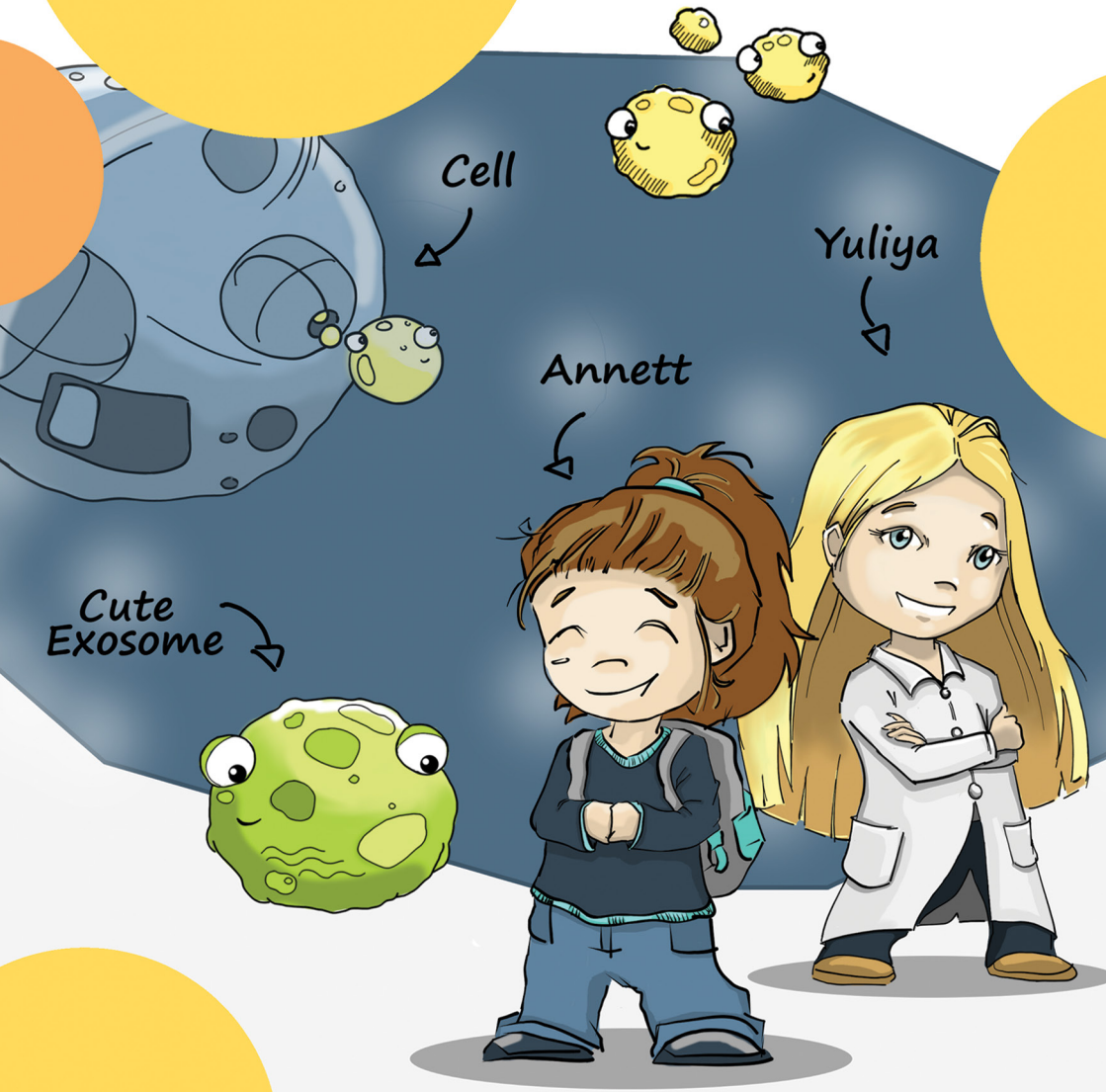
Yuliya Shakalisava & Annett Mueller

# Catch the Exosomes




An educational booklet about the fascinating world of exosomes

## Acknowledgements

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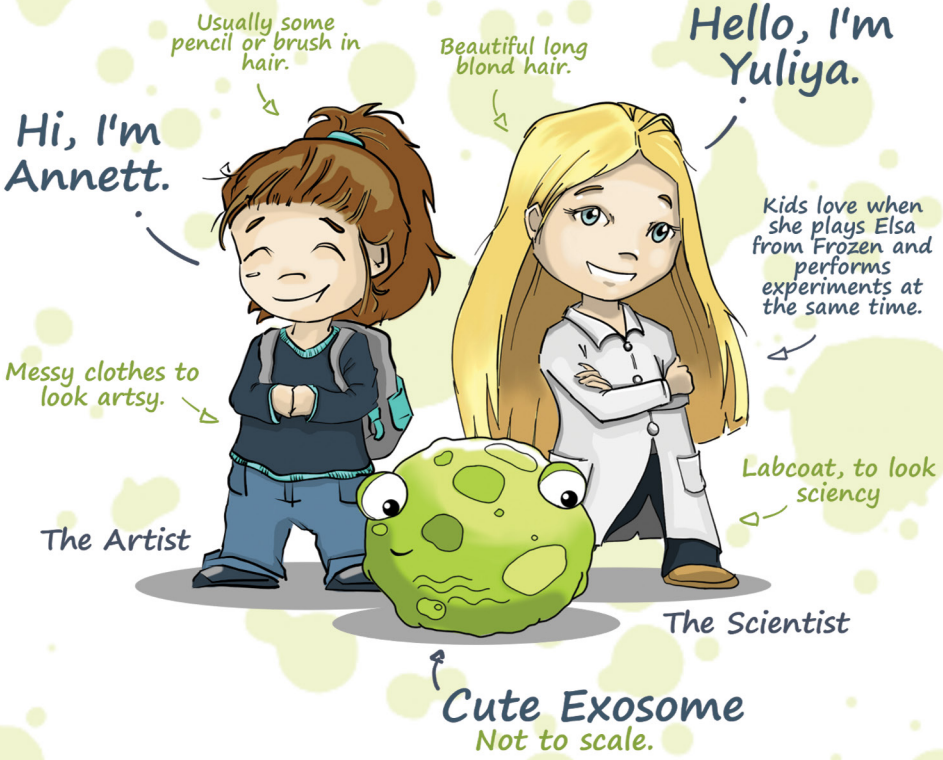
# Catch The Exosomes

An educational booklet about the fascinating world of exosomes

by
Yuliya Shakalisava and Annett Mueller

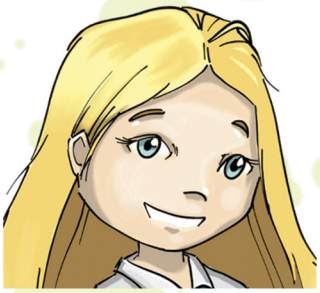



Text and Illustrations: SciViz Buddies

# Who we are...

This educational booklet was developed as part of an outreach project and aims to explain what we know about exosomes and interesting research in this area in an easy to understand and entertaining way. Are you excited? Great.

Before we start, we just want to introduce ourselves real quick:



I am Yuliya and I am a scientist. I love my work in the lab. The field of my research is analytical chemistry. I like to analyze things. In my free time I read cool science literature and play accordion. I am also a mom to two beautiful daughters.

I am Annett. I am a biologist and an artist. I was never able to choose between art and science and so I just combined the two and became an illustrator for science communication and in this booklet I also got to be the storyteller. In my free time I can usually be found somewhere in nature or on a volleyball court.

# Content

## Part 1
What are exosomes?

## Part 2
Why are they so interesting?

## Part 3
Catch me if you can!

# Part 1
## What are exosomes?

Who am I?

# What are exosomes?

That was one of the first questions I asked Yuliya. And she answered...

Scientists always say that!

"Well, that is a really good question.

Exosomes are so called extracellular vesicles or EVs. They are very, very small and can be found in all body fluids.

They can carry messages from one cell to another. Oh yeah ... and THEY DO NOT HAVE EYES!"

But they look so much cuter with eyes...
...and how does she even know yet?

# Got it? Not really?

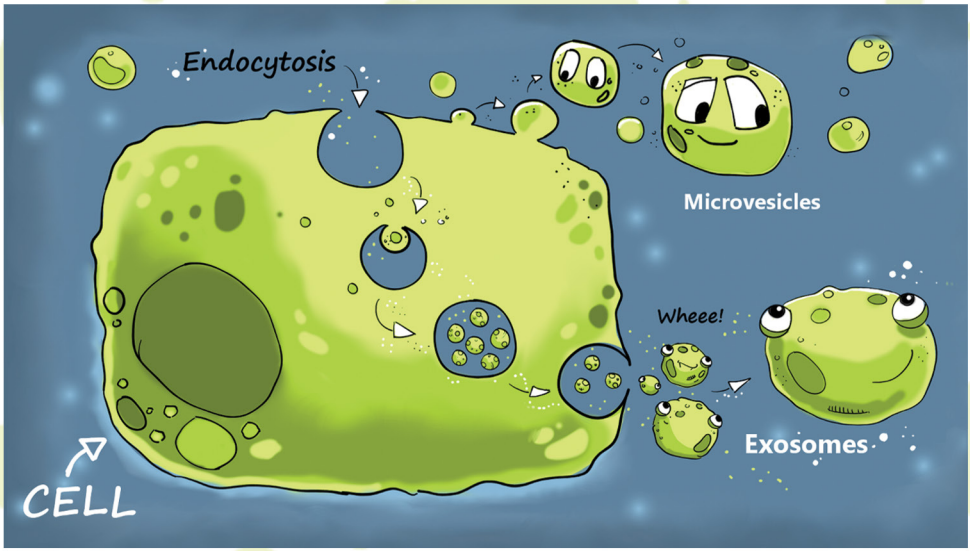
Well, don't you worry. That's what this book is for. We are going to explain everything in more detail. First I underlined all the important words in Yuliya's answer (which, given that she is a scientist is unfortunately almost every word...) and then hopefully I can make some helpful illustrations (or at least funny ones).

# Let's get started...

# Extracellular Vesicles (EVs)

You can think of extracellular vesicles (EVs) as tiny bubbles. They are produced by all the cells in your body. But not only that, the cells can release them into their environment. As a matter of fact, only then they are called EXTRAcellular vesicles instead of INTRAcellular (yeah... you will rock at that next pub quiz!).

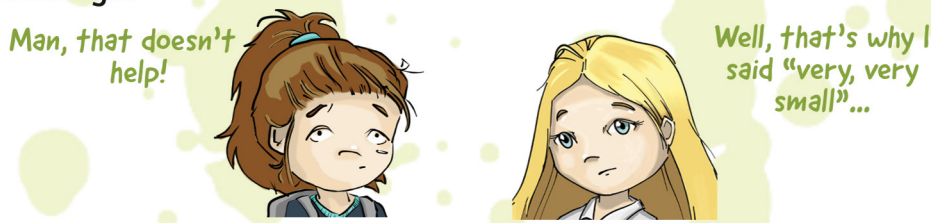
Exosomes are just one type of EVs. There are others and they are created in different ways. Exosomes develope due to a process called endocytosis. A cell folds its membrane inwards to build a bubble (the way you can fold a balloon inwards, by pressing your finger in it). Once the bubble is inside the cell it also folds its membrane inwards to build a smaller bubble. Once these bubbles leave the cell we can call them exosomes. Microvesicles on the other hand are formed by outward budding of the plasma membrane. They are of similar size or just a bit bigger than exosomes. And no, also no eyes unfortunately.




Biogenesis of cute exosomes and microvesicles. Both are extracellular vesicles.

# Exosomes are very small

Well, that is a somewhat vague statement coming from a scientist, haha! I asked Yuliya exactly how small 'very, very small' is and she said between 40-150 nanometres... and I just stared at her blankly...




Alright. 1 nm is 0,000 0001 mm and of course that doesn't help us either. Maybe you have an idea if you think an exosome is about 1000 times smaller than the thickness of a hair. No? Still not working... well, ehm... let's just say exosomes are very, very small...

# They can be found in all body fluids

Really means just that. They are everywhere! From blood, saliva and sweat to tears. Exosomes have been detected in all body fluids that have been tested. This is very handy, because you do not need to perform some complicated surgery to get them. It is enough to make someone cry... (just kidding).


Body fluids stored in totally inappropriate storage containers, with bad labels and under questionable storage conditions.

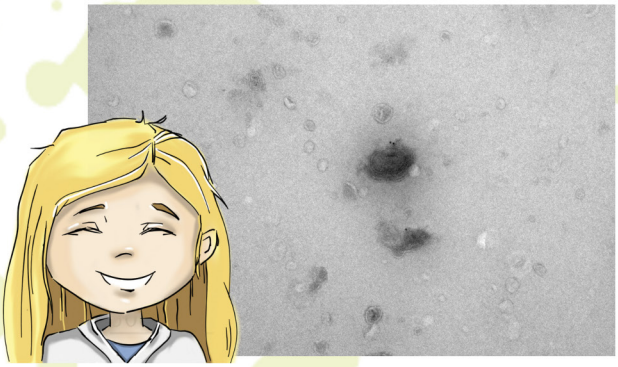
# Exosomes carry messages

This is actually one of the reasons why scientists are so interested in them. In the past exosomes where thought to be just the cells waste products, when in fact they play an important role in cell-cell-communication.
We will talk about that in more detail in the next chapter.

# Exosomes do not have eyes

That again... I bet you can't prove that they do not have eyes.

Actually, I can. Look! This is a picture of exosomes, that was taken under a Transmission Electron Microscope. See – No eyes!

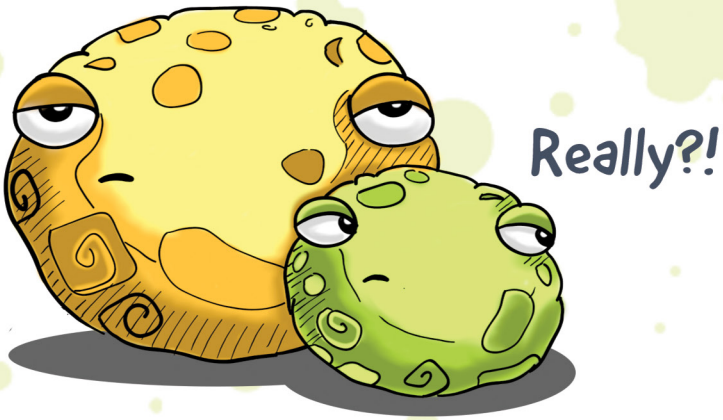


Well, ok. Turns out exosomes do not have eyes and the best part of being a scientist is being right ALL the time* (sigh!). BUT... The best part of being an artist is: Sometimes I can bend reality a bit and get away with it. And come on, admit it. They definitely should have eyes. It's just adorable!!!

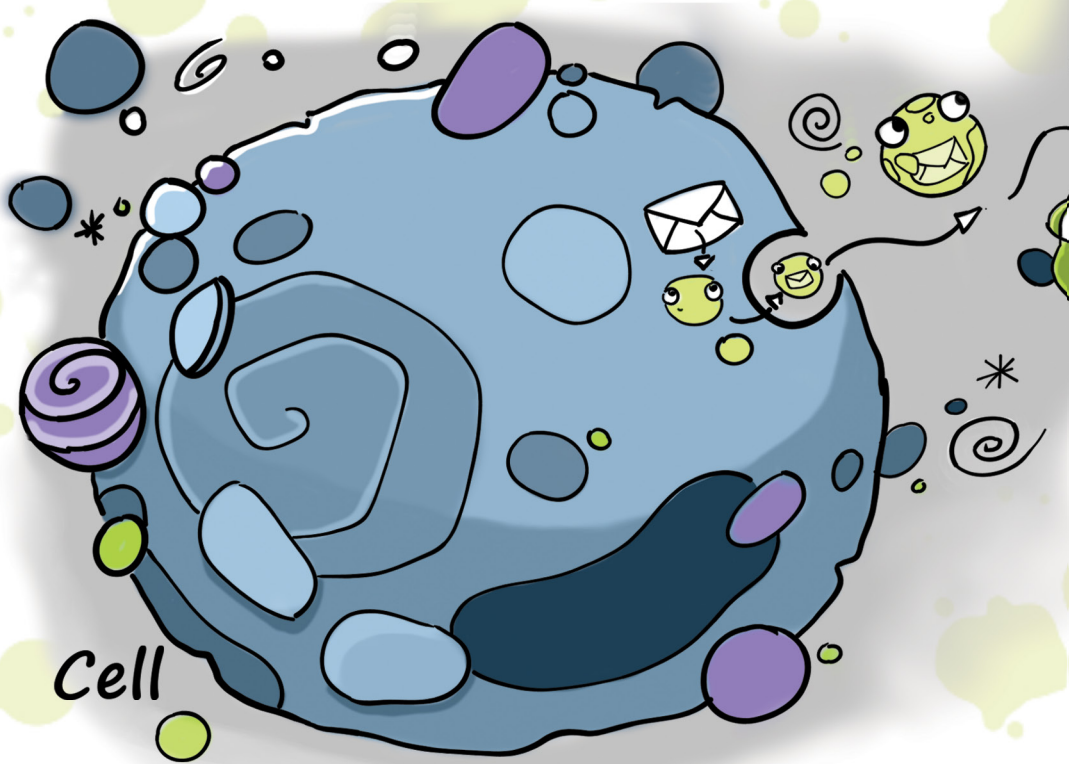
*Caution! One part of this sentence is not true. You may choose which one ;).

# Part 2

## Why are exosomes so interesting?



Extracellular Vesicles (EVs) were discovered about 50 years ago and scientists thought that they were only a way of the cell to get rid of waste products. But then, starting in 1983, some people looked closer and found out that EVs can be transferred between two cells. That means they play an important role in cell-cell-communication. What makes this so interesting is the fact that an EV (e.g., an exosome) will contain whatever message it is given by the cell that it comes from. For example, it takes up lipids, proteins or RNA and leaves the cell to carry these to another one. The other cell will take in the EV and now has all the information. They are basically little delivery guys.




This is good news and bad news. Good news, because cells have a way to communicate to each other, and you know: It's always good to have a great communication system. The bad news is, that exosomes and other EVs will carry any message that is given to it by the cell. That means they may also transport messages from "sick" cells and make the next cell "sick" as well. So, scientists suspect them to play a role in developing and spreading of several diseases (e.g., cancers, Alzheimer's disease).

# Wait...! What?

I thought you said they were amazing and potential superheros...?
That sounds awful.
It does, doesn't it? - BUT they could also be really helpful.
Especially in 2 ways:

**Don't shoot the messenger!**

## First:

The exosomes that indicate a disease can be found in all body fluids, just like all other exosomes. So, it is very handy to collect them. This means we could develop a blood test for example and use them to diagnose certain diseases.

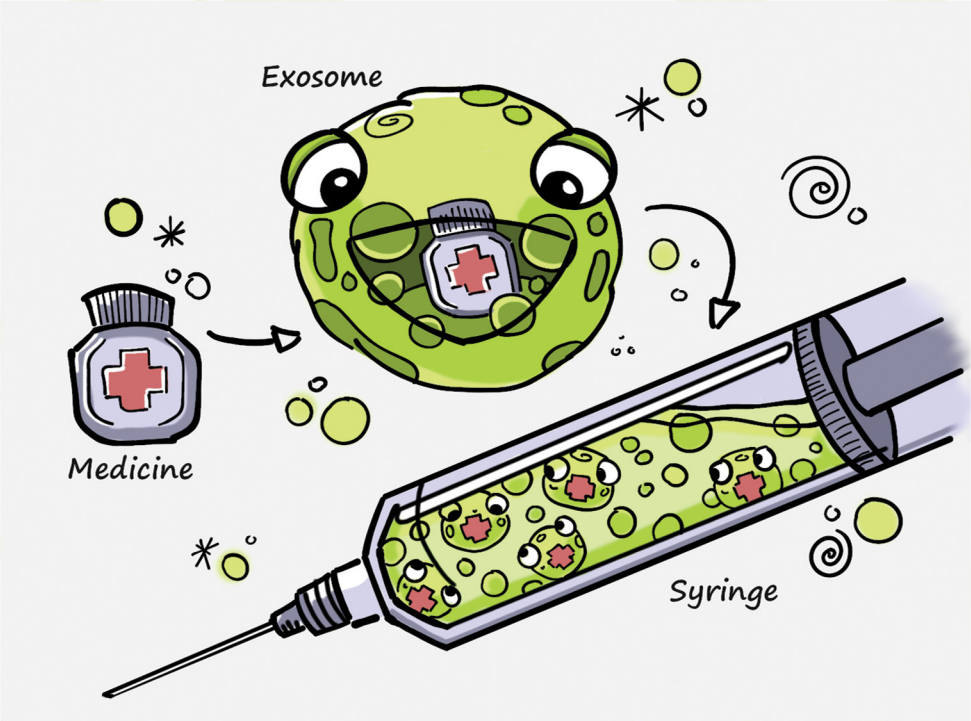
This is especially handy for those cells that are really far away and well hidden in our body, like brain cells.

No more need for invasive surgery once we have a good way of catching exosomes from body fluids!


Yeah, we all have loads of different exosomes in our bodies, coming from different areas.

# Second:

The fact that exosomes are just happy to deliver things (like a really good postman, never checking what's inside a package), they could also deliver drugs.



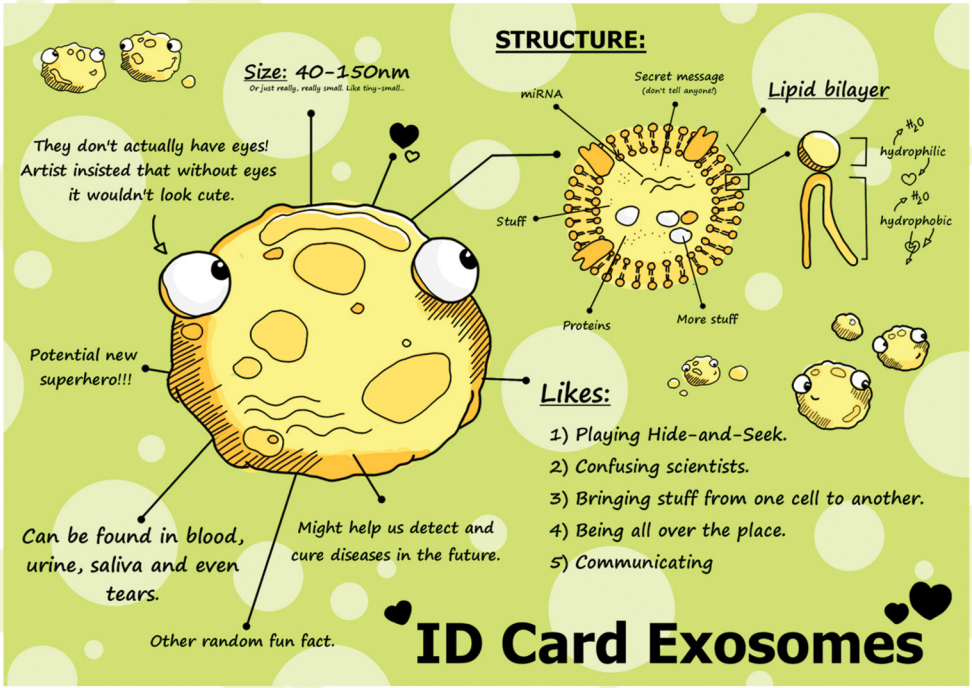

At the moment viruses are often used to deliver drugs (or therapeutical genes) into cells, but often the immune system of the patient reacts because of the virus as transport vehicle. If we could use exosomes there should not be an immune reaction because the cell does recognise the exosome as "an old friend" and not an "intruder".

# Summary/Cheat Sheet

Here is a little summary of what we already learned. Psst... it can also be used as a cheat sheet for those of you that really would love to but just can't find the time to read through the whole booklet.

## Exosomes...

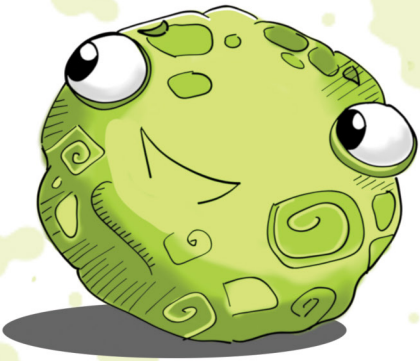
- are awesome.
- are made by all cells.
- can be found in all body fluids.
- deliver things and messages from one cell to another.
- may or may not have eyes.



# Part 3

## Catch me if you can!

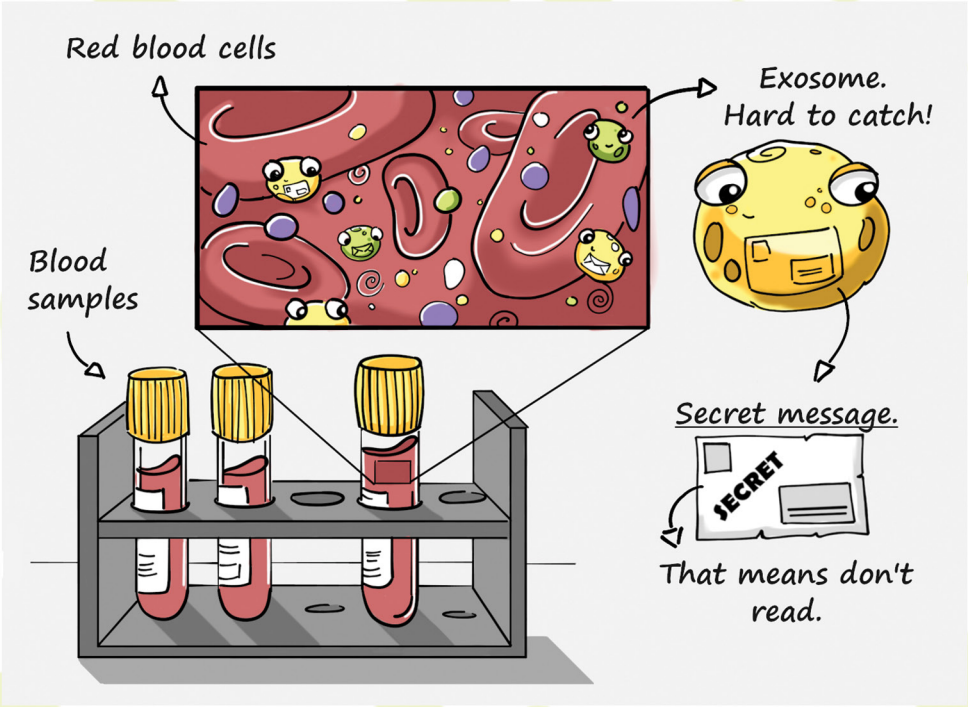
Come on!
It's gonna be fun.



# Excellent. What are we waiting for?

We now know that scientist would love to get their hands on the messages the exosomes are carrying. Nosy peope!*

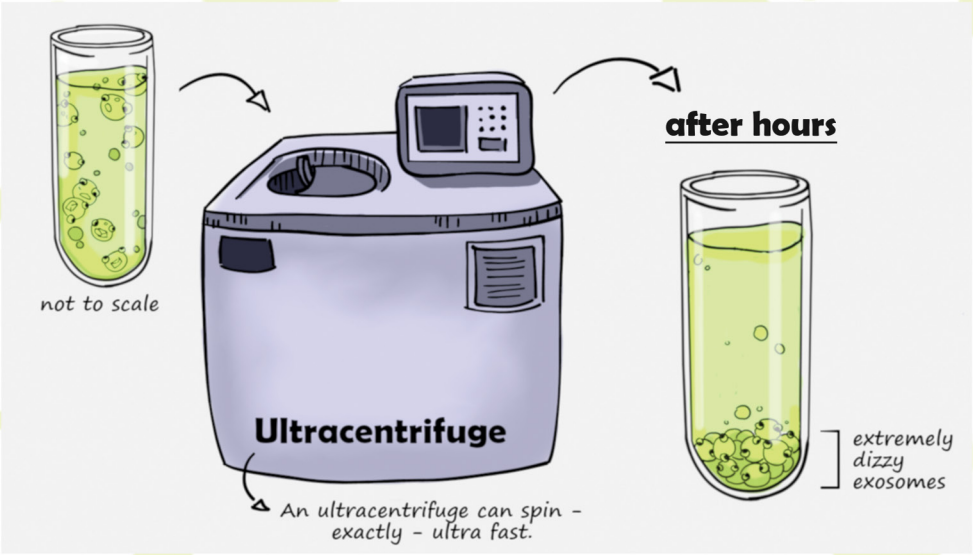
But before they can read these messages (which might as well be very private statements of affection... ever thought about that, science people? ...) the big challenge is to get the exosomes out of the body fluid (commonly out of the blood or urine).




* ok, ok ... tyou guys also try to help cure diseases by doing so. Just try to avoid reading the love letters, alright?

There are methods to get exosomes out of the blood or urine. We can spin them at a really really high speed in an ultracentrifuge until they are very dizzy and roughly in the same place.

The ultracentrifuge is a centrifuge optimized for spinning a rotor at very high speeds, capable of generating acceleration as high as 1 000 000 g (approx. 9 800 km/s²). Impressive, right?




Before we put the exosomes into the ultracentrifuge, we already separated them from a lot of other stuff with a normal centrifuge.

Of course, after a few hours in such conditions the EVs feel a bit bruised and battered, so scientists have developed faster and gentler methods to isolate them such as size exclusion chromatography or tangential filtration.

Another way is to use the special way they swim in liquids (density) to take them out.

But the thing is, it either might take very long time or there might be some other stuff in the sample that is the same size and density (lipoproteins). So, scientists are always scratching their heads to find a better way.

Yuliya, scratching her head and pondering ...

And this is what Yuliya's research is all about. She is trying to find a new way to get exosomes from blood. One that doesn't take forever and only collects exosomes and not all kinds of other things.

She also likes working with things that are very small - "micro". There is a technique that uses liquids in tiny channels/tubes, it's called microfluidics. So, this is the perfect fit.

## Micro-WHAT?!?

I know, I know. Just when you thought you got a broad understanding I throw in some other confusing term - blame science or Yuliya ;) ! But it's really quite interesting, I promise.

If you hear someone talking about microfluidics they talk about one of the following two topics:

1: The science of how fluids work in very tiny spaces (like channels that are smaller than a millimetre).

2: The technology of manufacturing microfluidic devices in which we can study how fluids work in tiny spaces.

The advantages of using microfluidics compared to conventional methods are:

- you only need a very small amount of sample
- it can be very fast (minutes)
- the device can be designed to conduct many experiments in parallel and that's pretty handy when you want to analyse a lot of samples.

What Yuliya does in the lab to separate exosomes is using the microfluidic format but also very different physical properties of exosomes - electrophoretic mobility (or how fast they move in the electric field). It is a very unique property to each molecule or particle that has a charge in the electric field.

This is how Yuliya's microfluidic device looks like.

The results are already promising that this method will allow us to separate exosomes from all other stuff that looks pretty similar. And we don't even need a whole day doing it.

# The end

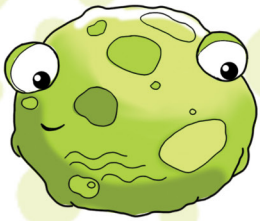
At least for this little booklet.
Yuliya is continuing with the development of the device and works on bringing the technology to the market with her startup EXIT071.

EXIT071

www.exit071.com

Keep in mind that scientists are still unsure and sometimes even disagree on many things related to exosomes. We need to do a lot more work to answer all the questions.

If you like my illustrations, come and visit me at:
www.scivizbuddies.com



See you in the lab!