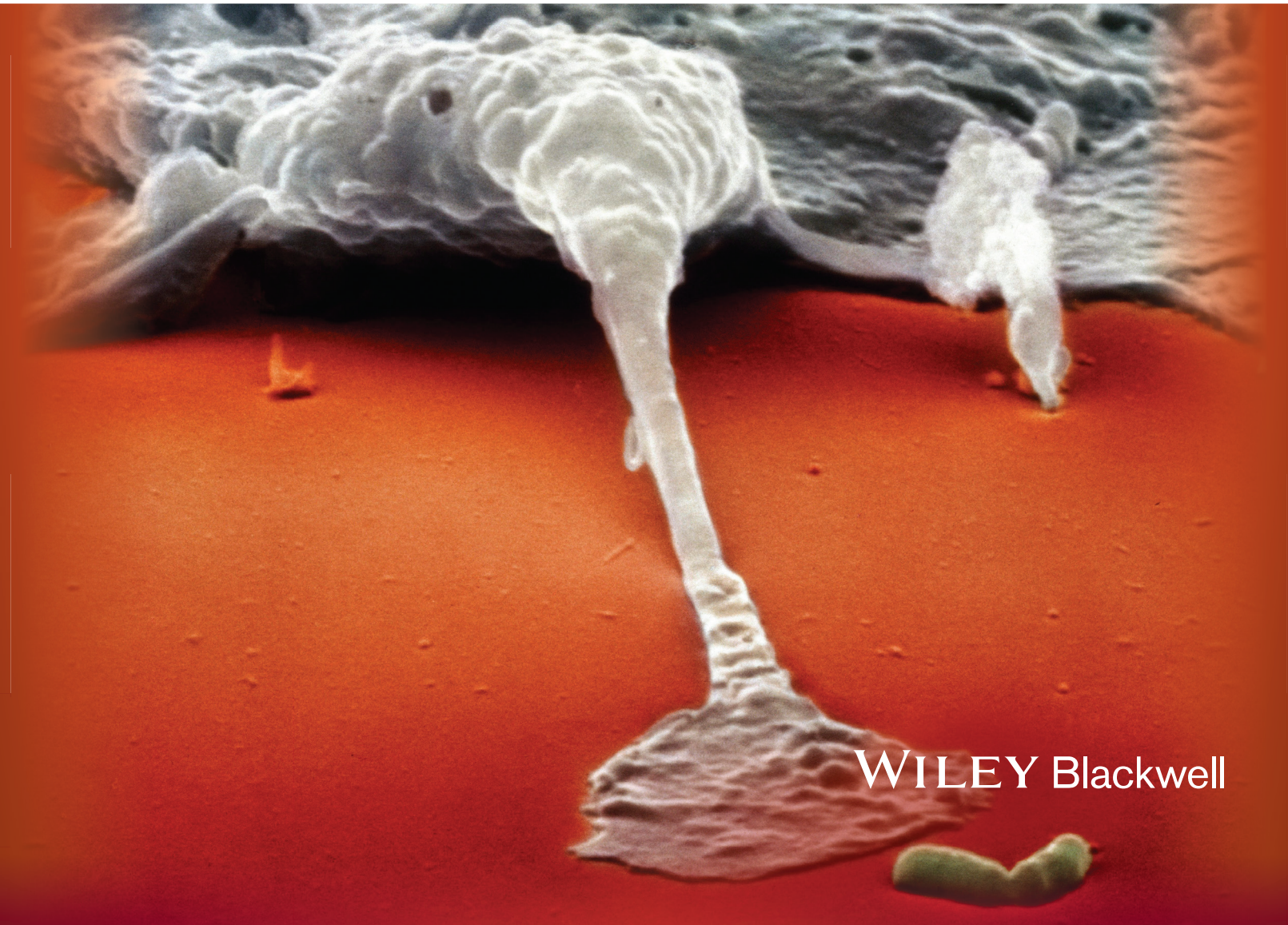
How The Immune System Works

5th Edition

Lauren Sompayrac



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I dedicate this book to my sweetheart, my best friend,
and my wife: Vicki Sompayrac.

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How to Use This Book

I wrote *How the Immune System Works* because I couldn't find a book that would give my students an overall view of the immune system. Sure, there are as many good, thick textbooks as a person might have money to buy, but these are crammed with every possible detail. There are also lots of "review books" that are great if you want a summary of what you've already learned – but they won't teach you immunology. What was missing was a short book that tells, in simple language, how the immune system fits together – a book that presents the big picture of the immune system, without the jargon and the details.

How the Immune System Works is written in the form of "lectures," because I want to talk to you directly, just as if we were together in a classroom. Although Lecture 1 is a light-hearted overview, meant to give you a running start at the subject, you'll soon discover that this is not "baby immunology." *How the Immune System Works* is a concept-driven analysis of how the immune system players work together to protect us from disease – and, most importantly, why they do it this way.

In Lectures 2 through 10, I focus more closely on the individual players and their roles. These lectures are short, so you probably can read them all in a couple of afternoons. In fact, **I strongly suggest that you begin by reading quickly through Lectures 1–10.** The whole idea is to get an overall view of the subject, and if you read one lecture a week, that won't happen. Don't "study" these 10 lectures your first time through. Don't even bother with the Thought Questions at the end of each lecture. Just rip through them. Then, once you have a "feel" for the system, go back and spend a bit more time with these same 10 lectures to get a clearer understanding of the "hows and whys."

In Lectures 11–15, I discuss the intestinal immune system, vaccines, allergies, autoimmune disease, the AIDS virus, and cancer. These lectures will let you "practice" what you have learned in the earlier lectures by examining real-world examples of the immune system at work. So after you have gone through Lectures 1–10 twice, I'd suggest you read these last five lectures. When you do, I think you'll be amazed by how much you now understand about the immune system.

As you read, you will encounter passages highlighted in blue, and words that are highlighted in red. These highlights are to alert you to important concepts and terms. They also will help you review a lecture quickly, once you have read it through.

In some settings, *How the Immune System Works* will serve as the main text for the immunology section of a larger course. For a semester-long undergraduate or graduate immunology course, your professor may use this book as a companion to a comprehensive textbook. As your course proceeds, reviewing the appropriate lectures in *How the Immune System Works* will help you keep the big picture in focus as the details are filled in. It's really easy to get lost in the details.

No matter how your professor may choose to use this book, you should keep one important point in mind: I didn't write *How the Immune System Works* for your professor. This book is for you!

LECTURE 1 An Overview

HEADS UP!

The immune system is a "team effort," involving many different players. These players can be divided into two groups: those that are members of the innate immune system team and those that are part of the adaptive immune system. Importantly, these two groups work together to provide a powerful defense against invaders.

INTRODUCTION

Immunology is a difficult subject for several reasons. First, there are lots of details, and sometimes these details get in the way of understanding the concepts. To get around this problem, we're going to concentrate on the big picture. It will be easy for you to find the details somewhere else. Another difficulty in learning immunology is that there is an exception to every rule. Immunologists love these exceptions, because they give clues as to how the immune system functions. But for now, we're just going to learn the rules. Oh, sure, we'll come upon exceptions from time to time, but we won't dwell on them. Our goal is to examine the immune system, stripped to its essence.

A third difficulty in studying immunology is that our knowledge of the immune system is still evolving. As you'll see, there are many unanswered questions, and some of the things that seem true today will be proven false tomorrow. I'll try to give you a feeling for the way things stand now, and from time to time I'll discuss what immunologists speculate may be true. But keep in mind that although I'll try to be straight with you, some of the things I'll tell you will change in the future – maybe even by the time you read this!

Although these three features make studying immunology difficult, I think the main reason immunology is such a tough subject is that the immune system is a "team effort" that involves many different players interacting with each other. Imagine you're watching a football game on TV, and the camera is isolated on one player, say, the tight end. You see him run at full speed down the field, and then stop. It doesn't seem to make any sense. Later, however, you see the same play on the big screen, and now you understand. That tight end took two defenders with him down the field, leaving the running back uncovered to catch the pass and run for a touchdown. The immune system is a lot like a football team. It's a network of players who cooperate to get things done, and focusing on a single player doesn't make much sense. You need an overall view. That's the purpose of this first lecture, which you might call "turbo immunology." Here, I'm going to take you on a quick tour of the immune system, so you can get a feeling for how it all fits together. Then in the next lectures, we'll go back and take a closer look at the individual players and their interactions.

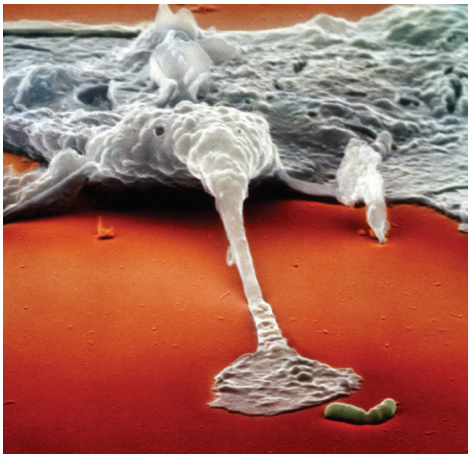
PHYSICAL BARRIERS

Our first line of defense against invaders consists of physical barriers, and to cause real trouble, viruses, bacteria, parasites, and fungi must penetrate these shields. Although we tend to think of our skin as the main barrier, the area covered by our skin is only about 2 square meters. In contrast, the area covered by the mucous membranes that line our digestive, respiratory, and reproductive tracts measures about 400 square meters – an area about as big as two tennis courts. The main point here is that there is a large perimeter which must be defended.

THE INNATE IMMUNE SYSTEM

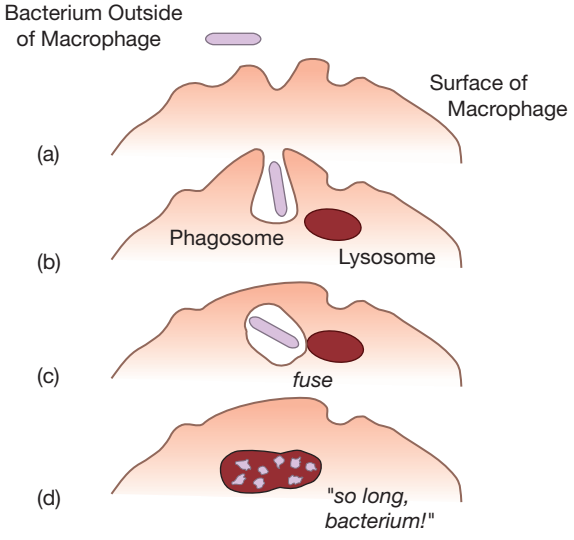
Any invader that breaches the physical barrier of skin or mucosa is greeted by the **innate immune system** – our second line of defense. Immunologists call this system "innate" because it is a defense that all animals just naturally seem to have. Indeed, some of the weapons of the innate immune system have been around for more than 500 million years. Let me give you an example of how this amazing innate system works.

Imagine you are getting out of your hot tub, and as you step onto the deck, you get a large splinter in your big toe. On that splinter are many bacteria, and within a few hours you'll notice (unless you had a lot to drink in that hot tub!) that the area around where the splinter entered is red and swollen. These are indications that your innate immune system has kicked in. In your tissues are roving bands of white blood cells that defend you against attack. To us, tissue looks pretty solid, but that's because we're so big. To a cell, tissue looks somewhat like a sponge with holes through which individual cells can move rather freely. One of the defender cells that is stationed in your tissues is the most famous innate immune system player of them all: the **macrophage**. If you are a bacterium, a macrophage is the last cell you want to see after your ride on that splinter! Here is an electron micrograph showing a macrophage about to devour a bacterium.



You will notice that this macrophage isn't just waiting until it bumps into the bacterium, purely by chance. No, this macrophage actually has sensed the presence of the bacterium, and is reaching out a "foot" to grab it. But how does a macrophage know that a bacterium is out there? The answer is that macrophages have antennae (receptors) on their surface which are tuned to recognize "danger molecules" characteristic of common microbial invaders. For example, the membranes that surround bacteria are made up of certain fats and carbohydrates that normally are not found in the human body. Some of these foreign molecules represent "find me and eat me" signals for macrophages. And when macrophages detect danger molecules, they begin to crawl toward the microbe which is emitting these molecules.

When it encounters a bacterium, a macrophage first engulfs it in a pouch (vesicle) called a **phagosome**. The vesicle containing the bacterium is then taken inside the macrophage, where it fuses with another vesicle termed a **lysosome**. Lysosomes contain powerful chemicals and enzymes which can destroy bacteria. In fact, these agents are so destructive that they would kill the macrophage itself if they were released inside it. That's why they are kept in vesicles. Using this clever strategy, the macrophage can destroy an invader without "shooting itself in the foot." This whole process is called **phagocytosis**, and this series of snapshots shows how it happens.

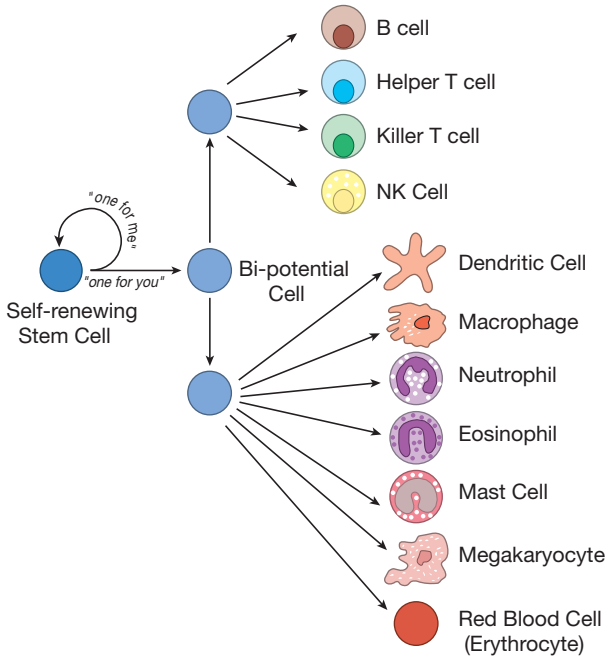


Macrophages have been around for a very long time. In fact, the ingestion technique macrophages employ is simply a refinement of the strategy that amoebas use to feed themselves – and amoebas have roamed Earth for about 2.5 billion years. So why is this creature called a macrophage? "Macro," of course, means large – and a macrophage is a large cell. "Phage" comes from a Greek word meaning "to eat." So a macrophage is a big eater. In fact, in addition to defending against invaders, the macrophage functions as a garbage collector. It will eat almost anything. Immunologists can take advantage of this appetite by feeding macrophages iron filings. Then,

using a small magnet, they can separate macrophages from other cells in a cell mixture. Really!

Where do macrophages come from? Macrophages and all the other blood cells in your body are made in the bone marrow, where they descend from self-renewing cells called **stem cells** – the cells from which all the blood cells "stem." By self-renewing, I mean that when a stem cell grows and divides into two daughter cells, it does a "one for me, one for you" thing in which some of the daughter cells go back to being stem cells, and some of the daughters go on to become mature blood cells. This strategy of continuous self-renewal insures that there will always be blood stem cells in reserve to carry on the process of making mature blood cells.

As each daughter cell matures, it has to make choices that determine which type of blood cell it will become when it grows up. As you can imagine, these choices are not random, but are carefully controlled to make sure you have enough of each kind of blood cell. For example, some daughter cells become red blood cells, which capture oxygen in the lungs and transport it to all parts of the body. In fact, our stem cell "factories" must turn out more than two million new red blood cells each second to replace those lost due to normal wear and tear. Other descendants of a stem cell may become macrophages, neutrophils, or other types of "white" blood cells. And just as white wine really isn't white, these cells aren't white either. They are colorless, but biologists use the term "white" to indicate that they lack hemoglobin, and therefore are not red. Here is a figure showing some of the many different kinds of blood cells a stem cell can become.



When the cells which will mature into macrophages first exit the bone marrow and enter the blood stream, they are called **monocytes**. All in all, you have about two billion of these cells circulating in your blood at any one time. This may seem a little creepy, but you can be very glad they are there. Without them, you'd be in deep trouble. Monocytes remain in the blood for an average of about three days. During this time they travel to the capillaries – which represent the "end of the line" for blood vessels – looking for a crack between the endothelial cells that line the inside of the capillaries. These endothelial cells are shaped like shingles, and by sticking a foot between them, a monocyte can leave the blood, enter the tissues, and mature into a macrophage. Once in the tissues, most macrophages just hang out, do their garbage collecting thing, and wait for you to get that splinter so they can do some real work.

When macrophages eat the bacteria on that splinter in your foot, they give off chemicals which increase the flow of blood to the vicinity of the wound. The buildup of blood in this area is what makes your toe red. Some of these chemicals also cause the cells that line the blood vessels to contract, leaving spaces between them so that fluid from the capillaries can leak out into the tissues. It is this fluid which causes the swelling. In addition, chemicals released by macrophages can stimulate nerves in the tissues that surround the splinter, sending pain signals to your brain to alert you that something isn't quite right in the area of your big toe.

During their battle with bacteria, macrophages produce and give off (secrete) proteins called **cytokines**. These are hormone-like messengers which facilitate communication between cells of the immune system. Some of these cytokines alert monocytes and other immune system cells traveling in nearby capillaries that the battle is on, and encourage these cells to exit the blood to help fight the rapidly multiplying bacteria. Pretty soon, you have a vigorous "inflammatory" response going on in your toe, as the innate immune system battles to eliminate the invaders.

So here's the strategy: You have a large perimeter to defend, so you station sentinels (macrophages) to check for invaders. When these sentinels encounter the enemy, they send out signals (cytokines) that recruit more defenders to the site of the battle. The macrophages then do their best to hold off the invaders until reinforcements arrive. Because the innate response involves warriors like macrophages, which are programmed to recognize many common invaders, your innate immune system usually responds so quickly that the battle is over in just a few days.

There are other players on the innate team. For example, in addition to the **professional phagocytes** like macrophages, which make it their business to eat invaders, the innate system also includes the complement proteins that can punch holes in bacteria, and natural killer (NK) cells that are able to destroy bacteria, parasites, virus-infected cells, and some cancer cells. We will talk more about the macrophage's innate system teammates in the next lecture.

THE ADAPTIVE IMMUNE SYSTEM

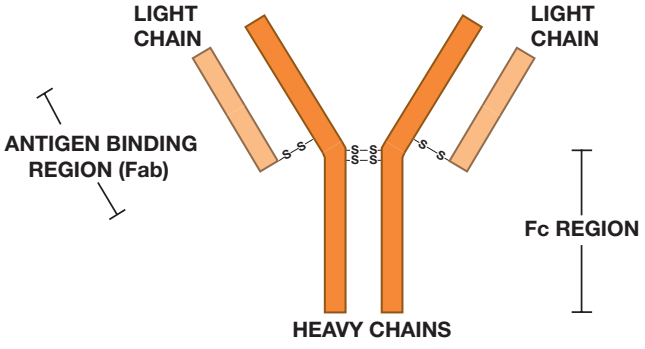
About 99% of all animals get along just fine with only natural barriers and the innate immune system to protect them. However, for vertebrates like us, Mother Nature laid on a third level of defense: the **adaptive immune system**. This is a defense system which actually can adapt to protect us against almost any invader. One of the first clues that the adaptive immune system existed came back in the 1790s when Edward Jenner began vaccinating the English against smallpox virus. In those days, smallpox was a major health problem. Hundreds of thousands of people died from this disease, and many more were horribly disfigured. What Jenner observed was that milkmaids frequently contracted a disease called cowpox which caused lesions on their hands that looked similar to the sores caused by the smallpox virus. Jenner also noted that milkmaids who had contracted cowpox almost never got smallpox (which, it turns out, is caused by a close relative of the cowpox virus).

So Jenner decided to conduct a daring experiment. He collected pus from the sores of a milkmaid who had cowpox, and used it to inoculate a little boy named James Phipps. Later, when Phipps was re-inoculated with pus from the sores of a person infected with smallpox, he did not contract that disease. In Latin, the word for cow is *vacca* – which explains where we get the word vaccine. History makes out the hero in this affair to be Edward Jenner, but I think the real hero that day was the young boy. Imagine having this big man approach you with a large needle and a tube full of pus! Although this isn't the sort of thing that could be done today, we can be thankful that Jenner's experiment was a success, because it paved the way for vaccinations that have saved countless lives.

Smallpox virus was not something humans encountered regularly. So Jenner's experiment showed that if the human immune system were given time to prepare, it could produce weapons that could provide protection against an intruder it had never seen before. Importantly, the smallpox vaccination only protected against smallpox or closely related viruses such as cowpox. James Phipps was still able to get mumps, measles, and the rest. This is one of the hallmarks of the adaptive immune system: It adapts to defend against specific invaders.

Antibodies and B cells

Eventually, immunologists determined that immunity to smallpox was conferred by special proteins that circulated in the blood of immunized individuals. These proteins were named **antibodies**, and the agent that caused the antibodies to be made was called an **antigen** – in this case, the cowpox virus. Here's a sketch that shows the prototype antibody, **immunoglobulin G (IgG)**.



As you can see, an IgG antibody molecule is made up of two pairs of two different proteins, the **heavy chain (Hc)** and the **light chain (Lc)**. Because of this structure, each molecule has two identical "hands" (**Fab regions**) that can bind to antigens. Proteins are the ideal molecules to use for constructing antibodies that can grasp attackers, because different proteins can fold up into a myriad of complex shapes.

IgG makes up about 75% of the antibodies in the blood, but there are four other classes of antibodies: **IgA**, **IgD**, **IgE**, and **IgM**. Each kind of antibody is produced by B cells – white blood cells that are born in the bone marrow, and which can mature to become antibody factories called **plasma B cells**.

In addition to having hands that can bind to an antigen, an antibody molecule also has a **constant region (Fc)** "tail" which can bind to receptors (**Fc receptors**) on the surface of cells such as macrophages. In fact, it is the special structure of the antibody Fc region that determines its **class** (e.g., IgG vs. IgA), which immune system cells it will bind to, and how it will function.

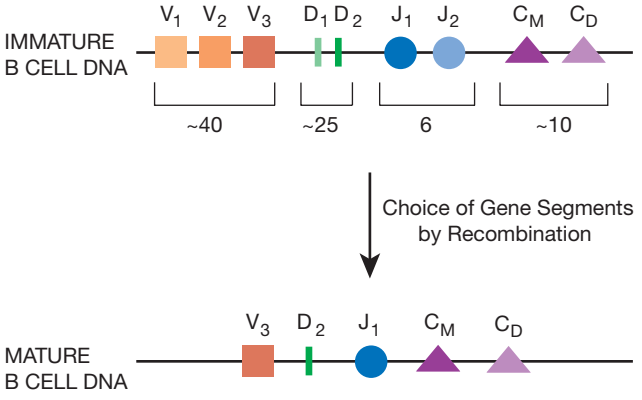
The hands of each antibody bind to a specific antigen (e.g., a protein on the surface of the smallpox virus), so in order to have antibodies available that can bind to many different antigens, many different antibody molecules are required. Now, if we want antibodies to protect us from every possible invader (and we do!), how many different antibodies would we need? Well, immunologists have made rough estimates that about 100 million should do the trick. Since each antigen-binding region of an antibody is composed of a heavy chain and a light chain, we could mix and match about 10 000 different heavy chains with 10 000 different light chains to get the 100 million different antibodies we need. However, human cells only have about 25 000 genes in all, so if each heavy or light chain protein were encoded by a different gene, most of the B cell's genetic information would be used up just to make antibodies. You see the problem.

Generating antibody diversity by modular design

The riddle of how B cells could produce the 100 million different antibodies required to protect us was solved in 1977 by Susumu Tonegawa, who received the Nobel Prize for his discovery. When Tonegawa started working on this problem, the dogma was that the DNA in every cell in the body was the same. This made perfect sense, because after an egg is fertilized, the DNA in the egg is copied. These copies are then passed down to the daughter cells, where they are copied again, and passed down to their daughters – and so on. Therefore, barring errors in copying, each of our cells should end up with the same DNA as the original, fertilized egg. Tonegawa, however, hypothesized that although this is probably true in general, there might be exceptions. His idea was that all of our B cells might start out with the same DNA, but that as these cells mature, the DNA that makes up the antibody genes might change – and these changes might be enough to generate the 100 million different antibodies we need.

Tonegawa decided to test this hypothesis by comparing the DNA sequence of the light chain from a mature B cell with the DNA sequence of the light chain from an immature B cell. Sure enough, he found that they were different, and that they were different in a very interesting way. What Tonegawa and others discovered was that the mature antibody genes are made by modular design.

In every B cell, on the chromosomes that encode the antibody heavy chain, there are multiple copies of four types of DNA modules (**gene segments**) called V, D, J, and C. Each copy of a given module is slightly different from the other copies of that module. For example, in humans there are about 40 different V segments, about 25 different D segments, 6 different J segments, and so on. To assemble a mature heavy chain gene, each B cell chooses (more or less at random) one of each kind of gene segment, and pastes them together like this.



You have seen this kind of mix-and-match strategy used before to create diversity. For example, 20 different amino acids are mixed and matched to create the huge number of different proteins that our cells produce. And to create genetic diversity, the chromosomes you inherited from your mother and father are mixed and matched to make the set of chromosomes that goes into your egg or sperm cells. Once Mother Nature gets a good idea, she uses it over and over – and modular design is one of her very best ideas.

The DNA that encodes the light chain of the antibody molecule is also assembled by picking gene segments and pasting them together. Because there are so many different gene segments that can be mixed and matched, this scheme can be used to create about 10 million different antibodies – not quite enough. So, to make things even more diverse, when the gene segments are joined together, additional DNA bases are added or deleted. When this **junctional diversity** is included, there is no problem creating 100 million B cells, each with the ability to make a different antibody. The magic of this scheme is that by using modular design and junctional diversity, only a small amount of genetic information is required to create incredible antibody diversity.

Clonal selection

In the human blood stream, there is a total of about three billion B cells. This seems like a lot, but if there are 100 million different kinds of B cells (to produce the

100 million different kinds of antibodies we need for protection), this means that, on average, there will only be about 30 B cells in the blood that can produce an antibody which will bind to a given antigen (e.g., a protein on the surface of a virus). Said another way, although we have B cells in our arsenal that can deal with essentially any invader, we don't have a lot of any one kind of B cell. As a result, when we are attacked, more of the appropriate B cells must be made. Indeed, B cells are made "on demand." But how does the immune system know which B cells to make more of? The solution to this problem is one of the most elegant in all of immunology: the principle of clonal selection.

After B cells do their mix-and-match thing and paste together the modules required to form the "recipes" for their heavy and light chain antibody proteins, a relatively small number of these proteins is made – a "test batch" of antibody molecules, if you will. These tester antibodies, called **B cell receptors (BCRs)**, are transported to the surface of the B cell and are tethered there with their antigen-binding regions facing out. Each B cell has roughly 100 000 BCRs anchored on its surface, and all the BCRs on a given B cell recognize the same antigen.

The B cell receptors on the surface of a B cell act like "bait," and what they are "fishing for" is the molecule which their Fab regions have the right shape to grasp – their **cognate antigen**. Sadly, the vast majority of B cells fish in vain. For example, most of us will never be infected with the SARS virus or the AIDS virus. Consequently, those B cells in our body which could make antibodies that recognize these viruses never will find their match. It must be very frustrating for most B cells. They fish all their lives, and never catch anything!

On occasion, however, a B cell does make a catch. And when a B cell's receptors bind to its cognate antigen, that B cell is triggered to double in size and divide into two daughter cells – a process immunologists call **proliferation**. Both daughter cells then double in size and divide to produce a total of four cells, and so forth. Each cycle of cell growth and division takes about 12 hours to complete, and this period of proliferation usually lasts about a week. At the end of this time, a "clone" of roughly 20 000 identical B cells will have been produced, all of which have receptors on their surface that can recognize the same antigen. Now there are enough B cells to mount a real defense!

After the selected B cells proliferate to form this large clone, most of them begin to make antibodies in earnest. The antibodies produced by these selected B cells are slightly different from the antibody molecules displayed on their surface in that there is no "anchor" to attach them to the B cell's surface. As a result, these antibodies are transported out of the B cell and into the blood stream. One B cell, working at full capacity, can pump out about 2000 antibody molecules per second! After making this heroic effort, most of these B cells die, having worked for only about a week as antibody factories.

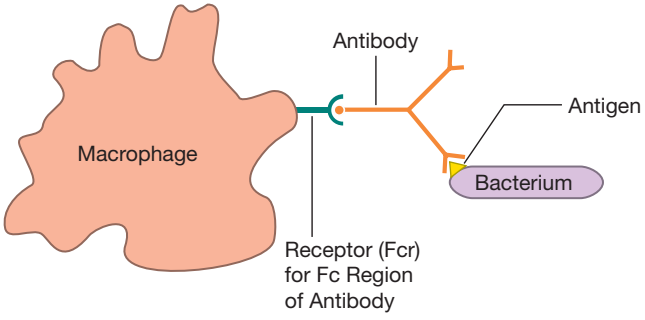
When you think about it, this is a marvelous strategy. First, because they employ modular design, B cells use relatively few genes to create enough different antibody molecules to recognize any possible invader. Second, B cells are made on demand. So instead of filling up our bodies with a huge number of B cells which may never be used, we begin with a relatively small number of B cells, and then select the particular B cells that will be useful against the "invader *du jour*." Once selected, the B cells proliferate rapidly to produce a large clone of B cells whose antibodies are guaranteed to be useful against the invader. Third, after the clone of B cells has grown sufficiently large, most of these cells become antibody factories which manufacture huge quantities of the very antibodies that are right to defend against the invader. Finally, when the intruder has been conquered, most of the B cells die. As a result, we don't fill up with B cells that are appropriate to defend against yesterday's invader, but which would be useless against the enemy that attacks us tomorrow. I love this system!

What antibodies do

Interestingly, although antibodies are very important in the defense against invaders, they really don't kill anything. Their job is to plant the "kiss of death" on an invader – to tag it for destruction. If you go to a fancy wedding, you'll usually pass through a receiving line before you are allowed to enjoy the champagne and cake. Of course, one of the functions of this receiving line is to introduce everyone to the bride and groom. But the other function is to be sure no outsiders are admitted to the celebration. As you pass through the line, you will be screened by someone who is familiar with all the invited guests. If she finds that you don't belong there, she will call the bouncer and have you removed. She doesn't do it herself – certainly not. Her role is to identify undesirables, not to show them to the door. And it's the same with antibodies: They identify invaders, and let other players do the dirty work.

In developed countries, the invaders we encounter most frequently are bacteria and viruses. Antibodies can bind to both types of invaders and tag them for destruction.

Immunologists like to say that antibodies can **opsonize** these invaders. This term comes from a German word that means "to prepare for eating." I like to equate opsonize with "decorate," because I picture these bacteria and viruses with antibodies hanging all over them, decorating their surfaces. Anyway, when antibodies opsonize bacteria or viruses, they do so by binding to the invader with their Fab regions, leaving their Fc tails available to bind to Fc receptors on the surface of cells such as macrophages. Using this strategy, antibodies can form a bridge between the invader and the phagocyte, bringing the invader in close, and preparing it for phagocytosis.



In fact, it's even better than this. When a phagocyte's Fc receptors bind to antibodies that are opsonizing an invader, the appetite of the phagocyte increases, making it even more phagocytic. Macrophages have proteins on their surface that can bind directly to many common invaders. However, the ability of antibodies to form a bridge between a macrophage and an invader allows a macrophage to increase its catalog of enemies to include any invader to which an antibody can bind, common or uncommon. In effect, antibodies focus a macrophage's attention on invaders, some of which (the uncommon ones) a macrophage would otherwise ignore.

During a viral attack, antibodies can do something else that is very important. Viruses enter our cells by binding to certain receptor molecules on a cell's surface. Of course these receptors are not placed there for the convenience of the virus. They are normal receptors, like the Fc receptor, that have quite legitimate functions, but which the virus has learned to use to its own advantage. Once it has bound to these receptors and entered a cell, a virus then uses the cell's machinery to make many copies of itself. These newly made viruses burst out of the cell, sometimes killing it, and go on to infect neighboring cells. Now for the neat part: Antibodies can actually bind to a virus while it is still outside of a cell, and can keep the virus either from entering the cell or from reproducing once it has entered. Antibodies with these properties are called **neutralizing antibodies**. For example, some neutralizing antibodies can prevent a virus from "docking" on the surface of a cell by binding to the part of the virus that normally would plug into the cellular receptor. When this happens, the virus is "hung out to dry," opsonized and ready to be eaten by phagocytes!

T cells

Although antibodies can tag viruses for phagocytic ingestion, and can help keep viruses from infecting cells, there is a flaw in the antibody defense against viruses: Once a virus gets into a cell, antibodies can't get to it, so the virus is safe to make thousands of copies of itself. Mother Nature recognized this problem, and to deal with it, she invented the famous **killer T cell**, another member of the adaptive immune system team.

The importance of T cells is suggested by the fact that an adult human has about 300 billion of them. T cells are very similar to B cells in appearance. In fact, under an ordinary microscope, an immunologist can't tell them apart. Like B cells, T cells are produced in the bone marrow, and on their surface they display antibody-like molecules called **T cell receptors (TCRs)**. Like the B cell's receptors (the antibody molecules attached to its surface), TCRs also are made by a mix-and-match, modular design strategy. As a result, TCRs are about as diverse as BCRs. T cells also obey the principle of clonal selection: When a T cell's receptors bind to their cognate antigen, the T cell proliferates to build up a clone of T cells with the same specificity. This proliferation stage takes about a week to complete, so like the antibody response, the T cell response is slow and specific.

Although they are similar in many ways, there are also important differences between B cells and T cells. Whereas B cells mature in the bone marrow, T cells mature in the thymus (that's why they're called "T" cells). Further, although B cells make antibodies that can recognize any organic molecule, T cells specialize in recognizing protein antigens. In addition, a B cell can secrete its receptors in the form of antibodies, but a T cell's receptors remain tightly glued to its surface. Perhaps most importantly, a B cell can recognize an antigen "by itself," whereas a T cell, like an old English gentleman, will only recognize an antigen if it is "properly presented" by another cell. I'll explain what that means in a bit.

There are actually three main types of T cells: **killer T cells** (frequently called **cytotoxic lymphocytes** or **CTLs**), helper T cells, and regulatory T cells. The killer T cell is