene expression is regulated through the use of histones. One images were retrieved from Essential Cell Biology Third Addition(Figure 5-32) and www.ncbi.nlm.nih.gov/books/NBK28290/.

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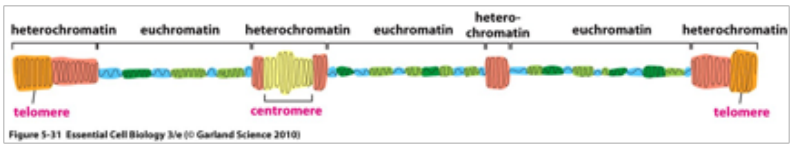

Figure 4a:

This is an image from Essential Cell Biology Third Addition(Figure 5-32).This figure illustrates the varying chromatin regions along the interphase chromosome. Heterochromatin and Euchromatin are each labeled. The heterochromatin regions display how tightly the chromatin is packed.The figure shows that the euchromatin regions are not packed as tightly. This figure supports the regulation of gene expression

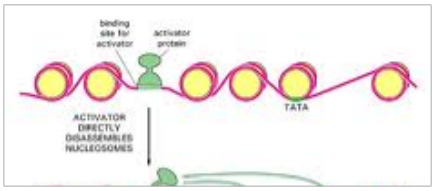

Figure 4 B

This image was retrieved from /www.ncbi.nlm.nih.gov/books/NBK28290/. This image displays the other way in which gene expression is controlled. A nucleosome blocks the transcription start site and the transcription apparatus cannot bind to the promoter.

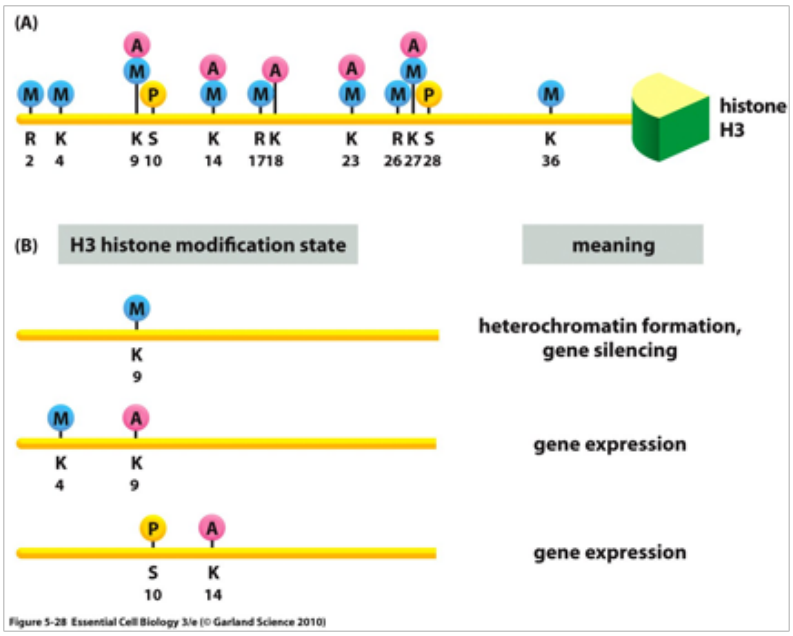

Figure 5

This is an image from Essential Cell Biology Third Addition (Figure 5-28). This image illustrates the modifications on histone tails. The modifications made to a histone tail dictates how that region of DNA is treated by proteins. This supports of all three of the processes in which histones regulate through the modifications of histones tails, the processes are replication, repair, and gene expression. Although this figure only displays the modifications made to the tail of histone H3, if the modification of the tail of histone H2A was displayed it would support the process of DNA repair.

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