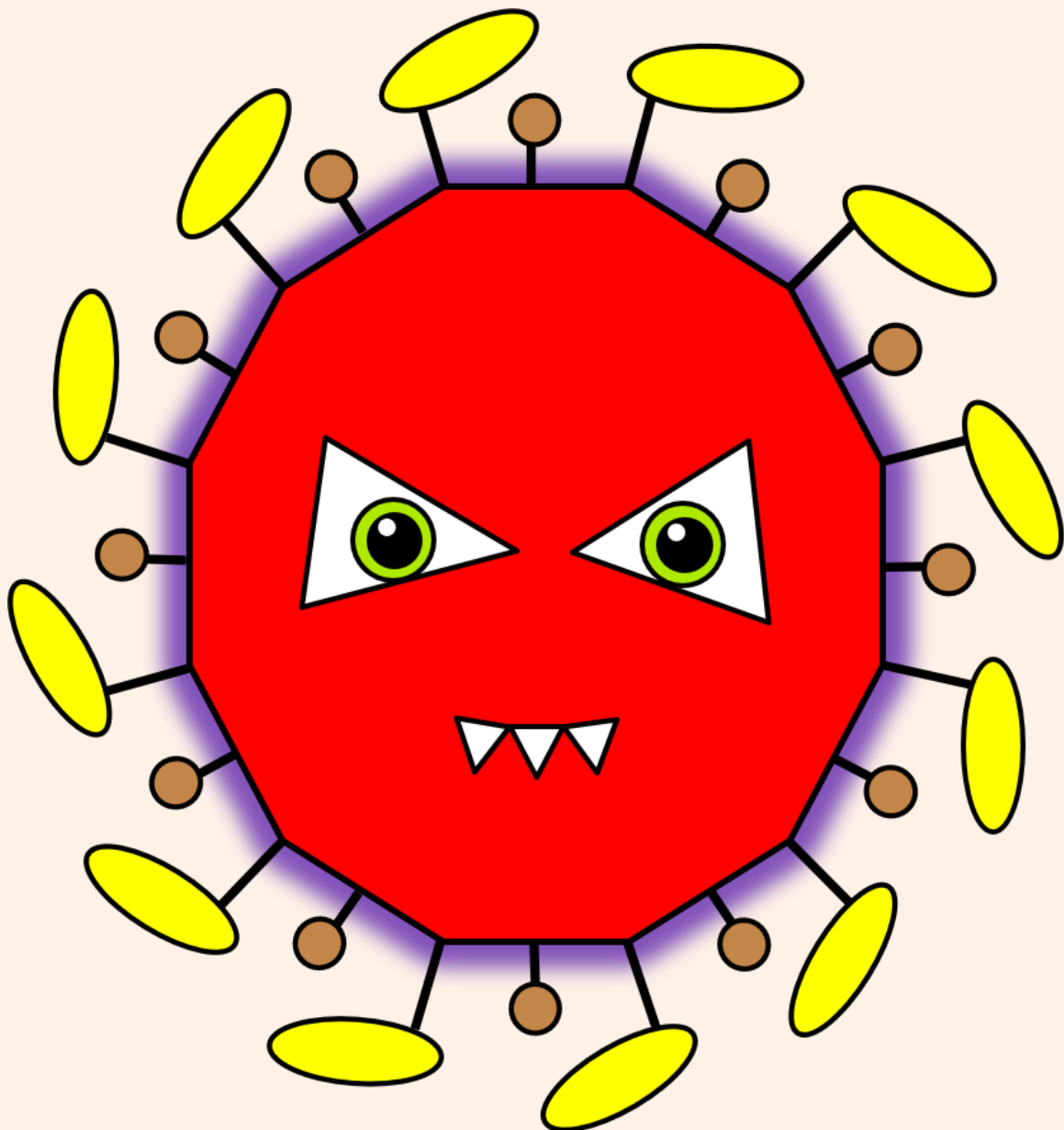


The Immunocytes and the coronavirus

A new enemy



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A new enemy

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Since we are born, we are threatened by many dangerous microbes that cause infection and death. To fight them, we need various defense cells, which we will call **immunocytes**.

On rare occasions, new infectious agents emerge in the world, to which our immunocytes may not be prepared. One of them is **Corina, the coronavirus**.

In this book, we will understand the global danger posed by Corina and learn how to help our immunocytes in this deadly battle.

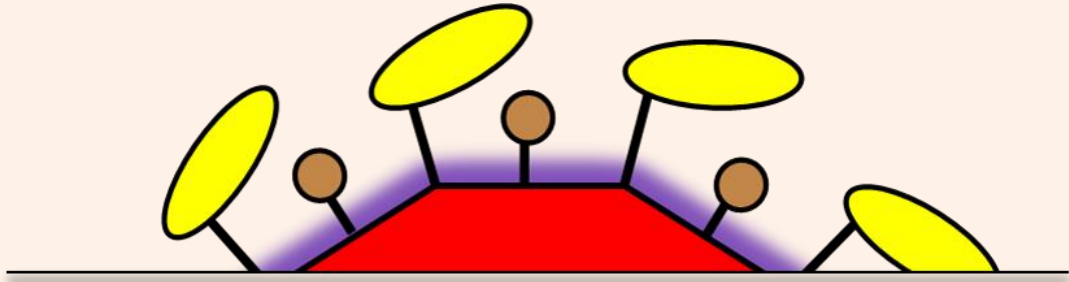
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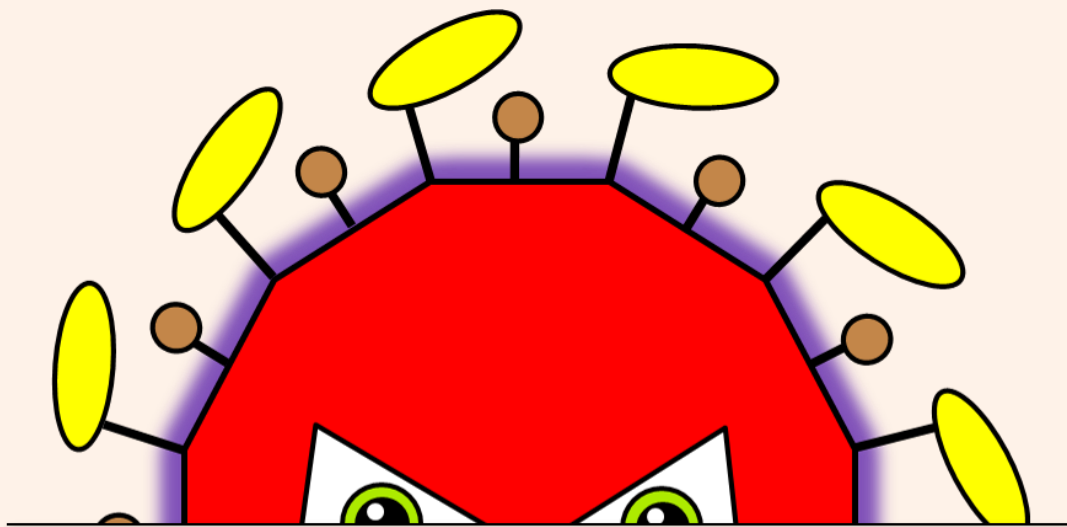
Chapter 1:

Corina, the coronavirus



Just 4 months ago, in December 2019, Dr. Li Wenliang, an ophthalmologist, alerted in the city of Wuhan (China) about some patients with an apparent new infectious respiratory disease.

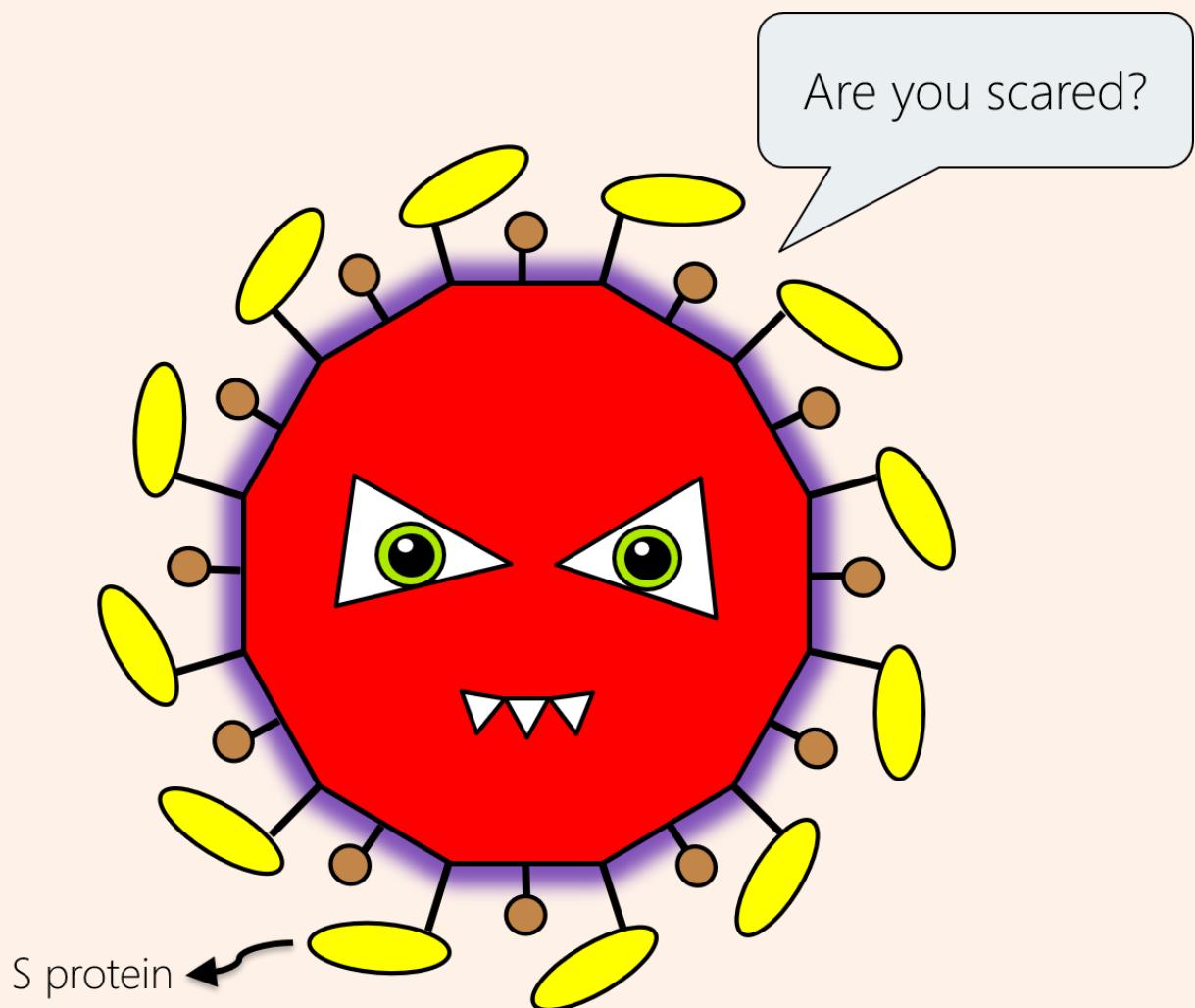
Initially ignored, even denounced for promoting "false alarms," Dr. Wenliang's alert was ratified shortly thereafter: many patients came to Wuhan hospitals with a clinical picture essentially characterized by cough, fever and severe respiratory distress, fatal in some cases.



Prominent scientists immediately looked for the causal agent. And, oh surprise, on January 7, 2020, a new infectious agent was identified. Humanity witnessed the appearance of ... Corina, the new coronavirus!

In scientific terms, Corina is actually called SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), and causes a disease called COVID-19 (coronavirus disease 2019).

Why is it important to know Corina? The answer is clear: it spread all over the world! In 4 months, it has infected 1,007,977 people and caused 52,771 deaths (official data as of April 2, 2020); its expansion is still uncontrollable.



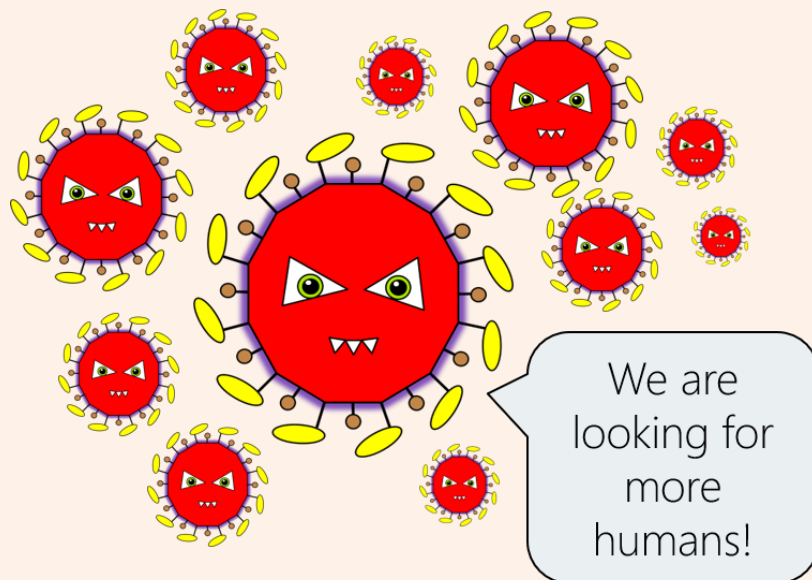
Chapter 2:

Corina attacks

Corina is an RNA virus (it has ribonucleic acid as genetic material). It cannot survive without a host. And it chose human beings!

Corina is dangerous for several reasons:

- It is a new virus. Therefore, scientists don't know it completely. Neither our immunocytes.
- It is quite contagious. On average, an infected person spreads the virus to 2 or 3 more people. Without control measures, viral propagation becomes exponential and uncontrollable.

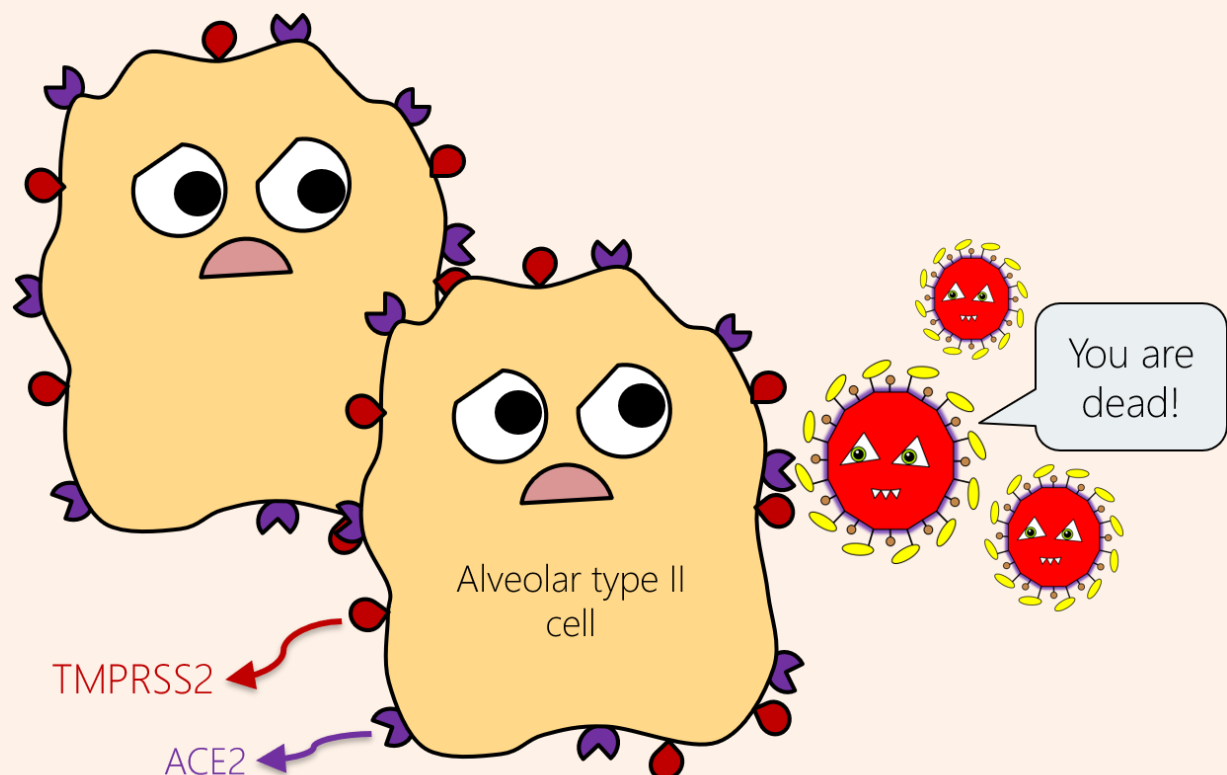


- It can be lethal. In general, 3% of infected people die. This percentage is higher in the elderly and patients with other diseases such as diabetes and obesity.
- Asymptomatic subjects can also spread the virus.

Corina is mainly transmitted through respiratory secretions. A cough, a sneeze, a touch of the face with contaminated hands, even the speech of an infected person at close range, can be sufficient to get the virus. Hence the importance of social isolation and hand hygiene.

In this way, Corina uses the S (spike) protein to bind a cell receptor named ACE2 (angiotensin-converting enzyme 2), expressed in respiratory epithelial cells including alveolar type II cells, which explains the preferred attack on the lung. Another membrane molecule that favors viral entry is the protease TMPRSS2. Our cartoon alveolar type II cells will be called Kjem and Yemi.

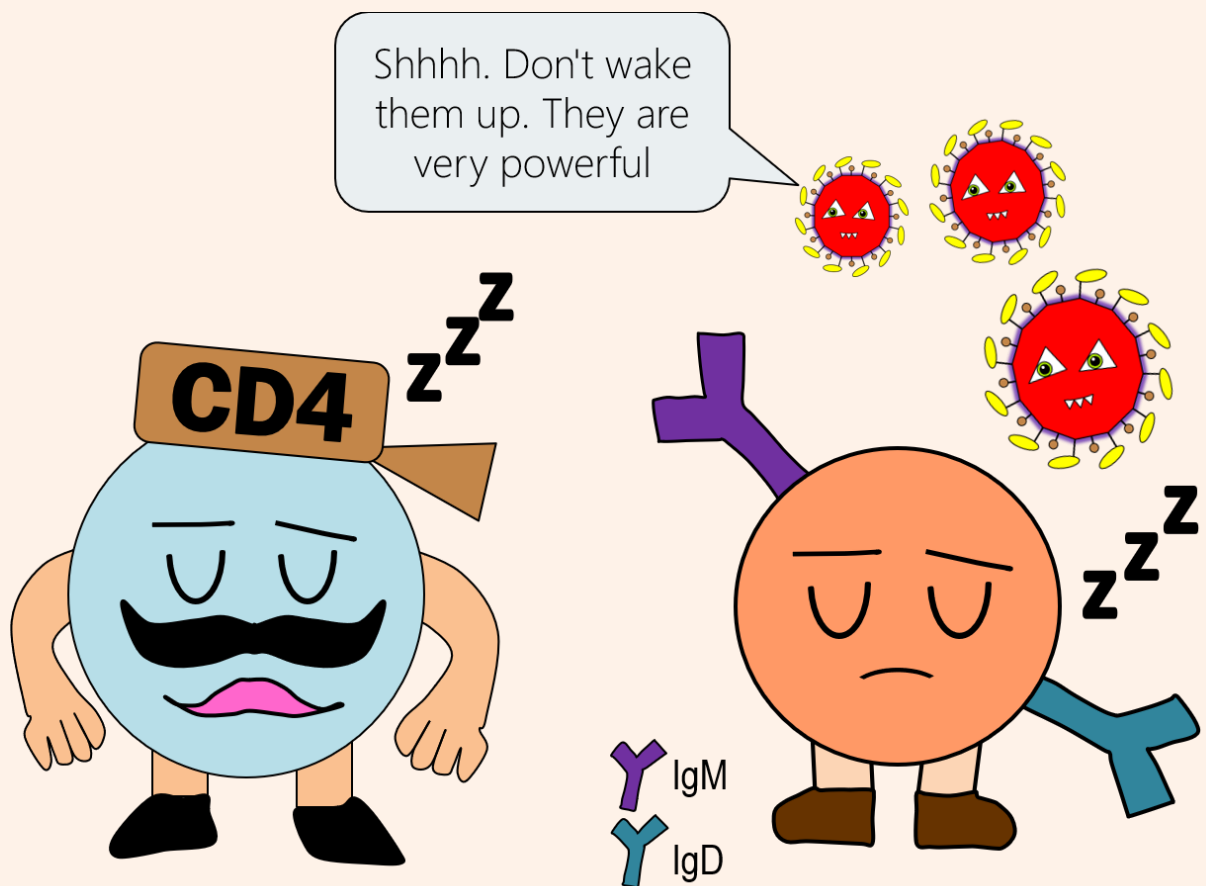
Once inside human cells, viruses use the cell's machinery to multiply.



Chapter 3: The immunocytes get surprised

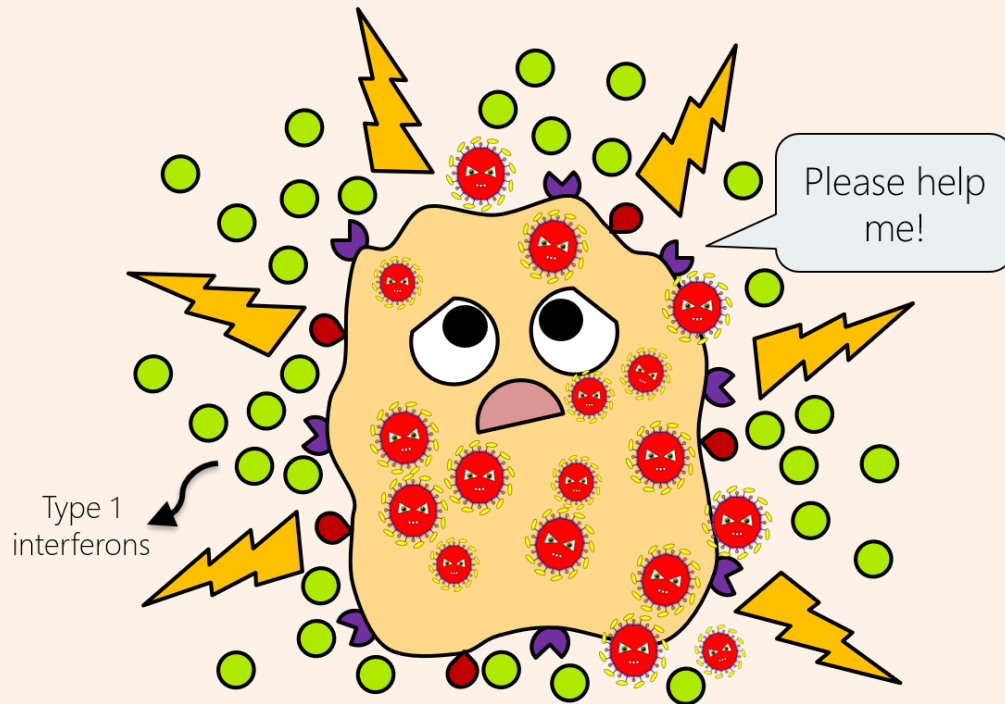
Where are our immunocytes? Normally, prepared to fight against dangerous infectious agents.

That's when we have a big problem. Our T and B lymphocytes, the most powerful adaptive immune cells, are not ready to face Corina because... she is a new virus!

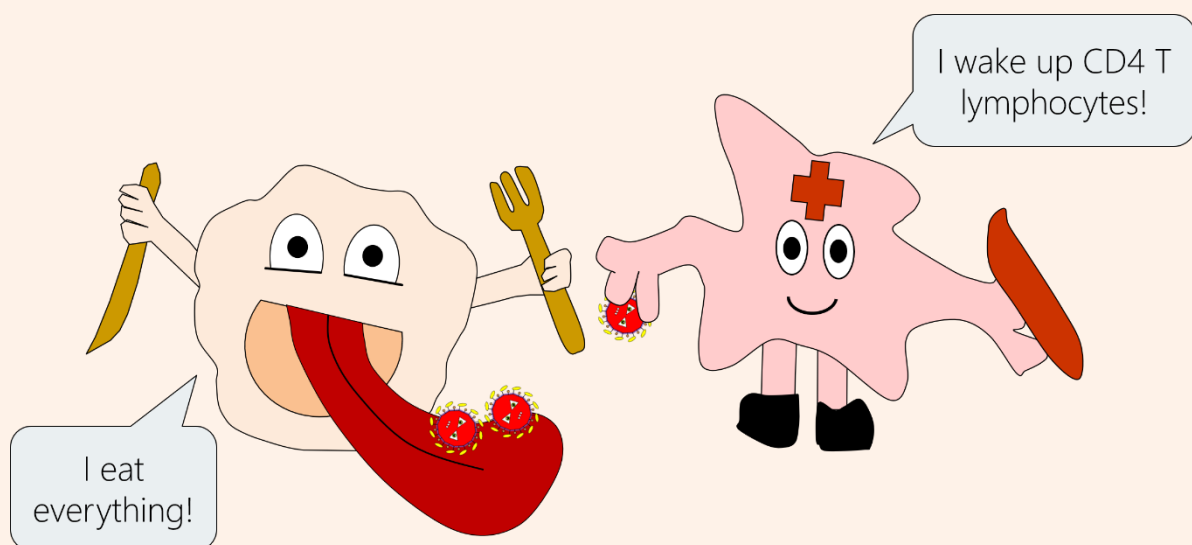


Activation of the powerful adaptive immunity will take weeks. Meanwhile, we must contain Corina with the first line of defense, that is, the innate immune system.

Typically, a virus-infected cell warns nearby cells by producing type 1 interferons, which "interfere" with viral reproduction and increase cellular antiviral resistance. Early production of interferons appears to be essential to rapidly eliminate Corina.



Innate cells that recognize and trap Corina include Fefon, the hungry macrophage, and Bertha, the vigilant dendritic cell, who also has the ability to activate adaptive immunity.

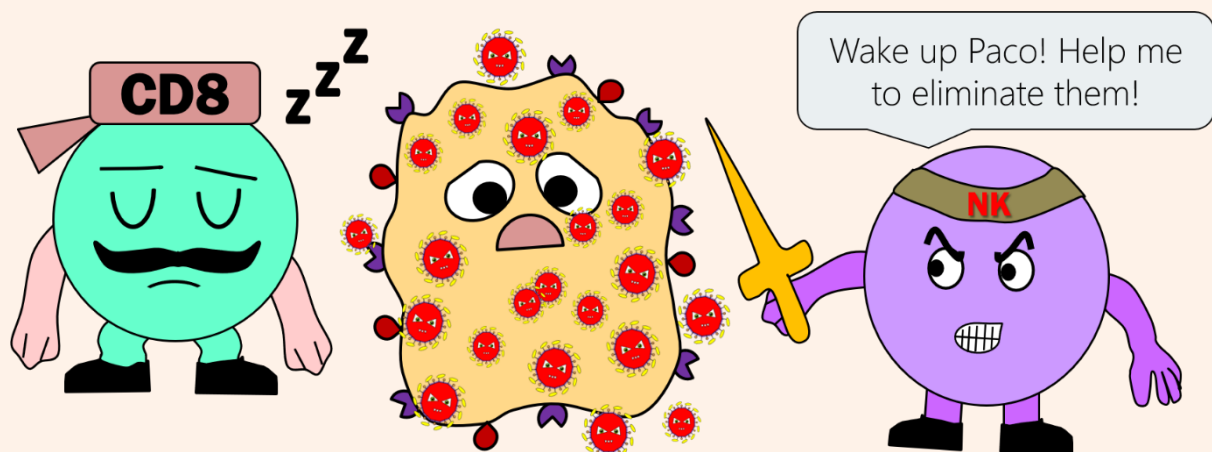


Chapter 4:

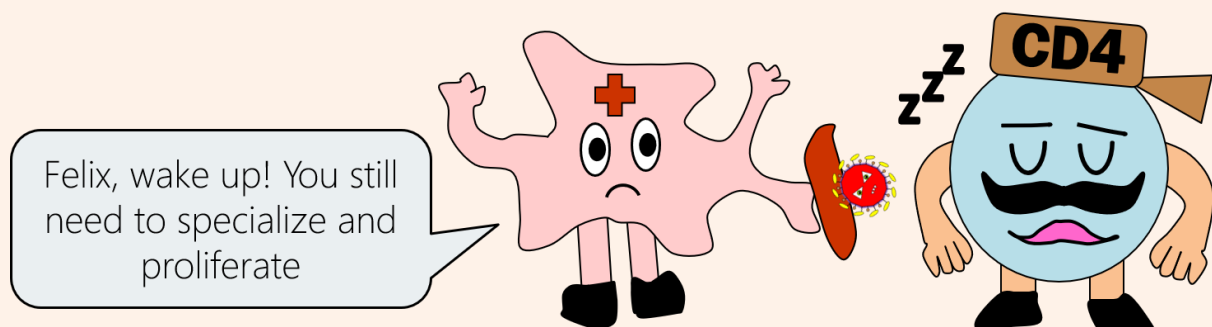
The power of the immunocytes

Following the viral attack, the immunocyte army is recruited to the infection site during the next hours to weeks, where they deploy many powers. In addition to Bertha and Fefon, the most important immunocytes involved in this battle are:

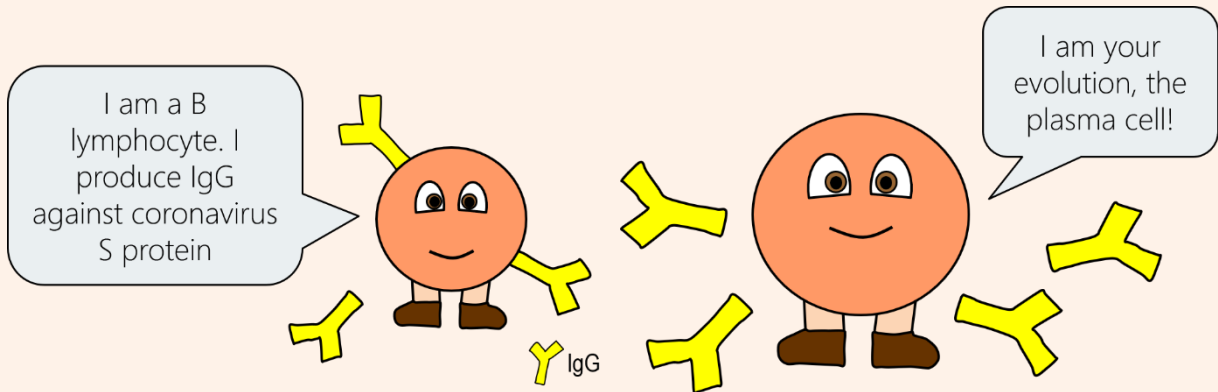
- Paul, the NK lymphocyte, and Paco, the T CD8 lymphocyte. They kill virus-infected cells. Paul is always ready to attack. Paco needs to be activated, a process that can take weeks.



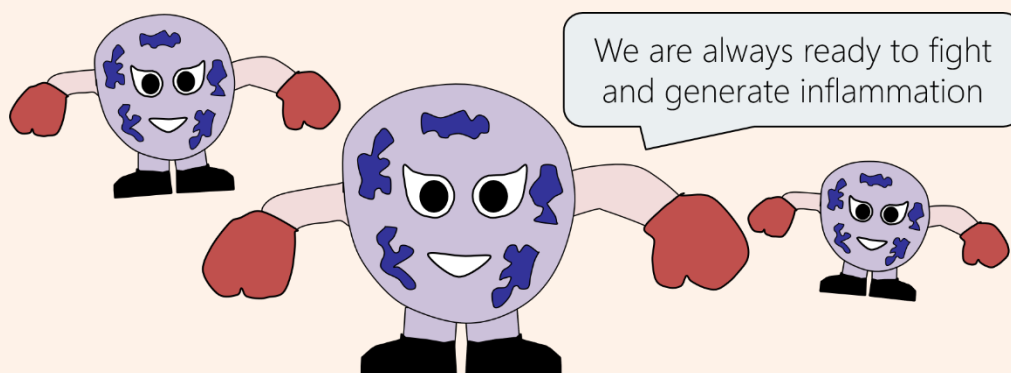
- Felix, the T CD4 cell, enhances or regulates the action of other immunocytes. The awakening of Felix is slow, similar to Paco's.



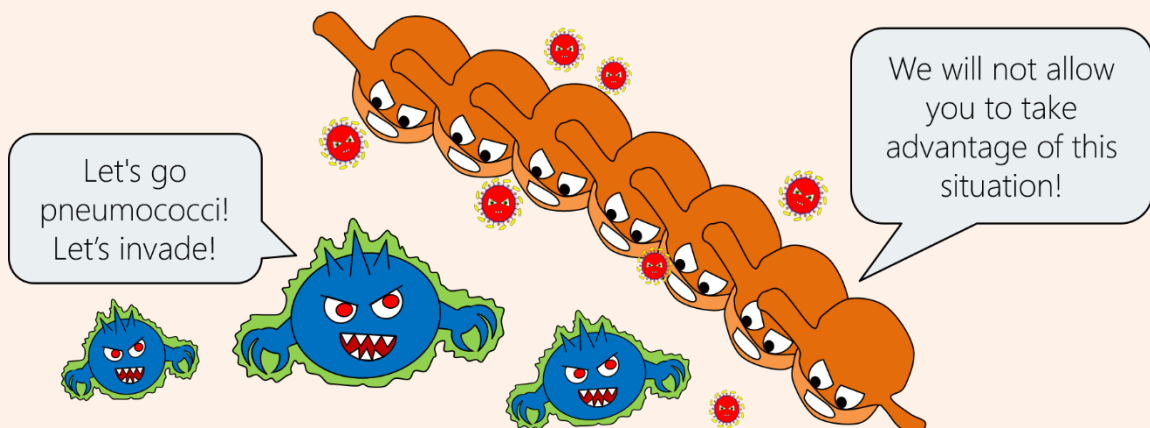
- Moli, the B lymphocyte, fabricates antibodies against Corona molecules. The specialization of Moli to achieve production of effective G-type antibodies (immunoglobulin G) can take weeks.



- Robert, the neutrophil, is attracted to infection sites and amplifies inflammation.

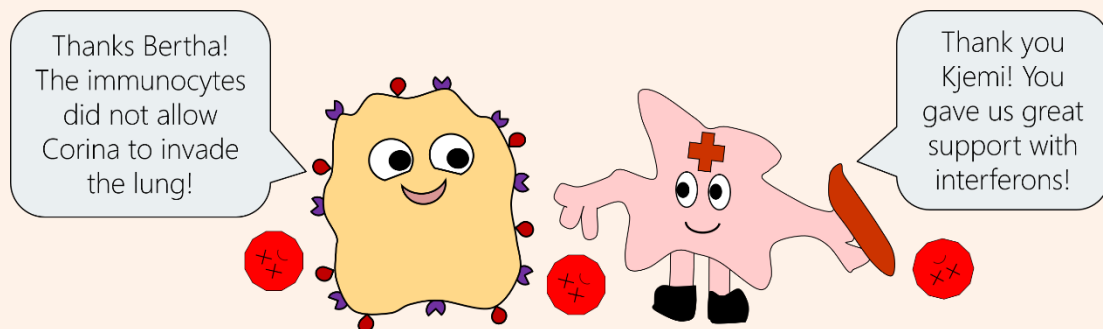


- Vilma and her friends, the epithelial cells, form a barrier that tries to impede superinfections by other enemies, such as the deadly pneumococcus.

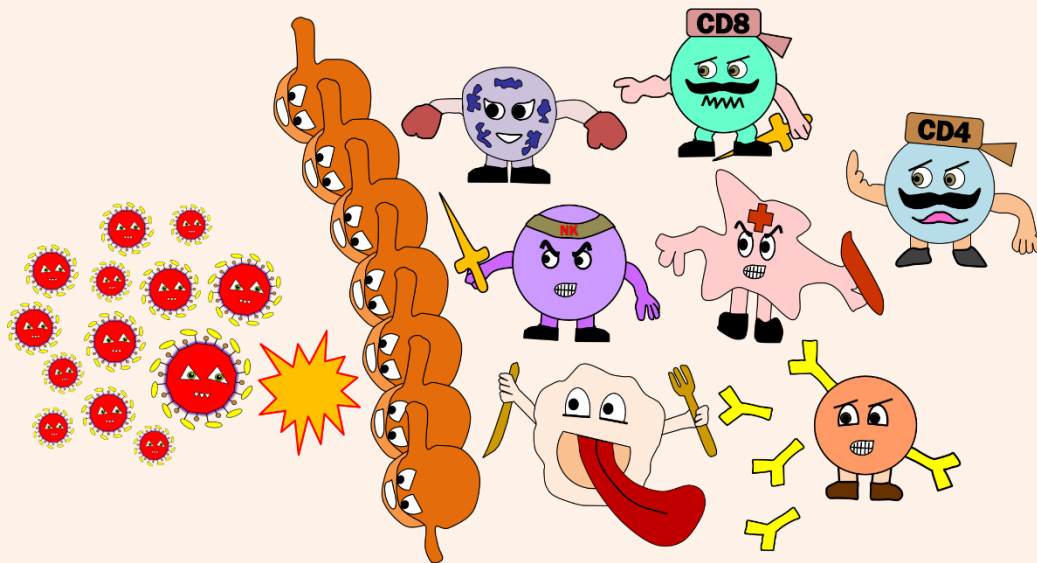


Chapter 5: Dangers of the battle

Overall, 80% of people infected by Corina develop mild or moderate symptoms, limited to inflammation of the upper respiratory tract, general malaise and fever. In these patients, the immunocytes eliminate Corina rapidly, preventing lung invasion.



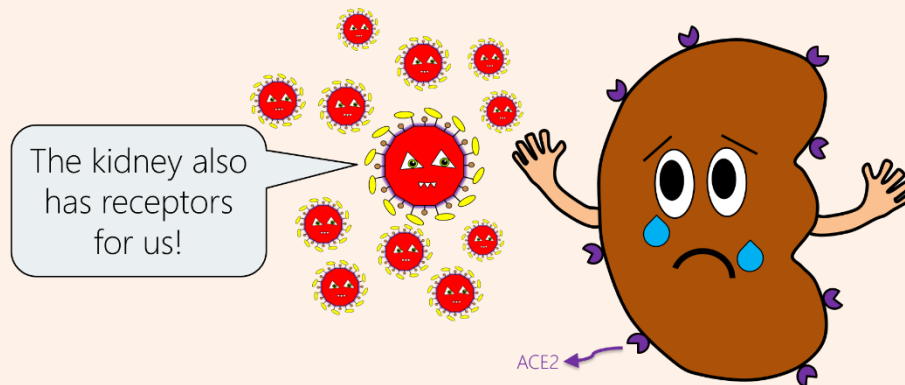
If Corina's attack is not detained in early stages, the battle between the powerful immunocyte army and the millions of viruses can become intense, explosive and often prolonged, extending to several organs.



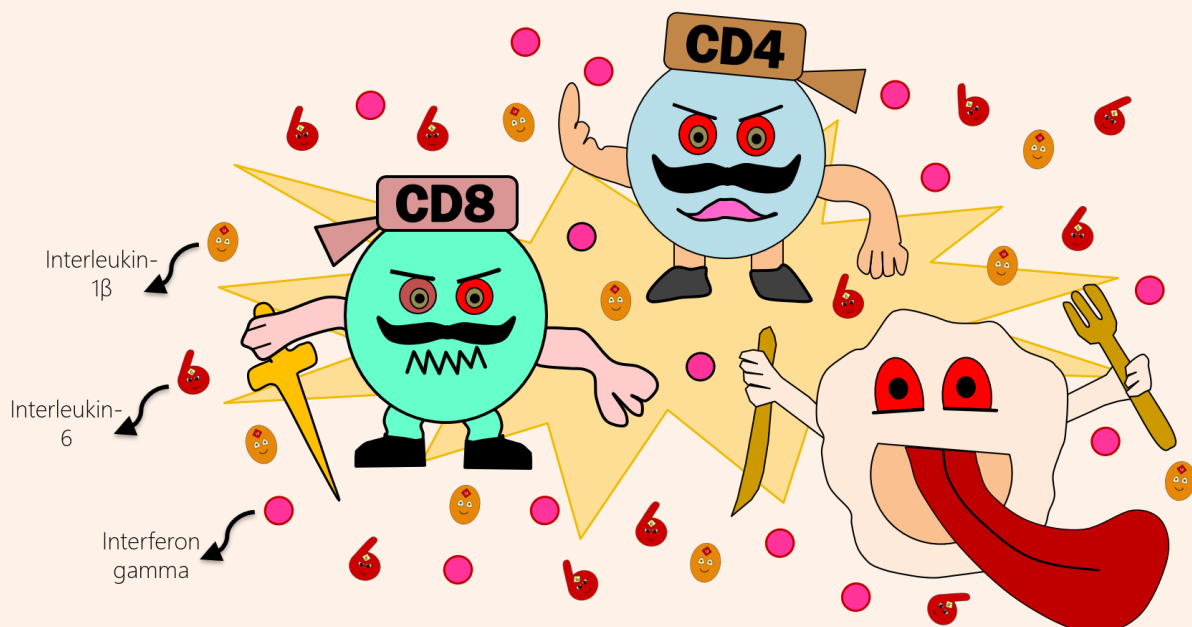
Given this, it is essential to avoid severe damage to vital organs, such as the lungs, kidneys, heart and brain.

Organ damage can be caused by:

- Direct attack by Corina, who looks for the ACE2 receptor in alveolar type II cells (lungs), oral and airway epithelial cells, enterocytes (gut), myocardial cells (heart) and renal tubular cells, among other cell types.



- Over-activation of the immunocytes, whose amazing power can cause more damage than the virus itself. "Hemophagocytic lymphohistiocytosis" and "macrophage activation syndrome" are extreme forms of immune dysregulation, catastrophic for many vital organs. The massive release of inflammatory molecules by lymphocytes and macrophages is called a "cytokine storm".

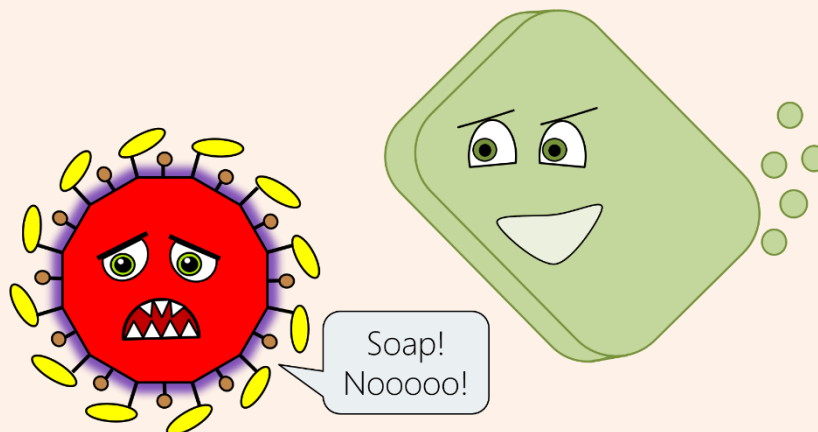


Chapter 6: Battle strategies

Sadly, 20% of people infected with the new coronavirus develop severe illness, 7% require intensive care unit support and 3.5% die.

World governments' response to this deadly virus has included several strategies:

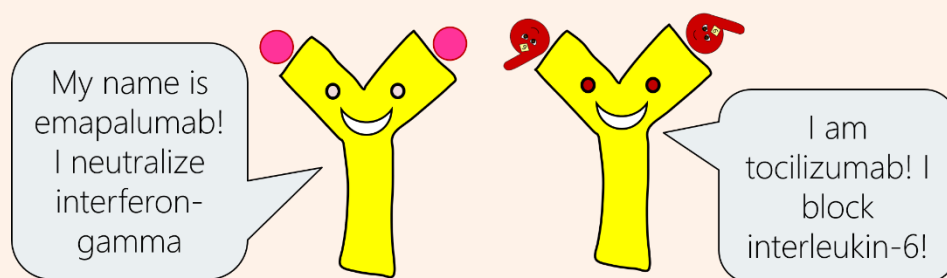
- Prevention of contagion through hand hygiene, travel restrictions, social distancing, disinfection of objects, use of face masks and technological tools such as mobile applications that warn of case proximity. However, disobedience of the population to authorities and shortage of protective material hinders the global application of these measures.



- Early diagnosis by detecting viral RNA in the respiratory tract mucosa of people with typical symptoms such as dry cough and fever. However, the availability of tests appears to be insufficient given the rapid spread of the virus.
- Equipment of hospitals and health personnel. It is regrettable that in several countries the corruption of the authorities,

accumulated over many years, is reflected in fragile health systems and unprotected health personnel against the virus.

- Identification and use of anti-Corona drugs: interferon alfa-2b, ritonavir, lopinavir, remdesivir, umifenovir, favipiravir, ribavirin, hydroxychloroquine, azithromycin, nafamostat, nitazoxanide and ivermectin, among others.
- Identification of predictors of severe disease: lymphopenia, high neutrophil-to-lymphocyte ratio, elevated ferritin, increased levels of some cytokines (e.g., interleukin-6) in blood.
- Use of immunosuppressants and immunomodulators in patients with immune over-activation: corticosteroids, tocilizumab, anakinra, ruxolitinib, emapalumab, human immunoglobulin.



- Use of plasma from recovered cases in critically ill patients.
- Development of vaccines, that is, non-infectious viral molecules that induce anti-Corona immunity in healthy people.
- Support to people in need due to economic and work crisis ("Happy are those who are concerned for the poor; the LORD will help them when they are in trouble." Psalms 41:1).
- Prayer to the Creator ("If they pray and turn from their evil ways, then I will forgive their sin and heal their land." 2 Chronicles 7:14), as the presidents of Paraguay and El Salvador did.

Chapter 7: Victory!

All the actions described in the previous chapter have not been sufficient to eradicate this pest globally.

Indeed, 5 days ago, when we wrote the Chapter 1 of this book, there were 1,007,977 cases and 52,771 deaths. Today, April 7, 1,431,706 cases and 82,080 deaths have already been reported (<https://www.worldometers.info/coronavirus>). Although the case-fatality rate for COVID-19 by age varies between countries and even cities, the elderly and people with chronic diseases (e.g., diabetes, cancer, chronic lung disease, cardiovascular disease, obesity, smoking) appear to have an increased risk of death.

Today, SARS-CoV-2 caused around 7,000 deaths, a significant fraction of the 151,056 deceased today in the world (<https://www.worldometers.info/en>). The next one can be me, can be you, can be anyone. The valid question in this context, and truly applicable since we are born, is: Am I ready to die?

Two thousand years ago, the apostle Paul wrote to the church of Philippi:

"For me, to live is Christ and to die is gain." (Philippians 1:21, The Holy Bible).

And to the church of Rome:

"If we live, we live for the Lord; and if we die, we die for the Lord. Therefore, whether we live or die, we belong to the Lord." (Romans 14:8, The Holy Bible).

And to his disciple Timothy, shortly before death:

"For I am now ready to be offered, and the time of my departure is at hand. I have fought a good fight, I have finished my course, I have kept the faith." (2 Timothy 4:6-7, The Holy Bible).

Was Paul crazy? Paul, the former persecutor of Christians, the witness of Stephen's death. Paul, the one who breathed threats and death against the followers of Jesus Christ, already risen. Paul, the intellectual religious transformed into a Christian by the power of the Lord Jesus, was fool for the majority of the world:

"For the message of the cross is foolishness to those who are perishing, but to us who are being saved it is the power of God." (1 Corinthians 1:18, The Holy Bible).

However, Paul knew who he believed in and was certain that death is victory, the passage to heaven for Christians.

"And that is why I suffer these things. But I am not ashamed, because I know whom I have believed and am persuaded that he is able to guard what has been entrusted to me until that day." (2 Timothy 1:12, The Holy Bible).

"There is reserved for me the crown of righteousness, which the Lord, the righteous Judge, will give me on that day, and not only to me, but to all those who love his appearing." (2 Timothy 4:8, Holy Bible).

As sure as I am. Glory to God! If you are not sure of the salvation of your soul, the Lord offers you the way:

"Jesus said to him, "I am the way, the truth, and the life. No one comes to the Father except through Me." (John 14:6, The Holy Bible).

In this little book, we learned about the global danger posed by Corona, the coronavirus, to humanity, as well as the protection conferred by a quick and balanced immune response.

I encourage you to share solutions, take care of yourself, help your family and your neighbor and, above all, look to God.

Juan Carlos Aldave, MD

Allergy and Clinical Immunology

Dedicated to:

- Dr. Li Wenliang and all the people who died from COVID-19.
 - Dr. Kelly Coba and Dr. José Mori San Román.
- Our children and adult patients with primary immunodeficiencies and allergies.
 - All my friends in Peru and the world.
- All professors who help us diagnose and treat our patients with primary immunodeficiencies.
 - My family.
 - Kjemí and Yemí.
- My brother Víctor (Fefon) and my sister Bertha.
 - My father Félix and my mother Bertha.

Collaborators:

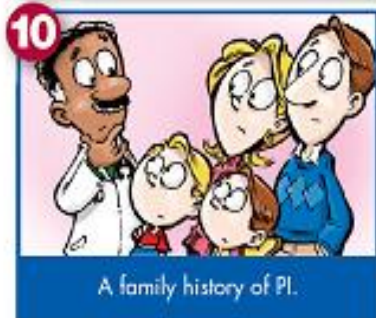
- Juan Félix Aldave Pita, MD.
- Bertha Alicia Becerra Sánchez.

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- Jeffrey Modell Foundation (Vicki, Fred, Jessica, Vanessa, Rachel, Jo Ann, Roger).
- Luke Society International.

10 Warning Signs of Primary Immunodeficiency

Primary Immunodeficiency (PI) causes children and adults to have infections that come back frequently or are unusually hard to cure. 1:500 persons are affected by one of the known Primary Immunodeficiencies. **If you or someone you know is affected by two or more of the following Warning Signs, speak to a physician about the possible presence of an underlying Primary Immunodeficiency.**



"These warning signs were developed by the Jeffrey Modell Foundation Medical Advisory Board. Consultation with Primary Immunodeficiency experts is strongly suggested.
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- Book 11: The armor of the Immunocyte Felix
- Book 12: The fantastic Interleukins
- Book 13: The Immunocytes and coronavirus

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