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Bioengineering and the Immune System: Engineering Super Cells

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Introduction

The immune system is at the heart of human health. The immune system's ability to protect our body from disease and intruders is extraordinary. This unit curriculum is designed to teach students the ways in which the body's immune system fights disease and battles intruders. As a way of teaching these multifaceted concepts, analogies which are familiar to the students will be used to teach the various jobs of the different immune cells. First, students will examine the specific role of each type of cell of the immune system in order to develop an understanding of the interdependence and complexity of these relationships. Through this examination, students will cultivate an understanding for malfunctions that can occur within the immune system and begin to think about ways to solve these malfunctions. Tuning the response and function of the immune cell will be the focus as students explore. Next, students will use the engineering design process to find solutions and solve problems that occur within this system. The engineering design process will offer a framework for students to explore, manipulate, and reorganize the forms and functions of immune cells. Students will work collaboratively in teams in order to analyze the parts of the cells and think about new ways to organize the structures of the cells which would enhance the function of the cells. Furthermore, students will experiment with various materials and technology to improve their designs of newly engineered cells. Finally, students will apply their knowledge and imagination to build a model of a cell, engineering an improved immune cell that would enhance the immune system or to solve a particular problem. Harnessing the power of these mighty defenders, students will create their own super cell.

Rationale

I teach fourth grade at John S. Martinez Elementary School in New Haven, Connecticut. My class is comprised of approximately twenty-seven students of whom 98% are Hispanic. John S. Martinez is in an urban setting where the students are from low income families. Within the classroom, my students are strapped with the demands of testing: Smarter Balance Testing (SBAC) as well as district math assessments, reading and language arts assessments. Because of the pressure of assessments, reading, writing, mathematics, social studies, and science compete for center stage, often squeezing the science curriculum to its bare bones. Students are unprepared for the rigors and expectations of the 21 st Century.

The expectations of the 21 st Century are high, as we are living in an age of exploration and enlightenment where the collaborative forces of science and technology offer access to a steady stream of new information; building, continuously sharing, propelling us forward toward to explore solutions for our greatest challenges. The challenges of world health, sickness, and disease can be addressed in new ways as we learn to access and use this plethora of information. Specifically, bioengineering the immune system is a new frontier in medicine. Breakthroughs can apply the tools of medicine and bioengineering; creating solutions that enhance the immune system to fight disease, infection, and cancers. This curriculum unit will infuse science, technology, engineering, and math into a curriculum unit, through the study of the immune system. Immersion into bioengineering will provide an opportunity for students to learn and practice the language, build wonder, foster excitement, and ignite a thirst for knowledge, quenching it as they work to find solutions. Ultimately, students will develop confidence and belief in their ability to ask questions, access information, and problem solve to find answers as they facilitate their own learning in their pursuit to design cells that improve the cells of the immune system, these mighty defenders of health.

Students will begin with the study of the body's immune system, its functions, and structures. Then, students will take a closer look at the different cells involved in the immune system and their functions. Specific roles of cells and the parts that these cells play in the system will be examined. In addition to studying the physical and structural differences of the various cells, how the immune system keeps the systems in balance will be studied. How does our immune system respond to pathogens? An exploration of causes for systems to break down and how these break downs could be corrected will be considered. Students will also learn about the effects of a weak immune system which may result in disease. Through multiple discussions, research, and activities students will learn about the causes of specific immune system failures as well as the groundbreaking solutions offered through bioengineering, genetic therapies, and drug delivery interventions. Since the opportunity to move through a cell membrane offer dynamic changes in cell behavior, nanotechnology will be introduced as a way of getting into the cell and solving these problems on the cellular and molecular level.

Building on this knowledge, students will study the relationships between the cells of the immune system and intruders through the use of analogy. The analogies to be used will be that of the different people and their roles within the community that keep the community safe. Familiar roles of defenders and protectors who live within the community will be used. Firemen, policemen, swat teams, doctors, and rescue workers will be employed to draw connection to the functions and relationships within the immune system. In addition to the relationships between these defender and invaders, students will think about the kinds of materials and technologies that help these defenders to rescue, guard, and protect. As students examine and explore these ideas, they will question how these materials and technologies enhance the effectiveness of one's job to protect and defend or increase efficiency, improving positive outcomes within the community system. Next, students would apply these ideas to cells within the immune system to enhance their functions. For example, a police officer wears a bullet proof jacket to protect himself again intrusive and deadly bullets. Might it be possible for a cell to have a bullet proof shield to protect it from a deadly invasion? Tasers paralyze. Can a cell be tasered or act like a taser itself, immobilizing a pathogen? Transceivers help to locate, rescue and find victims quickly. Can this concept be applied to finding a virus that eludes detection? Firemen wear protective gear specific to their conditions, such as extreme heat. Rescuers work as a team, communicating information quickly and often in order to be successful. Can communication be altered, blocked, or enhanced?

Students can also look to nature to find engineering solutions, noticing how nature offers solutions of its own. It is abundant in its models of remarkable and functional designs. For example, sea anemone have a poisonous coating which stops predators from consuming it. Additionally, students will look to the immune system itself to find ideas for tactics, strategies, and designs for specific obstacles. Finally, students will be encouraged to stretch their thinking and apply their knowledge to solve a problem. Student would strive to improve the immune system through the engineering design process. Harnessing the all that they have learned, students would engineer a super cell.

Pathogens

The central job of our immune system is to protect and defend our body against pathogens, or microscopic organisms. When pathogens invade our body, they can cause sickness and disease. Three major groups of pathogens are fungi, bacteria, and viruses.

Pathogenic fungi are eukaryotic microorganisms and are usually part of the plant kingdom which include molds and yeasts. Fungi produce spores and grow well in warm, dark, moist areas living on dead tissue. These conditions occur often between your toes or under your nails after long days covered with warm, sweaty socks. As a result, a common fungal infection called athlete's foot occurs. Other fungal infections are yeast infections and ringworm. Most fungal infections are eradicated by the immune system without notice, but when the immune system is compromised or suppressed, as with AIDS, fungal infections can take hold. Fungal infections are much more difficult to treat because of their eukaryotic cell structure. Unlike bacteria, fungi do not respond well to antibiotics and need to be treated with highly toxic chemicals. [1]

Bacteria, commonly referred to as, "germs", are single-celled, prokaryotes. Prokaryotes are microorganisms with no nucleus. They are living organisms able to move, eat, and reproduce. Bacteria are able to reproduce with incredible speed. In fact, one bacterium can become millions in just a few hours. [2]

There are many kinds of bacteria. Some are "good" bacteria, which aid in maintaining health and some bacteria are "bad" and can make you very sick. In actuality, we can live in harmony with thousands of good bacteria on our skin and in our intestines. For example, the good bacteria that live in the intestines help to break down food. However, harmful bacteria, called bacterial pathogens, can make you very sick. One example of a bacterial pathogen that can enter your body is the streptococcus bacteria. This bacterium is able to live on surfaces and can enter your body through the mouth. Upon entering the mouth, this bacterium directly invades the cells in your throat and kills them, which causes strep throat. Other bacterial pathogens can destroy cells indirectly by producing toxins when they replicate. Lyme disease is another example of an illness caused by bacterial pathogen which enters the body through the bite of a deer tick. Other harmful bacteria can enter the body through your airways. Examples of these bacterial pathogens are tuberculosis, meningitis, and chicken pox. Tuberculosis lives in the water droplets in the air and can cause infection when it is breathed into the lung tissue. Still other bacteria gain entry through the water and food we eat and drink. E coli and cholera are two examples of these deadly pathogens. There are many good bacteria, but our immune system is in a continuous battle against a host of bacterial pathogens as they try to gain entry into our body.

A virus is a tiny piece of DNA covered with protein. Although bacteria and viruses are both pathogens, they are very different. Viruses are much smaller than bacteria and can pass through small places that would filter out bacterial pathogens. Unlike bacteria, viruses are not considered to be alive. As a result, viruses are not able to reproduce like bacteria. Instead, a virus must take over a living cell and use its parts to replicate. The way a virus takes over a cell is by attaching itself to the cell membrane and then injecting its DNA into the cell. Next, the viral DNA uses the cell's parts to copy itself. In this way, the viral DNA hijacks the living cell's DNA and uses it to clone itself. The virus then continues to replicate in the host cell, like a factory, until the cell membrane can no longer contain this expanding volume. At this point, the infected cell explodes. This bursting event releases about 10,000 [3] viral clones, freeing them from the cell to find and infect new host cells. In this way, the viral pathogens are able to invade, multiply, and then simultaneously destroy their host cell while releasing thousands of new clones to invade new host cells. Carl Zimmer suggests that there are over 10 million times more viruses than there are stars in the universe . Imagine the spectrum of illness and diseases these viral pathogens cause. Some examples of a viral illnesses cause by these pathogens are influenza, rabies, herpes, hepatitis, and AIDs. Since, these viral infections are so challenging for the immune system, they are important foci of bioengineers.

The Immune System

Our immune system is a highly complex interconnected network of cells, vessels, and organs designed to fight pathogens and maintain our health. The immune response maintains our health as it applies three increasing levels of response to invading pathogens. Furthermore, these responses involve a wide range of extremely intelligent immune cells working together throughout the body. The circulatory system, the immune system, and lymphatic system collectively provide immune cells access to defend and protect every crevice of our anatomy where if needed, these amazing cells are able to communicate, organize, and work together in an orchestrated systematic attack on an invader.

The immune system is able to search, find, and destroy pathogens because it has a highly complex defense system which specializes in finding, recognizing, and responding to invaders. The immune system has a brilliant way to communicate, find, and identify a vast array of pathogens. Most importantly, immune cells are able to identify and distinguish between the body tissue, which is referred to as, "self," and invaders as well as infected tissue. Additionally, the immune system has a tiered system of strengthening attacks allowing it to wage war against a plethora of pathogens. To that end, the immune system has an arsenal of specialized troops, or cells that are able to destroy invaders. Furthermore, the immune system is able to remember every pathogen it touches. To summarize, the immune system is made up of a diverse group of highly intelligent cells, designed to carry out specific jobs within this defense process. This fleet of cells works together, communicating and organizing their attack against a pathogen.

Lymphatic System

The lymphatic system is an vital part of the immune system . The central function of the lymphatic system is to filter out and remove waste from body tissue. These waste products may include dead cells, pathogens, and toxins. The lymphatic organs include the lymph nodes, spleen, and thymus. These organs are connected by a network of lymphatic vessels, which act like drainage vessels. These vessels run almost parallel to the blood vessels. The lymph vessels structures are porous and allow immune cells and fluids to move easily between the blood and lymphatic systems. Waste from the bloodstream is able to leak into the lymphatic vessels, like a drainage tube. The lymphatic vessels are filled with a clear fluid called lymph that flows around the body tissue. Lymph fluid bathes body tissue and carries in nutrients. This lymph "bath" as it is referred to, also serves to remove waste materiel and excess fluids from body tissues. The lymphatic system allows immune cells access to tissue throughout the body. The lymphatic system is lined with lymph nodes shaped like small beans. You can easily feel your lymph nodes under your arms, on the sides of your neck, and in the groin. The lymph fluid flows through the lymph nodes carrying the waste products collected from the body tissue and blood. These waste products are filtered out as they flow through the lymph nodes. In this way, the lymph nodes serve as a filter to remove pathogens such as viruses, bacteria, or other foreign matter.. Once caught in the lymph nodes, pathogens are destroyed by white blood cells. When the body is fighting an infection, a lymph node will swell because of the ongoing battle. In addition to being a filtration system, the lymph nodes produce and store white blood cells. Furthermore, when needed, immune cells are released into the lymphatic vessels where they are able to make their way into the blood stream. In this way, the lymphatic system offers the immune cells roadways to access to all body tissue, filters out pathogen waste products, and makes and stores white blood cells the kill trapped pathogens. [4]

The organs of the lymphatic system play a central role in the development of the cascade of differentiated immune cells. The white blood cells, or lymphocytes, originate from stem cells located in the red bone marrow at the middle of our bones. However some immune cells travel to other organs to mature. One of these organs is the thymus, which is located just above the heart. The thymus gland is largest in the early teens and then slowly shrinks in old age to about the size of a grape. T-cells travel from the bone marrow to the thymus where they then develop fully. B-lymphocytes leave the bone marrow and travel to the spleen and lymph nodes, where they continue to produce.

Another organ of the lymphatic system is the spleen. The spleen serves to store and filter blood. This filtration removes and recycles abnormal and dead blood cells. When microbes and toxins are removed , they can activate a specific immune response. [5] To summarize, the lymphatic system plays a vital role in body's defense system, by using its body wide drainage vessels it is able to filter and destroy trapped pathogens and remove waste products. In addition, the lymphatic system is able to produce and deploying immune cells as needed.

Immune System: Search and Recognition

How is the immune system able to find and recognize such small invaders in the vast area of the body? There are three main reasons that the immune system is able to accomplish this feat. The first reason that the immune system is so effective at finding and recognizing invaders so well is because it sends out an exceptionally large number of immune cells that continuously patrol every inch of the body looking for invaders. These patrolling immune cells could be considered the Army. This army of soldier cells called phagocytic cells travel through the blood stream searching for pathogens. You were born with one division of this army, called the innate immune system and acquired the second division, the adaptive immune system, after birth through exposure to pathogens. These immune cells are able to immediately recognize certain microbes and pathogens and then destroy them. [6] The second reason that the immune system is able to find and recognize invaders is because each of these patrolling immune cells has many hyper- sensitive recognition receptors. The receptors could be thought of as little hands that cover each cell. A receptor is able to feel and touch, which allows it to recognize intruders. Each cell carries the equivalent of a thousand receptors or hands. As a result, collectively, these immune cells are able to effectively and to carefully patrol vast areas of the body, by searching, touching, feeling, and thus finding intruders. The third reason that the immune system is able to find and recognize intruders so well are because theses immune cells are very intelligent. Each cell has a very large nucleus , or brain, for thinking. The nucleus is filled with DNA. This brain power allows the immune cell the ability to distinguish between the self and intruder. In conclusion, the reason that the immune system is able to search and find invaders so well is because it is able to send out large numbers of incredibly clever immune cells to patrol the body with hypersensitive receptors that can and find invaders.

Immune Response

Immune cells continuously patrol the body, searching, ready to protect and defend. They patrol the body by traveling in the blood through the circulatory system hunting for and destroying pathogens. Many different immune cells are involved in the events in the battle of the immune response. The immune system is a complex multifaceted system made up of a variety of cells with specific jobs that work together in their tiered response to infection. This tiered defense system has a three tiered attacks that can escalate in its responses. The first line of defense focuses on keeping pathogens out of the body. The second line of defense kicks in when the first line of defense fails and pathogens enter the body. The third line of defense is the immune response, calling in the forces of both T-cells and B-cells. Each of the defensive responses employed by the immune system, relates directly to the battle status between the intruding pathogens and the body. To summarize, the immune response is a brilliant multifaceted, escalating system of organized methodical attacks, which is able to immobilize most pathogens.

First Line of Defense

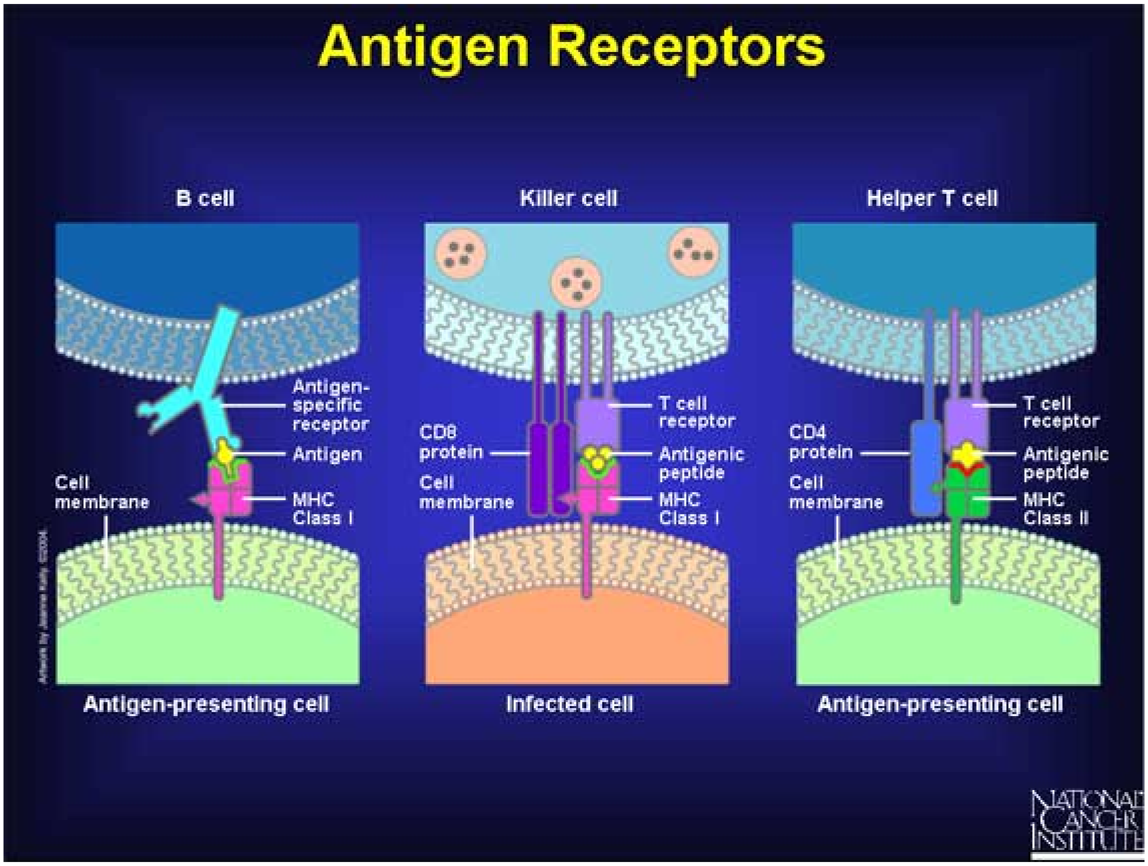
The central purpose of the immune system's first line of defense is to keep invaders out of the body. The immune system protects our body by blocking access to and guarding all points of entry. In this way, many pathogens are denied entrance into our bodies and are destroyed before they are even noticed. The largest organ of our body , our skin is like a wall or barrier covering our body and protecting it in the most fundamental way. There are three reasons why the environment on our skin inhibits the growth of or kills bacterial pathogens. One way the skin inhibits growth of bacteria is because it has a low PH. Another way the skin inhibits growth of bacteria is because the skin is coated with sweat and chemicals that kill bacteria. The third reason that the skin inhibits growth of bacteria on the skin is because the skin is covered with a thick coating of normal good bacterial flora, which crowds out pathogens. Only when the skin is opened by a wound can these pathogens enter. In addition to these three protections, the first line of defense involves guarding the gates of entry. These points of entry or gates are the mouth, the stomach, the nose, and the eyes. At each of these points, the guards serve to expel or destroy pathogens. Invaders are either expelled or destroyed by fluids, or are removed by reflexive actions, like coughs or sneezes, at the gates. One fluid used to guard the gates is mucus. The nose and throat are covered with a sticky mucus membrane that contains antibacterial enzymes which trap and kill pathogens before they are able to enter the lungs. Another fluid that guards the gates of entry is our tears. Our eyes secrete tears that contain an enzyme called lysozyme, which kills bacteria and washes pathogens away. Furthermore, saliva, an acidic fluid composed of destructive chemicals that prevents microbes from growing , guards the entrance of the mouth. Moreover, the stomach is filled with acidic fluids and enzymes that destroy most pathogens if they are ingested . Additionally, reflexive actions like coughing and sneezing will expel pathogens. In conclusion, the central purpose of the body's first line of defense is to provide a strong barrier that will keep out the pathogens or intruders and to guard all gates, or points of entry.

Second Line of Defense: Inflammatory Response

The inflammatory response is the immune system's second line of defense. The primary purpose of the inflammatory response is to get situations under control when the first line of defense fails. This inflammatory response kicks in when pathogens break through the body's barriers and enter the body from a cut, insect bite, or injury. The sequence of events is the same for the entry of all pathogens. However, the speed of the sequence can vary. [7] The first event of this sequence begins when pathogens begin to damage cells. When this occurs, the damaged cells send out chemical signals to "bring in the troops", or white blood cells to the site. Because of this chemical response, blood vessels widen resulting in an increased blood flow to the area allowing large numbers of phagocytes to be transported to the site. In this way, phagocytes, a type of white blood cells, respond to this signal and are transported to the area, flooding the site. Once the phagocytes arrive at the site, they begin the fight by eating anything that is not part of our body. The phagocytes are eating machines. They begin to engulf, digest, and destroy the pathogens. This process is called phagocytosis. In addition to phagocytosis, the inflammatory response uses heat and swelling to battle pathogens. The widen blood vessels and leaking fluid makes the area red, swollen, and warm to the touch. Chemicals released, as part of their immune reaction, also increase body temperature. As a result, the growth of pathogens slows down. [8]

Third Line of Defense: The Specific and Adaptive Immune Response

The third line of defense is activated when the second line of defense breaks down and the pathogens are outnumbering the phagocytes' ability to contain, control, and suppress the growth of pathogens. As a result of this break down, the infection becomes severe enough to cause the body to develops a fever. This fever then activates the third line of defense which is called the specific immune response. This third line of defense acts like calling in the "Special Forces." This defense is waged on two main fronts, and involves cells that are highly trained experts with specialized abilities.



http://www.cancer.gov/cancertopics/understandingcancer/immunesystem/AllPages

In responses to an invasion, or pathogen entering the body, the immune system begins to activate a cascade of multiple processes. This process begins when the macrophages, the patrolling cells, find an invader, or antigen. The macrophage cells engulf and digest the antigen, breaking it up into tiny pieces. Then, the macrophage displays this tiny piece of antigen on its cell surface. These little pieces are called antigen peptides. When an antigen is displayed on the surface of the macrophage cell it is called antigen presenting and plays an important role in the cascade of events of this immune response. Why is this antigen presenting process so important? Through "antigen presenting" the immune cells are able to communicate important information to each other. The antigen presented on the surface of the macrophage communicates the exact shape of the specific invader, or pathogen, to the Helper T-cell. This communication provides essential information needed for the ensuing level of attack.

Thus, the next key event in this sequential immune responses is the activation of Helper T- cells. Helper T-cells are activated (CD4) when they connect to the antigen presenting macrophage. During this connection, the macrophage releases a chemical called interleukin -1, which sends out a distress signal and stimulates the T- helper cells to release a chemical called interleukin -2, which initiates the next level response from the T-cells and B-cells. Also, while the Helper T cell is connected to the antigen presented on the macrophage, it physically senses the exact shape of the antigen. This communication allows the Helper T- cells to make their own protein receptors that will recognize the specific pathogens communicated by the antigen presenting macrophage. The Helper T- cell then displays these protein receptors on their cell surface. In this way, the T helper cell is then able to communicate this vital identifying information to the T-cells and B-cells. In this way, the Helper T-cell activates the next level of response.

Communicating this information, the Helper T- cells activate a parallel response, involving the initiation both the humoral and the cell- mediated immune response. The humoral immune response involves the B- cells finding and killing antigens in the fluids of our body. The cell-mediated response involves the Killer T-cells that will destroy the cells that have already been infected by the antigen. In the initiation of the humoral response, the Helper T - cells communicate the shape of the specific antigen to the B-cells. With this information, the B-cells are able to make an infinite number of antibodies specific to the antigen. In fact, the B- cell becomes a large plasma cell factory that produces identical copies of specific antibody molecules at an astonishing pace--up to 10 million copies an hour." [9]

In addition, the B-cells clone themselves creating a fleet of fighters. When an antigen is found, B-cell release antibodies that clump onto the pathogen . At the same time, the Helper T- cells activate macrophages that will then be able to go out in the body's fluids, to patrol and kill the specific antigens in the humoral regions, or fluids filled areas of our body.

Simultaneously, the Helper T- cells activate the cell- mediated immune response. The cell mediated response creates and activates Killer T- cells. These Killer T- cells clone themselves to produce many Killer T- cells. Then the Killer T- cells aggressively patrol the body searching for infected cells. They carry T-cell receptors (TCR) which are super sensitive, on their cell surface that will allow them to recognize a specific antigens on an infected cell surface. When a cell is infected, the fragments, or antigens, from the infecting pathogen are broken down and transported to the surface of the infected cell. These fragments are displayed on the cell surface as peptide antigens. The antigen is presented to the T- cell by a molecule called major histocompatibility complex (MHC). [10] If the T cell latches onto the peptide antigen, and fits, it signals the T-cell to destroy the infected cell. As a result, viruses within the host cell are destroyed along with the infected cell thus preventing further replicating. [11] Both the Killer T- cell and B -cells have super sensitive receptors on their surfaces, like little hands, that are able to recognize pathogens. However, the T cell receptors stay on the cell, while B cell receptors, or antibodies, can detach from the cell. The antibodies when released from the B cells bind to the antigens they find, fitting perfectly, like a lock and key or a handshake. In this way, the antibodies are able to neutralize pathogens. As the antibodies bind to the antigens, they begin to clump together which then flags the clumps for destruction by macrophages. Finally, some T- cells and B- cells hold onto the antigen information and become memory cells, patrolling the body remembering the specific pathogen, ready to destroy it on sight for several decades. [12]

Immunity

We develop immunity when we are exposed to a disease and our immune system is able to develop memory cells. The immune response to a secondary infection of the same pathogen will thus be stronger and faster because of these immune memory cells.

Recognizing "Self"

One of the most important characteristics of the immune system is its ability to discriminate between healthy body cells and foreign infected cells. Immune cells are able to make this distinction because they are able to interpret antigens on the surface of cells as either being foreign or as being self. Antigens could be thought of as name tags because they identify each specific cell by displaying its distinguishing protein. Immune cells recognize the body's own antigens as being different from invader cells because of the receptors they carry on their surfaces. The receptors of T-cells are able to recognize specific antigens which identify a vast number of invaders as targets. The T-cell receptors enable the cell to recognize and read the antigen that is on the body's own healthy cells and thus leave them alone. While maturing in the thymus, T-cells that react erroneously to an antigen made by the body, or "self," it will die off. In this way, T-cells with the potential to attack the body's own tissue are filtered out and do not survive. B- cell have a similar testing process in the bone marrow. As a result, T-cells and B-cells of the immune system are able to distinguish between the " self "and the invader, healthy body tissue versus pathogens; protecting healthy cells by targeting and eliminating infected cells and invaders. [13] Errors in this recognition process can result in autoimmune diseases like multiple sclerosis and rheumatoid arthritis.

Antibodies

Antibodies are proteins produces by the B-cells in our body as a response to an antigen. Antibodies all have a similar shape, like a "Y" . However, the shape of the top of the "Y" is directly related to the specific antigen that it is responding to. Our body can produce almost an infinite number and variety of antibodies. The antibodies dock, or attach to an antigen which marks it for destruction by macrophages. In addition, antibodies also clump around an antigen rendering it inactive.

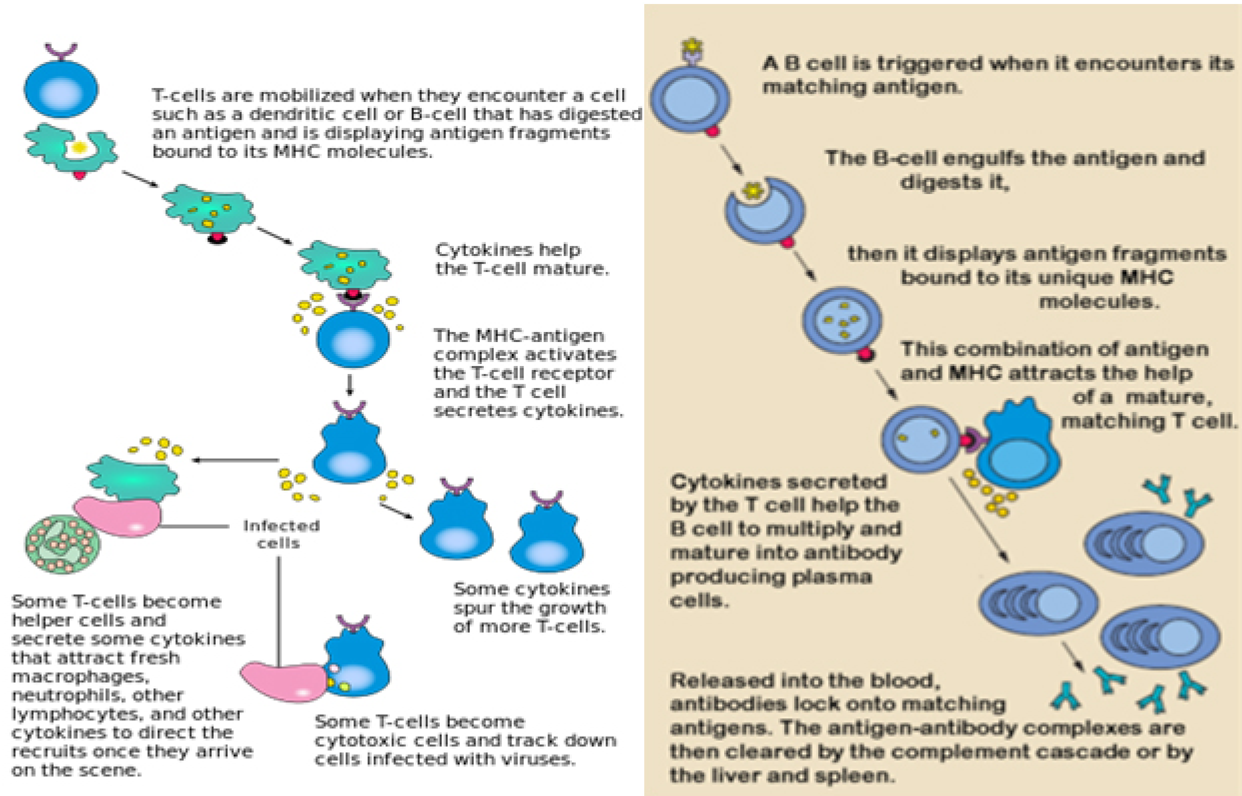
Cells of the Immune System

The immune system is made up of a multifaceted defense system involving many different types of white blood cells. These white blood cells, or leukocytes, each have specific jobs and have a life span of about 24 hours. White blood cells are made in the red bone marrow from stem cells. Each of the specialized immune cells originate in the bone marrow and develops through an evolving sequence that produces a highly specialized range of immune cell equipped to carry out participate in this sophisticated defense system. These cells include, monocytes and neutrophils, which are specialized phagocytes, as well as eosinophils and basophils which are involved in the inflammatory response.

Furthermore, B-cells and T-cells originate as stem cells in the bone marrow however, they leave the bone marrow before they are fully mature. T-cells, or lymphocytes, leave the bone marrow and travel to the thymus where they fully mature. Thus the "T" in T-cell stands for thymus. The T-cells are involved in the specific immune response, or third line of defense. The T-cells regulate the defensive actions of the B-cells and other cells in the immune response. There are many kinds of T-cells; examples of these cells are, killer T-cells, helper T-cells, and suppressor T-cells. [14]

Another immune cell is called the macrophage, or large phagocytes. [15] Macrophage is Greek for "big eater" [16] which is exactly what the macrophage cell does. Macrophages are immune cells that are active in the third line of defense. They engulf, digest and destroy pathogens and infected cells such as viruses, bacteria, and microorganisms. They then display the antigen, or tiny parts of the pathogen, on their cell surface thereby activating a higher level of defense. Macrophages are called antigen-presenting cells. By displaying the antigen, macrophages are able to communicate vital specific information about to identity of the pathogen to the Killer T-cells. This communication will secure the information necessary for the identification, attack, and destruction of the pathogen by attacking Killer T- cells.

Activation Sequences of the T-cells and B-cells of the Immune System



http://en.wikipedia.org/wiki/Adaptive_immune_system

T- Cells and B-Cells: Cell- Mediation Immunity & Humoral Immunity

The third line of defense and the two main immune responses are controlled by the T- cells and B-cell. These two responses are Cell- Mediation Immunity and Humoral Immunity. Both the T-cells and B-cells are lymphocytes, which are also referred to as white blood cells. These white blood cells are involved in the specific defenses of the immune system. Both the B- cells and T-cells have highly sensitive receptors, which allows them to recognize antigens. T-cells coordinate and regulate the responses of the immune system as well as attack infected cells. There are several kinds of T-cells.

B- cells are a type of white blood cell, that is made in the bone marrow. They are responsible for the Humoral response of the immune system. This means they are responsible for the immune activity in the body's fluids, or humors. These humors include, the blood, lymph, and body tissues. They are like the "Navy," patrolling the waters to keep us safe. When B- cells are activated by the T-helper cells, they differentiate into plasma cells which become antibody producing factories. B-cells produce specific antibodies for each particular antigen. B-Cells are capable of producing an infinite number of antibodies to different antigens. However, some B- cells do not turn into antibody factories, they become " memory cells" that will live for decades and are able to remember and recognize the antigens that they have been exposed to. [17]

T-cells are a type of white blood cell that are responsible for the cell- mediated immune response. T-cell are able to produce Killer T-cells, which target and kill the cells that have already been infected in the body tissue. The Killer T- cell is a type of activated T- cell that will aggressively seek out, dock against, and kill infected cells.

The immune system is able to survey the inside of a cell by reading the proteins displayed on its surface. The protein HLA (Human Luekiside Antigen) is the protein that enables the cell to display the contents of the inside of a cell on its surface. T- cells read the HLA protein on the cell surface as either self or invader. In this way, a virus hidden within the contents of the host cell will be revealed. When these protiens are displayed on the surface, the T-cell reads them as being foreign, and destroys the infected cell. [18][19]

Cells of the Immune System [20]

Cell	Analogy	Description
T- Cells- Generals	Helper T- cell Suppressor T-cell Killer T- cell	Stem cells that leave bone marrow in an immature state and, go to the thymus to mature and develop. Programmed response to one specific antigen. When it meets and recognized antigen, the T-cell multiplies, cloning itself, again and again. All clones recognize the same antigen. These cells then differentiate to become helper, suppressor , or killer cells. After the antigen is eradicated, the left over some T- cells become memory cells.
Helper T -cells	Oversee other t-cells- generals	Initiates humoral and cell mediated immune response
Killer T -cell_ cytotoxic T-cells	Eliminators	Kill cells that are infected
Phagocytes Macrophages	Army troops	Eaters! White blood cells: Eat any cell that is not self, digests and displays antigen. Macrophage wear parts of the pathogens they eat, or antigen, causing an immune response Activate: Helper T- cells and B-cells
B-Cell lymphocytes	Navy: Responsible for patrolling the fluids of our body, the Humor Response.	B-cells are programmed to respond to one specific antigen by producing and releasing one specific antibody. B-cells are activated upon contact with that antigen causing the cell to divide and continuously clone itself. Additionally, each of the clone produces antibodies which are releases into the blood stream and lymphatic system.
Antibodies	**Marines**	Chemical release by B- cells that are made to recognize and attach to a specific antigen, marking them for destruction or rendering it useless. Complex protein molecule specific to one antigen. Your body in capable of making billions of different antibodies.
Pathogens	Agents that cause	Bacteria, viruses, Fungi, Protists

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When Things Go Wrong

The greatest challenges to global health involve illnesses that defy, test, trick, attack and disrupt the functions of immune system. When problems occur with our immune system, the results are dire. Often, death, chronic illness, and life altering disease are the effects of an immune system failure. Problems that occur with the immune system can be grouped into three main categories. These categories include autoimmunity, when the immune system attacks its own body; hypersensitivity, when the immune system is overly sensitive as in allergies; and immunodeficiency, when the immune system is weakened or unable to respond to antigen as in AIDS. The many reasons for each of these breakdowns of the immune system continues to be a challenge to the medical field. However, the field of bioengineering is offering new hope for those who suffer from illness that involve the immune system.

Autoimmunity is when the immune cells are unable to distinguish between; "self," or the body's own cells and a foreign invader. Because of this lack of recognition, the immune cells attack the healthy body tissue too. One examples of illness caused by autoimmunity is multiple sclerosis. In the case of multiple sclerosis, the immune T-cells attack the myelin sheath that covers and insulates the nerve cell. These immune cells fail to recognize the myelin as "self", or part of the body. Unable to discriminate between the body tissue and invader, the T-cells attack the myelin as foreign, which causes inflammation and break down of the nerve tissue. As part of this response, the inflammation of the myelin can cause blockages or short circuit of neural communication. Signals from the affected nerves are not able to travel to and from the brain as needed resulting in disease symptoms. There are many symptoms which can be debilitating and often confine one to a wheelchair. There is no cure for MS. [21]

Hypersensitivity is an immune disorder cause by a heightened response to a non-threatening substance. For example, an allergy is a problematic response by the immune system to peanuts, pollen, eggs or mold, just to name a few. The immune system responds to the foreign substance as if it is a threatening pathogen. In this response, b-cell make antibodies to attack the allergen causing itchy watery eyes, inflammation of the skin, digestive system, airways, and /or sinuses. [22]

Immunodeficiency, or immunosuppression, is a condition where the immune system is not responding to an antigen effectively. This condition may be caused by a direct attack on the immune system or a congenital defect, the effect cripples the ability of the immune system to function properly. As a result, the affected person is left unprotected and vulnerable to a myriad of pathogens. Because of this, often a secondary infection can become life threatening. One example of an immunodeficiency disease is IgA. Those with IgA deficiency are unable to make IgA antibodies. Severe Combined Immunodeficiency Syndrome (SCID) is another example of a rare, but very serious immunodeficiency disease of the immune system. Babies born with this disease do not live very long because they do not have any B-cells or T-cells leaving them defenseless against pathogens. The treatments have been limited to bone marrow transplants and to, literally, put the child in a sterile, plastic bubble as protection. [23] In 1976 the movie, The Boy in the Plastic Bubble, was written and inspire by the real life stories of Davis Vetter and Ted DeVita who suffered from immunodeficiency. [24]

AIDS (acquired immunodeficiency syndrome) is an deadly immunodeficiency illness. It is the caused by the human immunodeficiency virus (HIV). The HIV virus directly attacks the immune system. The T- helper cell is the target of this virus. The virus invades the T- helper cells using the T-cell as its host. The HIV virus replicates itself within the host helper T-cell until the cell membrane explodes. With this explosion, the host helper T-cell is destroyed. At the same time, a fleet of new viral, HIV, pathogens are released to infect new helper T- cells. As a result, the immune response is compromised further as the disease progresses. This is because the helper T-cell is an important immune cell that is vital to initiating the immune response. The body's immune response is slowly eroded and is unable to launch an attack on invading pathogens. This leaves the infected person vulnerable to a secondary infection. As a result, of the weakened immune system, a minor exposure or infection can become life threatening. The HIV and AIDs viruses are spread by sexual contact or by infected blood or body fluids. It can take many years for one to show symptoms of the disease, which can be dangerous for the spread of the disease and the important health care of those infected. The disease has devastated many populations. Although there is no cure for HIV/AIDS, we now have medications that can slow the progression of HIV. There is greater hope now for improved therapies in the field of bioengineering. [25] [26]

Another problematic example of the immune system involves transplant rejection. Organ transplants are challenging because the immune system views the new organ as an invader. Although the immune system is doing exactly what it is supposed to be doing, this response can cost one a lifesaving organ transplant. Extreme care is given to matching and typing tissue as a way of preventing transplant rejection. If the immune cell receptors of the host person latch onto antigens from the organ transplanted and recognize it as non-self, then the immune system will react against the organ, attacking the transplanted organ. This response is like friendly fire, the immune system accidently attacking its own lifesaving organ. Immunosuppressant drugs are used to reduce transplant rejection, but these turn off the immune system and create other risks.

Applying the concepts of bioengineering to the immune system could offer relief and hope for those who suffer from these chronic and debilitating diseases and offer solutions that could, cure, or inhibit the progression of these illnesses. Could these answers lie in new ways to enhance, strengthen, or reinforce these mighty fighters to create a fleet of super cells?

Biomedical Engineering and the Immune System

When we think of bioengineering to improve or enhance the immune system and or its cells, one must first target a specific problem, break it down, and then explore solutions. How is the immune system failing? You may ask, how can I get the outcome I need? One approach to a solutions may lie in educating the system and cells as in a vaccination process. Another consideration would be to use a drug delivery system to cause a direct change. Alternatively, you may ask, do I change a cell behavior? A spectrum of genetic therapies might be considered, which could be game changers because they have the potential to alter cell behavior. On the other hand, structural changes to the cells may be a possible way to bolster cell function. At the heart of this work is to find a way into the cells. Getting into the cell will allow work on a cellular and molecular level, hence the exploration of nanotechnology.

Vaccines have proven to be a very effective way to protect our body against specific diseases. How exactly does a vaccine do this? Vaccines essentially teach the immune cells how to fight a specific disease. A vaccine teaches the immune cells how to fight a disease by activating the specific immune response, which after the battle, creates memory cells. To begin, the dead or weakened form of the pathogen is injected into the body. This activates the specific immune response of both the B-cells and T-cells. Next, the B-cells respond to the antigens by producing antibodies to fight the weaken pathogen. After the fight, both the T-cells and B-cells create memory cells that will recognize and destroy the specific pathogen for decades. Finally, in the event of a future exposure, the memory cells will immediately recognize and destroy the pathogen resulting in a faster and stronger immune response than the first. In the end, the vaccine prepares the immune system with ammunition and tools to recognize and destroy a pathogen to protect the body against future infection. Thus, the pathogen is often eradicating before it is even noticed. In the end, it is these memory cells that will be ready and waiting to attack quickly and effectively if a secondary infection occurred. This is the way we acquire passive immunity.

Genetic therapies can alter a gene, which will change the way a cell behaves. Gene therapies can be used to treat genetic disease. They can also change the behavior of the way an immune cell responses to a disease. However, genetic therapy is extremely challenging because the targeted gene must be located, and a specific corrective therapy must be developed. In addition, a viable vector must deliver the gene, and then the gene needs to be integrated into the cell's transcription and translation, ultimately altering the DNA of the cell in a permanent way. [27]

Dr. Tarek Falmy and his team of engineers at Yale University are stretching the boundaries of bioengineering in their cutting- edge work with nanotechnology and drug delivery which is both boosting the immune system and the effectiveness of cancer drugs. Dr. Fahmy's work with nanogel technology is a new and promising technology for the delivery of drugs to the micro environments of cancerous tumors. " The nanogels allow for the delivery of multiple drugs that can come out slowly over time to a specific cancer site, explains Dr. Falmy in his video interview with the New Haven Register. [28] "There is a promising path forward here for cancer therapy in general," said Yale bioengineer Tarek M. Fahmy, lead researcher and author of a new paper in the journal Nature Materials." [29] Furthermore, Dr. Tarek Falmy and his creative, visionary team of bioengineers are growing T-cells on nanotubes and are exploring genetic therapies and modifications that will enhance the cells, thus improving their functioning. These improved cells may be able to fight our most challenging diseases and offer hope to the once hopeless.

The Engineering Design Process

A revolutionary age of science and technology is before us, where what was once a dream is now a reality. Imagine what our students will be able to develop if given this knowledge to ponder, simmer, and grow; empowered to envision future treatments of their own. I cannot think of a more relevant topic than bioengineering at this time. With this knowledge, I believe my students will be inspired to think in new ways, experimenting with ideas they can imagine without fear, free to think – exploring the possibilities, and possibly improve human health, but more importantly experience the freedom to think.

Organizing learning around the engineering process offers the best of instruction; team work, inquiry driven, engagement, discourse, direct feedback of learning through trial and error , application of the highest level styles of thinking (evaluating, analyzing, creating) as students use all that they know to problem solve through a collaborative process, to create an original, novel solution. The best of instruction and learning is in the process of the engineering.

In order for student to design their own immune cell, students will need to learn the functions of the immune system and the immune cells. The activities are designed to build knowledge in preparation for building super cells in the engineering design process.

Activities and Learning Objectives

1.Objective: Students will be able compare and contrast the differences between the viral and bacterial pathogens in terms of their physical characteristic and how they cause disease.

Activity: Students will work with partners to compare and contrast a virus and bacteria using available resources to research the pathogens. Students will use a Venn diagram to organize and record information. Students will then use the Venn diagram to write one or more paragraphs comparing the two pathogens. As an option, student may want to pick two different specific pathogens

2. Objective: Students will be able to explain the central functions of the lymphatic system as well as the purpose of each organ in relation to the growth and development of immune cells.

Activity: Students will trace their bodies and then draw and label the lymphatic system including organs and lymph nodes. In addition, students will include captions under each organ, explaining the purpose and function of each as well as how the immune cells develop in each organ.

Demonstration: Wash a dirty playground ball and then pour the water through a coffee filter to simulate the way the lymphatic system washes cells and lymph nodes filters out bacteria and other microorganisms.

3. Objective: Students will learn how immune cells search, recognize, and eliminate pathogens by reading the presenting antigens to find an exact fit.

Activity: This is a game simulates the way immune cells search, recognize, and find invaders by reading presented antigens. Student will make a circle. Everyone will take off one shoe and put it in the middle. One student goes in the middle and picks a shoe from the pile. This student is the immune cell and the shoe symbolizes a specific antigen. When the game starts, the child moves around the circle searching for the perfect match. After the match it found, the student must try to fit the shoe on the student's foot, simulating the connection of immune cell and invader. If it is a perfect fit, the student is a "eliminated" and leaves the circle.

4. Objective: Students will demonstrate their knowledge of this immune sequence as they explain the sequence of events in the battle between a specific disease and the immune response systems. Students will demonstrate their knowledge as they create stories using analogies of community protectors for the functions of the various immune cells.

Activity: Create a story of the immune system through the use of analogies for the different cells corresponding to the protectors in the community. Students will write fictional stories personifying the immune cells with human characteristics that would reflect the job characteristics of the immune cells, (Patti Pathogen, Tommy T-cell,) Use the technologies of these guardians to create unique fictional super cells in the story. As an alternative, students can write a play and design costumes to show how the immune system works when an invader enters the body.

Activity: As a way of learning about the effects of living with a severe immune disorder, student can research and write a biography of the life of David Vetter, the boy in the bubble.

Activity: Create a First Aid Kit to support your immune system. Write a list of contents and an explanation for how each item will heal and protect your body against pathogens.

Activity: Students will work id groups to become experts of one specific cell in the immune system. As each group assembles their knowledge, it will be displayed on a wall mural illustration the immune process. The collective, collaborative work will build shared knowledge as students learn and display the interconnected relationships between the cells of the immune system.

Engineering a Super Cell

Objective: Student will apply their knowledge and understanding the immune system to design a super cell to solve a failure in the immune system or that will enhance this systems ability to fight a specific disease.

Activity: Group students in teams of three to five. Through the engineering process, students will apply their understanding of the immune system and its cell functions. Each team will pick a disease, identify the malfunction of the immune system and break it down into parts. Students will analyze the immune response, creating flow charts is a to analyze the process. Then, students will brainstorm possible solutions and generate questions to investigate. At this time, students can brainstorm uses of technologies learned from community protectors and observed from nature. In addition, students will consider genetic therapies to alter the cell DNA in order to change behaviors. Other engineering solutions students may include vectors for drug delivery or nano-bots that may consume pathogens. Still other ideas to create cells with protective coatings impervious to invaders. As part of this experience, students will work within the design process, brainstorming solutions with a team, exploring materials, creating models to test and learn what works and what doesn't, and then finally refine, build, and present the final product to the class; a might fighter and protector, their own engineered super cell.

Common Core Content Standards addressed in this unit

The Common Core State Standards aim to increase depth of content knowledge by integrating subject matter across the curriculum. An additional objective of the Common Core Standards is to strengthen reading comprehension skills and students' ability to use and understand more complex text. This unit addresses these issues directly through relevant, engaging subject matter of bioengineering.

Scientific Inquiry: Scientific inquiry is a thoughtful and coordinated attempt to search out, describe, explain, and predict natural phenomena.

Scientific Literacy: Scientific literacy includes speaking, listening, presenting, interpreting, reading, and writing about science.

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