Current research topics in immunology

And their difficulties and pitfalls

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Topics

1. What is happening
    a. In a healthy environment
        - Development of the immune system
        - Interaction of immune cells
    b. In a disease environment
        - cancer, autoimmity, disease, substance
2. How can we use the immune system

What is happening?

Development of the immune system

The development of immunity occurs during two separate phases.

1. The first takes place during fetal life. It is characterized by the production of immune cells (phagocytes and lymphocytes) with surface receptors for a range of potentially antigenic structures. This **seems likely** to be a highly regulated process in that mechanisms **must exist** even during fetal life to eliminate any newly produced cells that might react with accessible self-components.
2. The second phase of immunity development is characterized by adaptation in response to antigen stimulus, which starts at birth and continues throughout life.

Hayward, A.R. (1986). Immunity Development. In: Falkner, F., Tanner, J.M. (eds) Human Growth. Springer, Boston, MA. https://doi.org/10.1007/978-1-4613-2101-9_19

Difficulties:

1. When is a cell a «macrophage» or «DC»
2. Some cells are replaced by more »mature» versions
3. Annotation difficulties because:
    1. Cells might have different markers
    2. Might not have reached their final destination

Interaction of immune cells

Interactions between immune cells share principles of cell–cell contacts that are common to other cells such as epithelial and neuronal cells, but they also show a specific uniqueness in their capacity to form and to resolve rapidly, as well as an unforeseen variability in their appearance and function.

Difficulties:

1. By-stander activation
2. Cell – cell interaction (immune- and other)
3. LOTS of interleukins and other cytokines

The disease environment

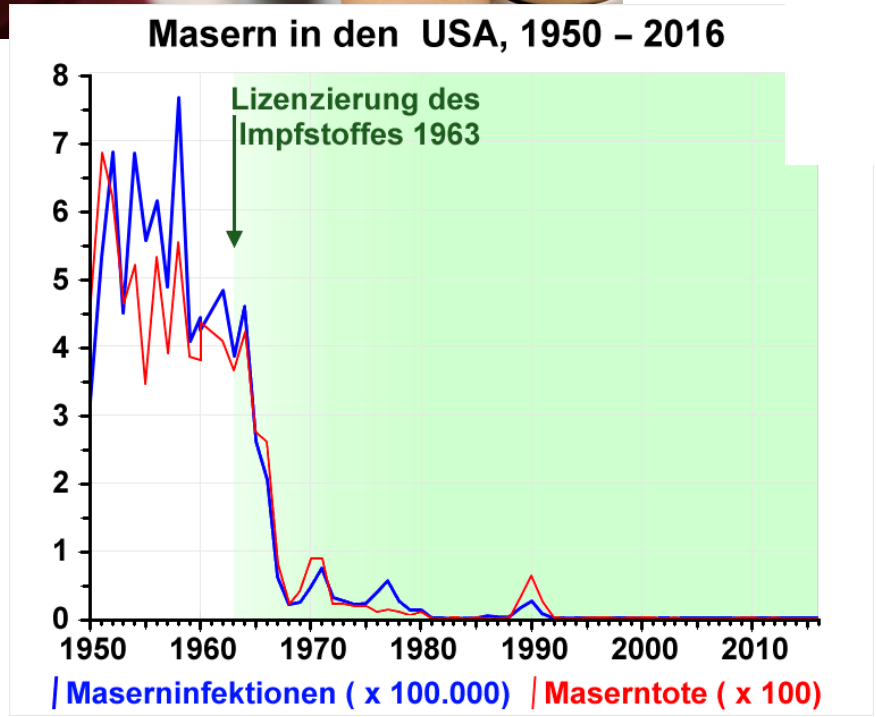
The tumor microenvironment is a complex ecosystem surrounding a tumor, composed of cancer cells, stromal tissue (including blood vessels, immune cells, fibroblasts and signaling molecules) and the extracellular matrix.

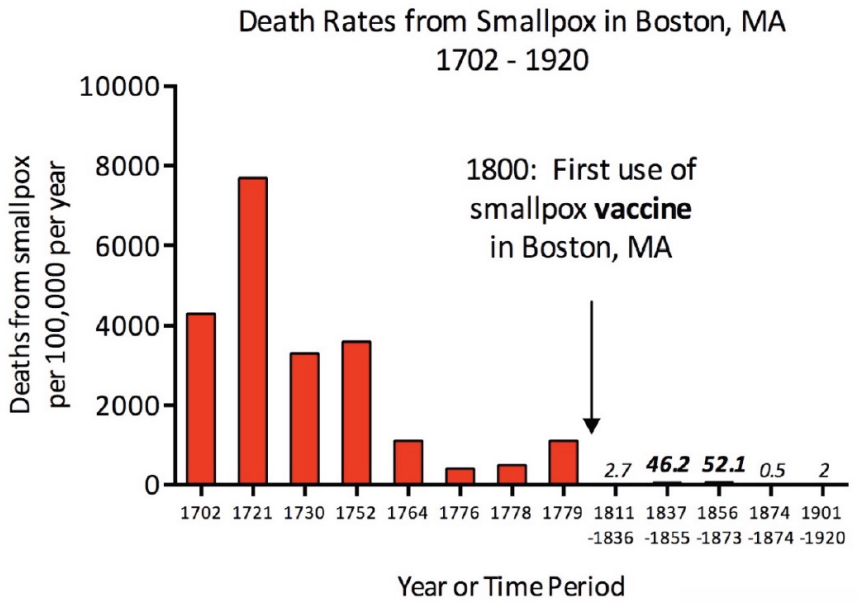
Difficulties:

1. When is a cell a «macrophage» or «monocyte»
2. Annotation difficulties because:
    1. Cells might have different markers
    2. Contains cells you might not expect there
    3. Cells are mutated to a point where annotation is difficult

How can we use the immune system

Vaccines





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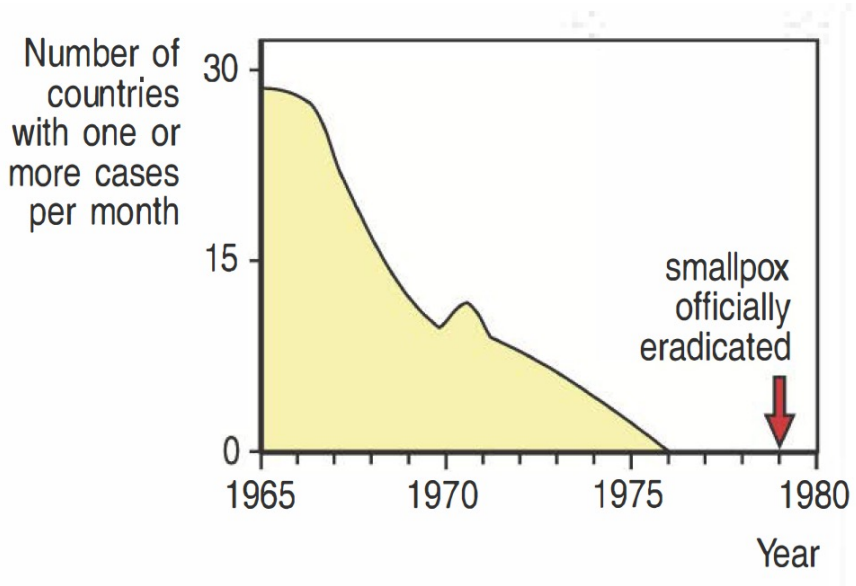


Vaccine (Protein)

1.) Formaldehyde

- Used to kill viruses
- Produced by the body when metabolizing alcohol (in toxic abounts).
- Every pear contains more formaldeyde than a dose of vaccine.

LD_{50} = 100 mg/kg -> 7g (70kg)
1 pear contains 0.17% of the deadly dose
7g/10mg = 700 pears = 210kg pears

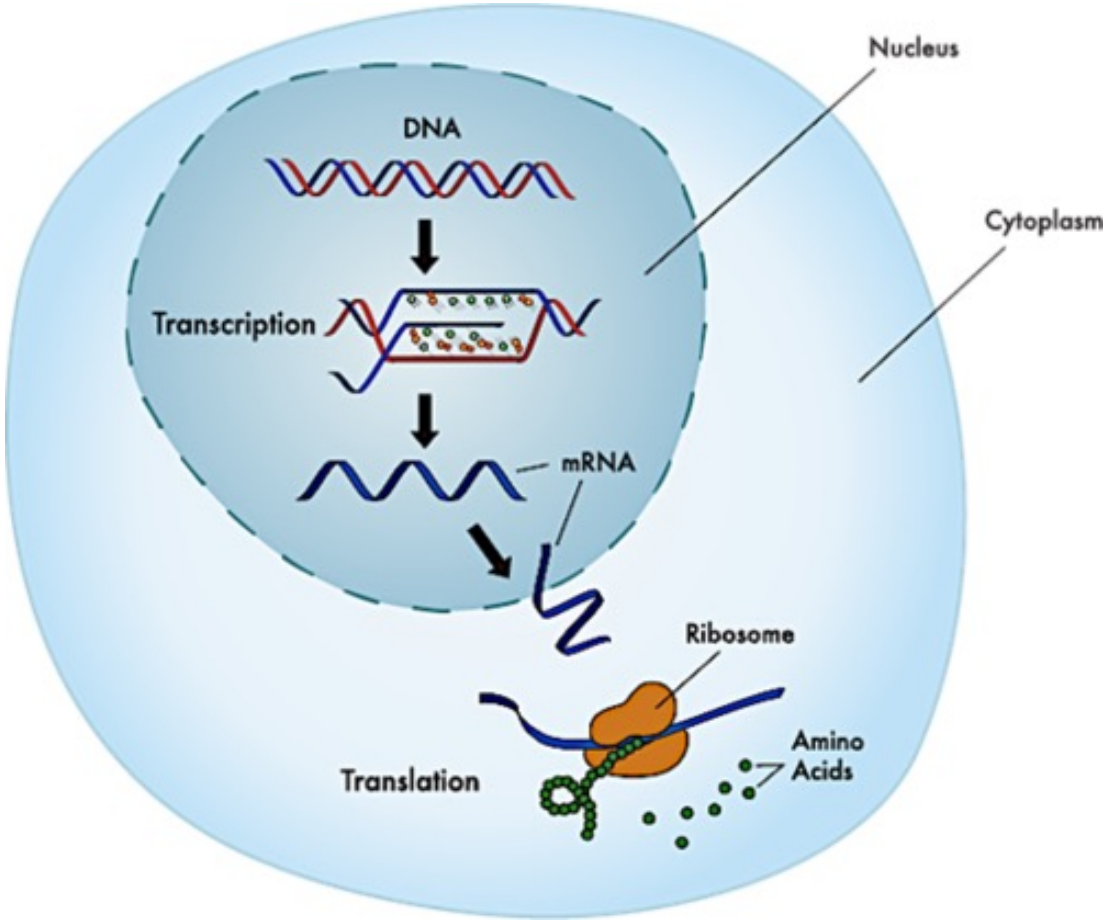
2.) Aluminium

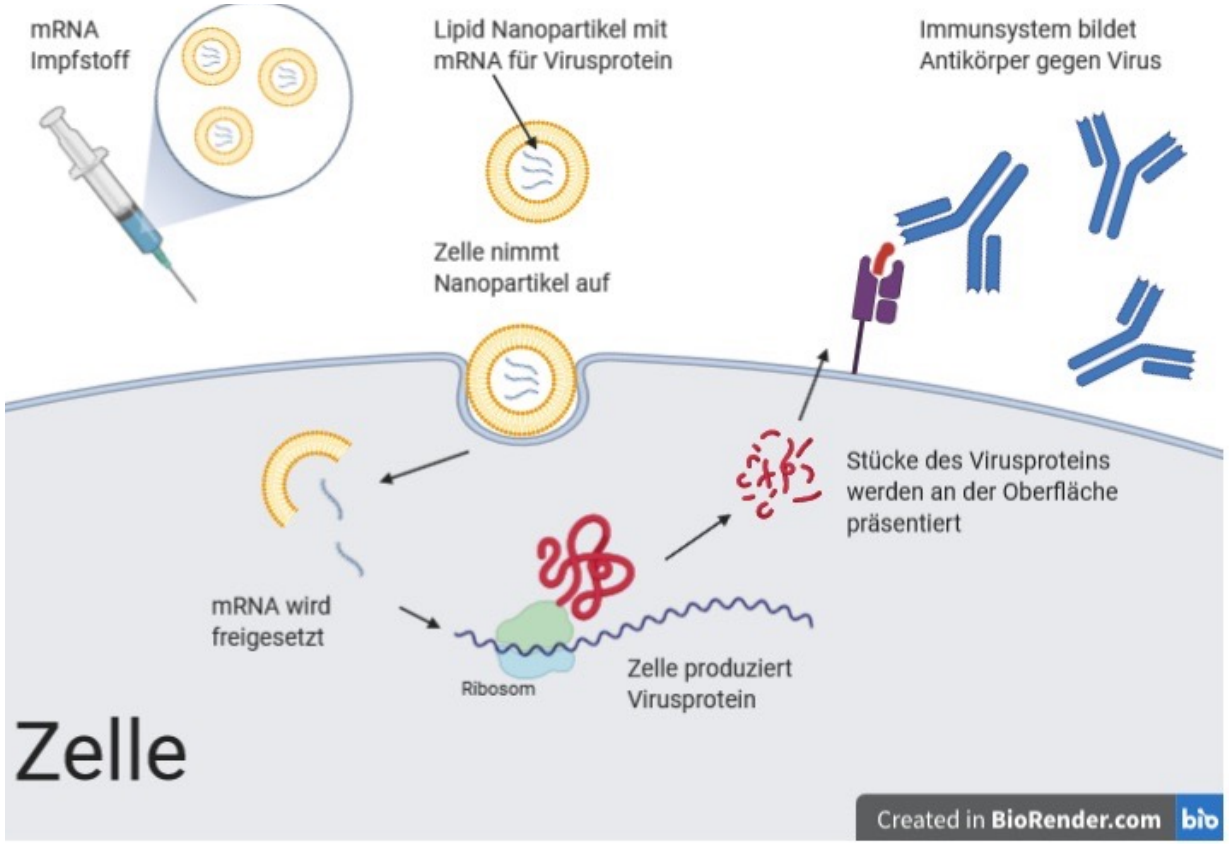
- Used as a «danger» signal
- An adult takes in 7 bis 9 mg aluminium per day.
- Vaccines currently on the market contain 0,125mg to 0,85mg

LD_{50} = 320 - 1587 mg/kg -> 22 – 111 g (70kg)
vaccine (1mg) = 0.004% - 0.0009% of the deadly dose

Vaccine (RNA) (BioNTech, Moderna, CureVac,...)

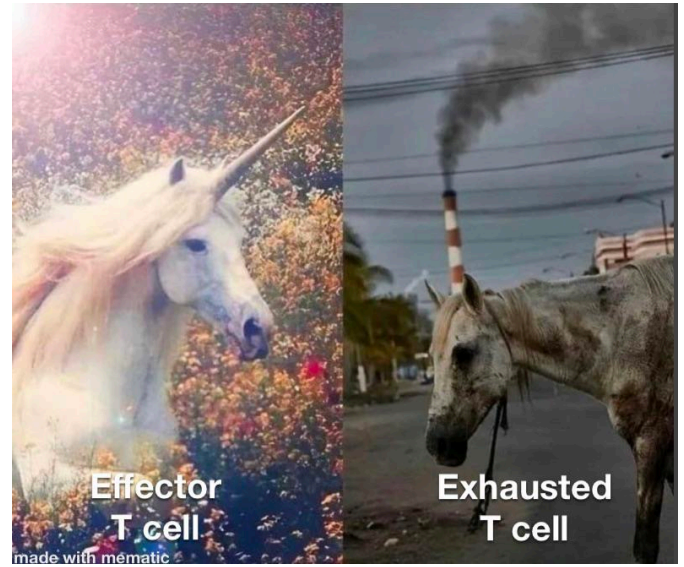
How does the RNA get into the cell?



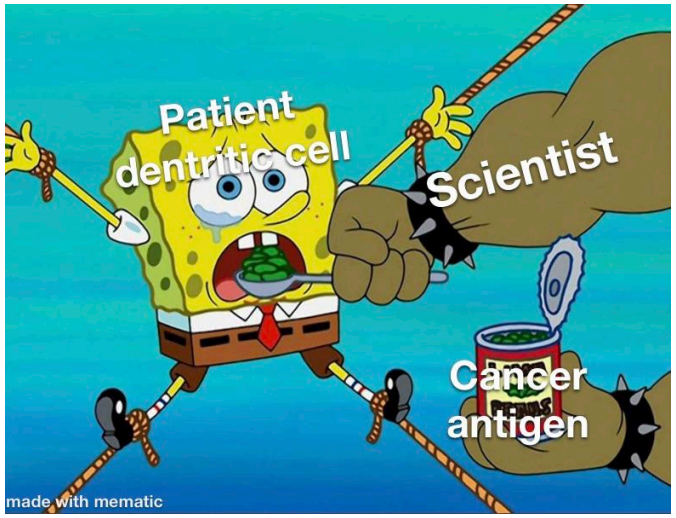


Cancer treatment

Checkpoint blockade
When T cells (specially $CD8^+$ T cells) see “too much” antigen they become exhausted and stop killing their target cells. This is a natural protection against autoimmune activation. Some drugs can prevent exhaustion and keep the T cells activated.



Car T cells
T cells are extracted from a patient and mutated to recognize a specific (tumor) protein. After injecting back into the patient, these CD4 or CD8 T cells get activated.
The protein currently used is CD19, the B cells marker.
Patients who received a car T cell therapy do not have B cells anymore and the treatment can not me stopped or revered.



Adoptive Cell Therapy
DC or T cells (TIL – Tumor infiltrating lymphocytes) are extracted from the patient and expanded in vitro. DCs are loaded with cancer antigen. After injection back into the patient the hope is they lead to an increased response against the tumor.