HOW STRONG IS YOUR IMMUNE SYSTEM?

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HOW STRONG IS YOUR IMMUNE SYSTEM?

Leading scientists reveal
how to bolster your body's natural defenses
against cold, flu & disease.

BY FRANK TUFARO, PH.D.

ALLERA PRESS

Dr. Yancey Gillespie, UNIVERSITY OF ALABAMA-BIRMINGHAM

· How the immune system works
· Autoimmune disease
· Allergies and immunity
· Aging and disease
· Wake up your immune system!

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Preface

Frank Tufaro, Ph.D.

Let’s start right off with a brief quiz. How many times have you eaten live poliovirus—on purpose?

a) Once was enough for me.

b) Three times, of course!

c) Are you kidding me?

B is the correct answer, of course!

Did you know that most infants in North America are fed three strains of live polio as a way to prevent polio infection in the future? It sounds incredible and kind of dangerous, but it’s true—and it works.

Here’s how it works. As an infant, you were most likely fed vaccine strains, or special weakened strains, of polio to teach your immune system what polio looks like. Your immune system remembers this and can quickly and effectively kill any

subsequent polio that it may encounter. The vaccine strains are called “ live” because they actually colonize your intestines for several days and reproduce many copies of themselves, just like a does. In this way you are“ vaccinated against polio.”

This discovery, and the discovery made in the eighteenth century that deliberate infection of healthy people with certain strains of cowpox virus (from a cow!), could prevent smallpox in humans, is a cornerstone in the foundation of modern medicine and has allowed for the total wordwide eradication of smallpox, with polio soon to follow.

Consider that there were only 1,315cases of polio infection worldwide in 2007. Compare this with the more than 58,000 people infected in 1952 during the last polio epidemic in the United States. Moreover, it is estimated that more than 20 million people were infected worldwide between 1840 and 1950.

The discovery of vaccines for eradicating these extraordinarily successful pathogens represents monumental human achievements that will have to

be replicated in the future as new threats emerge. Where will the next threat come from?

The answers to these and other compelling questions are the driving force behind the creation of this book. Your immune system is your ultimate guardian, and the success of vaccines relies entirely on your ability to mount an effective immune response when faced with danger.

When I first started my career as a research scientist and professor in the department of microbiology and immunology at the University of British Columbia, I taught a course in virology (the study of viruses) to two hundred or so senior students at eight in the morning. I began most lectures with a question such as the one above, or with this one:

How many of you havebeen infected with herpes?

I would raise my own hand and ask, “All of us?” The students would slump down in their seats. Some looked around at each other. A few giggled. Several looked shocked. The question was certainly provocative and woke them up, as was my intent!

When I followed up with, “ How many of you have had chicken pox?” they all raised their hands but were still confused.

It was a bit of a trick question. Many types of herpesviruses infect humans. Chicken pox is caused by a herpesvirus, varicella zoster, which is similar to the herpes simplex virus that causes cold sores. I knew that 95percent or more of my students would have had chicken pox while growing up. Therefore, virtually all them had been previously infected with a herpesvirus! They were indeed happy to learn this.

This book is designed to wake you up as well. Our goal is to provide answers to important questions you may have about your immune system, infections, cancer, autoimmunity, and what you can do to stay healthy.

The battle between viruses and our immune system is an ancient one that is still raging. Why are certain viruses potentially deadly (Ebola, HIV), while others are merely a nuisance (the cold virus,

for example)? Which virus can cause cancer? Can this be prevented? Can your immune system prevent cancer?

Fortunately, as you will learn from this book, our immune system has some pretty sophisticated weapons for fighting back, especially if it is working at its peak. We know that stress, poor diet, lack of sleep, and even medications can weaken the immune system.

We also know that your immune system’s effectiveness increases from birth until the teenage years but then undergoes a subtle decline throughout the rest of your life. This decline leads to impairment in coping with infectious agents that can cause disease and illness. This book will suggest ways to stay strong.

Scientists are also beginning to take advantage of the destructive nature of viruses to develop potent new virus- based drugs to kill diseases such as cancer. As an example, for the past thirteen years I have worked with my colleagues on developing

herpes simplex viruses for treating brain tumors. Yes, it is possible to genetically modify viruses in the research laboratory to harness their ability to kill certain cells (that's what a cold sore is—certain cells dying), while not killing others. If we can make viruses kill only cancer cells in the brain without killing normal brain tissue, that could be a potent new therapy for this deadly disease.

Finally, we'll look at theeffectivenessof abalanced approach to treating health- related issues, in an approach known as" integrativemedicine," in which weincludethebest of both conventional therapiesand alternativetreatmentsfrom other cultures.

I have called on several world- renowned experts in immunology, virology, and vaccines to help ask and answer some important questions. Much of the book relies on a question- and- answer format, because we want you to easily find topics that are important to you.

We believe you will find this book both informative and enjoyable, and the next time someone asks

you something like, " How can I get the flu if I was just vaccinated?" you will be able to say, " I just read this great book. . . ."

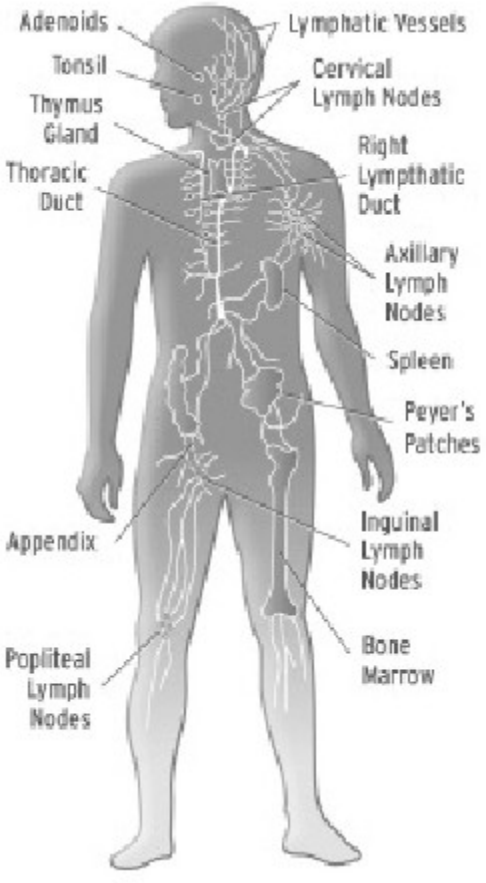
INTRODUCTION

Your Immune System

We live in a swarm of viruses, bacteria, parasites, fungi, and foreign proteins, all aiming to harm us. Happily, we have an immune system, whose main purpose is to protect us from these harmful microorganisms.

Our skin and mucous membranes provide an effective first defense against invaders. Tears, saliva, and mucous can sometimes flush away, trap, or otherwise inhibit invading pathogens, so that they do not gain entry to our bodies. In addition, the acidic environment of the stomach is also a barrier to infection. If these defenses are breached, invaders will face a rapid response by cells of the innate immune system.

This subset of immune cells, which include phagocytes (neutrophils, macrophages) and natural



COMPONENTS OF THE IMMUNE SYSTEM

killer (NK) cells, must act quickly to destroy invaders, even on first encounter. Fortunately for us, these cells are capable of recognizing many common, essential features of pathogens, such as microbial DNA, sugars, and proteins and possess the " weapons" to destroy them. No prior exposure is required. Simply put, this part of the immune system is hardwired by our genetics to recognize these invaders and destroy them.

Another extremely important part of our immune system is called acquired immunity. As the name suggest, we acquire this type of immune response when we are exposed to foreign substances. This type of immunity requires prior knowledge of the invader, and therefore is not instantaneous. On our first exposure to a specific microorganism, our immune system undergoes a permanent change so that it can " remember" what this invader looks like. This is usually a highly specific response mediated in part by lymphocytes, which are the agents of acquired immunity. The

beauty of this system is that once the immune system has committed the invader to memory, it can respond quickly and effectively the next time it encounters this invader (and its close cousins).

Our immune system also has to learn very quickly what belongs to us (our DNA, proteins, sugars) and what belongs to potential threats (virus DNA, foreign proteins, tumor cells). It also has to recognize the foods that we eat (foreign) without constantly trying to destroy them.

Unfortunately, this ability can sometimes break down, which can lead to some forms of autoimmune disease. Our immune system occasionally mounts an inappropriate immune response to our own molecules, which can itself cause disease. No system is perfect.

Like our own memories, immune" memory" changes throughout our lifetime as we encounter new things and forget old ones. The immune system can " forget" things as we get older (or perhaps the invaders have changed so that they are no longer

easily recognized.) Thus, our immune system may be well equipped to fight off the flu virus that we caught last year but not the slightly different one that will be spreading this year. Pathogens adapt. Our immune systems respond. It is an elegant and ongoing dance of survival.

FAST FACTS

THREE WAYS TO BOOST YOUR IMMUNE SYSTEM WITH KNOWLEDGE

1. BEWARE OF DISEASE

They say the world is flat, and while that may be great for global commerce, it's not so great for preventing the spread of disease. The international borders are open, creating an avenue for harmful microorganisms (viruses, bacteria, parasites, and fungi) to find their way to your front door as efficiently as any package delivered by FedEx.

A shift in weather patterns can also affect the transmission and potentially harmful properties of infectious agents. For example, shifts in bird migration patterns, changing wind currents, and increased tropical storm activity may whip up microorganisms in such a way that they can spread more easily.

The Trust for America's Health states that at least 170,000 Americans die annually from newly emerging and reemerging infectious diseases, a number that could increase dramatically during a severe flu epidemic or outbreak of an unknown disease. These diseases could endanger us both at home and overseas, put our military at increased risk, and conceivably fuel political instability in developing nations.

While much attention and funding has gone toward thwarting bioterrorist attacks, there has not been as much focus on naturally occurring perils such as severe acute respiratory syndrome (SARS), dengue fever, hepatitis C, and Methicillin-resistant Staphylococcus aureus (MRSA). And while you're keeping a wary eye out for these new pathogens, don't be surprised when we see a reemergences of more familiar diseases such as measles, mumps, and tuberculosis.

The message here is that identifying, treating, and eliminating infectious diseases must remain at the forefront of medical research. Because of the sheer

numbers of pathogens swarming around us, this war will never be won. You can win many battles, however, by, taking steps to keep your immune system working at its peak.

2. REMEMBER THAT SOME BACTERIA ARE BENEFICIAL

Cleanliness may be a culprit when it comes to allergies and autoimmune diseases. Based on studies of countries where antibiotics are not commonly prescribed, scientists have come up with the "hygiene hypothesis." This hypothesis suggests that we may have gotten too far away from the soil in our modern lifestyles. An increase in the use of processed foods and enhanced sanitary conditions may have rendered our immune systems less effective. We have sterilized the very systems that have kept us healthy. Remember, our immune systems must come into contact with potential invaders so that they can know their enemies!

As our culture has evolved from agricultural to industrial, researchers say we may have lost some important

connection to our immune system strength along the way, namely, the microorganisms from the soil that surrounded our food stocks. While nobody's yet developed a cuisine consisting completely of the earth's crust, don't be surprised to see some attempts to provide the essential balance and exposure to bacteria that previous generations enjoyed. Being too clean may be a double-edged sword that can hurt us as well as the invaders.

3. GET COMFORTABLE WITH VIRUSES!

Now that you've been convinced by the hygiene hypothesis to buddy up with some of the more helpful forms of bacteria, you may as well take the final leap and get comfortable with the other friends of the immune system, the viruses. While you may think of all viruses as "alien life forms," consider that up to one-third of our human DNA probably originated from viruses. In fact, researchers now believe that our survival as a species depends on our coexistence with bacteria.

Scientists don't consider a virus a living thing. That's because a virus is merely a relatively small piece of genetic material (RNA or DNA) that cannot reproduce itself unless it gains entry to a "host cell"—that could be our cells! A virus must find a host, infect that host by entering a cell, and take control of that host cell machinery to replicate itself. This can be quite a spectacular process. Consider that a polio virus, which is a small piece of RNA only 7,381 units long, enters a cell with 3 billion units of DNA. Despite its small size, the polio virus RNA encodes several extremely powerful proteins designed to take over the cell. They are so powerful that only two hours after the virus enters the cell, that cell is dead, having reproduced millions of copies of new poliovirus, which spill out to infect even more cells.

Here's another reason to start seeing viruses in a new light. They have an incredible work ethic that could put us all to shame, and they are speed demons that make copies of themselves much faster than our human cells can. While this is dangerous if you're

dealing with a lethal viral invader that threatens your health, it's possible that the viruses we all carry around with us helped us get to where we are—they helped us to evolve.

Finally, some immunologists are now using viruses to fight other diseases. By studying what a particular virus can do, these researchers are able to remove the elements of a virus that have disease-fighting capabilities and use these elements to enhance or add to potential therapies for treating cancer patients, for example. Several stories in this book describe work in the field known as viral therapy.

Chapter 1

Dr. Yancey Gillespie

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- How the immune system works
- Autoimmune disease
- Allergies and immunity
- Aging and disease
- Wake up your immune system!

How does the immune system work?

Our immunesystem isactually two systemsin one, both of which aremadeup of avery diverseset of cells and functions, much likeahighly trainablearmy. Someimmunecellsareready from birth to fight most

foreign invadersof your body. Thesecellsarepart of theinnateimmunesystem. Othershaveto learn how to fight theforeign invaders. Thesearepart of the adaptiveimmunesystem. Theimmunesystem hasto betrainableor adaptive, sinceso many different kinds of viruses, bacteria, fungi, parasites, and other microorganismswant to useyour body asfood.

Each of these innate or adaptive immune cells possesses a key to a lock. The innate cells are born with it, but the adaptive cells have a blank key that has to be cut to fit a lock.

What are the locks these keys are opening? The locks are on the foreign invaders, and when the immune cells open a lock, they are stimulated to divide and produce more immune cells just like themselves. These immune cells possess powerful means to kill foreign invaders, so once the immune cell gets stimulated, it kills until there are no more locks. That's how the immune system works.

We have all these immune cells, but there are a lot of microorganisms out there: infectious disease

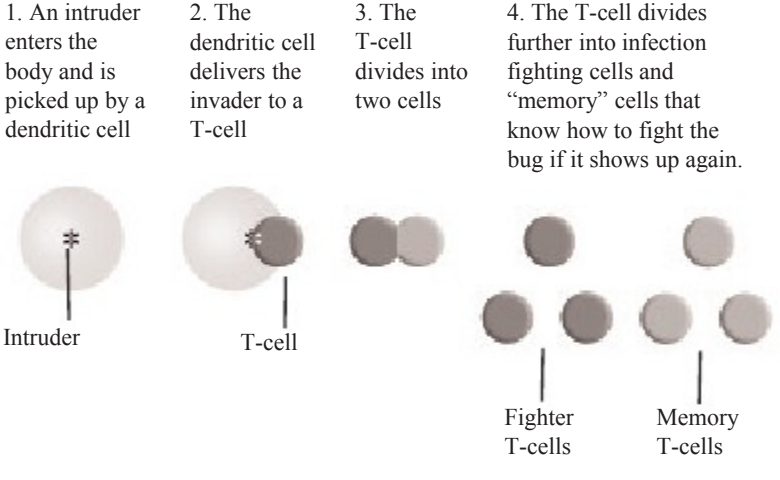
agents, tumors, protein materials from plants or animals. The reason we have these two kinds of immune cells is so that we can be protected initially by the innate cells until the immune system can program itself to fight all the infectious agents off.

Here's an example. Say a nasty bacteria like streptococcus A invades your throat and begins to attack your cells for food. Your body sends all kinds of immune cells to the rescue, and the immune system determines that it needs a set of keys that fit the streptococcus A locks—but there are hundreds of locks!

To addressthis, our immunesystem uses an amazing trick wecall the" generation of diversity." Theimmunesystem isactually ableto produceall kindsof keysby stimulating theright cells. Wecall thesekeysantibodies, madeby theBlymphocytes, and antigen receptors, madeby theT lymphocytes. Each Bcell or T cell hasadifferent key, and thusan entirearmy of cells isgenerated with many, many different specificities: custom immunecells on thefly.

Each immune lymphocyte does this by keeping a portion of these antibody, or antigen, receptor proteins constant, while reshuffling the rest of the molecules to customize their effect. This reshuffling or cutting of the keys allows our adaptive immune system to develop millions of combinations, out of which a few are able to recognize the invader. The

HOW YOUR IMMUNE SYSTEM REMEMBERS INVADERS



immune cells with the right keys are preserved through a process called memory, and when the invader tries again, they are ready to swing into action. In this way, our immune system can recognize an almost infinite number of threats to our bodies.

What is auto-immune disease?

As we have seen, the immune response is a subtle, sophisticated system designed to do very specific things. And there are control mechanisms to keep the immune system in check.

Think of the immune system like a bulldog that you want to attack only intruders, not friends. The leash you have on the dog keeps it from attacking indiscriminately.

But in autoimmunity, that leash is missing. To complicate matters, our immune system is made of a lot of components. If some of those components aren't working right, your immune system can get

turned on, but there's nothing to turn it off again. It tends to keep attacking.

And the more experienced the immune system gets with what's its attacking, the more vicious it becomes in its attack. The leash is gone! There's no control system.

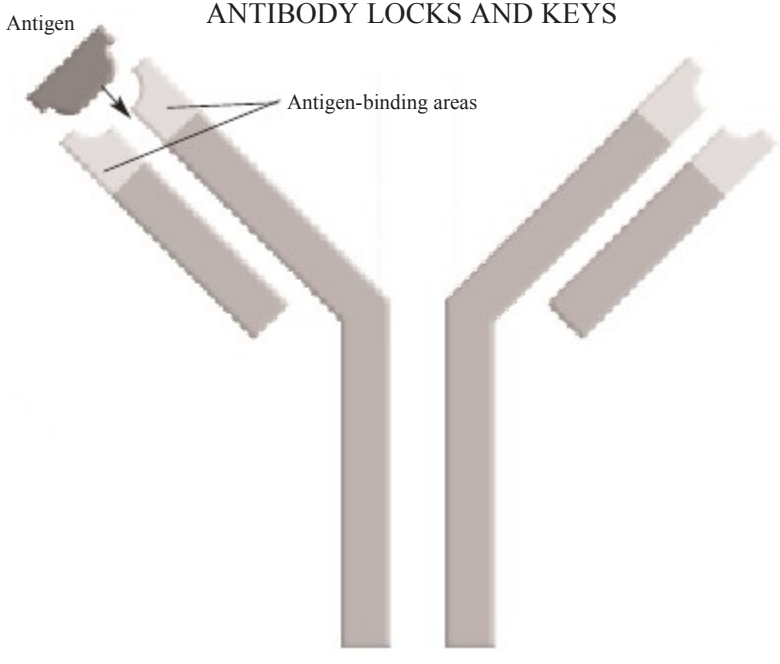
How can our immune system become stronger?

Diversity is important.

You don't want all the immune cells to recognize the same lock. Remember the generation of diversity. You want custom immune cells. If all the immune cells were the same, and a bacterium came along with locks that the keys don't fit, that bacterium could run rampant through your body and kill you. That's why you need all the different keys.

This immune cell diversity happens in the gene within the immune cell. Those genes can mutate within cells, producing a multitude of changes—millions and millions of different combinations.

ANTIBODY LOCKS AND KEYS



Antibodies are proteins found in your blood. Your immune system uses them to identify and neutralize foreign antigens, such as bacteria and viruses. Antibodies are produced by a B cell, a white blood cell. Antibodies are all similar to one another, with the exception of a small region at the tip. This area is wildly variable, allowing millions of antibodies with slightly different structures to exist. Each antibody binds to a specific antigen; an interaction similar to a lock and key.

And somewhere in all those combinations is the cell with the perfect key to unlock the lock.

That cell gets turned on and expands, making more cells like itself. All these new cells have the same key that fits the lock to defeat the virus or the microorganism or tumor.

Once a cell is determined to be the one with the right key, that cell “ wins.” It makes multiple copies of itself very quickly.

These new cells possess the same key and are sent out with the instructions to go open the lock and destroy the foreign invader. They quickly attack the bacterium or the virus- infected cell and eliminate the threat.

Our immune cells receives instructions?

Theimmunesystem usesasort of elementary school education process. Your immunecellsarecreated in thebonemarrow, and someof thesecells(called T lymphocytes) aresent to immunesystem school in an

organ called thethymus. Thethymusliterally presentsto thecells all theantigenspresent in thebody. But sometimesaT cell’skey opensthewrong lock, a lock that isactually beneficial to thebody. Say it opensalock on aheart musclecell. Wecan’t let it open that lock, so it hasto die. Cellswith keysto forbidden locksarewiped out, and the“ educated” T cellscan then leaveto form theprotectivearmy.

In autoimmunedisorders, thecell can makeakey that it’snot supposed to make, escaping “ elementary school.” That key bindsto or attackssomething beneficial to our body. It’smuch moredifficult to kill those cellsoncethey’vegotten out.

Theimmunesystem isvery complex in itsnumbersand typesof cells. Along with theT lymphocytes, educated in thethymus, wealso haveB lymphocytes, theantibody- producing cells. Becausethesecells wereinitially discovered in thebursa, alymphoid organ found only in chickens, westill call them B cells. But in humansantibody cellsareactually generated in thebonemarrow and migrateout to

largeantibody- producing organsand tissues, such as thespleen, tonsils, and lymph nodes.

Much likean army, therearedozensof typesof T cells, each onewith adifferent function. Someareregulatory T cells, somearekiller T cells, somearecellsthat suppress invaders, and somearecellsthat help B cellsmakeantibodies. Theimmunesystem is really ahugecommunity of systemsthat work together.

Does the immune system exist everywhere in the body?

The immune system exists everywhere in your body except the brain. The brain has several ways to keep the immune system out. The only time parts of the immune system can gain access is when there is physical trauma or damage.

In the case of trauma, immune system cells enter the brain and say, “ What is all this stuff? We’ve never seen it before.” The brain is full of nervous system cells that seem foreign to the immune

system, because the immune system and the nervous system evolved separately.

When the brain is injured and the immune system enters, reactions can occur. For instance, our brain cells use a certain protein to insulate axons and dendrites, so that if they happen to touch, they don’t short- circuit. Multiple sclerosis is thought to be an autoimmune allergic reaction to this insulating protein.

Are allergies related to the immune system?

Some people are genetically predisposed to allergies. Their immune system makes the wrong kind of antibody, called Immunoglobulin E (IgE). IgE recognizes things like peanuts or pollen and it produces the wrong response. This antibody binds to the antigen, and when it does it activates cells known as eosinophils.

When the IgE combine with the eosinophil, the eosinophil release histamines and other bad things

that have a very potent responses in the body. They manifest themselves as allergic reactions: the watering of the eyes, and causing the muscle in your trachea to contract so that you are not able to breathe. Not good reactions.

Now eosinophils are not all bad. They are actually present in very small numbers in the blood, and they are very important in fighting parasitic infections. As humans were evolving from scavengers to settlers, we had exposure to lots of parasites. Eosinophils probably kept us alive because of their ability to attack and kill parasites. But today they mainly produce these allergic responses.

How does aging affect the immune system?

In the elderly, the immune system has pretty much petered out, so the elderly are more susceptible to bacterial and viral diseases. A younger person who becomes ill can spend a few days in bed and then be up and running. But because an elderly person's

immune system has weakened, it needs something to heighten its awareness. It needs something to help it reactivate.

Our immune system has an " on" switch and an " off" switch. When the immune system encounters something foreign, it gets turned on. But in the process of getting turned on, the immune system activates a mechanism that will turn it off—it's part of the leash we talked about. After the immune response has had sufficient time to eliminate the foreign invader, it will get turned back off. Most biological systems work this way.

But it gets even subtler. These" ons" and " offs" cycle up and down. When you're young, the cycles are very strong. As you age, the on and off cycles continue, but not as strongly.

To be honest, we don't completely understand what limits the responsiveness of the immune system as we age. We do know the cells that evoke the immune response wear out and have to be replaced. But fewer cells are made in the bone marrow, and

the immune system education system begins to close down. In essence, the immune system becomes ineffective because the cells that are generated as a result of the immune response get tired, die, and are not replaced.

So as you age, you need to slap your immune system in the face to wake it up. You need it to produce more cells so that it can look for harmful invaders. That way, when the flu or a bacterial or viral infection occurs, your immune response will be heightened. It will be ready to work.

To stay safe, especially if you are older, you want to keep your immune system tuned up. Then it's ready, it's watching and waiting. Otherwise, as you age, it will simply lose interest.

FAST FACTS

THREE WAYS TO BOOST YOUR IMMUNE SYSTEM WITH YOUR NATURAL DEFENSES

1. TAKE CARE OF YOUR SKIN

Your skin is the external barrier, the immune system's first line of defense. Your skin maintains the entire immune system within its borders and keeps foreign elements and pathogens at bay.

Not merely a surface layer, your skin is an incredibly complex organ that is interconnected with your nervous system and your immune system. The skin protects the body's storehouses of folate, a B-complex vitamin that is an important part of cellular growth, helping the body replicate DNA when cells divide. The skin is where the manufacturing of vitamin D takes place: when our bodies

our exposed to certain types of sunlight, they convert cholesterol to vitamin D.

And don't forget those bodily fluids that, along with the skin, also form a first line of defense: tears flush out the eyes, and your saliva contains enzymes that are part of the immune system.

Feeling lousy during a cold can be viewed as a good sign that your immune system is operating in high gear. For instance, coughing and sneezing is your body involuntarily ejecting pathogens from your respiratory tract (although some scientists suggest that the viruses themselves stimulate coughing and sneezing as a way to find freedom on the airwaves and locate new hosts to conquer and infect).

2. OPTIMIZE YOUR IMMUNE SYSTEM ORGANS

While the brain, heart, and lungs receive a good deal of attention, you certainly don't want to neglect those organs that are integral to a highly functioning immune system. These essential organs are organized as the lymphatic system, coordinating the creation,

specialization, and distribution of white blood cells, called lymphocytes, that fight infection.

Approximately five hundred lymph nodes are located throughout your body, and they link with each other by way of lymphatic vessels. The lymph is a clear waterlike fluid that transports lymphocytes and other substances for use throughout the body.

Try fighting off pathogens without your thymus. This organ is where your lymphocytes come to learn their specialized and intricate tasks, before entering the bloodstream in service to the system. Make a fist. Now you know the size of your spleen, located in the upper abdomen above the stomach and under the rib cage. The spleen plays an important role in filtering out foreign substances and forming lymphocytes.

The blood vessels that carry the blood cells and the bone marrow where they are created round out the major organs making up the highly intricate lymphatic network. Bone marrow is a supple type of tissue found in the hollow interior of your bones, and the marrow in large bones produces new blood cells.

While bone marrow makes up less than 5 percent of body weight, it certainly carries its weight in the overall immune system. All the cells of the immune systems are initially derived from this source. It all begins with the bone marrow.

3. TAKE SPECIAL CARE OF YOUR CELLS

Who has the best cellular coverage? Your immune system just might be the winner when it comes to putting cells to work for the detection, defense, and disposal of pathogens and other foreign invaders. Without the estimated 10 trillion (or more) cells, your body would suffer a lot of dropped calls when it comes to fighting off viruses, bacteria, and other infections. And when they wear out and die, they are replaced by new cells.

While red blood cells carry oxygen to body tissue using the bloodstream, white blood cells carry the day when it comes to the immune system and the complex functions of immune response. These white blood cells are also called leukocytes, which is Greek for "white cell."

When the T lymphocyte white blood cells (or T cells) that are educated in the thymus detect a foreign invader, they set off the immune response to the particular antigen (antigen is short for the antibody generation that follows the immune response).

Those antibodies are made from proteins created by the B lymphocyte cells (or B cells), and they are soon at work attaching themselves to the antigens and inhibiting their progress. Or there may be an all-out response to the pathogen that results in inflammation. That's when some really specialized cells, such as neutrophils and macrophages, show up.

Neutrophils like to congregate around the site of an infection, but they can never be accused of loitering. They set to work immediately, ingesting and killing the invading microbes. Macrophage (literally "big eater") cells are scavengers that like to engulf and digest pathogens, removing all the debris to the landfill.

Given all that your immune system cells do to protect you, it seems only fair that you should take care of them so they can work at optimal performance levels.

Chapter 2

Dr. Charles Grose

M.D., UNIVERSITY OF IOWA

- Do vaccines work?
- Measles, mumps, and tetanus
- How not to get the flu
- Asthma and your immune system
- Chicken pox or shingles?
- The most fascinating virus
- How we catch colds

How do vaccines work?

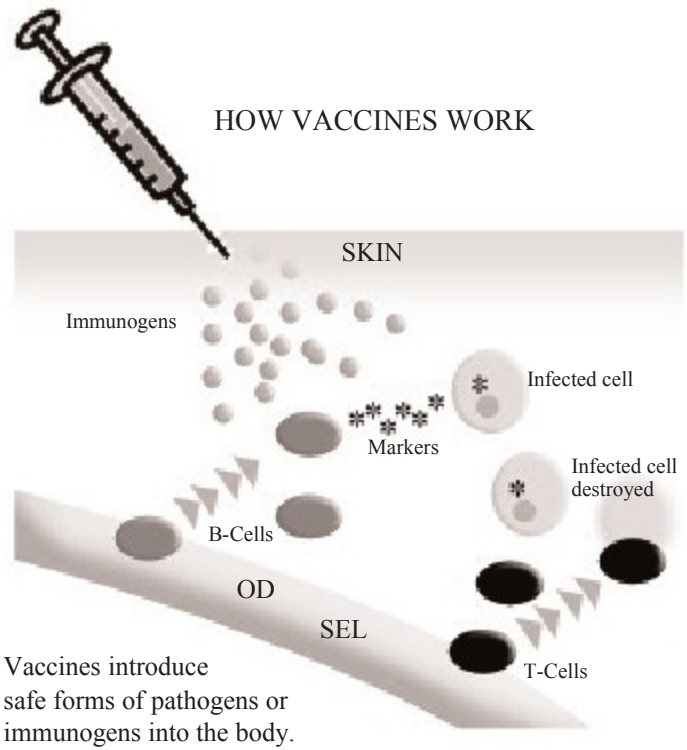
There are vaccines that give you lifelong protection, and there are other vaccines that do not.

Everyone has had the measles, mumps, and rubella vaccines in childhood. These vaccines work so well that immunity to the viruses or bacteria they address is lifelong.

Why? It depends on the organism, the bacteria or virus that infects you. Measles, mumps, and rubella are very stable viruses—every generation is essentially very similar to the previous generation. Those who get the measles now essentially have the same version of the virus that existed in Roman times.

When you have the measles and your antibody response kicks in, it kills the virus. The virus is no longer in your body. It never comes back, since your immune system has memory cells. Those cells stay in places such as your bone marrow for the rest of your life.

If you go to an exotic country and the measles virus lands on you, the memory cell in your body remembers that you once had the measles or the measles vaccine. The memory cell essentially wakes



Vaccines introduce safe forms of pathogens or immunogens into the body. Immune B cells recognize the immunogens and produce antibodies which bind to foriegn particles and mark them for destruction. T-Cells divide rapidly, identify the body's infected cells and kill them.

up your body and makes more measles antibodies. That's why you have a lifelong response.

Tetanus, which causes lockjaw, is another great example. Everyone gets a tetanus vaccination in the United States, at about two months old. If you had a tetanus vaccine at any time, you will have at least partial protection for the rest of your life.

The first time tetanus vaccines were used was during World War II, and the USArmy was the only army that gave their soldiers this vaccination. Tetanus are bacteria that live in the soil, so if you are fighting a war, you're going to get a lot of wounds and possible contamination with tetanus bacteria. But because of this effective vaccine, the United States had no cases of tetanus during the War.

What about the flu? Why doesn't our immune system adapt to each new strain?

With influenza, the flu, it works the other way. Influenza viruses are genetically unstable. They

change every year, and thus you have to get a new flu vaccine each year. There are usually two new flu strains every year, so the immune response to the flu has better odds if you have the flu shot.

But the vaccine only lasts for that year, because the next year, a new flu strain or two arrives, so the antibodies made for this year's strain don't protect you against the next.

Interestingly, all the flu strains start in Southeast Asia. They migrate from Southeast Asia through Europe and then to the West Coast. And then they move across the country. It takes approximately a year to get to the East Coast.

Is there a way to stop the flu from getting through?

There is no way to stop the flu, short of halting all international air travel. Our global economy allows us to fly all over the world, and the flu virus loves to ride along on those trips. The flu is spread by

humans, especially airline personnel who hop from destination to destination. They are an ideal mode of transmission for the virus.

Once the flu has arrived, closing schools is not such a bad idea. That way school- age children don't get sick at school and bring the flu home. We can learn from the British in World War II: Because of bombings, children were sent out from London to live with rural families. They didn't get the flu because they weren't interacting with other children.

Why is the flu so dangerous for the elderly and the very young?

The elderly truly are at the front line. The flu virus grows in the lining of the lungs, and the lungs' capacity to fight off the virus diminishes as we age. Add to that the fact that 40 percent of the generation born in the 1920s and 1930s smoked. Even if they smoked for ten years and quit, there is still damage to lungs.

And children between the ages of one and five are more likely to get severe influenza. By age six children accumulate antibodies for about six to seven strains, yet there are twenty to forty flu strains out there. So children younger than six who are attacked for first time by a virus their immune systems have never seen don't have much protection.

What about the flu vaccine?

The World Health Organization will isolate a late-2007 or early- 2008 version of the virus to be used for the fall 2008 vaccine. They take a sample—usually from Taiwan—of the predominant strain most likely to spread. Then it takes four to six months to prepare the vaccine.

Sometimes a miscalculation is made, and a strain that's not selected for the vaccine appears.

Are all vaccines safe?

Two issues have been raised about the safety of vaccines. One was raised by an English scientist about twenty years ago. This scientist published a paper that associated measles, mumps, and rubella vaccinations with autism. This caused a great stir and, while the paper was subsequently withdrawn, its effects have been long- lasting.

The second issue is the thiomerisol, or mercury, component of vaccines. Vaccines come either in single- dose or multiple- dose vials—typically ten doses per vial. It's much cheaper to create a vaccine multiple- dose. Obviously, there is a separate dose for each person, but you only use one vial of the vaccine. If you put a needle into the vial, there's always a very small chance that bacterial will contaminate the vaccine. Traditionally, the vaccine manufacturers used to add a compound that is a derivative of mercury, because mercury will not allow bacteria to grow in the compound.

The scientific name for this derivative is thiomerisol.

As you receive multiple vaccines containing tiny amounts of thiomerisol over the course of your childhood, you could, by argument, experience a cumulative negative effect.

This controversy was raised about five years ago in the United States. The National Institute of Medicine reviewed this argument and published a report saying they found no evidence of a significantly high accumulation of thiomerisol. Nevertheless, the furor had enough of an impact that the pharmaceutical manufacturers have removed thiomerisol from almost all vaccines.

The one exception is the influenza vaccine in multiple- dose vials, because that vaccine must be produced on the order of 100 million doses a year. The pharmaceutical companies say they cannot possibly produce 100 million single- dose vials of the influenza vaccines; they have to manufacture in multiple- dose vials.

This mercury debate, which has generated a lot of controversy, persists on both sides.

Does chicken pox come from chickens?

Chicken pox is actually related to the chick*pea,* because the size of the welt on the skin is about the size of a chickpea. In the Middle Ages, the English coined the name. It came from the French word for chickpea, *chichepois.*

Three infectious pox diseases feature eruptions on the skin, and their names are mostly related to the size of the pustules. Smallpox is so named to differentiate its pimple- size welts from the much larger welts of syphilis, also known as “ great pox.”

Chicken pox is another of those viruses. Until recently, every child in the United States acquired chicken pox during childhood. In 1995a chicken pox vaccine was introduced in the United States and approved by the FDA. Now everybody has been

immunized against chicken pox. Your children's children will never see the disease.

What is the connection between chicken pox and shingles?

Once you have measles and your antibody response kicks in, it kills the virus. The measles virus is no longer in your body and never comes back.

But after you have chicken pox, the virus travels through your nerves back to your spinal column and just sits there for the rest of your life. When you get to be seventy years old or so, your general immunity starts to wane, and occasionally the virus wakes up and comes back out of your nerves. That's what gives you shingles, or zoster. It's exactly the same virus you had when you had chicken pox.

Zoster is the Greek word for " girdle," the kind of girdle that wraps around the body like a belt. With zoster, the virus comes from the spine and creeps around to the front of the body. We don't often hear

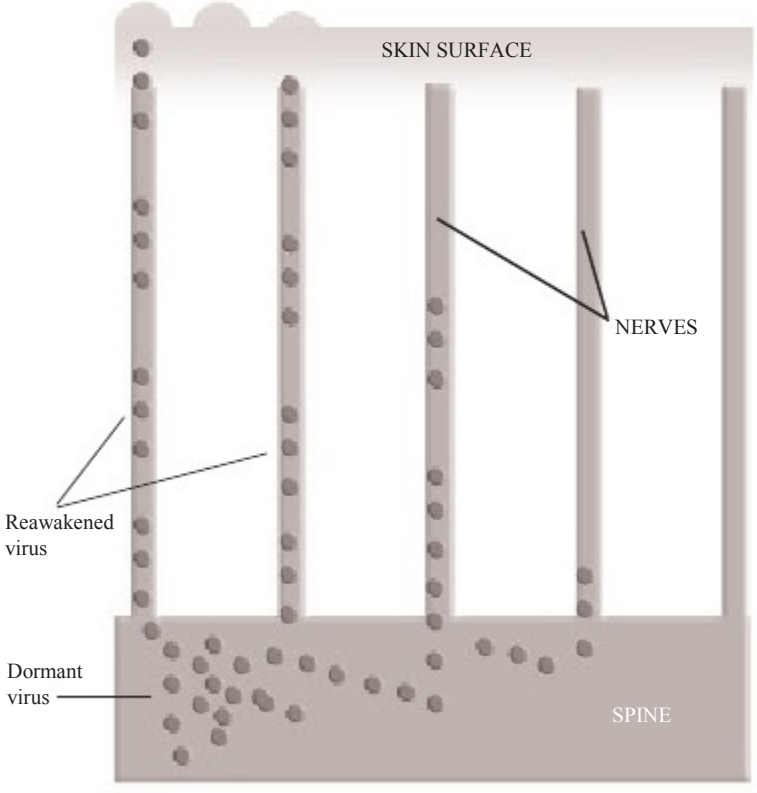
about shingles, yet the really bad cases can do damage to your nerves. In the elderly, it can make its way into eye nerves and can even cause blindness. It can also go into the nerves in your arms and legs. As a result, even an elderly person who is very capable and energetic can have significant pain and be debilitated for weeks.

Zoster has the longest latent period of any known virus. It can sit in your body for fifty, sixty, even seventy years before it wakes up. However, there's now a vaccine for shingles, and it's recommended for when you reach sixty.

What virus do you find most fascinating?

Epstein- Barr is a very old virus, and it's the one that causes infectious mononucleosis, " mono" for short. Infectious mono is very hard to spread; it can only be spread through saliva. It not only takes saliva, it takes lots of saliva. It really is a " kissing disease." You can't just get it if someone casually sneezes on

SHINGLES AND CHICKEN POX



Once you're exposed to chicken pox, the virus continues to live in your spine for the rest of you life. As you age, your immunity lessens and the virus reawakens, making its way through your nerves, back to the skin surface.

you. You can't get it from a drinking fountain. It does require some effort: You have to kiss someone. And though you only get it once, it stays with you for life.

Here's another interesting fact: Mono only occurred after the Industrial Revolution. You won't find mononucleosis in the medical textbooks of the 1500s. Before the Industrial Revolution, everyone lived in a one- or two- room house, everyone slept in the same room and used the same dishes. Children in primitive or ancient cultures got mono from sleeping in the same beds and eating off the same dishes. But, while these children were all exposed to mono, they were too young to show symptoms.

You only get symptoms if you contract the virus as an adolescent or as an adult. So infectious mono is a disease of modern culture. Also, it is one of the few diseases that is common among the higher economic classes. In fact, the higher the economic class, the higher likelihood of mono. Why? If you had mono, it meant you lived in bigger houses and

didn't sleep in the same bed as your siblings or have your food chewed for you by your parents. That would have exposed you earlier, protecting you as an adult. It's the reverse of most diseases.

Is asthma related to viruses?

Asthma is an imbalance, actually a hyperimmune response. The wheezing associated with asthma is symptomatic of this response.

Interestingly, children on farms are shown to have far less asthma, even though they have more exposure to all the pollens and ragweed. Why? Because they develop antibodies that a city person doesn't have.

There is new information that an unrecognized infection with some rhinoviruses increases the likelihood that young children will develop asthma in early childhood. Early rhinovirus infection may exacerbate an imbalance in the immune system.

Is there any connection between rhinoviruses and a rhinoceros?

There is no connection or transmission of rhinoviruses from the animal community to humans. *Rhino-* is simply from the Greek word for " nose." Rhinoviruses are the most common viruses affecting humans and the cause of the common cold.

We say that we have "caught" a cold. It usually feels like it catches us.

We are ultimately helpless against colds. Rhinoviruses are quite prevalent, and there is really no way to stop them. What we can do, however, is try to mitigate the symptoms of a cold when we have one.

There are about eighty rhinoviruses floating around—and some say there are closer to a hundred—but there's no common antigen protein and no single antibody. A vaccine approach to rhi-

noviruses has failed time and time again; there is no consistent way to generate an immune response. The good news is that you have complete lifelong protection from a specific strain once you have it. You'll never get that particular virus again.

Why does a cold initially take up residence in the nose and throat?

While your internal body temperature may be 98.6 degrees, rhinoviruses can only live at about 90 degrees, which happens to be the temperature of the nasal lining. Like it or not, that part of your body is an ideal habitat for a rhinovirus.

Why do we tend to get colds in the winter?

easy answer is that in summertime children aren't in school, spreading the rhinovirus germs to each other and bringing them home to their parents. Viruses spread best in the humidity and temperature of win-

ter, at a time when everyone is spending more time indoors and in closer proximity to each other.

Are rhinoviruses spread by sneezing?

Rhinoviruses don't spread that easily in the air, but they like to attach to surfaces. Rhinoviruses are hardy and spread quickly. It starts with nasal secretions that get on hands, and then spread. Everything you touch becomes fair game for transmission.

When you have a cold, you blow your nose, so there's a Kleenex out there spreading the germ on your behalf. Saliva is another way that viruses travel.

So, what's the answer? The best we can do is close the schools during cold season and create surfaces less receptive to the viruses.

Are viruses are here to stay?

Viruses are a part of nature and also a part of your natural lifespan, your own evolution. There are

certain viruses you get and fight off when you are between the ages of one and twelve and others that you contract in your late teens and in your twenties.

But even if we completely sanitized our homes, schools, and public spaces, we would just be deferring the issue to later years. If everything becomes too clean, we may actually get more ill more often.

FAST FACTS

THREE WAYS TO BOOST YOUR IMMUNE SYSTEM WITH YOUR DIET

1. DON'T MAKE INTAKE MISTAKES

Avoid foods that foul up a finely tuned immune system. Stay away from sugars and high-fructose syrups. One of the significant setbacks of sugar is that it raises the insulin level, which limits the release of growth hormones, with the eventual effect of inhibiting the immune system.

White blood cells thrive on vitamin C, but when sugar levels go up, glucose and vitamin C compete for entry into your cells. When vitamin C loses that contest, your immune system loses. And stay away from enriched, bleached, and non–whole grain flours because your body uses them just like it uses sugars.

Diets high in fat may weaken your immune response by toning down the performance of T lymphocytes. Transition away from trans fats especially. These are found in margarines and in many fast foods, packaged and frozen foods, and commercial baked goods. Trans fats are known to be factors in chronic low-grade inflammation, so that your immune system expends resources dealing with the damage of the inflammation rather than its core mission of defense.

Nutritionists advise limiting your fats to 30 percent of daily intake and getting your daily dose from unsaturated fats such as canola oil, olive oil, nuts, seeds, and avocados. Optimize those omega-3 fatty acids to help fight inflammation and let the immune system go after the antigens.

Maintaining a proper balance in your daily diet is very important. Crash diets and nutrient shortfalls raise your risk for infection, while overeating has been shown to lower T lymphocyte levels.

2. GO PRO WITH PROBIOTICS

Look for live active cultures, such as the kind you find in yogurt and kefir. These cultures are the helpful forms of bacteria, the ones known as probiotics that stimulate immune-related cells in your gastrointestinal tract. Acidophilus is the general name for this group of probiotics found in milk and yogurt products that create a healthy digestive system.

There's a fascinating trade-off going on in your gut. Certain types of bacteria are allowed to remain in the digestive tract, as long as they agree to deal decisively with even nastier forms of bacteria and microbes that pass through.

Stress and poor diet can upset the balance of bacteria in the gastrointestinal tract. You want your gut in good shape; otherwise the immune system will be preoccupied with gastrointestinal battles and it will neglect other areas of vulnerability.

3. KNOW YOUR NUTRIENTS AND VALUE THOSE VITAMINS

The great thing about feeding your immune system is the wide variety of food groups you'll encounter in the process. You'll be amazed at the multitude of colors and flavors and textures of foods that are great for fighting off disease. Here are fifteen fantastic food groups to place on your list when you travel to the grocery store or farmer's market, or even order from a restaurant menu:

· Berries
· Citrus fruits
· Cruciferous vegetables (cabbage, broccoli, cauliflower, kale)
· Fish
· Grapes and raisins
· Herbs and spices
· Honey
· Melons
· Nightshades (eggplant, tomato)

· Olives
· Root vegetables
· Seeds and nuts
· Soy foods
· Tea
· Yogurt

And as you incorporate the numerous beneficial nutrients that boost the immune system, there is an entirely new cast of characters to consider. Here are three that you may not know about:

Bromelain: This protein-digesting enzyme, found only in pineapple, has anti-inflammatory attributes. Before you head to the produce aisle, remember that just eating a pineapple will not give you a great deal of extra bromelain, because it is mostly concentrated in the stem, which is not nearly as tasty. So you might try a supplement. But pineapples are also a great source of vitamin C and the immune-boosting trace mineral manganese.

Ellagic acid: This plant nutrient and antioxidant is found in blackberries, blueberries, raspberries, and

strawberries. Those same berries are also succulent sources of vitamin C and manganese.

Vitamin K: This vitamin promotes blood clotting when we're injured. Vitamin K is also an antioxidant that deactivates free radicals. Vitamin K is found chiefly in leafy green vegetables such as spinach and Swiss chard, as well as in avocados, kiwifruit, and cruciferous vegetables such as broccoli, cabbage, cauliflower, and kale.

Chapter 3

Dr. Grant McFadden

PH.D., UNIVERSITY OF FLORIDA

- What is a virus?
- Ebola and HIV
- Bird flu and arboviruses
- How viruses jump from animals to humans
- Viruses vs. the immune system
- Viruses that kill cancer

What is a virus?

A virus is simpler than a cell. It's still debated whether or not viruses are actually " alive," since all viruses need a living host to survive. Both the host

and the virus interact constantly. All viruses have the same genetic code as we do. They build proteins the same way.

But viruses are amazingly prevalent. There are at least 100 million virus particles in a single vial of seawater. One- quarter of the human genome consists of remainders of ancient viruses, the ancestral genetic “ droppings” of former virus infections of human beings and other primates. It’s worth remembering that we have been coexisting with viruses for a very long time, and that most viral infections cause no symptoms at all.

Viruses are very picky about their host species. A lot of viruses pass right by humans and look for other animals or hosts.

Are viruses intelligent?

Viruses can be said to have a form of intelligence. They are surprisingly sophisticated in their own way. They know the host’s immune system and all

the tactics an immune system uses to try to eliminate a virus.

This is not a one- sided war, in which the immune system does all the fighting; viruses can actually inhibit the immune system. For instance, some very intelligent viruses create anti- immunity molecules in the form of a“ cloud” of immunity inhibitors around them. This serves to neutralize the immune system. Other intelligent viruses have learned how to hide from the host’s immune system.

You could call this the“ anti- immune” system of the virus. When you have a disease, it is because the virus has won the battle, but when you recover from a viral infection, then the host has won.

How long does a virus survive?

There is an interesting correlation between the type of virus and how long it takes for a virus to kill the cells it inhabits. For example, the HIV virus wants to kill you slowly; it wants to keep you alive long

enough to replicate and pass on the virus to someone else.

The Ebola virus has an 80 to 90 percent kill rate. Yet Ebola can't really be considered a long-term threat because it needs hosts in order to replicate and reproduce. If it kills off everyone, there won't be any hosts left. In fact, Ebola outbreaks in monkeys or human beings in Africa tend to " burn out" quickly because the virus grows too fast in these hosts and kills too quickly to form a longer- lasting epidemic.

Smallpox is a human- only virus that killed millions of people in the twentieth century alone, but if it had eradicated all humans, it would be gone. That scenario is really not in the best long-term interest of a virus, because it will die off also. In fact, when viruses have lived in one host species for a very long time, they tends not to kill as many of theirs hosts as viruses that have recently leapt onto that host species. So viruses evolve and adapt just like we do.

Is there such thing as an unsuccessful virus?

Yes. That would be a virus that is so good that it quickly wipes out all its hosts. In terms of evolution, there are successful viruses, which have staying power and unsuccessful viruses, which are so lethal that they can't find any more hosts and so disappear.

A virus will be a short- term resident if all it knows is how to defeat the innate immune system, because it will most likely be killed off by the acquired immune system. Longer- term resident viruses " know" both the innate and acquired immune systems and stick around to fight.

Speaking of the Ebola virus, why do some of these lethal viruses originate in Central Africa?

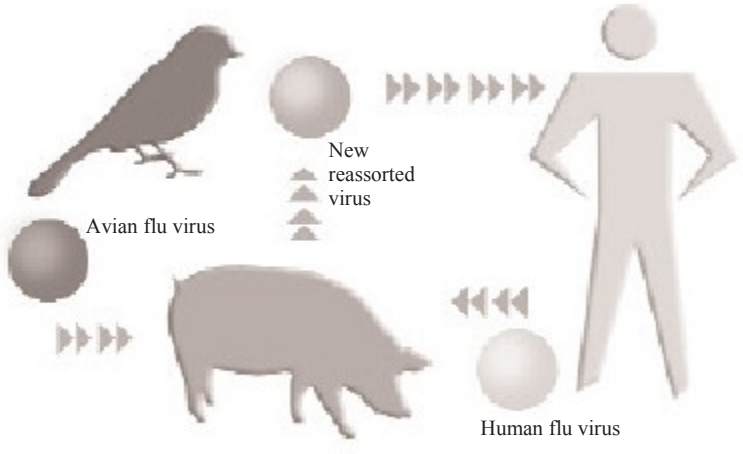
There's tremendous biological diversity within a small geographical area, with more species living more closely together. Those higher concentrations also harbor a wider spectrum of viruses. Nature is

able to conduct more experiments in the ideal setting of a tropical rainforest. Think of Africa as one of nature's " testing labs."

How do humans get the flu virus from birds?

The host for the influenza virus has always been present in nature. Many " human" influenza viruses are actually bird viruses and can reside in ducks. Bird populations migrate, congregate, and build up the virus. The bird virus then gets into the pig population, especially in places like China, where ducks are raised very close to pigs, and then humans can get the virus from the infected pigs. Then transmission happens human to human via the upper respiratory tract. In this case, the bird virus has gotten into humans with pigs acting as the " middlemen."

FLU TRANSMISSION



Influenza ("flu") viruses contain two major proteins on their outer membrane termed H (hemagglutinin) and N (Neuraminidase). These proteins help the virus to recognize and gain entry to its appropriate host cell so that it can replicate itself (and give you flu symptoms in the process!). If a cell becomes infected with two flu viruses at once, either in a human or in an animal, the genes of the virus can intermingle and form viruses with a combination of proteins from the two viruses. In this way, a "bird" flu virus can be mixed with a pig or human virus, for example. When this happens, an epidemic can occur because our immune system has no "memory" of having seen this strange new virus.

What is an arbovirus?

An arbovirus is the truncated name for a virus that is transmitted by arthropods, specifically insects. Malaria, yellow fever, West Nile fever, and dengue fever are well- known arboviruses that use the mosquito as the vector, or method of transmission, to deliver the virus. Arthropods pass on the virus by biting, which allows the virus to enter the blood-stream of the new host.

Are there any other viruses we should know about?

There is a rare infectious virus disease called monkeypox, caused by the monkeypox virus. Monkeypox is usually found among rodents and only in Africa. It is not transmitted human to human. But in 2003 there was a small epidemic in the Midwest.

Monkeypox appeared in Illinois, and it looks as if it had been transmitted by an imported African rat

that came into contact with prairie dogs, then finally with humans. People suspected of having monkeypox were hospitalized, but there were no deaths related to the outbreak. It was a close call, nonetheless. I call it the“ warning shot” of a virus, or pathogen. Scientists worry that this kind of event could happen again, or even that this virus might find a new “ home” in North American rodents such as prairie dogs.

As mentioned before, viruses learn from each encounter with the immune system of a particular species. They learn, and the immune system learns. There’s a state of tension between them, which results in the host and the virus evolving together.

To review, the innate immune system is there in place before any virus finds or threatens its host. The acquired immune system is adaptive and is developed following an encounter with an infectious disease, creating a particular set of self- protection instructions for the host to create antibodies against future threats by that same virus or pathogen.

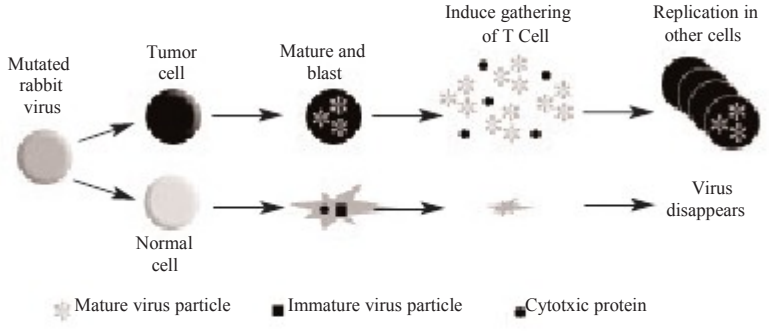
Vaccines work to bolster the acquired immune system. They are synthetic tricks used to fool the acquired immune system into thinking it has been infected with the real virus. A vaccine tricks the body into thinking it's infected, stimulates an innate response, and leads to an acquired long- lasting response and strong defense.

Are viruses purely evil?

I am particularly interested in an Australian rabbit virus. Over time, it has evolved into something less lethal than it originally wasand hassomevery interesting characteristics. Although thevirus isdangerousto rabbits, it iscompletely harmlessfor humans.

Specifically, we are looking at this rabbit virus as a possible treatment for human cancer. The rabbit virus likes to live within the environment of rabbit cells. So we asked, what other kind of cells would a rabbit virus like? What if it liked human cancer cells and killed them as if they were just like rabbit cells?

ONCOLYTIC VIRUS



An oncolytic virus is a virus that is able to infect and kill cancer cells, while leaving normal cells unharmed, making them potentially useful in cancer therapy. Replication of oncolytic viruses both facilitates tumor cell destruction and also produces dose amplification at the tumour site. They may also act as vectors for anticancer genes, allowing them to be specifically delivered to the tumor site.

It turns out that it did. In the lab, we have adapted the rabbit virus and made it safe for humans but still a killer of human cancer cells. Then we have manipulated the rabbit virus, taking genes out of the virus and adding something to it that turns it into a sort of " hot rod." We actually strip out the rabbit-

killing genes and insert a cancer killer. Then we take human cancer cells (in mouse models of human cancer) and infect them with the adapted rabbit virus.

So we've found a way to use a virus that in nature is dangerous only to rabbits as a weapon to kill cancer in humans.

FAST FACTS

THREE WAYS TO BOOST YOUR IMMUNE SYSTEM WITH YOUR LIFESTYLE

1. SLEEP

While no one will recommend that you induce a stupor to stimulate your immune system, deep, restful sleep plays an important role in bolstering your natural defenses. It appears that both the length and depth of sleep contribute to our abilities to fight off infectious disease and other invaders. Sleep deprivation has been linked to higher bacteria levels, while plenty of sleep can help one resist those same bacteria.

Cutting back on sleep-hindering additives like alcohol and caffeine can only help. Weight loss will help also, because you'll sleep more comfortably and breathe easier as you rest.

2. LOVE YOUR WAY TO IMMUNITY

A little loving might go a long way toward bolstering your immune system. A study in the late 1990s showed that people who have sex once or twice a week receive a small boost to their immune system, or at least to one factor integral to the immune system known as immunoglobulin A. Abstinence and high-frequency lovemaking didn't seem to do the trick. Undoubtedly there will be further studies and a long list of volunteers!

Sex incorporates several other stress-reduction components such as exercise and touch. As a gym substitute, a sex session can burn up two hundred calories, about the same as running fifteen minutes on a treadmill. Putting two bodies together may end up being one more way to make more antibodies.

3. BURN YOUR WAY TO A BALANCED SYSTEM

When we are overweight or have high levels of cholesterol and triglycerides, the cells in our immune system are less capable of recognizing and fighting off viruses

and bacteria. Experts recommend doubling physical activity each day, which could involve choices as simple as taking the stairs instead of the elevator, walking the kids to and from school, and parking as far away as possible from the office building or shopping mall.

Consistent exercise in the form of brisk walking, jogging, running, biking, or swimming is optimal for keeping your immune system organs and cells in optimal shape. But don't forget other social activities such as ballroom dancing, team sports, and martial arts. Another bonus of strenuous exercise? You'll sleep better!

Chapter 4

Dr. Akiko Tanaka

PH.D., TAMPA BAY RESEARCH INSTITUTE

- Integrative medicine
- Pinecone extract
- Balance in the immune system
- How nature protects us
- Aging and immunity
- How to live longer

Can folk medicines help the immune system?

In Japan, there is an understanding that traditional remedies are important. For example, herbs or plant bark pinecone are traditionally boiled in water in a big kettle; in my family, we drink this extract like a tea. It's a primitive method but effective in boosting the immune system.

In the East, the study of herbal medicine is known as Kampo, and Eastern pharmacists practice Kampo. Some college students study the subject of " pharmacognosy," and many medical doctors practice Kampo.

In my training we studied hundreds of herbs, learning the Japanese and Latin names for them all. We studied dried leaves and barks, examining the chemical components. In Japan the practice of using herbs has continued for centuries even. Why? Because it works!

Consider ginseng, for example. For years and years, ginseng has been used in Japan, China, and Korea as a general tonic to strengthen the whole system, reinforcing vital energy, increasing resistance to various diseases, and prolonging life.

Can a combination of traditional folk remedies and Western medicine help build a strong immune system?

Yes, Western culture is adapting the lessons learned from other cultures that have a scientific basis for their effectiveness.

For instance, in many culturesgreen teaisatraditional beverage, apart of everyday ritual. Wenow know that green teacontainsantioxidantsthat slow theaging processand havebeen shown to lower cholesterol.

Combining traditional folk remedies and Western medicine is called integrative medicine. Much of Eastern tradition and culture is based on the search for simple, practical ways to promote health and prevent disease. Integrative medicine is beginning to reveal the scientific basis for the usefulness of traditional healing plant extracts. By applying the modern technologies of Western science, we seek to explain the wisdom embedded in the practice of Eastern medicine.

HOW STRONG IS YOUR IMMUNE SYSTEM?

INTEGRATIVE MEDICINE

It's important to remember that integrative medicine doesn't dismiss Westernized medicine. Rather, it complements conventional Western medicine by combining the advantages of alternative medicine with extensive laboratory testing. It takes anecdotal evidence and supports it with hard scientific data.

We study traditional remedies that are derived from folklore and anecdotes. We focus on those remedies that are known to have a positive effect on health and are low risk and low cost. We then take the extra step to have these remedies rigorously tested by in vitro (cell culture), in vivo (animal), and by human clinical trials characteristic of conventional Western medicine.

What process do you use to analyze potential immune system remedies?

We start by shredding a dried form of the herb or plant or turning it into a powder.

We then extract the most likely molecules, purify them, and add them to cell cultures to see how they interact with cells in vitro. We might end up with two or more molecules from the same plant that affect the immune system differently.

Once we have isolated the effective molecules, we investigate them in animals (in vivo). In vivo studies may show that these molecules act differently than they do in in vitro experiments. For example, certain molecules may be destroyed or altered by elements of the digestive system (enzymes, pH levels, and gut bacteria) that are not present in cell culture. These digestive elements might help—or destroy—the plant molecules.

Finally, we examine their effectiveness in humans in clinical trials. This is the conventional discovery pathway for Western medicine.

Can you give us an example of something you're working on here at the Tampa Bay Research Institute?

We have identified the active chemical components in an extract of the pinecone, long used in Japan to promote health and longevity.

Specifically, the components in pinecone extract are capable of promoting conversion of human peripheral blood mononuclear cells (PBMC) to mature dendritic cells (DC).

Why is this important? DC are the most potent antigen- presenting cells of the immune system. As soon as the DC recognize a foreign invader or abnormality (such as an infectious agent, cancer, or immune disorder), the DC instruct “ troops” (other immune cells) to eradicate the problem.

The ability of DC to detect, process, and present foreign material (antigens) to other immune cells is of central importance in eliciting an effective response against bacterial- and viral- infected cells and cancer cells. Scientists believe that harnessing the power of DC will be useful in developing new generations of more refined and effective vaccines.

You talk about the balance of folk remedies and Western medicine. Is balance important to the immune system?

Balance means you are healthy. If you emphasize only one thing, that’s not good for you. The immune system is very regulated: Certain cells in the immune system are the“ generals.” And when these generals give instructions, the rest of the army follows their orders. This highly regulated system is a form of balance.

As you age, your immune system becomes less effective. Thus, an older person who is fighting a disease has a weaker immune system, and balance is lost.

However, if you balance that loss with a traditional folk remedy such as a pinecone extract (which has been validated by Western scientific methods), you have created a way to optimize this regulated system. You have corrected an imbalance.

Besides our internal immune system, how else does nature help us defend us against pathogens and disease?

Plants have always been key to human health. In ancient times, plants were often the only medicines readily available to the common person. The Greeks used an aspirinlike substance from the bark of willow trees to relieve pain and fever. The health benefits of pinecones were first documented in 500 AD by Greek physicians.

It really shouldn't be all that surprising. Look at the traditional Japanese drink sake: It contains eight herbs and is believed to ward off some of the more common ailments, such as colds and flu.

How do these plant-based remedies work with Western medicine?

Wealso study what wecall " adjuvants." An adjuvant isahelper or catalyst that may not necessarily do

anything significant on itsown. But in thepresence of theright components, it triggersareaction.

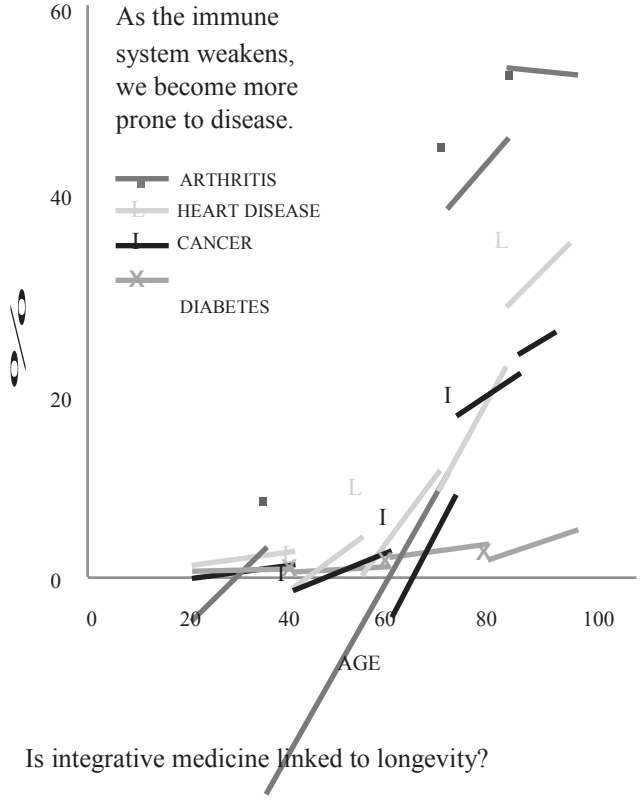
For example, when delivered along with avaccine, that samepineconeextract was found to significantly boost theimmuneresponseto thevaccine. The pineconeextract has no direct anticancer properties but significantly enhancestumor cell death when delivered along with chemotherapy.

Aging is an inevitable part of life. How does it affect our immune system?

Aging takes its toll. As we age, our immune system gradually loses its ability to defend us. We become increasingly susceptible to infections, autoimmune disorders, cancer, and so on.

Think of it like a mountain range. The peak of your immune system strength occurs around age twenty, and then you slowly begin descending the slope for the rest of your life. It's not a steep slope, but it's a decline nonetheless.

AGING AND THE IMMUNE SYSTEM



Is integrative medicine linked to longevity?

Certainly. I look at the culture of my childhood in Japan. The Eastern lifestyle promotes longevity.

Japan has approximately 40 percent of the population of the United States but in an area a little smaller than the state of California. It's a very dense population with lots of stress from everyone living and working so closely together. But everyone lives a long time. How do they do it?

First, everybody walks, regardless of their age. Exercise and diet are of critical importance. There is also the collective wisdom—the cultural teachings—that is woven into daily life and passed from generation to generation. And everyone knows of herbs that are beneficial to healing.

The Allera Immune System Assessment

Instructions:
Check the first box under each category and receive 1 point
Check the second box and receive 2 points
Check the third box and receive 3 points

1. Exercise
   I don't exercise at all.
   I walk briskly, for at least thirty minutes, four to five times a week.
   I run, swim, or bike vigorously four to five times a week.

2. Antioxidants
   I eat fruits and vegetables occasionally.
   I eat two to three portions of fruits and vegetables daily.
   I eat five portions of fruits and vegetables daily.

3. Sleep
   Getting a good night's sleep is challenging.
   I get deep, restful sleep occasionally.
   I experience deep restful, sleep almost every night.

4. Calorie Intake
   I have no idea how many calories I consume.
   I have no plans to reduce my daily calorice intake.
   I plan to reduce my calorice intake in order to boost key infection-fighting cells.

5. Intimacy and the Immune System
   I spend a good deal of time alone.
   I have a few friends and a pet, and I get along with family members.
   I make deep personal connections with my spouse or a significant other, with friends and family members.

6. Proactive Measures

I figure the bacteria I already have in my system will keep me protected.

I eat yogurt occasionally.

I take prebiotics and probiotics to boost immunity.

7. Acceptable Fats

I frequently eat mayonnaise, fried foods, and foods prepared with butter, lard, and coconut oil.

I limit my intake of fried foods and occasionally eat foods prepared with healthy oils.

My meals are prepared exclusively with sunflower, olive, canola and soya oils, soft margarines and nonstick vegetable sprays.

8. Smoking

I smoke.

I don't smoke, but am exposed to second-hand smoke frequently.

I don't smoke and I'm rarely exposed to second-hand smoke.

9. Stress

I am overwhelmed by the stress in my life.

I am aware of the causes of stress in my life and am addressing them.

I am proactively understanding and addressing stress factors that put a strain on my immune system and make me more susceptible to viruses.

10. Levity

I don't have much to laugh about.

Occasionally, I will see the humor in a situation or enjoy a joke.

I laugh frequently, including at myself, and I cause others to laugh.

11. Meal Management

I eat three big meals a day, and often go back for seconds.

I eat three meals a day, and pay some attention to portion size.

I eat smaller meals more frequently, and pay close attention to portion size

12. Addressing the Aging Immune System

Aging affects the immune system? The older I get, the better I feel!

I understand that aging directly affects the immune system, but I'm not sure that I can do much about it.

I understand that aging directly affects the immune system, and I am actively taking measures to boost my immune system as I age.

IMMUNE SYSTEM ASSESSMENT

12 - 18 points: You are putting a lot of strain on your immune system

19 - 27 points: You are on the road to immune system strength

28 - 36 points: You are an official booster of your immune system

ABOUT ALLERA HEALTH

Allera Health Products, Inc. is a research and development company dedicated to providing innovative natural products that enhance the immune system. Headquartered in St. Petersburg, Florida, the biotechnology company was founded in 2005. Allera holds the exclusive license for Proligna®, developed by scientists at the Tampa Bay Research Institute.

ImmunExtra® isanutritional supplement derived from Proligna®, apatented pineconeextract that supportsimmunehealth. Prolignaisquickly gaining areputation asan effectiveimmune- support compound. Also called PPC (polyphenylpropenoid-polysaccharidecomplex), it iscomposed of two of the most important natural compoundson earth, lignin

HOW IMMUNEXTRA IS MADE

and polysaccharide, and is a potent antioxidant.

The health benefits of pinecone extract were first documented in 500 AD by Greek physicians. Ingesting pinecones or teas brewed from them has long been associated with improved health in Japan.

In modern- day Japan pinecone extract is used to maintain wellness.

In the United States, there has been more than twenty years of positive human experience with pinecone extract, as well as published research on its benefits.

Proligna® is only available in ImmunExtra®, a once- a- day nutritional supplement that optimizes your immune system.

Fresh, renewable pinecones harvested from the forests of Wisconsin are put through a patented process that extracts active molecules. The liquid extract is tested extensively for purity and to ensure that it does not contain environmental contaminants. After being dried to a powder it is packed into vegetarian capsules.

Allera Health Products follows Good Manufacturing Practices to ensure quality and purity, and all testing is performed by independent laboratories that comply with FDA standards and practices.

You can find ImmunExtra® in fine health food stores. To find one close to you, or for additional information, please visit ImmunExtra.com.

ABOUT THE SCIENTISTS

Dr. Yancey Gillespie, University of Alabama-Birmingham

Dr. Gillespie obtained B.A. (Biology & Chemistry), M.Sc. (Cytogenetics) and Ph.D. (Immunology & Immunogenetics) degrees at the University of Mississippi, finishing in 1971. Following a NCI post-doctoral fellowship at the University of Kansas Medical Center, he joined the Department of Pathology.

In 1975, he joined Scripps Clinic and Research Foundation in La Jolla. In 1977, he moved as Assistant Professor of Pathology to the University of North Carolina- Chapel Hill. In 1977, he transferred to the Department of Surgery, Division of Neurosurgery to direct the Brain Tumor Immunology research program. In 1986, Dr. Gillespie came to UAB as tenured Associate

Professor of Surgery to direct brain tumor research efforts in the Division of Neurosurgery. He is Professor of Surgery with secondary appointments in Departments of Microbiology and Cell Biology. Dr. Gillespie is Director of the UAB Brain Tumor SPORE, and leader of Brain Tumor Tissue and Brain Tumor Animal Models Core Facilities.

The main thrust of Dr. Gillespie's research is to develop and test specific therapies for treatment of malignant primary brain tumors in adults and children, with a special emphasis on tumors of glial origin. One major focus is development and characterization of replication conditional herpes simplex viruses that are both oncolytic for glioma cells and express foreign therapeutic genes. Gene transfer includes both pro- drug converting enzymes and cytokines under different promoter systems.

A secondary focus is the ability of conventional therapeutics (radiation, chemotherapy) to enhance the replication and spread of HSV throughout the tumor mass.

This effect is being studied at the cellular and molecular levels to determine how it can be best exploited as a therapeutic strategy. These systems are validated by in vitro assays before being advanced to safety and efficacy assessment in a variety of murine models of intracranial malignant gliomas.

Dr. Charles Grose, University of Iowa

Dr. Grose is Professor of Pediatrics and Director of theDivision of InfectiousDiseasesat theUniversity of Iowa’s Children’s Hospital. He received his residency and research fellowship training at theAlbert Einstein College of Medicine in New York and the University of California Medical Center, San Francisco.

His research interests include Varicella- zoster virus, the virus that causes chickenpox in children and shingles in the elderly. He studies the components of the virus, employing a variety of molecular biology techniques. He also uses the newest imaging techniques, to determine the sites on the virus that

interact with the cell. Recently, Dr. Grose's team has discovered the first mutant strain of varicella- zoster virus ever found anywhere in the world. Thereafter, he has collaborated with the National Microbiology Laboratory in Canada, in a project to completely sequence 11genomes of varicella- zoster virus and to divide the viruses into clades.

Dr. Grose has also studied Epstein Barr virus and human herpes virus type 8. He documented the association of Epstein Barr virus infection (infectious mononucleosis) with certain neurologic diseases. He has examined HHV- 8 prevalence in low risk populations. This virus causes Kaposi sarcoma in patients with AIDS. Three to five percent of otherwise healthy people in the United States are infected with this virus. While it is not known how the virus is transmitted from person to person, the team is currently studying neonates in Iowa to determine if the virus is transmitted at time of delivery or shortly thereafter.

Dr. Grose has been associated with the Center for Emerging Infectious Diseases and Iowa Biosciences

Advantage program for undergraduate students at the University of Iowa. He is also a board member of the VZV research Foundation. His research is carried out in collaboration with groups at the National Microbiology Laboratory in Winnipeg, MB, Canada; Stanford University, California, and University of Buffalo, New York.

Dr. Grant McFadden, University of Florida

Dr. Grant McFadden received the Ph.D degree (Biochemistry) in 1975, from McGill University in Montreal, Canada. He has held faculty positions at the University of Alberta and the University of Western Ontario, and was a visiting sabbatical Professor at Harvard Medical School. He was awarded a prestigious Canada Research Chair (Tier I) in Molecular Virology in 2001and in 2005he was awarded a Howard Hughes Medical Institute International Scholarship.

He was inducted as a Fellow of the Royal Society of Canada in 2004, the Canadian Academy of Health

Sciences in 2005, and the American Academy of Microbiology in 2007. In 2006, Dr. McFadden relocated to the University of Florida in Gainesville and he is currently a Professor in the Department of Molecular Genetics and Microbiology at the University of Florida.

Dr. McFadden is recognized as a world leader in the field of virology. His lab studies how poxviruses that cause immuno- suppression interact with the host immune system. The McFadden lab pioneered the field of viral immune subversion (also called " anti- immunology"), and he is credited with the discovery of a wide spectrum of virus- derived inhibitors of the immune system. His lab also investigates host- virus tropism, and the deployment of poxviruses for oncolytic virotherapy for the treatment of cancer. He is consulted internationally about issues relating to dual use technologies and bioterrorism, particularly with respect to smallpox.

In 1997, McFadden co- founded Viron Therapeutics, Inc. (with Dr. A. Lucas) to explore the

use of viral proteins for therapeutic purposes against inflammatory diseases. In 2005, Viron was awarded the International Prix Gallien Award for new early stage Biotech Companies. To date, McFadden has published over 250 scientific papers and reviews.

Dr. Akiko Tanaka, Tampa Bay Research Institute

Dr. Tanaka is dedicated to solving the puzzle of one of life's most daunting challenges – life- threatening diseases.

Dr. Tanaka came to the United States from Japan in 1971, without knowing the English language and with the goal of a making a difference. She has overcome many obstacles as a woman scientist, courageously venturing into biomedical research and mentoring many young women who wished to enter fields traditionally dominated by men.

Her most notable scientific achievement has been the development of a folk remedy into a commercial dietary supplement known as

ImmunExtra®. Manufacturing and marketing of this product is overseen by Allera Health Products, Inc., formed in 2005. ImmunExtra™ is now undergoing preliminary clinical trials with several collaborating institutions.

The knowledge gained through Dr. Tanaka's long- term research efforts has contributed to our understanding of the cause, cure and prevention of such chronic, debilitating diseases such as AIDS, hepatitis C and certain cancers associated with herpes- virus infections.

Of equal significance, Dr. Tanaka co- founded the Tampa Bay Research Institute in 1981. She has ventured onto the frontiers of biomedicine, helping to popularize the concept of Integrative Medicine, in which modern biomedical research is afforded the insights provided by the practice of folk medicine. As Integrative Medicine is developed further, it may provide important guidance in advancing the concepts of preventative medicine. The Tampa Bay Research Institute is dedicated to meeting the most

imminent needs of humankind in its quest for cures and disease prevention strategies.

Dr. Tanaka has received numerous awards for her accomplishments in science and service to mankind, and in 2005she received an Honorary Doctor of Science degree from Eckerd College.

Frank Tufaro, Ph.D., Allera Health Products

Dr. Tufaro istheCEO of AlleraHealth Products, a research and development company dedicated to providing innovative, natural products that enhance the immune system. Headquartered in St. Petersburg, Florida, the company was founded in 2005.

Allera holds the exclusive license for Proligna®, a Pinecone extract developed by scientists at the Tampa Bay Research Institute. Allera's first product, ImmunExtra®, is the only supplement that contains Proligna, an all natural, preservative- free, patented, botanical compound first studied in Japan and developed by scientists at the Tampa Bay Research Institute in Florida.

ImmunExtra® comes to market after more than 15years of rigorous research on the pinecone extract that is the basis for Proligna®. Extensive research indicates that pinecone extract optimizes immune cell activity to help the body combat germs and viruses that may cause illnesses.

Dr. Tufaro is a former professor of microbiology and virology at the University of British Columbia. During his 17- year tenure, he published extensively in the areas of virology and cancer.

He was one of the original founders of Neurovir, Inc., a Vancouver- based biotech company with a mission to develop herpes- simplex virus oncolytic vectors for treating cancer. Dr. Tufaro initially served as Chief Scientific Officer, where he managed all aspects of drug development, including FDA interactions and contract manufacturing. He then served as CEO, during which time he negotiated and executed the successful merger of NeuroVir with MediGene AG, a public company headquartered in Munich, Germany.

Following the merger, Dr. Tufaro was appointed the Managing Director of the U.S. subsidiary of MediGene AG. In that capacity, he hired and led a team of 15Directors and VPs, including representatives from manufacturing and process development, pre- clinical, QA/ QC, regulatory, clinical, and business development. Within 18 months, he developed MediGene, Inc. into a fully integrated drug development company of 55employees located in two facilities in San Diego.

From MediGene, Dr. Tufaro worked with several biotech start- up companies to develop successful financing and product development strategies.

He remains active in both the business and scientific arenas and serves on the Scientific Advisory Boards of several public and private companies.

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www.allerahealth.com
www.immunextra.com