

Acute Lymphoblastic Leukemia from the Perspective of Immune Cells: A Book to Help Children Understand Cancer

Honors Thesis

**Presented in Partial Fulfillment of the Requirements
For the Degree of Bachelor of Arts in Biology**

In the College of Arts and Sciences
at Salem State University

By

Irune Aparicio

Dr. Gwen Scottgale
Faculty Advisor
Department of Biology

Commonwealth Honors Program
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Abstract

Acute Lymphoblastic Leukemia (ALL) is the most common type of childhood cancer. According to the American Cancer Society 3 out of 4 childhood leukemia cases are ALL, and the main treatment for these patients is chemotherapy. There are various tools that doctors and nurses use in order to effectively communicate with these young patients and their families about what this type of leukemia is, and what chemotherapy will do in order to help. There are children's books on cancer, but they are mostly coping aids or answer general questions. My children's e-book however invites the young reader (6 to 14-year-olds) into the world of immune cells, by following the life of a T-cell as he learns about his environment and how to interact with other immune cells to fight against ALL and protect their human. The reader also witnesses how the cells react to the chemotherapy, and their journey after treatment. My goal for this creative project is that it will serve as another educational tool for patients with ALL. Also, I hope that it inspires its audience and gets them excited about science. Even though this children's book is written with scientific detail, the concepts are presented in a simple and attainable way, enabling my young audience to comprehend what ALL is, unlocking their perception towards the disease with this new approach.

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Acknowledgements

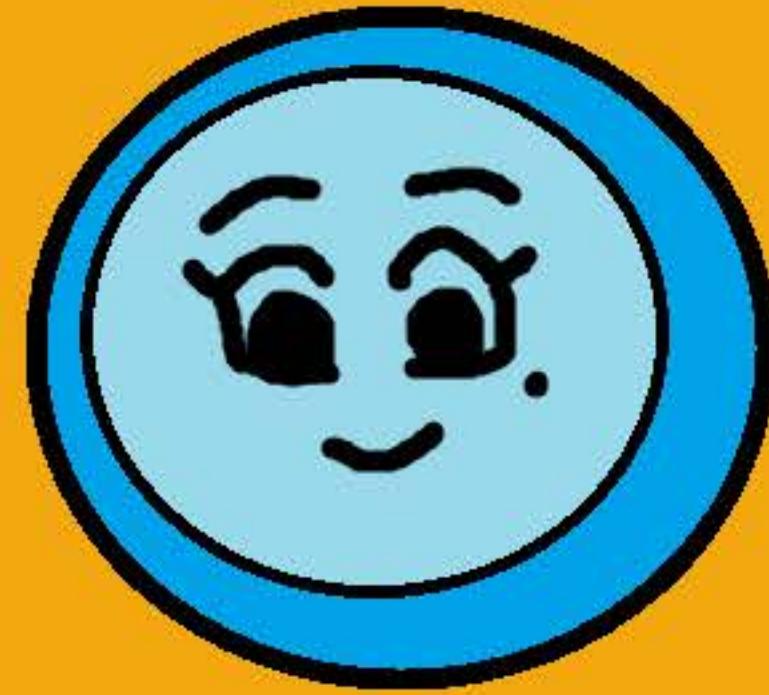
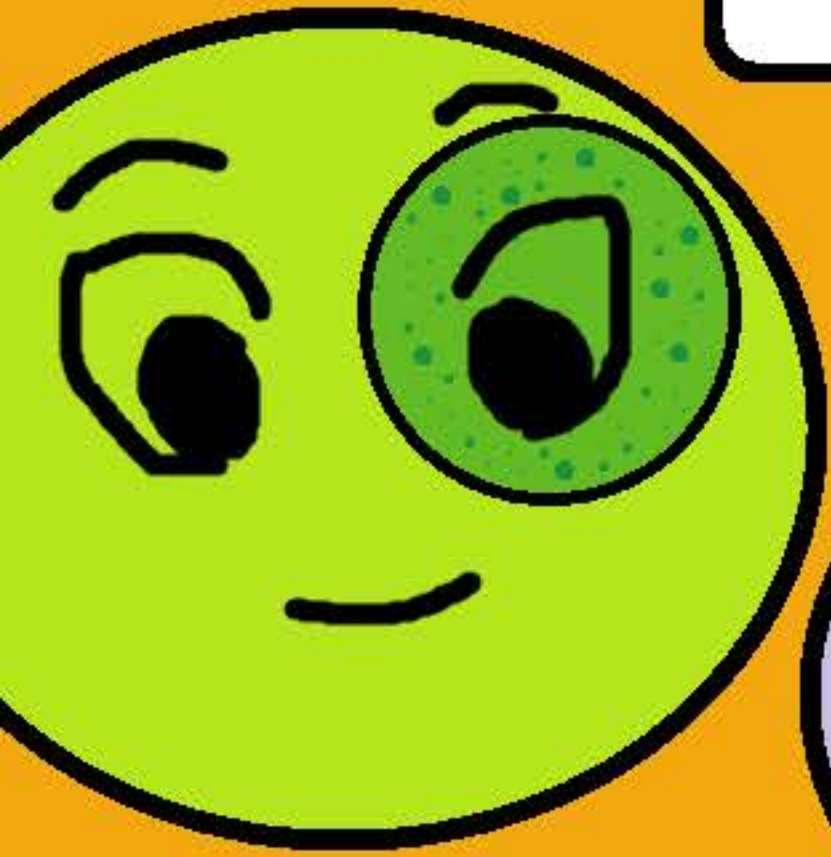

Gwen Scottgale, Ph.D., for guiding me through this process and for her essential constructive criticism.

Alan Aparicio, for helping me brainstorm ideas for the story's ending.

My young violin students Jeremy and Rosie, for giving me feedback on a couple of subjects regarding my thesis that allowed me to get a better idea for what my target audience can understand and is attracted to.



Acute Lymphoblastic Leukemia from the
Perspective of Immune Cells:
A Book to Help Children Understand Cancer

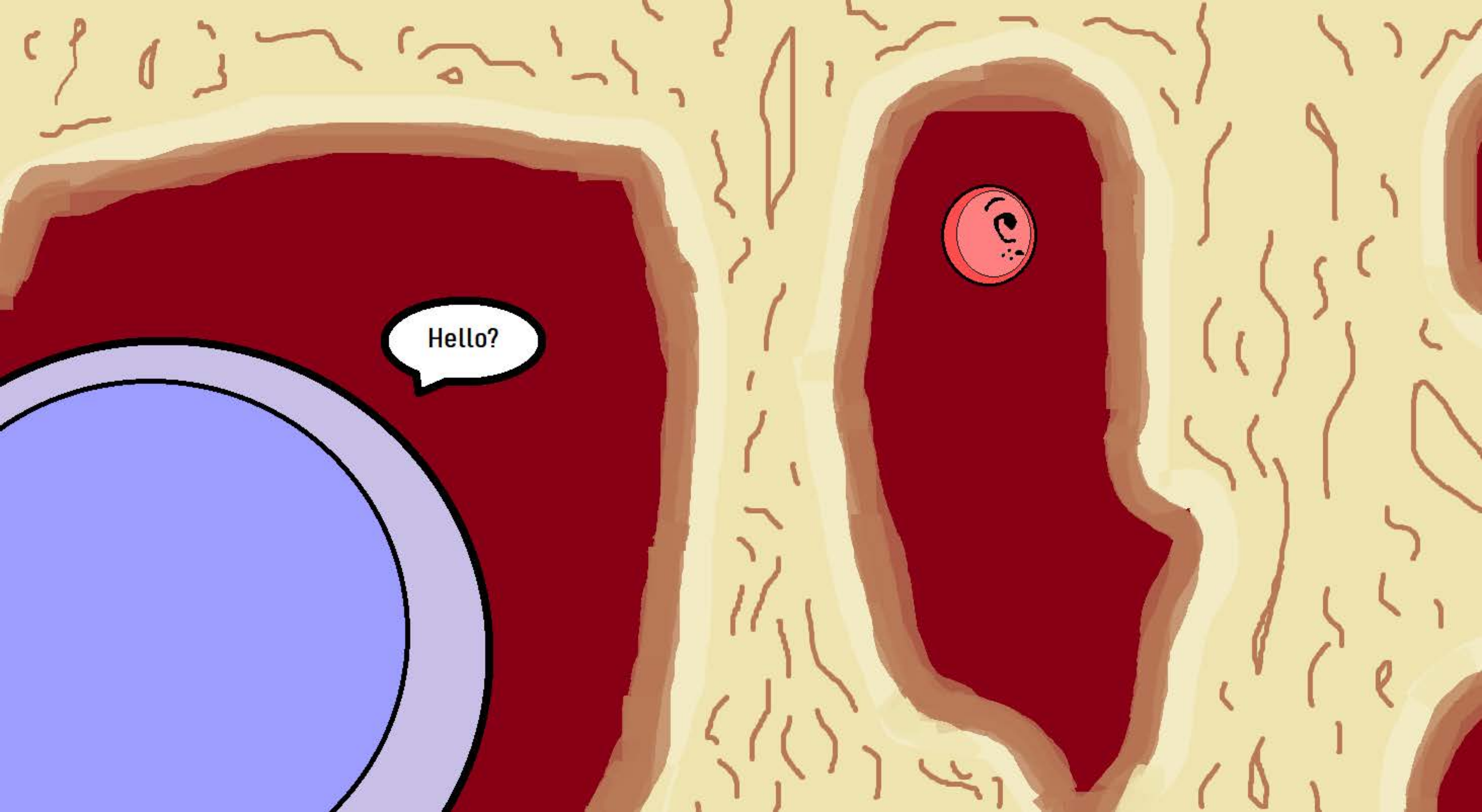


Written and Illustrated by Irune Aparicio

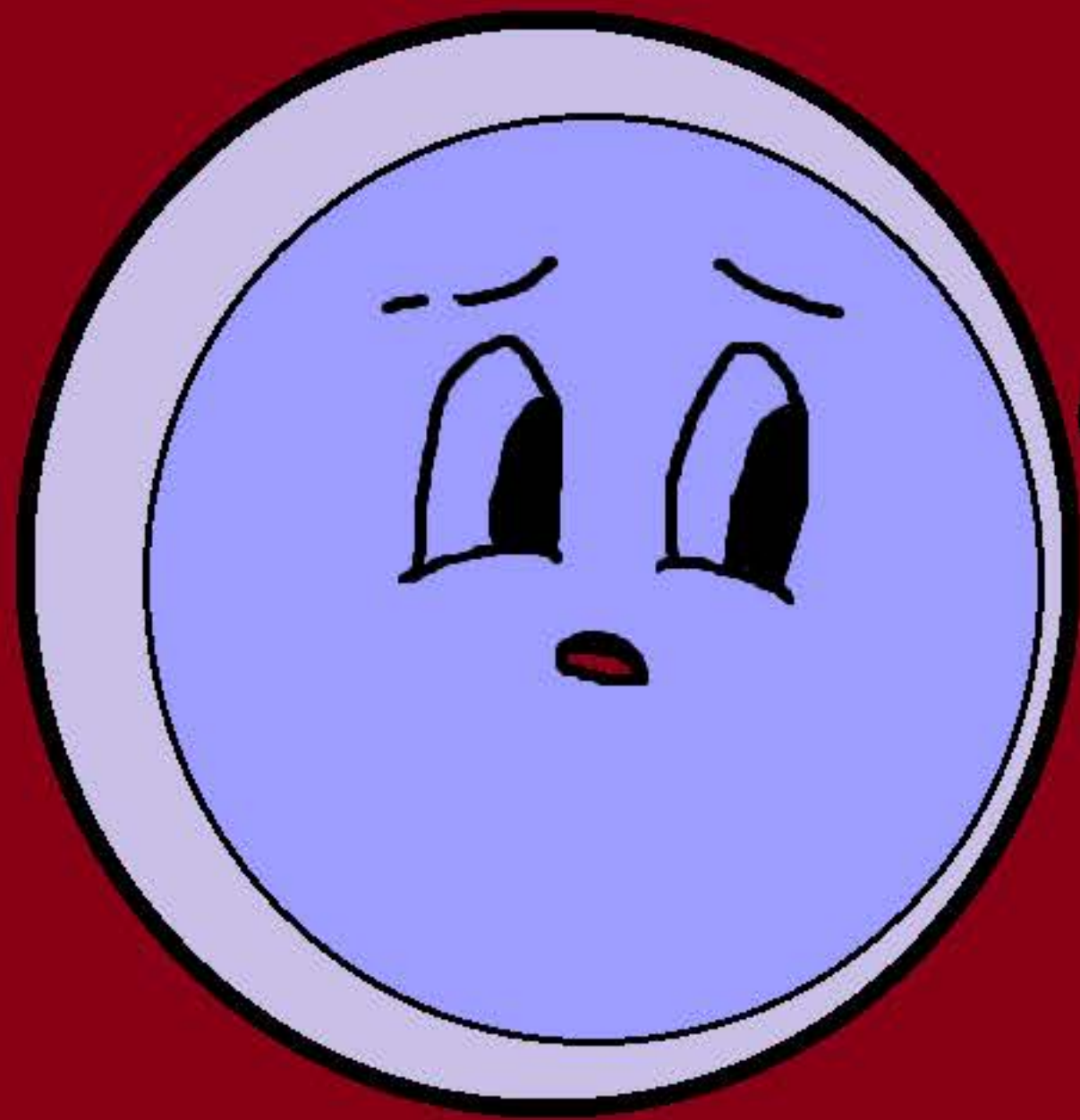




Huh? Where am I?



Hello?



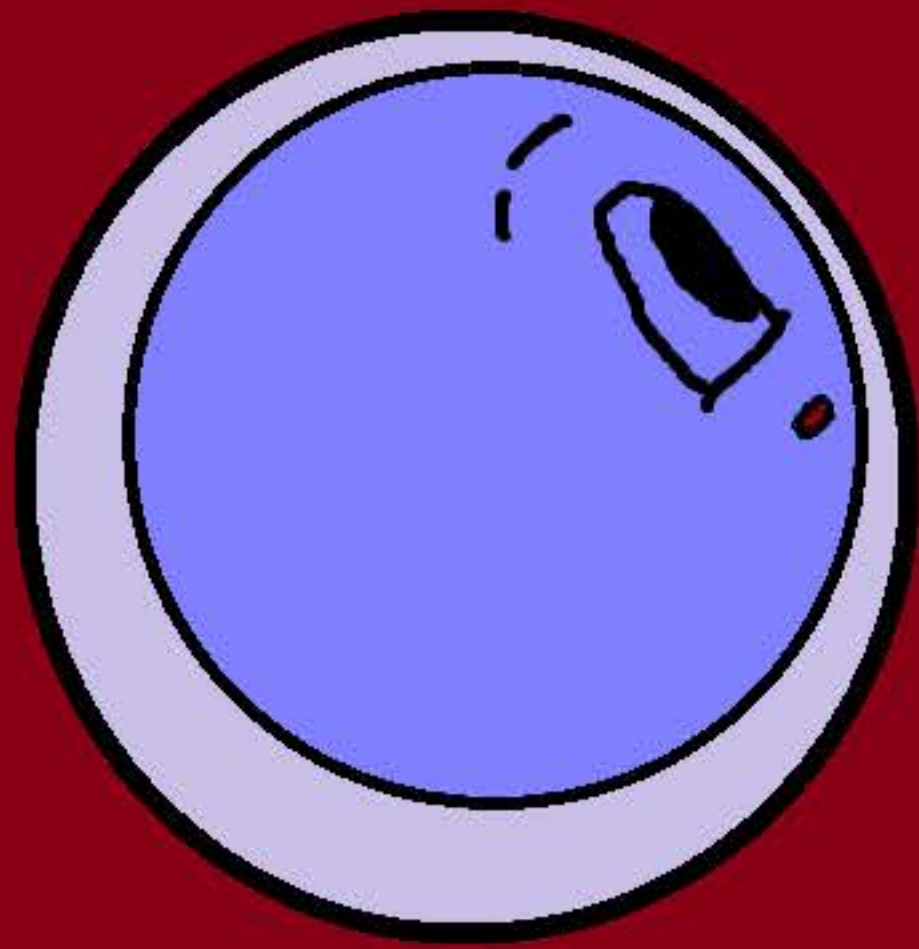
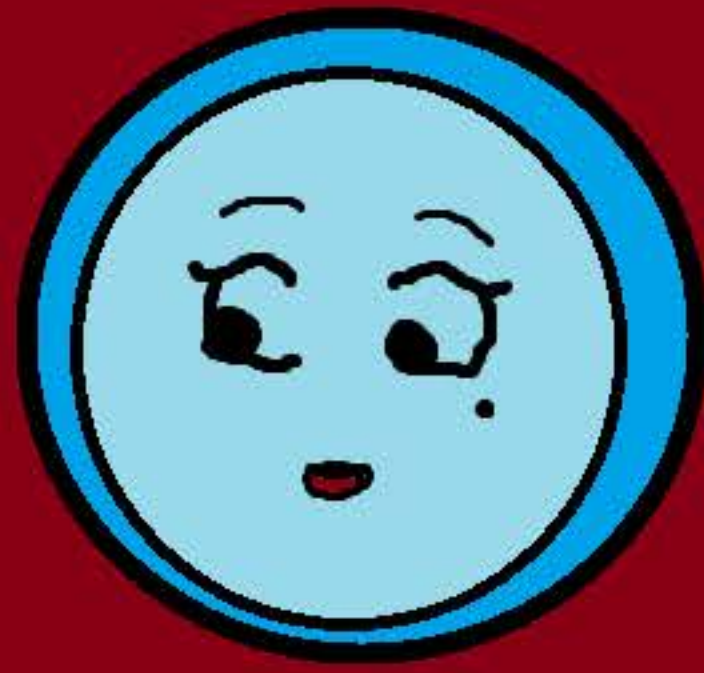
Do you know
where we are?

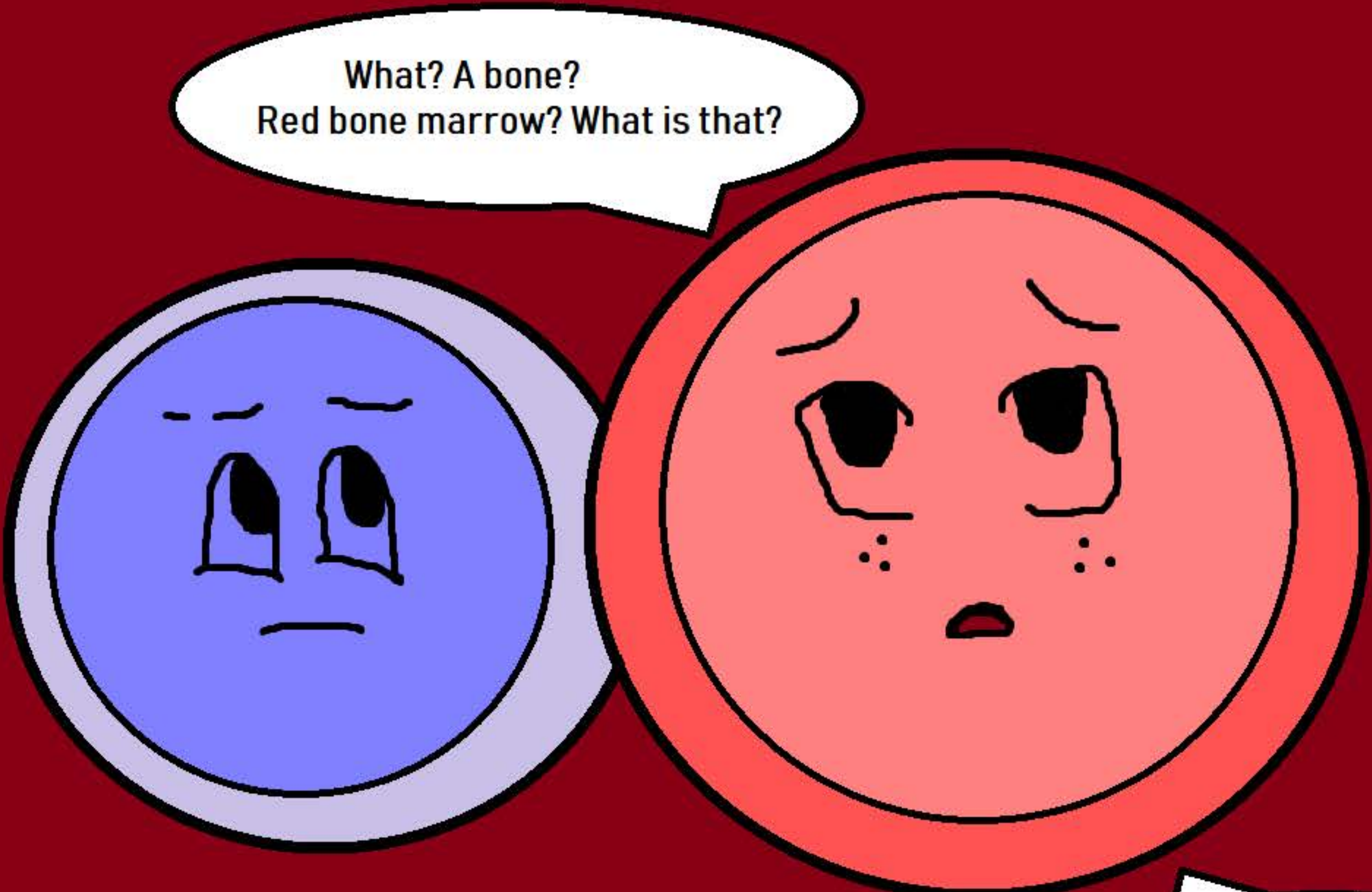
Uh... Hello...



I'm sorry,
but no.

You are both inside a bone, to be more specific, you are inside this bone's red bone marrow.

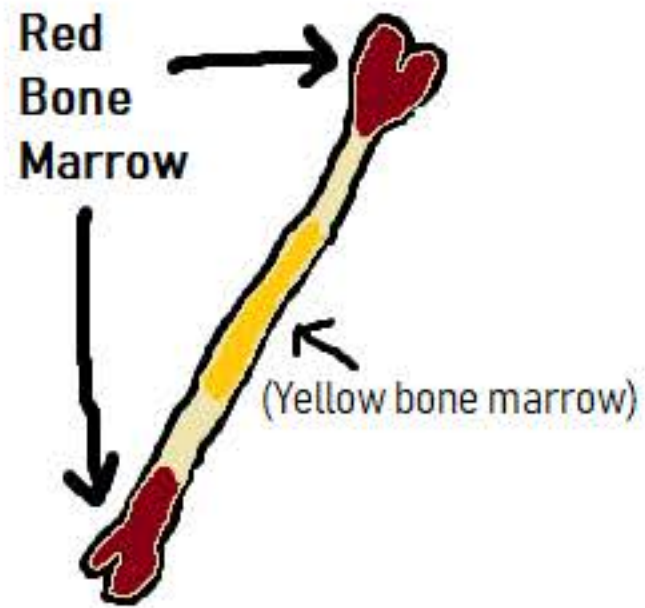




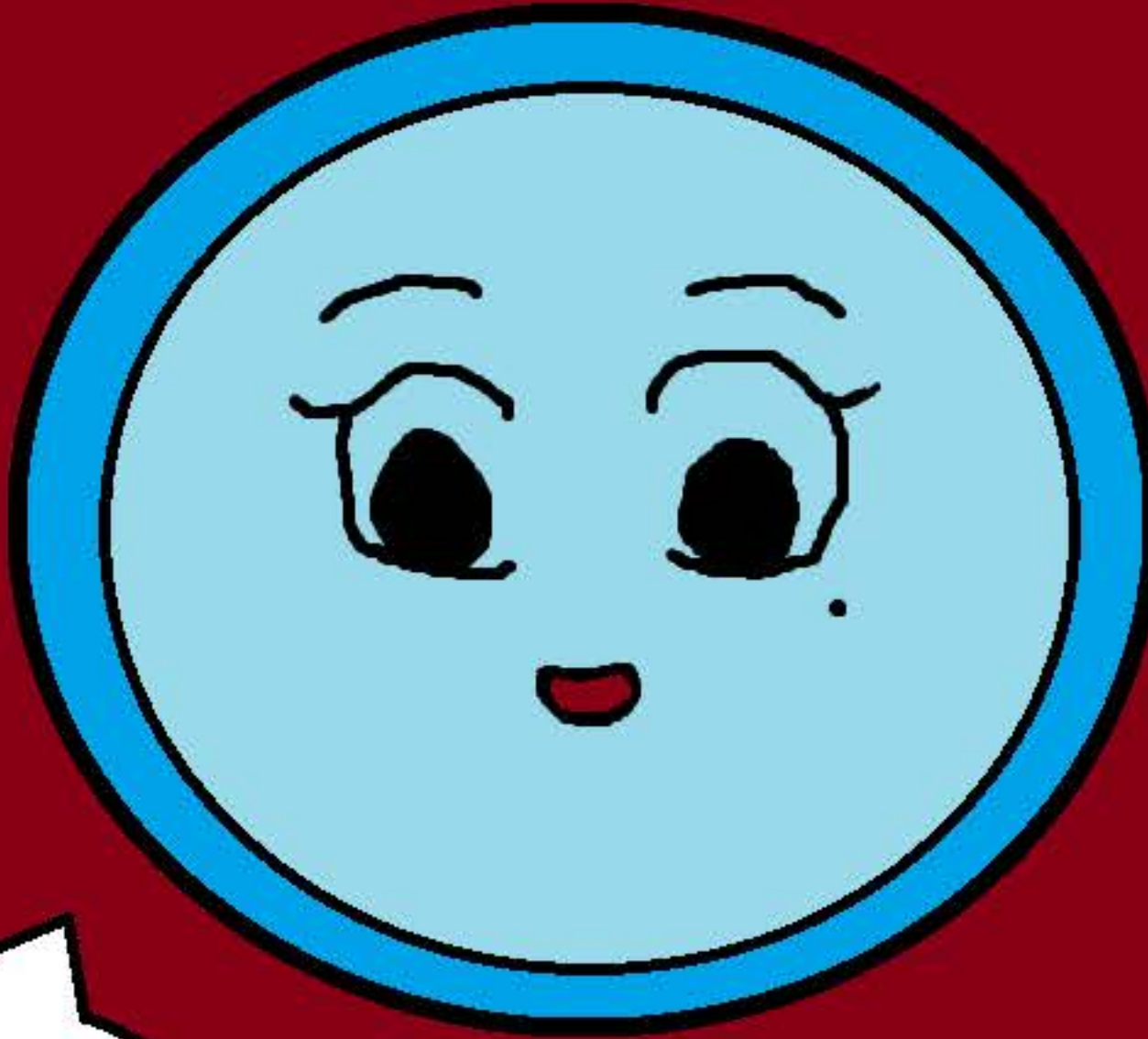
What? A bone?
Red bone marrow? What is that?

And, who are you?

Inside a Bone



A bone is part of a skeleton, the skeleton protects our human's organs and helps them move.

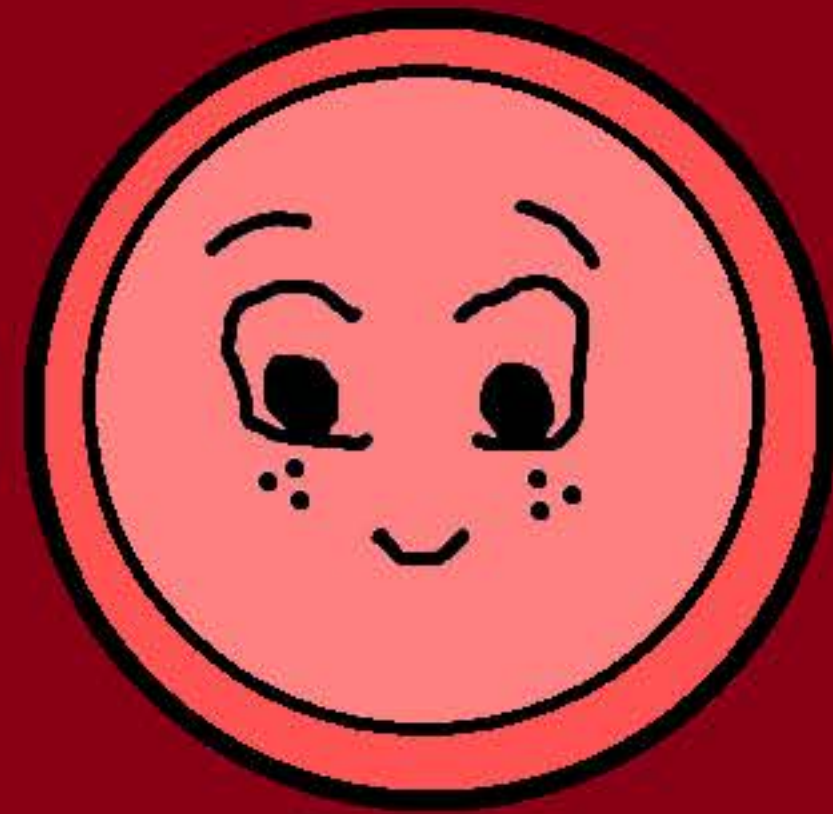
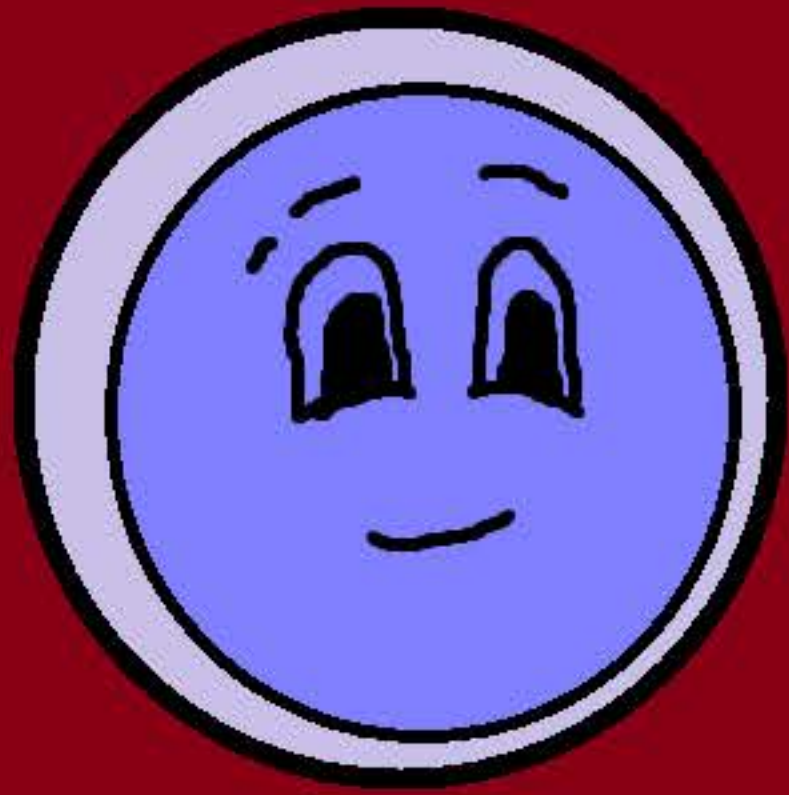


Like myself,
my name is Ava.
I'm a Helper T cell,
Nice to meet you both.

Bone marrow is the
hard spongy-looking
material inside bones.

In this part of the bone
marrow, called the red
bone marrow, is where
red blood cells and most
white blood cells are born.

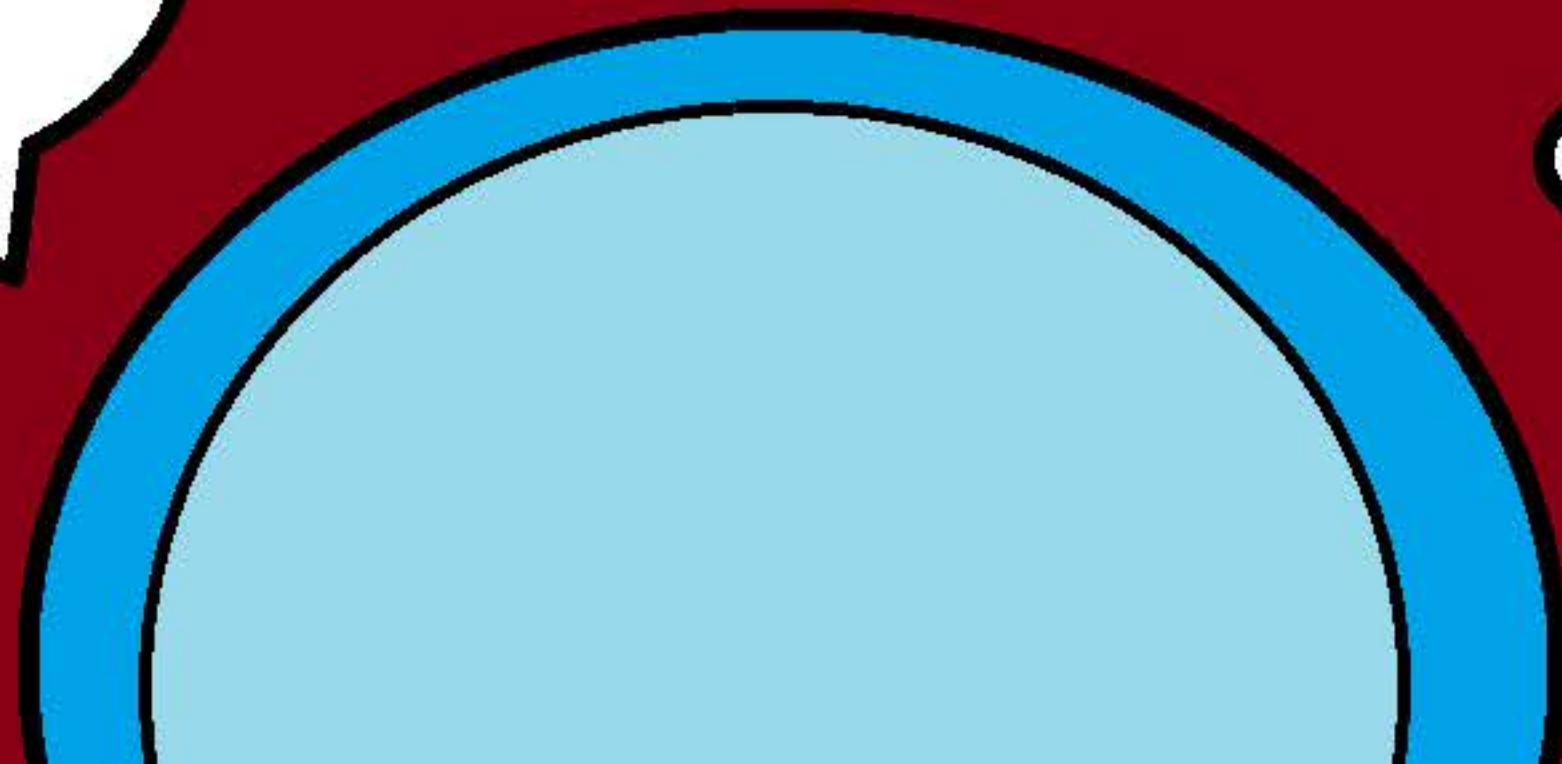
Looks like a sponge because
of the little holes.



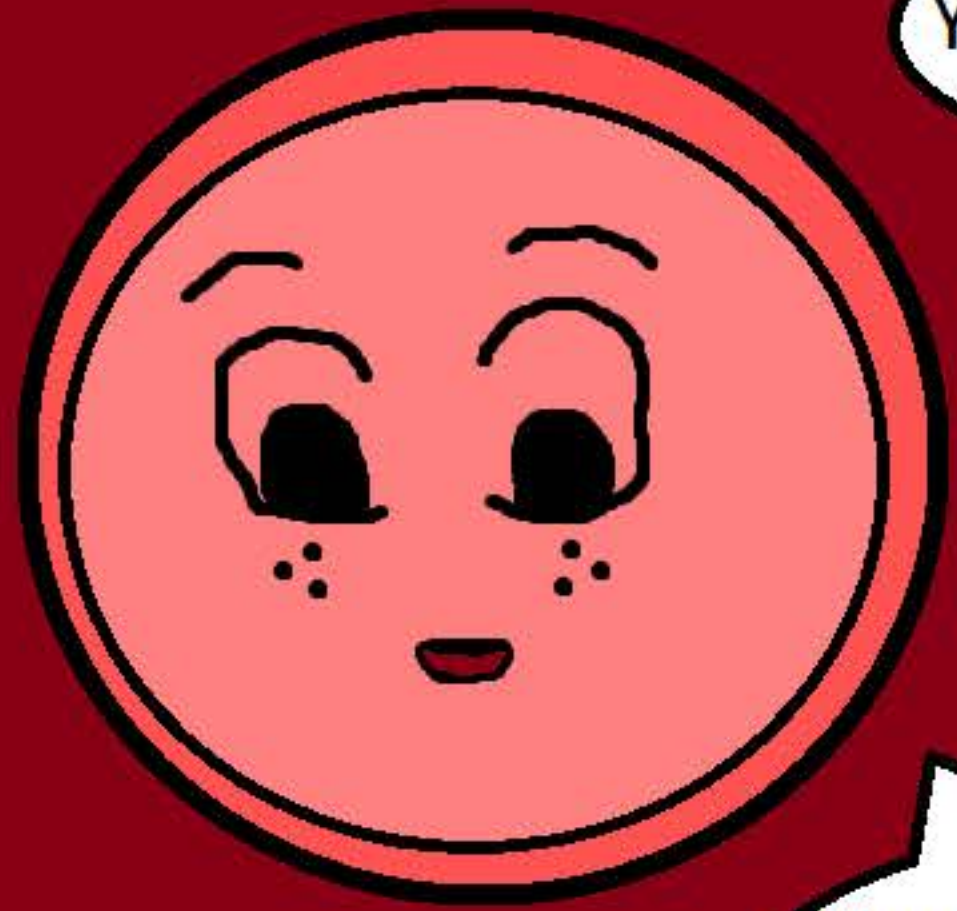
I'm guessing you
two are new white
blood cells.

Welcome to the team!

Do you have names?



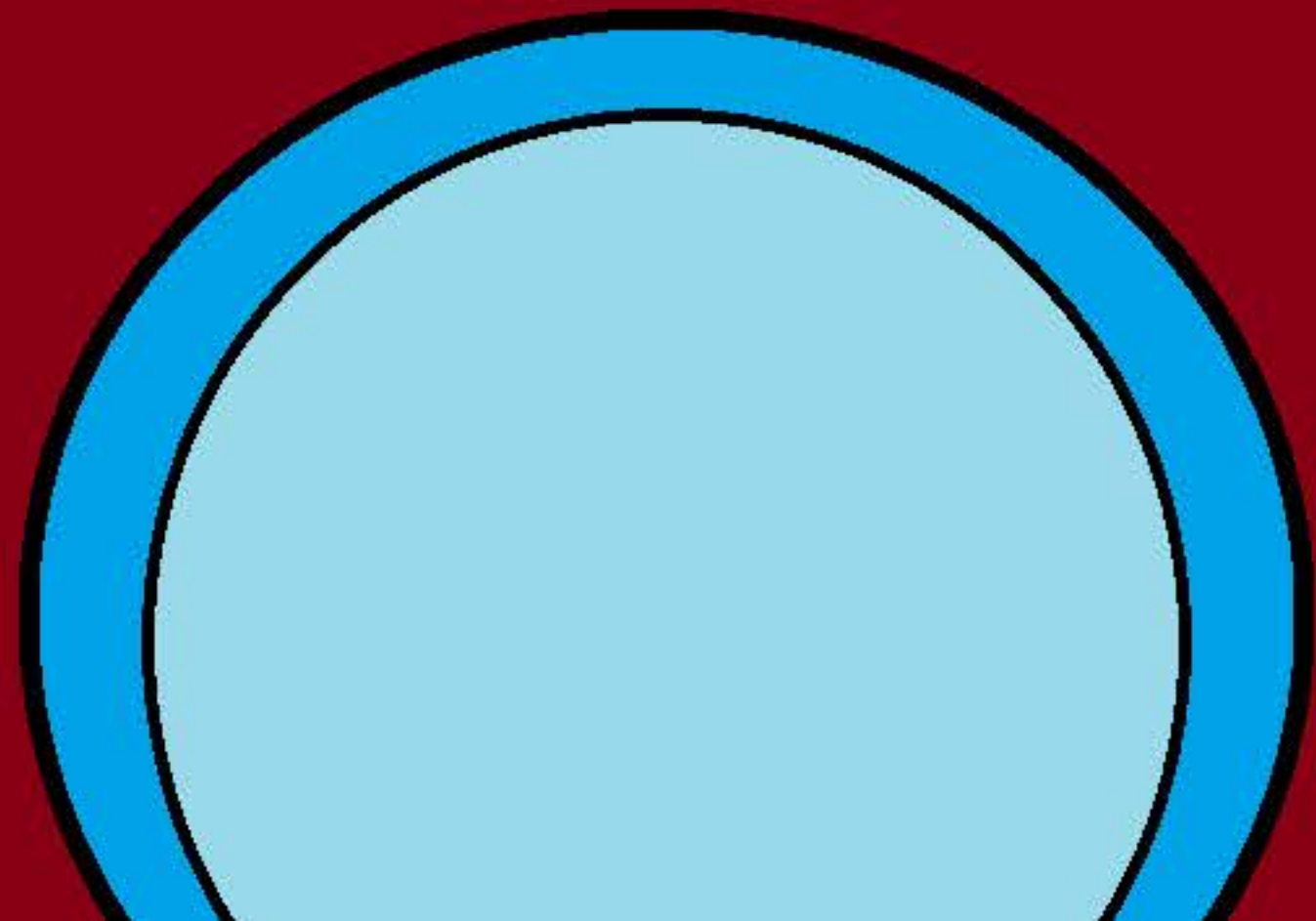
Yes, my name is Tim.



And I'm Neo.



Hey Ava, you said that you are a Helper T cell, is that a type of white blood cell?





Nice to meet you both!

And yes that is correct, a Helper T cell is a type of white blood cell, or WBC.

My specific type of WBC specializes in communicating with other immune cells, who are also different types of WBCs.

I help organize an immune response that protects our human's health.



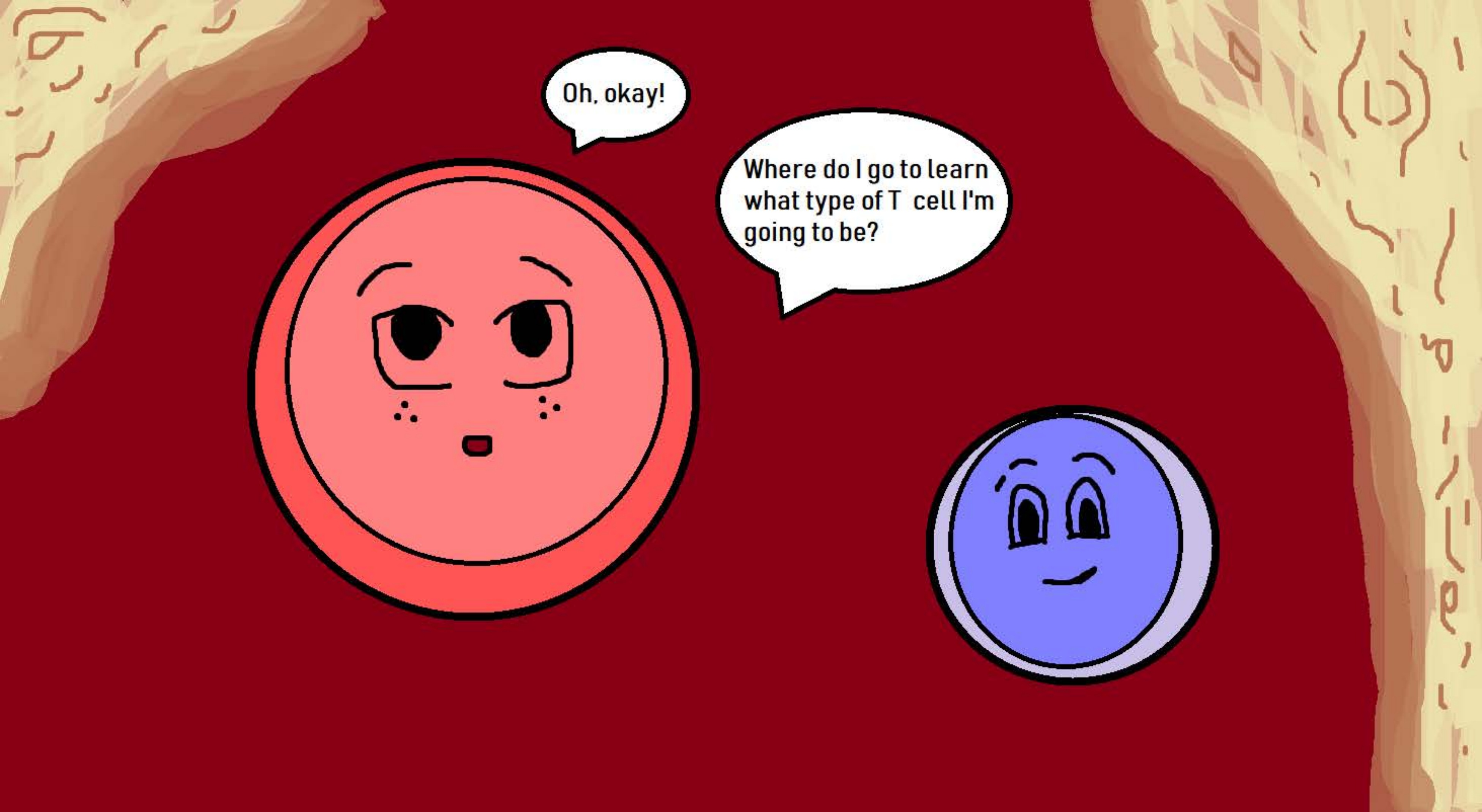
Really? Why?

Looking at you Tim, I believe you are also a type of T cell.

Because, you have those small spots on your face, like me.

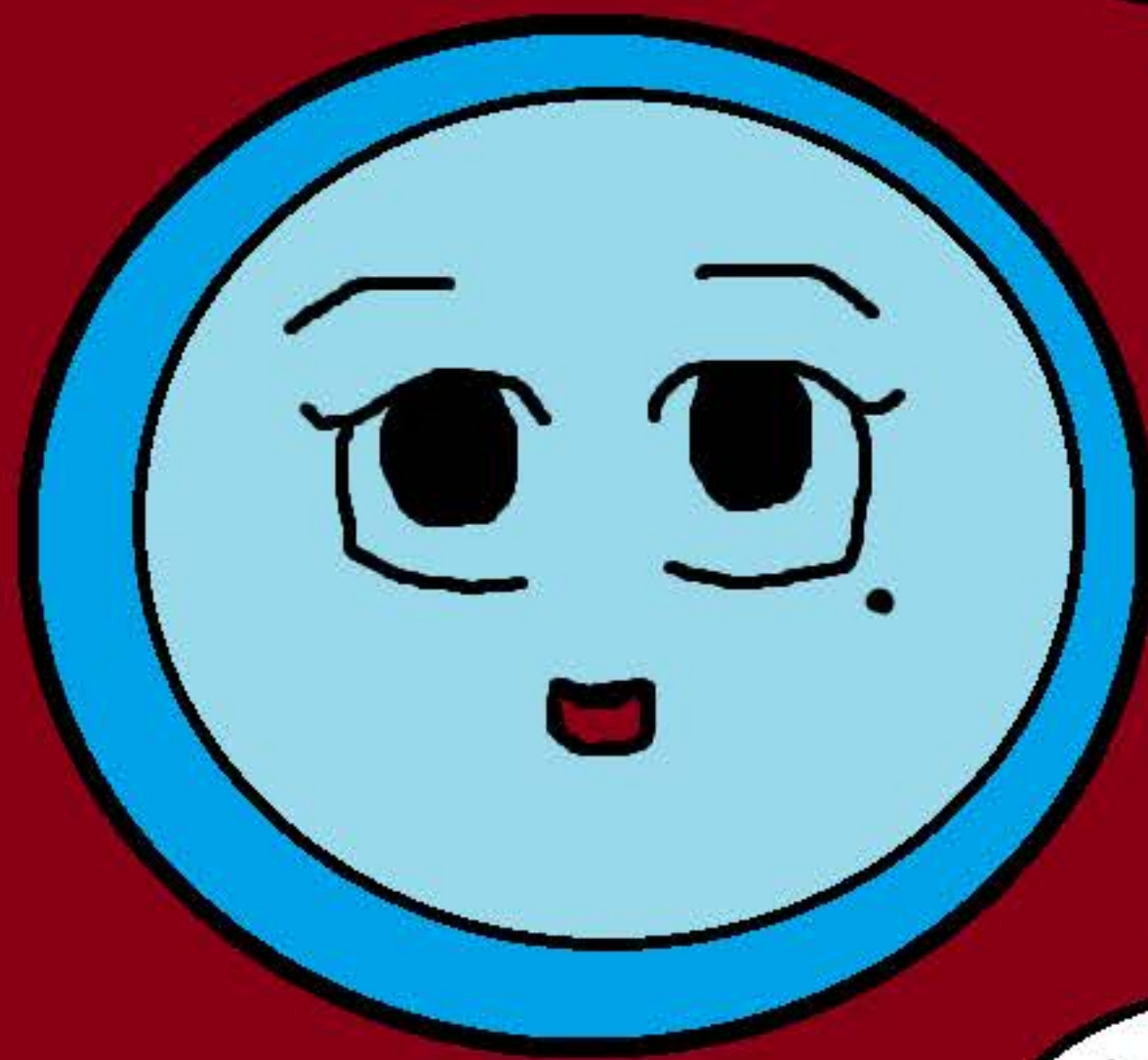
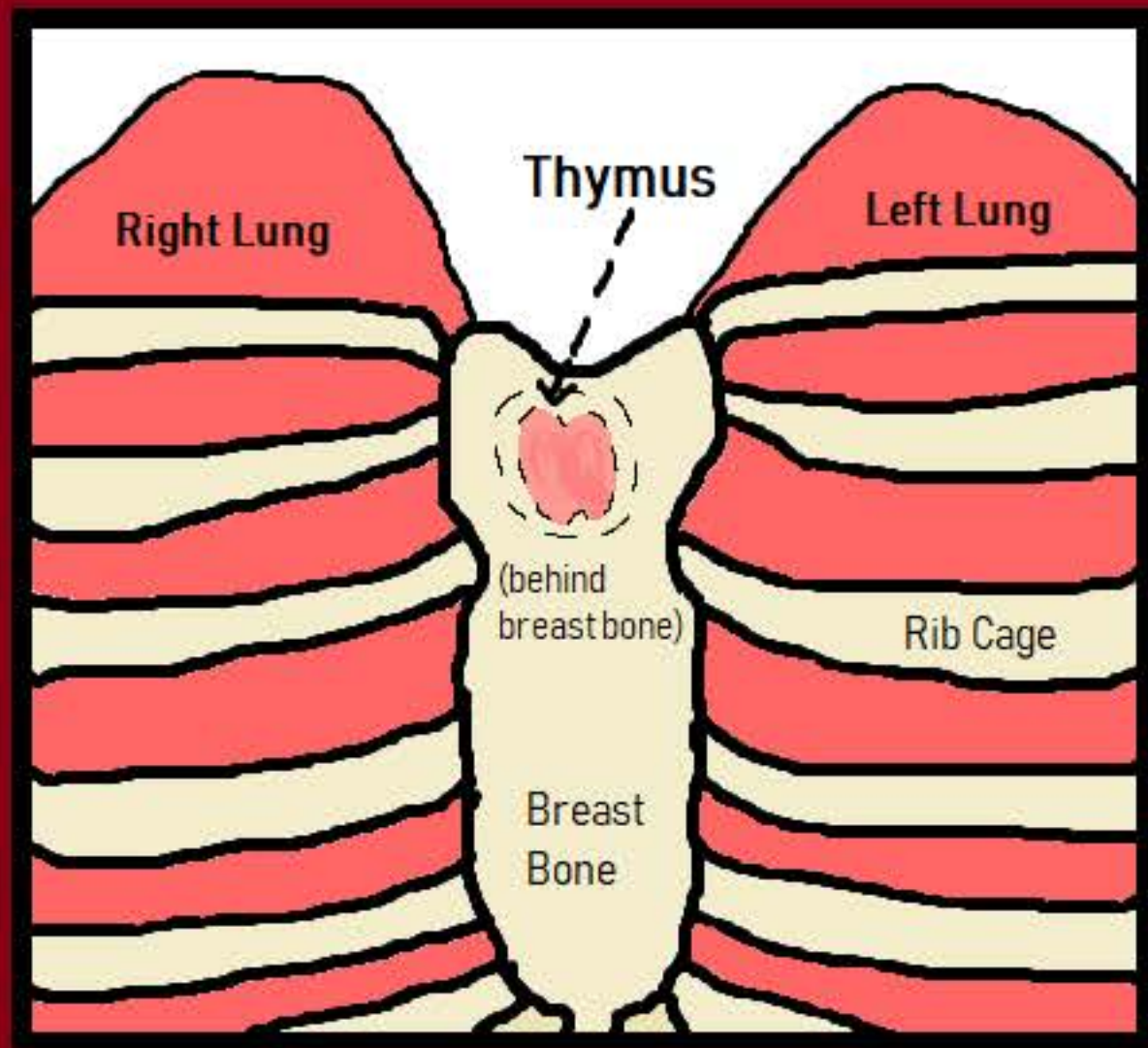
But since you are new and don't know what type of T cell you are going to be, you are an immature T cell for now.





Oh, okay!

Where do I go to learn
what type of T cell I'm
going to be?

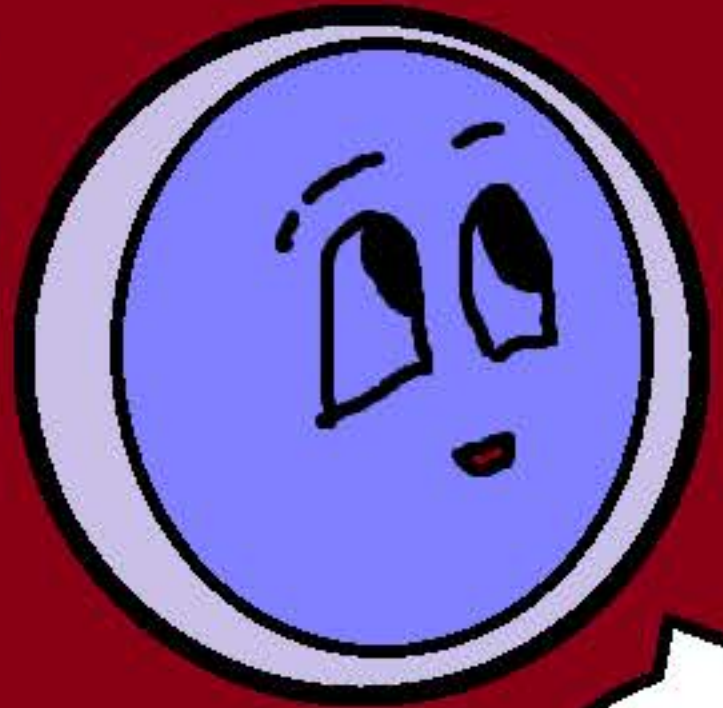
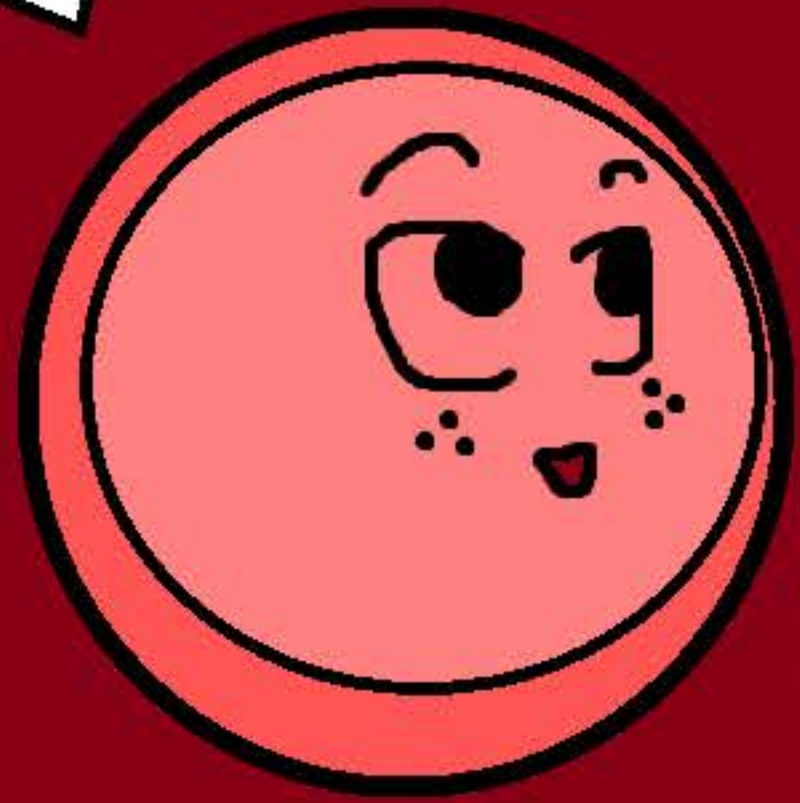


In our human's Thymus.

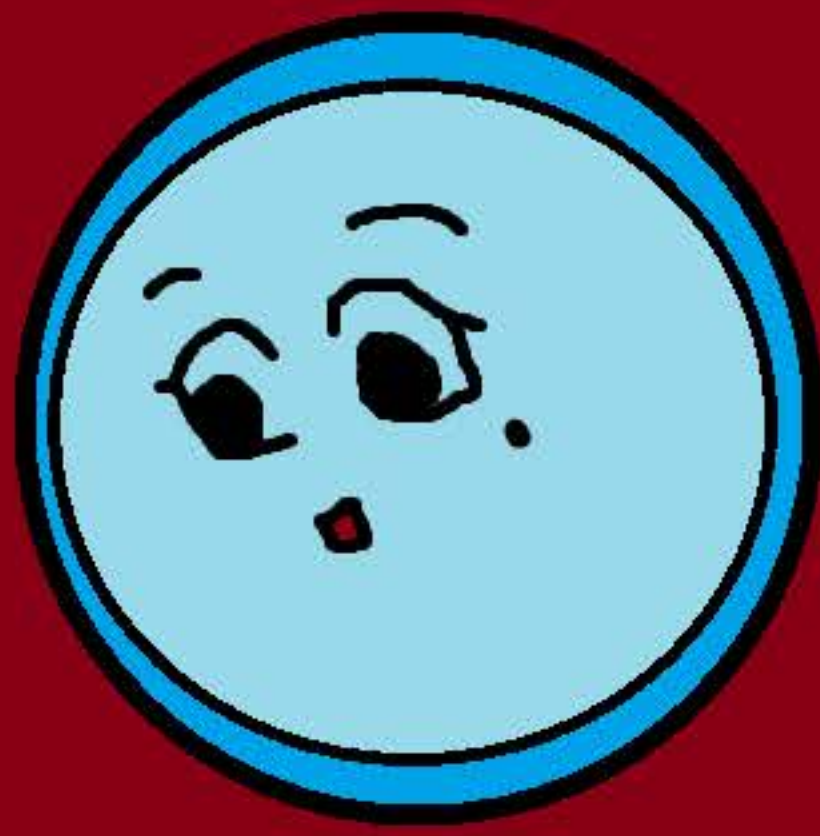
It's a small gland in the top of the chest, underneath the breast bone, and in between the lungs.

I can take you there if you'd like!

Yes please!

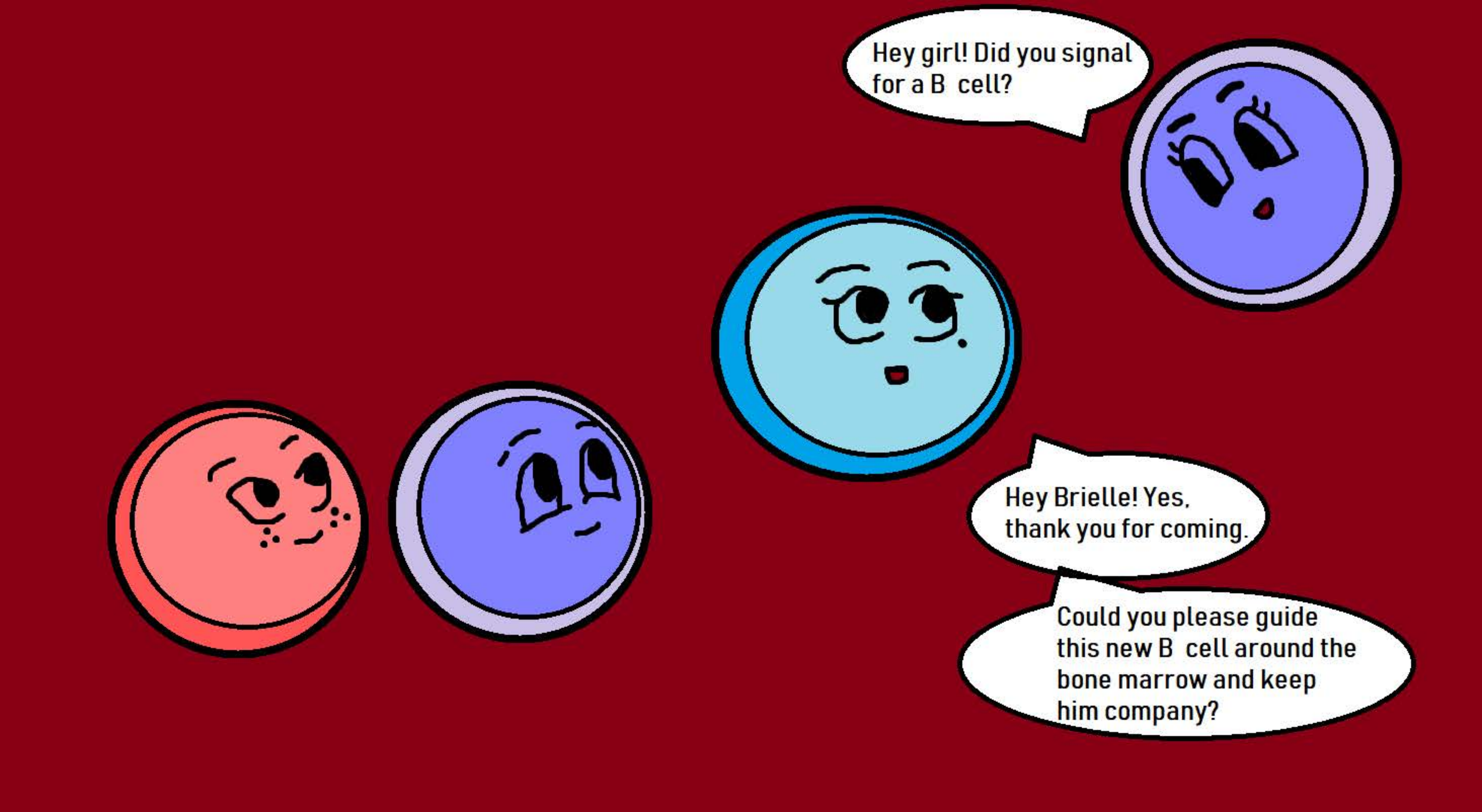


Thank you.



Sure! Just let me signal to a nearby B cell that I know to come help Neo.

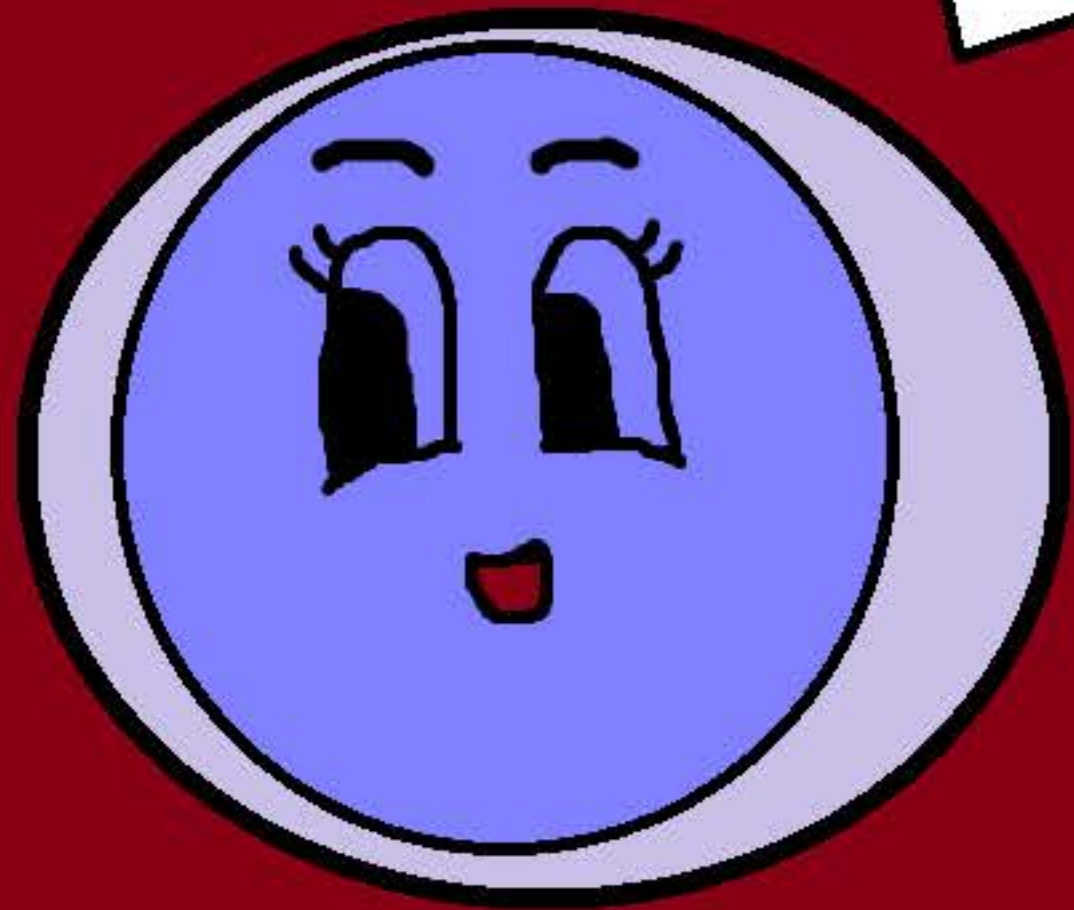
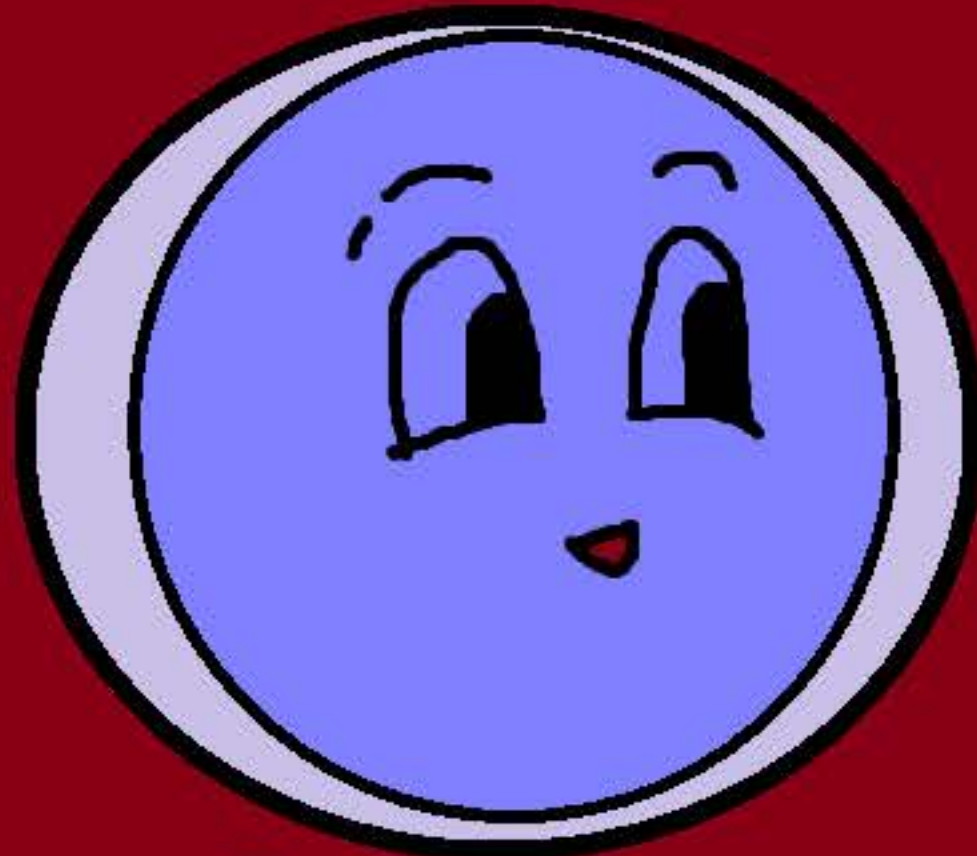




Hey girl! Did you signal for a B cell?

Hey Brielle! Yes, thank you for coming.

Could you please guide this new B cell around the bone marrow and keep him company?

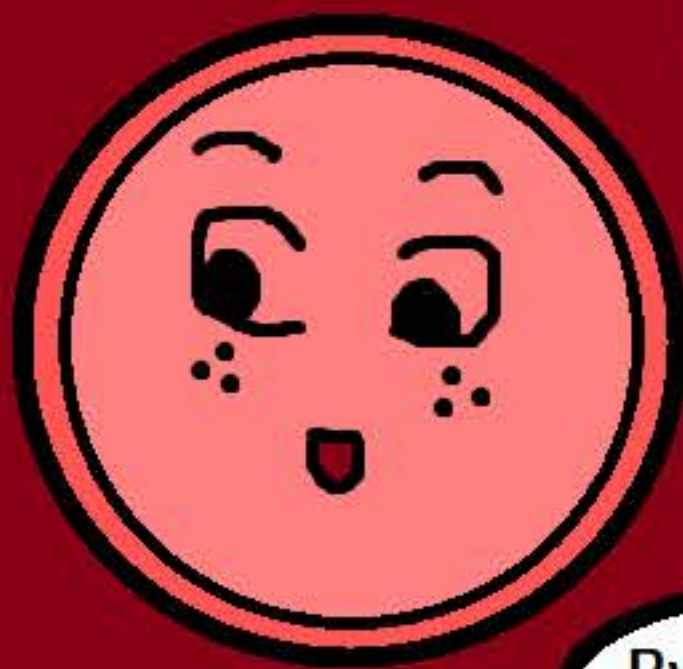
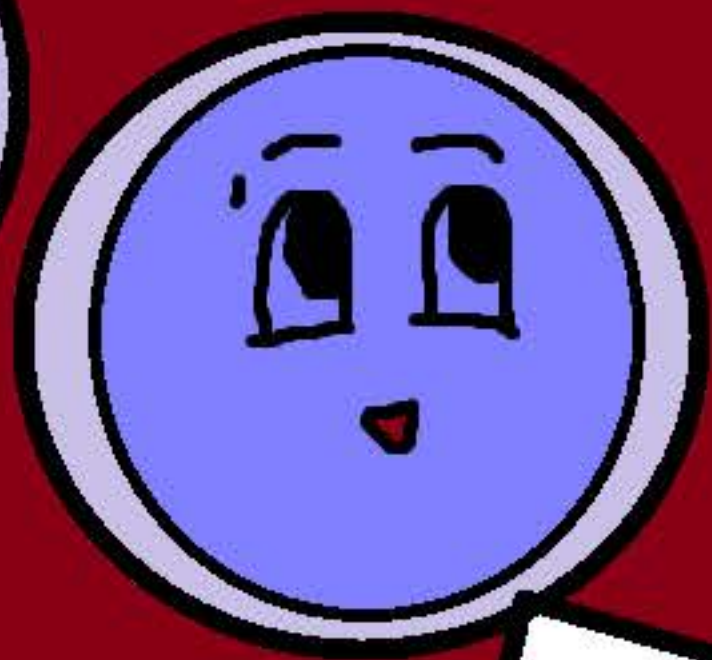
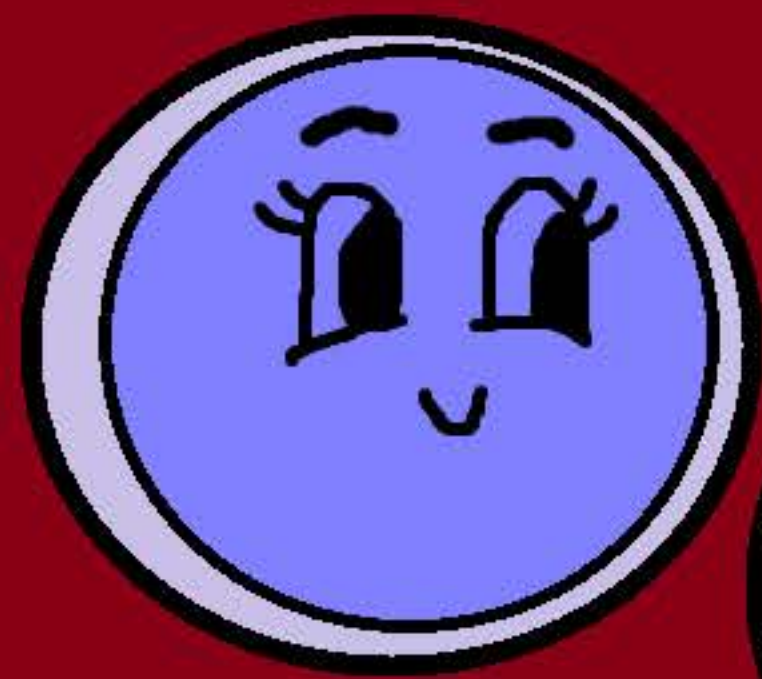


It would be my pleasure!

Hello new guy,
my name is Brielle.
I'm a fellow B cell.

Nice to meet you Brielle,
I'm Neo.



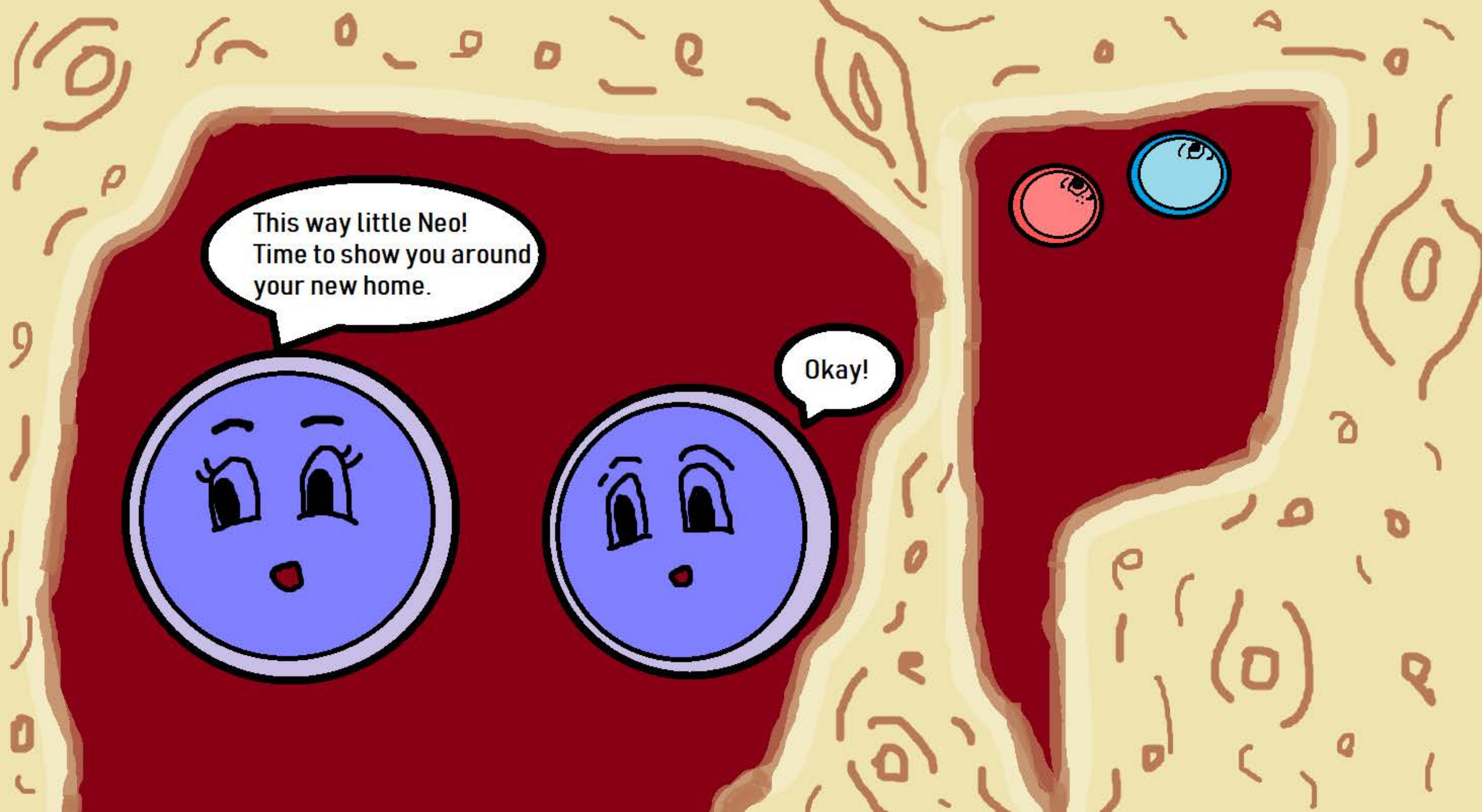


Now that Neo is taken care of, it's time to say your goodbyes for now. But don't worry, you'll see each other again.

B cells and T cells work together all the time.

Bye Neo, good luck!

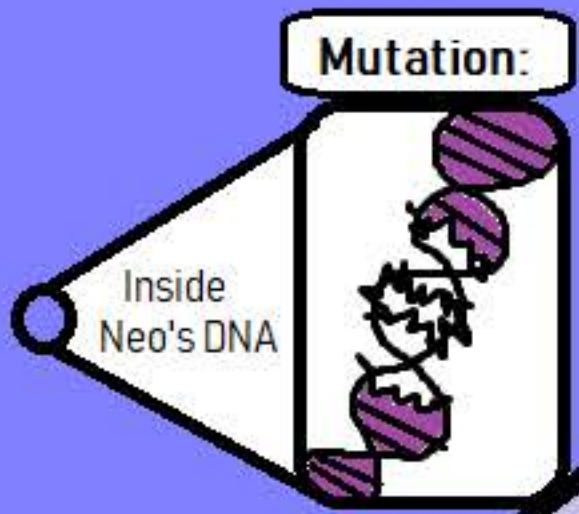
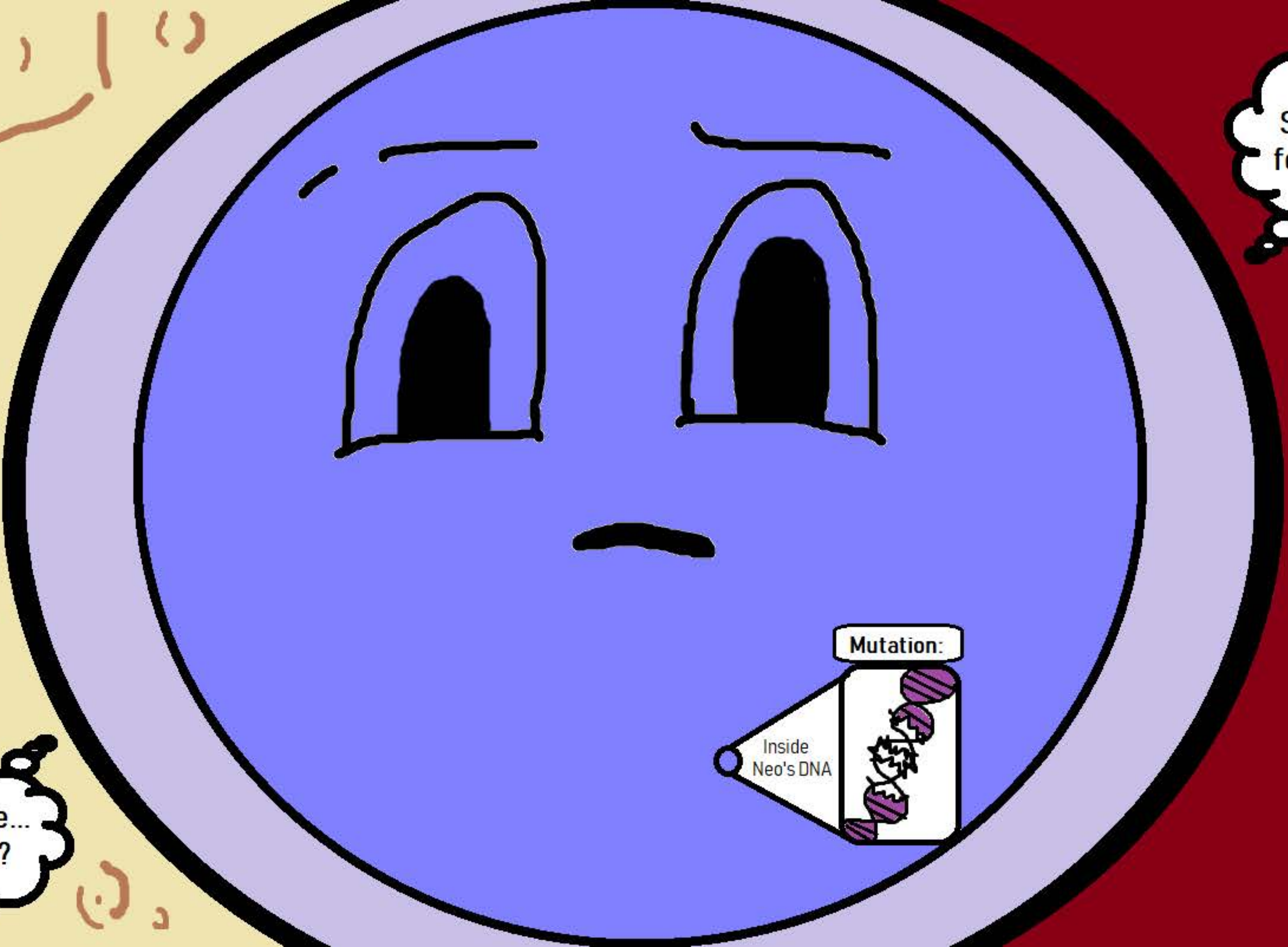
Same to you Tim! I look forward to seeing what type of T cell you mature into.

A cartoon illustration of a cave. The cave walls are a dark red color, and the floor is a light yellow color with brown, wavy lines representing rocks or uneven ground. In the foreground, two blue, round characters with large, expressive eyes and small red mouths are looking towards the right. The character on the left has a speech bubble above it. In the background, two more characters are visible: one is red and one is blue, both with large eyes, looking towards the foreground. The overall style is simple and colorful.

This way little Neo!
Time to show you around
your new home.

Okay!

Uh...
Something
feels wrong...



Inside me...
am I sick?

Inside the Blood Vessels

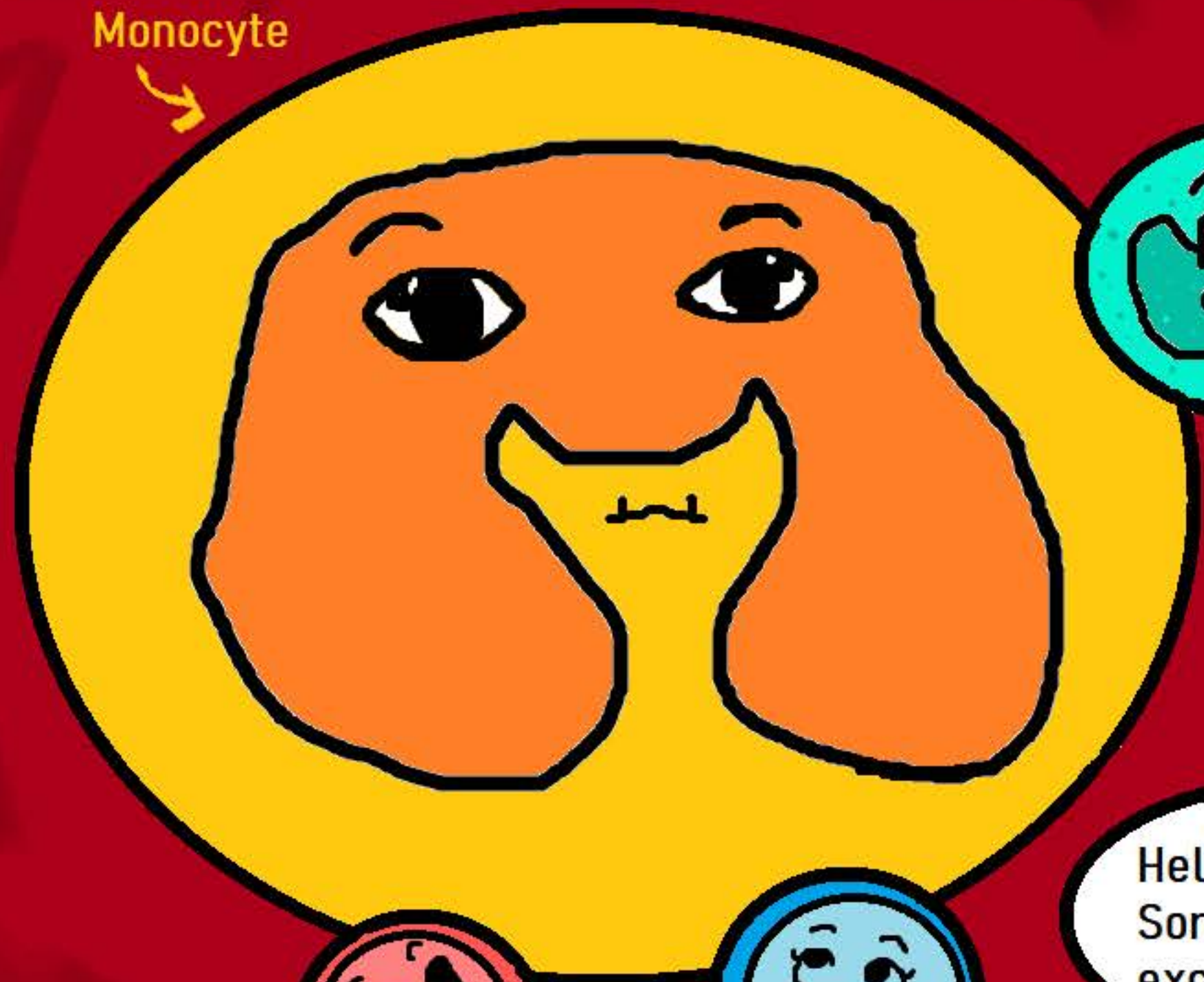
Ava, where are we now?

We are inside a blood vessel Tim.

That's where red blood cells and white blood cells, like us T cells and other types of immune cells, travel in order to get to different places in our human's body.

Monocyte

Neutrophil



Hello there!
Sorry guys, please
excuse us.

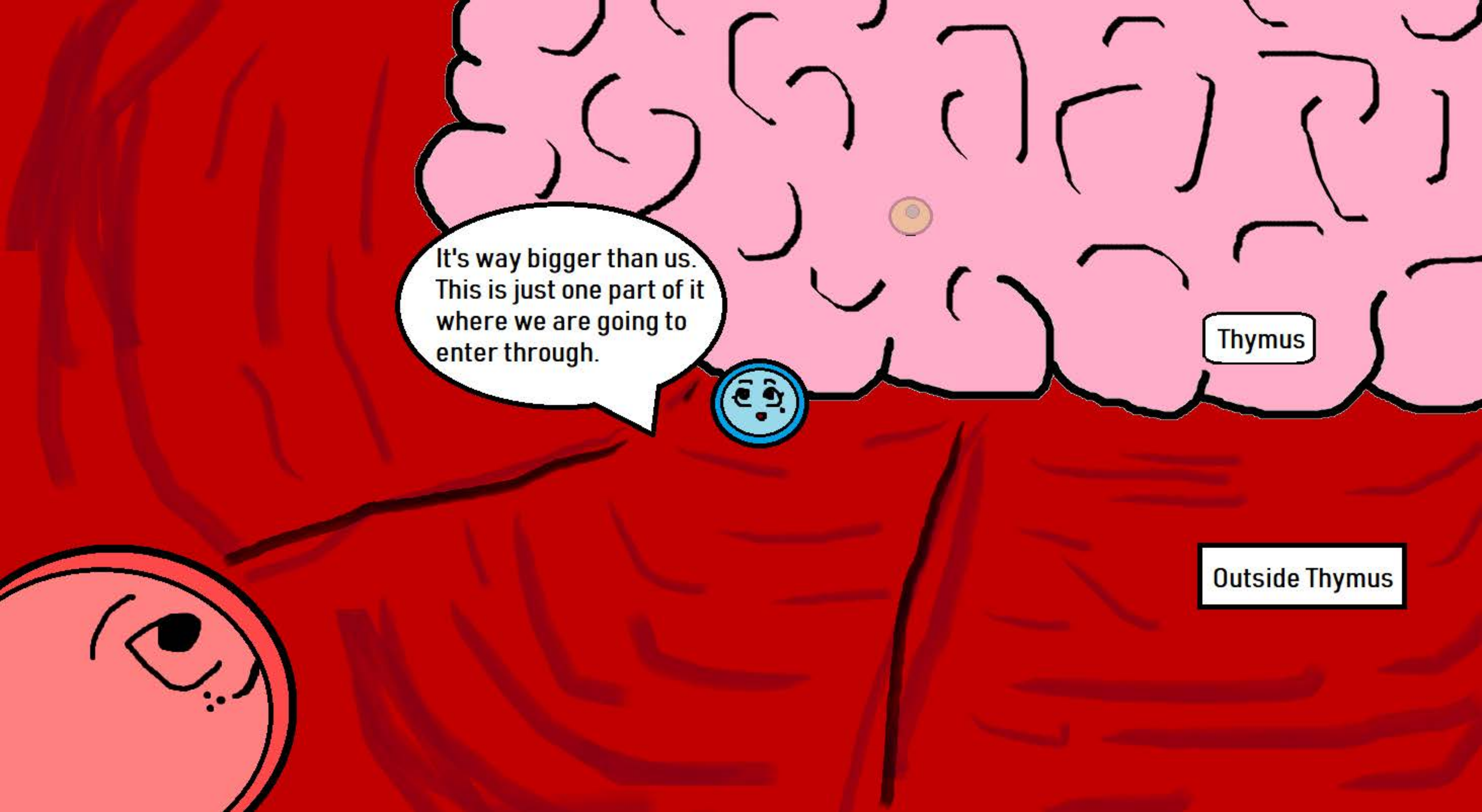
Whoa, he's
huge...



Those guys looked
so cool!
And important...

I wonder if I
will become as
awesome as them.

Ava:
Tim we are
here!



It's way bigger than us.
This is just one part of it
where we are going to
enter through.

Thymus

Outside Thymus

Hello!
Are you a
T cell too?

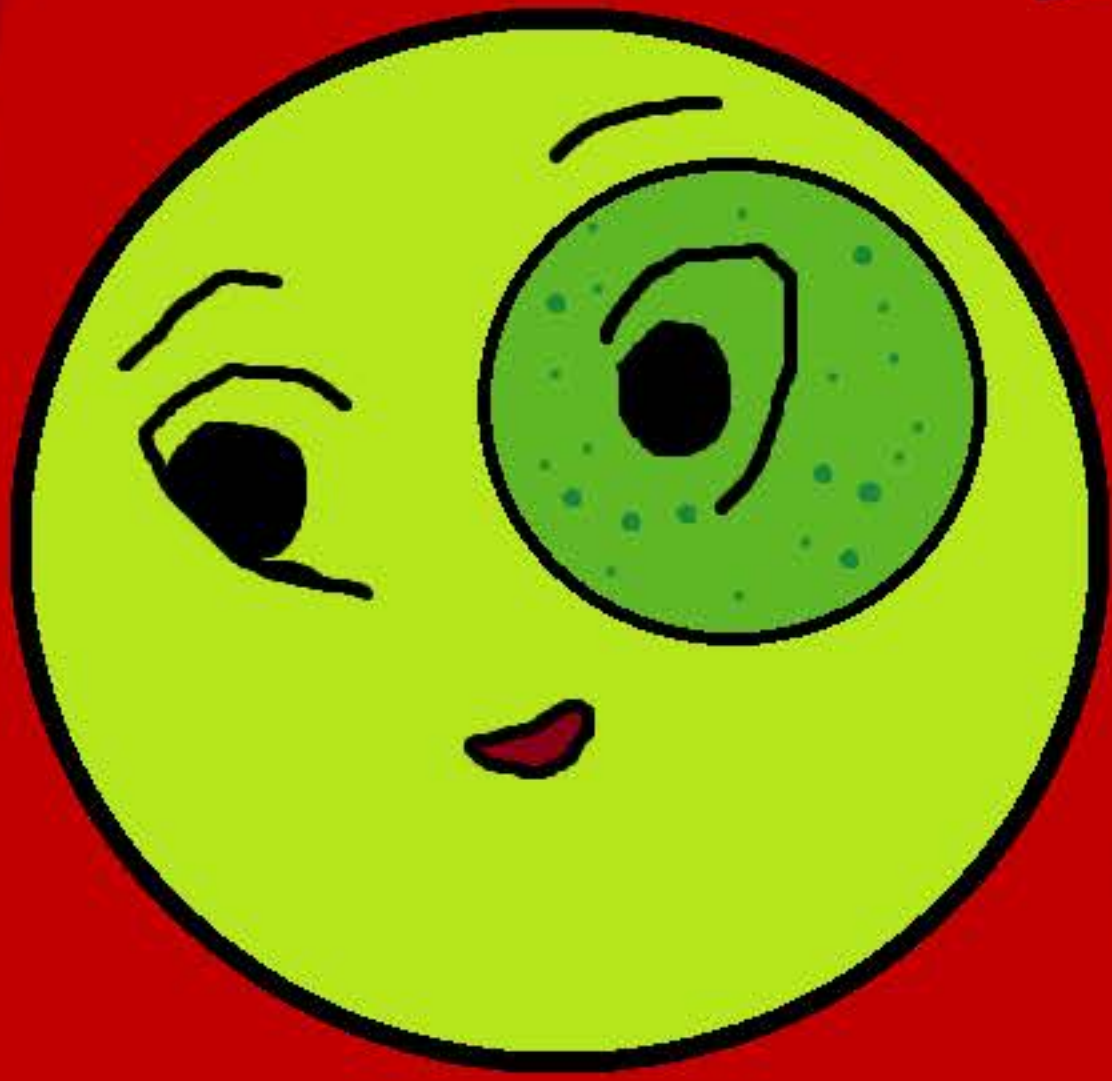


Hi Bebel!
Come meet Tim,
a new T cell!



Hello Ava.





No Tim, I'm a Natural Killer Cell.


My job is to dispose of cells that have been infected by viruses, also...

... to be the first responder in the fight against cancer.

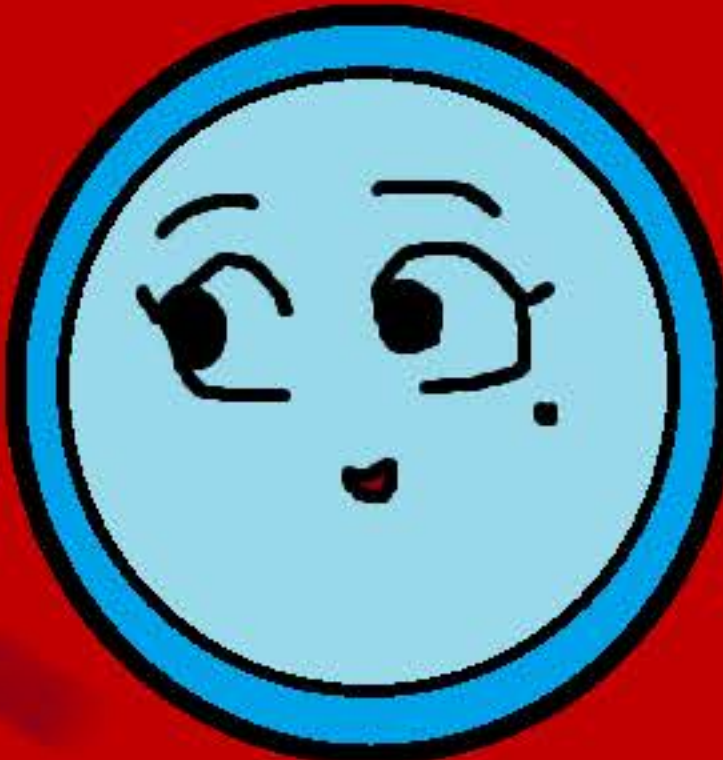
Wow!



I'm actually doing my visits to different parts of the body right now.



The red bone marrow is next, I have to keep working, but it was nice to meet you!



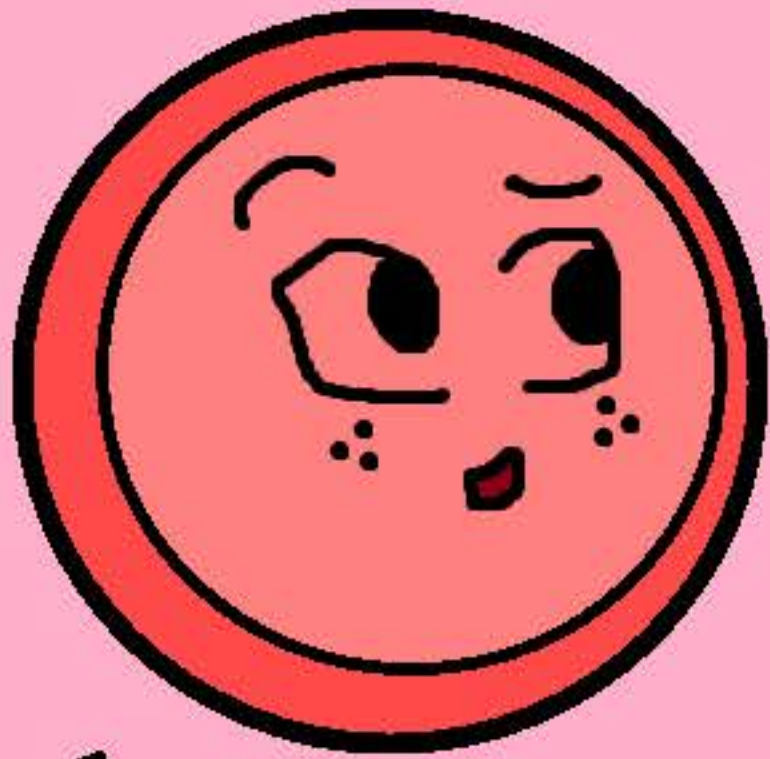
Okay, bye Bebel!
See you around!

Inside the Thymus

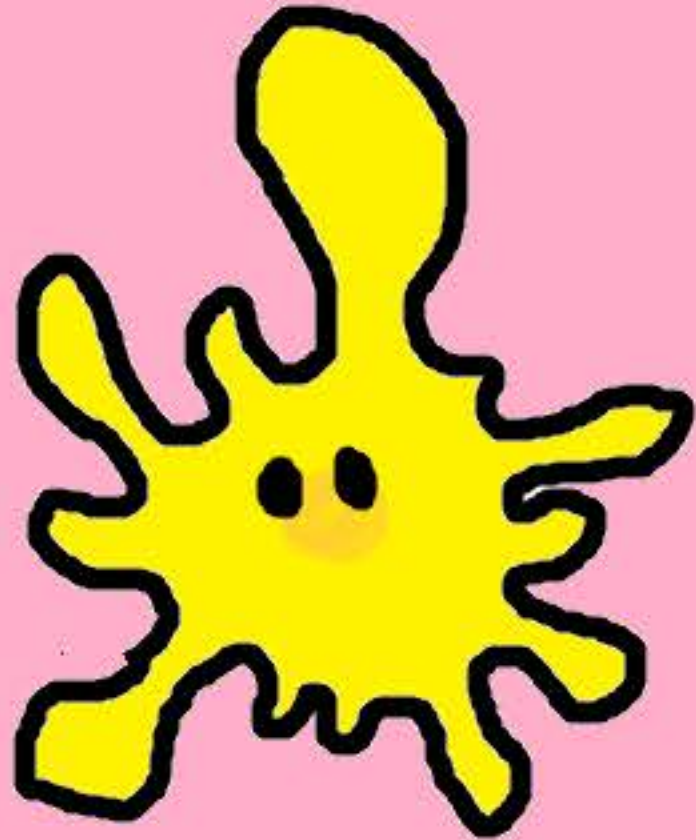


Here we are!
Welcome to the
inside of the
Thymus.

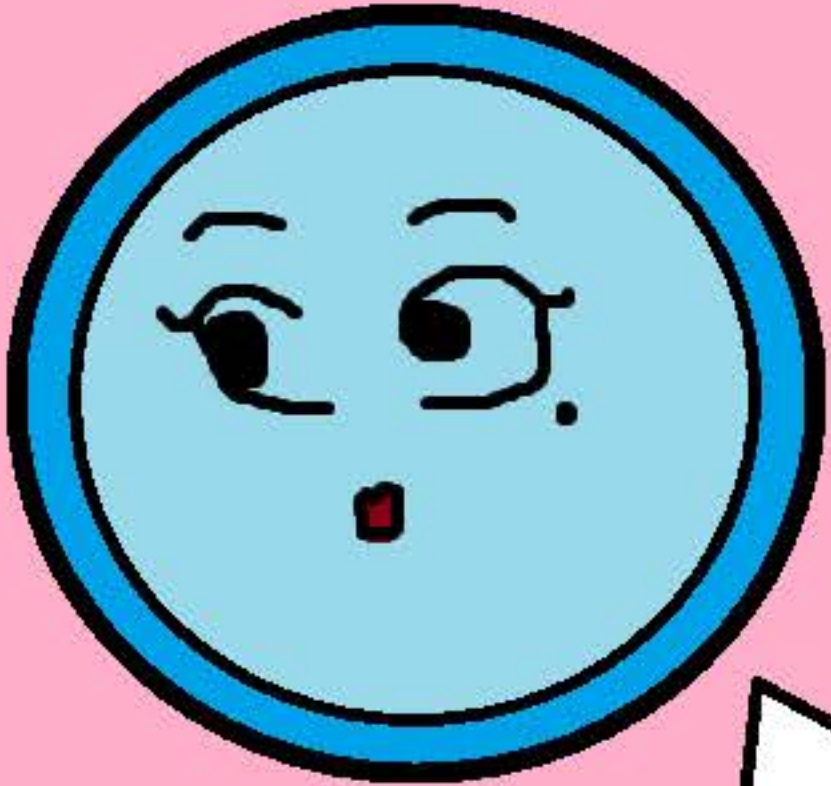




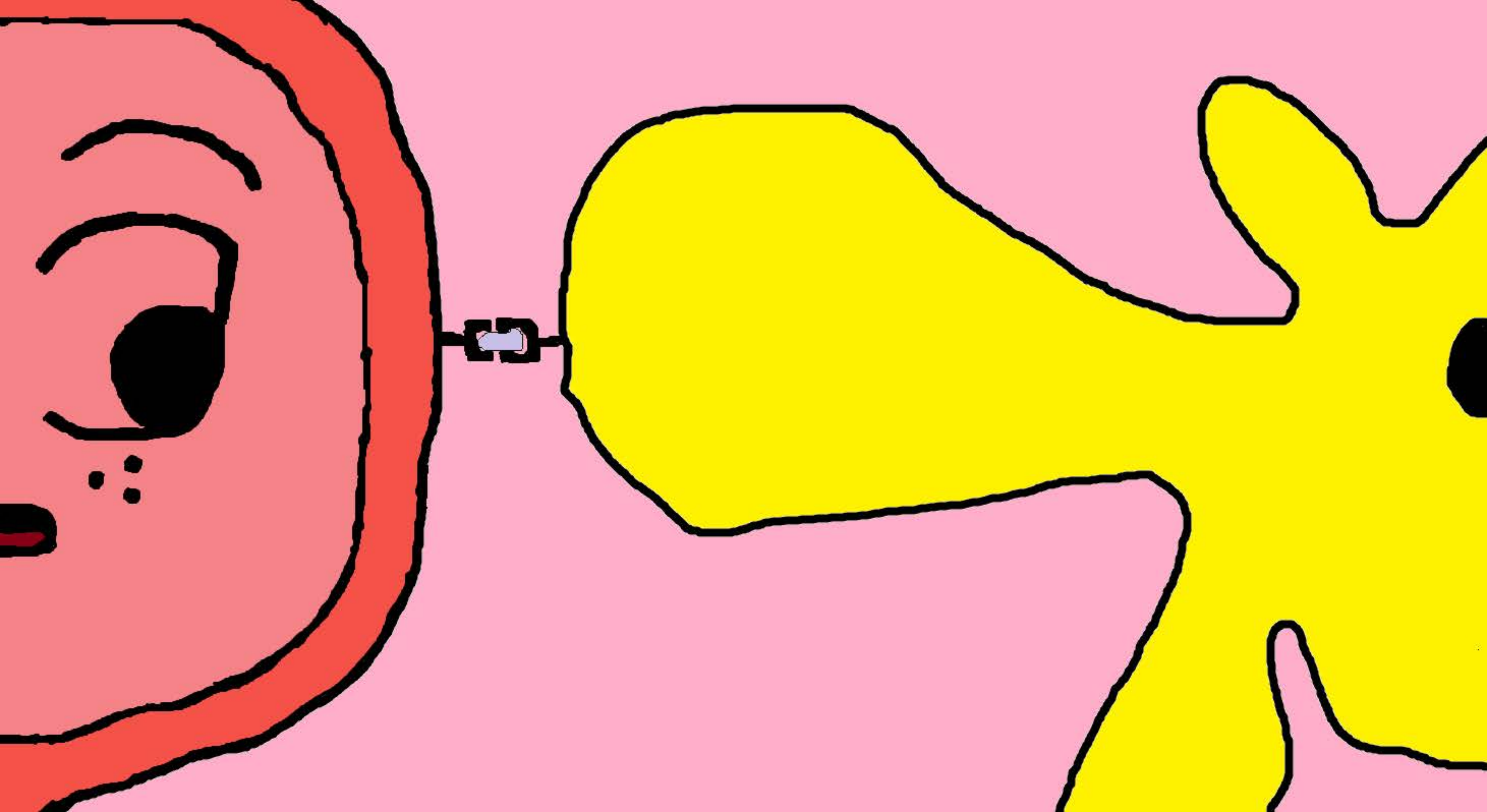
Ah, okay...

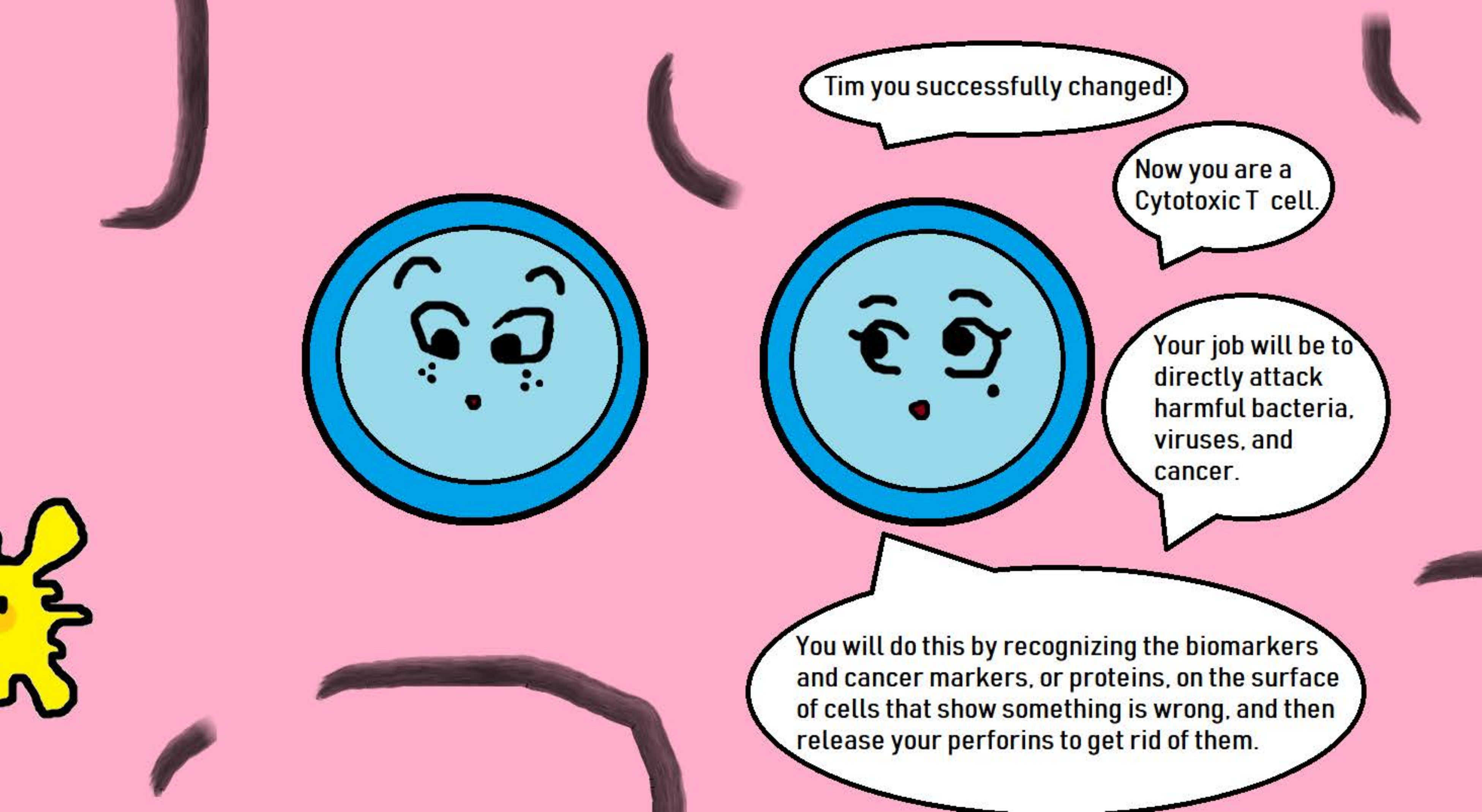


Tim, this is an Antigen Presenting Cell.



It will give you the protein with the information you need for the type of T cell that you're going to become.





Tim you successfully changed!

Now you are a
Cytotoxic T cell.

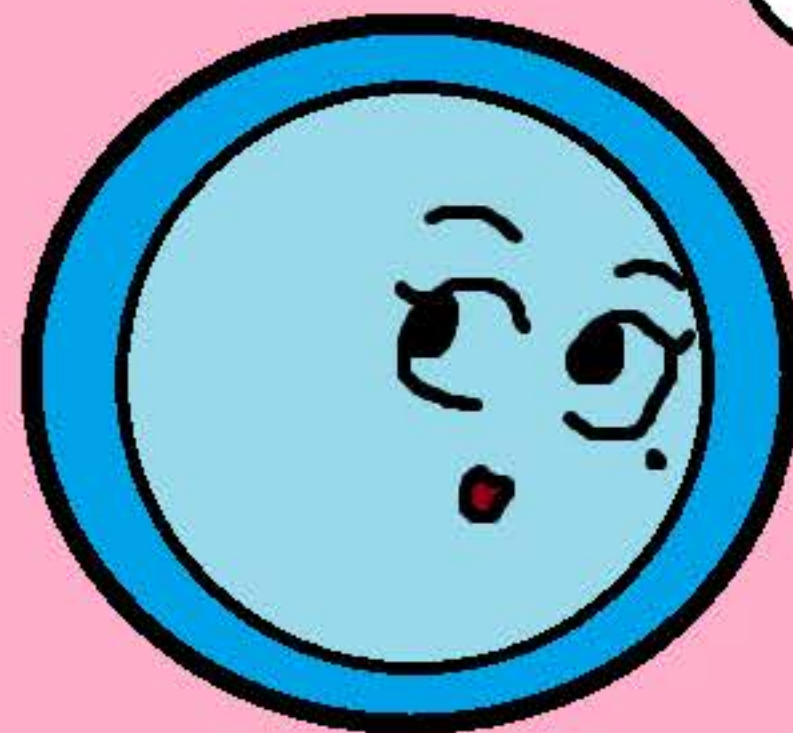
Your job will be to
directly attack
harmful bacteria,
viruses, and
cancer.

You will do this by recognizing the biomarkers
and cancer markers, or proteins, on the surface
of cells that show something is wrong, and then
release your perforins to get rid of them.

That sounds like a lot of responsibility...

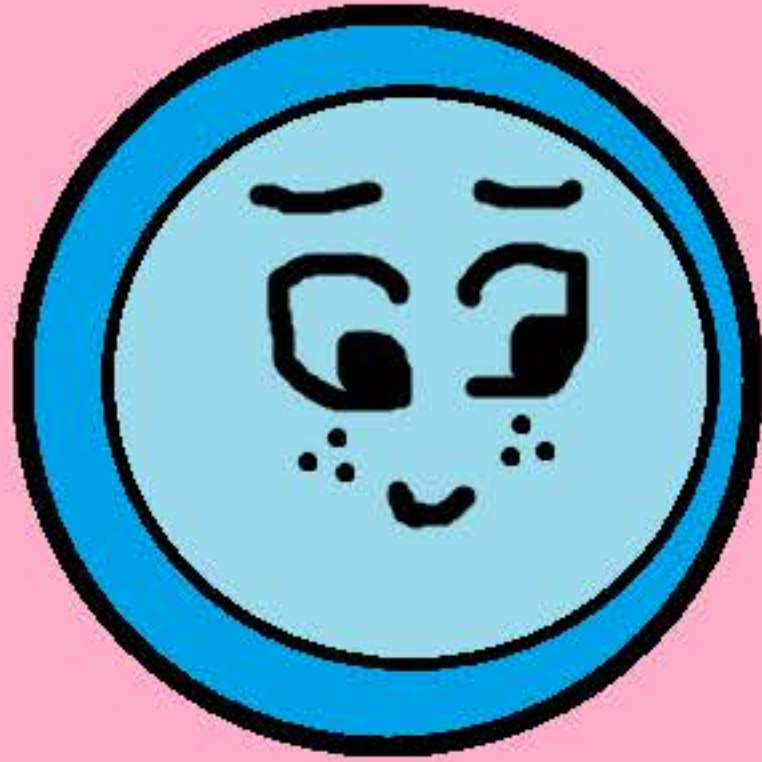
Ava, what if I make a mistake?

This is all very new to me, and what if I don't have the courage to do my job when the time comes?



I understand that you may feel afraid...

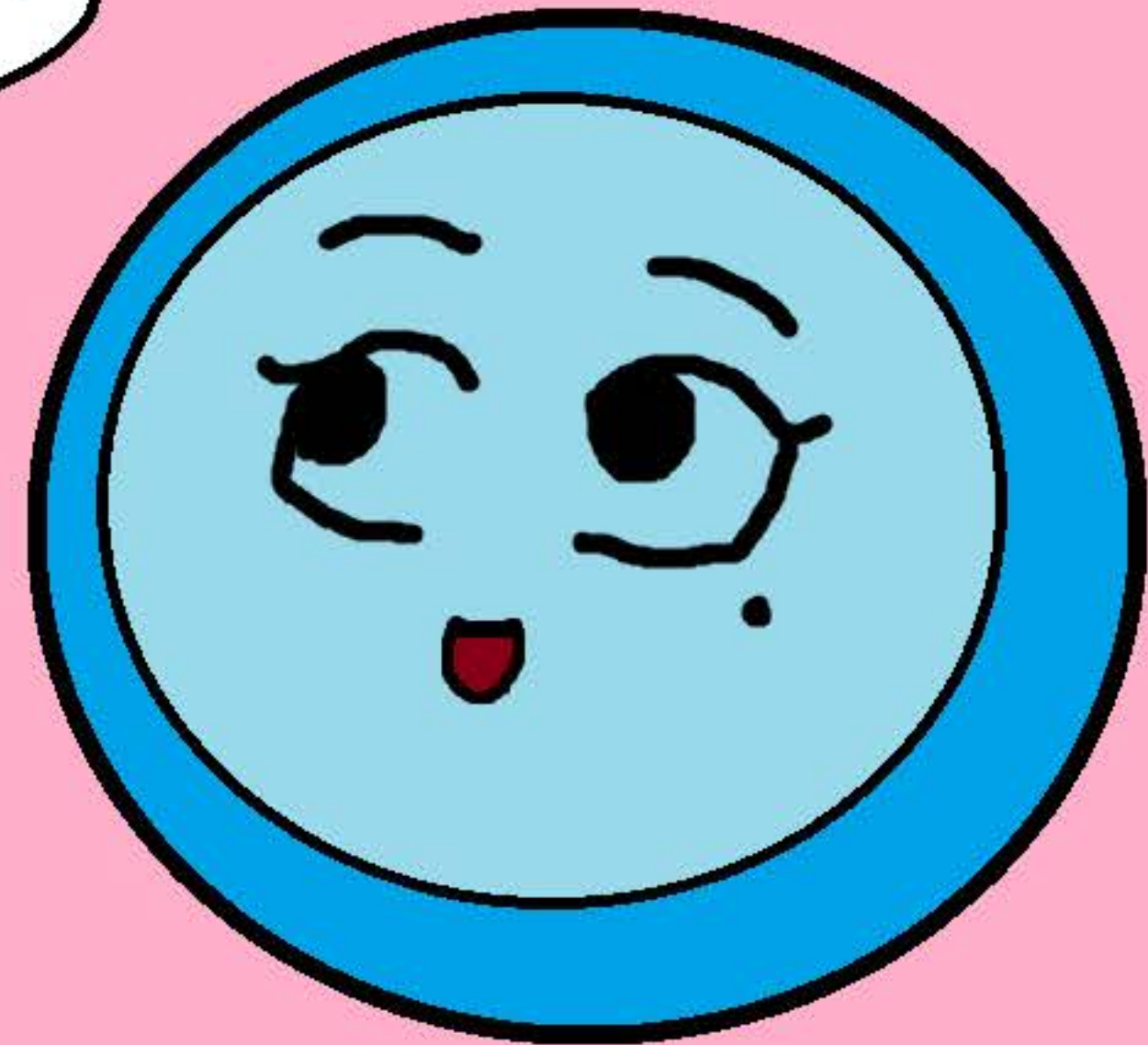
.. but be confident in knowing that you are not alone.



We will support and encourage each other to do our best,

all while remaining positive and pushing ourselves to go beyond our limitations.

So Tim, hold your head high, and remember that there are other cells working along side you, who are cheering for you and will help you prevail.



Meanwhile, back in the Red Bone Marrow

Bebel! Over here!



Brielle? What's wrong?

Something strange is happening with the new B cells, but we don't know what it is!

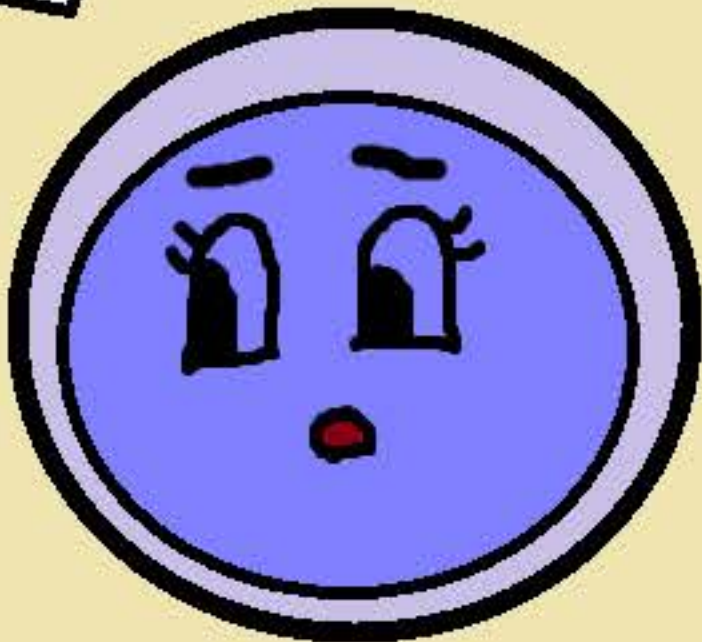


Okay, please take me to one of these new B cells.



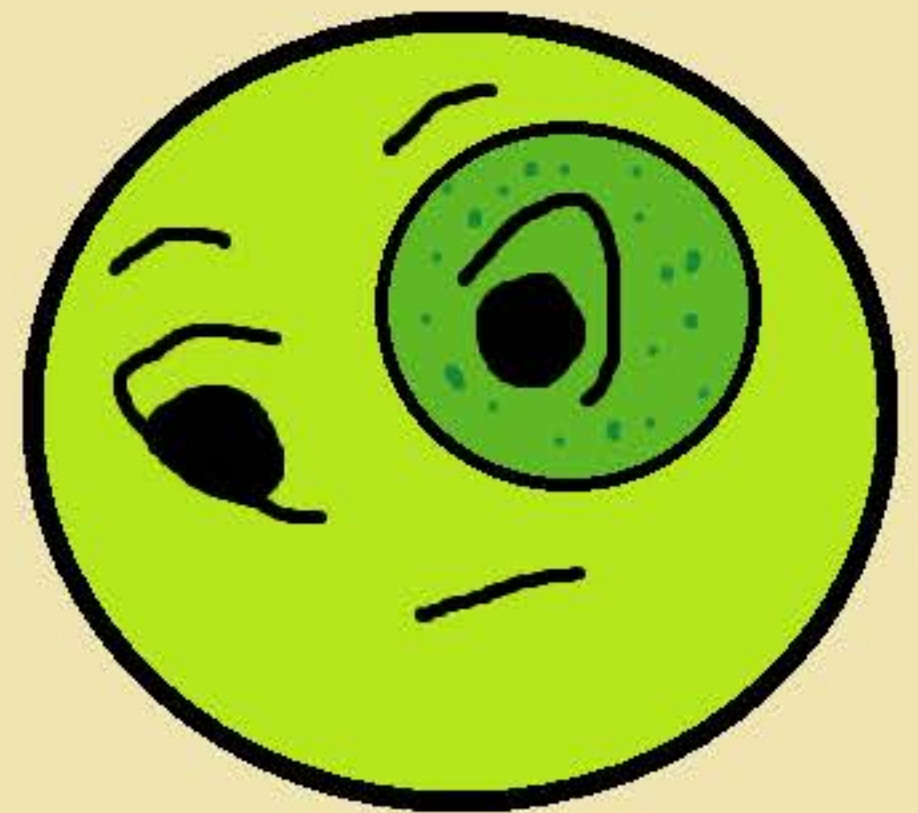
Ah! Neo, another clone?

Yeah...



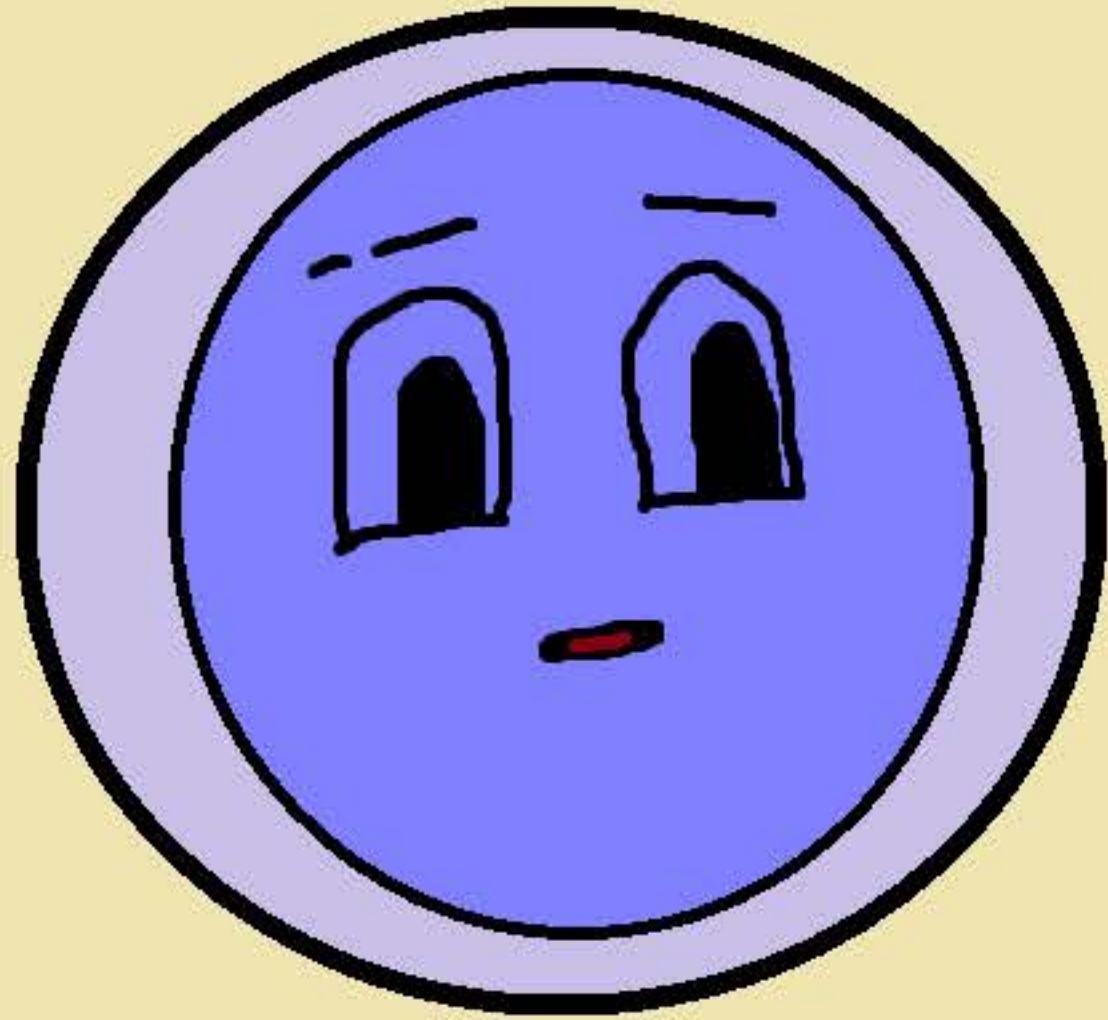
and there is something wrong with this one too, it's not acting like a normal B cell should.

Also, like the other clones, it keeps destroying and attacking all the wrong targets with its antibodies.

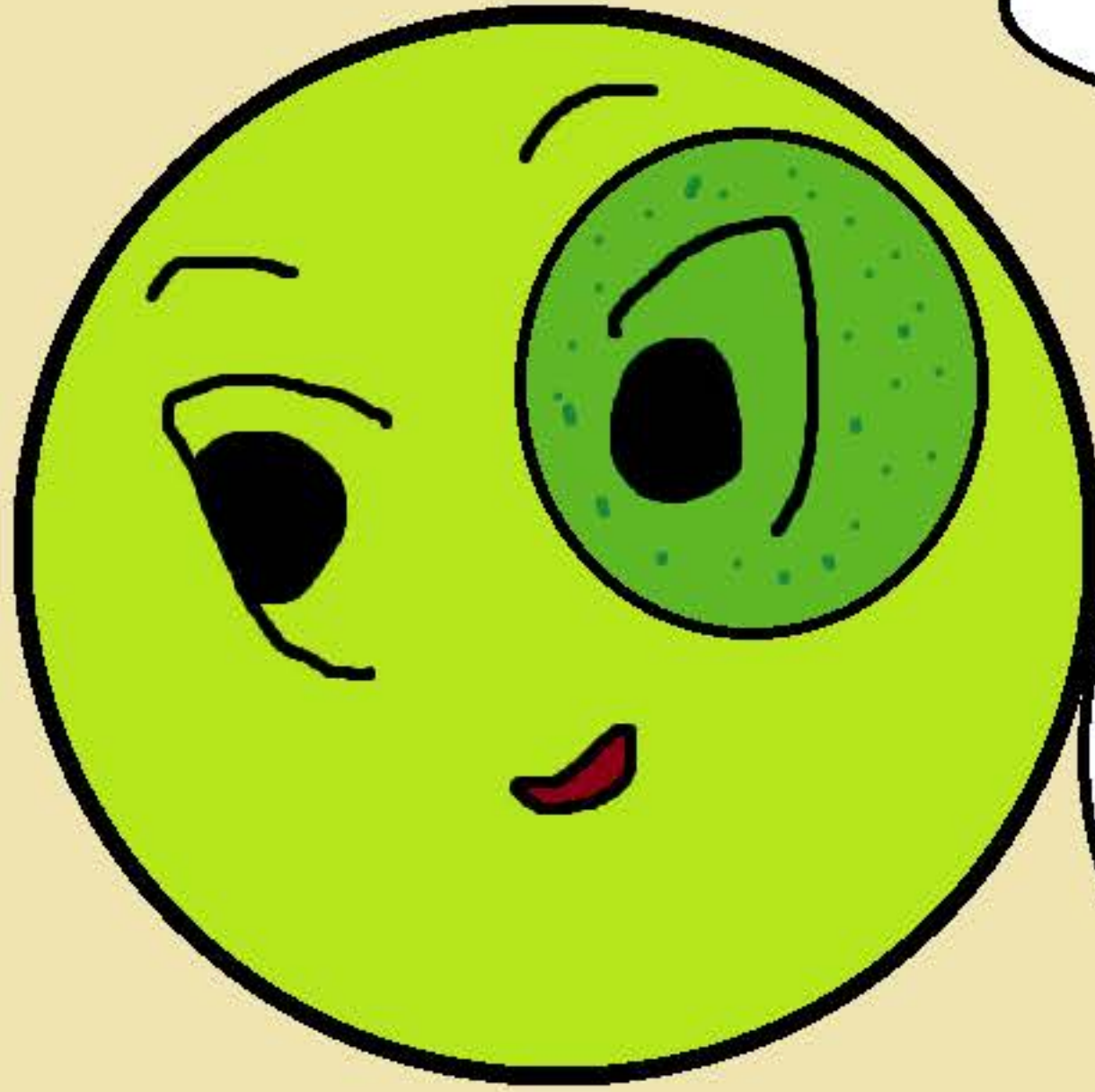


Antibody

A blood protein made to counteract a specific antigen (toxin or foreign thing).

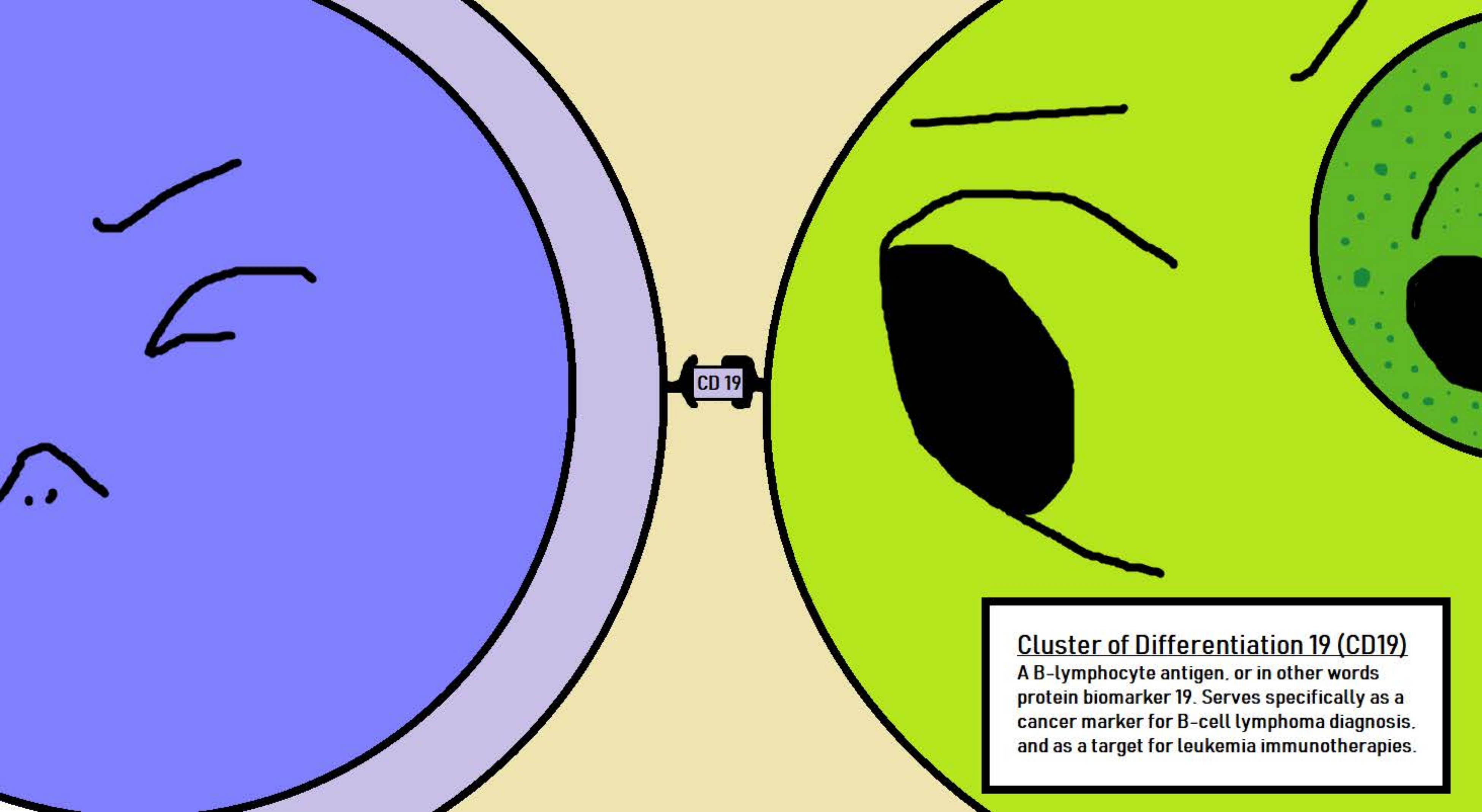


Okay.



Hi there Neo, I'm Bebel and I'm a Natural Killer Cell.

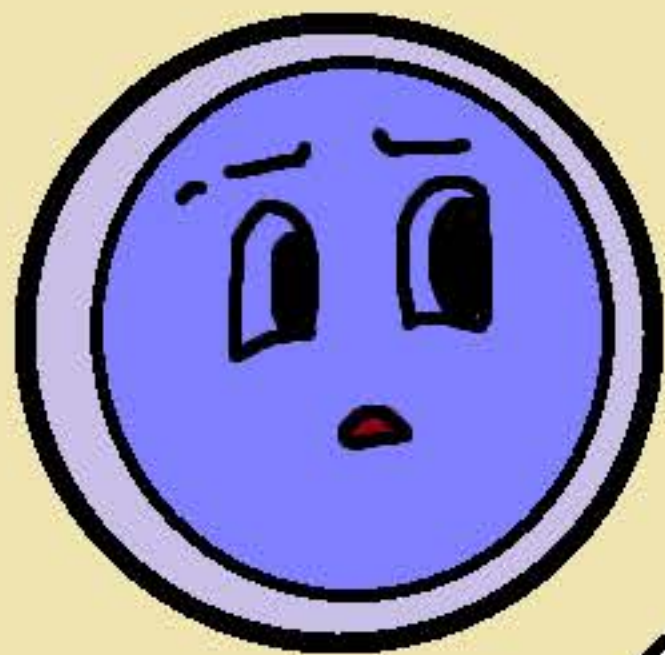
Try to relax, I'm just going to read the protein biomarkers you are presenting on your surface to see if I can recognize what the problem is.



CD 19

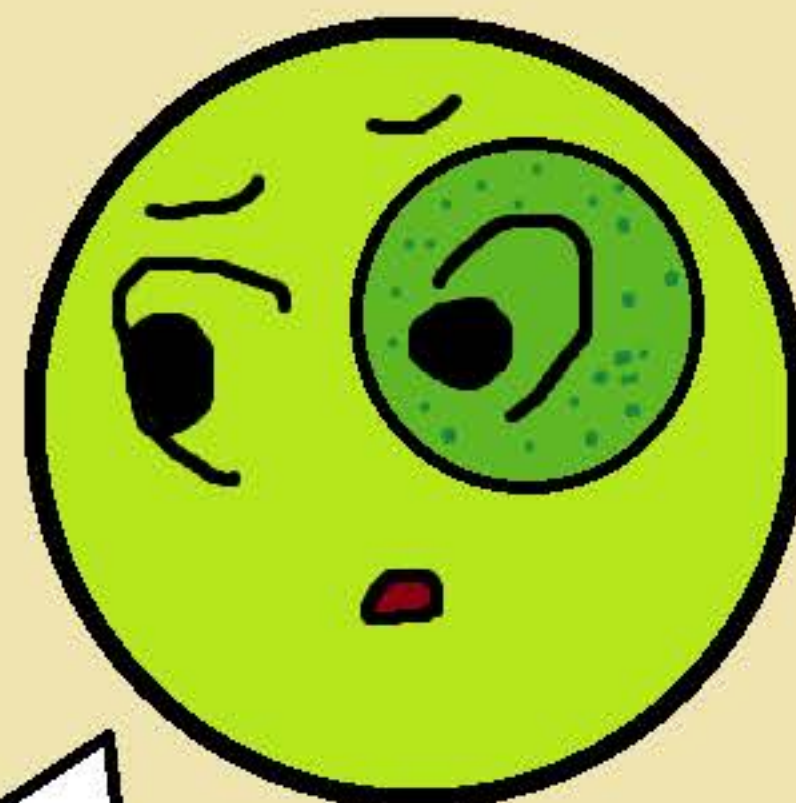
Cluster of Differentiation 19 (CD19)

A B-lymphocyte antigen, or in other words protein biomarker 19. Serves specifically as a cancer marker for B-cell lymphoma diagnosis, and as a target for leukemia immunotherapies.



What is it Bebel?

It's a mutation Neo, in your DNA, and this specific mutation is causing Acute Lymphoblastic Leukemia.

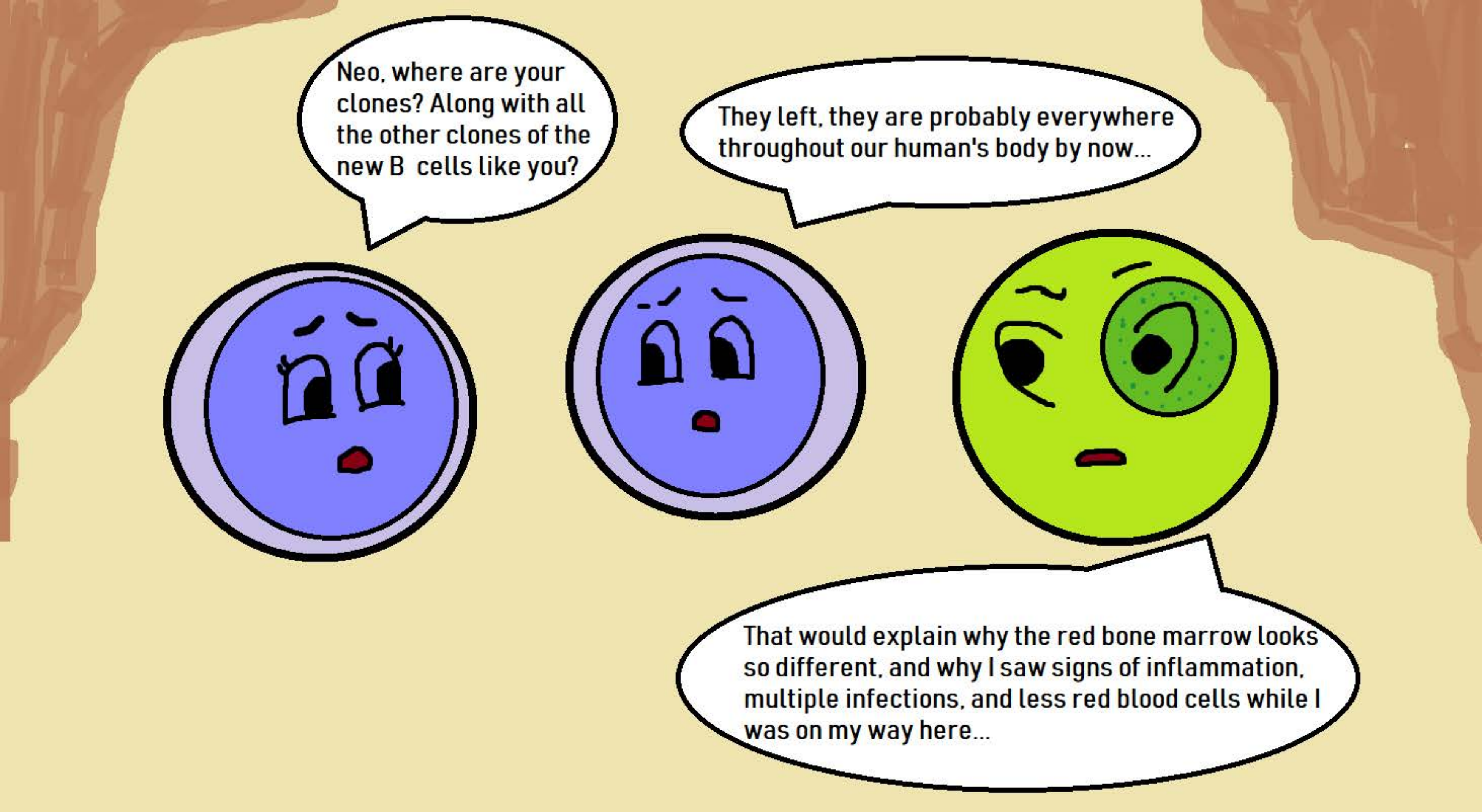


What? A mutation? Leukemia?

Is that why I'm making clones so quickly? And do all the clones I make carry this mutation?

This type of mutation causes a cancer that is acute, fast growing or cloning, of lymphoblasts or immature white blood cells in the red bone marrow and other blood making organs. Making this a leukemia type because it is involved with the blood.

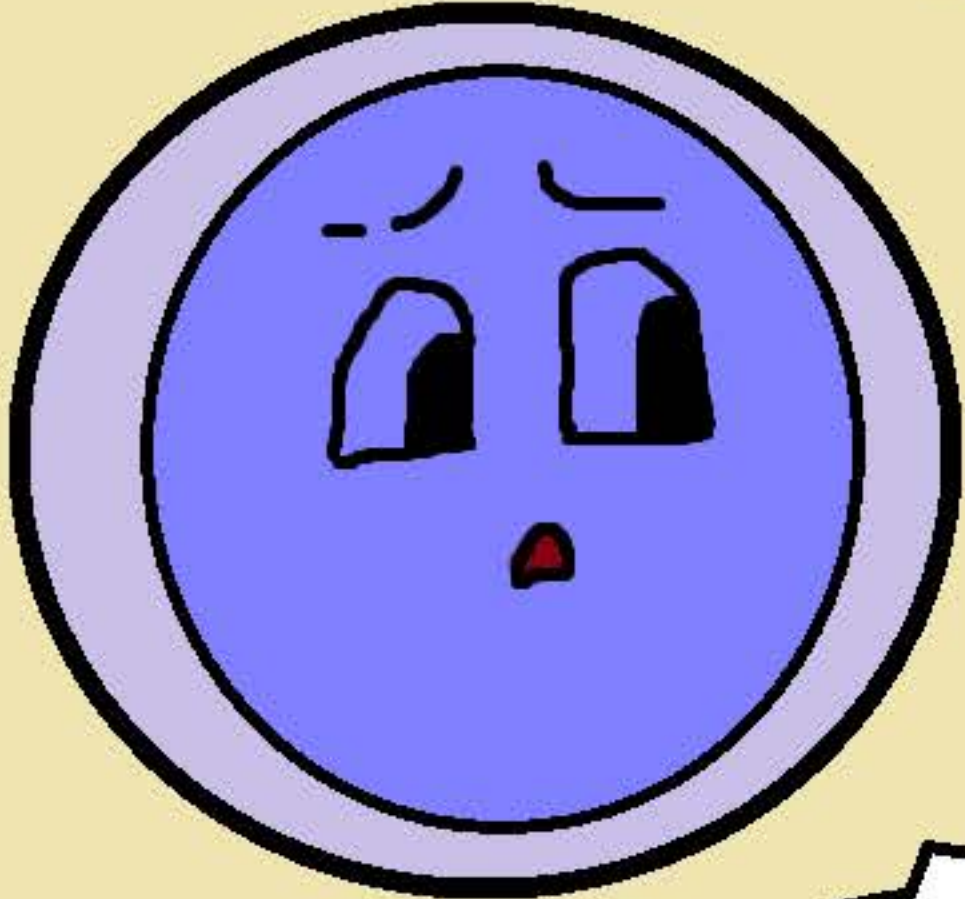
Yes.



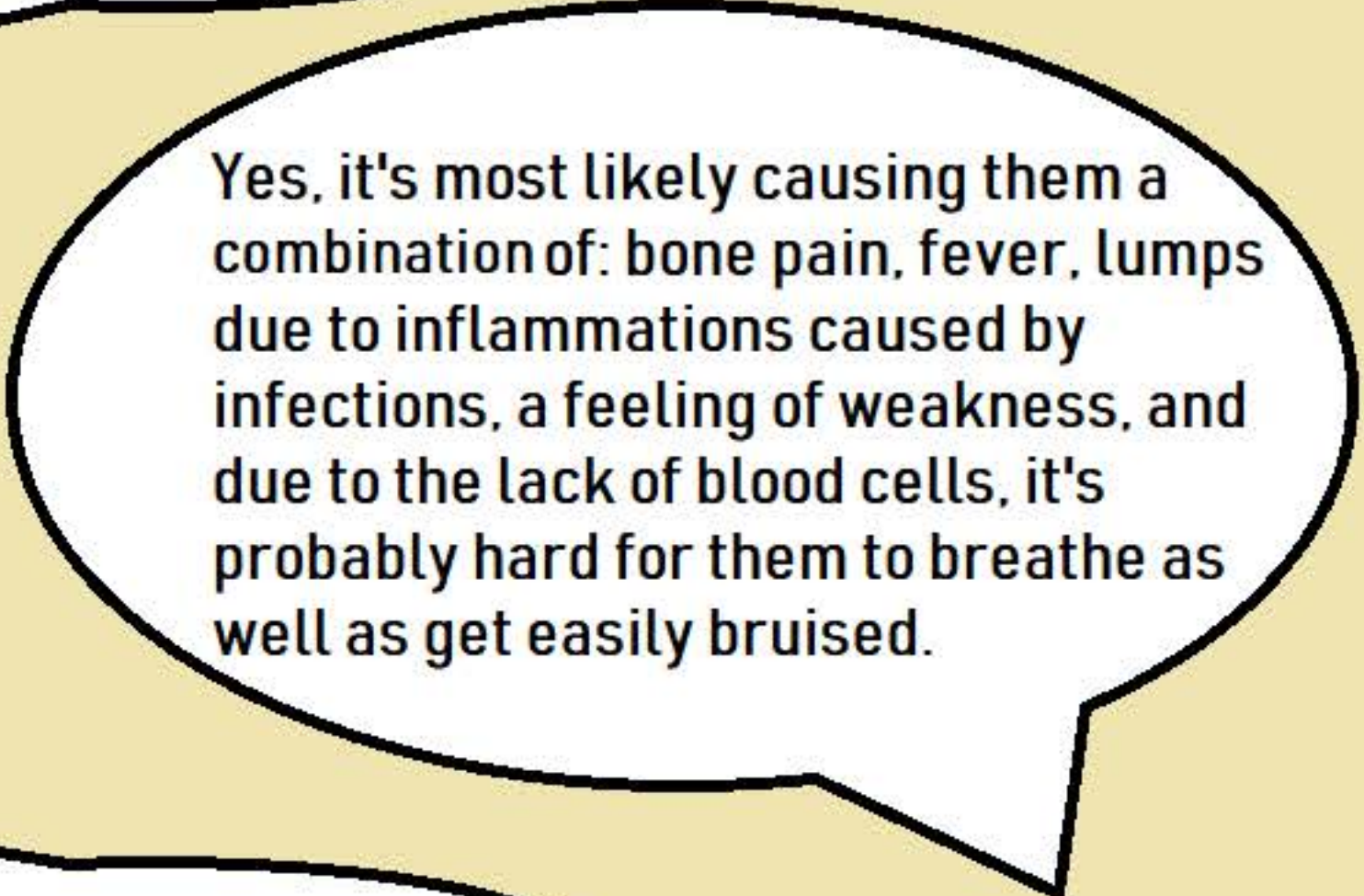
Neo, where are your clones? Along with all the other clones of the new B cells like you?

They left, they are probably everywhere throughout our human's body by now...

That would explain why the red bone marrow looks so different, and why I saw signs of inflammation, multiple infections, and less red blood cells while I was on my way here...



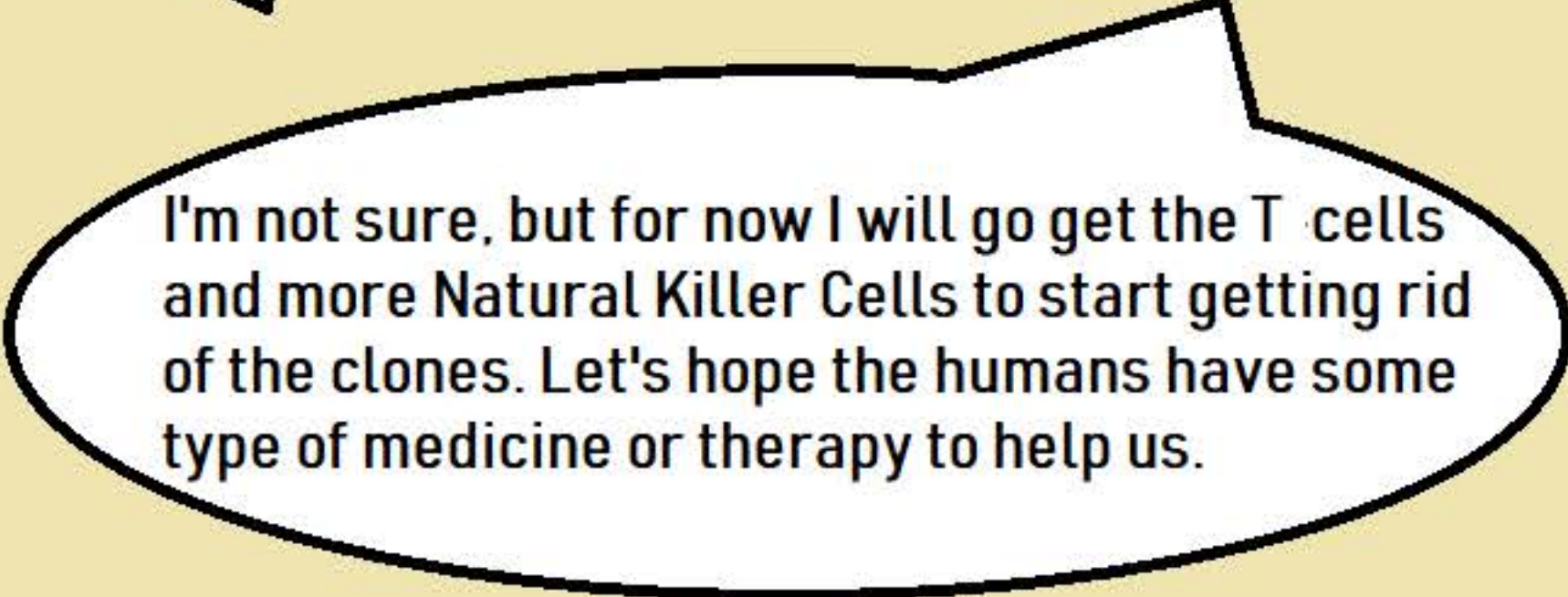
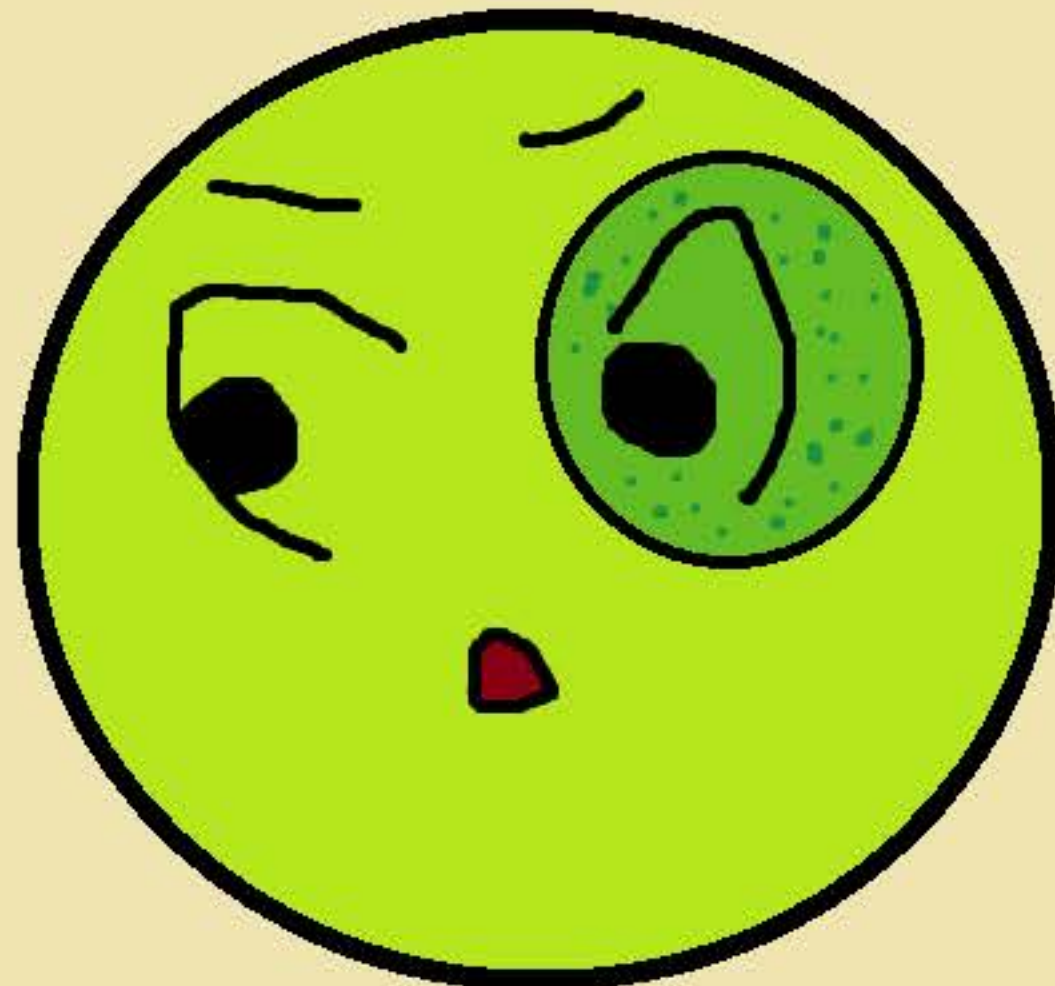
Is that hurting our human?



Yes, it's most likely causing them a combination of: bone pain, fever, lumps due to inflammations caused by infections, a feeling of weakness, and due to the lack of blood cells, it's probably hard for them to breathe as well as get easily bruised.



Oh no! How can we stop it?



I'm not sure, but for now I will go get the T cells and more Natural Killer Cells to start getting rid of the clones. Let's hope the humans have some type of medicine or therapy to help us.

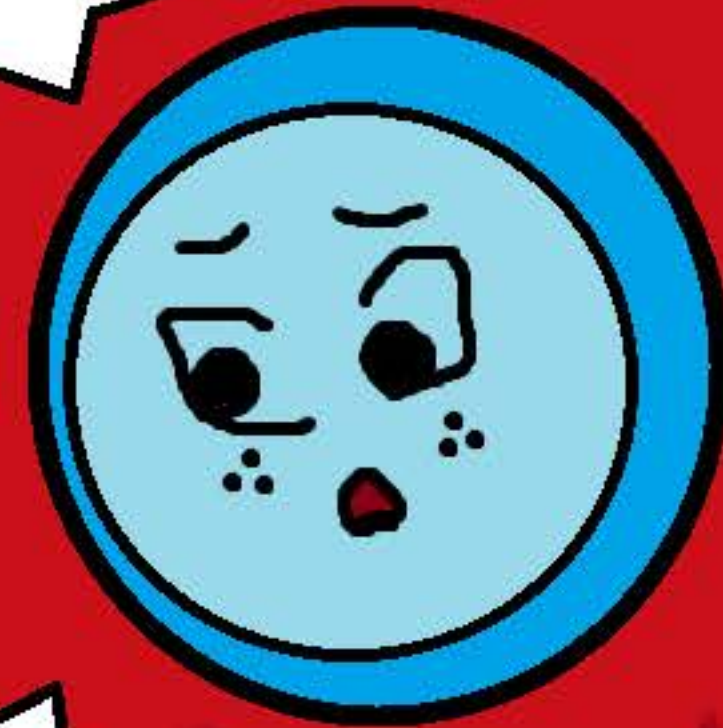
Back in the Blood Vessels

Ava, why are we going back to the bone marrow?

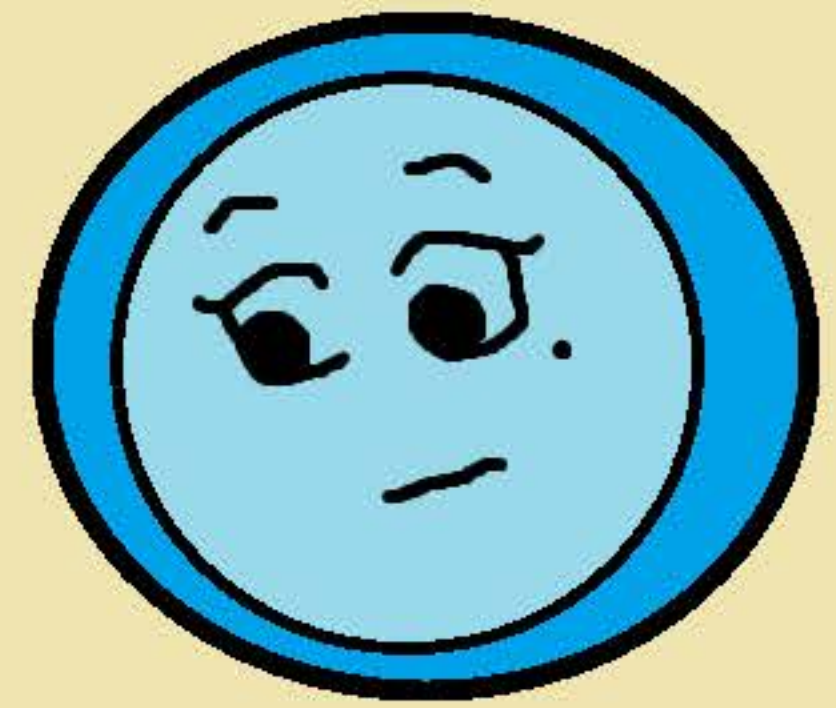
The Natural Killer Cells are signaling for help. They need us to organize a bigger attack on a lot of B-cell clones that are carrying a mutation.

What does this mutation do?

It causes the B-cell antibodies to target and attack the wrong protein signals and biomarkers, harming our human instead of helping them.



In the Red Bone Marrow

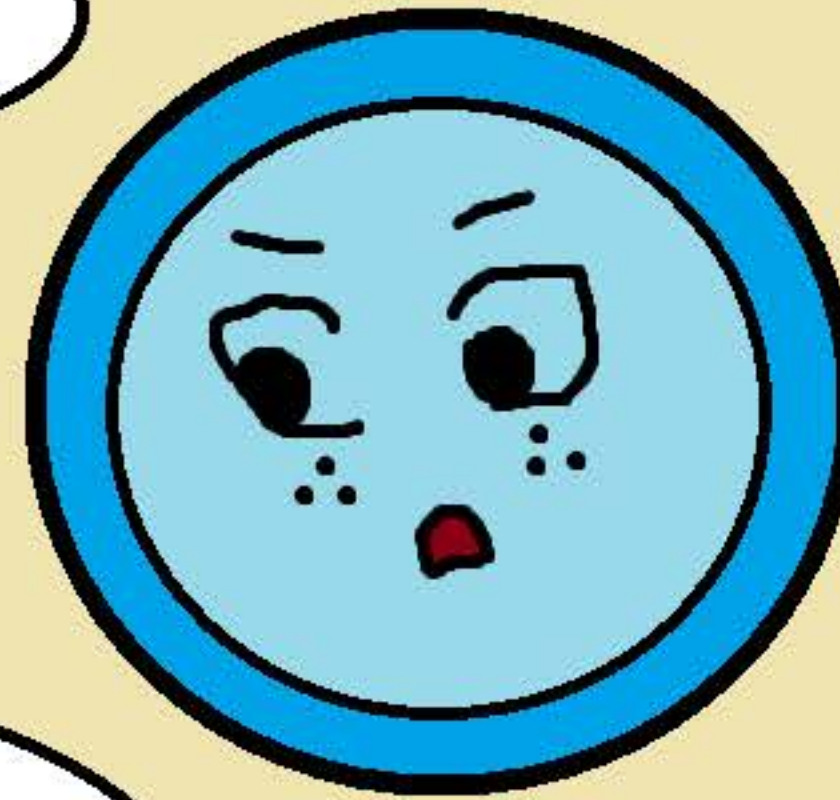


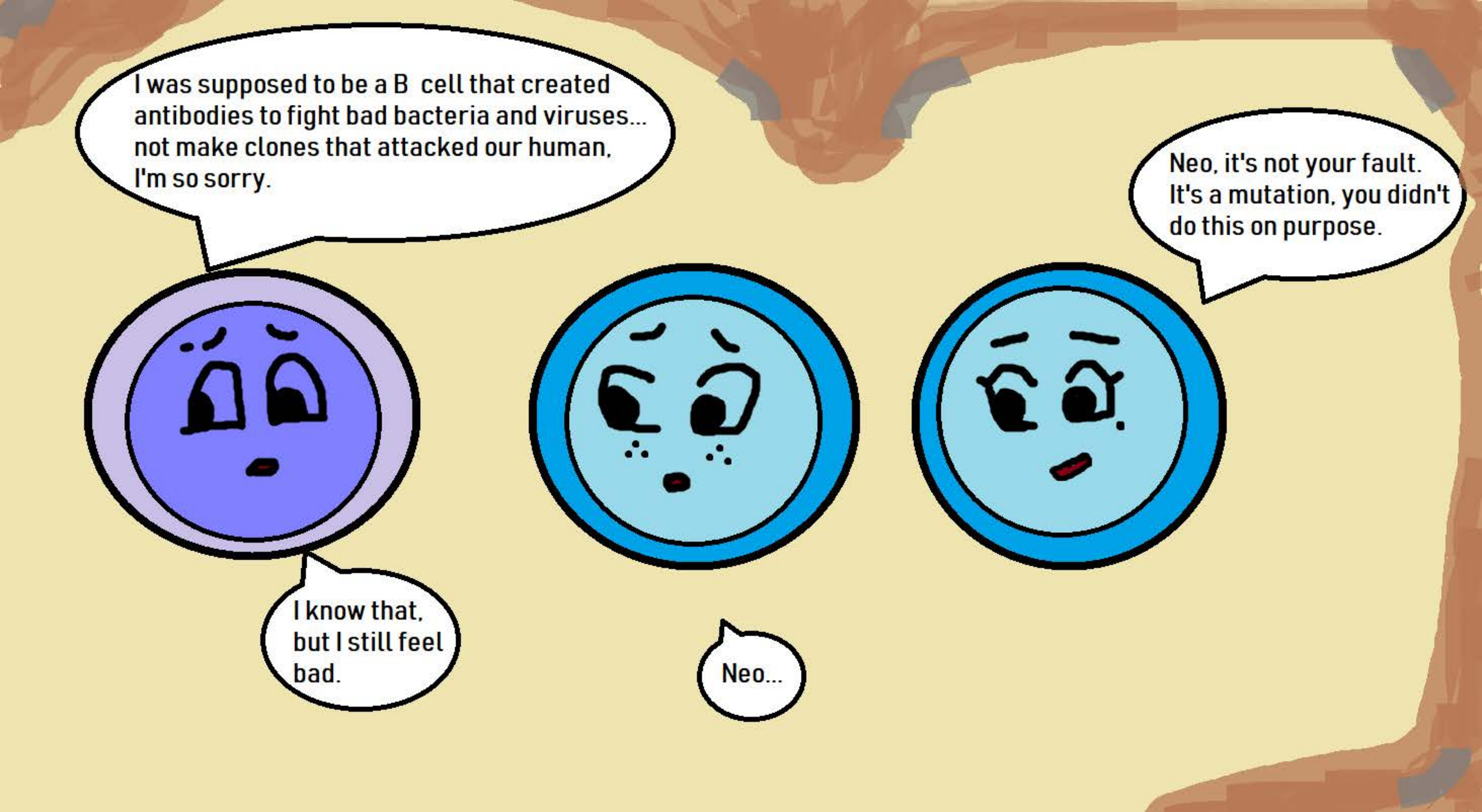
Tim! Ava!

Neo! Are you okay, do you know what's happening?

Yes, thank you for coming to help.

And about the clones... you guys should know that I'm one of those immature B cells whose mutated clones are causing all of this harm.






I was supposed to be a B cell that created antibodies to fight bad bacteria and viruses... not make clones that attacked our human, I'm so sorry.

Neo, it's not your fault. It's a mutation, you didn't do this on purpose.

I know that, but I still feel bad.

Neo...

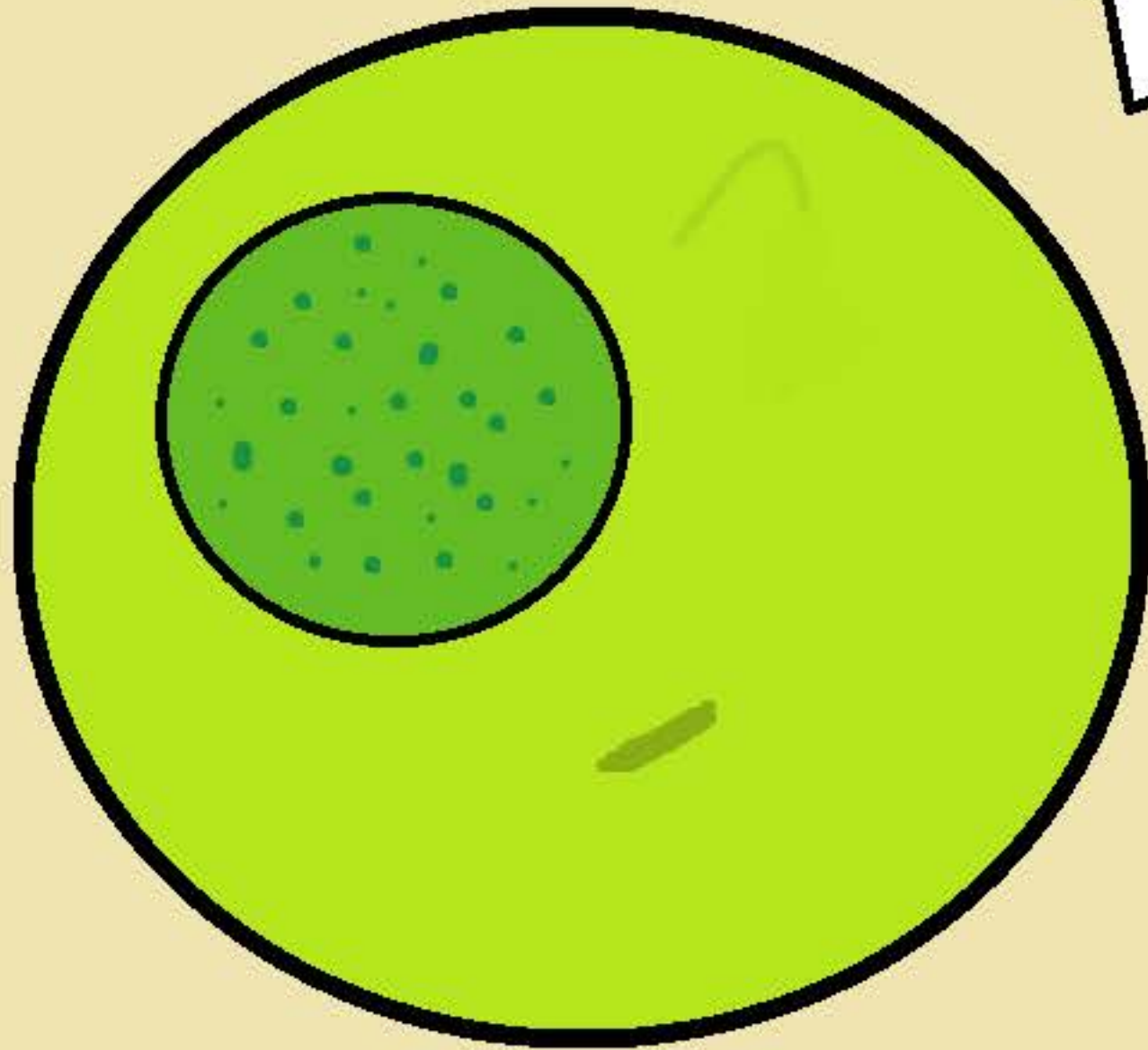


Tim! Ava! You came
just in time.

Tim. I see that you are a Cytotoxic T cell now.
you may be able to help me with something.

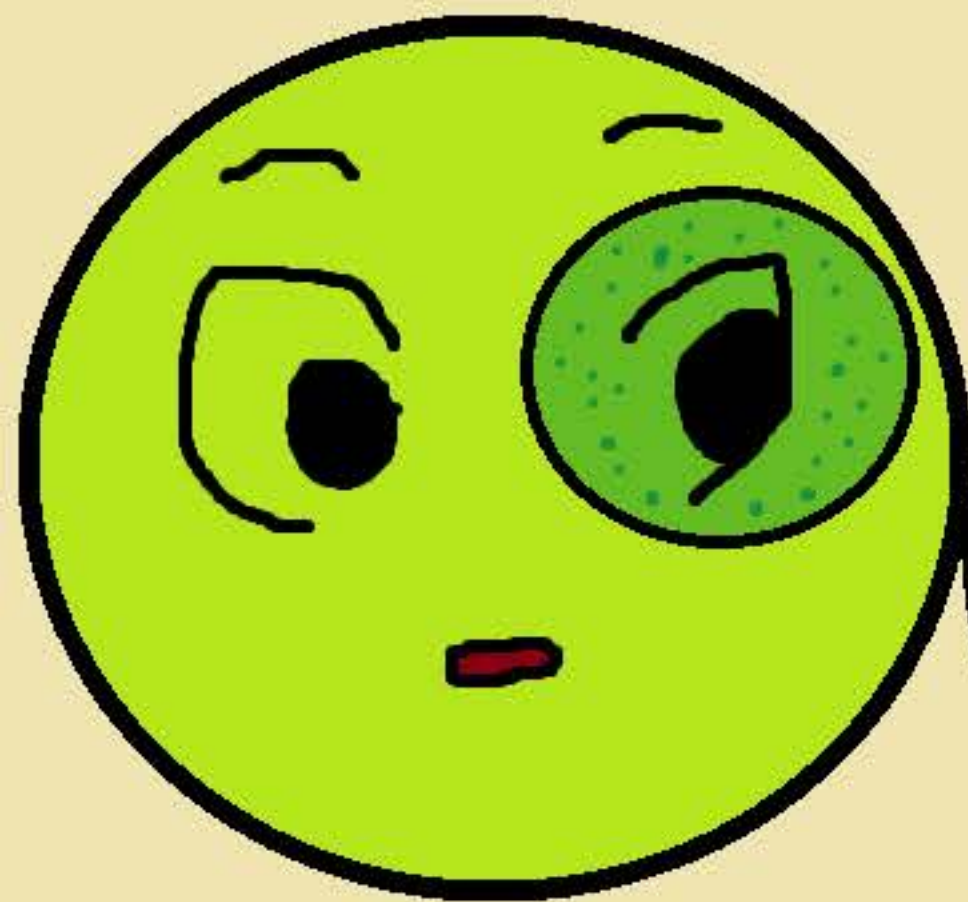
Yeah sure... what is it?

You'll see.
everyone follow me.



We are now deeper inside the red bone marrow, where I managed to find one of the clones that have been causing problems.

I already tried to kill it, but I'm having trouble recognizing its cancer marker that allows me to kill it... which is why I want Tim, a new Cytotoxic T cell, to try.



Because you are a T cell Tim, your receptors are more specific than mine.

Wait, but Bebel, you are a Natural Killer Cell... if you couldn't do it, what makes you think I can?

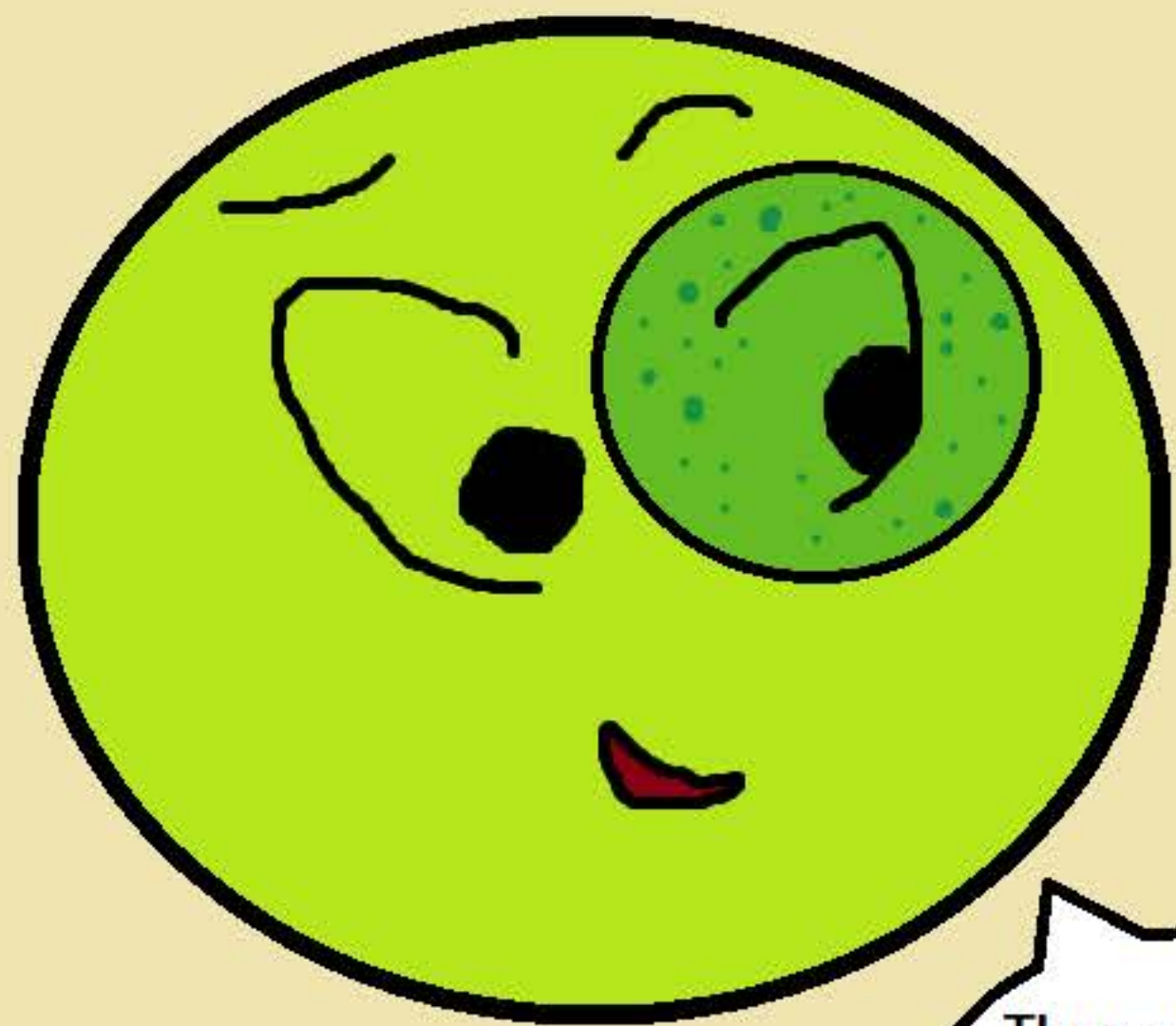


He's right Tim, remember that protein that the Antigen Presenting Cell gave you back in the Thymus?

Yeah...

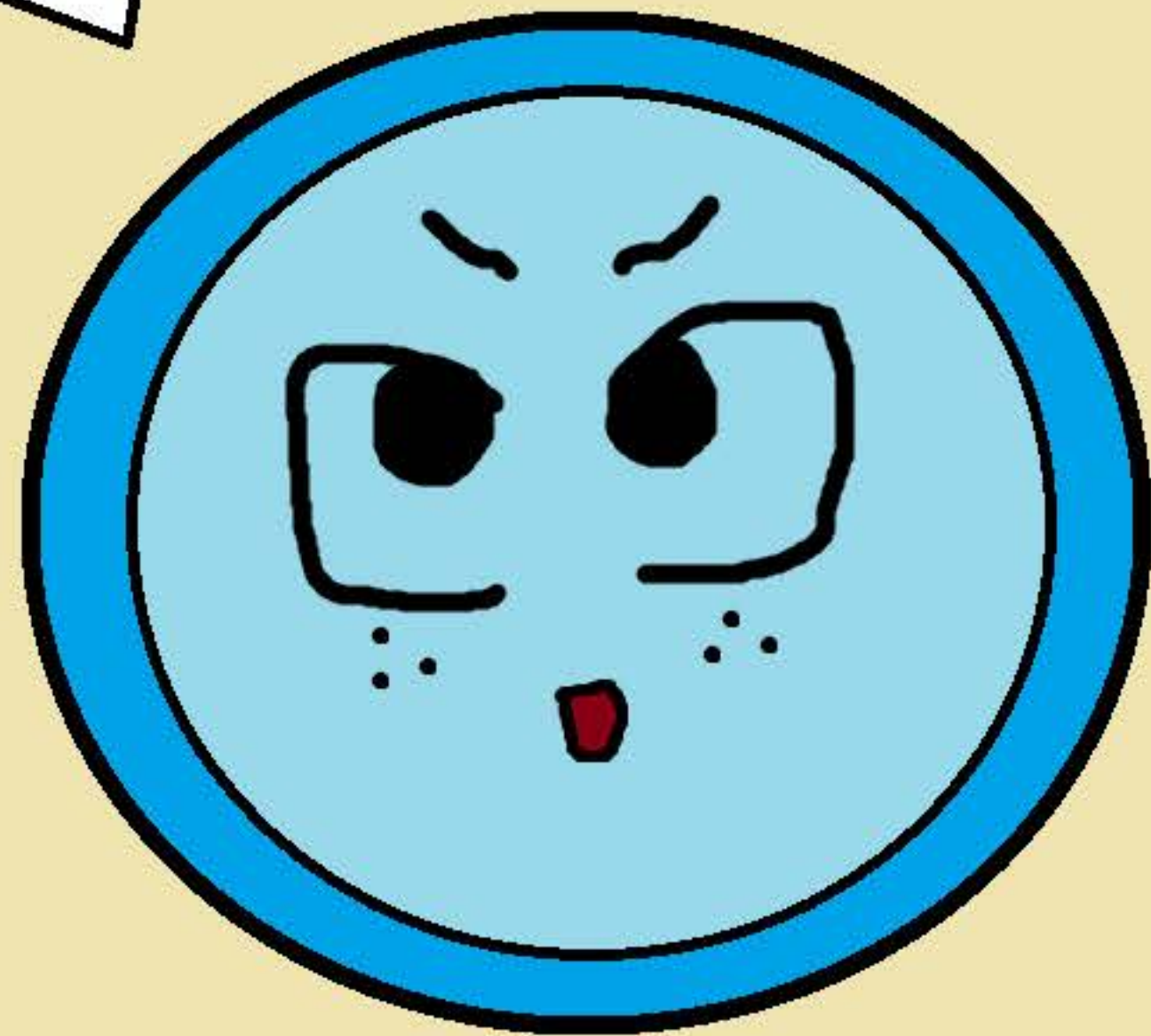


Well that protein could have been the same one being expressed on these clones surfaces, making you gain special receptors that can recognize and kill them.



There you go!
That's a better
attitude!

Okay then, I don't know yet if I'm
actually able to do what you guys
just said, but I'm willing to try!





I really don't know if I can do this... but this is not the time to be afraid!

I will gather courage and keep pushing forward, I have to do my part!

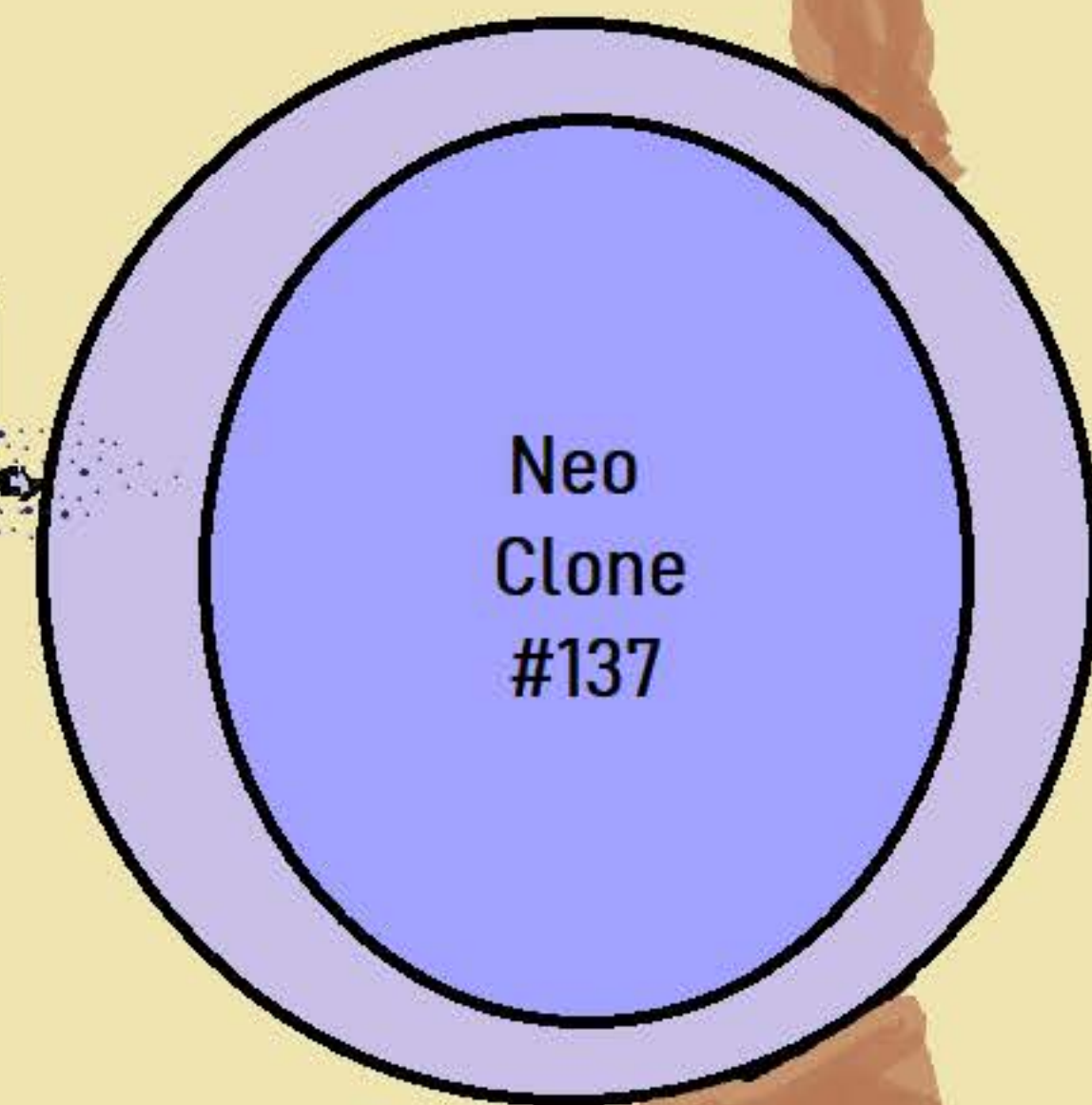
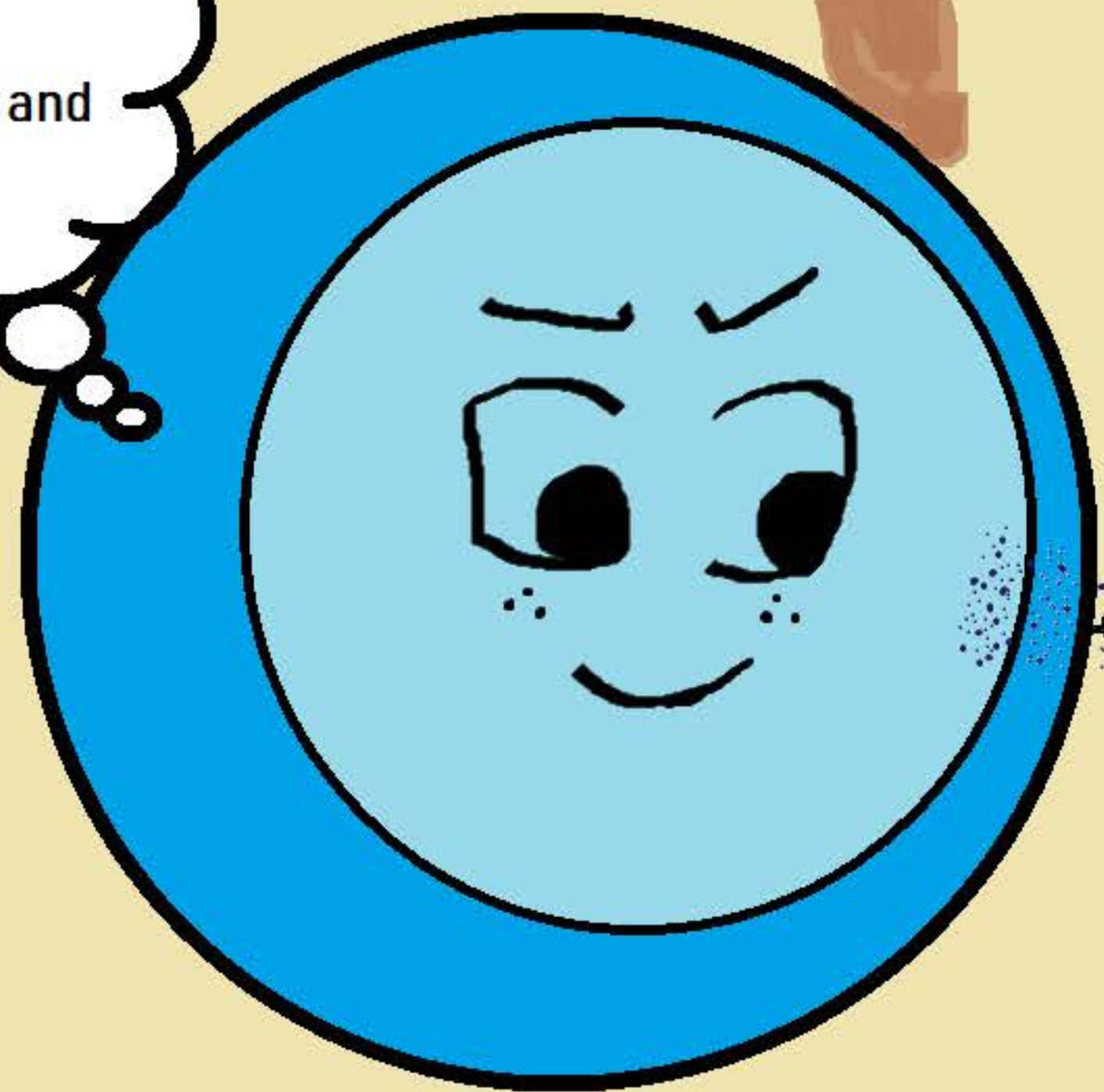
Neo
Clone
#137

CD 19

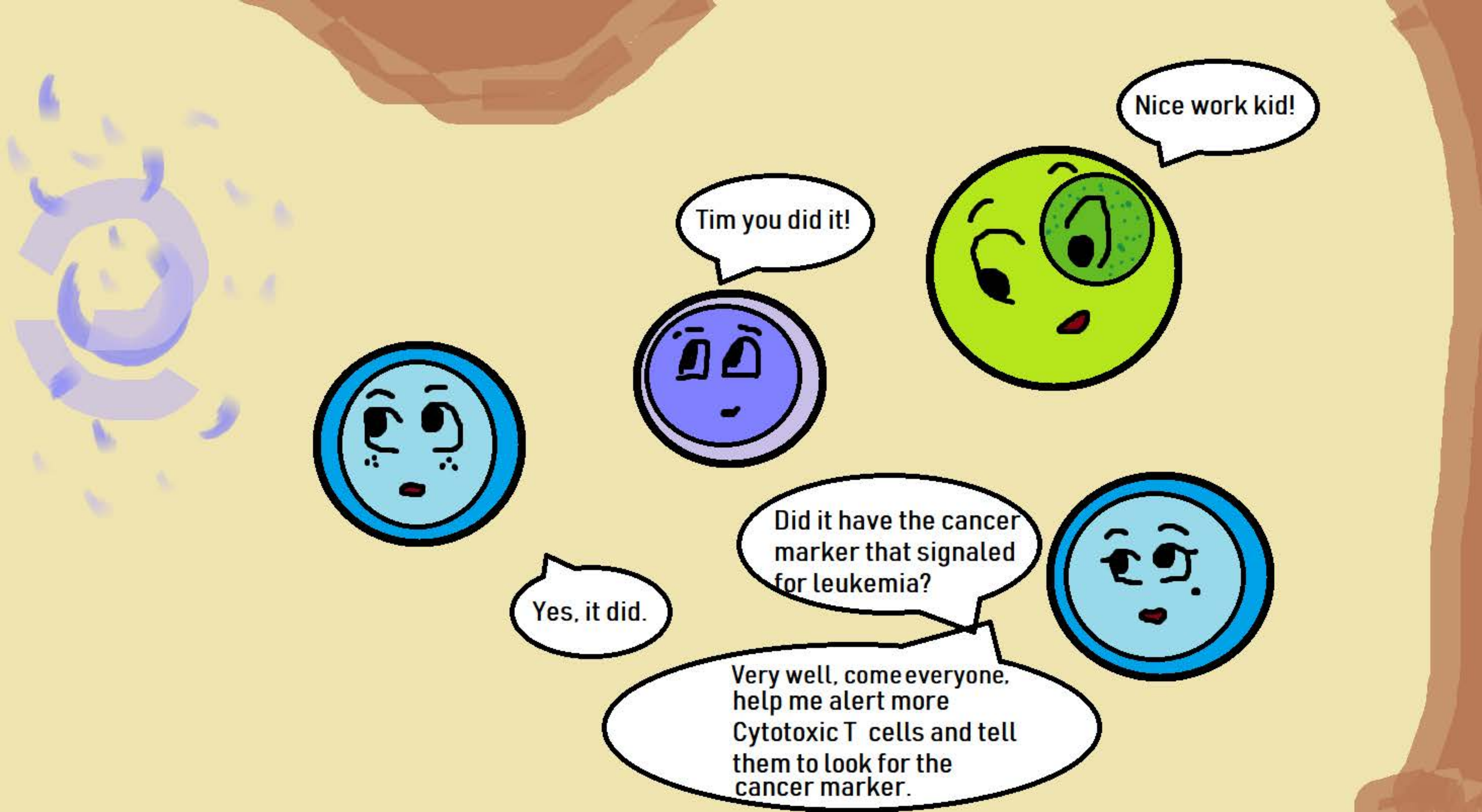
Ah! I can recognize it!
It's the cancer marker
for what's causing the
leukemia.

Which means...

...I can release my special toxic molecules called perforins and defeat it!



Neo
Clone
#137



Nice work kid!

Tim you did it!



Did it have the cancer marker that signaled for leukemia?

Yes, it did.

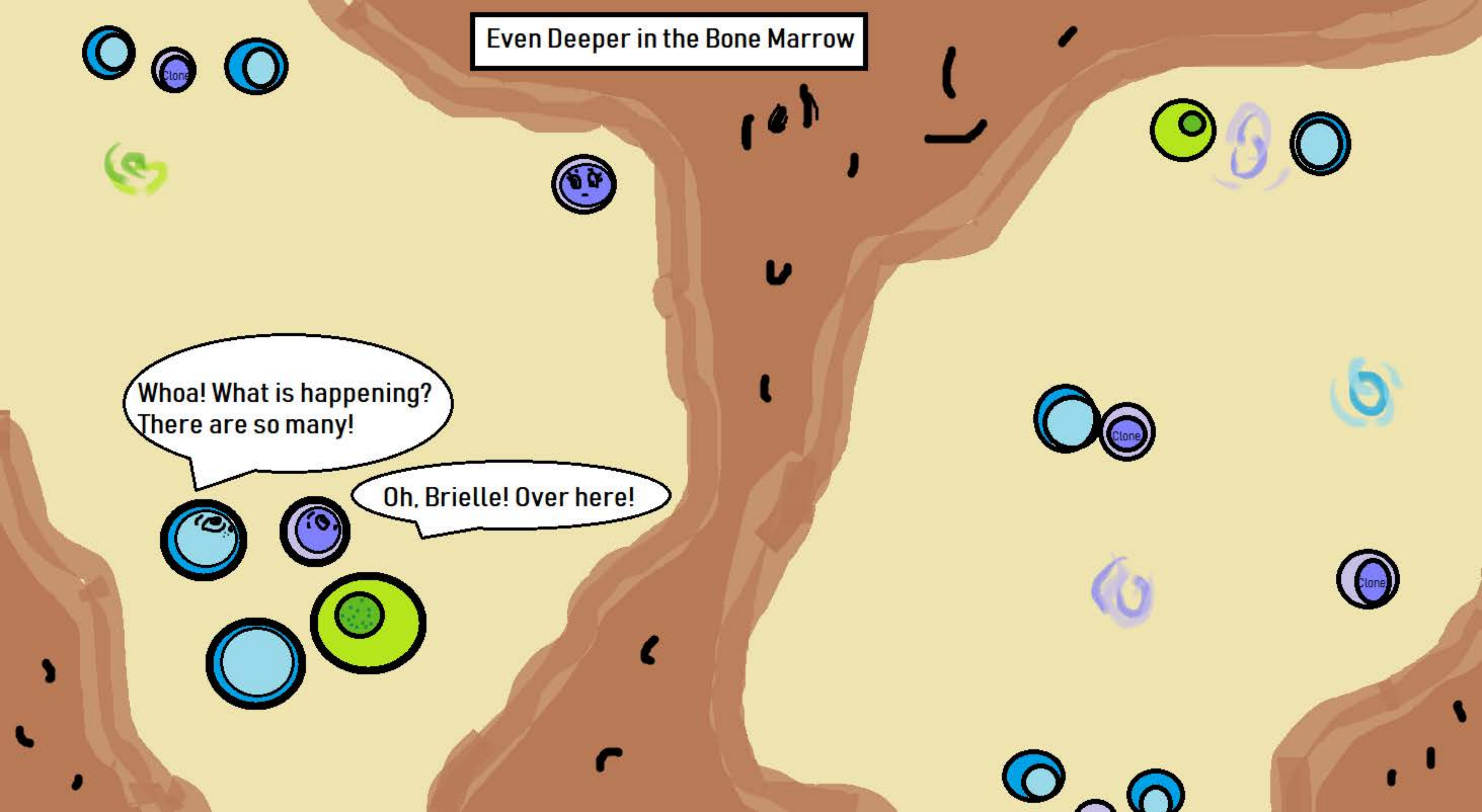


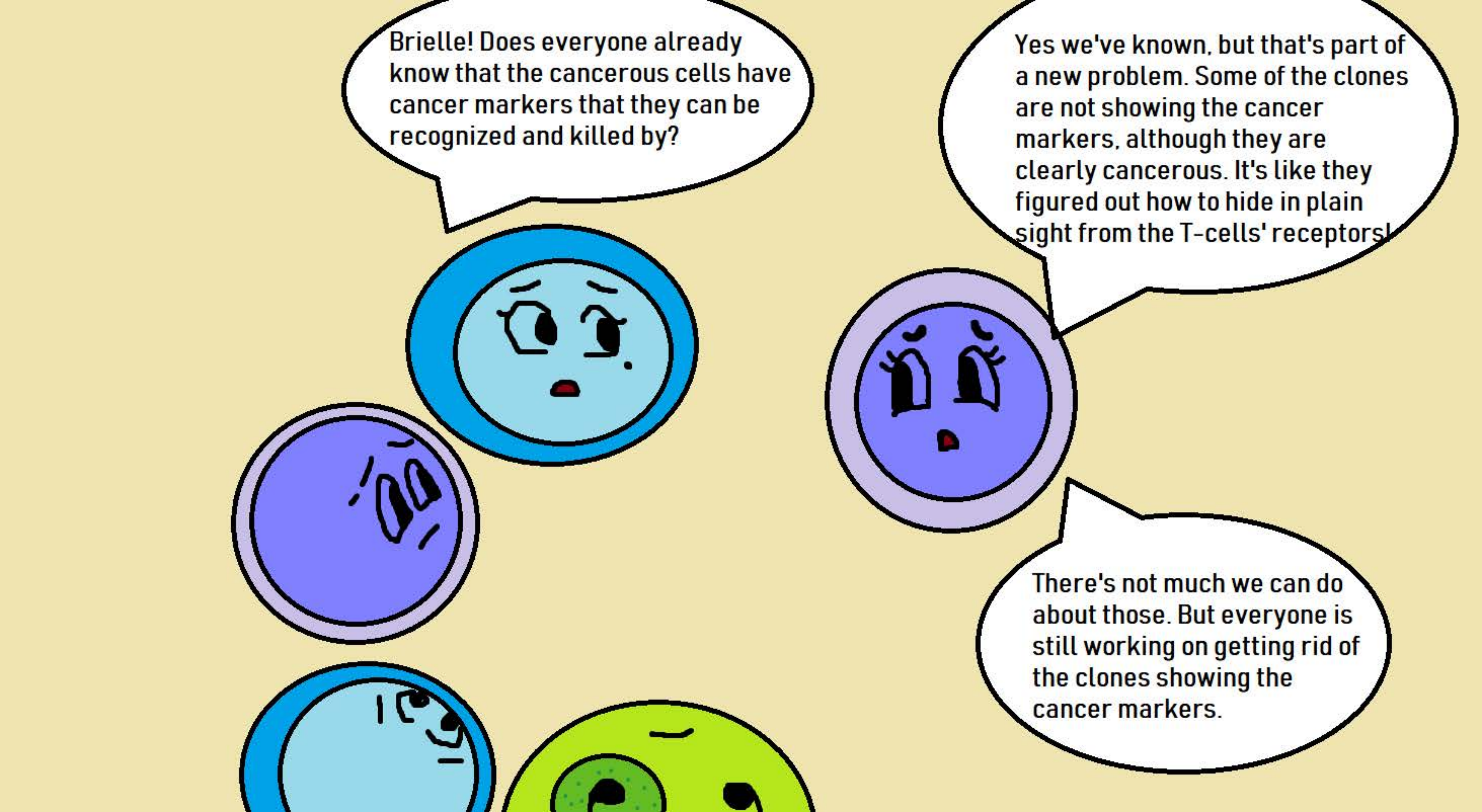
Very well, come everyone, help me alert more Cytotoxic T cells and tell them to look for the cancer marker.

Even Deeper in the Bone Marrow

Whoa! What is happening?
There are so many!

Oh, Brielle! Over here!

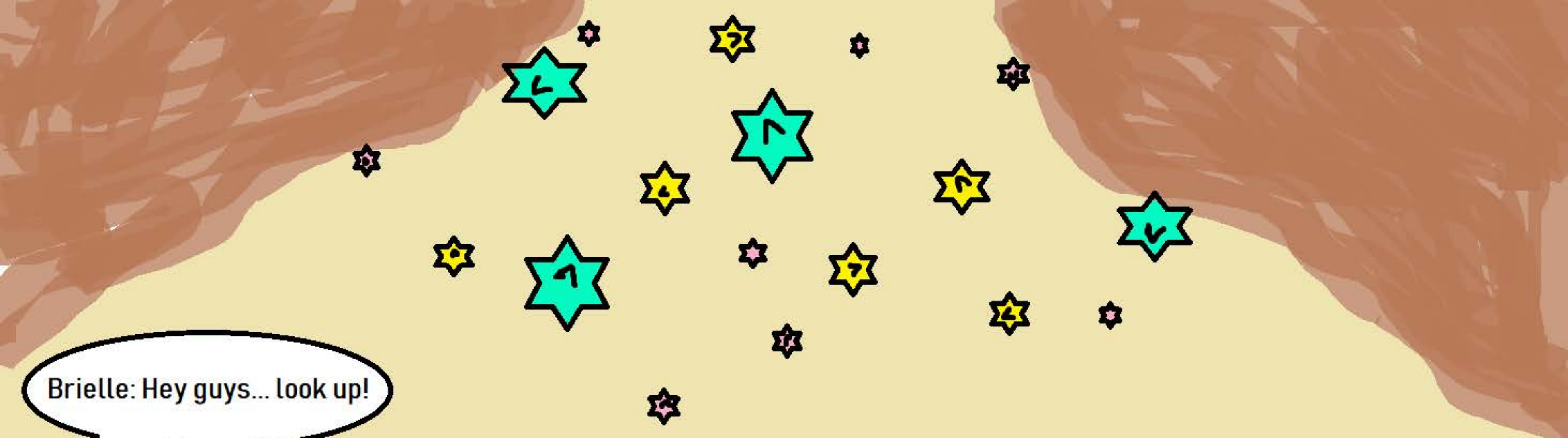




Brielle! Does everyone already know that the cancerous cells have cancer markers that they can be recognized and killed by?

Yes we've known, but that's part of a new problem. Some of the clones are not showing the cancer markers, although they are clearly cancerous. It's like they figured out how to hide in plain sight from the T-cells' receptors!

There's not much we can do about those. But everyone is still working on getting rid of the clones showing the cancer markers.




Brielle: Hey guys... look up!

Tim: Whoa... what are those?

Bebel: It looks like different types of human-made treatments...

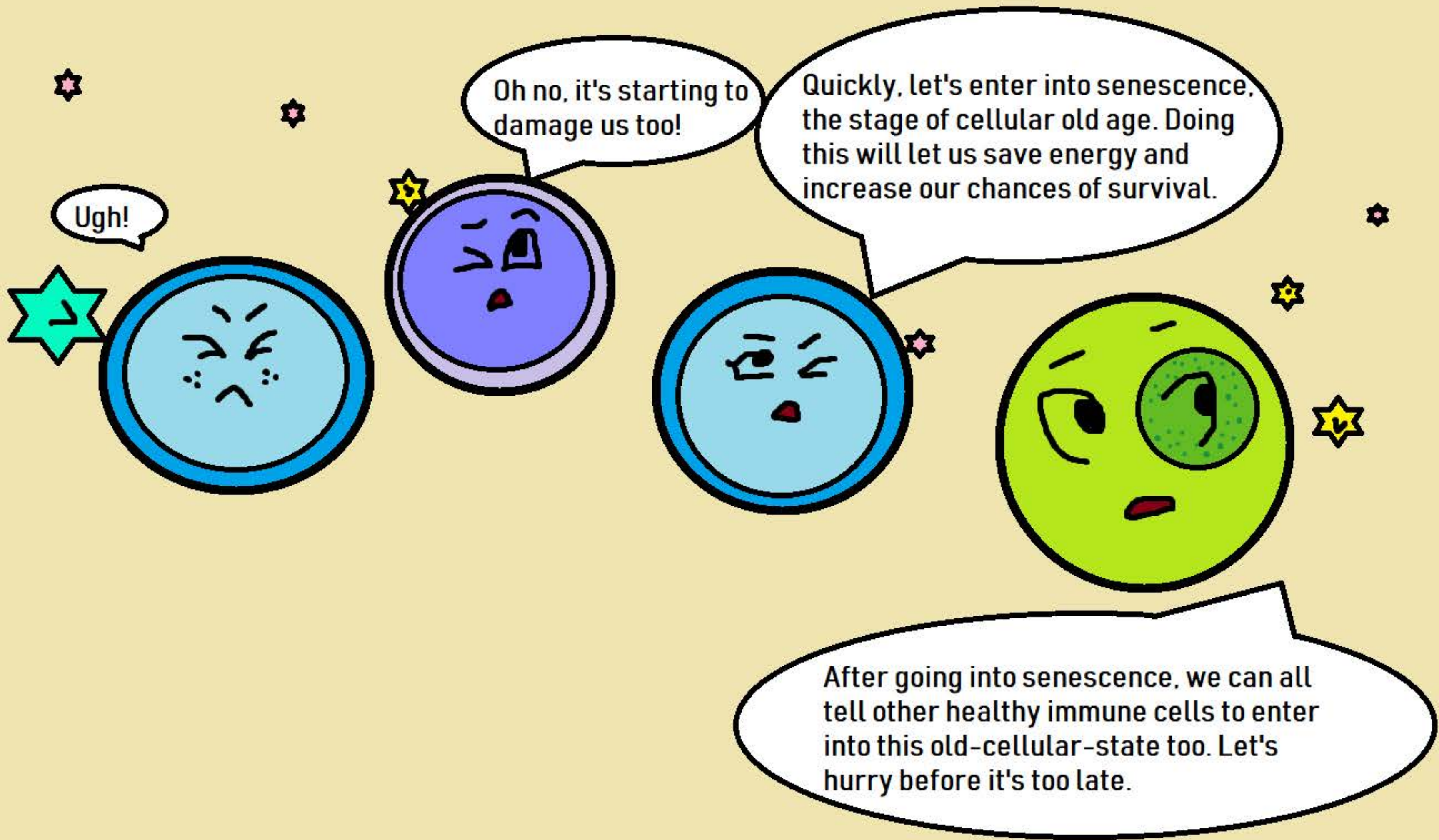
Ava: Perhaps some type of chemotherapy medicine has been given to our human to help us defeat the leukemia.

Neo: Will it work?



Tim: It definitely looks like it's working!

Yes, but maybe it's working too well... it's affecting the healthy cells too, look!




Ugh!

Oh no, it's starting to damage us too!

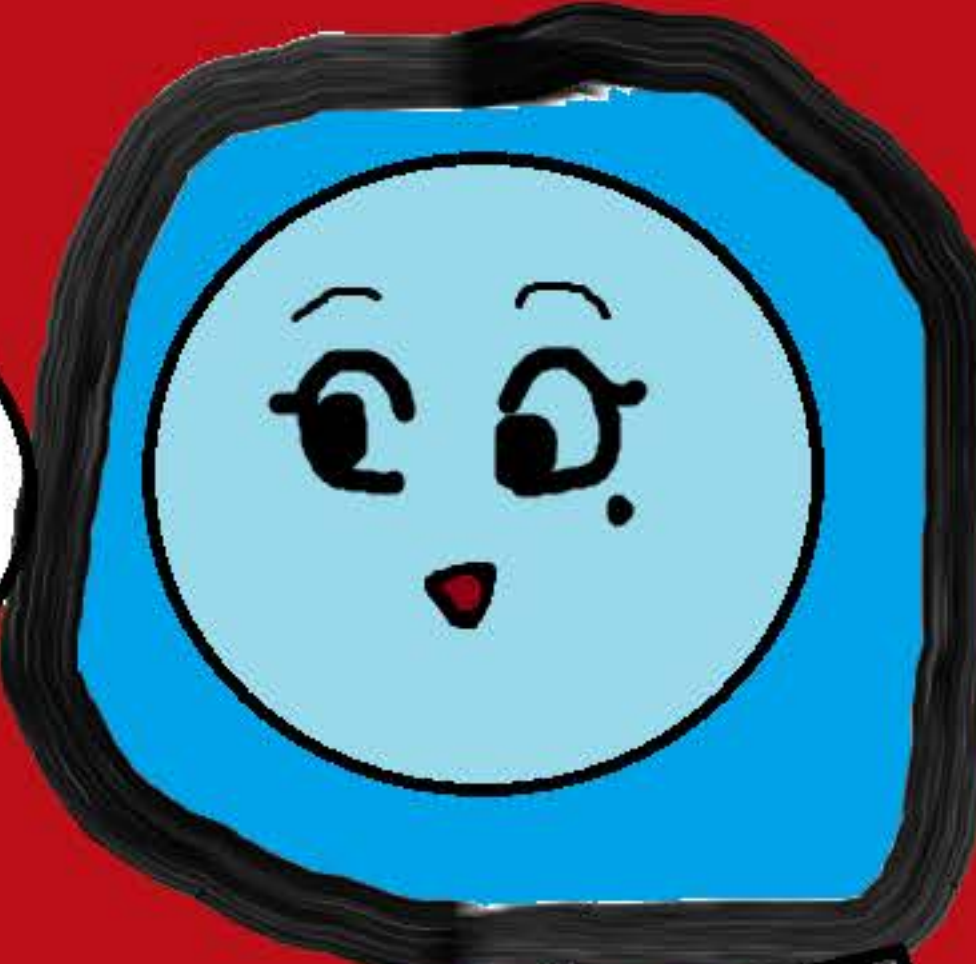
Quickly, let's enter into senescence, the stage of cellular old age. Doing this will let us save energy and increase our chances of survival.

After going into senescence, we can all tell other healthy immune cells to enter into this old-cellular-state too. Let's hurry before it's too late.

About One Month Later, Inside the Red Bone Marrow



We look awful, I can't believe it took that medicine so much time to finally get rid of the cancer cells so that the leukemia could go into remission.



It's not exactly over yet Tim. Hopefully this never happens, but this leukemia could attack again with new cancer cells in the future.

Really? What can we do to be ready? Just in case.

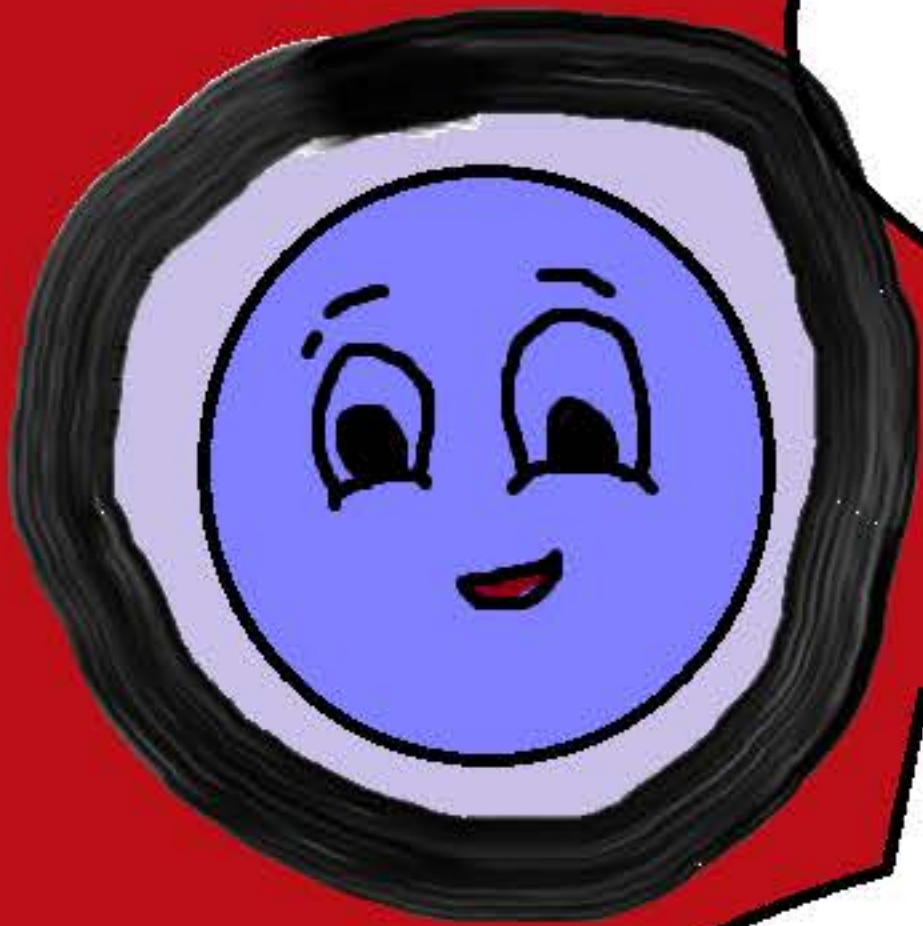
There are Memory T cells that can also recognize the cancer marker and remember it, making them able to fight this cancer effectively if they ever see it again for years to come.



What? Why?

Neo...

Guys, I'm going to exit out of my senescence stage and allow myself to pass away.



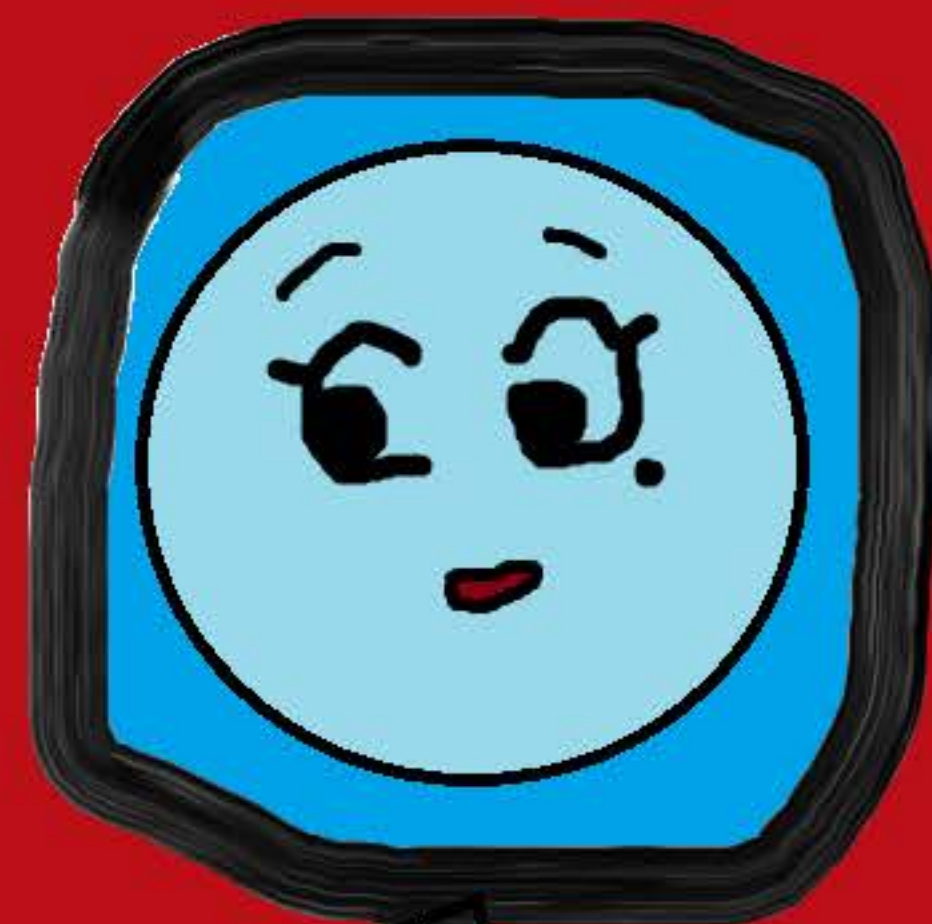
The mutation is still active in my DNA, so I could accidentally start making those cancer clones again. Therefore, it's a sacrifice I'm willing to make, I can stop the mutation inside of me with my passing.

I'm at peace with that decision, really. It would allow me to redeem myself and serve our human one last time. Also think about this, my name Neo means "new", and I have a chance to give everyone a new beginning, so I'm doing it. With no regrets!

If that's truly what you wish Neo,
to serve our human in that final
way. I understand and support you
on your brave decision.



Thank you Tim, I'll miss everyone,
but this is for the better.



You know we'll all miss you too
Neo. Go remembering that none
of this was your fault.

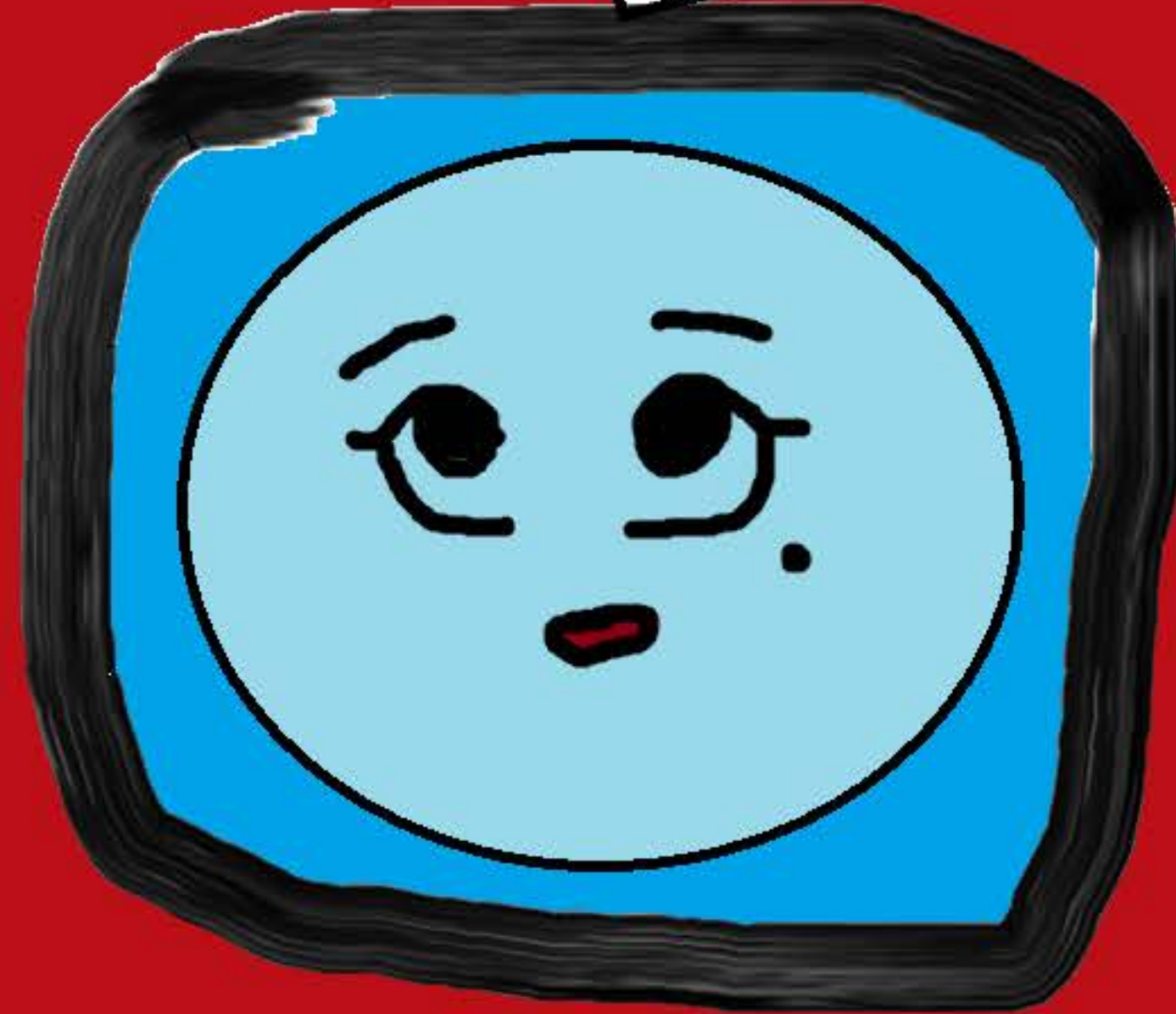


Goodbye Neo.

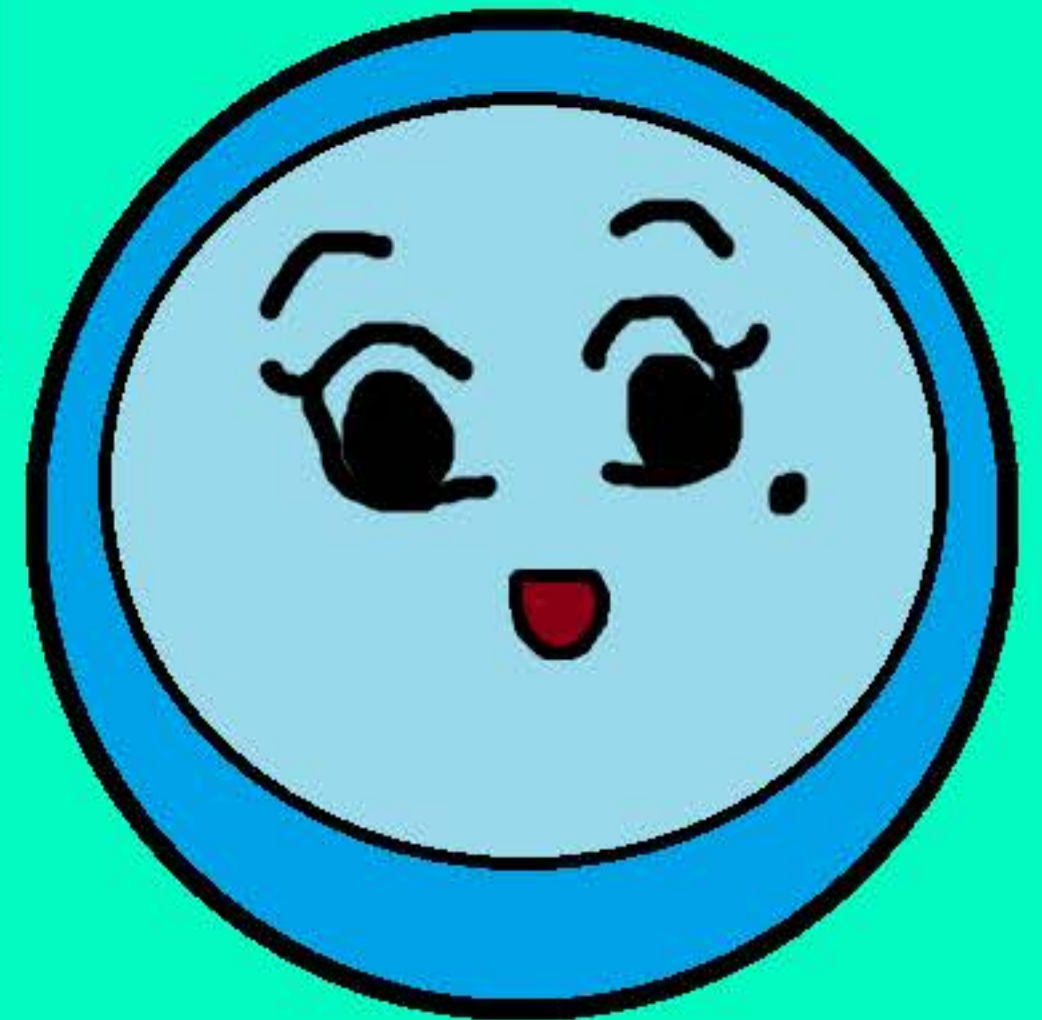




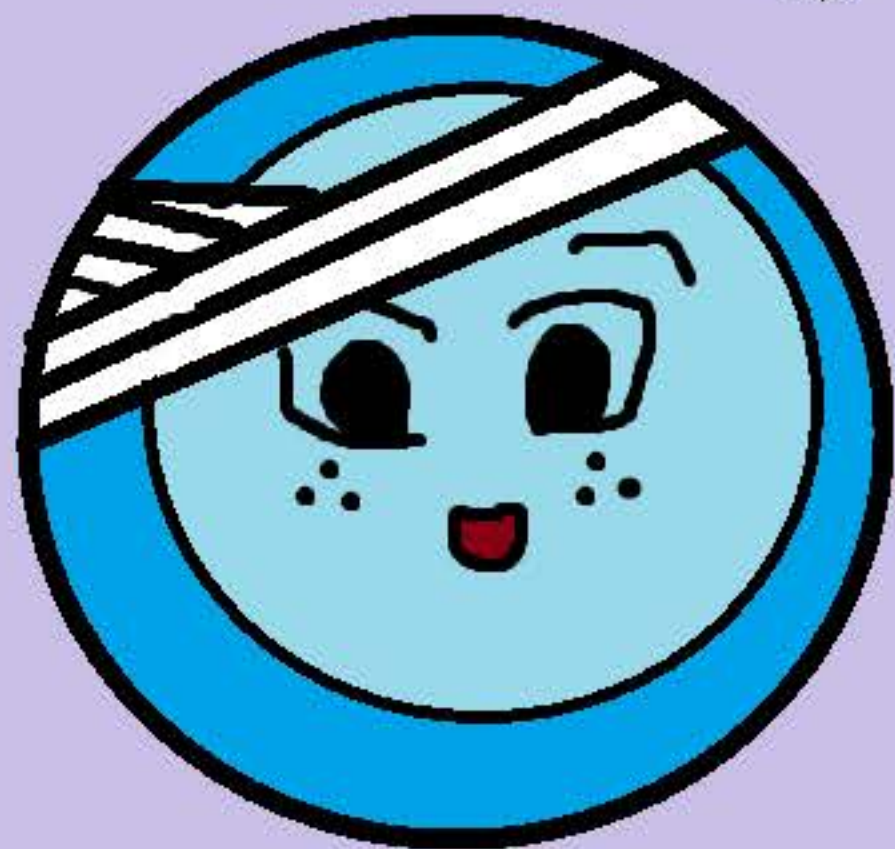
Neo's memory will live on in the Memory T cell, and give us a fighting chance against this leukemia if there is ever a next time.



We are immune cells, we work together to protect our human from pathogens (microorganisms, bacteria, viruses), and cancer. Our journey has come to an end for now, but yours may be just starting, in the middle, or almost at the end. Whichever phase of your battle with cancer you may be in, know that your immune cells, like us, are fighting for you and are doing their best! Stay strong, stay positive, and stay open. Openly share your feelings, thoughts, worries, and emotions with the people around you. They love you, and so do we, your cells.



The End.



Author's Notes

Acute Lymphoblastic Leukemia (ALL) is a cancer of the bone marrow, hence the name leukemia, started by early forms of white blood cells also called lymphocytes, that is quickly growing or spreading for which it receives the name acute (cancer.org, 2019). ALL is the result of a mutation in immature B cells that causes them to quickly replicate into multiple cells carrying the mutation (clones in the story). ALL occurs mostly in children between the ages of 6 and 14 years old, but can occur at any age whether infant or adult. Lastly, current survival rates include a percentage of 98% of pediatric patients enter into remission within weeks of starting treatment, and 90% of those pediatric cases can be cured after 10 years of remission (stjude.org, 2019).

The reason for why I chose to write about ALL is because out of all childhood leukemias, ALL occurs in about 3 out of 4 pediatric leukemia patients (American Cancer Society, 2019). I wanted to write a story that would be relatable to most pediatric patients. What separates ALL from other types of leukemia and cancers, is that it's a cancer of the bone marrow by B cell or T cell mutation, which clones quickly and can spread throughout the body via the blood. For this story, in order to not confuse the audience, I chose to have the B cells start the cancer and the T cells remain unaffected by the mutation. According to the cancer.org website, this type of leukemia can spread to the patient's lymph nodes, central nervous system, liver, spleen, and other organs (this varies depending on the patient). Scientists and researchers are finding that there are several factors that could cause or provoke childhood leukemia. These are called risk factors, which include: genetic, lifestyle-related, and environmental factors. Among the genetic risk factors that come from the parent's bloodline, genetic syndromes like Down syndrome, inherited immune system problems such as Bloom syndrome and Schwachman-Diamond

syndrome, and having a sibling with leukemia are included as risk factors for developing ALL (American Cancer Society, 2019). Lifestyle-related risk factors, that are more for an adult's chance of developing ALL, include: being overweight, smoking, too much exposure to the sun, and excessive consumption of alcohol. Environmental risk factors, are outside influences that have an effect on a person's physiology. These include high levels of radiation exposure, exposure to chemotherapy drugs like etoposide and cyclophosphamide while treating a previous cancer, or other chemicals like benzene, and immune system suppression due to intensive treatment (like an organ transplant). Besides these possible risk factors, there are not many known lifestyle or environmental risk factors directly linked to ALL. Therefore, there are no known preventions for ALL as of now. This is significant in understanding that in the majority of ALL cases, there is nothing that could have been done in order to prevent its development in the patient (American Cancer Society, 2019). Neo, the B-cell in my story that sorrowfully and inexplicably carried the mutation for ALL, was my way of showing the audience this idea of unpredictability.

When it comes to treatments, chemotherapy is the main treatment for ALL. Chemotherapy is usually induced in 3 phases that can span over a time of 2 to 3 years. These phases are called Induction, Consolidation, and Maintenance (St. Jude's, 2019). I would like to discuss the Induction phase, since it is the first phase of chemotherapy and it's the phase that my story ends with. During Induction, patients typically receive a combination of 3 drugs for their first month of treatment. These chemotherapy drugs are L-asparaginase and vincristine, and usually dexamethasone (a steroid drug) (American Cancer Society, 2019). I illustrate these drugs as little star-shaped molecules with 3 different colors for the 3 different drugs. I also write

“About 1 Month Later” toward the end of the story in order to keep a timeline of how long it has been after the Induction phase.

Consulting the sources listed in my bibliography is how I derived ideas and inspiration for my own interpretation of how immune cells look and the overall plot of the story. I did this in order to represent ALL and these immune cells in their roles and physiological interactions. This contextual information is what influenced me both theoretically and artistically in my drawings and story for this creative project. I wished to achieve an eye-catching and relatable story that ALL patients could gain insight to, and readers not impacted by ALL in their lives could also learn about ALL from this creative project. Hopefully I accomplished making this story relatable by taking the creative freedom to personify the cells by giving them facial features and feelings. I wanted the audience to see themselves in my characters, so that it would be easier for them to stay engaged in these cells’ journey through ALL. Although I took creative freedom in how I illustrated and simplified ideas, I tried my best to stay true to the nature of these cells and ALL. My first goal was to make this children’s book a good starting point for anyone interested in understanding how ALL works. My second goal was to spark inquisitiveness in the reader for these cells and the scientific field that studies them. I learned a great deal about ALL through making this book. From how the cells interact with each other, to how the chemotherapy affects these cells during and after treatment. I wish that I would have drawn some things like the cell receptors with more detail, or included Chimeric Antigen Receptor T cell therapy (CAR T therapy) as an immunotherapy option, but perhaps this is a revision I could do in the future. Thank you for reading, hopefully like me, you have a new insight of ALL and the immune cells that are in the front line of defense against it.

Irune A.

Cast of Characters

While I was creating characters for my book, I kept in mind that I wanted to introduce the audience to the leading cells that are front-and-center in the fight against cancer.

Tim

Tim is a Cytotoxic T cell, he is one of the main characters of my story, and also one of the main types of cells doing the actual fighting against the cancer cells. I named him Tim in order for his name to start with the same letter of the type of cell he is, “T.” Making it easier for the reader to remember what type of cell he is. I needed a Cytotoxic T cell in order to show the audience how these specific T cells can recognize the cancer markers on cancerous cells and cause their apoptosis, or cell death. Doing so by releasing their perforin, which penetrates the cancerous cell’s membrane, ultimately destroying the cell.

Ava

Ava is another type of T cell, although the hint of a “T” is not in her name. However, her name can be translated to “living one” or “joyful,” a personality I thought would be perfectly fitting for someone who loves to help. Therefore, Ava was created to be a helper T cell in my story. She is also a main character, for her role as a helper T cell is crucial in the organization and recruitment of other immune cells in the formation of an immune response against cancer. Which helper T cells accomplish by communicating with other cells by secreting chemical signals. Since she helps, I use her voice often throughout the story to explain the more complicated subjects, like science terms and settings or parts of the body.

Neo

A story about Acute Lymphoblastic Leukemia (ALL) needs an explanation for how this type of Leukemia started. For that I created the character of Neo, a newly made immature B cell born in

the red bone marrow like Tim. I wanted the audience to see one B cell that was born with the mutation, although multiple B cells in ALL can be born with a mutation at the same time. The purpose for Neo was not only to show how this mutation starts the replication of cancerous clones, but for the reader to see that these cells carrying the mutation are not evil cells. They are just cells who had something wrong with their DNA, even though they are called malignant, they are not to be feared. After all, like Neo, they can't control the fact that they carry a mutation that causes ALL either.

Bebel

Bebel is a Natural Killer cell; these cells specialize in fighting virally infected cells and cancer cells. The reason for why I needed a Natural Killer cell in the story, is because Natural Killer cells are the first to encounter the cancerous clones or cells, and then call on T cells for help. As you can see on Bebel's nucleus, he has multiple differently sized dots which represent the cytokines and toxic granules that this type of immune cell uses in order to penetrate the infected cell's membrane and kill it.

Brielle

Brielle is a B cell who Ava calls upon to keep Neo company in the red bone marrow while her and Tim make their trip to the thymus. Brielle is a minor character in this story, but she is there to represent the other B cells that don't carry the mutation and are healthy.

Parts of Human Body and Settings for the Story

Red Bone Marrow

Both Red Blood Cells (RBCs) and White Blood Cells (WBCs) are created in the red bone marrow. Red bone marrow can be found in the majority of flat bones, like hip bones, and towards the heads or tips of long bones, like a femur (thigh bone) or humerus (arm bone). The red bone marrow is the main setting in my story, because ALL is cancer of the bone marrow. You can see that in the beginning of the story the red bone marrow background is red, but when Ava and Tim return it is more of a brown and bone color. This was my way of representing the cancer of the bone marrow and less RBCs being present.

Blood Vessel (and Lymphatic System)

In the story we see Tim and Ava traveling from a source of red bone marrow to the Thymus in order for Tim to mature. Blood vessels and the lymphatic system are what white blood cells use as a means of transportation through out every part of the body. For the sake of simplicity, I chose to illustrate this transportation as the inside of a tunnel-like structures representing the inside of blood vessels.

Thymus

The Thymus, located behind the breast bone, is the site where an immature T cell matures, goes through selection and differentiates or identifies with a specific T cell role, depending on the antigen that is presented to it by an Antigen Presenting Cell. This location was important to the story, for it is where Tim matures and becomes a Cytotoxic T cell and is able to recognize the cells with the cancer marker. The scene in the Thymus is important for the reader to understand how specific roles are assigned to T cells. Ava in this story has already become a helper T cell and has been through this maturing and selection process herself. The reason for why I didn't

show this for her though, was because I wanted her to be a mature cell from the start so that she could help Tim.

Although these were the key settings for my story and plot, immune cells can be found everywhere throughout the body. Not just the locations mentioned in my children's book.

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