

# SARS-CoV-2 ASEP seminar

Prof. Dr. Klaus Eyer

Assistant professor IPW

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- Due to the time frame, we will try to touch as many topics as possible as deep as possible
- If you need additional information feel free to use the Q and A session
- Various level of information – we are trying to strike a balance here

In this first part, we will

- **get some basics of vaccines and vaccine-mediated protection,**
- **talk about different vaccine formats,**
- **and the chances and risks of mRNA vaccines,**

guided by your questions.



# Vaccine-mediated protection

Immunization (WHO):

- Key component of primary health care
- Critical to the prevention and control of infectious-disease outbreaks
- Prevention: amongst the best health investments

## Key concepts:

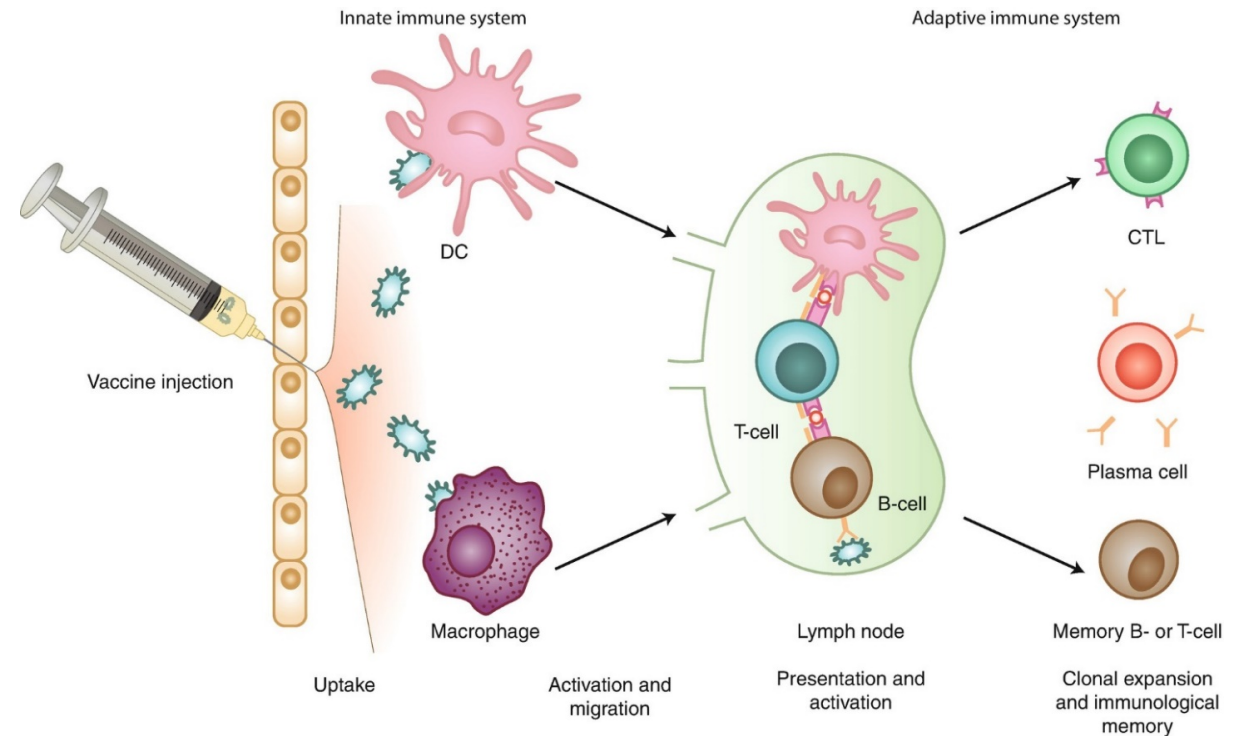
### Protection and long-term memory

Vaccines need to induce effector functions (such as neutralizing antibodies) to be protective; these functions need to be present over time

### Initiate and sustain the immune response

### Antigen as well as formulation thereof

What does vaccination do to our body. How does it make us immune?



Jiskoot *et al.*, *Pharmaceutical Biotechnology*, 281-304, 2019.

# Vaccine-mediated protection

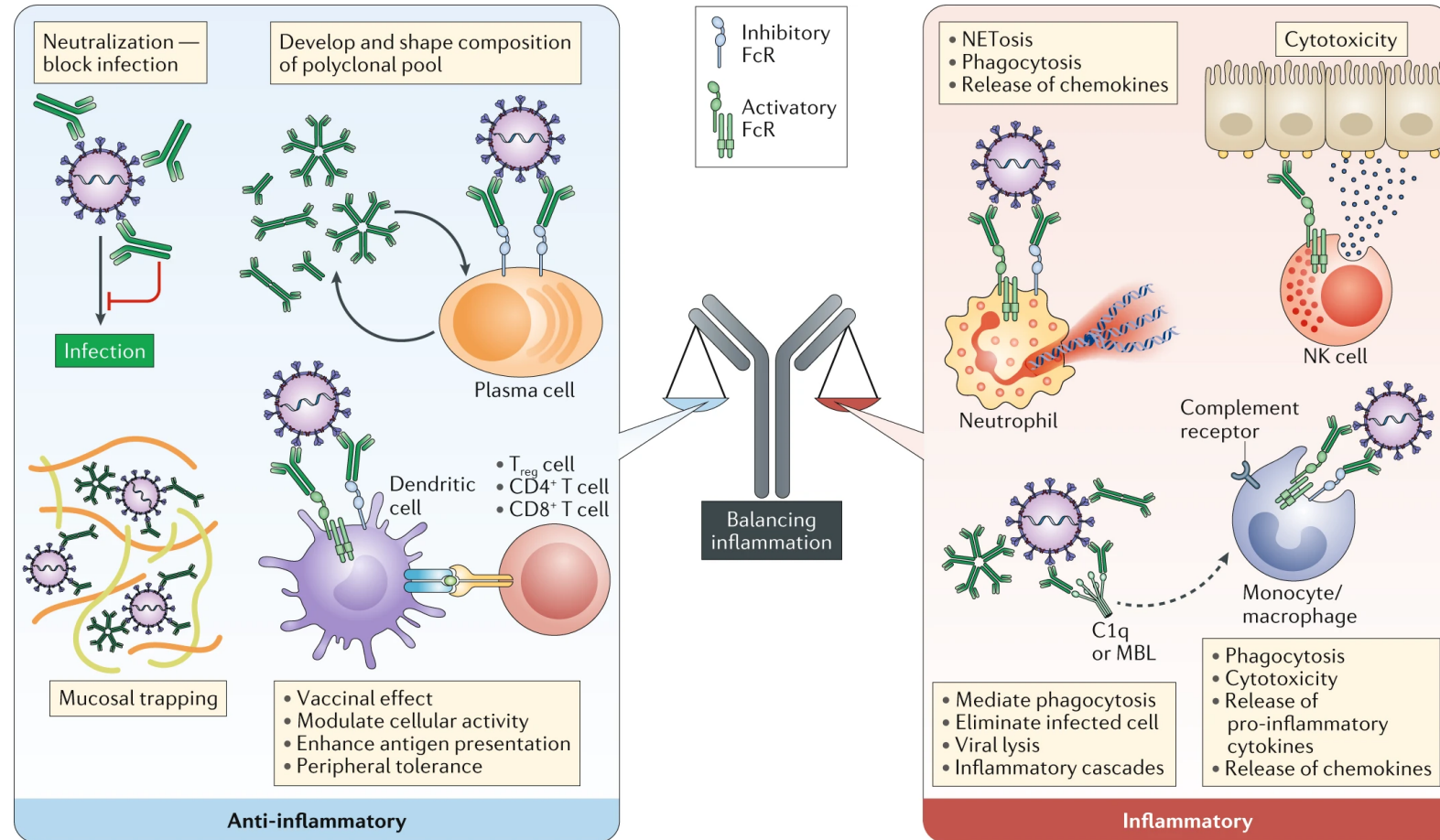
What does vaccination do to our body. How does it make us immune?

Vaccines need to induce effector functions such as

- Generation of specific killer cells (CD8+ T-cells)
- Activation of innate immunity
- Antibody mediated functionalities

such as **immune complexes, neutralization, complement, or other**

- Other...



Zohar and Alter, Nature Reviews immunology, 2020.

# Neutralizing antibodies

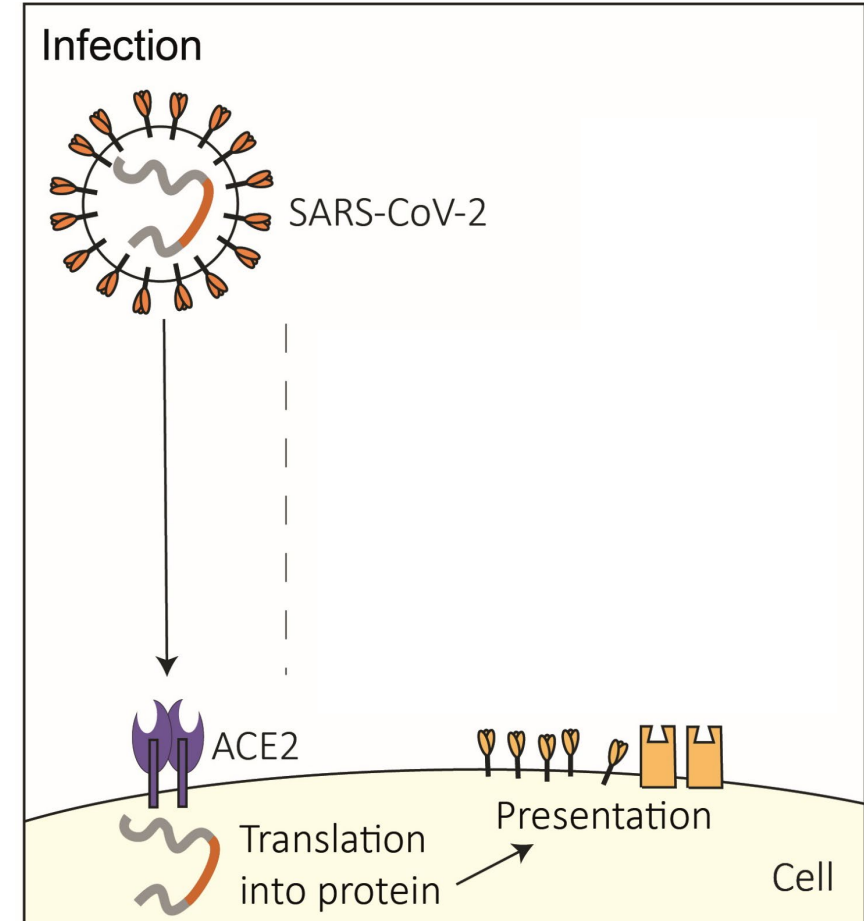
What does vaccination do to our body. How does it make us immune?

## Neutralizing antibodies as the current lead for protection

Functional: Neutralizing antibodies (nAbs) against the Spike receptor binding domain (RBD)

Zost *et al.*, Nature, 2020.

Barnes *et al.*, Nature 2020.



Simplified state-of-the-art

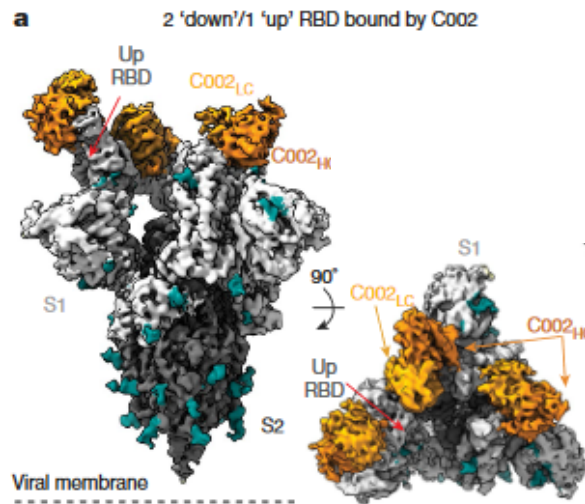
# Neutralizing antibodies

What does vaccination do to our body. How does it make us immune?

## Neutralizing antibodies as the current lead for protection

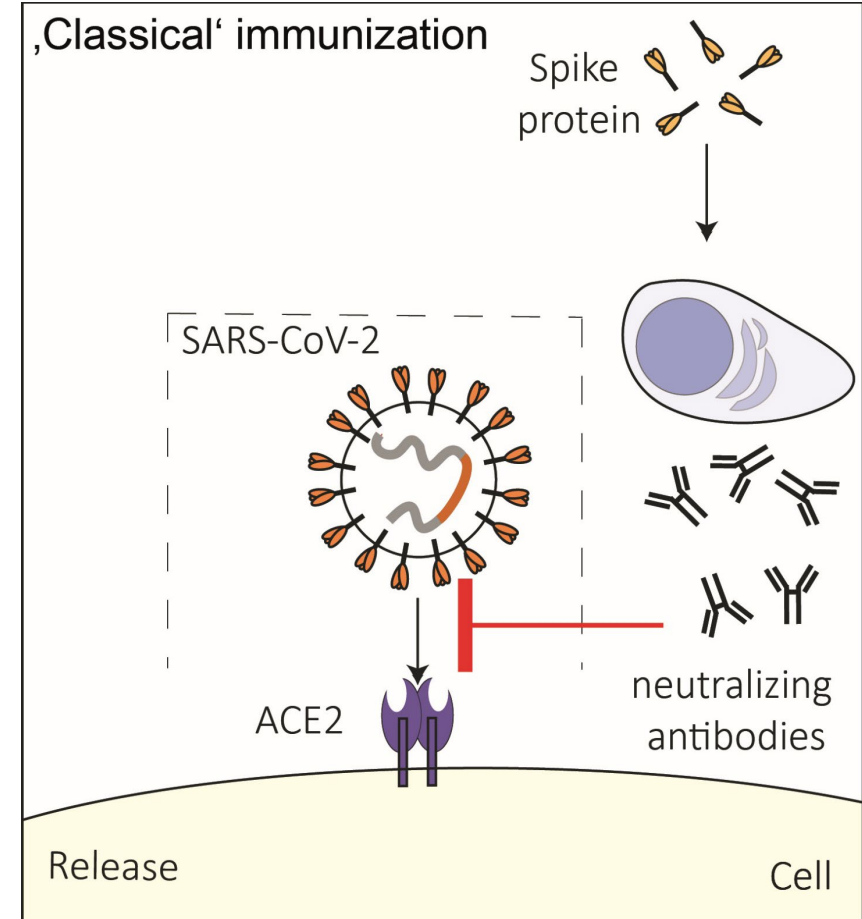
Functional: Neutralizing antibodies (nAbs) against the Spike receptor binding domain (RBD)

### Article



Zost *et al.*, Nature, 2020.

Barnes *et al.*, Nature 2020.



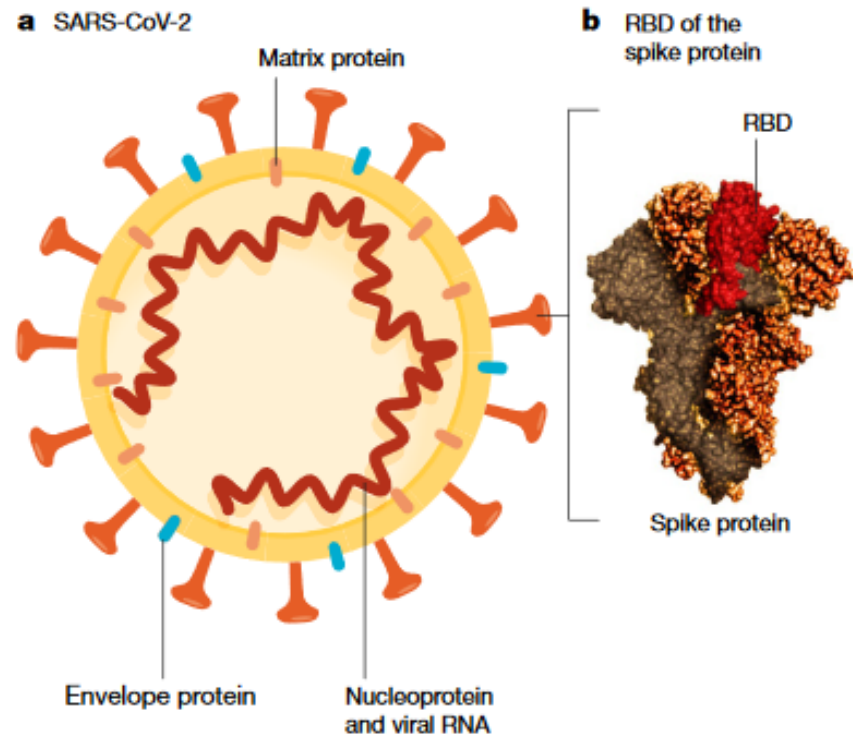
Simplified state-of-the-art

## Outcome measured in current vaccination studies

(ex. NCT04674189, 2<sup>nd</sup> outcome measuring individual SARS-CoV-2 neutralizing antibody titer)

# SARS-CoV-2 vaccination strategies

How do the vaccines (Moderna, Pfizer-Biontech, AstraZeneca, Sputnik *etc.*) differ from each other?



Krammer, Nature, 2020.

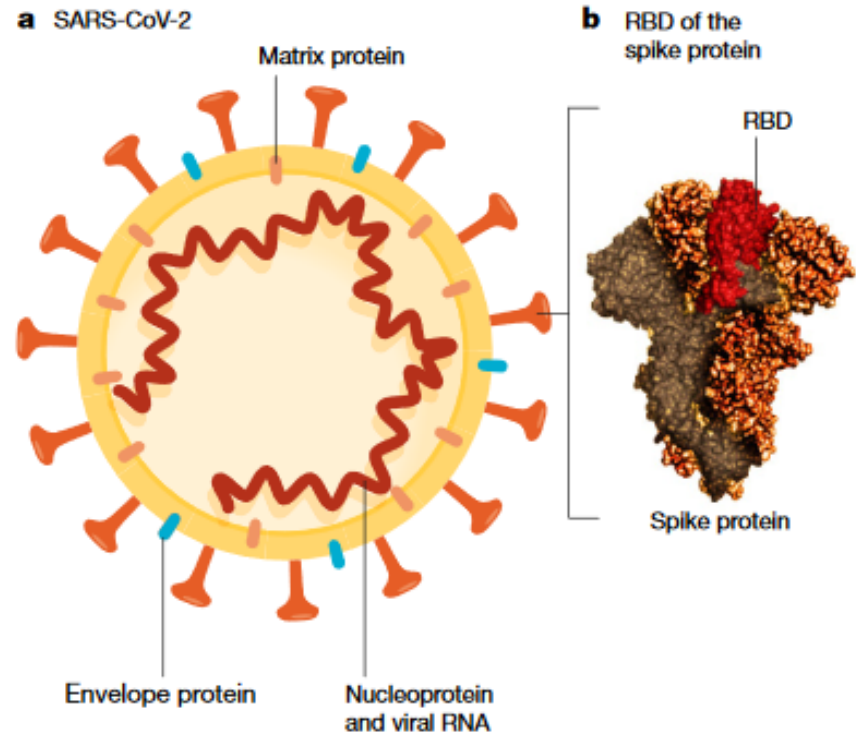
Good ressource: Nature News Feature, 2020.

05.03.2021

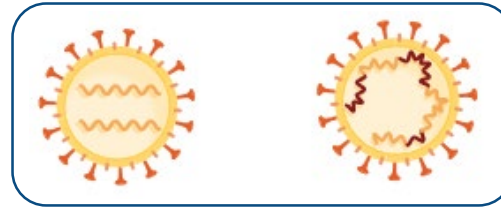
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# SARS-CoV-2 vaccination strategies

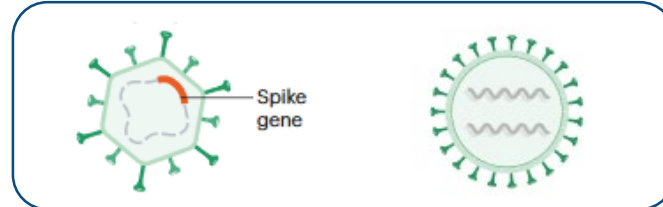
How do the vaccines (Moderna, Pfizer-Biontech, AstraZeneca, Sputnik etc.) differ from each other?



## Broad categories:



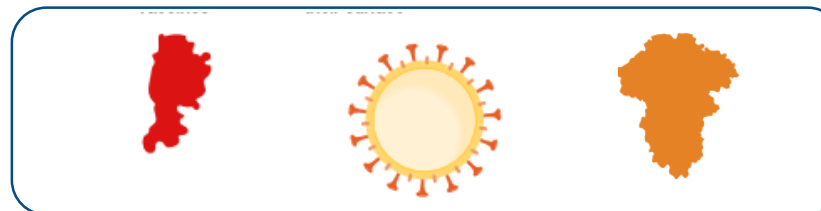
Virus-based (same virus)  
inactivated  
attenuated



Viral vector (different virus)  
Replication incompetent  
Replication competent



Nucleic-acid based  
DNA  
mRNA



Protein-based  
Recombinant  
Virus-like particles

Krammer, Nature, 2020.

Good ressource: Nature News Feature, 2020.

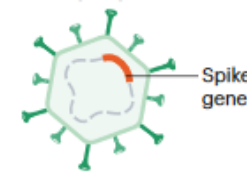


# SARS-CoV-2 vaccination strategies

Can the immunosystem react to the vaccine vector? Can the vector exaggerate or dampen the response?

## Examples for viral vectors, non-replicating:

Ad26.COVS.S (Janssen Vaccines & Prevention (Johnson & Johnson))



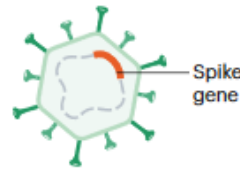
Gam-COVID-Vac (Gamaleya Research Institute of Epidemiology and Microbiology, Health Ministry of the Russian Federation)

AZD1222 (ChAdOx1 nCoV-19) (University of Oxford und Astra Zeneca)

Often used adenovirus type 5 and type 26 as recombinant versions; or virus from other species

# SARS-CoV-2 vaccination strategies

## Examples for viral vectors, non-replicating:



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Gam-COVID-Vac (Gamaleya Research Institute of Epidemiology and Microbiology, Health Ministry of the Russian Federation)

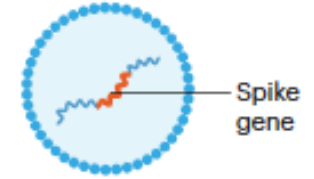
AZD1222 (ChAdOx1 nCoV-19) (University of Oxford und Astra Zeneca)

## Example for spike-based vaccine:

NVX-CoV2373 (Nanoparticle vaccine; contains purified pieces of spike protein, Novavax)



## Examples for mRNA vaccines:

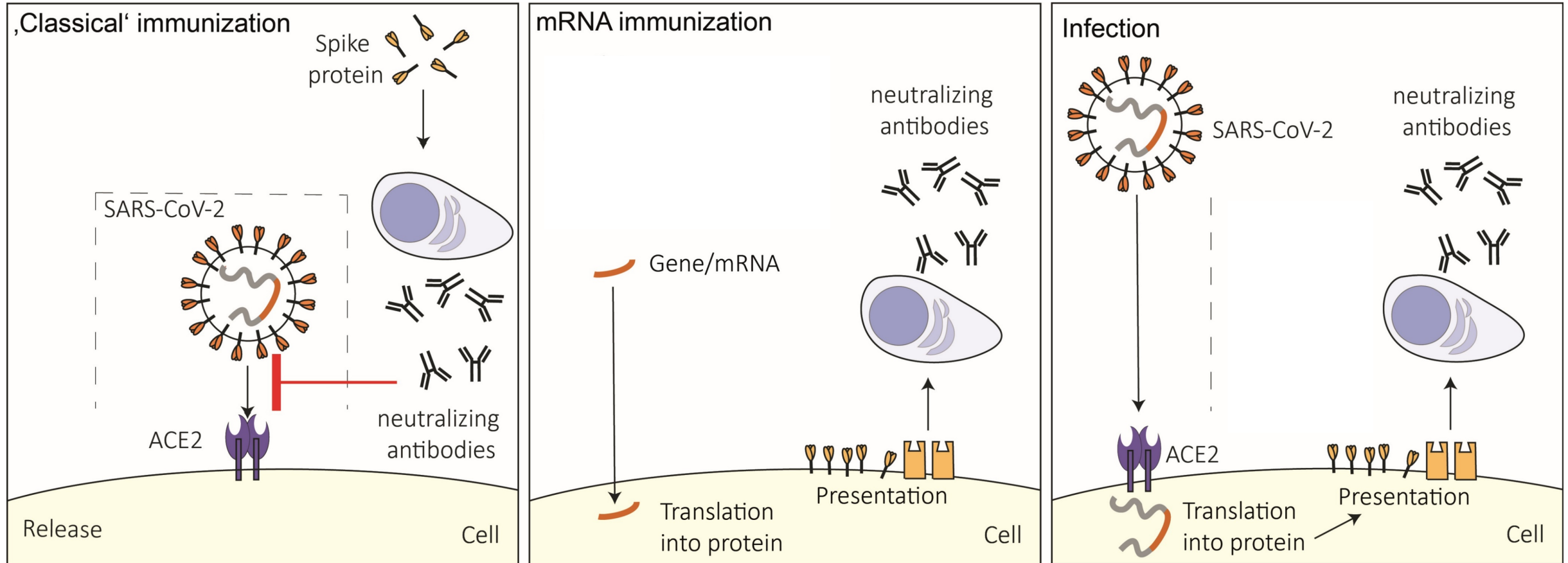


BNT162b2 (BioNTech RNA Pharmaceuticals/Pfizer)

mRNA-1273 (National Institute of Allergy and Infectious Diseases/Moderna)

CVnCoV (CureVac)

# SARS-CoV-2 vaccination strategies: mRNA



# SARS-CoV-2 vaccination strategies: mRNA

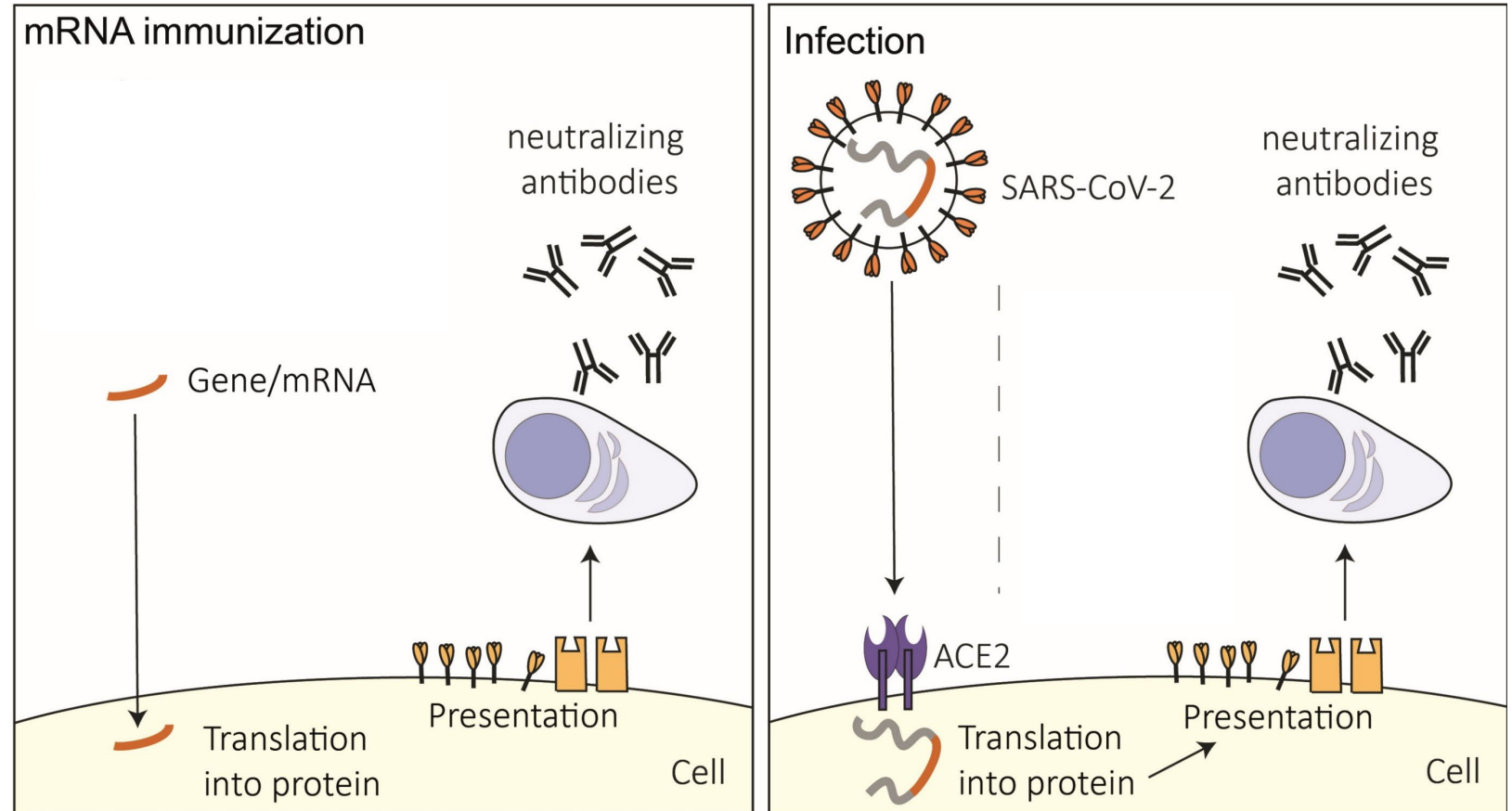
mRNA vaccines:

Similar engagement of immune system

Local uptake and protein production by host cells (intramuscular, deltoid) for a short time (days-week?)

**Advantage:**  
Quality control/rapid adaptation

**Challenge:**  
stability, distribution





# SARS-CoV-2 vaccination strategies

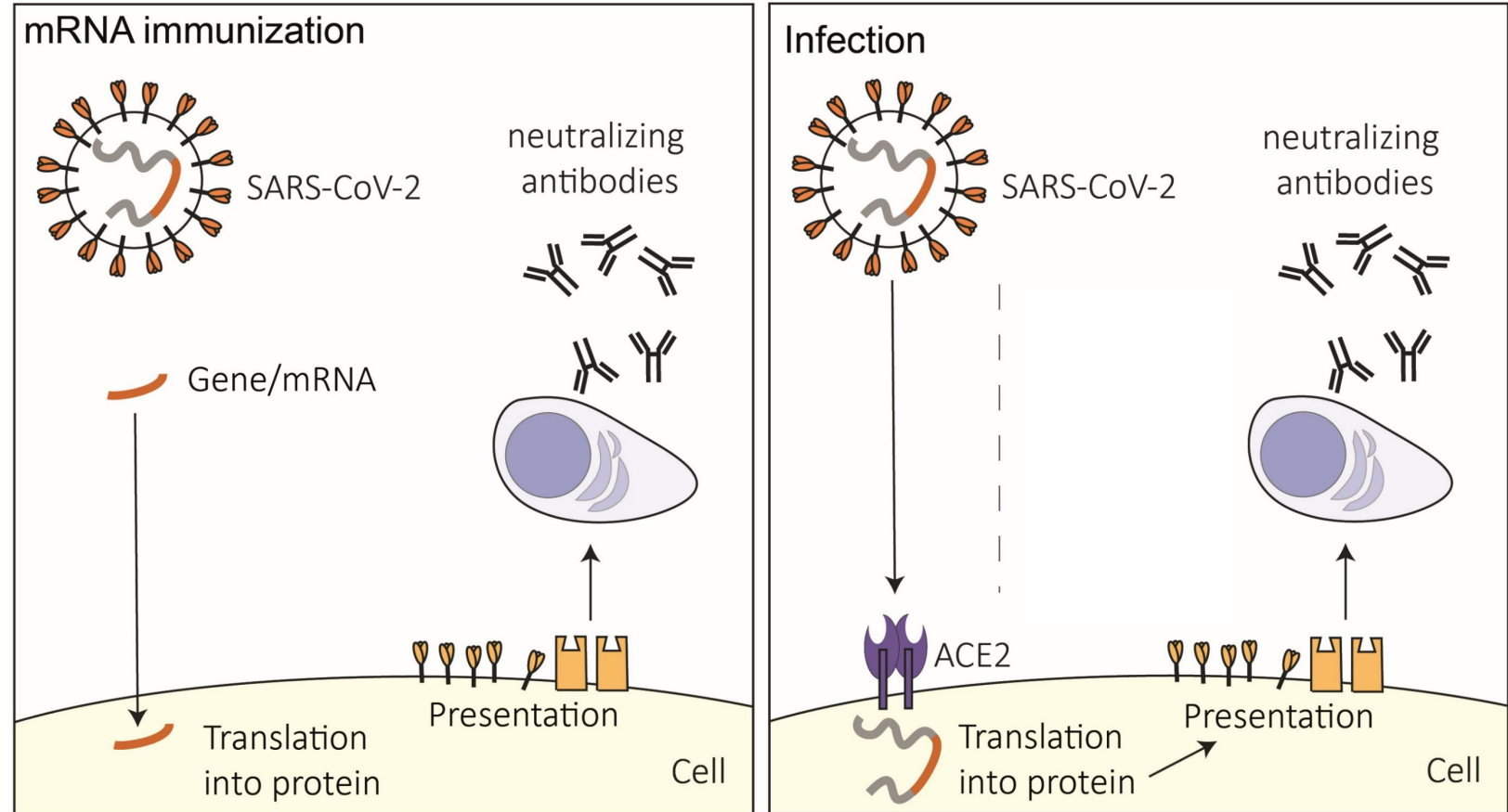
Is there a risk that mRNA could transfect host cells and modify the human genome?

mRNA is translated into protein

No integration into DNA of the host – no modification of host DNA (no transfer to future generations)

**Integration into host genome needs...**

- Reverse transcriptase (RNA to cDNA)
- Primer for mRNA (specific for viral RNA)
- Retroviral integrase (recognises **viral** DNA)



# SARS-CoV-2 vaccination strategies

Are the people informed which vaccine (so which brand) is given to them? Are they able to choose? Which vaccination is assigned to you and why?

## Examples for viral vectors:

Ad26.COVS.2.S (Janssen Vaccines & Prevention (Johnson & Johnson))

Gam-COVID-Vac (Gamaleya Research Institute of Epidemiology and Microbiology, Health Ministry of the Russian Federation)

**AZD1222 (ChAdOx1 nCoV-19) (University of Oxford und Astra Zeneca, 5.3 Mio)**

## Example for spike-based vaccine:

NVX-CoV2373 (Nanoparticle vaccine; contains purified pieces of spike protein, Novavax, 6 Mio.)

## Examples for mRNA vaccines:

**BNT162b2 (BioNTech RNA Pharmaceuticals/Pfizer, 3 Mio.)**

**mRNA-1273 (National Institute of Allergy and Infectious Diseases/Moderna, 13.5 Mio.)**

CVnCoV (CureVac, 5 Mio.)

Bold: CH Government ordered/pre-ordered vaccines (source BAG)

Red: Approved vaccines in CH

Blue: In approval process

(information retrieved: 20/02/2021)

# SARS-CoV-2 vaccination

How can vaccines induce long-term immunity if a infection cannot? What exactly is the difference in the effect of the vaccine and an infection at the molecular level?

## Neutralizing antibodies as the current lead for protection.

Various levels of neutralizing antibodies in infected patients

Wu *et al.*, Nature, 2020.

Lau *et al.*, Nature Comm, 2021.

Duration of protection after infection is not clear, but decreasing levels of neutralizing antibodies are reported, re-infection seems possible

Marot *et al.*, Nature Comm, 2021.

### From viral point-of-view:

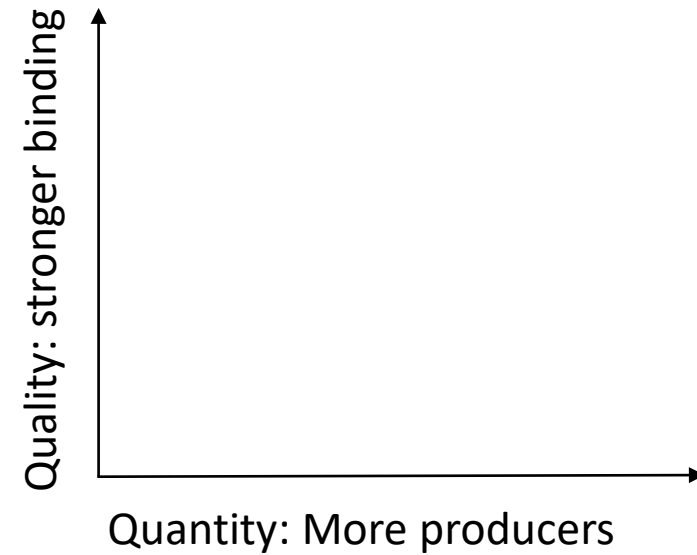
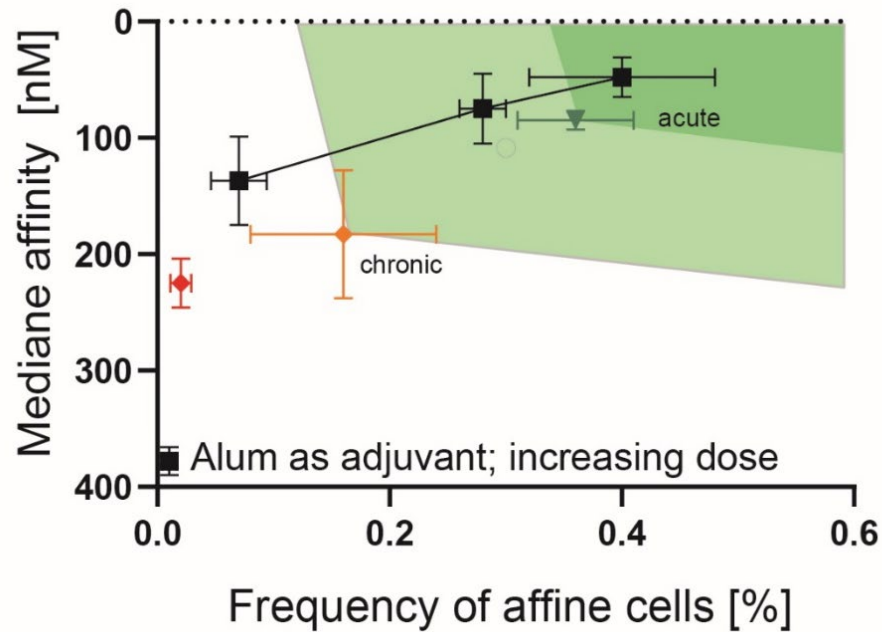
Only spike protein  
No other viral proteins are present  
(Kopecky-Bromberg, Journal of Virology, 2020): ORF3b, ORF6 and NP function as IFN antagonists)

### From vaccine point of view:

Vaccine formulation and dose is critical!  
Multifunctional components influencing each other

# Vaccination and Immunity

How can vaccines induce long-term immunity if a infection cannot?



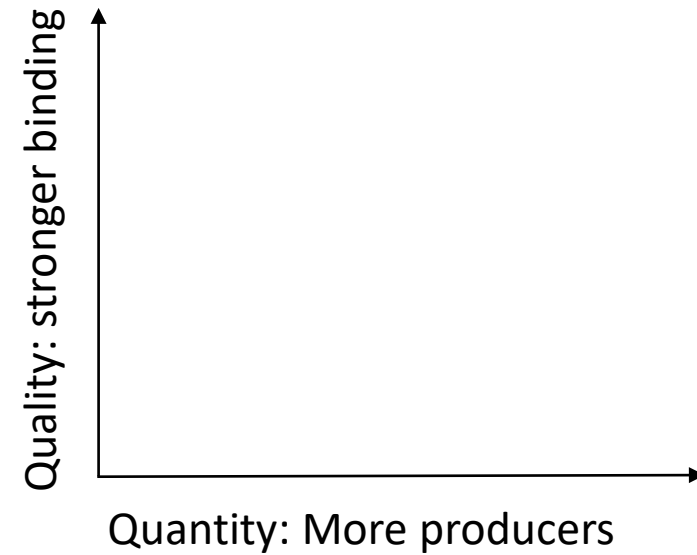
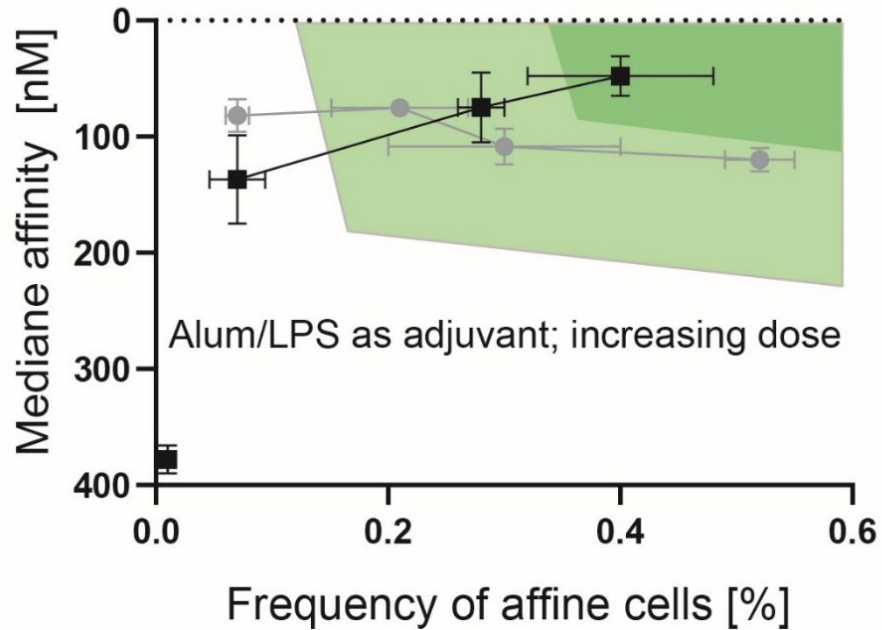
infection  $\neq$  immunization: Route, response, stimulation, dynamics, efficacy are different

Kräutler et al., Cell Reports, 2020.  
Eyer et al., The Journal of Immunology, 2020.  
Rybczinska *et al.*, Vaccine, 2020.  
Unpublished data.



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## ETH Zurich

Prof. Dr. Klaus Eyer

Functional Immune Repertoire Analysis

HCI H 433

Vladimir-Prelog-Weg 1-5/10

8093 Zürich - Schweiz

+41 44 633 74 57

klaus.eyer@pharma.ethz.ch

<https://eyergroup.ethz.ch/the-group.html>

FIRA\_Eyer (@EyerFira) | Twitter

Often used adenovirus type 5 and type 26 as recombinant versions; or virus from other species



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