

HUMAN PHYSIOLOGY, BIOCHEMISTRY
AND BASIC MEDICINE

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Preface

How this book was conceived and came about is in many respects a book unto itself. Laurence Cole, PhD, an author, was a professor of obstetrics and gynecology at University of New Mexico and an affiliate and associate professor at Yale University. He was a scientist and a medical student reproductive biology teacher. He was chief of the division of women's health research.

Dr. Cole started the USA hCG Reference Service, a small business run from his new home in Angel Fire, in the mountains of New Mexico. The USA hCG Reference Service ran blood and urine laboratory tests and consulted with physicians worldwide in cases of gestational trophoblastic disease and cases of women not-pregnant positive in hCG gestational tests. The USA hCG Reference Service only occupied Laurence's time for just 1 day in each 14 days.

Laurence could not stand all the free time he had, since, in essence for 13 of 14 days, he was doing nothing, other than just standing and staring at the incredible mountains surrounding Angel Fire. Laurence was so used to thinking about reproductive science and dreaming reproductive science that he sat by the computer and started writing. In 2012 and 2013, Laurence wrote a comprehensive physiology and medicine textbook on human reproduction for medical students entitled "The Biology and Medical Dynamics of Human Reproduction" Nova Science Publishers 2014, ISBN 978-1-62948-832-5. In 2013, Laurence wrote other medical books, including "The Glycopeptins," Nova Science Publishers, 2014 ISBN 978-1-63321-833-8.

In 2014, Laurence kept writing, preparing the second edition of the monograph "Human Chorionic Gonadotropin (hCG)," Elsevier Insight, ISBN 978-0-12-384907-6. Next, Laurence prepared talks on human biology for presentation at Texas high schools, which is when he considered writing a high school human biology textbook. He proposed this book to Nova Science Publishers. They responded with a solid No!, saying they do not publish high school textbooks. Laurence then proposed the same high school science book to Elsevier. Elsevier also said No!, saying they only publish university undergraduate and graduate school books, but instead suggested an undergraduate and graduate student book on human biology.

Angel Fire is located at 8400 ft altitude. In the summer, the temperature rarely exceeds 75 degrees. However, the sun is different at 8400 ft altitude. The solar rays or infra-red heat is very much more intense in Angel Fire, such that 75 degrees feels on the skin like 90-100 degrees. I had sat outside in the sun at our house for 1 h and my forehead felt like it was on fire. I then went inside to get away from the sun and sat alone on the sofa. That is when I suddenly came up with the book title *humanology*, a book that combined all aspects of physiology with biochemistry and anatomy, or a book that looks at every conceivable aspect of what makes a human. I was sold. I wrote to Elsevier proposing the book "Humanology," a comprehensive book covering all -ologies of humans. A new book for undergraduate students at university.

What is humanology? What does the word mean? I was able to find three dictionaries that listed the word humanology. What was found, however, was a mishmash of definitions with different biological and psychological meanings.

The Merriam Webster Dictionary, <http://nws.merriam-webster.com>.

Humanology (noun): the balance between the wealth mindset and the spiritual self. The science that deals with human aspects for betterment of relationships and self-confidence. The process and use of the mental, emotional, physical and spiritual states of a human being.

The Syntheory Dictionary, <http://www.syntheory.com/refs/glossary.html>.

Humanology—the current author defines humanology as the scientific study of humanity. It draws upon all of the existing theories of psychology as well as all of the known arts and spiritualities.

The Wikipedia Encyclopedia, <http://philosophyofreason.wikispaces.com>.

Humanology is the study of human beings. It is a neologism used within POR to identify the difficulty of using science to study human beings. Humanology consists of all serious attempts to apply scientific reasoning to *Homo sapiens*. By definition, humanology includes psychology, sociology, anthropology, and all similar academic specialties.

I start this book with one simple definition on humanology: Humanology is one science describing the actions, all physiological and biochemical behaviors, and an introduction to medical behavior of humans. It is the science of everything human.

I soon started to realize that I needed partners for writing this book, my co-authors or partner authors. Partners with expertise in biochemistry, human physiology, and human psychology. I thought about Peter Kramer, PhD, a nutritional biochemist. Laurence Cole and Peter Kramer both studied together on their biochemistry PhDs at Medical College of Wisconsin in Wauwatosa, Wisconsin, 1978-1982. I always

remember that Christmas when Peter and I, who both drove very old Volkswagen Beetles at that time, said that we will meet for lunch down at the tavern on Wisconsin Avenue. Wisconsin Avenue in Wauwatosa is very hill-ridden with dozens of ups and downs. There was at least a foot of fresh snow on the ground and no traffic. Stephen left the medical complex and went over the first hill on a car-deserted Wisconsin Ave and unwittingly his car rotated around six or seven times coming over the brim of the first hill, skiing in every direction.

I followed him, lost all control, and did the same thing coming over the hill spinning around and around. My spinning car slapped side into side into Peter's car as I came down the hill. I remember the front door of Peter's car falling off, tumbling flat into the snow, then a few minutes later the back door falling off. Then 10 min later, his front wheel dropped 90 degrees, and finally his back wheel falled flat 90 degrees. All I could do is laugh. All we all could do is laugh and laugh as we walked into the tavern for lunch. Peter's old beetle had had it.

I remember that after lunch and drinking a couple of beers, coming outside and looking at the cars, all we could do is laugh more looking at Peter's door-less and wheel-less dead skeleton car. We ordered taxis to take us home. This story here is one of unraveling a car, yet here we write a book on unraveling humans piece by piece.

Stephen seemingly traced Laurence all across the United States. Laurence Cole first moved east to University of Michigan in Ann Arbor, Michigan. Stephen moved east to Notre Dame University in Notre Dame, Indiana. Laurence moved further east to Yale University in Connecticut, and Stephen moved east shortly afterward to University of Connecticut. We always kept in touch, worked together, and hiked together on weekends. Now Stephen lives in the Philippines where he co-authors this book by e-mail with me.

This comprehensive text is designed to give the undergraduate student a thorough

understanding of the workings of a human being, encompassing the workings of the brain and mind, the workings of the organs or body, the underlying biochemistry, and a broad introduction to medicine. Such knowledge is essential to a career in the medical field.

The book starts by looking at the bodily units ([Section 1: Human Body Formed by Units](#)). Here we examine the underlying cells and inspect the biochemistry at the roots of the functioning of the human body. We also investigate the underlying DNA and genetics of the human body and how it all works.

The book then examines the anatomy and biology of the human frame ([Section 2: Human Frame](#)). First, by examining the human skeleton, then inspecting the skin, ligaments, and muscles of the human body. Third, this section examines apoptosis and the underlying mechanism by which we grow and age. The third section is a comprehensive examination of human physiology ([Section 3: Human Organs](#)), looking at system by system how the body functions and what different organs look after.

The fourth section of the book examines in detail how humans evolved or came about

([Section 4: Human Evolution and Pseudo-evolution](#)). It looks at how humans evolved from primates, how *Homo sapiens* first appeared, including details about early life and how it slowly became civilized. [Section 5](#) deals with human nutrition, diet, and fitness and obesity ([Section 5: Nutrition](#)).

[Section 6](#) is an introduction to basic human medicine ([Section 6: Human Diseases and Treatments](#)). This section selects multiple categories of disease, genetic defects, infection, cancer, cardiovascular disease, hydatidiform mole, diabetes, and ovarian cysts. It tries to introduce each disease category, examine its underlying physiology and biochemistry, and explain the basic mechanisms of disease.

It is believed that a comprehensive understanding of all six sections of this book will provide students with complete knowledge of the workings of human beings, or an appropriate introduction with the vast science of humanology.

Laurence A. Cole, PhD
Peter R. Kramer, PhD



Section 1

Human Body Formed by Units

1.1

The Cell

The cell is the unit of all animal and plant, prokaryotic and eukaryotic, life. There is single cell life like the amoeba, oligocell life like some plankton, and multicell life like humans. Humans actually contain 3.0×10^{13} cells or 30 trillion cells. If you imagine that an average speck of dust weighs just 0.75 μg , then the average 70 Kg man comprises the weight of 93 billion particles of dust. Considering both values, the average cell in the human body weighs just a tiny fraction of the mass of a speck of dust, 1/323 of a speck of dust. The cell is the basic human makeup or unit, a tiny fraction of a speck of dust.

This minuscule body, a fraction of the size of a speck of dust, is an entire village full of organelles or shops and business facilities. There is the mitochondrion, which is like the village power station, the nucleus, where the village mayor controls the village council or chromosomes and orders what is to be made and when, the rough endoplasmic reticulum and ribosomes, which are like the local village factory, hard at work manufacturing the village's need for proteins, and the Golgi apparatus, another village factory, hard at work refining the synthesized proteins. Then there is the lysosomes or local village dump degrading the molecules not needed by the cells. All buildings in the

village or fraction of a speck of dust work happily and eagerly together.

Figure 1.1.1 shows a representative human cell. While there are thousands of types or classes of cells in humans, each is different in shape, makeup, and function. A very general cell is shown in Figure 1.1.1. The number of each organelle varies in each cell type, and some cell types contain specialized functional organelles, which are not shown. Each cell is centered by a nucleus and within each cell is a nucleolus. Each cell has a smooth and rough endoplasmic reticulum, ribosomes, Golgi apparatus, mitochondria, lysosomes, centrioles, and microtubules. Shown are secretory vesicles emerging from the Golgi apparatus as a representative cell (Figure 1.1.1).

THE PLASMA MEMBRANE

The plasma membrane is the envelope that encloses the entire cell. The envelope is made up of molecules called phospholipids. These are fatty acids with a charged or polar group on the head, and two long noncharged fatty tails comprising carbon and hydrogen atoms. Many different lengths of fatty acid tails, saturated

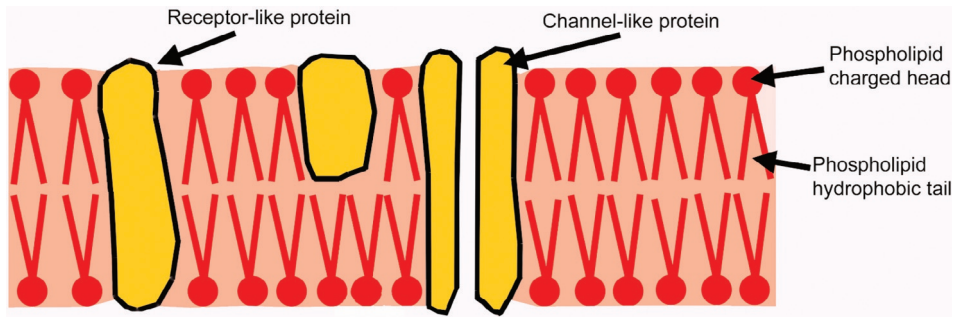


FIGURE 1.1.3 The lipid bilayer structure of plasma membranes.

which contain the genes for ribosomal ribonucleic acid (rRNA), serve as the substance for nucleolar structure. Ribosomal assembly in the nucleolus begins with the transcription of pre-rRNA. During transcription, ribosomal and nonribosomal proteins attach to the RNA. There is modification and cleavage of pre-rRNA and incorporation of more ribosomal proteins and 5S rRNA into maturing preribosomal complexes.

As shown in Figure 1.1.4, the nucleus is a ball filled with chromatin, a DNA-protein complex, with the nucleolus, and multiple loose chromosomes. Each human cell contains 23 pairs of

chromosomes or in 46 total. The nucleus is the site where DNA is replicated, and DNA is transcribed to make messenger RNA (mRNA) signals to start the process of translation or protein synthesis which occurs in ribosomes in the cell cytoplasm (all the cell body except the nucleus).

The function of the nucleus is to maintain the integrity of the genes on chromosomes and to control the activities of the cell by regulating gene expression through mRNA signals. The nucleus is the control center of the cell. Because the nuclear membrane is impermeable to large molecules, nuclear pores are required that regulate nuclear transport of molecules across the envelope. The pores cross both nuclear membranes, providing a channel through which larger molecules must be actively transported by carrier proteins while allowing free movement of small molecules and ions into the nucleus. Movement of large molecules like proteins and mRNA through pores is needed for gene expression and the maintenance of chromosomes.

The nuclear envelope contains thousands of nuclear pores (Figure 1.1.4). Nuclear pores are large protein complexes that cross the nuclear envelope, which is the double membrane surrounding the cell nucleus. The proteins that make up the nuclear pore complex are known as nucleoporins. Each nuclear pore complex is composed of approximately 30 distinct proteins.

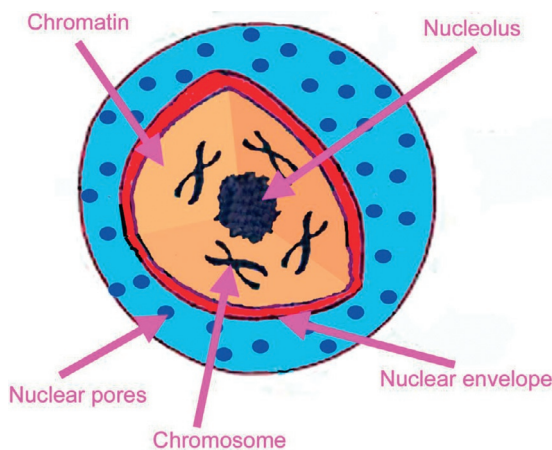


FIGURE 1.1.4 The nucleus and nucleolus.

ROUGH ENDOPLASMIC RETICULUM AND RIBOSOMES

The ribosomes are the site of translation of mRNA to produce polypeptides (long strips of amino acids) and proteins (folded polypeptides). Ribosomes are found both attached and nonattached to the rough endoplasmic reticulum (see [Figure 1.1.1](#)). Ribosomal RNA (rRNA) exists as 30S or small rRNA that hold the mRNA, and large 50S rRNA where protein synthesis occurs (see [Figure 1.1.5](#)). As illustrated in [Figure 1.1.5](#), the mRNA binds amino acid-specific transfer RNA (tRNA) that have the corresponding RNA anticodon sequence. The tRNA carries the specific amino acids and places them together in sequence.

The surface of the rough endoplasmic reticulum is studded with ribosomes and has a rough appearance when viewed under an electron microscope. The binding site of the ribosome on the rough endoplasmic reticulum is the translocon. However, the ribosomes are constantly being bound by and released from the rough endoplasmic reticulum. A ribosome only binds to the rough endoplasmic reticulum once a protein-nucleic acid complex forms in the cytoplasm. This special complex forms when a free ribosome begins translating the mRNA of a protein destined for a secretory pathway. The first 5-30

amino acids encode a signal peptide, a molecular message that is recognized and bound by a signal recognition particle. Translation pauses and the ribosome complex bind to the rough endoplasmic reticulum translocon where translation continues with the protein forming in the rough endoplasmic reticulum membrane. Following translation, the protein is processed in the endoplasmic reticulum by a signal peptidase, which removes that short signal peptide. Ribosomes at this point may be released from the rough endoplasmic reticulum back into the cytosol.

The membrane of the rough endoplasmic reticulum links to the outer layer of the nuclear envelope ([Figure 1.1.1](#)). While there is no continuous membrane between the endoplasmic reticulum and the Golgi apparatus, transport vesicles shuttle translated proteins between these two compartments. Transport vesicles are surrounded by coating proteins called COPII, which target vesicles to move proteins to the Golgi apparatus to complete processing.

The rough endoplasmic reticulum has multiple functions. These include manufacture of enzymes and secreted proteins. Glycosylation is the process whereby sugars are added to proteins as side chains. Initial glycosylation of proteins, as in N-linked or Asn-linked glycosylation, occurs in the rough endoplasmic reticulum. Glycosylation continues in the Golgi apparatus. If the protein is properly folded, a glycosyltransferase adds a root 14-sugar backbone (2-N-acetylglucosamine, 9-branching mannose, and 3-glucose at the end) to Asn residues. The root oligosaccharides are processed further in the rough endoplasmic reticulum and Golgi apparatus to make the final glycosylated protein.

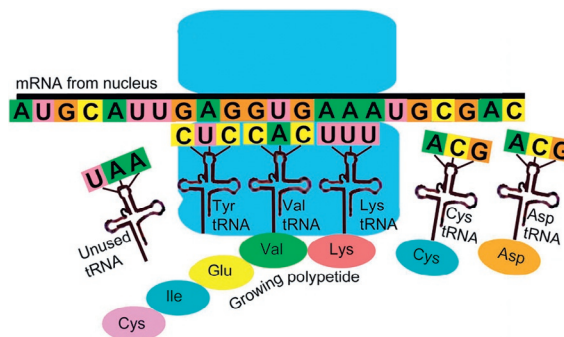


FIGURE 1.1.5 Translation of mRNA into polypeptide sequence occurring in ribosomes.

SMOOTH ENDOPLASMIC RETICULUM

The smooth endoplasmic reticulum functions in many metabolic processes. It synthesizes lipids, phospholipids as in plasma membranes,

and steroids. Cells that secrete these products, such as cells of the testes, ovaries, and skin oil glands, have an excess of smooth endoplasmic reticulum. The smooth endoplasmic reticulum also carries out the metabolism of carbohydrates and steroids. In muscle cells, the smooth endoplasmic reticulum regulates calcium ion storage. The smooth endoplasmic reticulum like the rough endoplasmic reticulum is connected to the nuclear envelope. The smooth endoplasmic reticulum comprises tube-like structure located near the cell periphery. These tubules or tubes sometimes branch forming a network that is reticular in appearance. The network of smooth endoplasmic reticulum allows for an increased surface area to be devoted to storage of key enzymes.

GOLGI APPARATUS

The Golgi apparatus is an organelle found in all animal cells (Figure 1.1.6). It was first identified in 1897 by the Italian physician Camillo Golgi and thereafter named after him. The Golgi apparatus plays an important role in the synthesis of proteoglycans, mixtures of amino acids and sugars, which are molecules present in the extracellular matrix of animals. It is also a major

site of carbohydrate synthesis or glycosylation of proteins. Proteins are *O*-glycosylated in the Golgi apparatus and *N*-glycosylation is completed in this organelle. This includes the production of glycosaminoglycans, long unbranched polysaccharides the Golgi then attaches to a protein synthesized in the endoplasmic reticulum to form proteoglycans.

Another task of the Golgi involves the sulfation of certain molecules passing through its lumen via sulfotransferases that gain their sulfur molecule from a donor called PAPS (3'-phosphoadenosine-5'-phosphosulfate). This process occurs on the glycosaminoglycans of proteoglycans as well as on the core protein. Sulfation is generally performed in the trans-Golgi network. The level of sulfation is very important to proteoglycan signaling abilities as well as giving the proteoglycan its overall negative charge.

Transport vesicles carry proteins from the rough endoplasmic reticulum to the cis face of the Golgi apparatus, where they fuse with the Golgi membrane and empty their contents into the Golgi lumen. Once inside the lumen, the molecules are modified, glycosylated, or sulfated, then sorted for transport to their next destinations.

LYSOSOMES

The lysosomes are spherical vesicles each containing hydrolytic enzymes, which are capable of breaking down or degrading virtually all kinds of biomolecules, including proteins, nucleic acids, carbohydrates, lipids, and cellular debris. Lysosomes contain more than 50 different enzymes, which are all active at an acidic environment of about pH 5.0. Thus, they act as garbage dump system of the cell by digesting unwanted materials, whether proteins, carbohydrate, nucleic acid, or other cell debris in the cytoplasm.

Enzymes of the lysosomes are made on the ribosomes of the rough endoplasmic reticulum.

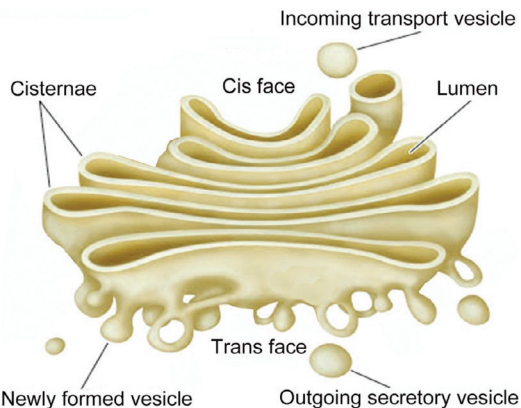


FIGURE 1.1.6 The Golgi apparatus.

The enzymes are released from Golgi apparatuses in small vesicles that ultimately fuse with lysosomal acidic vesicles. Extracellular materials such as microorganisms taken up by phagocytosis, macromolecules by endocytosis, and unwanted cell organelles are fused with lysosomes in which they are broken down to their basic molecules. Thus, lysosomes are the recycling units of a cell. Synthesis of lysosome enzymes are controlled by nuclear genes. Mutations in the genes for these enzymes are responsible for more than 30 different human genetic diseases, which are known as lysosomal storage diseases.

MITOCHONDRION

Mitochondrion is considered to be the power stations of animal cells, in that this is the site of production of adenosine triphosphate (ATP), the power source of all animal energy. ATP is cleaved to form adenosine diphosphate (ADP) to release the bond energy. The ATP power source generation is driven by a remarkable ionic process called oxidative phosphorylation, which is driven by the oxygen we breathe and NADH and FADH₂ from sugar degradation. [Chapter 1.2](#) examines oxidative phosphorylation. Oxidative phosphorylation in mitochondria follows the equation of life, $1\text{Glucose} + 6\text{CO}_2 + 38\text{ADP} \rightarrow 6\text{CO}_2 + 6\text{H}_2\text{O} + 38\text{ATP}$.

The number of mitochondria in a cell varies widely by organism and tissue type. Many cells have only a single mitochondrion, whereas others can contain several thousand mitochondria, depending on the energy needs of the cell. Mitochondria are composed of compartments that carry out specialized functions, and include the outer membrane, the intermembrane space, the inner membrane, and the cristae and matrix.

Although most of a cell's DNA is contained in the cell nucleus, the mitochondrion has its own independent genome stored in a circular DNA loop in the mitochondrion. Mitochondrial

DNA codes for mitochondrial proteins. Oddly, mitochondria and mitochondrial DNA is strictly inherited through the reproduction pathways from the mother only.

Many enzymatic pathways occur in the mitochondrion, generally those involving ATP. The citric acid loop or Krebs cycle, the key pathway of acetyl-CoA usage and conversion of sugars to CO₂, and generation of energy (NADH and FADH₂) occurs inside the mitochondrion, as does fatty acid β -oxidation, a pathway that generates much ATP.

The concentrations of free calcium in the cell can regulate an array of reactions and is important for signal transduction in the cell. Mitochondria can transiently store calcium in a cell. Mitochondrion also controls cell apoptosis or cell death in a cell. An ion channel is formed on the outer mitochondrial membrane in response to certain apoptotic stimuli (see [Chapter 2.3](#) Apoptosis, Growth, and Aging).

MICROTUBULES AND CENTRIOLES

Microtubules are a part of the cellular skeleton, found throughout the cell. These tubular polymers are made of the protein tubulin and grow an average length of 25 μm . The outer diameter of a microtubule is about 24 nm, while the inner diameter is about 12 nm. They are found in all animal cells and are formed by dimers of two globular proteins, α and β -tubulin. Microtubules are important in a number of cellular processes. They are involved in maintaining the structure of the cell and, together with microfilaments and intermediate filaments, form the cellular skeleton. Microtubules provide platforms for intracellular transport and are involved in a variety of cellular processes, including the movement of secretory vesicles within a cell. They are also involved in cell division (mitosis and meiosis), including the formation of mitotic spindles, which are used to pull apart chromosomes.

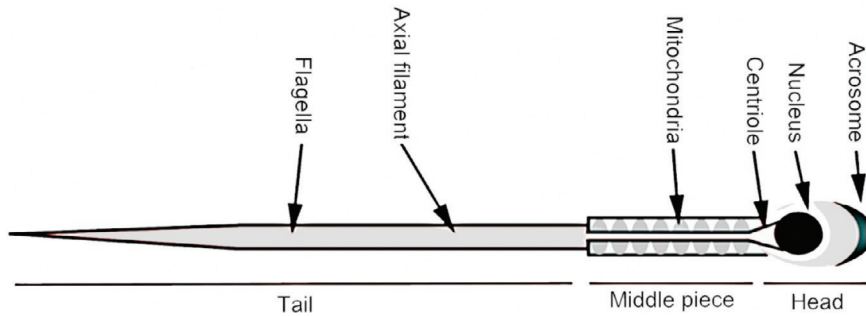


FIGURE 1.1.7 Spermatozoon.

Centrioles are made from tubulin or microtubules. They form cylindrical structure from nine sets of microtubule triplets, arranged in a cylinder. Centrioles are involved in the physical division of cells, in the organization of the mitotic spindle.

CELLS, CELLS, AND MORE CELLS

Cells have hundreds of shapes in the human body serving different purposes and functions. Looking, for instance at a spermatozoon or mature sperm cell, the nucleus is in the head of the spermatozoon and the mitochondrion or power source is all together in the middle piece of the spermatozoon to provide power axial filament movements (Figure 1.1.7).

The erythrocyte or red blood cell is a cell with no nucleus at all and therefore is missing most other cellular organelles. All the space is used for storing the protein hemoglobin. The erythrocyte cannot divide or make itself and is made by bone marrow cells. The erythrocyte in humans is the principal means of delivering oxygen to the body tissues via the blood flow through the circulatory system. Many extreme cells are found in humans all basically built around the structure shown in Figure 1.1.1. Spermatozoon and erythrocytes are examples of extreme cells.

CHAPTER KEYWORDS

Know these keywords and what each word refers to as well as its function. Read over the list. Are all these keywords familiar?

- Bilayer
- Centrioles
- Chromatin
- Cis-Golgi
- Cytoplasm
- COPII coating proteins
- Erythrocyte
- Golgi apparatus
- Golgi cisternae
- Golgi lumen
- Lysosome
- Messenger RNA
- Microtubules
- Mitochondrion
- Nuclear pores
- Nuclear envelope
- Nucleus
- Nucleolus
- Plasma membrane
- Phospholipid
- Ribosome
- Ribosomal RNA
- Root 14 sugar backbone
- Rough endoplasmic reticulum

Secretory vesicle
 Smooth endoplasmic reticulum
 Spermatozoon
 Trans-Golgi
 Transfer RNA
 Transport vesicle

INTERNET REFERENCES

Use these references to find out more.

en.wikipedia.org/wiki/Nucleolus
en.wikipedia.org/wiki/Cell_nucleus
en.wikipedia.org/wiki/Endoplasmic_reticulum
en.wikipedia.org/wiki/Ribosome
en.wikipedia.org/wiki/Golgi_apparatus
en.wikipedia.org/wiki/Mitochondrion
en.wikipedia.org/wiki/Microtubule
en.wikipedia.org/wiki/Centriole
en.wikipedia.org/wiki/Spermatozoon
en.wikipedia.org/wiki/Red_blood_cell

CHAPTER QUIZ

Answer these questions. Do you know the answers, holy cow! Check yourself out in this quiz, and prove that you are a humanology wiz.

1. The nucleolus is located where and does what?
 - a. Located on smooth endoplasmic reticulum, site of mRNA translation
 - b. Located in lysosome, responsible for transport within cell
 - c. Located within the nucleus, site of ribosome assembly.
 - d. Located in plasma membrane, responsible for receptor synthesis
 - e. Located adjacent to plasma membrane, processes ribosomal RNA
2. What is a lysosome, what is its function?
 - a. Vesicles containing hydrolytic enzymes to degrade molecules
 - b. Part of plasma membrane, permits anions to assess cells
 - c. Vesicles that control transport of molecules within cells
 - d. Site of production of ribosomes
 - e. Site of production of ribosomal RNA
3. Mitochondrial cytochromes are coded for by:
 - a. Chromosomes in the nucleus
 - b. Mitochondrial circular DNA
 - c. By mRNA on the endoplasmic reticulum
 - d. By lysosomal DNA
 - e. None of the above
4. The mitochondrion of cells is the site of:
 - a. Glycolysis and the citric acid cycle
 - b. Oxidative phosphorylation and apoptosis regulation
 - c. Apoptosis regulation and fatty acid synthesis
 - d. Protein synthesis and fatty acid degradation
 - e. Glycolysis and gluconeogenesis
5. The plasma membrane contains:
 - a. Phospholipids and imbedded sugars
 - b. Phospholipids and imbedded proteins
 - c. DNA and microzymes
 - d. Imbedded proteins and sugars
 - e. Imbedded proteins and DNA