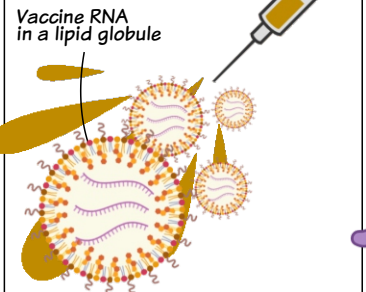


ONCE UPON A TIME... AN RNA VACCINE

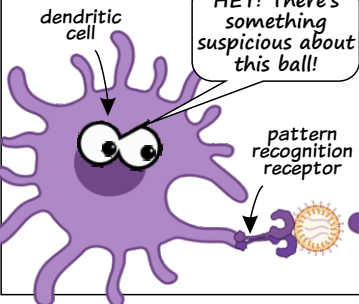
EPISODE I: ANTIBODIES STRIKE BACK @MikaelNiku

Veterinary Biosciences, University of Helsinki, Finland

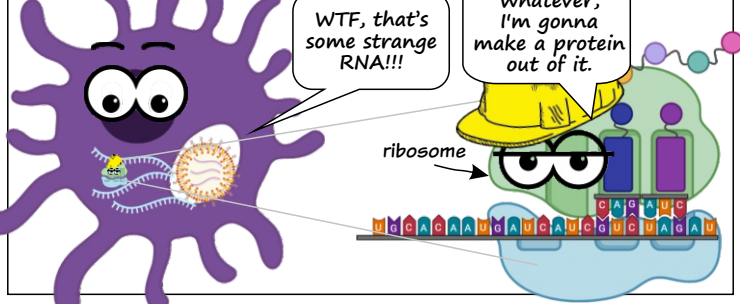
An RNA vaccine is a synthetic strand of RNA that codes for the coronavirus spike protein, packed into lipid globules.



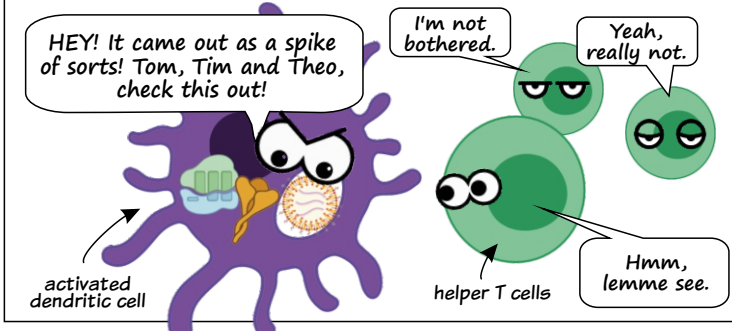
Dendritic cells are the border guards of the immune system with the mission of identifying structures typical of bugs.



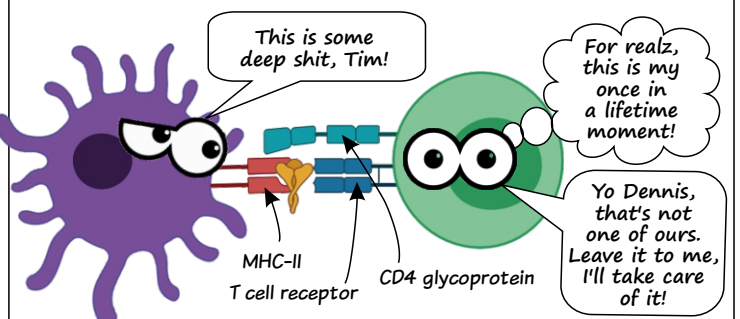
Dendritic cells pull the vaccine globules inside themselves, admitting the RNA to the cytoplasm. Cellular ribosomes manufacture the protein the RNA codes for, just as if it were the cell's own messenger RNA. Structures typical of bugs activate dendritic cells.



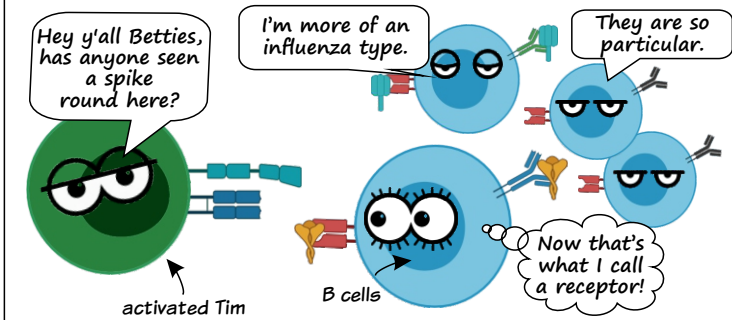
Dendritic cells present the viral spike produced by the vaccine (conventional vaccines already contain it). Helper T cells are the officers of the immune system who, when necessary, initiate full-scale defences.



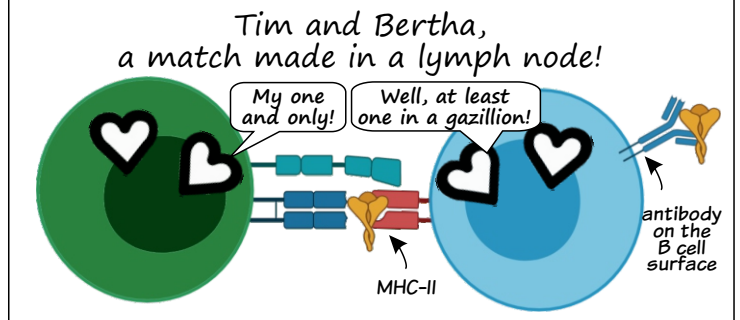
The viral component is carried by MHC protein molecules, and helper T cells identify it with their T cell receptors. Each helper T cell has a unique receptor that is capable of recognising only a single target that is foreign to the body.



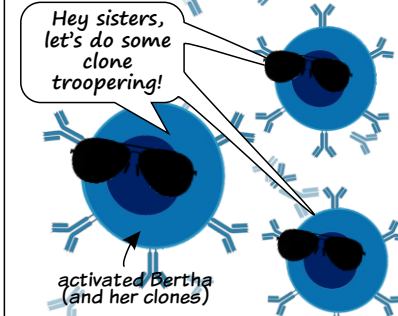
Helper T cells activated by dendritic cells are now able to kick into gear the rest of the defence system, such as antibody-producing B cells. But they only activate the B cells that have recognised the same target.



Each B cell also produces a specific antibody. When a B cell and a helper T cell that both recognise the coronavirus spike meet, the T cell activates the B cell, giving it permission to act.

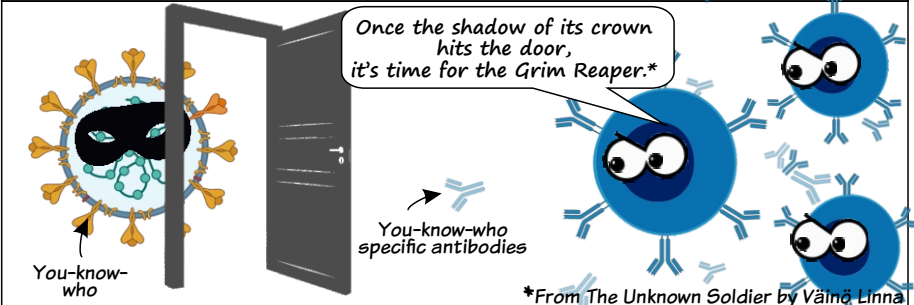


The activated B cells divide, resulting in a large group of B cells that recognise the same target: the coronavirus spike.



Later, in an overly popular all-night cafe ...

If the actual coronavirus enters the body, it will face B cells and the antibodies produced by them, targeted precisely at the spike protein of this specific virus. The antibodies attach to the spike and prevent the virus from functioning. The immune system also includes other fighting troops, but that's a story for another time.



English translation by Lauri Mäkelä, edited by Julie Uusinarkaus, University of Helsinki Language Services
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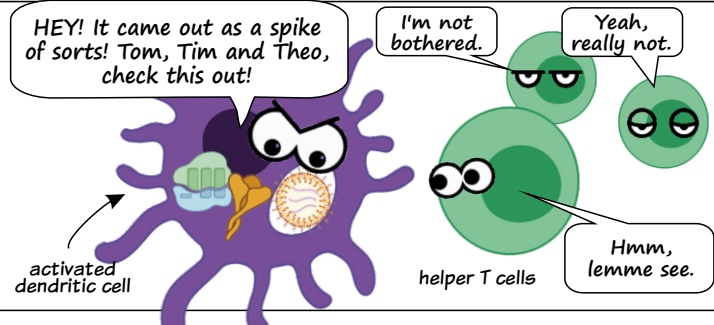
That's not all, folks! Also check out **Episode II: Attack of the T Cell Clones**

ONCE UPON A TIME... AN RNA VACCINE

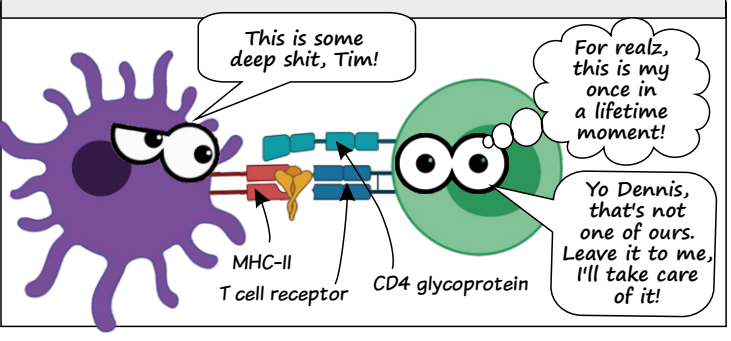
EPISODE II: ATTACK OF THE T CELL CLONES

@MikaelNiku Veterinary Biosciences, University of Helsinki, Finland

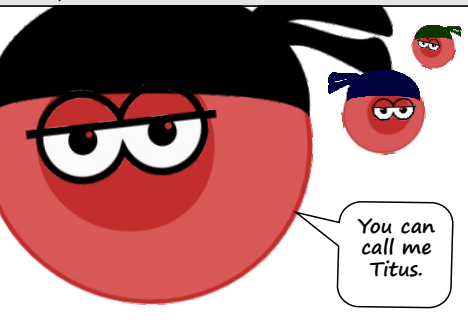
In the previous episode: dendritic cells ate the vaccine globules, and the vaccine RNA initiated the production of the coronavirus spike protein in the cells. The vaccine globules and the tuned-up RNA activated the dendritic cells to let T cells know that the spike is a bad guy.



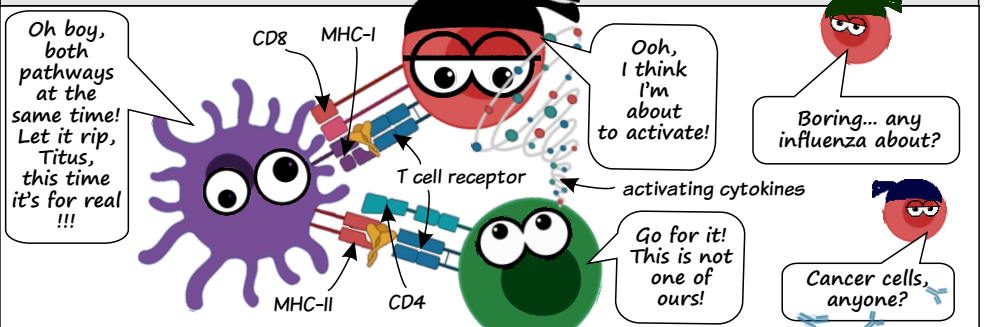
You know the drill: using their receptor, helper T cells recognise the viral component carried by MHC molecules. Each helper T cell has a unique receptor that is capable of recognising only a single object that is foreign to the body.



Now, a third figure appears, a baby-faced killer: the cytotoxic T cell. Its mission is to kill any corrupted cells.



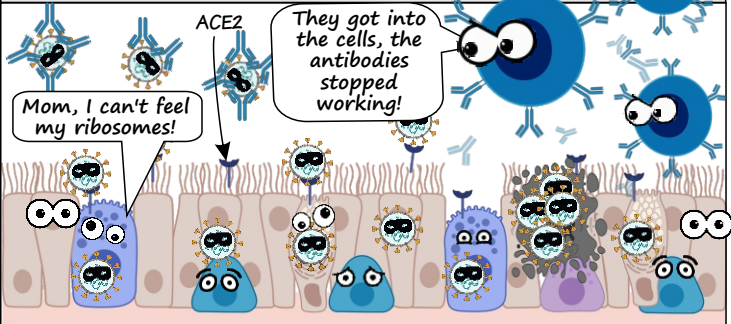
Titus is a contract killer, and for safety reasons both Dennis and Tim are needed to activate it. Like helper cells, each killer also has a specific target. Titus only kills cells with the coronavirus spike on them.



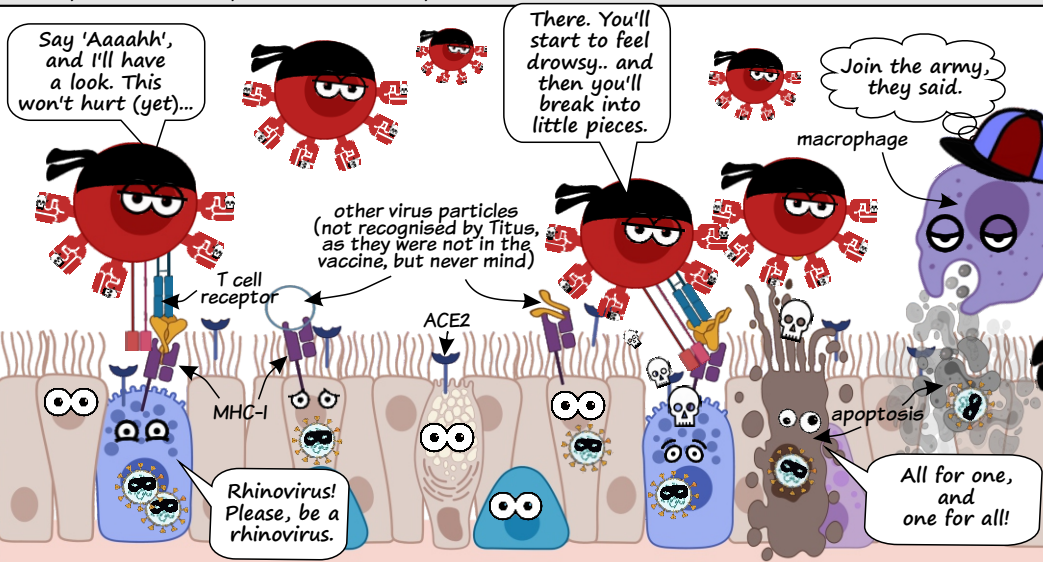
The activated killer Titus is like the Phantom, only armed with a hundred fists, each with its own skull ring. Titus divides, and suddenly there are a gazillion Tituses in the body, all of them targeting the coronavirus spike.



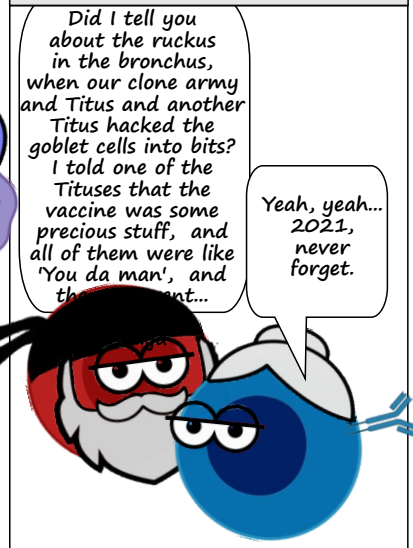
One day the action starts: a coronavirus attack which antibodies are unable to control entirely. Epithelial cells in the airway are infected by coronavirus.



Epithelial cells reveal their viral infection by presenting viral components on their surface. Killer T cells give the cells that have turned into viral factories the order to initiate self destruction, or apoptosis. Macrophages clean up the mess, and epithelial stem cells repair the damage.



Some T and B cells become long-lived memory cells which remain ready and waiting, should the virus take another shot later.



ONCE UPON A TIME... AN RNA VACCINE

EPISODE III: THE VARIANT MENACE

@MikaelNiku
Veterinary Biosciences, University of Helsinki, Finland



Once a virus enters a cell, it starts to replicate. An enzyme called RdRp (RNA-dependent RNA polymerase) produces copies of the viral genome using components pilfered from the cell.

You can call me AI.

AI is a good guy who happens to make mistakes every now and then (though the coronavirus polymerase is pretty accurate for a viral enzyme). The mistakes are known as mutations.

Now listen here, you whiner. You can't make an omelette without breaking eggs. Do it yourself if it's not good enough for ya! Oh yeah: you people can't even copy RNA from RNA!

New viruses produced on the basis of the mutated genome are called variants. Since mutations often have no effect on the virus, they only matter to viral genealogists. Some mutations render the virus useless. However, some mutations alter the virus's functioning in a way that may be harmful to humans. These are known as Variants of Interest (VOI).

ordinary variants (no visible change)

variant of interest (VOI)

unfortunate variants

HEY! Where my spikes at!?

Sorry buds, AI's tail-light warranty just expired.

Is that the KING?!?

Why do I have streamers in place of my genes?!?

Some of the VOIs can actually turn out to be increasingly feisty viruses. They are called Variants of Concern (VOC).

VOC B.1.1.7

VOC P.1

VOC B.1.351

The spikes of the Brit... er, the B.1.1.7 has a mutation that makes it cling tighter to the surface of human cells, which is why this variant is more easily transmitted.

In addition, the South Af... the B.1.351 variant and the Bra... the P.1 variant have spikes whose shape is different enough to prevent the antibodies designed for the standard model spikes to properly attach to them.

an ACE2 receptor on the surface of a human cell

a spike on the surface of the B.1.1.7 variant

a perfect fit!

not a match!

an antibody induced by a standard model vaccine

BERTHA! Wake up!! I caught a REAL virus!! Remember this spike? Wasn't this in the vaccine?

Sorry Dennis, but he's not really my type.

Are you in Wuhan tonight? Do you miss me tonight? Are you sorry we drifted apart?

a B cell activated by the standard model vaccine

a shredded virus

It takes a couple of weeks to train new lymphocytes.

This here is a c-o-r-o-n-a-v-i-r-u-s.

Do I really have to start from the beginning AGAIN?*

naive B cell

helper T cell

For realz, this is my once in a lifetime moment! Hey, déjà-vu!*

* See Episode I

Wow, things can get ugly in no more than a couple of weeks?! I know! Fortunately some of the B cells are able to identify the variant as well. And you didn't forget about T cells, did you? They kill infected cells to prevent the virus from replicating - and they are not as easily fooled by variants! Thus, even the coronavirus bogeyman is reduced to a bout of flu for most people.

What, didn't we have a couple of weeks for reckless abandon?!?

But we got a head start thanks to the vaccines!

I don't understand what Bella sees in those guys!

These guys thought they'd be safe and sound inside cells. Thanks for the tip! You'll feel a small pinch.

The pleasure is all my neighbours'.

T cells instruct the infected cells to die a clean death

Macrophages clean up the mess (and bits of virus)

Yeah, yeah.

Keep your chin up, mates! I'm outta here.

bronchial cells

ACE2

English translation by Lauri Mäkelä, edited by Julie Uusinarkaus, University of Helsinki Language Services
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SARS-Cov-2 RNA polymerase structure: David Goodsell / Protein Data Bank Molecule of the Month 9/2020 (doi:10.2210/rcsb_pdb/mom_2020_9)