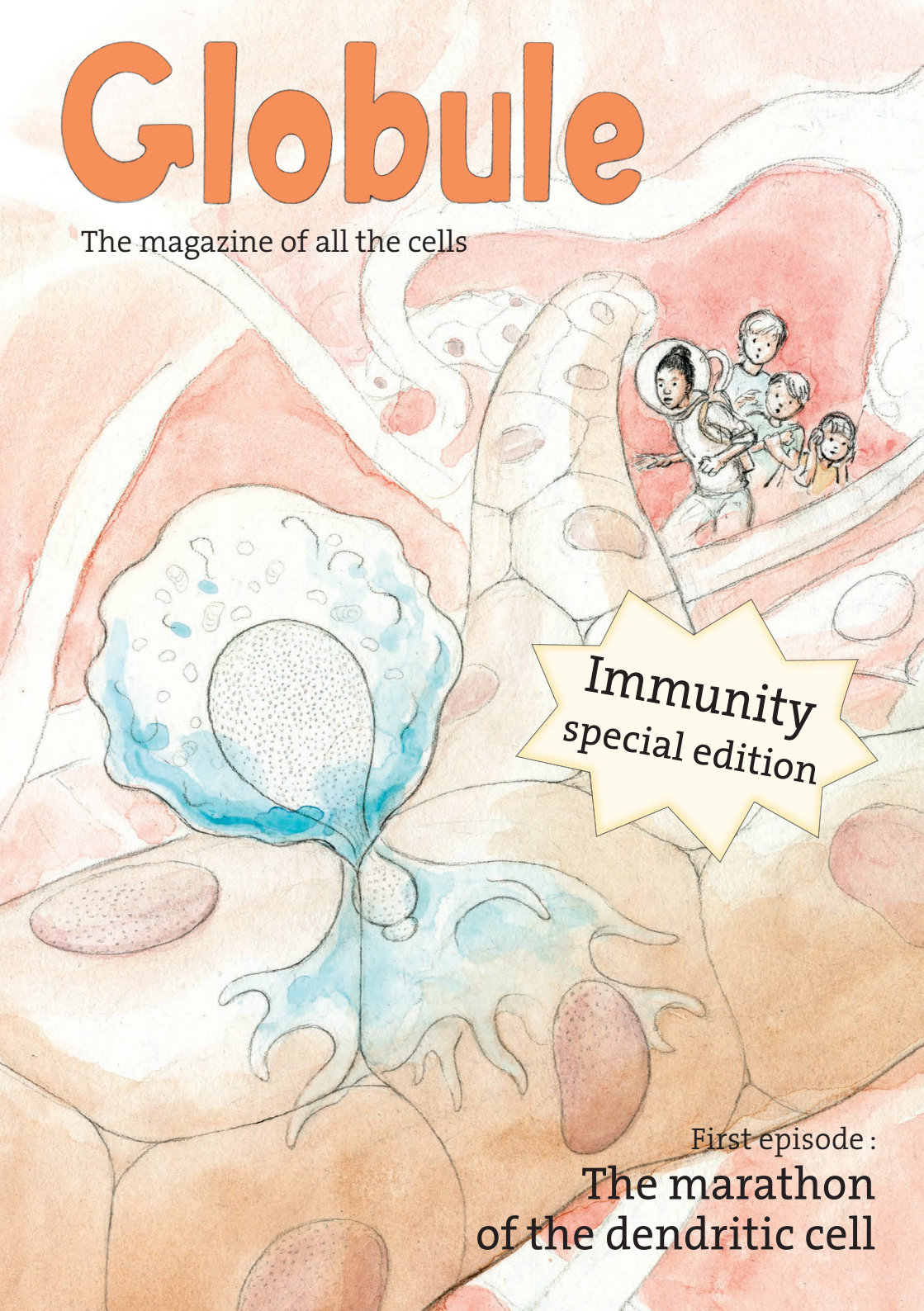
Globule

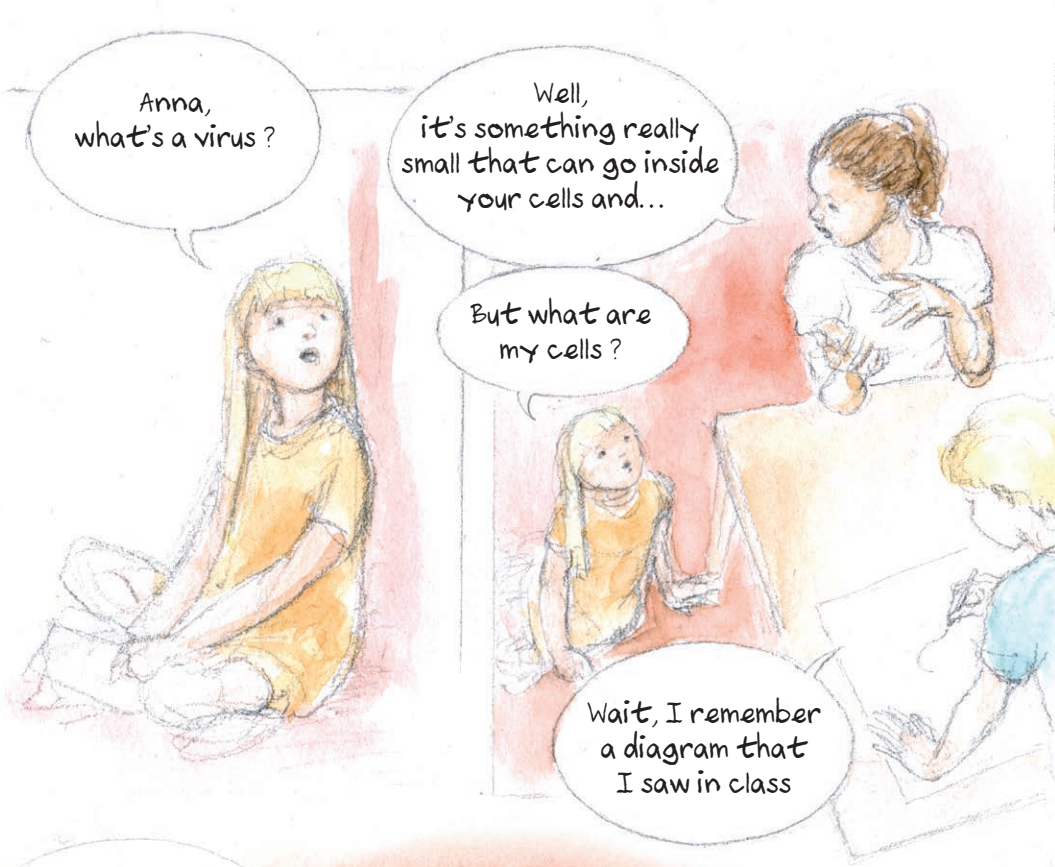
The magazine of all the cells

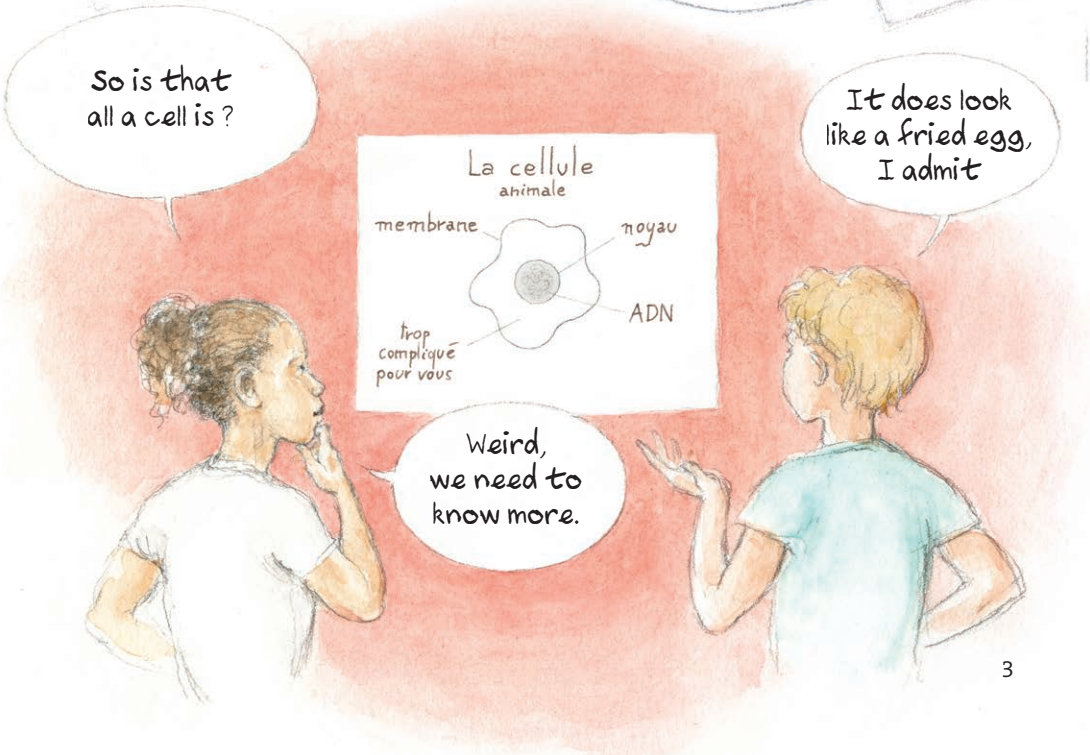


Immunity
special edition

First episode :
The marathon
of the dendritic cell

Somewhere in France, April 2020...





I have an idea ! what if we made a newspaper about cells ?

Super ! But how do we go about it ?

We'll search for information... Well, scientists know everything, right ?

Do you really think so ? But they talk about such tiny things ! You can't even see them !

What about Clementine ? She is very small. She can see really small things.

No, that won't work.

What we really need is a microscope

I'll get a hold of one of those. But most importantly, we must recruit reporters on the ground!

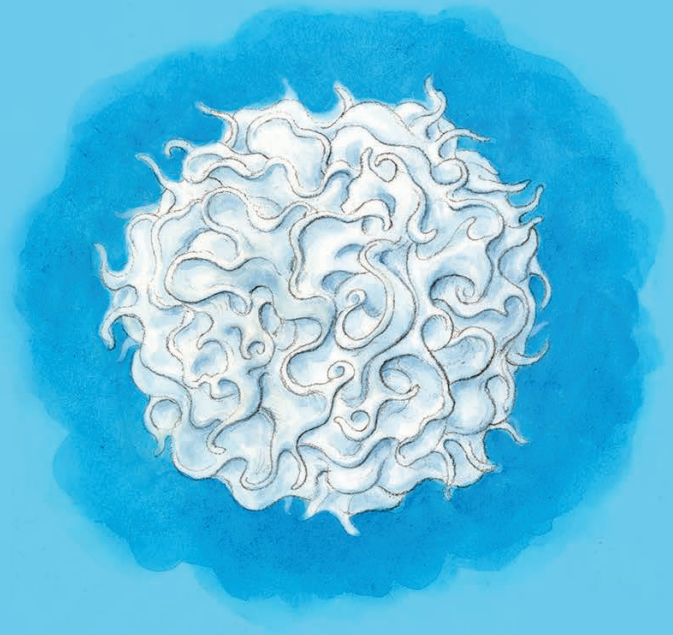
Let's make a poster to put in every laboratory.

Little One, little One... you'll see! I am going to draw those cells.

And that is how it all began....

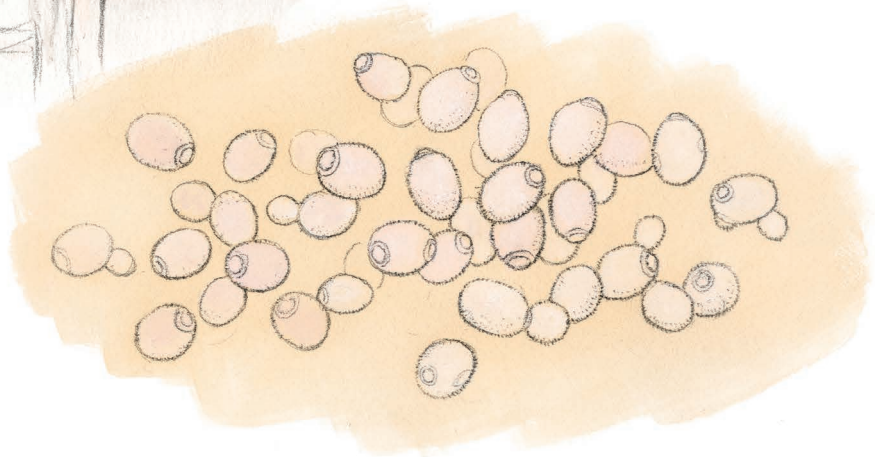
Globule

The magazine of all the cells



Story line, text and drawing: Renaud Chabrier
Scientific Advice: Matthieu Piel and Ana-Maria Lennon
English translation: Chloe Bulinski

The first candidates for the job of cell reporter arrived on a small glass slide, with a label on which the word "Yeast" has been beautifully written. Very excited, we slip it under the microscope and we discover a strange landscape: It is as if a multitude of small elongated eggs were stuck in clusters. Nothing moves and the atmosphere seems as calm as a Sunday morning. Curious behavior for a job interview...



Editor: Is anyone here?

Yeast: Uh, yeah! *(yawning)* Excuse us..... we worked all night long.

Editor: Oh, sorry. But are you really candidates to be reporters?

Yeast: Yes, yes, absolutely.... Just imagine: We work for you all year long, yet you hardly know us! We help you every day to make bread, pastries, croissants, beer... We even produce sugar along the way!

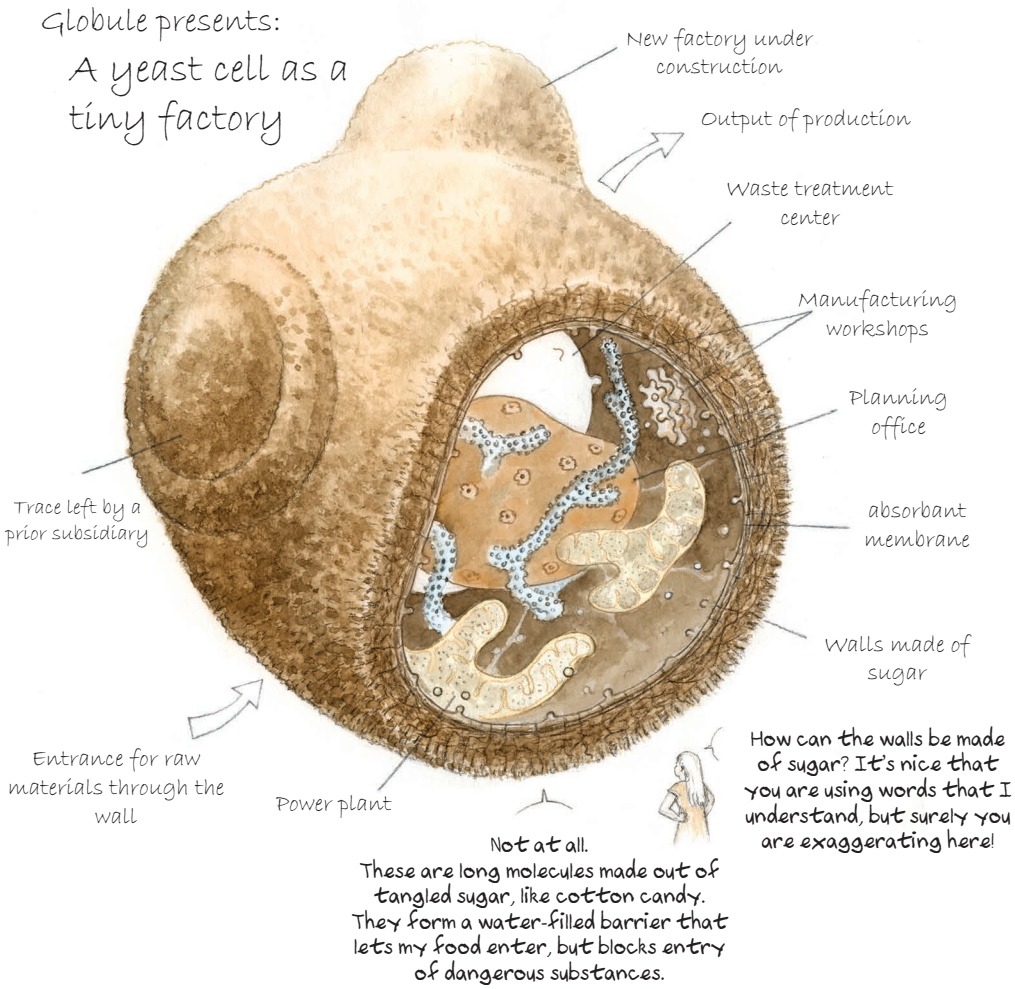
Editor: Wow! That's a tough life!

Yeast: Hmm, not quite. We take advantage of the situation rather well. As long as it is reasonably warm, wet and there is sugar to eat, it's a party for us and we bring out the champagne! Whenever there are small bubbles like in bread, or something fermented in what you eat, it means that we have had a veritable feast.

Editor: So, what do you propose to report on?

Yeast: A section on cooking, of course! But not just cooking! You aren't going to believe this, but we belong to the mushroom family. Mushrooms with only a single cell, but mushrooms just the same. Everyone talks about animals or plants, but who can talk to you about mushrooms? (babbling)... Excuse me, we're really low on sugar right here on this microscope slide.

After the interview with the yeast cells, everyone agrees: they can report for subsequent issues of Globule. But for today, they seem far too sleepy.



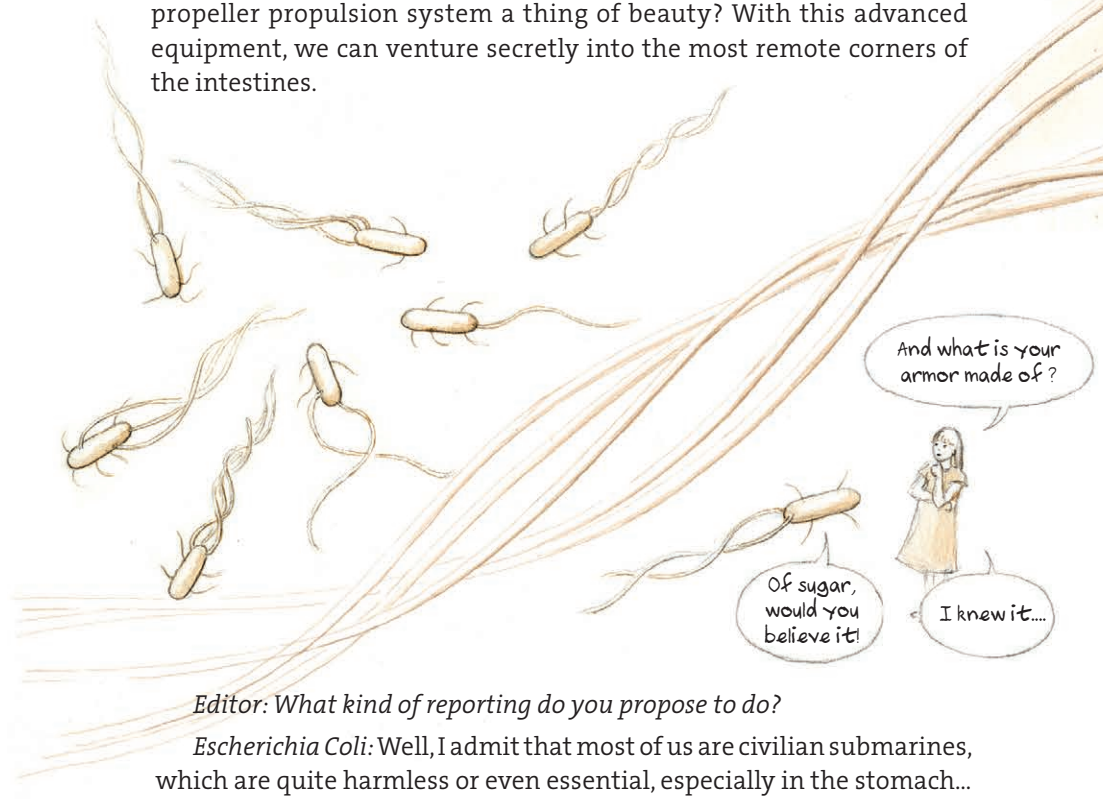
We then look at the second set of candidates. Curiously, they are enclosed in a small tight box, labeled with an unpronounceable name: Escherichia Coli.

Editor: Wow, what a change!

Escherichia Coli : Haha, welcome from the bacteria, green-horn! Here we do not wait for our food to fall on us all ready to eat, we process it ourselves.

Editor: You remind us of little submarines.

Escherichia Coli: Absolutely, deckhand! Pirate submarines, to be more precise... Isn't our double-hulled, armored submarine, with its propeller propulsion system a thing of beauty? With this advanced equipment, we can venture secretly into the most remote corners of the intestines.



Editor: What kind of reporting do you propose to do?

Escherichia Coli: Well, I admit that most of us are civilian submarines, which are quite harmless or even essential, especially in the stomach... But what young people like you want to see is adventure and conquest, right? Well then, right now our armada is secretly preparing a generalized infection, so it's just the time to come aboard!

Globule presents: the navigator bacteria

1 - Rotating motor
2 - Extra-long propeller
3 - Armoured double membrane
4 - Docking cable
5 - Mission intructions
6 - Workshop
7 - Poison syringe
8 - Antibacterial torpedo

We interrupt our interview as quickly as we can. It will be absolutely necessary to investigate these furious madmen - it is a matter of public health! But we are not yet equipped for such a dangerous mission.

We only have one more applicant, a third sample mysteriously labeled, "DC".

Editor: "DC", what do those initials mean?

DC: Well, in laboratories, this is a our nick-name. Our full name is "Dendritic Cell".

Editor: That may be your full name in English, but we cannot tell what it means at all.

DC: Me neither! That is why I and the other DCs are so interested in your investigations into cells! Scientists have given us this name, and I would really like to understand why.

Editor: It isn't just your name that is weird; your shape is... surprising.

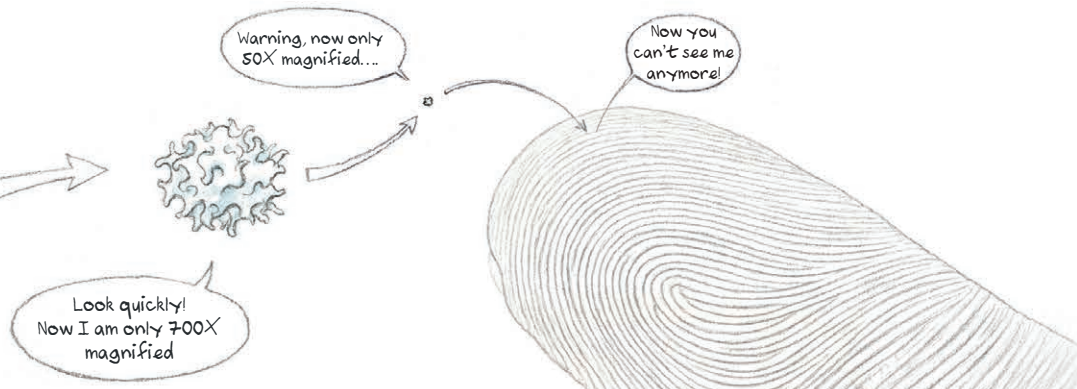
The yeast and bacteria were inside a nice little rigid shell, but your membrane is changing constantly.

It grows on one side, it shrinks on the other ... It looks like a cross between a rose, a ball of tentacles and the erupting lava of the sun. You never feel lost or confused?

DC: Oh, on the inside I'm very organized. And anyway, I do not need to lock myself inside a protective shell, since I live inside a much bigger body that already has a protective skin.

Editor: Whom do you live inside of?

DC: Inside of YOU ! I am part of your body. More precisely, I am Simon's dendritic cell # 194902005!



Simon: But I don't know you!

DC: That's perfectly normal. You can not feel it, but I spend my time walking around just underneath your skin. So here is what I propose: I will do a completely new report on the undersides of the skin and in exchange you can help me understand why I was given a weird name, "Dendrictic Cell".

Editor: It's a deal!

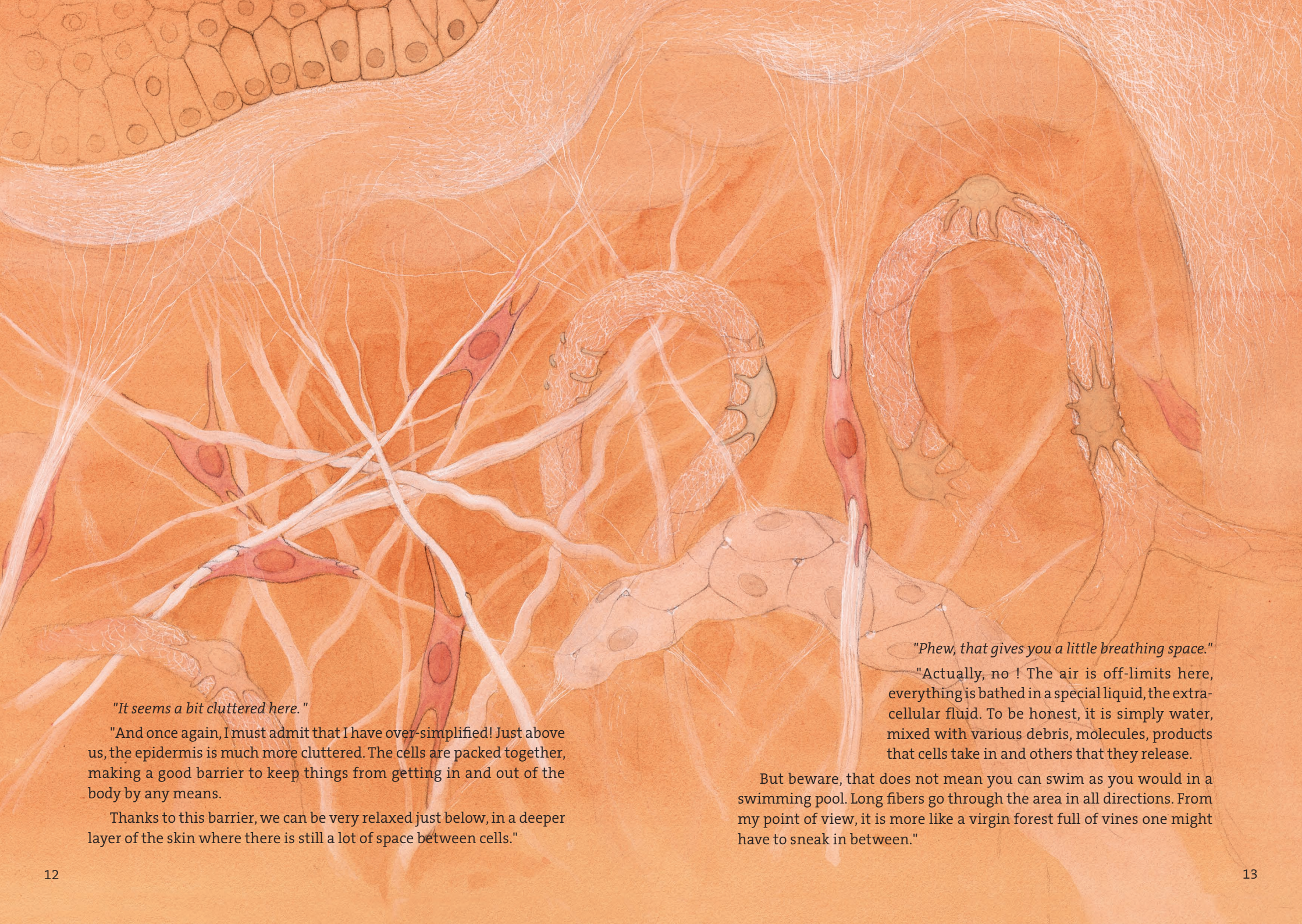
With these words, the dendritic cell starts shrinking and shrinking..... and starts to burrow into Simon's skin. Radio contact is quickly established:

"Delta-Charlie, Delta-Charlie, it's the Editor talking, everything all right?"

"Delta-Charlie, here. I hear you loud and clear! I have found my patrol area; I'm sending you the first pictures. We are at a depth of 2 millimeters under the Surface of Simon.

Daylight still filters in so far.

The atmosphere is golden, it is very pretty."



"It seems a bit cluttered here."

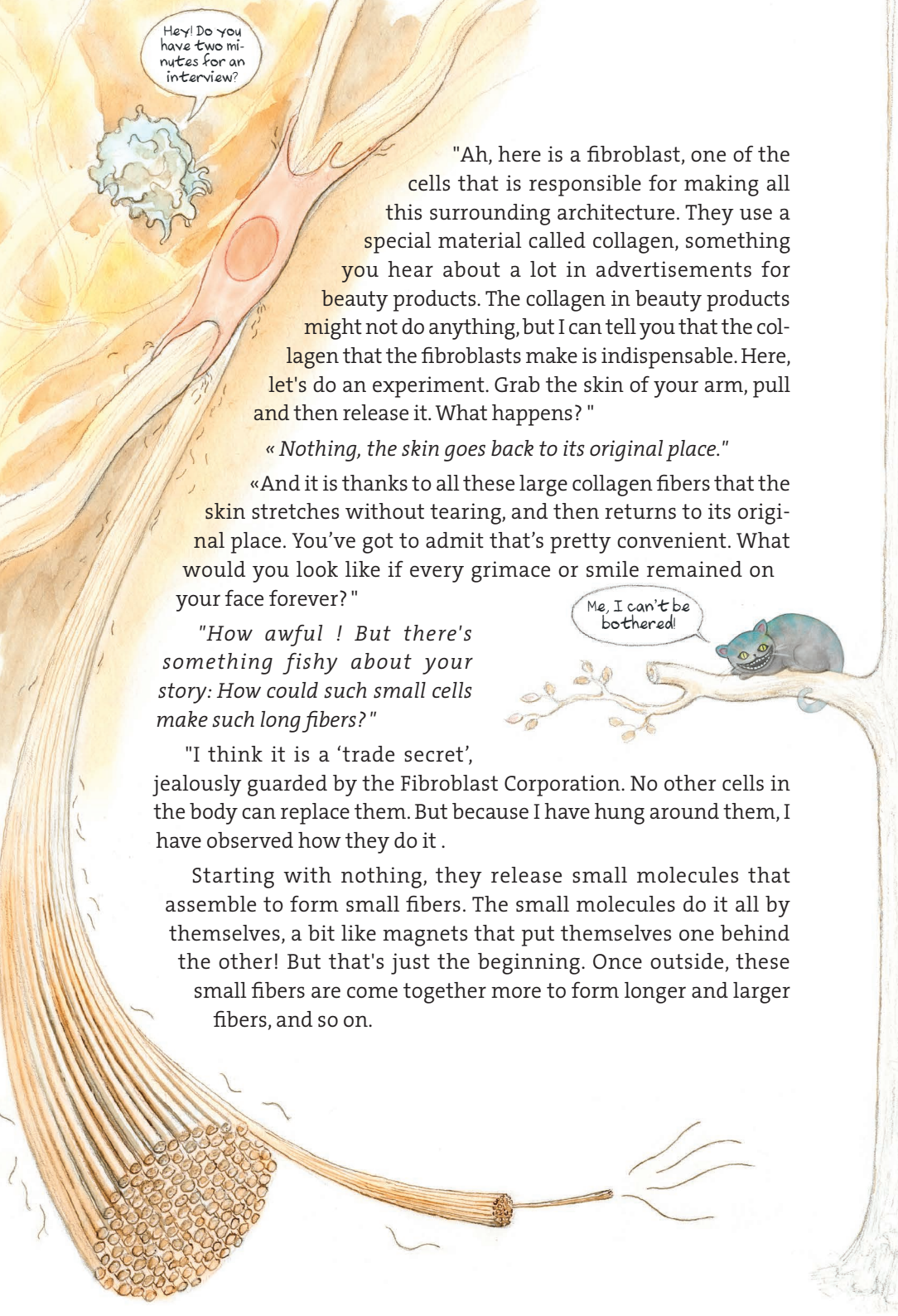
"And once again, I must admit that I have over-simplified! Just above us, the epidermis is much more cluttered. The cells are packed together, making a good barrier to keep things from getting in and out of the body by any means.

Thanks to this barrier, we can be very relaxed just below, in a deeper layer of the skin where there is still a lot of space between cells."

"Phew, that gives you a little breathing space."

"Actually, no ! The air is off-limits here, everything is bathed in a special liquid, the extra-cellular fluid. To be honest, it is simply water, mixed with various debris, molecules, products that cells take in and others that they release.

But beware, that does not mean you can swim as you would in a swimming pool. Long fibers go through the area in all directions. From my point of view, it is more like a virgin forest full of vines one might have to sneak in between."



"Ah, here is a fibroblast, one of the cells that is responsible for making all this surrounding architecture. They use a special material called collagen, something you hear about a lot in advertisements for beauty products. The collagen in beauty products might not do anything, but I can tell you that the collagen that the fibroblasts make is indispensable. Here, let's do an experiment. Grab the skin of your arm, pull and then release it. What happens? "

« Nothing, the skin goes back to its original place."

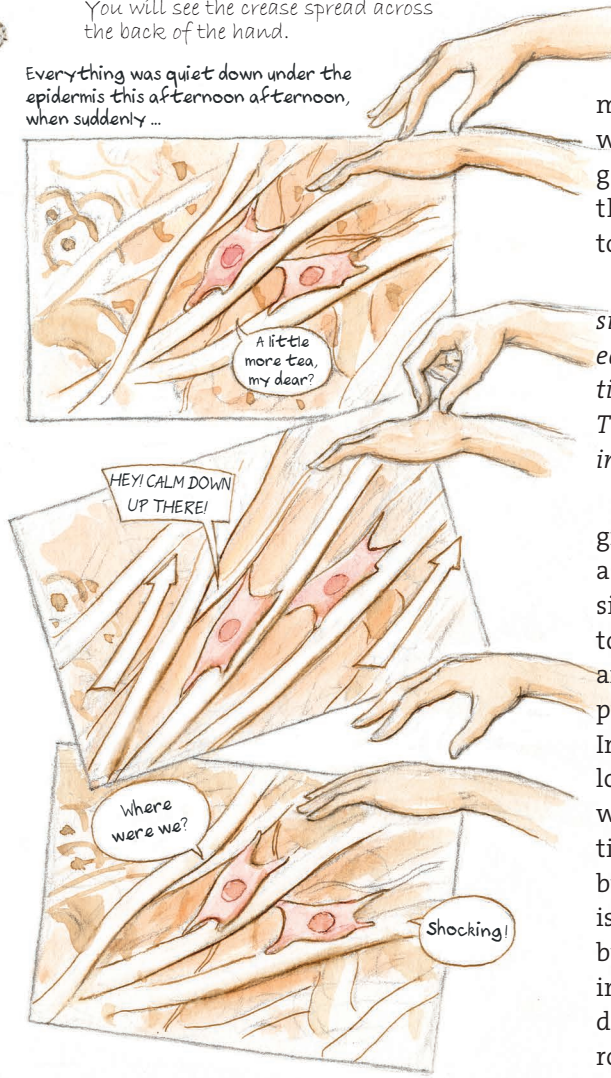
«And it is thanks to all these large collagen fibers that the skin stretches without tearing, and then returns to its original place. You've got to admit that's pretty convenient. What would you look like if every grimace or smile remained on your face forever? "

"How awful ! But there's something fishy about your story: How could such small cells make such long fibers?"

"I think it is a 'trade secret', jealously guarded by the Fibroblast Corporation. No other cells in the body can replace them. But because I have hung around them, I have observed how they do it .

Starting with nothing, they release small molecules that assemble to form small fibers. The small molecules do it all by themselves, a bit like magnets that put themselves one behind the other! But that's just the beginning. Once outside, these small fibers are come together more to form longer and larger fibers, and so on.

Test your collagen!
Pull your skin as shown in the picture:
You will see the crease spread across the back of the hand.



It sounds like the way one makes a huge boat rope ; one winds together bigger and bigger strands. Except that here the strands wind themselves together into a rope!"

"Okay, but once they are outside the fibroblast cell, how can each strand know in which direction the rope is supposed to grow? They could just as easily tangle into big clumps like vermicelli."

"Fibroblasts have devised a great trick: At first glance, it looks as though the big ropes are just sitting there with fibers clinging to them. But actually, the ropes are constantly contracting, which pulls lightly on the small strands. Imagine that you are pulling on a long rope that is hanging on the wall at one end: the rope becomes tighter, not just where you pull, but all along. For the fibroblast, it is the same: without moving, just by pulling, it helps the molecules in each strand align in the right direction throughout the big ropey collagen fiber."

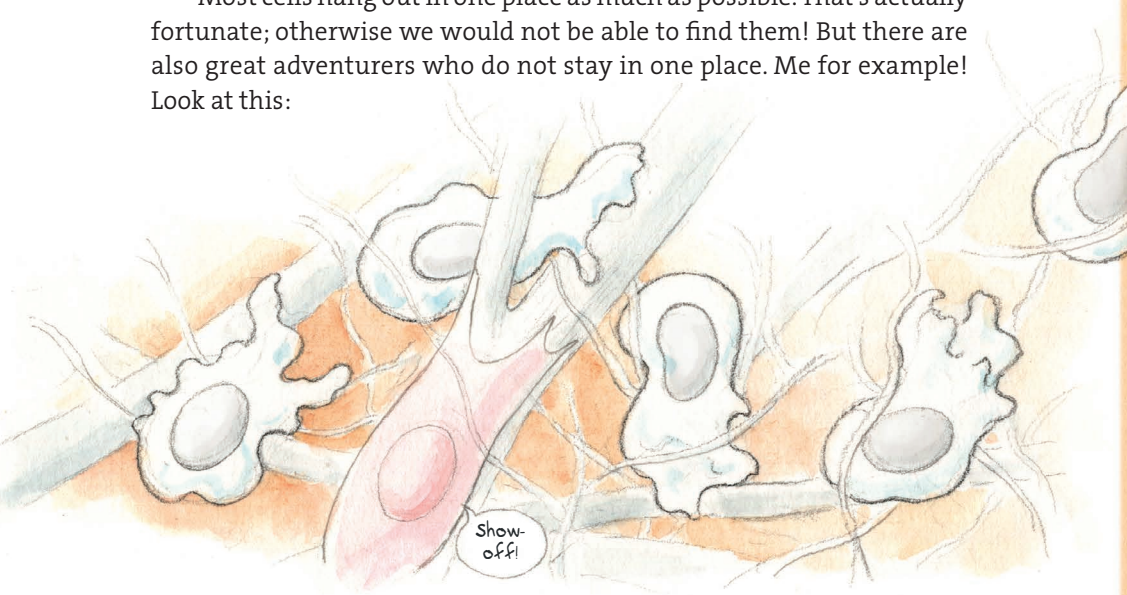
Thanks to the collagen fibers, the cells only undergo a little deformation, even if they are pulled over a very long distance relative to their length. Thus, they keep all their usual neighbors. Other fibers that are more elastic then bring everything back into place.

For multicellular organisms, it is very important to make fibers that are much longer than the cells, thus allowing the body to hold together.

Plants do not have collagen: they use lignin and cellulose. It is cellulose fibers that allow wasps to make nests, and humans to make paper and books.

"Well those fibroblasts discovered a way to get this work done without leaving the comfort of their armchair. Are all the cells in our bodies like that?"

"Most cells hang out in one place as much as possible. That's actually fortunate; otherwise we would not be able to find them! But there are also great adventurers who do not stay in one place. Me for example! Look at this:



Impressive no? ... Hello? You still there?"

"Excuse us, but that was a bit slow."

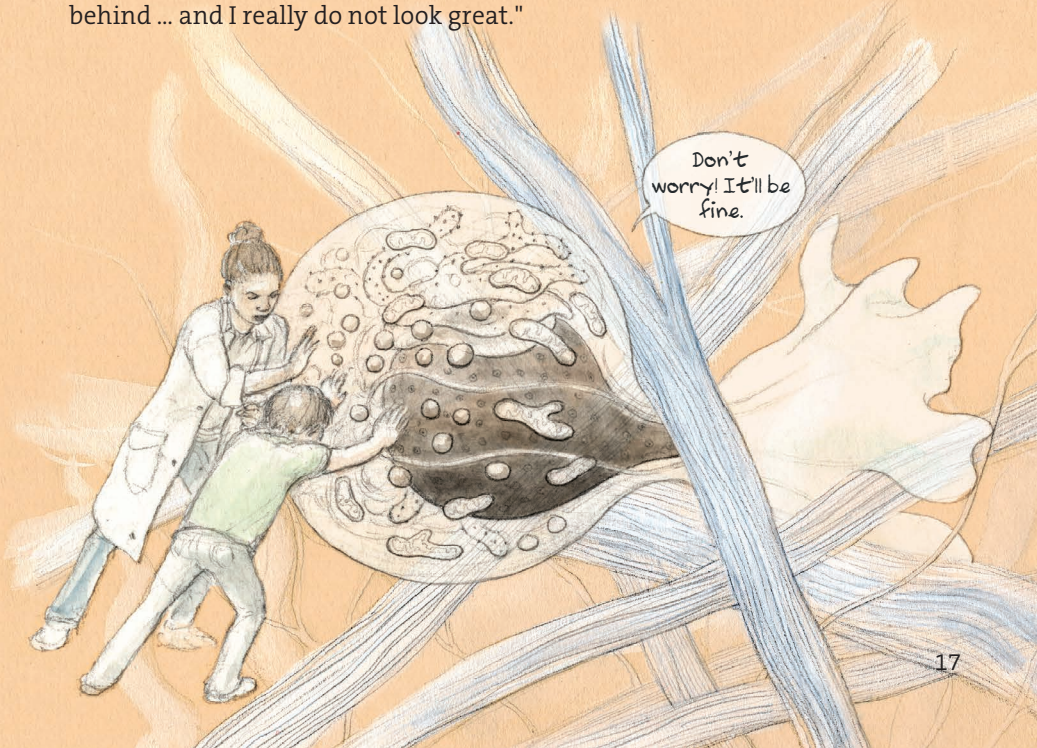
"How is that slow? It only took me 6 minutes to move 3 times my length! Excuse me; that makes me the fastest cell in your body! And this speed is notwithstanding the fact that I have to crawl through an inextricable tangle of fibers. Put yourself in my place: completely surrounded by thick vines lying tightly against one another, without hands to grab onto them, how would you move through them?"

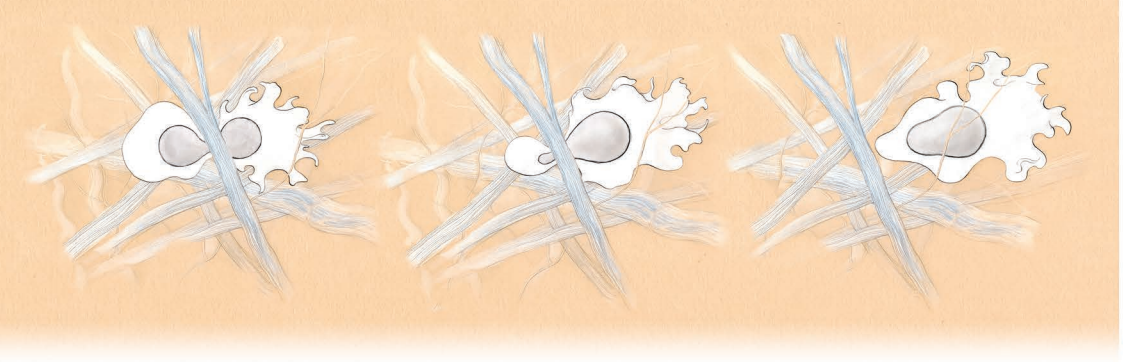
"From that point of view, it does look more difficult ...."

"Yes, but I do have a a few special tricks. First I can easily deform my membrane so that I can squirm through tight passages. When I find a tunnel that looks promising, even if it seems small, I press my body against the fibers all around me, and I lean on all sides to move in the right direction. When snakes sneak through branches, or when the mountaineers climb a rock "chimney" by leaning against the walls, they do the same thing."

"So, this whole collagen matrix is not really an obstacle for me. On the contrary, I need it to advance. Without it, if you put me on a glass slide, for example, I will feel very stupid. Without the matrix guiding or supporting me, I would spread out like an egg on the slide. Only, when I find myself wedged tightly between other cells and collagen fibers, my proper shape returns and I feel so full of energy!

So much so that I often have the idea to squeeze through tiny holes, scarcely 2 micrometers. That's 10 times smaller than me! Though in such cases I feel as though I am a little bit stuck. The biggest problem is getting my nucleus through. My nucleus is a large sac that contains ultra-valuable information that mustn't be damaged, inside a double reinforced membrane that does not deform so easily. And as long as I do not manage to get it through, there's a whole bunch of things left behind ... and I really do not look great."





"Well, of course, I am not going to be defeated so easily. I simply make a small special ring (see the next double page) that will tighten around the nucleus at the hole, until it can slip through as I wish. At the back the membrane stretches until... yes... oh! I'm on the other side! And I am ready to start moving again!"

"Don't you spend all your time practicing this kind of skill?"

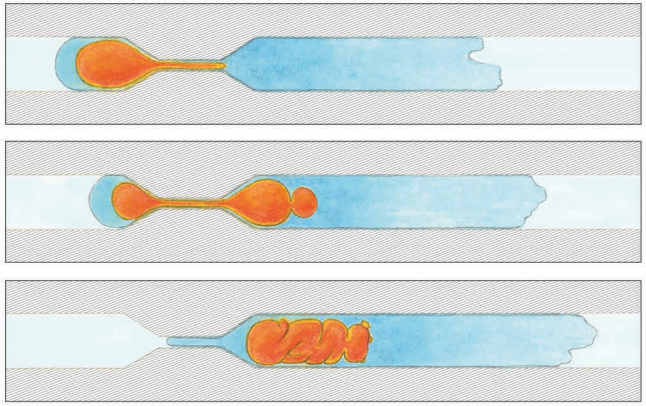
"No, of course not. If I do all this effort, it is only to satisfy my own passion. You know, I'm a great collector."

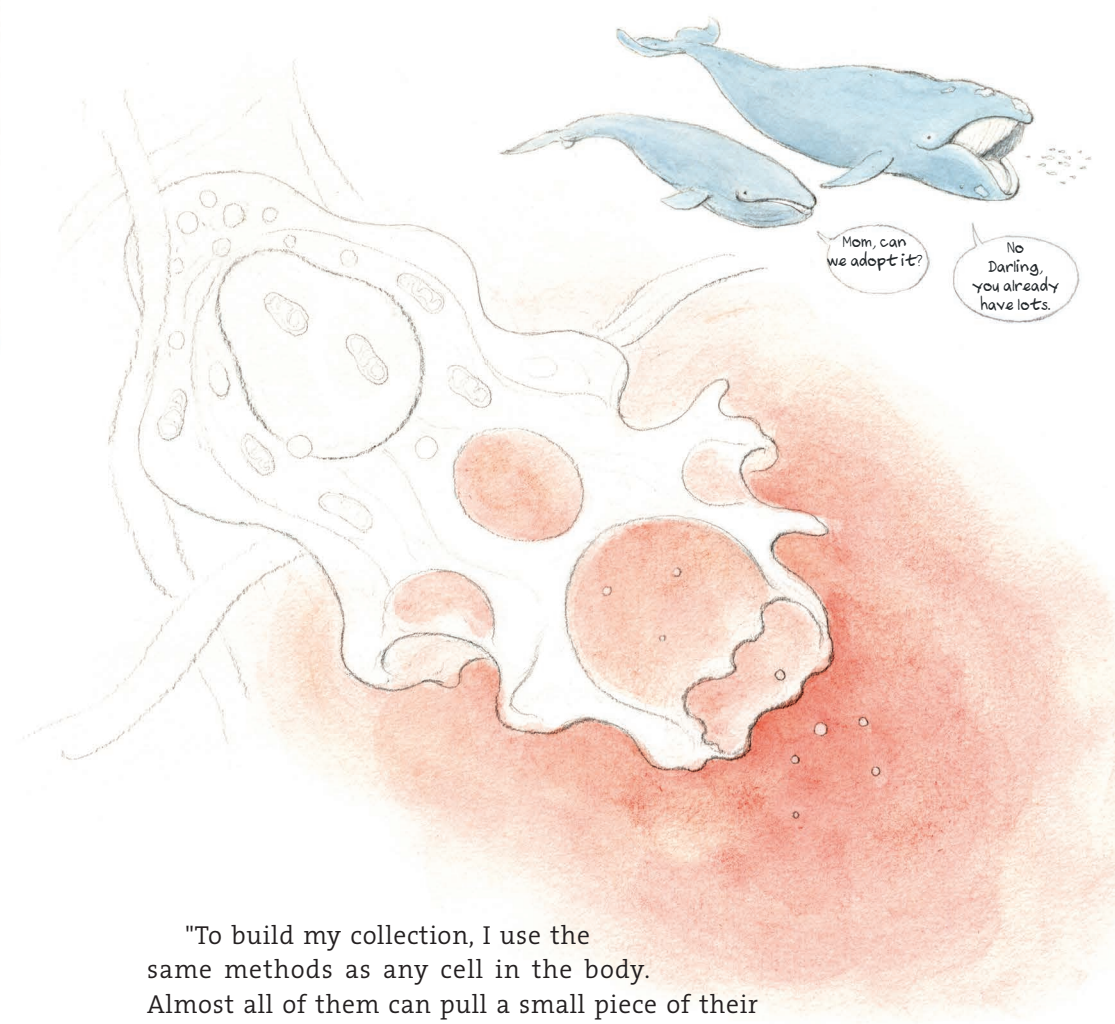
"What do you collect?"

"Everything. Absolutely everything that I find in the extracellular liquid. Pieces of proteins, bits of DNA, fragments of sugars. There are always things going on here: the blood circulation brings some driftwood, cells spit out other things. Still others self-destruct to leave room for the newest ones... Cleaning services do what they can, but sifting through this molecular potpourri that is left is my greatest happiness."

SCOOP ! The dendritic cell is not as supple as it thought it was!

DCs like to sneak through narrow passages and researchers have learned from experiments: Looking specifically at the nucleus (shown in orange), they realized that it frequently broke in the process. The dendritic cell must quickly repair it, otherwise it faces immediate death!





"To build my collection, I use the same methods as any cell in the body. Almost all of them can pull a small piece of their membrane inward, until it comes off with a tiny drop of liquid inside. Then you're all set: the products that were outside the cell just now are inside now, contained in a small sac called a "vesicle".

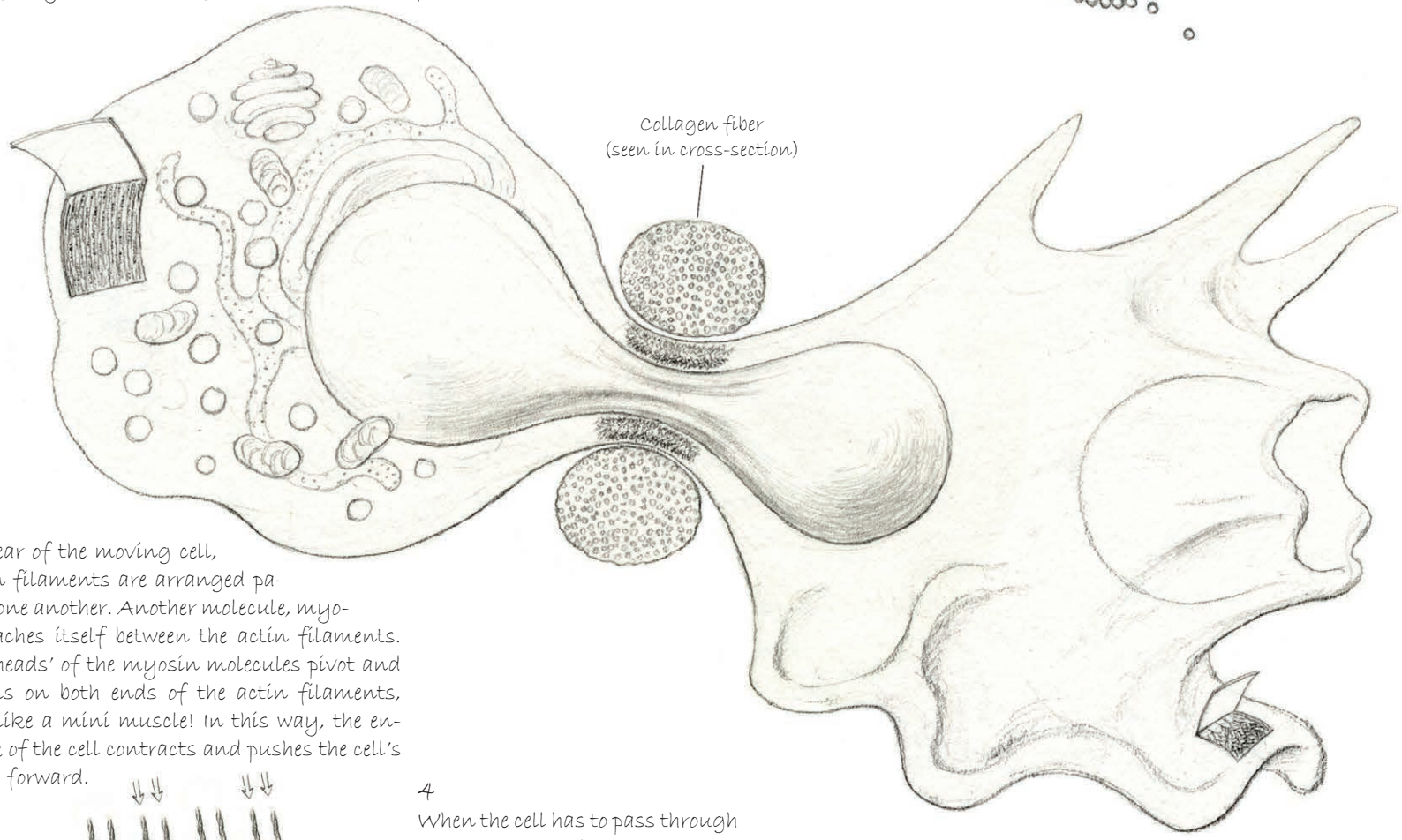
The problem is that this only works when the things you want to absorb are already close to the membrane. Me, I want more! So I adopted the technique of a balleen whales such as the Right Whale (this technique is called "macropinocytosis" by researchers): I deform my cell membrane into a kind of immense mouth that closes around a big drop of liquid. It's several thousand times the volume of a vesicle, more or less! Then I put this drop in and filter. It's always a surprise, what is going to be found at the bottom of the net!"

* From the Greek : μακρός (large), πίνω (drink) and κύτος (cell), that is to say "a cell taking a big drink"

Globule presents:

Under the hood of the DC

We now know that a dendritic cell moves around, but how does its interior machinery make this happen? It has no muscles and bones like us, but it does have something else: a "cytoskeleton" that allows the DC to change its shape in many surprising ways. Let's take a guided tour with 5 stops.



1

One of the main molecules of the cytoskeleton is called actin. Very abundant in the cell, it can assemble all by itself into long filaments. The filament's growth creates a small pushing force that the cell makes use of.

2

At the front of the cell, protrusions in the form of fingers or thin petal-shaped sheets form to help the cell explore new directions. Just inside the membrane, the actin grows and pushes the membrane out! The filaments of actin connect with each other, so the force generated by the growth of adjacent filaments adds up to a substantial membrane-pushing force.

3

At the rear of the moving cell, the actin filaments are arranged parallel to one another. Another molecule, myosin, attaches itself between the actin filaments. Small 'heads' of the myosin molecules pivot and this pulls on both ends of the actin filaments, exactly like a mini muscle! In this way, the entire back of the cell contracts and pushes the cell's contents forward.

4

When the cell has to pass through a small hole and the nucleus resists, the branched actin filaments still grow. But this time it grows both outward and inward. This forms a ring that compresses the nucleus, allowing it to slip into the narrow passage.

5

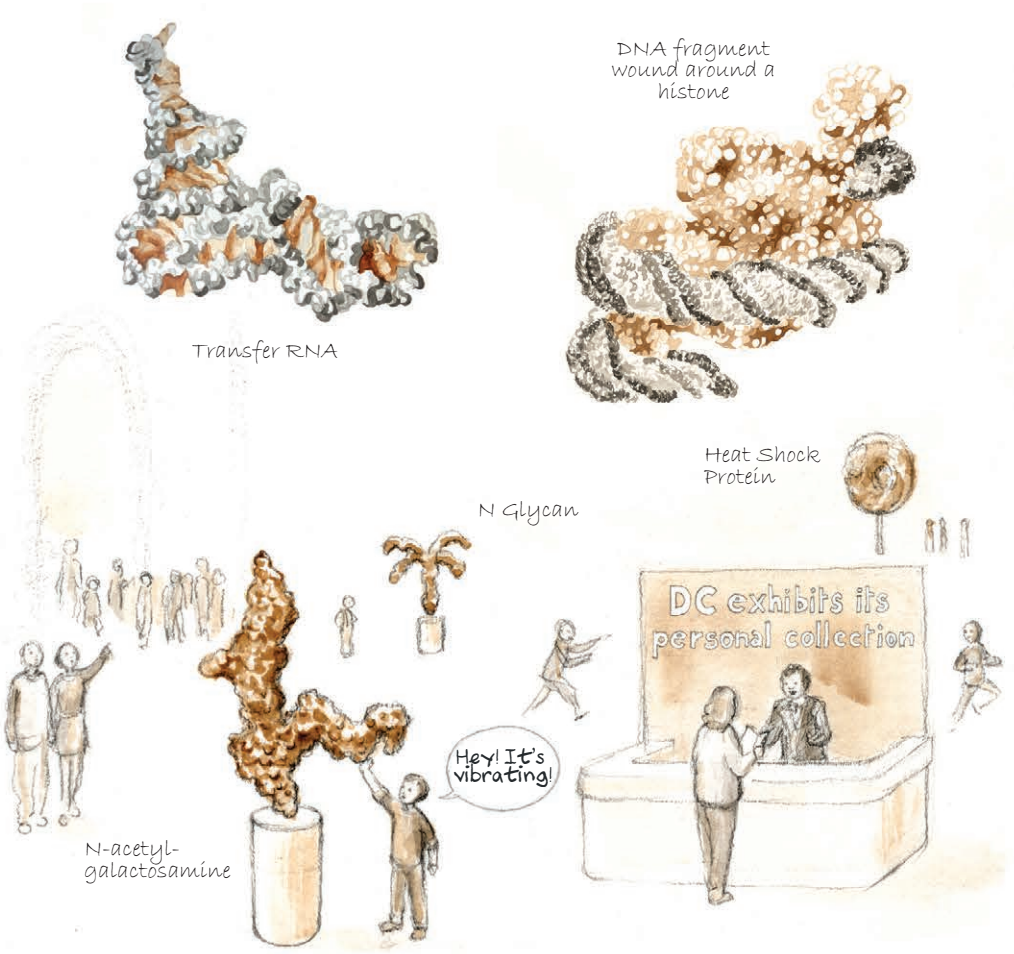
And how does the DC swallow liquid? Well, researchers still don't know! They suspect, though, that actin and myosin are involved, but the mechanism probably won't be discovered for a few years. Who knows, maybe YOU will discover this!

"And where do you put the things you find?"

"Hmm..... that's a little delicate to talk about. Can we keep that between the two of us, until I retire?"

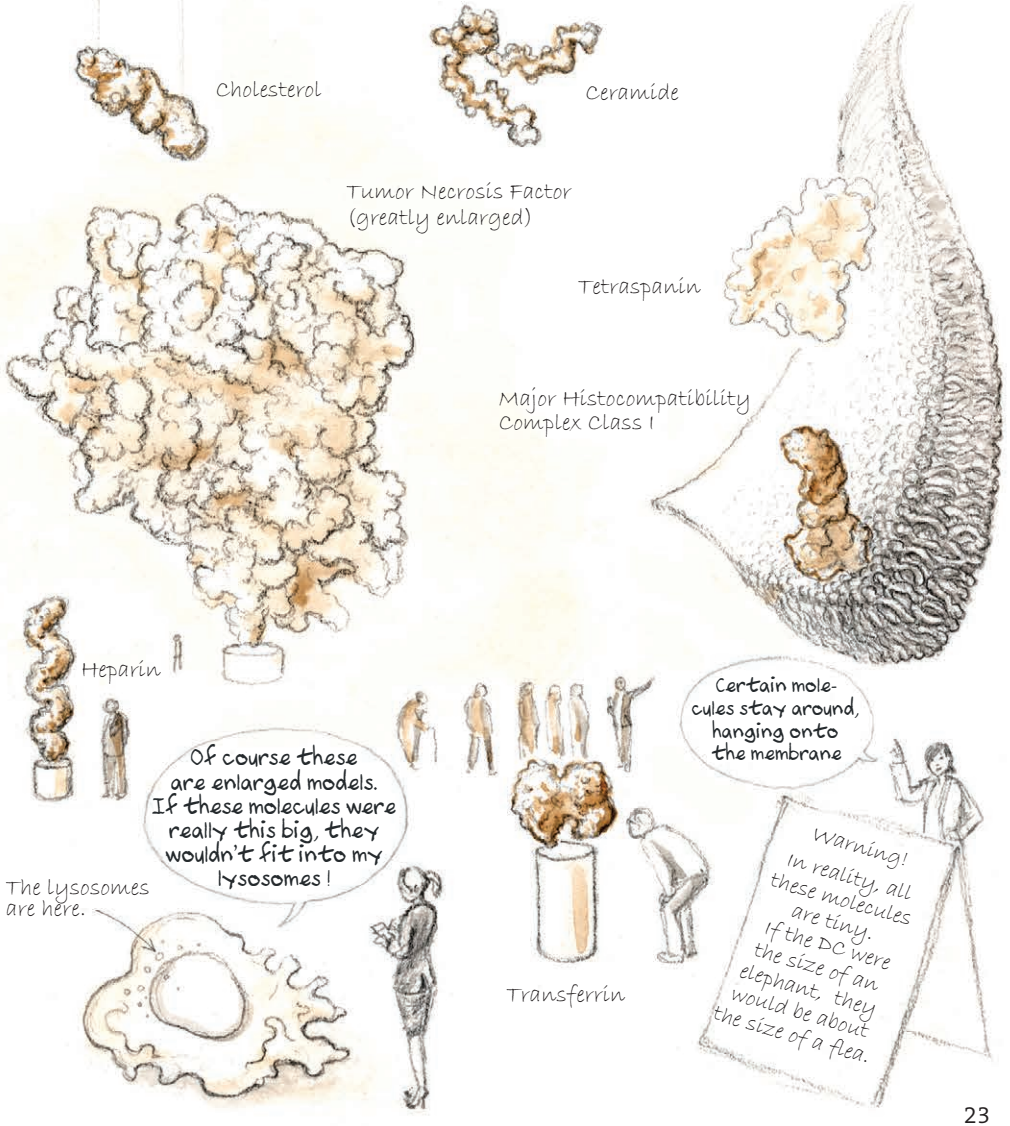
"Of course!"

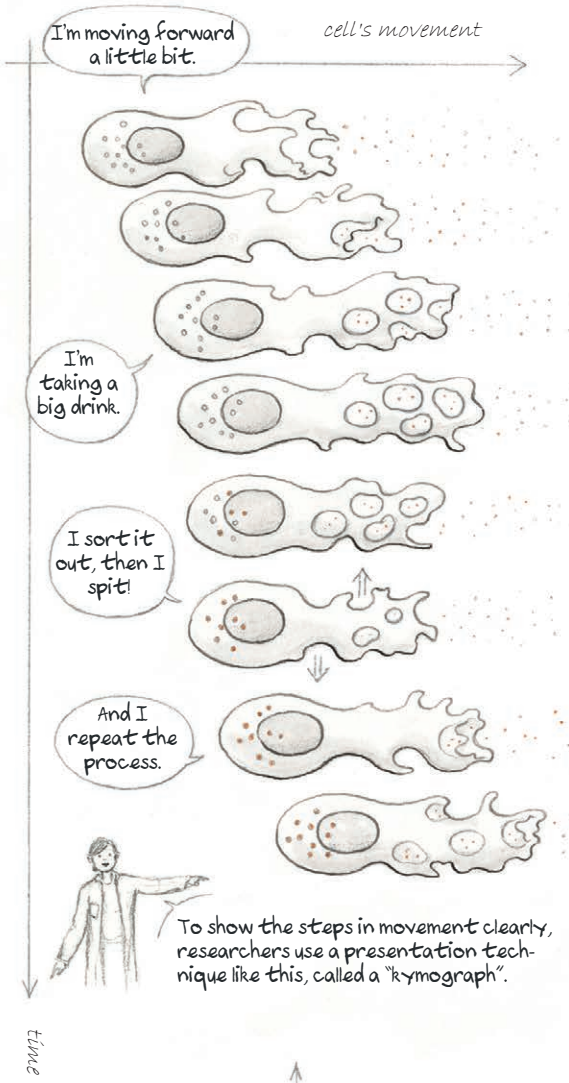
"Well, all of Simon's cells produce chemical waste, molecules they need to get rid of. They have their own waste treatment plants for this purpose; scientists call these "lysosomes". Only, I wanted to keep all these waste products, all the rubbish I find... Therefore, I tinkered with my lysosomes. Instead of destroying and methodically neutralizing the products I put in them, my lysosomes simply cut them into smaller pieces to store them."



"When you have done all your fishing, then you rest a little?"

"You would not think so. It's a real obsession, my collection! I've hardly absorbed and filtered a few drops when I feel like going out again to collect more! What if a new find was just waiting for me a little farther away? So I sneak out again, eat again, then I sneak, then I eat... Actually, I do not remember doing anything else since I left ESCD (elementary school of DC)."





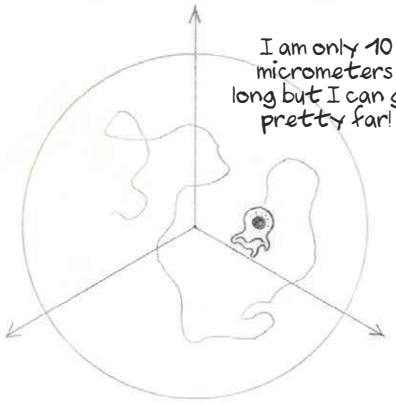
"It's kind of repetitive, isn't it?"

"Do you think so? It's actually an incredibly effective strategy to find things ... especially when you don't even know what you're looking for!"

"Sounds difficult, though."

"Imagine that you're on a big beach. You know there are some interesting things hidden in the sand, but you do not know what. To explore the beach, you have to walk around. But you can't dig around in the sand while you're walking. And when you are searching in the sand, you always stay in the same place. So you have to do both: walk, stop to search, walk again, etc... Exactly like me!

In this way, I can get a very good idea of everything in my territory. Look, it stretches between that capillary there, that big fiber and the surface of this muscle... Impressive, right? Nearly 1000 times my volume! Come on, it's time for me to take you on a tour around the property..."



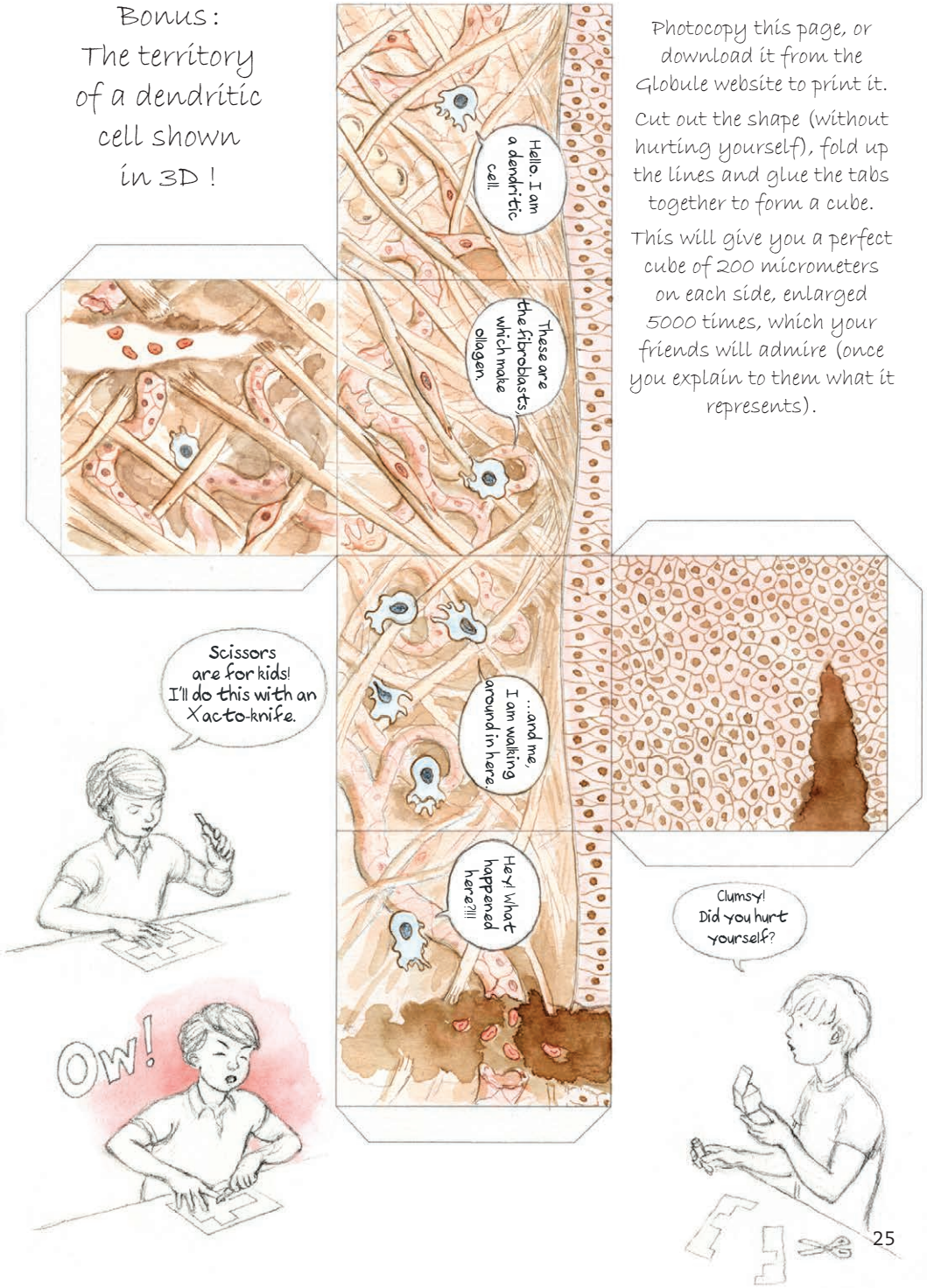
The area explored by a DC corresponds approximately to a sphere that is 100 micrometers in diameter: even if DC is so small, the size of its territory is at the border of what we can see with our eyes.

Bonus: The territory of a dendritic cell shown in 3D !

Photocopy this page, or download it from the Globule website to print it.

Cut out the shape (without hurting yourself), fold up the lines and glue the tabs together to form a cube.

This will give you a perfect cube of 200 micrometers on each side, enlarged 5000 times, which your friends will admire (once you explain to them what it represents).



"...What the heck happened here?"

"It's Simon – He just cut himself. But it's ok, it's hardly bleeding."

"It is clear that you are not able to see this! If it isn't wrong to gawk at this, I can survey how much damage has been done here: The membrane that separates the epidermis and the dermis is all torn, and there is extracellular fluid escaping! Let's look at how many collagen fibers have been cut. Well, a few hundred, that's not too bad. Obviously, there are also blood capillaries just under the skin that have been cut and red blood cells have escaped. We can't do anything about that. All this is not very serious; the bigger problem is that microbes may surely have slipped in here in the meantime. Simon, did you at least have clean hands? Oh, not so much? Well, at least it's an opportunity to see the famous white blood cells at work. This will be a show, your readers will be happy!"

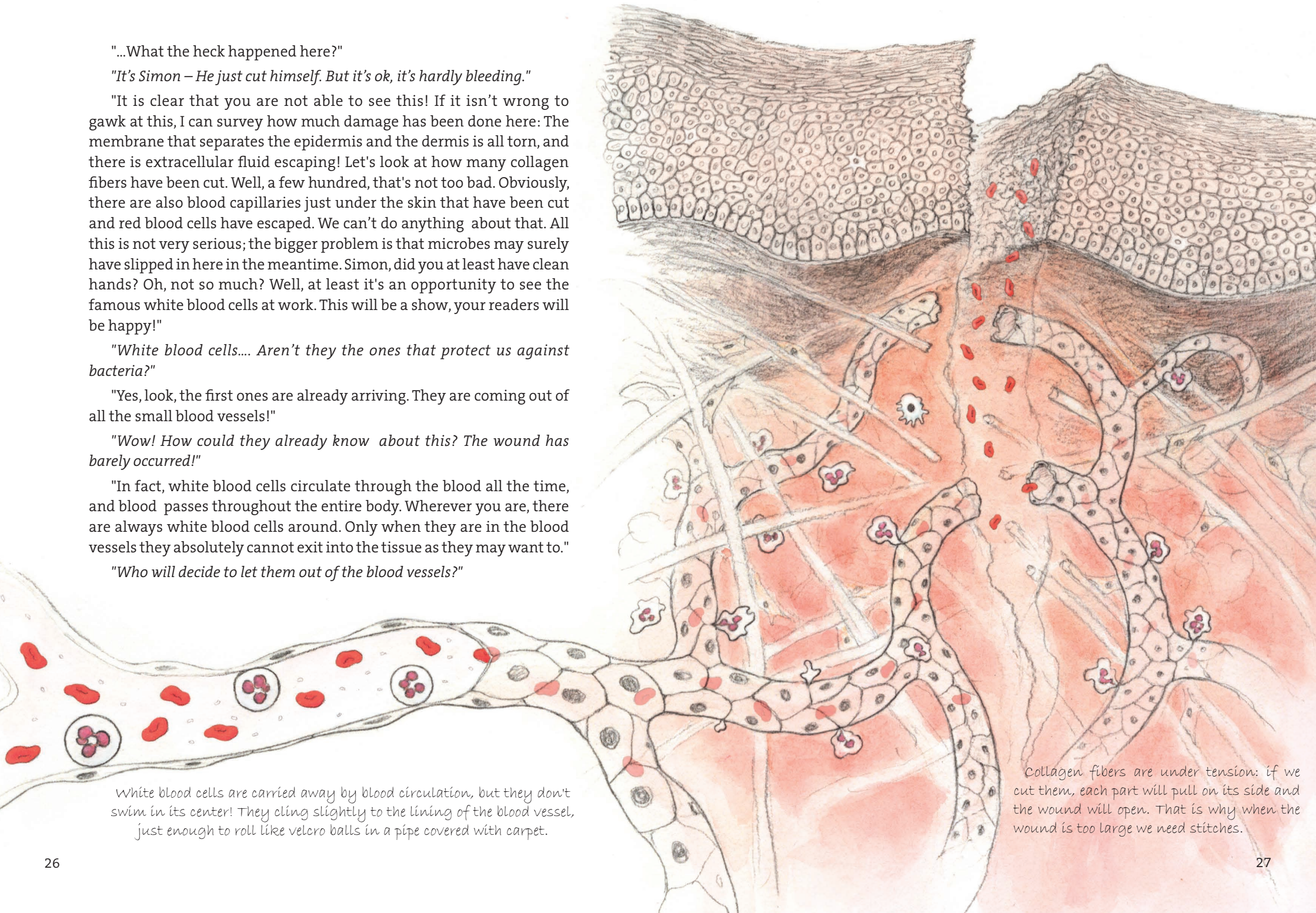
"White blood cells.... Aren't they the ones that protect us against bacteria?"

"Yes, look, the first ones are already arriving. They are coming out of all the small blood vessels!"

"Wow! How could they already know about this? The wound has barely occurred!"

"In fact, white blood cells circulate through the blood all the time, and blood passes throughout the entire body. Wherever you are, there are always white blood cells around. Only when they are in the blood vessels they absolutely cannot exit into the tissue as they may want to."

"Who will decide to let them out of the blood vessels?"



White blood cells are carried away by blood circulation, but they don't swim in its center! They cling slightly to the lining of the blood vessel, just enough to roll like velcro balls in a pipe covered with carpet.

Collagen fibers are under tension: if we cut them, each part will pull on its side and the wound will open. That is why when the wound is too large we need stitches.

"Imagine that the lining of the blood vessels is also made of cells that are tightly bound to each other. In case of injury, chemical signals released by damaged cells and their neighbors quickly alert these cells to the damage. They then insert new molecules onto their cell surface; these molecules stop the white blood cells that are traveling by. Once stopped, the white blood cells have only one obsession: to go out into the tissue. They sneak between the cells of the vessel lining, and if necessary, they even go right through it! By the hundreds of thousands, the white blood cells sworm out of the capillaries, and arrive at the scene of the crime.

The first ones on the spot are cells called neutrophils. They know how to eat or poison germs, but their most spectacular strategy is to create large sticky nets."

" A bit like spiders do?"

"Yes and no. Because in casting their net... the neutrophils self-destruct; they explode their own nucleus! No other cell in the body would ever choose such selfless destruction, but here it is for a good cause. The immense DNA molecules that carry the genetic information in the nucleus are spread all over. Being incredibly long, and as sticky as half-cooked spaghetti, they make an effective net. The microbes find themselves trapped and poisoned at the same time. But that is not the end of the story, because some bacteria know how to cut the mesh of the net.

Fortunately, the macrophages arrive a little later. These are like a Tyrannosaurus Rex for germs, always prowling around the body.

When the macrophages happen upon an intruder who has dared to enter the tissues, it doesn't stop to count to three : it just swallows it in a large vesicle.

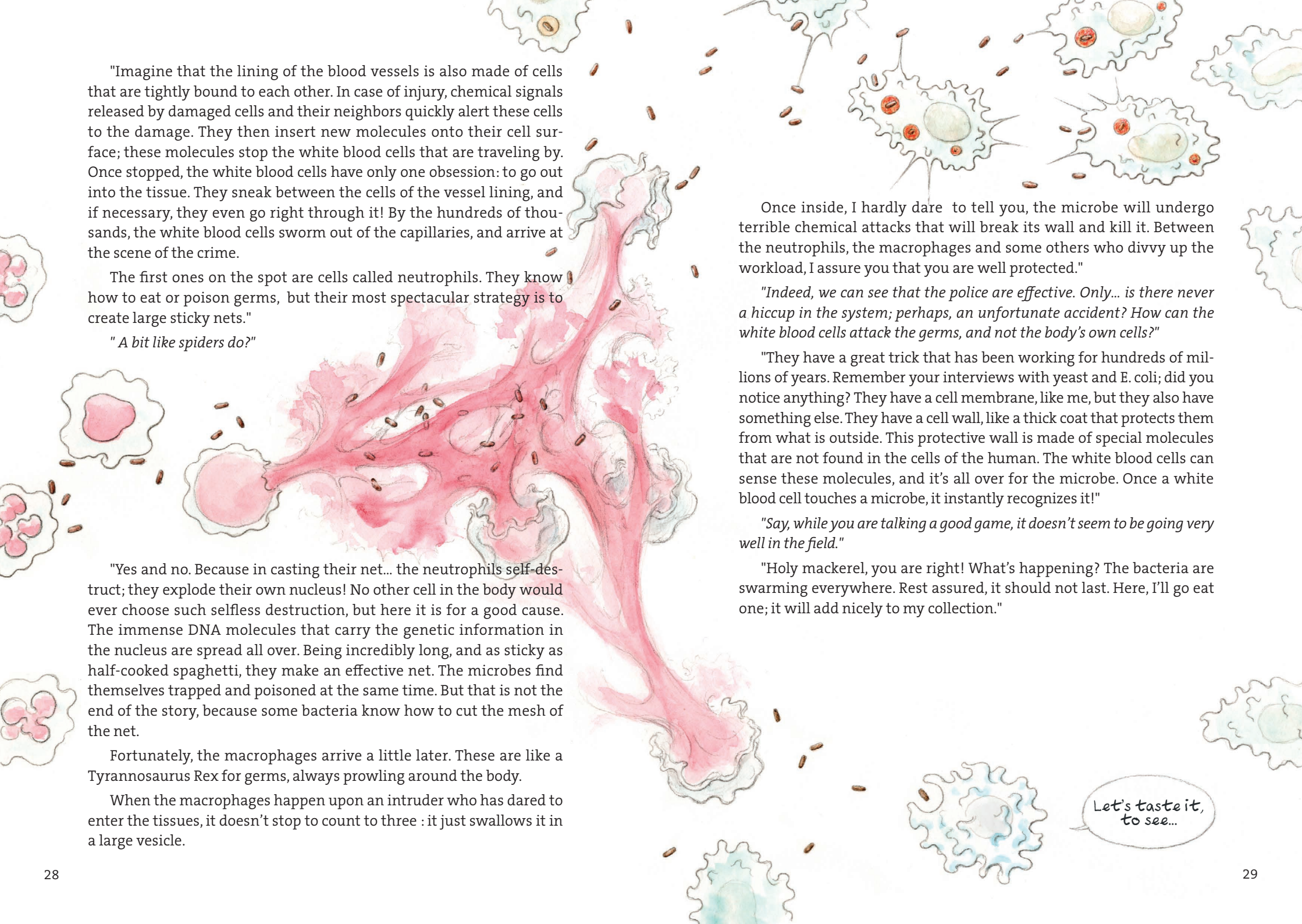
Once inside, I hardly dare to tell you, the microbe will undergo terrible chemical attacks that will break its wall and kill it. Between the neutrophils, the macrophages and some others who divvy up the workload, I assure you that you are well protected."

"Indeed, we can see that the police are effective. Only... is there never a hiccup in the system; perhaps, an unfortunate accident? How can the white blood cells attack the germs, and not the body's own cells?"

"They have a great trick that has been working for hundreds of millions of years. Remember your interviews with yeast and E. coli; did you notice anything? They have a cell membrane, like me, but they also have something else. They have a cell wall, like a thick coat that protects them from what is outside. This protective wall is made of special molecules that are not found in the cells of the human. The white blood cells can sense these molecules, and it's all over for the microbe. Once a white blood cell touches a microbe, it instantly recognizes it!"

"Say, while you are talking a good game, it doesn't seem to be going very well in the field."

"Holy mackerel, you are right! What's happening? The bacteria are swarming everywhere. Rest assured, it should not last. Here, I'll go eat one; it will add nicely to my collection."



Oops ! We lost our connection with DC for a few minutes.

When the signal is restored, its voice has changed. We sensed that something had happened.

"Delta-Charlie, are you OK? What happened?"

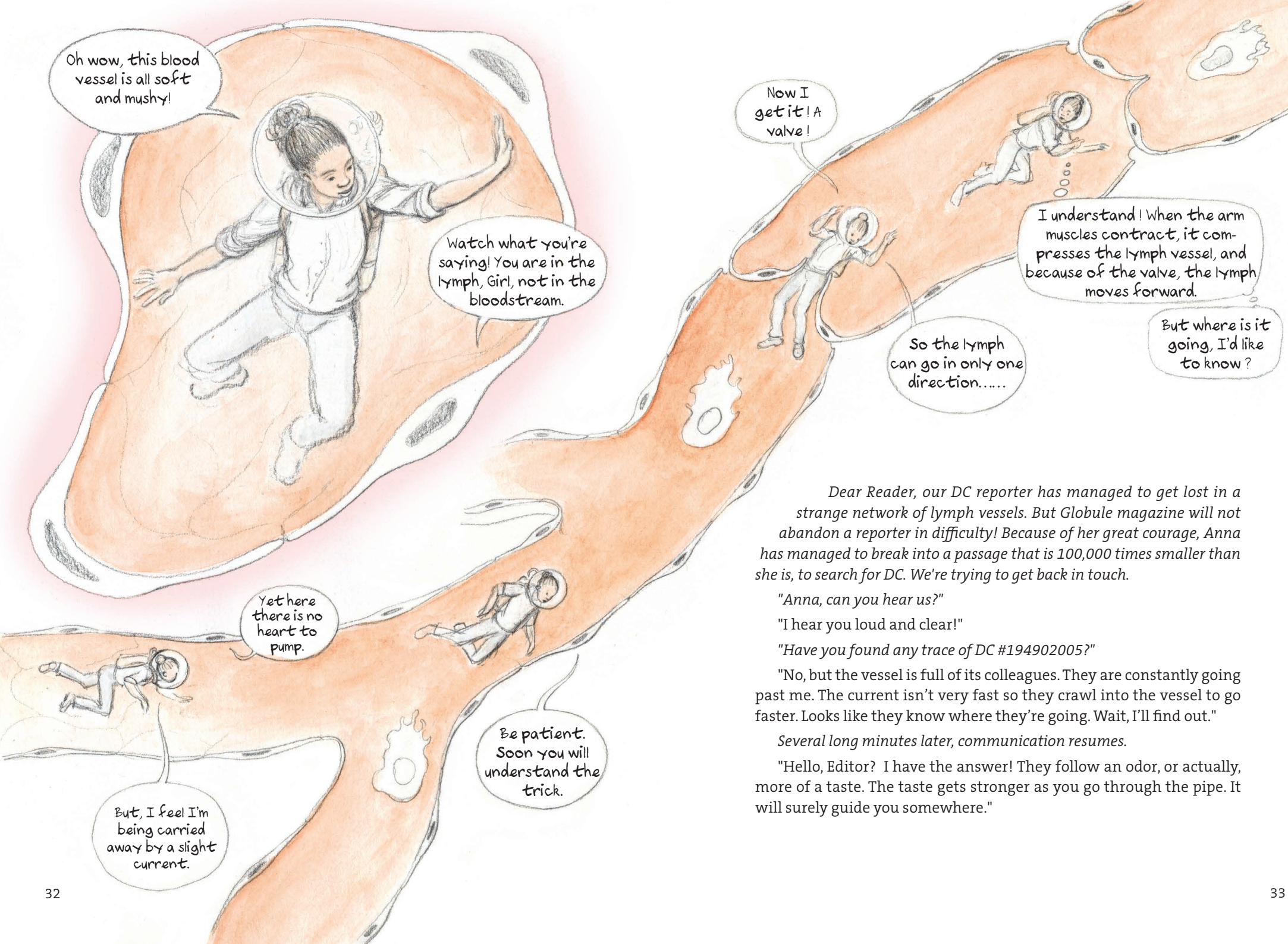
"This microbe I ate ... I am having an odd reaction to it. Looks like I also have detectors for bacteria wall molecules. But how can that help me? I am not a great warrior like a neutrophil or a macrophage.

The strangest thing is that I no longer feel like moving around as usual. I stopped on the spot, I am taking samples from every side, collecting all the information I can about these bacteria. I think it's my new obsession. It must be said, however, that these bacteria are unique. I have no idea how they can do it, but they are resisting all of Simon's emergency responders. And I had total confidence in our immune defenses!

Oh, and now the microbe has given me an irresistible urge to leave. Farewell friends, I have something important to do!"

Simon: « But wait! What's going to happen to me now, with all these invincible bacteria in my finger? Hello, are you there? Hello?"

This time, DC really isn't responding anymore. The editor feels helpless: We lost our reporter, and a member of the editorial board seems in danger of death! What to do?



Dear Reader, our DC reporter has managed to get lost in a strange network of lymph vessels. But Globule magazine will not abandon a reporter in difficulty! Because of her great courage, Anna has managed to break into a passage that is 100,000 times smaller than she is, to search for DC. We're trying to get back in touch.

"Anna, can you hear us?"

"I hear you loud and clear!"

"Have you found any trace of DC #194902005?"

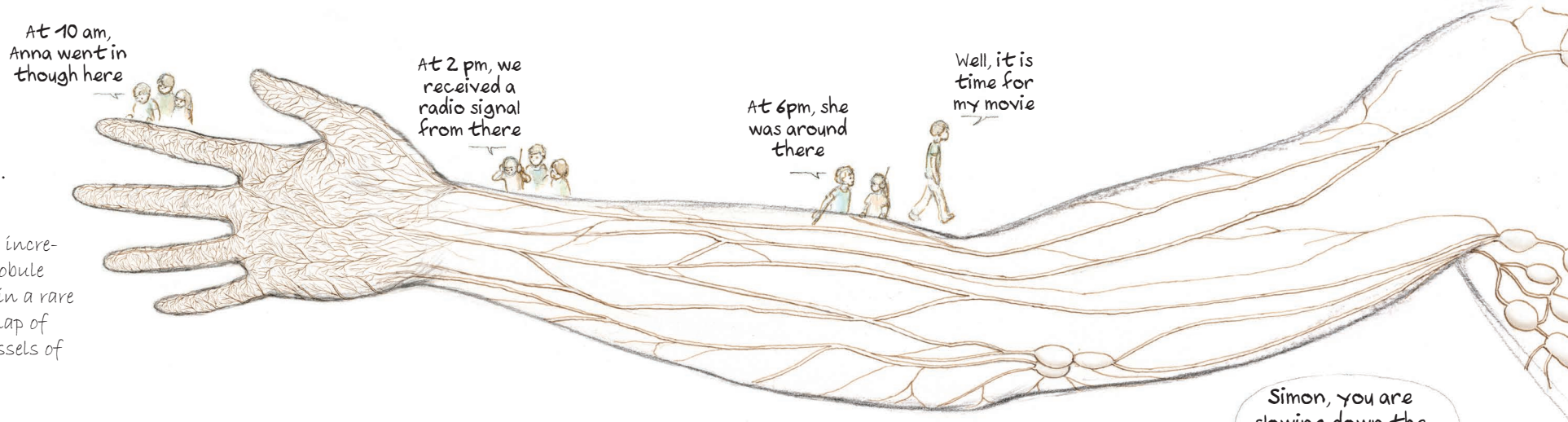
"No, but the vessel is full of its colleagues. They are constantly going past me. The current isn't very fast so they crawl into the vessel to go faster. Looks like they know where they're going. Wait, I'll find out."

Several long minutes later, communication resumes.

"Hello, Editor? I have the answer! They follow an odor, or actually, more of a taste. The taste gets stronger as you go through the pipe. It will surely guide you somewhere."

A long journey...

To follow Anna's incredible journey, Globule managed to obtain a rare document : the map of the lymphatic vessels of Simon's arm.



"But I have been moving for more than an hour and I still have no idea... Simon, can you move around a little bit? Obviously this is what moves me forward."

Simon: "You're thinking only of yourself! Now you're asking patients to do gymnastics!"

"Frankly, you still don't look sick, at least from our view inside here. Here there is a joyous symphony of hisses, blood passing through the vessels next to mine, and everything seems OK..."

Again, we lose the communication for a long time...

Much later, we finally hear Anna's voice:

"Oh, now my vessel is getting bigger and bigger, it seems that I've arrived somewhere. Yes, the lymph is flowing into a big lobby... What a crowd! All the cells are packed together like commuters in a train station at rush hour. To find our dendritic cell in here is going to be impossible! There are thousands, tens of thousands...

But it's not just that: Other round cells look like they are bumping up against the dendritic cells. Hmm, how can I describe it? They seem to be very affectionate with one another. The two kinds of cells are sticking together and kissing each other. The dendritic cells, especially, are extending their tentacle arms in all directions, and the other cells are curling up in them."

to get the answers go page 31 and page 42!

We hear a voice interupting Anna:

"Ma'am, what are you doing here? We are in the midst of preparing for war !"

Anna: "Sorry. I would never have guessed. Um, could you tell me where I am ?"

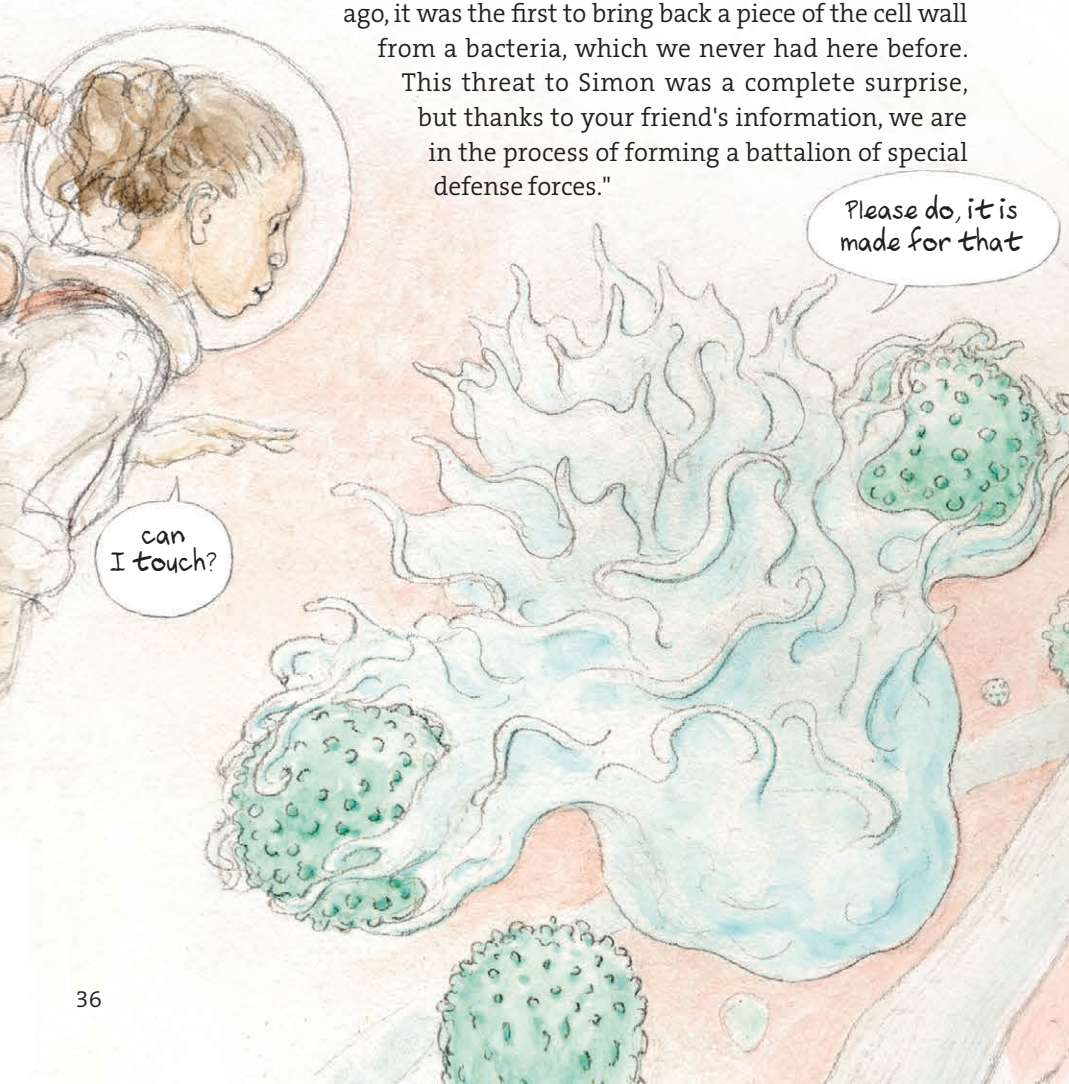
"You are in the lymph node, My Dear. A few hours ago, it was much more peaceful around here. But a message of the utmost importance has come to us. Imagine that there is an attack of germs, somewhere towards the end of this arm."

Anna: "Oh yes! I just came from there."

"So, what are you doing? Quick, show me the molecules you brought from there! I understand that you are tired from your trip, but put in one last effort! Do you need me to show you what to do? Look at me, you have to extend yourself out at the edges like petals. And cover your surface with the whole repertoire of small fragments of molecules that you have stored in your lysosomes. It's important to get as many nearby cells as possible to bind to them."

Anna: "I'm sorry, I didn't bring anything with me, I didn't have time to think about it! And anyway, I am not a dendritic cell; I am just searching for DC #194902005."

"What, is it a friend of yours? What a hero! A little while ago, it was the first to bring back a piece of the cell wall from a bacteria, which we never had here before. This threat to Simon was a complete surprise, but thanks to your friend's information, we are in the process of forming a battalion of special defense forces."



Anna: "Will Simon be saved?"

"Of course, with the help of all the round cells that are cozying up to the dendritic cells. They are called lymphocytes. They are formidable killers of microbes, but they do not attack them in the same way as neutrophils and macrophages do. Instead of having the usual microbe recognition system, which usually works well, but sometimes fails, they each have a special and unique recognition system, each different from that of its neighbor. And there are so many of them! Every day, hundreds of thousands of new ways of recognizing microbes are created at random. Amazingly, no one knows which ones will turn out to be useful!

Each new lymphocyte spends its time traveling from one lymph node to another, snuggling up to each dendritic cells, one after another. If the lymphocyte embraces a DC that presents it with pieces of molecules from microbes, as happened today, then, Bingo! We know then that that DC has the right sensors to neutralize the new threat. The chosen lymphocytes then start to multiply. This causes the lymph nodes to swell, to the extent that you can sometimes feel it by touching them. As soon as this army of identical lymphocytes is numerous enough, it sets out to assault the microbes."

Anna: "I am eager to see that! But first: where is DC ? I am so glad we just found it!"

"Um... It isn't really here."

Anna: "Did it leave again?"

"Oh no, it couldn't go any farther. Do you know the story of the first marathon runner? It was a Greek warrior who ran 40 kilometers to bring an important message to Athens. Legend has it that on his arrival he collapsed and died of exhaustion. Well, after DC's long trip, moving through the tissues and the lymphatic vessels, it was exhausted. So after delivering its message, it breathed its last breath. I gathered what was left of it to show to the others. I am a dendritic cell that never moves out of the lymph node, so I have time on my hands."

Anna: "Is DC dead? Oh no! That is so sad!"

"It's not really like that! You know, your friend DC lived a full life. Thanks to it, the human in whose body we live (I believe that his name is Simon, right?) will be able to live for a long time. And even without this wound, DC would have lived only two more days."

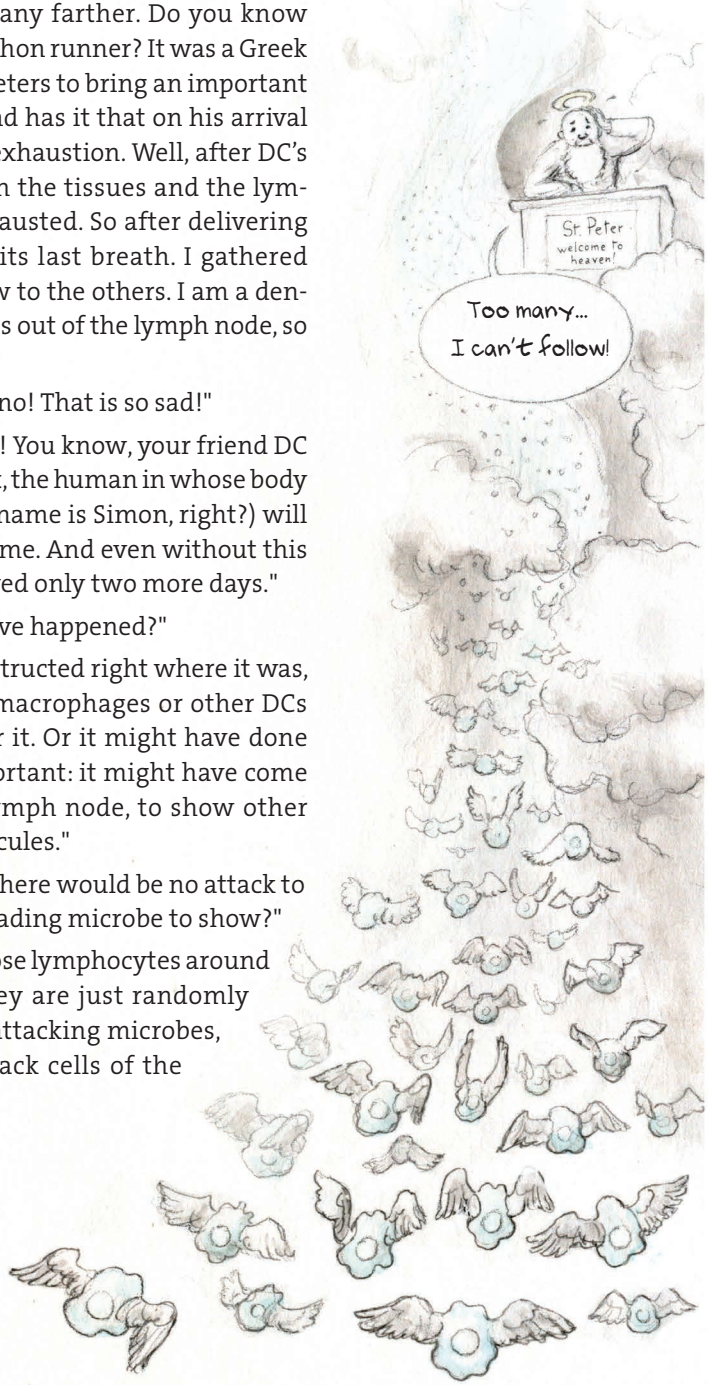
Anna: "What would have happened?"

"It would have self-destructed right where it was, just under the skin, and macrophages or other DCs would have filled in after it. Or it might have done something else very important: it might have come back here itself, to the lymph node, to show other cells its collection of molecules."

Anna: "But why, since there would be no attack to report on, no pieces of invading microbe to show?"

"Well, do you see all those lymphocytes around us? They are not bad, they are just randomly programmed. Instead of attacking microbes, many of them might attack cells of the

How many DC's are born and die everyday in the human body?

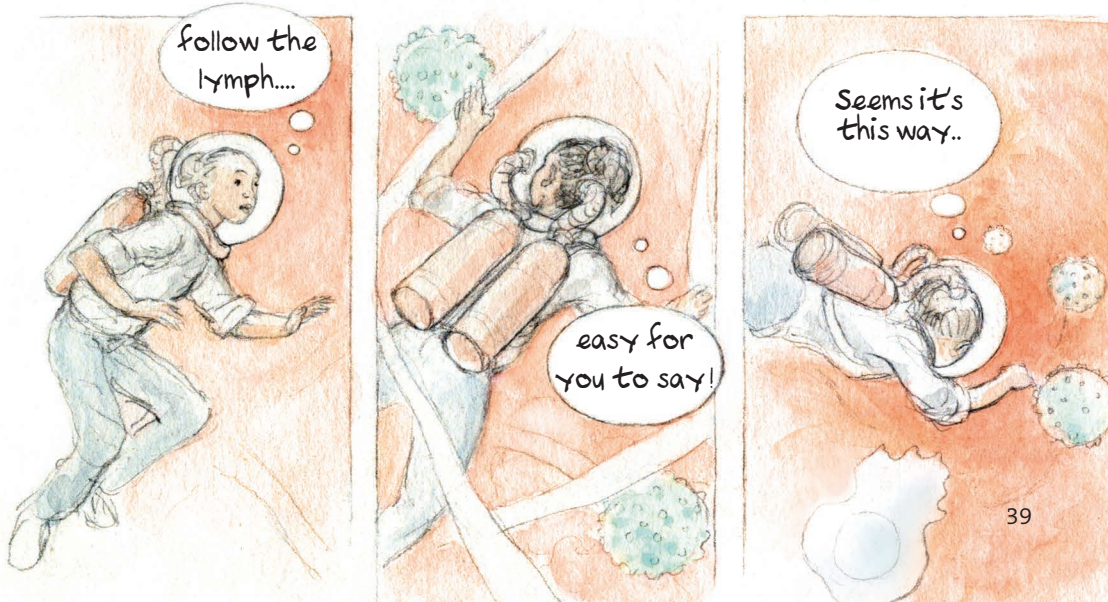


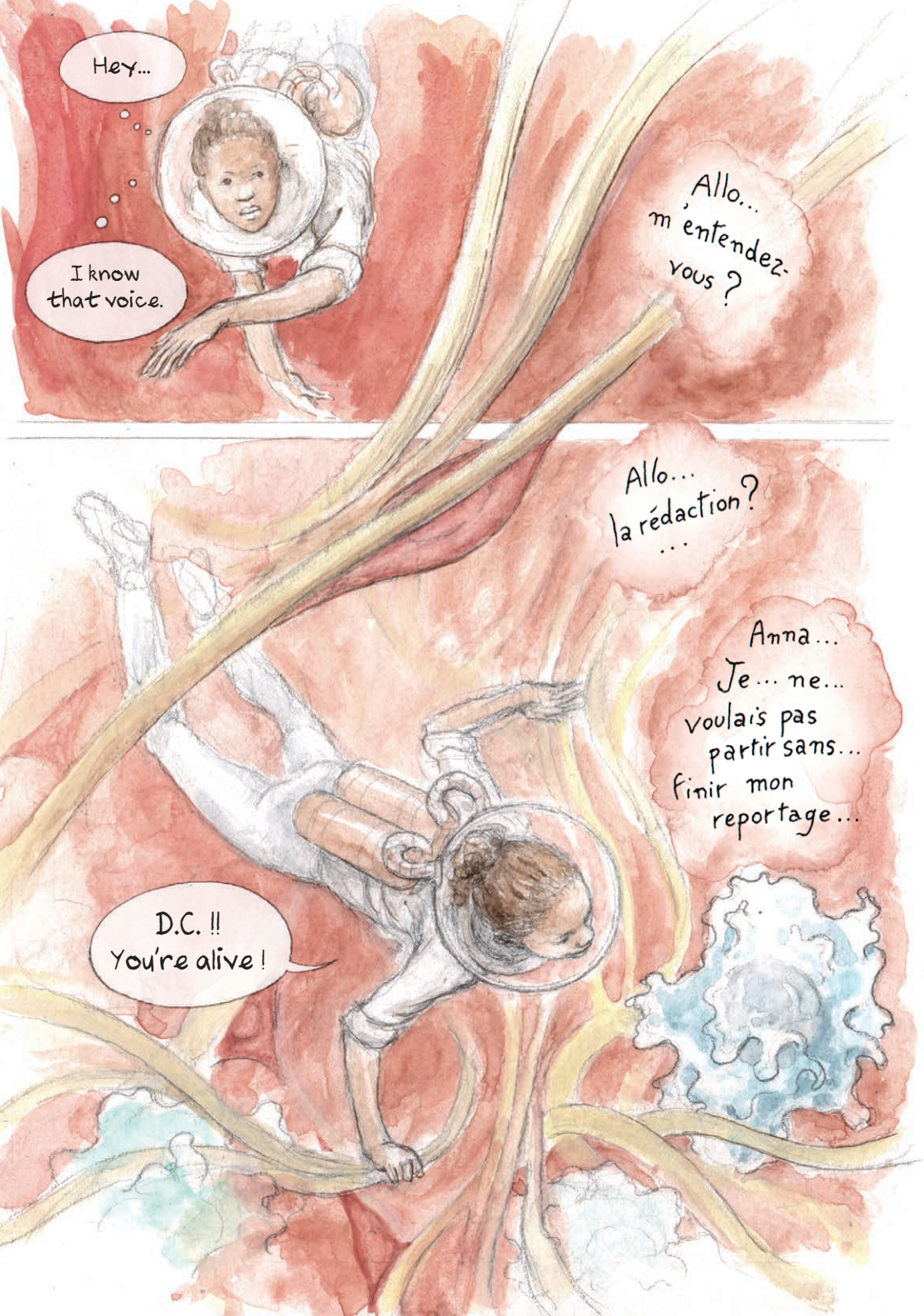
body if they are released like that. Those lymphocytes need to be eliminated. But, how to know which ones are dangerous?

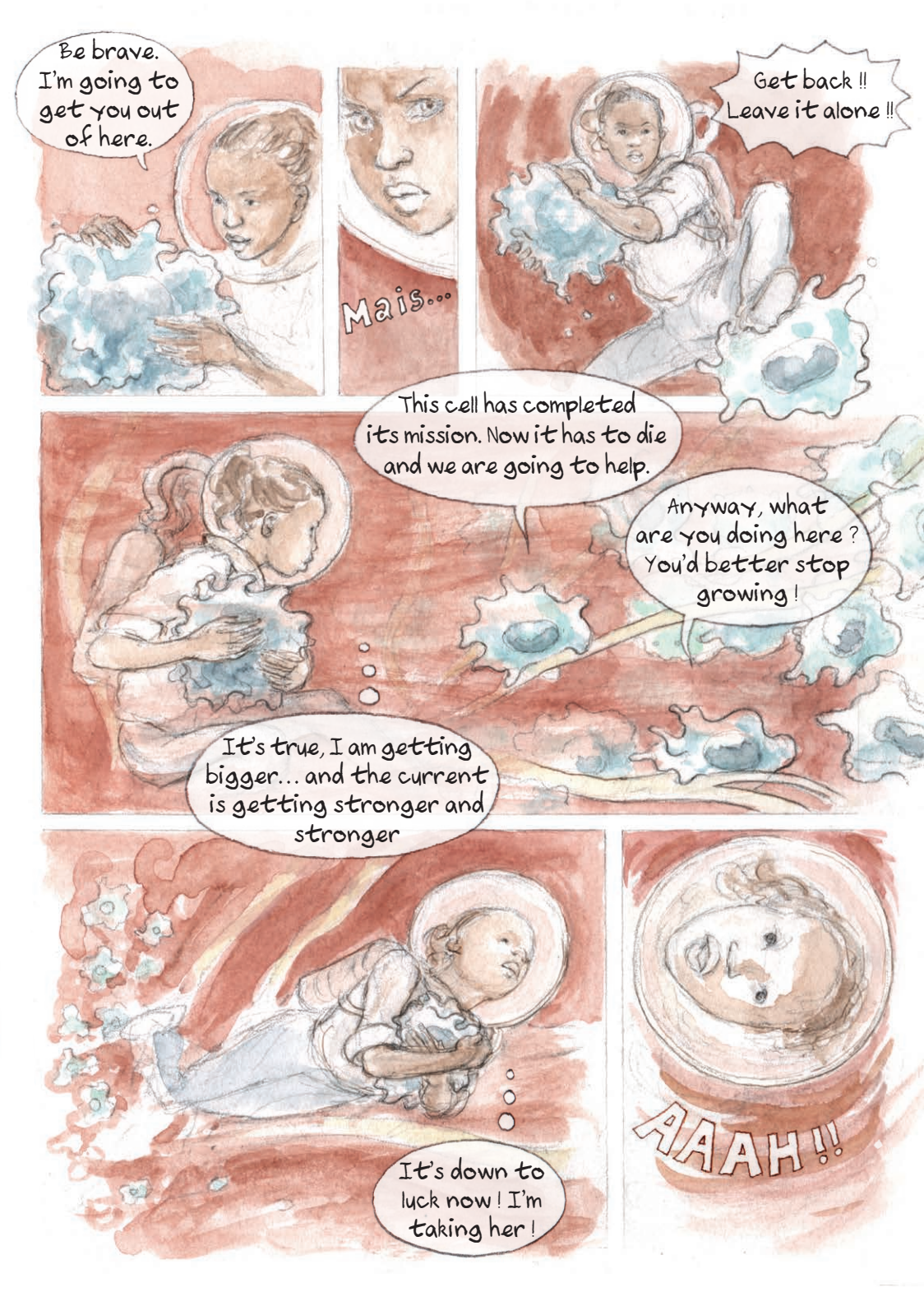
That's where travelling DCs help us again. Whenever one of them comes back into the lymph node without having encontered any infection, its collection of molecules consists only of fragments from our own body. When kissing the DC, lymphocytes that react agressively are identified right away: it shows that they could attack where they are not supposed to. I assure you, they are eliminated without further notice!"

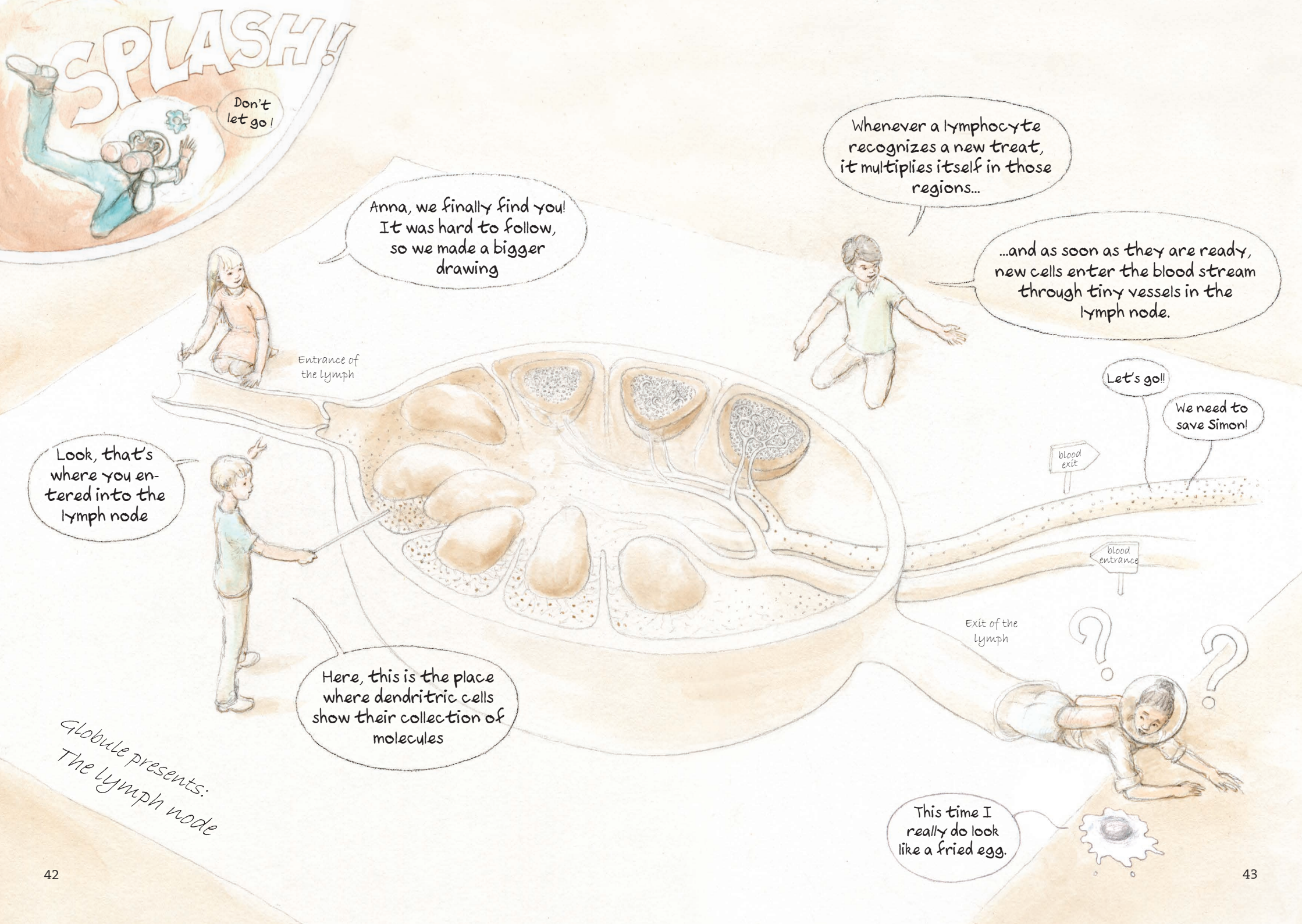
Anna: "I would really like to understand this! Do I have to go back on the same path that I took?"

"That is out of the question, Girl! First, the lymph is a one-way path. To reach the infection, the lymphocytes travel through the blood vessels. This isn't a very direct route, and even scientists don't really understand how they find their way. They think that the DC manages to give them the information that enables them to stop at the right place. Whatever you do, don't try to follow them, or you might get lost forever inside Simon's body! And besides, I really think it's time for you to go back to where you came from. Follow the lymph! Bye-bye!"




Hey...
I know that voice.
Allo... m'entendez-vous ?
Allo... la rédaction ? ...
Anna... Je... ne... voulais pas partir sans... finir mon reportage...
D.C. !! You're alive !


Be brave. I'm going to get you out of here.
Mais...
Get back !! Leave it alone !!
This cell has completed its mission. Now it has to die and we are going to help.
Anyway, what are you doing here ? You'd better stop growing !
It's true, I am getting bigger... and the current is getting stronger and stronger
It's down to luck now ! I'm taking her !
AAAH !!



Globule presents:
The Lymph node

To continue the adventure, follow us on www.globulemag.org

This work received support from PSL Research University and from the grants ANR-11-LABX-0038 and ANR-10-IDEX-0001-02. It has also been suported by DCBiol Labex and Institut Curie.

Globule would like to thank Ameya Murukutla and Bertsy Goïc, for their research and their contribution to the drawings, Daria Bonazzi, Chloé Bulinski, Marie-Christine Chabrier, Iris Chabrier-Trinkler, Emma Neaves, Aurélie Faure de Peybeyre, Carsten Janke, Maria Magiera and Jérôme Robert, for their support, and finally Arthur Charles-Orszag, Klemens Rottner, Pablo Vargas, Danijela Vignjevic and all the researchers that answered all our questions.

A very big thank you to the magazine La Hulotte, from which this book is largely inspired.

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THE • GLOBULE • GLOSSARY

In biology, there are important ideas that aren't always easy to understand.

Here are a few terms that you encountered in the story you just read:

Molecule: molecules are the smallest objects that make up living matter. They are themselves made up of atoms bound to each other. The living world uses molecules that are found everywhere, such as water, but also molecules that are only manufactured by living beings. These can be very large molecules, such as proteins or DNA (see pages 22-23).

Membrane: In general, a membrane is a thin surface that separates two fluids. In living organisms, membranes are made up of special molecules called lipids. These membranes separate the inside and the outside of the cells, as well as the compartments within the cells, such as the macropinosome on page 19, or the nucleus on page 17.

Cell: All living organisms are made up of cells. Some are made up of only a single cell (bacteria, yeast), others of a very large number of cells. The cells are separated from the environment by a membrane, and they contain a multitude of molecules that are necessary for them to function. All cells are capable of dividing to give rise to two daughter cells, thus perpetuating themselves.

Nucleus: All cells contain deoxyribonucleic acid (DNA) which is a 'memory' molecule within which the genetic information is found. The information necessary for the cell to make its own proteins is encoded in the DNA. Some cells (like ours or yeast cells) gather the DNA into a compartment separated from the rest of the cell by a double membrane. It is called the nucleus, and it is often the only component shown on a drawings of a cell, even though the cell contains many others interior components. This precious 'bag' that the cells carry sometimes poses problems for them to squeeze through narrow passageways (see page 18).

Organism: Biologists use the word 'organism' when referring to individuals of a living species. Multicellular organisms contain organs such as the heart, brain or skin. Unicellular organisms include organelles such as the nucleus or lysosomes (described on page 22).

Tissues: In organisms that contain a large number of cells, some cells group together to produce the different parts of the organs, which are called tissues. In the skin, we can distinguish three tissues, from the most superficial (closest to the outside) to the deepest: the epidermis, the dermis and the hypodermis. At the beginning of our story, DC is living in the dermis. On page 27, Simon's epidermis and dermis get cut.

Immunity: This term refers to an organism's defenses against attacks by other organisms that might make it ill (e.g. bacteria or viruses, which are commonly referred to as microbes). To defend itself, the organism must be able to recognize threatening microbes. It does this by reacting to certain molecules that it detects on the surface of these microbes. There are two types of immunity:

Innate immunity: These are weapons the organism always has on hand. They are built from blueprint genetic material an organism has inherited. These weapons are deployed very quickly but they are not specifically targeted or adapted to all of the different types of microbes. On pages 26 to 29, it is innate immunity that takes place.

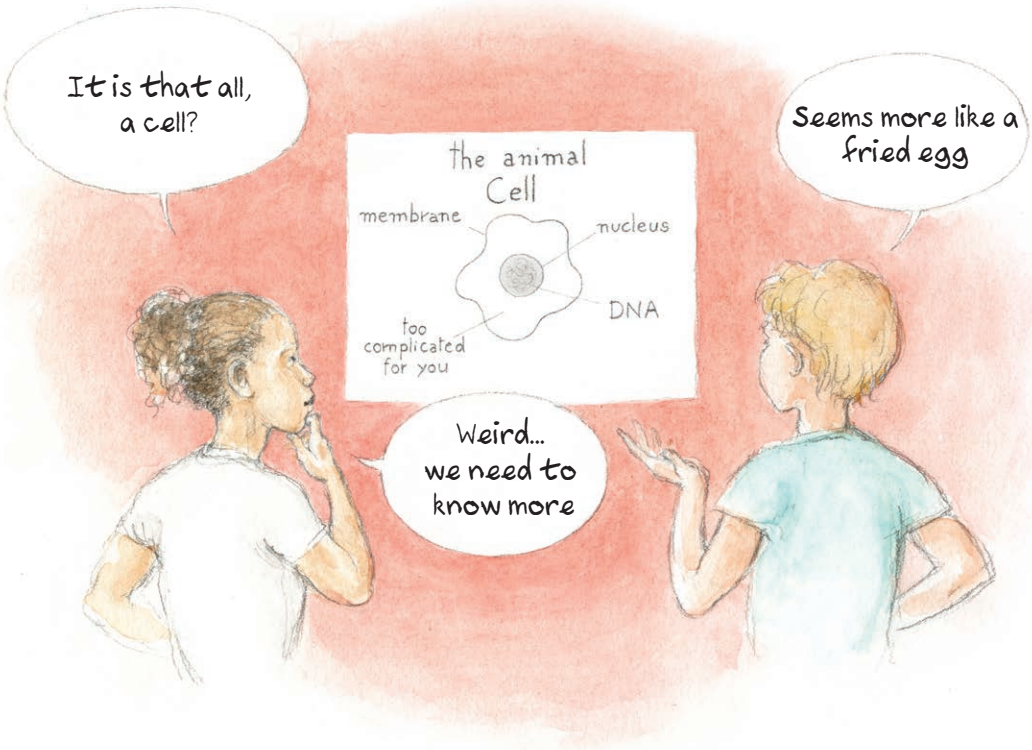
Adaptive immunity: This allows the body to manufacture weapons called antibodies, which are [made by cells called lymphocytes and are] specially adapted to a particular threat. To select these weapons and identify the most effective ones, the organism tests them on molecules from the aggressors, which are called antigens. The role of a dendritic cell is to collect fragments of molecules from the attacking microbe and carry them to the lymph node, where the DC then helps to select the lymphocyte that is capable of making the appropriate antibodies. This is the story that we have told in this magazine. Once a specific antibody has been selected to recognize an antigen, the lymphocyte that makes it will divide into many daughter cells in order to mass-produce this particular antibody. The next time it is attacked, the organism will know how to make the correct antibodies very quickly. In this way the organism is immune to the threat posed by this particular attacker. Vaccination makes use of this mechanism : when we are immunized with the molecules of microbes, we will avoid letting that microbe make us sick the next time our body is attacked by it.

Here is the first issue of Globule, the newspaper that finally lets the cells speak.

Science is fascinating with its galaxies, black holes and particles, but there also exists an amazing world, much closer to us. This world simply gives us life.

Globule invites you to discover this world and to know it better.

No matter if you are ten, if you know nothing about cells or if you are a well-trained biologist, be assured that Globule will surprise you!



Free distribution in the context of Covid-6 crisis
ISBN 978-2-9563725-1-6