Sound of Science
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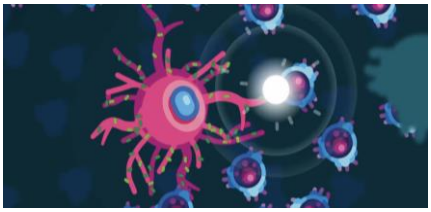
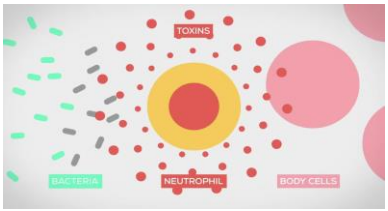
Innate immune system(先天免疫系統)

Your immune system is perhaps the most important, complex, yet interesting part of your body: it is present in basically every part of your body, it works in an enormous variety of ways, and it can save you while killing you, yet most people know barely anything about it, which is the reason why today I am going to discuss the first part of your immune system, your first line of defense – the Innate Immune System. Let's start by discussing the largest organ of your body, the thing that covers you from head to toe—**SKIN**

Part 1: Your Skin

Imagine a desert, without any food or water anywhere and with weird acidic fumes in the air not enough to kill you, but enough to be very annoying and irritating. Now imagine there are groups of random people holding gigantic axes chasing you down the moment they see you to eat you, and to make matters worse the sand has geysers underneath that from time to time shoots huge chunks of sand, potentially including you and the random people from before straight into outer space. That is what pathogens (living things that cause disease like bacteria and viruses and so on) experience when they are on your skin. Your skin has properties such as:

- Has nothing for bacteria to eat
- Is Impermeable to water (contaminated water cannot pass through your skin)
- Made of dead cells (Viruses cannot survive without living things to infect)
- Hosts Friendly bacteria that kill all unfriendly things
- Releases acid 'sebum' (makes it a terrible place to live for pathogens)
- Constantly replaces itself (while shedding older dead cells with pathogens on them)

Essentially, your skin is impenetrable unless we cut straight through it, which is why in order to show you the rest of your innate immune system, we are going to cut straight through it.

Part 2: The Cut

You were cutting the vegetable of your choice in your kitchen one day when you felt a slight but sharp pain on your finger. When you look down onto it, you see a slightly bleeding cut. It did not hurt much at all, so you kept on going with your day being mildly annoyed. **Though you as a person are not really affected by the cut at all, in the cellular level around where your cut is, a gigantic catastrophe has essentially just occurred**. Millions of cells were ripped apart and obliterated in an instant and all your cells in that general area are panicking. Not to mention the millions of pathogens and previously friendly bacteria living on your skin had just found a much better place to live than wherever they were at before – it's warm, there's food everywhere just up for grabs, and even some pathetic, helpless cells to hunt and eat – That is the situation on your finger. As you go to grab a band aid to cover it up, millions of pathogens have already entered your wound and started to wreak havoc. Your body does not like chaos: it wants everything to go exactly as you want it to, and right now these pathogens are disrupting the peace in your finger. Now that you know the situation, it is time for you to see for yourself how different parts of your innate immune system work together to keep you safe and alive.

Part 3: Your Soldiers – Macrophages and Neutrophils

By now, a bunch of your immune cells called macrophages and neutrophils would have seen what has happened on your finger. They follow the stream of cytokines (the language of immune cells) which speak of screams, death and chaos and eventually arrive at the battlefield. Let's start with

neutrophils because what they do are a bit simpler – they kill, and nothing else, but they are extremely good at that. They have a few extremely effective ways to kill pathogens, like:

- Phagocytosis. It basically means neutrophils can eat things, and in this case their food are the things trying to kill you.
- Granules. Essentially little pockets of death they can throw at things and when they burst it kills everything it comes into contact with, including your own cells.
- Neutrophil Extracellular Traps (just call it a NET). It is a net made of a neutrophil's own DNA. They rip themselves apart and throw their DNA at their enemies, which acts like a net with sharp things on it – it traps and cripples pathogens.

What they do is brutally murder, throw their NET at the enemies when they get exhausted and cannot fight anymore, and just die. Killing yourself to kill enemies might not sound like the smartest thing to do, but remember, you have trillions of neutrophils and make a hundred billion more every day, so odds are you are not running out any time soon.

Neutrophils have a problem though – they are too good at killing, to the point where they kill everything around them, including your own cells, when going after pathogens. They are so powerful that having them fight for too long will hurt you more than your enemies can. Even so, our bodies keep them around because they are just so effective at killing pathogens. We also keep them around because we have ways to keep them under control. This is where the macrophages come in. Macrophages are simpler in terms of how they kill enemies. The only thing they can really do is phagocytosis (they eat your enemies alive too) but they have a few more jobs. For example:

- They eat your enemies (as I said before)
- They clean up the battlefield littered with dead bodies of your cells and your enemies (by eating them)
- They recycle the materials in what they eat and lets your body reuse them (Your immune system, and the rest of your body, does not waste)
- They calm down your neutrophils when your enemies are mostly dead before they do any more damage to your own cells than they have to (by eating the neutrophils)
- Many of them kill themselves when your enemies are mostly dead (constantly having too many of them around is a waste of resources)

As you can see, they eat a lot, which would not be a surprise if you knew their name literally means "Great Eater". They do a really important job though – they keep your innate immune system under control. Without them, your own innate immune system will do way more harm than good, considering your immune system (innate or adaptive) is easily strong enough to kill you. Now is probably the time to introduce a really important concept about your immune system – *they require constant stimulation to keep fighting*. If your immune cells are not constantly told to keep fighting, they will kill themselves by having an internal timer run out and causing apoptosis (the way cells kill themselves without causing a mess) or just by exhaustion. It is actually quite the ingenious idea – more enemies means more stimulation, which means more immune cells stay alive. On the other hand, less enemies means less stimulation, which means less immune cells stay alive and more kill themselves. It is a way for your own immune system to keep itself under control, and your macrophages help with this through their own ways. These two combined allow your immune cells to fight enemies as effectively as they can, while keeping the collateral damage to your own cells to a minimum.

There is one more thing these two types of cells do that is a huge help in the fight against the pathogens that just entered the cut on your finger. They cause *inflammation.*

Part 4: Inflammation and the Complement System

Inflammation is the reason why your wounds hurt after a while and why the wounded area feels warm. It is also the reason why many of you are still alive after countless wounds which might have killed you otherwise. It is something dying cells (excluding those who kill themselves, i.e. those that

die by apoptosis) or certain immune cells can trigger through releasing certain cytokines (the language of the immune system). When inflammation happens, it has the following effects:

- The blood vessels leading to the area dilate (they expand in a sense), causing more blood to flow towards the area with the wound (and in our case, your finger)
- The wounded area becomes warm (caused by the previous point)
- Your blood vessels become more permeable, i.e. things go through it easier (by literally poking holes through your blood vessels), which combined with the first point lets in more immune cells and the complement system into the wounded area
- The wound swells (as a side effect of the previous point)
- The wound begins to hurt (caused by the previous point because the swelling could apply pressure on your pain receptors, essentially giving you pain)

The increase in temperature caused by inflammation makes it hell (almost literally) for your enemies, but your immune cells actually like the heat, and so do your cells when they are trying to fix themselves and heal. Let's go back to the situation on your finger real quick. At this point, you are starting to feel a bit of ambient pain on your finger, and you are increasingly annoyed. More and more immune cells are reaching the wound, but the fight is not quite over yet. Suddenly out of nowhere, holes start appearing all over the pathogens, and their guts leak all over the place. The pathogens are also being seemingly grouped up into large clumps for your phagocytes (the cells that eat things, like macrophages, neutrophils, and the dendritic cells that we are going to talk about later). That is the work of the complement system. They are filled with an insane amount of absolutely terrible names like C1INH, MASP-2 and C4bp, so I am not going to mention them here. This is all you need to know about them:

- It is essentially a bunch of proteins that just float around in your blood until it touches a pathogen
- The proteins of the complement system stick themselves into the cell membranes of pathogens (basically their skin)
- The proteins stuck onto the cell membranes of pathogens can stick to other complement system proteins, which can then stick themselves to more pathogens, eventually forming a big clump, which makes it a lot easier for your phagocytes to eat them
- It can also turn into a bunch of knives in the blink of an eye and rip holes into whatever the proteins stuck themselves to
- It can stop pathogens from doing the stuff they are supposed to do, including stopping them from killing your cells
- It can activate immune cells, keep them from killing themselves, make them keep fighting and can guide the immune cells to the pathogens

It is kind of oversimplified, but that is all I can do without making it a billion times more complicated. TLDR, it makes it easier for your eating cells (phagocytes) to eat things, makes your eating cells continue to eat things, cripples and kills anything that tries to kill you, and generally makes the lives of the pathogens trying to infect you absolutely miserable.

Before I end this off, there is one more type of cell that you need to know about in the innate immune system. It is the cell that brings in help when the pathogens are too powerful and your innate immune system starts to fail. It brings in backup when you need it and activates the second and much more powerful half of the immune system. This cell is called…

Part 5: Dendritic Cells

Dendritic cells are responsible for calling in the big guns, your adaptive immune system. I am not going to discuss the details of how they do it here because it is pretty complicated and irrelevant unless I want to talk about the adaptive immune system as well, which will open another gigantic can of worms. They are essentially more refined versions of your macrophages, and they have to be. If your innate immune system is a gun, your adaptive immune system is a nuclear bomb, and if that goes out of control, you are very dead, which is why dendritic cells need to do a bunch of complicated stuff before they can even activate a part of the adaptive immune system. Here is an extremely oversimplified version of what they do:

- They grab things at eat things (just like macrophages do)
- Instead of digesting and recycling the materials, they keep the stuff they eat as it is (which essentially makes them a mailman of information from the battlefield, because you can tell what is going on in a wound just by looking at what they eat)

- They travel through your lymphatic system (kind of like your circulatory system with the blood vessels, except not) to find the adaptive immune system

After that, they do a whole bunch of stuff to activate the adaptive immune system, but because it is very hard to activate the adaptive immune system, the more the dendritic cells do their thing (more dendritic cells mean a worse infection), the higher the chance of activating the adaptive immune system, but hopefully it does not get activated at all and the cut on your finger, with all the intruders dead, heal itself eventually.

Summary

Alright, that was a lot of information, so let's go over all of it one more time:

- Your skin is near impenetrable for pathogens (disease causing living things) and is a terrible place to live for them
- When a bunch of cells die and panic (like when your skin gets cut by a knife), they shoot panic cytokines (the language of the immune system) all over to place to alert the innate immune system
- Neutrophils show up to kill everything in their way through a variety of methods
- Macrophages eat pathogens, keep neutrophils under control and clean up the battlefield
- Neutrophils, macrophages and panicking dead cells cause inflammation, which hurts your enemies but helps you with fighting and healing
- The complement system makes enemies easier to eat, get more immune cells to battle and outright kills the pathogens
- Dendritic cells collect information and shows it to the adaptive immune system in hopes of activating it

There is so much more about the innate immune system alone that I was not able to cover it, and there still is the entire adaptive immune system. Keep in mind that a lot of this is oversimplified to fit in three pages and to let people understand it easier. If you are interested in the immune system, I highly recommend the book *Immune, A Journey into the Mysterious System That Keeps You Alive* by Philipp Dettmer. It is honestly a great read and the information is presented in a way that makes it very easy to digest, so I recommend anyone interested to go check it out. I hope you learned something from this newsletter and see you next time!

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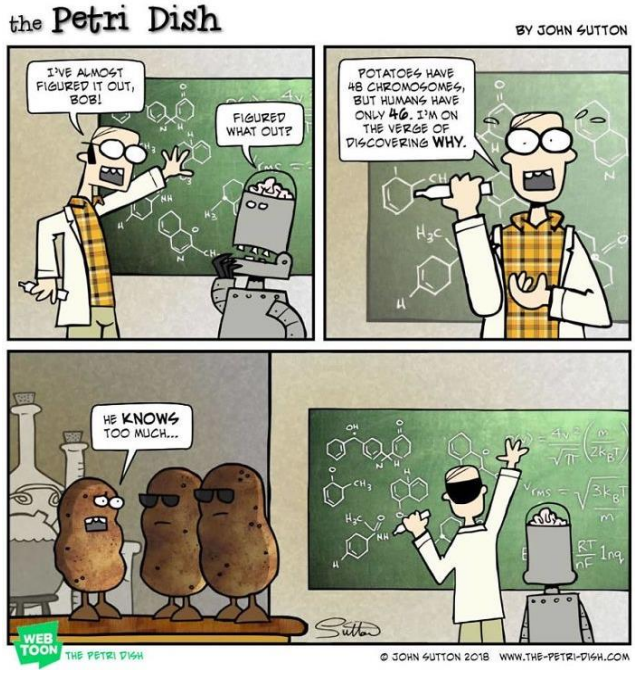

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