Proteins: Not Just a Food Group

1.1 Introduction to Proteins

All organisms that sustain life contain proteins within their cells that help them carry out their daily functions. Proteins make up around fifteen percent of a human’s body weight and along with carbohydrates, lipids, and nucleic acids proteins are considered a basic building block of life. One might be surprised at how diverse and extensive the functions of proteins truly are. Proteins are needed for structural stability, biochemical reactions, fighting off infections, hormone secretion, food metabolism and much more. Proteins can be produced in the body through protein synthesis or obtained through eating protein rich foods such as fish, eggs, nuts, and meats. Eating protein can help human bodies to repair or replenish the supply of proteins in the body. Proteins can be very important in the diets of those with missing or have ineffective proteins that help the body perform some of its basic functions.

Unfortunately, only eating proteins can send someone into ketosis. Ketosis usually occurs in people who cut out almost all carbohydrates and diary from their diets and only eat chicken, beef, pork, fish, nuts, and eggs. This is because many of these high protein foods are also high in fat. When an abnormal amount of fat is being metabolized in the body there is a higher level of ketone bodies throughout the body as well. This high level of ketone bodies is what defines someone as being in a state of ketosis. Many fad diets such as the Adkins diet promote this type of nutrition for weight loss but can be very dangerous. The dangers of this type of diet are that one can lose muscle mass, lose energy, and cause long term damage to the liver, heart, and metabolism of any individual undergoing frequent phases of ketosis. Just like everything else in life, proteins are great in moderation and especially when accompanied by carbohydrates, fiber, and fats. In the rest of this chapter, the molecular structure of proteins, protein synthesis, protein folding, and membrane proteins will be explained.

1.2 The Molecular Structure of Proteins

The building blocks of proteins are amino acids. There are twenty-one amino acids and various combinations of amino acids result in vastly different proteins. Amino acids are usually classified into three different groups: essential, nonessential, and conditional. The essential amino acids are histidine, isoleucine, leucine, lysine, phenylalanine, threonine, tryptophan, and valine. The nonessential amino acids are alanine, asparagine, and aspartic acid. The conditional amino acids are cysteine, glutamine, glycine, proline, serine, and tyrosine. Conditional amino acids are amino acids that may not be produced in the body due to a malfunction such as catabolic stress. These conditional amino acids can be obtained through eating certain foods. Despite the three different categories of amino acids, every amino acid has the same general features such as side chains, an amine group, and a carboxyl group. An amino group consists of a nitrogen atom that is single bonded to one, two, or three hydrogens. If the amino group of an amino acid is stationed at the end of the molecule and is not bonded to any other atoms, it will contain three hydrogens. If it is bound to one other atom than it will contain two hydrogens and if it is bond to two other atoms it will only contain one hydrogen.

A carboxyl group consists of a carbonyl and a hydroxyl group. A carbonyl is a carbon double bonded to an oxygen atom and hydroxyl group is an oxygen single bonded to a hydrogen atom. These are the molecules that make up the basic structure of every amino acid. The chemical makeup of the side chains is what differentiates each amino acid from the others. Amino acids can get linked together through peptide bonds. A string of amino acids bound together by peptide bonds are known as the primary or beginning structure of a protein. Certain side chains of amino acids can have varying properties such as being negatively charged, positively charged, polar, nonpolar, etc. These properties influence the types of bonds that it can form with other amino acids. Charged (negatively or positively) side chains can usually form ionic bonds and polar side chains can usually form hydrogen bonds. Covalent bonds are rarely found between amino acids. However, cysteine has been known to form them occasionally. Peptide bonds link the carboxylic acid end of one amino acid to the amino end of another amino acid. No other ends can be joined together. It is important to remember that peptide bonds are covalent bonds. This becomes very important later when learning about proteases.

Proteases cleave proteins at their peptide bonds. Therefore, it is important that covalent bonds are strong because peptide bonds hold proteins together but they are not permanent fixations because that would cause a lot of metabolic problems. Proteases start protein catabolism or the break down of proteins and the break down of proteins that we eat is very important for replenishing our amino acid supply and providing energy for the body. It is interesting to note that the foods that are very protein rich can be different than foods that are rich in amino acids. Foods that are rich in amino acids are pumpkin, leafy greens, avocados, wheat, chia seeds, watercress, and almonds to name a few.

1.3 Protein Synthesis

Protein synthesis is a very in-depth process that can be quite confusing at times. However, this section will explain the basic foundation of protein synthesis without trying to add in all of the confusing terminology that only college level or above students would need to learn. Basically, protein synthesis is comprised of a few fundamental steps: 1. DNA is replicated. 2. DNA is changed into RNA through transcription and 3. RNA is changed into a protein through translation. Protein synthesis is often referred to as the central dogma of biology because it is essential to every single living organism!

Step one is a basic step that DNA undergoes all the time, even when not involved in protein synthesis. Just like it is a good idea to save a paper that you are writing in more than one place on your computer, it is a good idea to have replicate copies of DNA in case any of it ever got lost or destroyed. DNA replication is quite easy for cells to do because it is just making an identical copy of the DNA that is already in the cell. Lots of enzymes and proteins are used to conduct this process but we will only talk about a few of them here. The first enzyme involved in DNA replication is helicase. Helicase unzips the double helix of DNA in order to make a “Y” shaped replication fork. Making a replication fork is essential to DNA replication because it allows the existing DNA to act as a template to make the new identical copies. Since the Y shape gives us two strands, one strand will be in the 5’ to 3’ direction and it is called the leading strand. The other strand is in the 3’ to 5’ direction and is called the lagging strand. DNA polymerase is the enzyme that assembles nucleotides to unpaired strands, but it can only read nucleotides in the 5’ to 3’ direction. This is quite a big problem for the lagging strand because it runs 3’ to 5’! Therefore, DNA polymerase has to synthesize the lagging strand in 5’ to 3’ fragments called Okazaki fragments. The synthesis of the lagging strand is not continuous like the synthesis of the leading strand. However, DNA polymerase doesn’t work alone. It needs small RNA primers to come before it and show DNA polymerase where to start. Base pairing is very important for DNA replication, so DNA polymerase’s role in this process is crucial. DNA polymerase adds nucleotides to the leading and lagging strands so that they will become double sided again but it doesn’t add these nucleotides randomly. There are five nucleotides with the assigned letters ATCGU. ATCG are used in DNA and ACGU are used in RNA. Nucleotides can only pair up with their assigned partner and DNA polymerase has to be able to recognize this. C always pairs with G and A always pairs with T (or U when dealing with RNA). However, DNA polymerase isn’t perfect so a proof reading mechanism works to check and make sure the DNA has been replicated correctly. If a mistake is found, a protease will cut or excise that piece out and DNA polymerase is given the opportunity to fix it. Once everything is correct, an enzyme called DNA ligase comes in and seals up the strands into two identical double stranded DNA strands. After DNA replication, we have two identical double stranded daughter strands. One strand is made of the template DNA and one strand is the complementary to the template strand.

Transcription, as it is stated in step two, is the process of converting DNA to RNA. It is important to note that during transcription, RNA polymerase is used instead of DNA polymerase but their functions are the same. There are three main steps to completing transcription: initiation, elongation, and termination. During the initiation phase, RNA polymerase binds to DNA at a sequence called the promoter. A promoter is a sequence of DNA specifically designed to attract and bind to RNA polymerase, so that RNA polymerase knows where to start working. Once bound, elongation can occur. During elongation, RNA polymerase adds nucleotides to the 3’ end of the new growing chain. This can go on for quite some time and does not end until a stop codon is found. A stop codon is three nucleotides that code for the RNA polymerase enzyme to release the growing polypeptide strand that is has been adding nucleotides to. This process is called termination. Once termination has occurred, transcription has ended. The products of transcription are mRNA that code for proteins and contain the nucleotide U instead of the nucleotide T. After transcription is over there are necessary processes that have to occur in order to keep the new mRNA strand from getting degraded or damaged. A cap is put on the 5’ end of the mRNA and a tail made up of lots of the nucleotide A in a row is placed at the 3’ end of the mRNA strand. Sections of the mRNA strand that do not code for proteins (called introns) are cut out and thrown away. DNA replication and transcription both occur within the nucleus of a cell.

The third step in protein synthesis is done outside the nucleus on organelles called ribosomes. Just like transcription, translation has initiation, elongation, and termination steps. In order to start translation, some equipment has to be set up. The equipment is actually a complex that involves the mRNA strand and the small and large subunits of a ribosome. The mRNA strand and three initiation factors bind to the small subunit of the ribosome. This is the initiation stage of translation and it puts the whole process into motion. From then on, a tRNA structure carries amino acids that are complementary to the mRNA strand in order to build the polypeptide chain into a protein.

The first amino acid added is always methionine because every start codon is the nucleotide sequence AUG. A codon is three nucleotides in a row that code for an amino acid. After methionine is added, the mRNA strand is fed through the ribosome and the tRNA is able to read the next codon and therefore add the next amino acid. As the strand grows, the amino acids stay connected to each other and the tRNA in the order that they were brought to the sequence. Therefore, multiple tRNAs work this process, each one bringing a different amino acid. This process continues until a tRNA reads a stop codon nucleotide sequence, which causes no more amino acids to be added to the chain and the mRNA strand to disassociate from the ribosome. After this, the amino acid chain can be folded into a fully functional protein.

1.4 Protein Folding

Once the mRNA stranded is fully translated, it is in its primary structure. A protein’s primary structure is defined as amino acids linked together. It typically looks like beads on a string at the molecular level. Once the protein starts to fold a little bit, it enters its secondary structure. A protein at its secondary structure can either be a beta sheet or an alpha helix depending on the way it was folded. In an alpha helix conformation, the peptide chain is wound together very tightly and resembles a spring. The backbone of the polypeptide sequence or chain forms the inside of the spring and the side chains form the outside of the spring. An alpha helix is stabilized by hydrogen bonds from the amine group of one amino acid to the carbonyl group on another amino acid that is four amino acids to the left or right of it. In beta sheets, the chains of proteins are held together by hydrogen bonding between amine groups of totally separate protein chains. Therefore, beta sheets can link together multiple proteins instead of just coiling the same polypeptide chain into a different conformation like alpha helices seem to do. Overall, they are both considered to be secondary structures despite their differences due to the fact that they both form geometrical shapes due to hydrogen bonding. The next step in protein folding is the tertiary structure. At the tertiary level, the beta sheets and alpha helices fold into one another. The polypeptide chain is now a protein in three dimensions instead of two. In fact, the protein’s designed shape appears at this level. The protein can now be fully functioning wherever it is designed to work in the body.

Denaturation is a process in which protein folding is altered and can occur when excess heat or extreme pH levels are experienced. This can be permanent or reversible depending on where in the body it occurred and what type of protein was involved. The last protein structure is the quaternary structure of proteins. The quaternary structure of proteins is common for fibrous and globular protein, which is defined as the aggregation of multiple different protein subunits into a final specific shape. These protein aggregations can take on very complex shapes. The reason why these proteins would come together is that the usually can only function when joined together. Therefore, they are not a complete or fully functioning protein until they have joined and entered their quaternary structure. Not all proteins have the ability or need to form into the quaternary structure. Just like it is mentioned above, some proteins are fully complete and functioning at the tertiary structure level. Protein folding is extremely important and any misstep in this process can lead to serious human diseases and defects.

1.5 Membrane Proteins

Every single cell inside the human body contains an outer membrane called the plasma membrane that holds all the contents of the cell inside the cell. This is a very important structure to sustain life and it would not be fully functioning without membrane proteins. The plasma membrane provides stability and selective permeability for all cells. This means that it gives the cell a barrier from things that could be harmful to it but also allows nutrients and necessary proteins and enzymes to come into the cell. Several proteins on the plasma membrane make selective permeability possible. Two very important membrane proteins are peripheral proteins and integral proteins. Most of the time, peripheral proteins are bound lightly to the outside surface of the membrane. However, some peripheral proteins can touch part of the inner bilayer of the plasma membrane. Peripheral proteins are also more abundant that integral proteins. Since peripheral proteins are mainly on the surface of the plasma membrane, they are generally used as receptors for signal transduction. Signal transduction is the way that cells throughout the body communicate. Peripheral proteins are good at this because they can sense and bind with things outside of the cell membrane. Integral proteins are embedded inside the plasma membrane and some can span the entire membrane. Integral proteins are sometimes also called transmembrane proteins if they span across the entire length of the membrane (from the outside of the cell to the inside of the cell). These proteins are great for letting ions or other small molecules into the cell. Integral proteins are bound very tightly to the membrane and are not easily separate from the membrane once there. This is a good thing because if they ever left the membrane, they would not longer serve any purpose to the cell. However, harsh detergents can cause integral proteins to dissociate from the membrane, which can be very damaging to a cell. In contrast, when peripheral proteins are removed from the plasma membrane, the bilayer is not harmed at all. In fact, peripheral proteins can dissociate from the plasma membrane quite easily without the use of harsh chemicals. It is important to note that the plasma membrane is not a rigid structure. The plasma membrane is very fluid and mobile and can move and change shape quite easily. Some of the proteins in the plasma membrane can move throughout the lipid bilayer quite easily. Integral proteins move literally throughout the bilayer quite often, but peripheral proteins tend to stay in place. Transport proteins are also important proteins that work with the plasma membrane. It is not easy for any molecule to come into a cell or leave a cell due to the plasma membrane bilayer. Transport proteins help pump important ions and molecules in or out of the cell depending on the concentration gradient or energy provided for active transport. If the transport protein is using the concentration gradient of an ion in order to bring it in or push it out of a cell then it is considered facilitated diffusion, which is a form of passive transport. It is considered passive transport because it does not require energy. Active transport is used by a transport protein with the help of ATP when it needs to bring in an ion or release an ion or molecule from the cell against the concentration gradient. This is considered active transport because it requires energy. All of the different proteins that are associated with the plasma membrane are important for functionality. If any class of these proteins were eliminated from the plasma membrane, all of our cells could burst, shrivel up, or become non-functional. Proteins are a part of so many different essential processes to the lives of our cells, tissues, organs, and bodies.

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