Tinkering With the Blueprints of Cells and Notre-Dame

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Rule-to-Build-By:

The building plans of both nature-built architecture and man-made architecture are continuously being tinkered with in order to achieve the best design.

What:

To illustrate this rule-to-build-by, viruses and humans tinker with the plans of nature-built structures while throughout history humans have changed the interior and exterior plans of Notre-Dame cathedral in Paris.

How: The animal cell is a complex nature-built structure whose "blue prints", or building plans lie within its DNA, which is kept in the nucleus. However, the replication and synthesis of that cell's DNA can be halted when a virus infects that cell by injecting its own viral DNA into the cell. Viruses are genetic parasites that are motile and use cells to replicate their own DNA. Viruses store their DNA inside a protective capsid protein coat in the bacteriophage head and they also have tails that extend out from below this structure. There is a diverse array of different viruses and their genome type usually falls into the category of either double-stranded DNA or single-stranded RNA (Alberts et al., 2010).

One way in which the virus inserts its DNA into the cell is by attaching to the plasma membrane of its host cell at certain receptor sites where it is engulfed. When the virus merges with the plasma membrane and moves into the cell, the protein coat is shed. A second way the virus can enter the cell is to attach to the plasma membrane and insert its tails through the plasma membrane and into the cell. Once the tails are inside, the virus pushes the DNA down and into the cell through the tails. Inside the cell, the viral DNA undergoes transcription once the virus has commandeered the host cell's DNA replication and protein synthesis machinery to replicate its own DNA (Fraenkel-Conrat, 1969).

The process of replicating the viral DNA is the same as the process that the cell's DNA goes through. To start with, DNA is comprised of a four different nucleotide subunits, adenine (A), cytosine (C), guanine (G), and thymine (T). These four nucleotides form base pairs in which adenine and thymine go together and cytosine and guanine go together. The backbone is comprised of the sugars and phosphates that bind these nucleotides together. When the nucleotides are arranged in a specific order, they create a gene that can be transcribed to create RNA, which in turn is translated into a protein. The process of replicating the viral DNA creates DNA helixes that are identical to the original DNA. The sites at which replication of the viral DNA begins are known as replication origins and can be found within a sequence of nucleotides that constitute the promoter region. It is here where the replication machinery assembles, and part of that machinery includes the DNA polymerase, which binds to the replication origins and begins to unzip the DNA (Alberts et al., 2010). As it unzips the double helix, the DNA polymerase forms two replication forks at the replication origin. The replication machinery uses each DNA strand as a template to create new daughter strands. These new daughter strands run in opposite directions as they're being made because the DNA polymerase adds subunits to the 3'end. Thus the leading strand is formed continuously because subunits are added easily to its growing 3'end as it

grows in the 5'-3' direction while the other strand, the lagging strand is made discontinuously. The lagging strand is made discontinuously because it grows starting with its 5' end. It begins to grow by forming small series of short DNA strands known as Okazaki fragments. In turn, these small Okazaki fragments are joined together to from the lagging strand, creating one continuous strand. (Alberts et al., 2010).

Once the DNA is replicated, it undergoes transcription. During transcription, an RNA polymerase binds to the promoter regions of the viral DNA known as replication origins. Once bound, the RNA polymerase uses the DNA as a template to synthesize RNA (Alberts et al., 2010). RNA is similar to DNA but it is made of ribonucleotide subunits, and instead of tymine, it contains uracil, which pairs with adenine. To start transcription, the RNA polymerase unzips the DNA and transcribes one of the strands into a single strand of RNA. The newly formed RNA strand then goes to a ribosome where its triplet codons are translated into viral protein (Alberts et al., 2010).

At this point, the virus has replicated its DNA and synthesized multiple new copies of itself in the form of virus phages. These virus phages have their own set of viral DNA that is identical to the original virus and is stored inside capsid protein coats (Fraenkel-Conrat, 1969). When the concentration of these virus phages accumulate, the cell bursts and the newly made viruses spread out into the extracellular space of the host organism and infect other cells and tissues.

This event can have drastic effects on the functionality of the architecture of the cells that have been infected. Once infected, they are no longer able to function correctly because they have been taken over by the viruses and cannot replicate their DNA successfully. An example in which the blueprints of a cell's architecture have been altered is a cell that has been infected by tumor viruses, in particular the polyoma virus. In this case, the polyoma virus has incorporated its viral DNA into the genome of its host through reverse transcriptase, which in turn compromises and changes the structure of that organism's architecture through the creation of tumors. (Fraenkel-Conrat, 1969).

On the other hand, humans now have the ability to alter the building plans of nature-built structures through stem-cell research. There are two types of stem cell research: therapeutic cloning and gene therapy (Kelly, 2007). In general, stem cell research involves taking an early embryo from a female donor and changing the building plans of all the embryonic stem cells that have the potential to differentiate into different types of cells (Alberts et al., 2010). The point at which cells begin to embark on their differentiated path is when the fertilized egg forms into a blastocyst. The blastocyst consists of an outer layer of cells known as the trophoblast and a mass of embryonic stem cells inside known as the inner cell mass (Scott, 2006). The embryonic stem cells inside the blastocyst begin to differentiate into three different types of cells: ectoderm, endoderm, and mesoderm. Each of these types of cells will grow to become specific organs and tissues that help make an organism.

Stem cell research has taken the building plans of these nature-built stem cells to the next level by allowing scientists to alter the design so that the cell will differentiate into a different type of cell than the one it was originally going to be. To begin the process of therapeutic cloning with stem cells, a somatic cell from a patient's body is fused with a donated unfertilized egg whose nucleus has been removed. This is known as somatic cell nuclear transfer (Kelly, 2007). Once the zygote, which is totipotent becomes a blastocyst, the inner cell mass is isolated and placed in petri dishes where the plans for the stem cells' final structure can be manipulated (Scott, 2006). These human embryonic stem cells (hESCs) that are pluripotent, are then subjected to injections of different types of growth factors that will promote them to grow into a certain types of tissue (Kelly, 2007) Growth factors are proteins that when bound to a specific cell protein, act as an enzyme to phosphorylate and activate other proteins. This phosphorylation acts as a switch that turns on certain processes. Two types of growth factors, nerve growth factor (NGF) and epidermal growth factor induce stem cells to differentiate into nerve or epithelial cells. The leukemia inhibitory factor (LIF) induces stem cells to differentiate into bone, cartilage, smooth and striated muscle. Transforming growth factor (TGF) induces stem cells from bone marrow to differentiate into adipocytes, also known more commonly as fat cells (Kelly, 2007). The second type of stem cell research, gene therapy involves the culturing and growing of stem cells from patients with genetic diseases. These stem cells with their malfunctioning genes are introduced to a normal-working DNA sequence through a process known as genetic editing. In genetic editing, the proper working DNA with its complete coding region and regulatory regions is added to the stem cells (Kelly, 2007). Once the gene sequence is tinkered with, these stem cells give rise to daughter cells that have reprogrammed blueprints, which in turn provides the cells with the plans to create an even better functioning architecture. At this point, the reprogrammed cells with the functioning gene are reinserted into the body of the patient (Kelly, 2007). Over recent years, scientists have developed the ability to engineer an array of different types of stem cells by changing their DNA, or building plans. Now, a stem cell that starts as one particular type of cell can have its design tinkered with to become a whole new different cell type.

Both scientists and viruses have influenced and changed the building plans of nature-built structures. Similarly, multiple master builders have tinkered with the building plans of the Notre-Dame cathedral in Paris throughout its

building history. Their changes to the cathedral are what we see today, in particular the changes of Eugène Viollet-le-Duc. The building of Notre-Dame commenced in the year 1163 under the direction of the first master builder who was hired by Maurice de Sully, the bishop of Paris. The original plan of Notre-Dame that Maurice de Sully created included a five-bay apse and choir area with an eight-bay nave and finally a large façade with two towers. This plan was a four-elevation plan that consisted of a large nave arcade, an arcade, a gallery, and a clerestory. The second master builder took over the plans of the cathedral in 1177, and changed the rose occuli in addition to adding triple arcade units to the second level. This change in the plan gave the cathedral a heightened sense of spaciousness because it reduced the wall surfaces (Erlande-Brandenburg, 1997/1998). During the 1200's the third master builder started the grand western façade, and after his death the fourth master builder took over. The fourth master builder kept the original four-elevation plan but modified it by extending the clerestory windows, which increased the building's sense of spaciousness and loftiness. He also kept the uniform design of the arcade supports while introducing a new complex support system. In this new addition to the building's plan, he used four engaged columns as par of the support system. This change can be seen today in the façade wall where the method of coursed masonry is applied, and lancet windows are present in the towers (Erlande-Brandenburg, 1997/1998). Later on, the cathedral was subject to ruin both by defects in its architecture and by angry French citizens who dismantled a lot of the cathedral's sculptural program. Notre-Dame remained in disrepair until Eugene Viollet-le-Duc started to restore the building in the 19th century in 1843. In his restoration, he added to the exterior plan of the cathedral a whole sculptural program of gargoyles that can be seen today adorning the cathedral. While restoring the cathedral, Viollet-le-Duc aimed to create a revised version of the original building plans. To do this, he restored the spire that had been lost over the crossing, changed the southern window, and restored the original four-level elevation at the crossing inside the cathedral, which can still be seen today (Erlande-Brandenburg, 1997/1998).

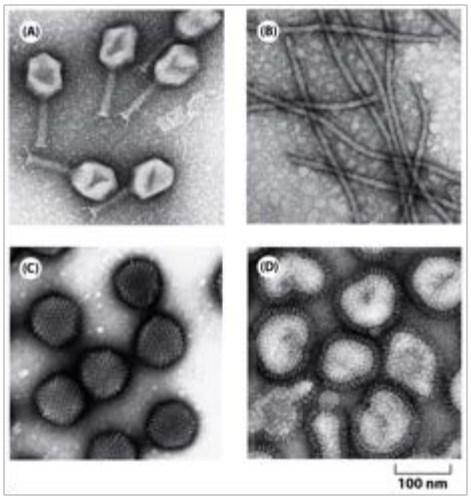
Why: Both viruses and human stem cell research alter the building plans of nature-built architecture while master builders such as Viollet-le-Duc have tinkered with the building plans of Notre-Dame cathedral. In both cases, there is an evolutionary advantage to the changing of the building plans.

To start with, this building rule is evolutionarily advantageous for the virus because it can commandeer its host cell's replication machinery to replicate itself, which can alter the functioning abilities of the cell's architecture. Over time, viruses have evolved in such a way that they can co-evolve with their host, which can be seen today with plants and animals. Although for the most part we associate viruses as being a negative thing, there are good viruses. These provide benefits for their host when they alter the building plans, which in turn affect the functioning of the host's architecture. In one case, it has been noted that when plants were introduced with four different RNA viruses, Brome mosaic virus, Cucumber mosaic virus, Tobacco mosaic virus and the Tobacco rattle virus, they were better able to survive in drought conditions (Chen et al. 2008). When the plants were injected with the viruses, the viruses actually gave the plants and increased tolerance to drought conditions. Over time, when these infected plants replicate, they will pass on this advantageous virus. This can also be seen in the genomes of current day humans whose ancestors' genomes were infected with human endrogenous retroviruses HERVs. These retroviruses altered the genome of our ancestors, which benefited our ancestors because by altering the genomes, they encoded for proteins that carry out essential functions in the placenta. Over evolutionary time, these HERVs have been passed on down to us through generations and still exist in our genomes today (Villarreal, 2005).

In regards to stem cell research, the evolutionary advantage of being able to manipulate and change the building plans of stem cells is that patients who have lost normal functioning cells due to diseases have the ability to replace them with reprogrammed stem cells. In the use of genetic stem cell therapy and therapeutic cloning, the advantages are that stem cells can be reprogrammed using somatic cells from the patient's body, which reduces the chances that the reprogrammed stem cells will be rejected by the patient's immune system.

The current day architecture of Notre-Dame cathedral is very different from its original architecture. Over time, multiple architects, including Eugene Viollet-le-Duc, have changed its structure, and it is through this continuous tinkering that Notre-Dame has come to assume the best design. This changing was advantageous in that each architect added his own design to the building, making it a more stable yet lofty and beautiful cathedral. Today, we appreciate these changes that have been made to the cathedral's building plans because it represents an amazing collaboration of ideas from multiple master builders who all envisioned it as a perfect edifice in which to honor God.

Figures:



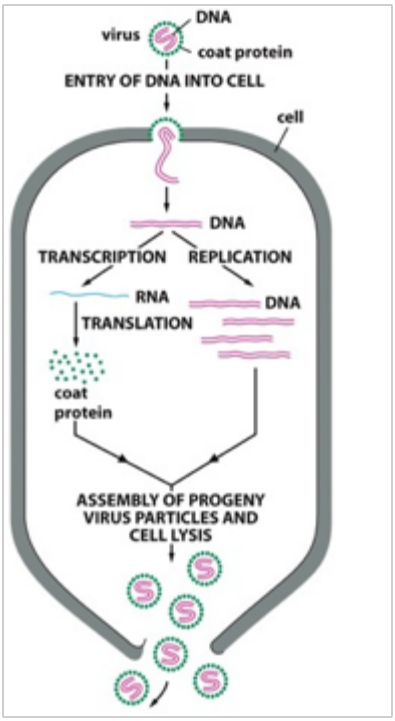
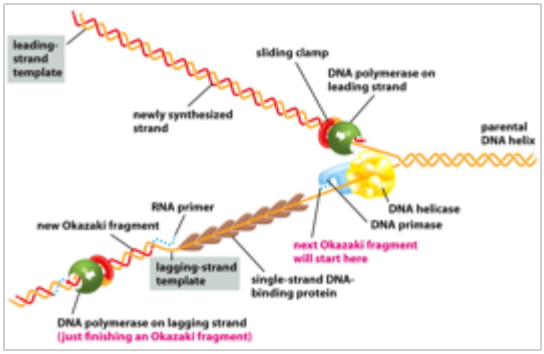


Figure 1 shows the different types of viruses that exist and how they can commandeer a cell's replication machinery to replicate their own DNA in order to replicate themselves (Alberts et al., 2010).



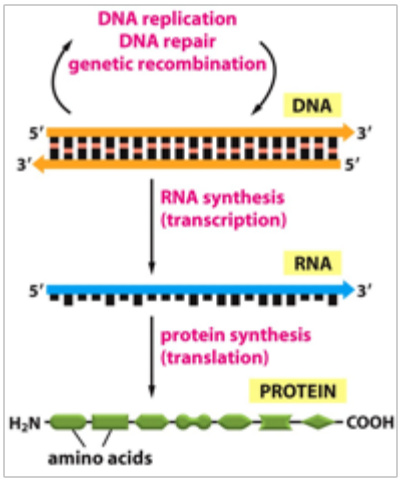
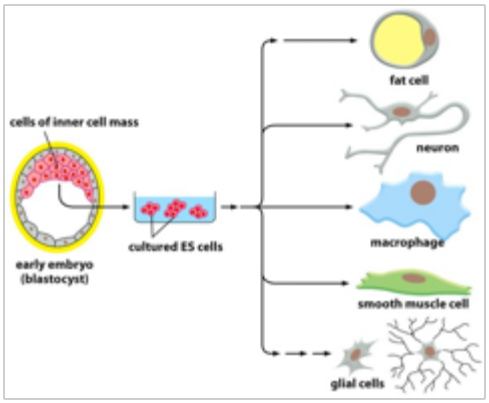
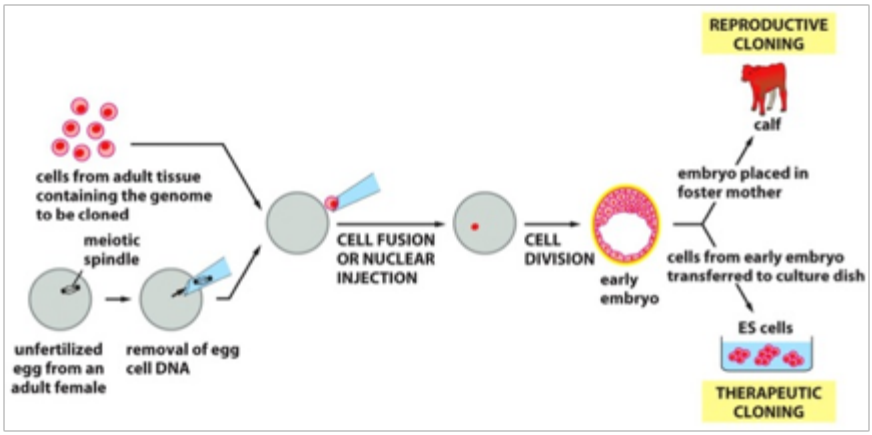


Figure 2 shows the process of DNA replication, transcription and translation of normal DNA in a cell. A virus's DNA will undergo the same process once the virus has taken control of the cell's replication machinery (Alberts, 2010).





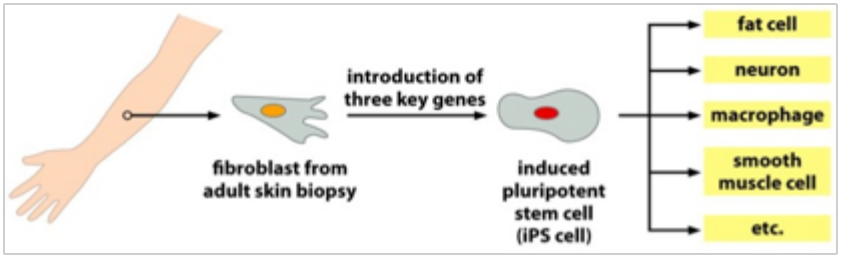


Figure 3 shows that embryonic stem cells that make up the inner cell mass of a blastocyst are pluripotent and have the ability to differentiate into different types of cells. Two types of stem cell research, therapeutic cloning and gene therapy are also shown here (Alberts, 2010).

Figure 4 shows the original plans of Notre-Dame cathedral in Paris (Erlande-Brandenburg, 1997/1998), and the first picture shows part of Eugene Viollet-le-Duc's interior restoration seen today that features the original four-elevation (Wheeler, 2008) along with his gargoyles and the reconstruction of the spire that was lost over the crossing (Ryan-Small, 2010).

References:

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