Dear Editor,

Please find enclosed a modified and complete version of my high school textbook chapter manuscript “The Basics of Cancer”. To address the concerns and comments raised by the 5 reviewers, I have made the following changes to improve my manuscript. I hope these changes further clarify my manuscript and make it acceptable for publication in Microreviews in Cell and Molecular Biology.

Sincerely,

Taytum Crockett

**Reviewer 1:**

1. I found the comments from this reviewer to be helpful and encouraging. This reviewer wanted me to provide more sources, as well as further explain severity and death rate of cancer.
2. I did not make any changes to my manuscript regarding these comments. As most of my chapter was explaining the basics behind cancer, I found a vast majority of talking points from the National Cancer Institute website. I did not further explain the severity and death rate because I did not want to make my chapter lengthier, and also felt that it would disrupt the overall flow of my manuscript.

**Reviewer 2:**

1. I found the comments of this reviewer to be helpful and encouraging. This reviewer wanted me to provide more sources, as well as further explain the key terms I used in my manuscript.
2. Again, I chose to not provide more sources for the same reasoning for reviewer 1. However, I did provide definitions at the end of my chapter for all the key terms I used.

**Reviewer 3:**

1. I found the comments of this reviewer to be encouraging. The reviewer provided no comments as to what they would like to see improved.
2. I did not make any changes to my manuscript based on this reviewer.

**Reviewer 4:**

1. I did not find the comments of this reviewer to be helpful. They wanted me to provide my opinion on my topic.
2. I did not make any changes to my manuscript based on this reviewer. As this is an informational manuscript, I do not want to provide my personal opinion on the topic.

**Reviewer 5:**

1. I found the comments of this reviewer to be encouraging. The reviewer provided no comments as to what they would like to see improved.
2. I did not make any changes to my manuscript based on this reviewer.

The Basics of Cancer

**Introduction**

What is cancer? You have more than likely met or know of someone who has this disease, as it is very prevalent around the world today. **Cancer** is the condition in which cells grow uncontrollably at any location in the body. This is a genetic disease, which occurs in the body because of uncontrollable cell division, damage to the body’s DNA due to **carcinogens**, or gene inheritance. Normally, the body is able to identify cells that have damaged DNA and kill those cells before they can become cancerous, but that is not always the case. Cancer cells have adapted in order to grow without a signal to do so, ignore signaling altogether, spread to different areas of the body, and have even found a way to tell the immune system to keep them alive and help them grow.

**The Body’s Cells and Cancer**

There are many different cells that make up the human body, and all of these cells can be involved in the formation and development of cancer. **Somatic cells** are any type of cell located in the body that is not a sperm or egg cell. Some examples of these cells include blood cells, skin cells, and connective tissue cells.

 There are three different types of skin cells that are involved in the development of cancer formation. **Basal cells**, which are located at the bottom portion of the epidermis (the outer layer of the skin), are constantly dividing in order to replace squamous cells. In other words, basal cells eventually become squamous cells. **Squamous cells**, which are located at the top portion or the epidermis, are constantly shedding and being replaced. When you get a sunburn after being outside in the summer, your skin starts to peel and gives way to a newer layer of skin underneath. This is an example of how squamous cells shed, which are then replaces by basal cells. **Melanocytes**, which are located in between basal and squamous cells, produce the brown pigment melanin, which is responsible for our skin color.

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| Epidermis |
|  Dermis |
| Subcutis |

 Squamous cells

 Melanocytes

 Basal Cells

Figure 1. **Layers of the skin**. There are three layers of the skin, epidermis, dermis, and subcutis. The three different types of cells that make up the epidermis of the skin include squamous cells, melanocytes, and basal cells.

 Our body contains both innate and adaptive cells, which are white blood cells that are responsible for immunity. All of these cells can help the body fight cancer but can also become cancerous themselves. **Innate cells** are the first line of defense in our body that are responsible for **innate immunity**, which we were born with. **Natural killer cells** are a type of innate cell that can kill both infected and tumor cells by exposing them to enzymes that are harmful to them. Another type of innate cell, **macrophages**, engulf and kill foreign pathogens and other harmful organisms. **Neutrophils** are a type of innate cell that helps our body fight against infection, and they are often our immune system’s first responder. They locate and travel to the infection site, ingest the harmful organisms responsible for the infection, and release enzymes to kill them. **Dendritic cells** and **mast cells** are other innate cells that boost the immune system’s response and play a role in exactly *how* our immune system responds.

 The second line of defense in our body are called adaptive cells, which are responsible for **acquired immunity**. We develop acquired immunity through exposure to foreign pathogens and vaccines. This allows our adaptive immune system to identify and respond to foreign pathogens that our innate immune system does not recognize or cannot kill. Our adaptive immune system is made up of **T lymphocytes** (T cells) and **B lymphocytes** (B cells), both of which develop from our stem cells in the bone marrow, and work to determine our immune response specificity.

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| **INNATE IMMUNITY CELLS** | **FUNCTION** |
| Natural killer cells | Kill infected cells by exposing them to enzymes |
| Macrophages | Engulf and kill foreign pathogens and other harmful organisms |
| Neutrophils | Help fight infection and are the immune system’s first responder |
| Dendritic cells | Boost the immune system’s response |
| Mast cells | Help determine how the immune system should respond |
| **ADAPTIVE IMMUNITY CELLS** | **FUNCTION** |
| T lymphocytes (T cells) | Determine immune response specificity |
| B lymphocytes (B cells)  | Determine immune response specificity |

Figure 2. **Types of immunity cells and their functions**. The body has both innate and adaptive immune systems that contain different types of cells to help them function.

 While there are hundreds of different types of cells that our body produces, this is just a small example of types of cells that can continue to grow unchecked, eventually turning cancerous.

**Genes and Cancer**

 As mentioned earlier in the chapter, cancer is a genetic disease due to uncontrollable cell division, damage to the body’s DNA due to cancer causing agents, or genetically inherited through our parents. All of these factors are a result of or can lead to gene mutation, which then results in the development of cancer. Though there are many genes that play a role in cancer, there are four different genes that are more prevalent than the others.

 **Proto-oncogenes** are genes that are involved in normal cell growth and division in the body. However, if proto-oncogenes are mutated or have drastically increased activity, they can become an oncogene. **Oncogenes** are mutated forms of proto-oncogenes, which leads to abnormal cell growth. In other words, oncogenes are the genes that are responsible for the development of cancer. **Tumor suppressor genes**, which make tumor suppressor protein to control cell growth in the body, are another type of gene that can mutate and lead to cancer. After mutation, tumor suppressor genes tend to make less tumor suppressor protein, leading to abnormal cell growth. Inside the nucleus contains a protein that aids in the control of both cell division and cell death. This protein is made by the **p53 gene**, which can mutate and lead to cancer. Mutation of the p53 gene usually decreases the amount of protein that is produced, which can lead to abnormal cell division.

**Types of Cancer**

 Due to the many different types of cells that can mutate and turn cancerous, there are many different types of cancer that the body can develop. The different types of cancer in the body are directly related to where exactly they are located.

 **Carcinoma** is a type of cancer that is located in the skin or the tissue lining of internal organs. This is the most common type of cancer, and it is usually caused by exposure to ultraviolet (UV) rays from the sun. Another type of skin cancer is called **melanoma**. As mentioned earlier in the chapter, melanocytes are the cells that produce melanin for our skin color. Melanoma usually appears as a mole on the body due to the overproduction of melanin. This type of skin cancer is usually caused by exposure to UV rays and the use of tanning beds or lamps.

 **Sarcoma** is a type of cancer that is located in the body’s bone and soft tissues such as fat, muscle, and cartilage. DNA mutations of these tissues are usually due to exposure of chemicals that cause cancer or radiation. Another type of tissue cancer, known as **Leukemia**, is a type of cancer that occurs in the body’s blood-forming tissue (bone marrow). DNA mutations of blood cells generally lead to an increased number of abnormal blood cells being produced in the body.

**Lymphoma** is a type of cancer located in the body’s immune system cells. This type of cancer develops when a lymphocyte mutates and begins to grow rapidly. **Multiple myeloma** is another type of cancer that is located in the bone marrow, which is caused by increased growth of unusual plasma cells.

The rapid cell growth and division that causes cancer can lead to **tumors**, which is an abnormal tissue mass made up of cancer cells. There are many different types of tumors that can develop, and they can be either cancerous or **benign** (not cancerous). Examples of such tumors are brain tumors, neuroendocrine tumors, and spinal cord tumors. Brain tumors are due to abnormal cell growth in the body’s brain tissue, and spinal cord tumors are due to abnormal cell growth in or next to the body’s spinal cord. Neuroendocrine tumors are a little more complex than just abnormal cell growth. These tumors are normally located in the gastrointestinal tract of the body and are a result from overproduction of cells that release different hormones in response to what the body’s nervous system instructs it to do.

As mentioned earlier in the chapter, cancer cells have found a way to spread to different areas of the body. **Metastasis** (metastatic cancer) is the spread of cancer cells from the site of first formation to somewhere else in the body. This does not cause a new type of cancer to form, so if the individual has lung cancer and those cells spread to the pancreas, that individual is still considered to only have lung cancer.

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| **MOST COMMON CANCER TYPES AROUND THE WORLD** |
| Breast cancer |
| Lung cancer |
| Prostate cancer |
| Colon/rectum cancer |
| Melanoma |
| Bladder cancer |
| Non-Hodgkin lymphoma |
| Kidney/renal cancer |
| Endometrial cancer |
| Leukemia |
| Pancreatic cancer |
| Thyroid cancer |
| Liver cancer |

Figure 3. **Most common types of cancer around the world**. According to the National Cancer Institute, this is the list of the most common types of cancer around the world in 2020.

**Testing for Cancer**

 With the development and progression of cancer, medical professionals and researchers have developed different types of testing methods that are used to diagnose cancer. Testing for cancer can be achieved by **imaging**, **biopsy**, and laboratory testing.

 Different imaging techniques used to test for cancer include computerized tomography (CT) scans, bone scans, magnetic resonance imaging (MRI), positron emission tomography (PET) scan, ultrasounds, and x-rays. Imaging techniques allow medical professionals to view the body’s bone and organs, allowing them to locate where cancer is located in the body. Imaging also helps to see if the cancer has spread and what stage the cancer is in.

 A biopsy allows medical professionals to test for cancer in the body by analyzing it for abnormal cell growth. For instance, if it is suspected a person has skin melanoma because of the abnormal shape of a mole, that individual’s doctor will remove a portion of that mole and send it to a laboratory for testing. Biopsies can also be achieved by removing a suspected bodily fluid, such as plasma, with a needle and sent to a laboratory for testing.

 Along with biopsies, there are other laboratory tests that allow medical professionals to test for cancer. An individual suspect to have cancer, such as bladder cancer, may have to have a blood or urine sample sent to a laboratory in order to identify any abnormalities in the body that may be caused by a cancer that is not seen by imaging or biopsy.

Due to the vast number of different types of cancer, a person may be only subject to one type or all types of testing.

**Treating Cancer**

 Although there have been many advancements and improvements in medical technology, medical professionals have yet to find a cure for cancer. Though there is no cure, there are different types of treatments an individual with cancer may go through. Medical professionals and researchers have also discovered some successful preventatives for cancer that is advised to people all over the world.

 Surgery, chemotherapy, and radiation therapy are some of the most common cancer treatments that an individual may go through. When going through a surgical procedure, most individuals hope to remove as much cancer in their body as possible. Surgery is usually used for tumor removal in different parts of the body. **Chemotherapy**, which is the use of a specific type of drug to kill cancer cells, in the most common method of cancer treatment. Some examples of chemotherapy drugs include Altretamine, Carboplatin, and Cisplatin, and they can be used alone or as a combination. **Radiation therapy** is the use of energy beams (radiation beams) to shrink different types of tumors and kill cancer cells.

 Some other examples of cancer treatment include bone marrow transplant, hormone therapy, immunotherapy, and cryoablation. Bone marrow transplants are used in hopes of a donor’s stem cells to replace damaged stem cells of the patient. Hormone therapy aims to remove or block different hormones in the body to stop cells from growing, and **immunotherapy** utilizes and individual’s immune system to help fight or kill cancer cells. Some examples of immunotherapy include in situ vaccines, nanoparticles, and checkpoint inhibitors. **Cryoablation** is a cancer treatment procedure that repetitively freezes and thaws cancer cells in order to stop them from growing and killing them.

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| **TYPE OF CANCER THERAPY** | **HOW IT WORKS** |
| Chemotherapy | Uses drugs in order to kill cancer cells and shrink tumors |
| Radiation therapy | Uses sources of high energy radiation in order to kill cancer cells and shrink tumors |
| Immunotherapy | Uses different substances to help an individual’s immune system fight cancer |
| Cryoablation | Uses freezing methods to stop the growth of cancer cells and kill them |

Figure 4. **Types of cancer therapy and their method of action**. According to the National Cancer Institute, these are basic methods of cancer therapy and how they are used to treat or kill cancer.

 Medical professionals and patients alike hope to prevent cancer from occurring as much as possible. Preventative measures include using sunscreen when going outside into the sun, avoiding tobacco products such as cigarettes and chewing tobacco, maintaining a healthy diet and exercise regimen, receiving all suggested vaccinations, and attend routine doctor’s office visits.

 Cancer is a frightening disease that many people hope to never have, and that many hope to beat. There are numerous factors that lead to the formation and further development of cancer, and medical professionals are still unsure as to what exactly causes specific types of cancer. Will we ever live in a cancer free world? With the continuation of medical advancements, as well as the increase of the survival rate, there is a possibility.

**Key Terms**

**Acquired immunity:** immunity that has developed once the immune system responds to a foreign substance, microorganism, or antibodies

**B lymphocytes:** a white blood cell that is responsible for the production of antibodies

**Basal cells:** small cell that makes up the epidermis

**Benign:** tumors that are not cancerous

**Biopsy:** removal of a tissue or cell sample for a pathologist to examine for cancer

**Cancer:** disease in which cells divide uncontrollably

**Carcinogens:** a substance that causes cancer

**Carcinoma:** a type of cancer that starts out in the skin or tissues of internal organs

**Chemotherapy:** a type of cancer treatment that utilizes drugs to stop the uncontrollable growth of cancer cells

**Cryoablation:** a procedure that freezes and destroys abnormal or cancerous tissue

**Dendritic cells:** cells found in body tissue that boost the immune response

**Imaging:** process of taking pictures inside the body

**Immunotherapy:** a type of cancer treatment that uses different substances to either suppress or stimulate the immune system

**Innate cells:** white blood cells that mediate innate immunity

**Innate immunity:** immunity that a human is born with

**Leukemia:** cancer that begins in blood-forming tissues (such as bone marrow)

**Lymphoma:** cancer that begins the immune system cells

**Macrophages:** a white blood cell that kills microorganisms and removes dead cells

**Mast cells:** a white blood cell that is found in connective tissue, which plays a role in the immune system response

**Melanocytes:** a type of cell located in the skin (and eyes) that produces melanin

**Melanoma:** a type of cancer that begins in melanocytes

**Metastasis:** the spread of cancer cells from the origin to another part of the body

**Multiple myeloma:** a type of cancer that starts in plasma cells

**Natural killer cells:** immune cells that contain granules loaded with enzymes the can kill either virus-infected cells or tumor cells

**Neutrophils:** a type of white blood cell that helps the body fight infection

**Oncogenes:** mutated form of a gene involved in normal cell growth

**p53 gene:** a gene that creates a protein that plays a key role in the control of cell division and cell death

**Proto-oncogenes:** gene involved in normal cell growth

**Radiation therapy:** a type of cancer treatment that uses high-energy radiation sources to shrink tumors and kill cancer cells

**Sarcoma:** a type of cancer that starts in bones and soft tissues

**Somatic cells:** all cells in the body that are not reproductive cells

**Squamous cells:** a cell found in tissues such as skin, as well as the lining of organs, the respiratory tract, and the digestive tract

**T lymphocytes:** a white blood cell that helps protect the body from infection

**Tumor:** an abnormal tissue mass that forms when cells are growing uncontrollably

**Tumor suppressor genes:** a gene that makes tumor suppressor protein to help control cell growth

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