

Vaccines for special populations

Immunological considerations

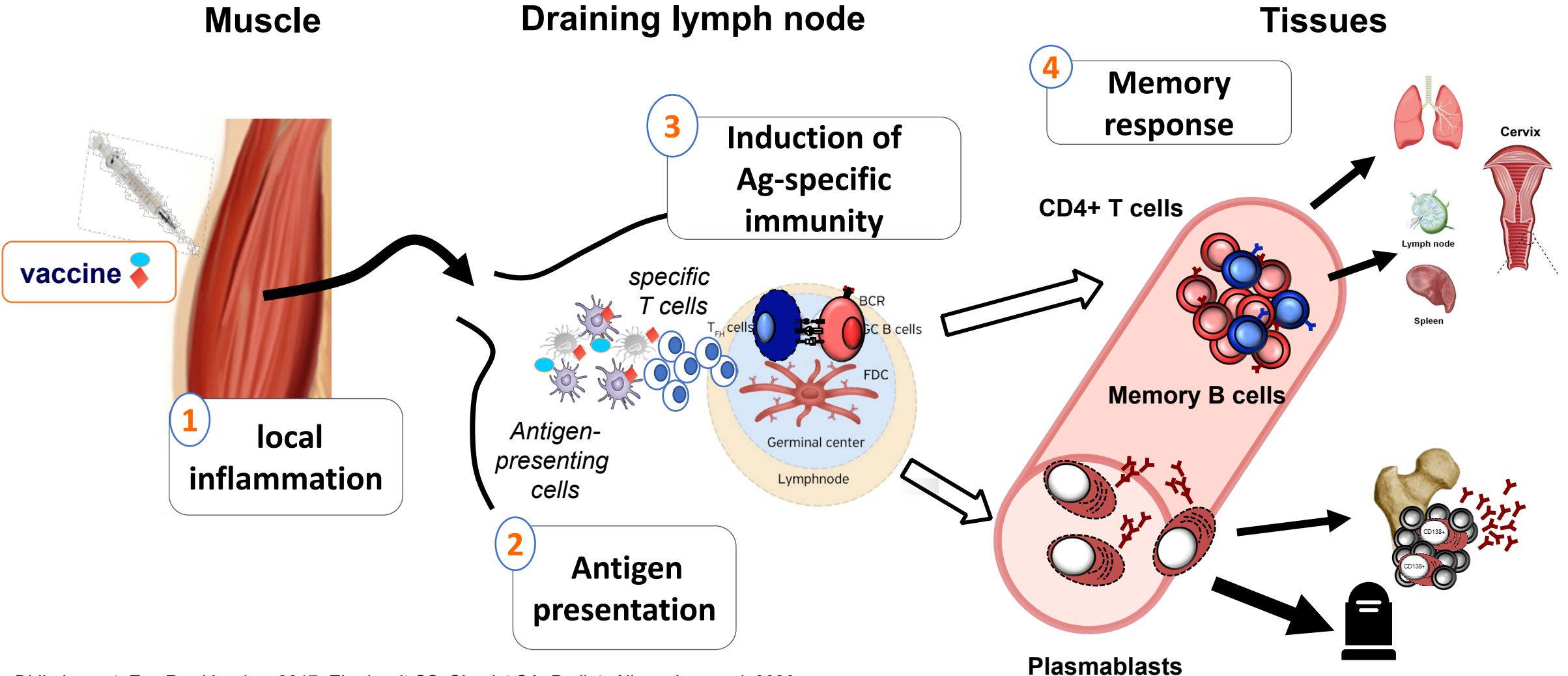
Prof. Arnaud Didierlaurent
Geneva Center of Vaccinology

Global Vaccine and Immunization research forum
March 28th 2023

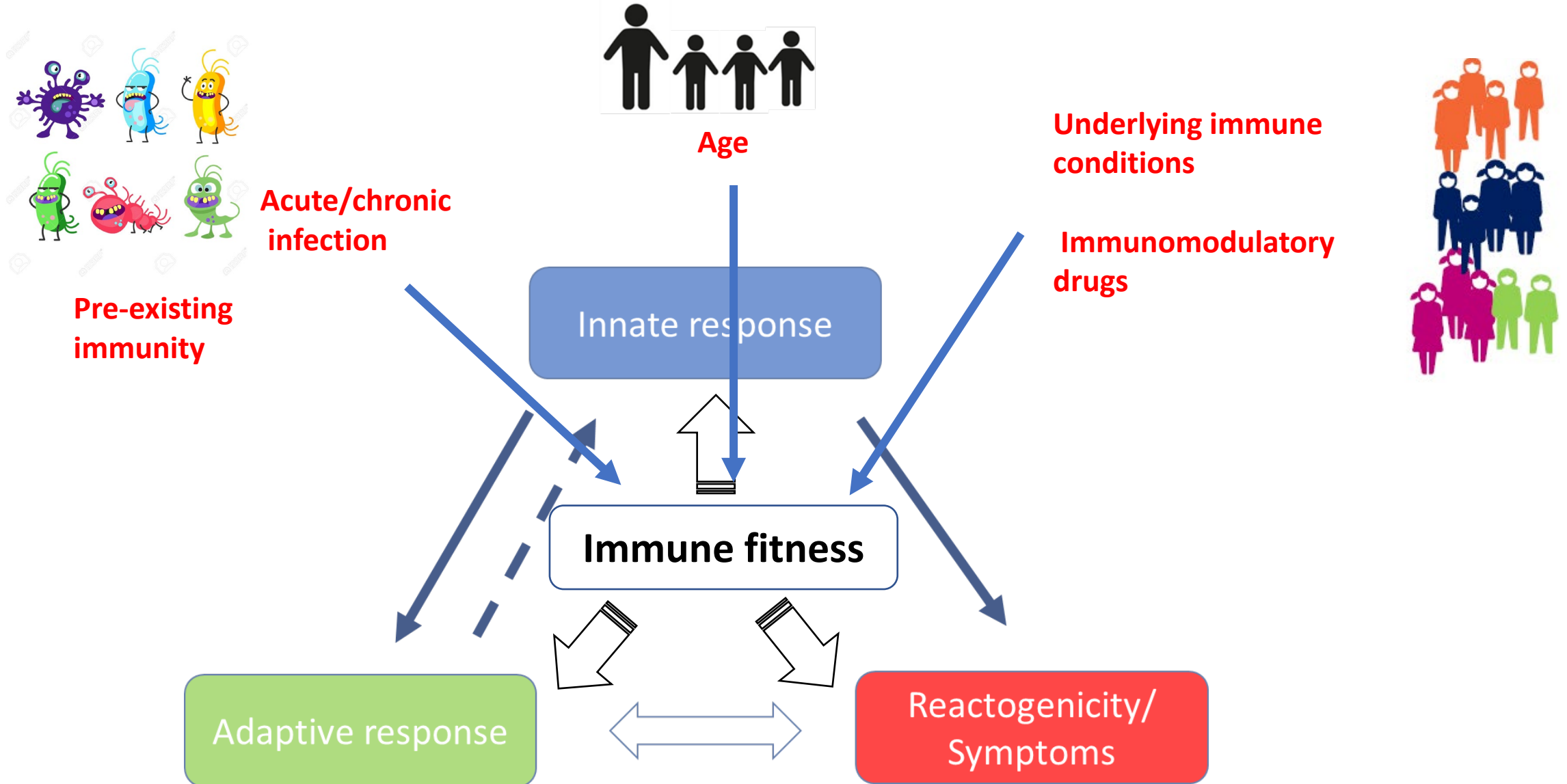
Different steps in the vaccine response

Transient innate response (0-72h)

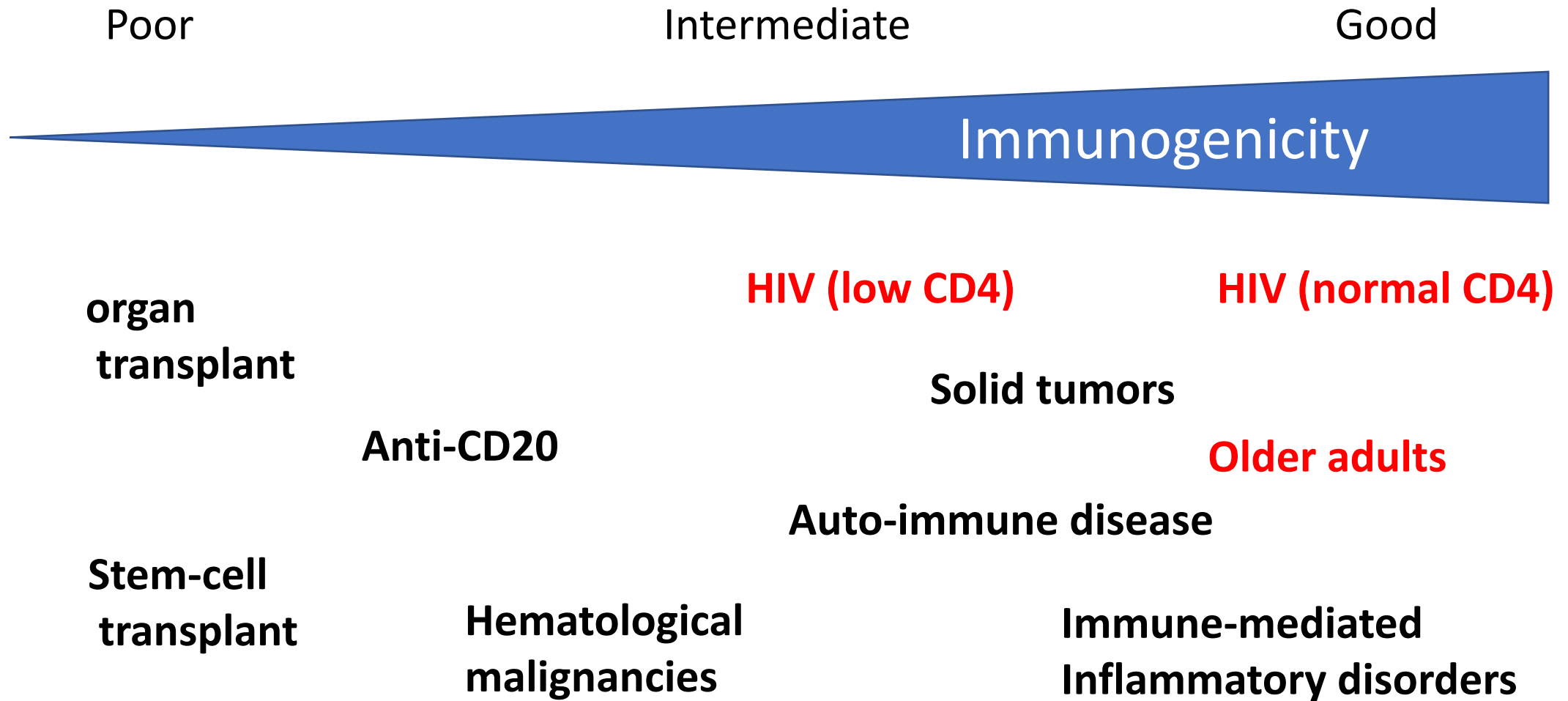
Antigen-specific response (months/years)



Different factors that influence the vaccine response

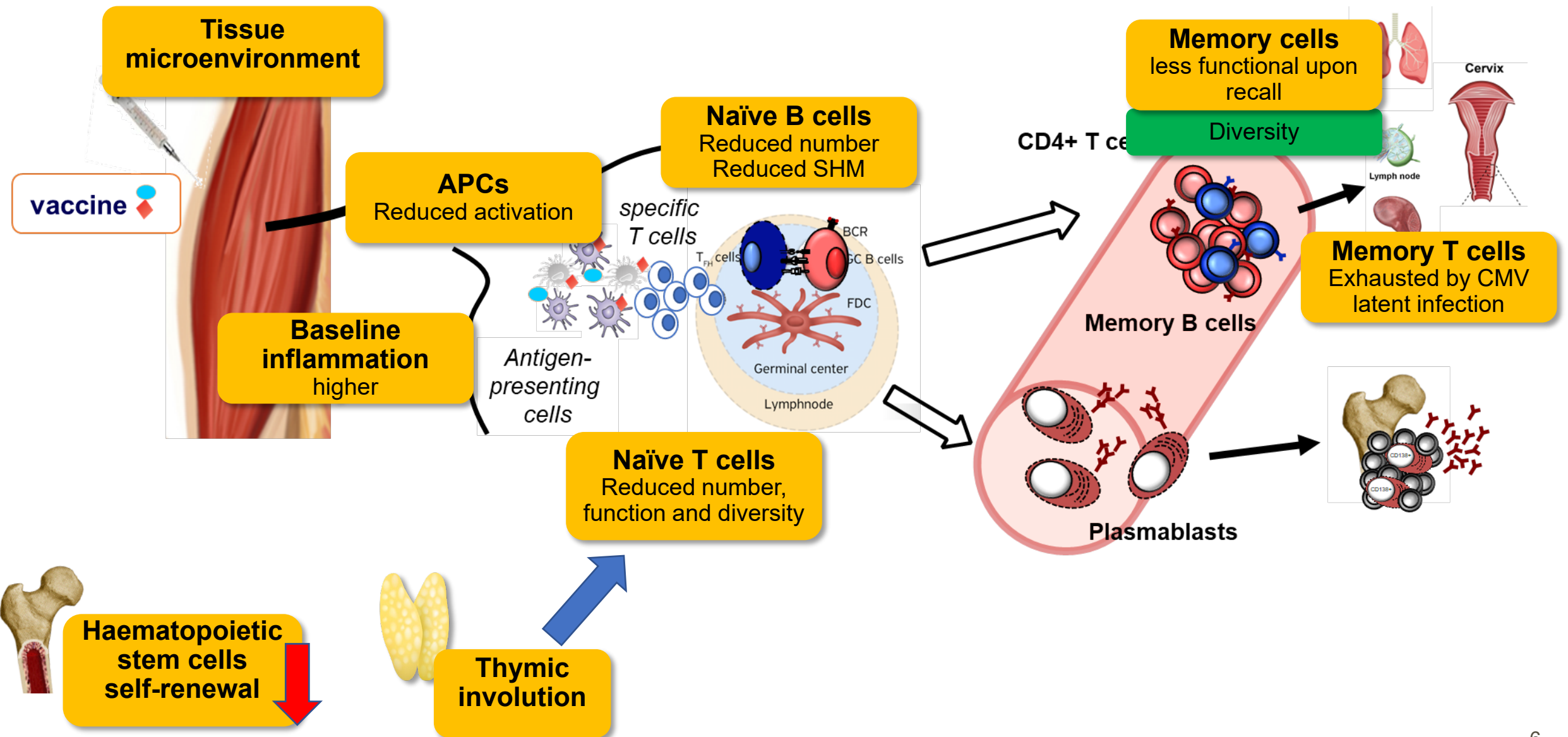


Vaccine immunogenicity across vulnerable population



Older adults

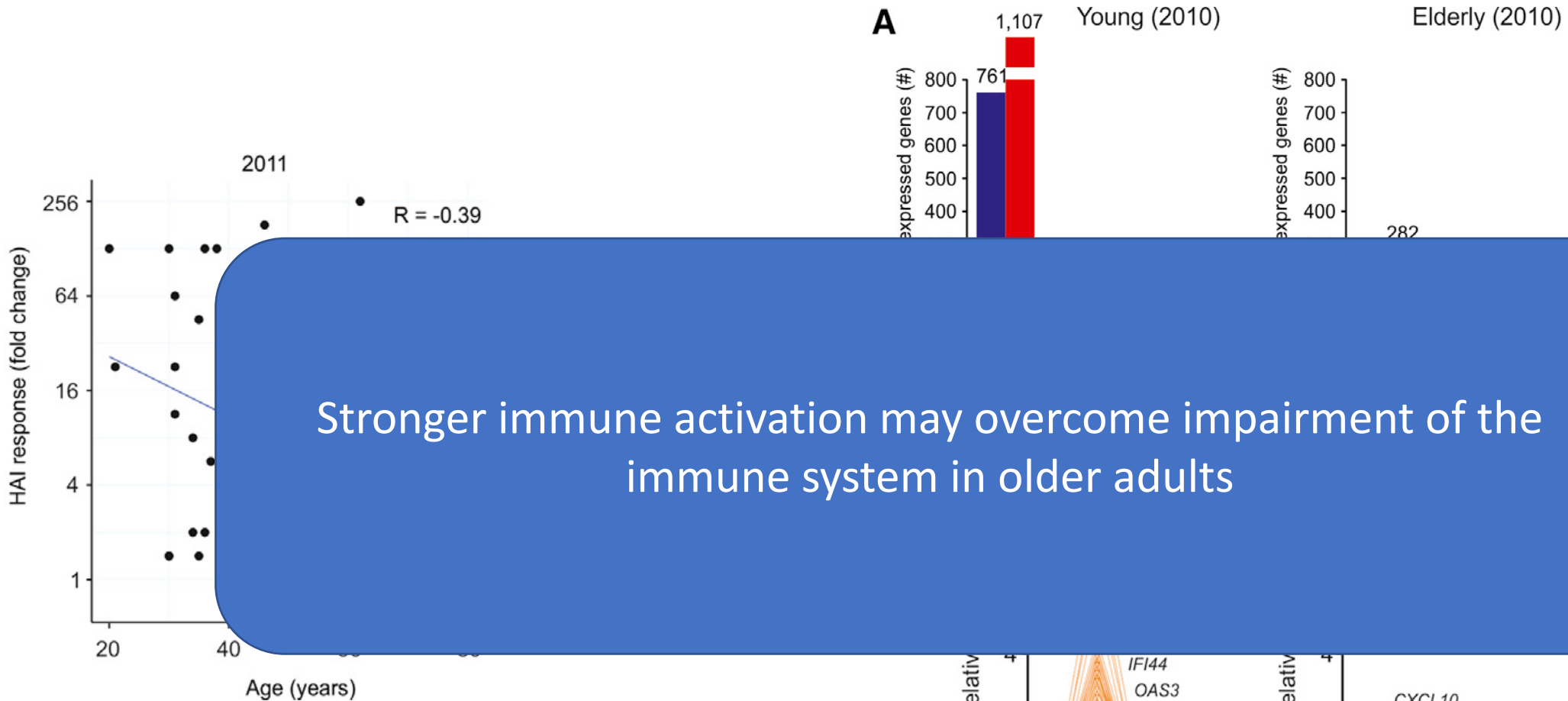
Impairment of immune cell function with age



Evidence of reduced immune response in older adults

- Reduced T cells^{1,2} and antibody-secreting cells^{3,4} to seasonal Flu vaccines
- Reduced T cells⁵ and antibody response⁶ to Hepatitis B vaccine
- Reduced potency of antibody after pneumococcal vaccination⁷
-

Evidence of reduced vaccine-mediated immune activation in the older adults



Stronger immune activation may overcome impairment of the immune system in older adults

Reduced innate activation (e.g. interferon) in the older adults

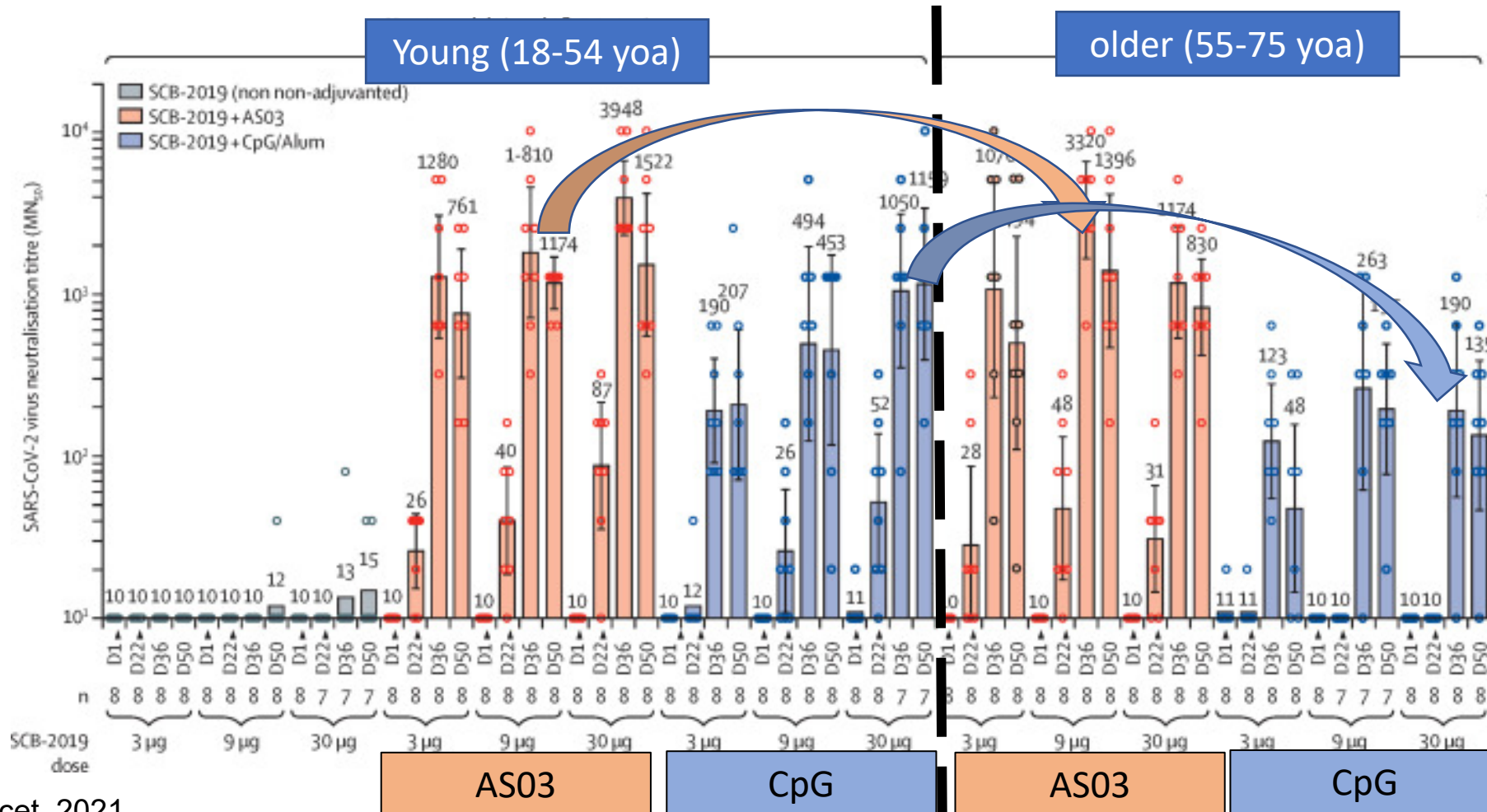
Stronger immune activation in the older adults may improve vaccine response

- Higher antigen content -> high-dose Flu vaccine
- Use of adjuvants:
 - MF59 in Flu vaccine
 - CpG in Hepatitis B vaccine
 - AS01 in the recombinant Zoster vaccine

Some adjuvants may work better in the older adults

S-Trimer (SCB-2019), adjuvanted with CpG or ASO3
Healthy adults
phase 1- antigen dose finding

days 1 22 36 50



Dose of adjuvant

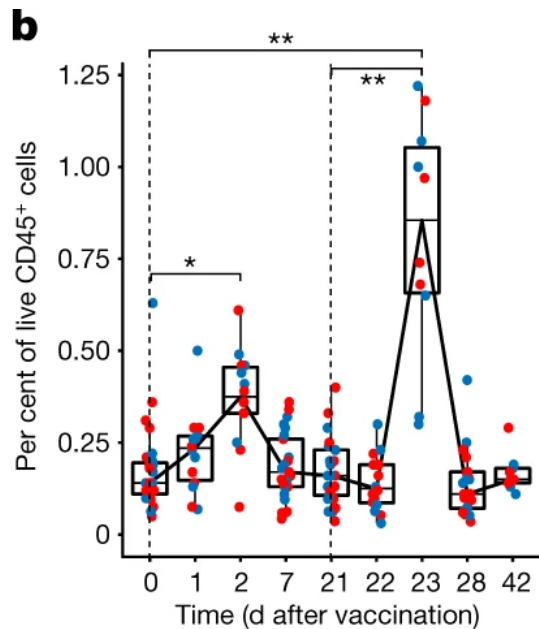
Neutralizing antibodies

mRNA vaccines can also activate the innate immune system, similar to adjuvanted vaccines

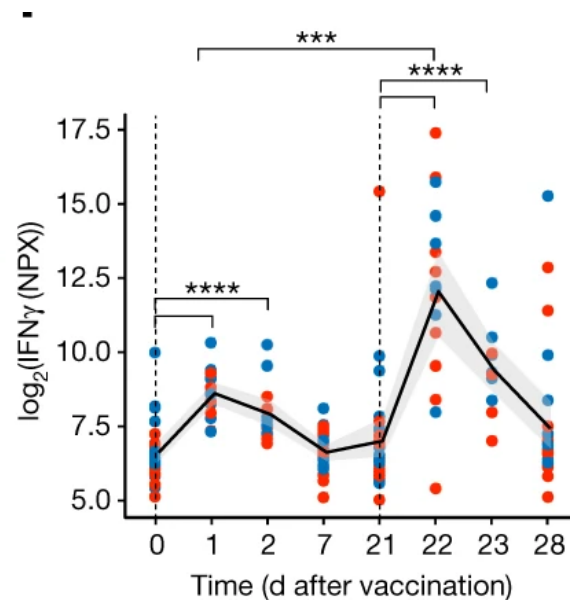


Bali Pulendran's group
N=27

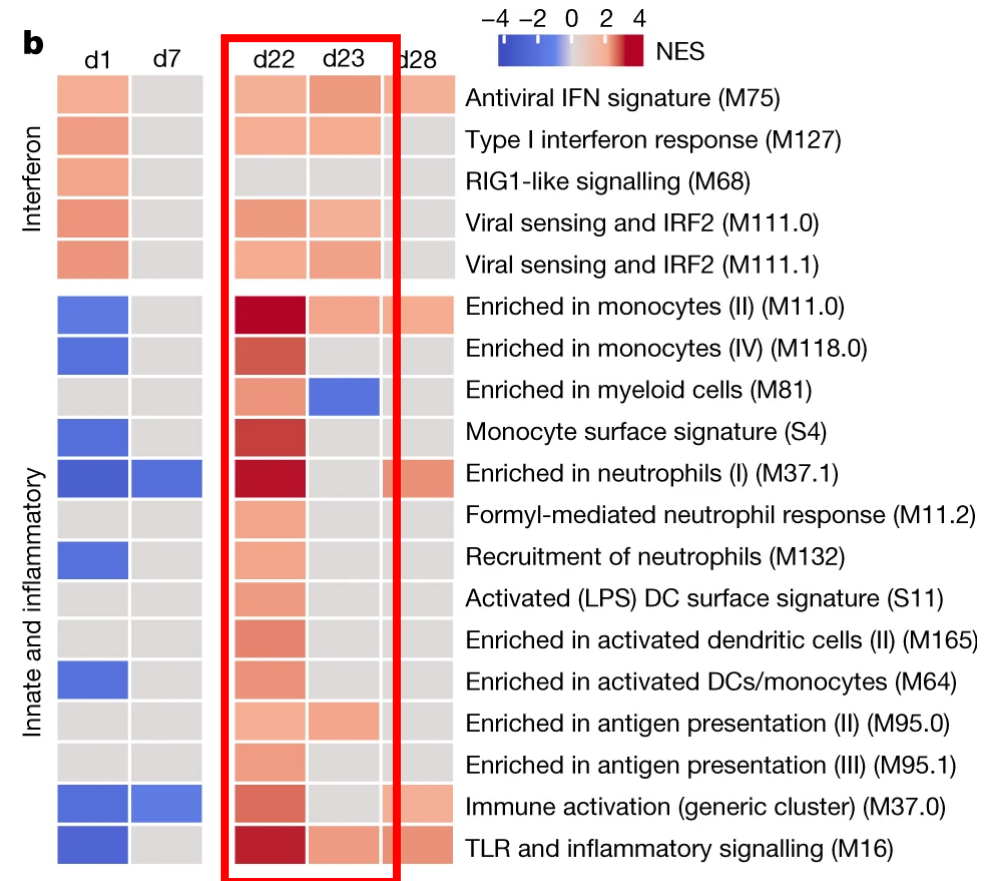
Transient increase in blood monocytes (CD14+16+)



Transient increase in IFN γ /IP-10

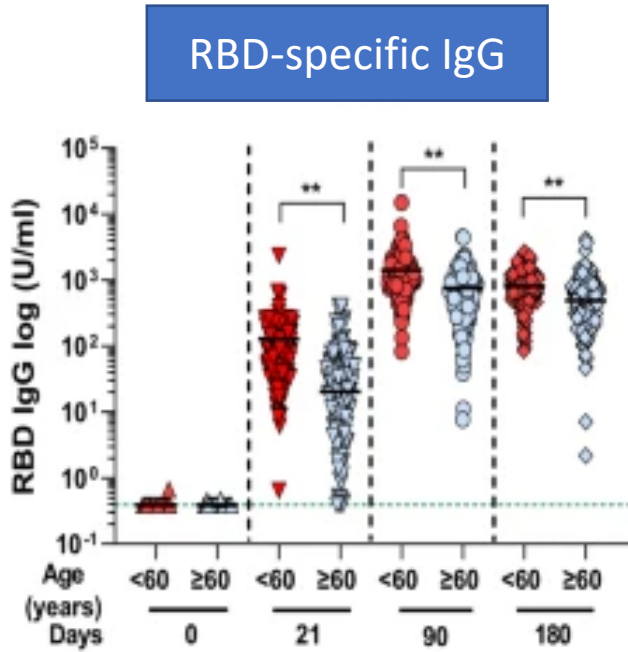
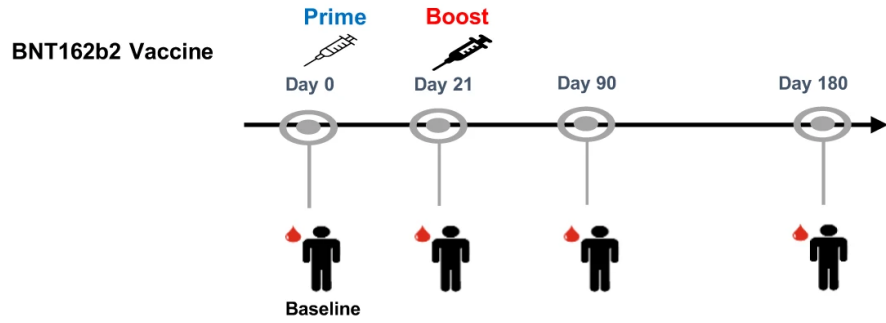


Interferon signature also seen with adjuvant
Comparison young and older adults???

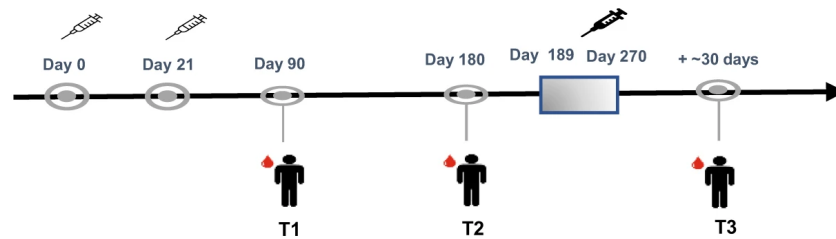


Use of mRNA generate robust immune response in all age groups but remains lower in the older adults

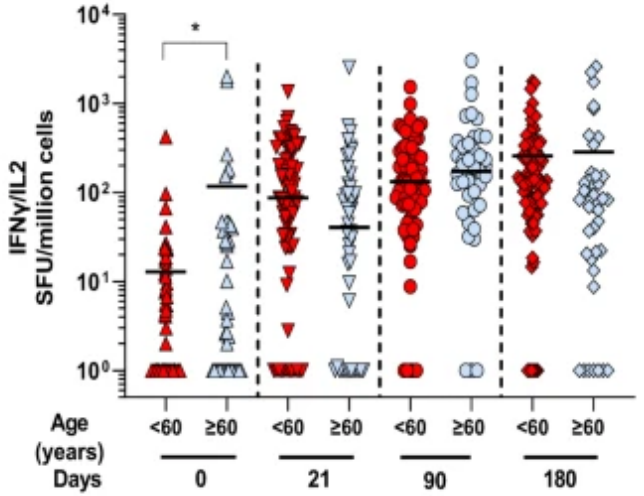
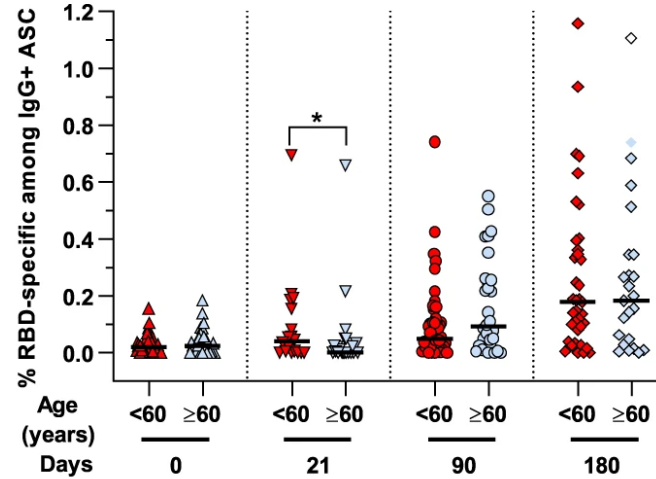
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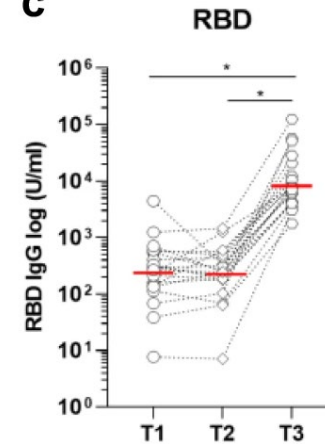
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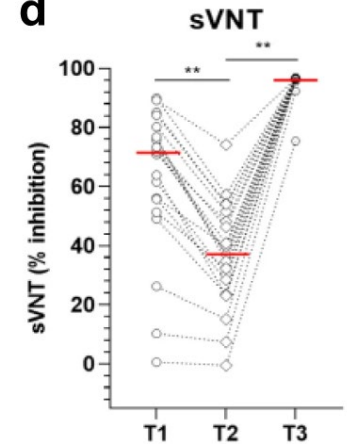
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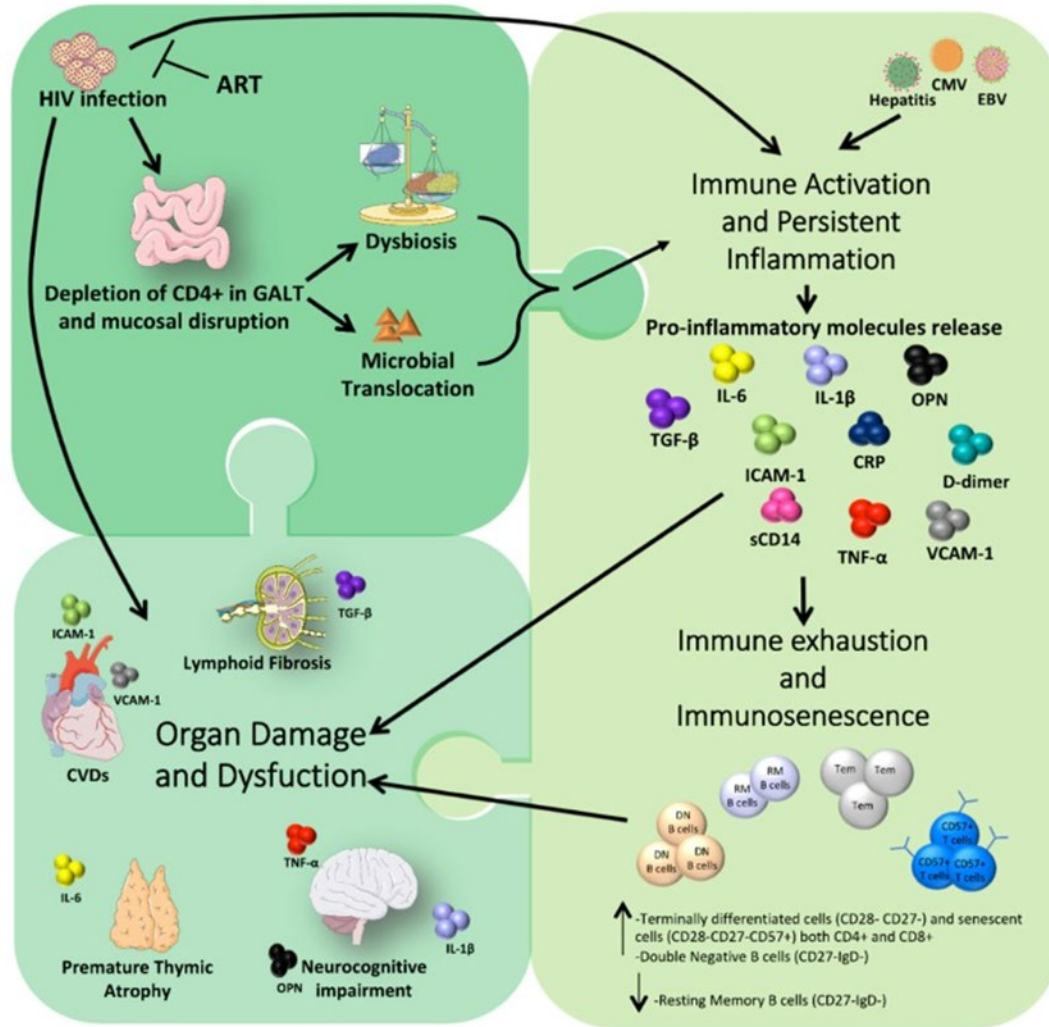


Key considerations for vaccination of older adults

- Impairment of immune cells in older adults is well documented and largely explains the observed reduced immune (and reactogenic) response to vaccines
- Reduced innate fitness in older adults may be aggravated by comorbidities -> needs to be considered!
- Higher immune stimulation with new vaccine platforms can overcome age-related decline in immunity

People living with HIV

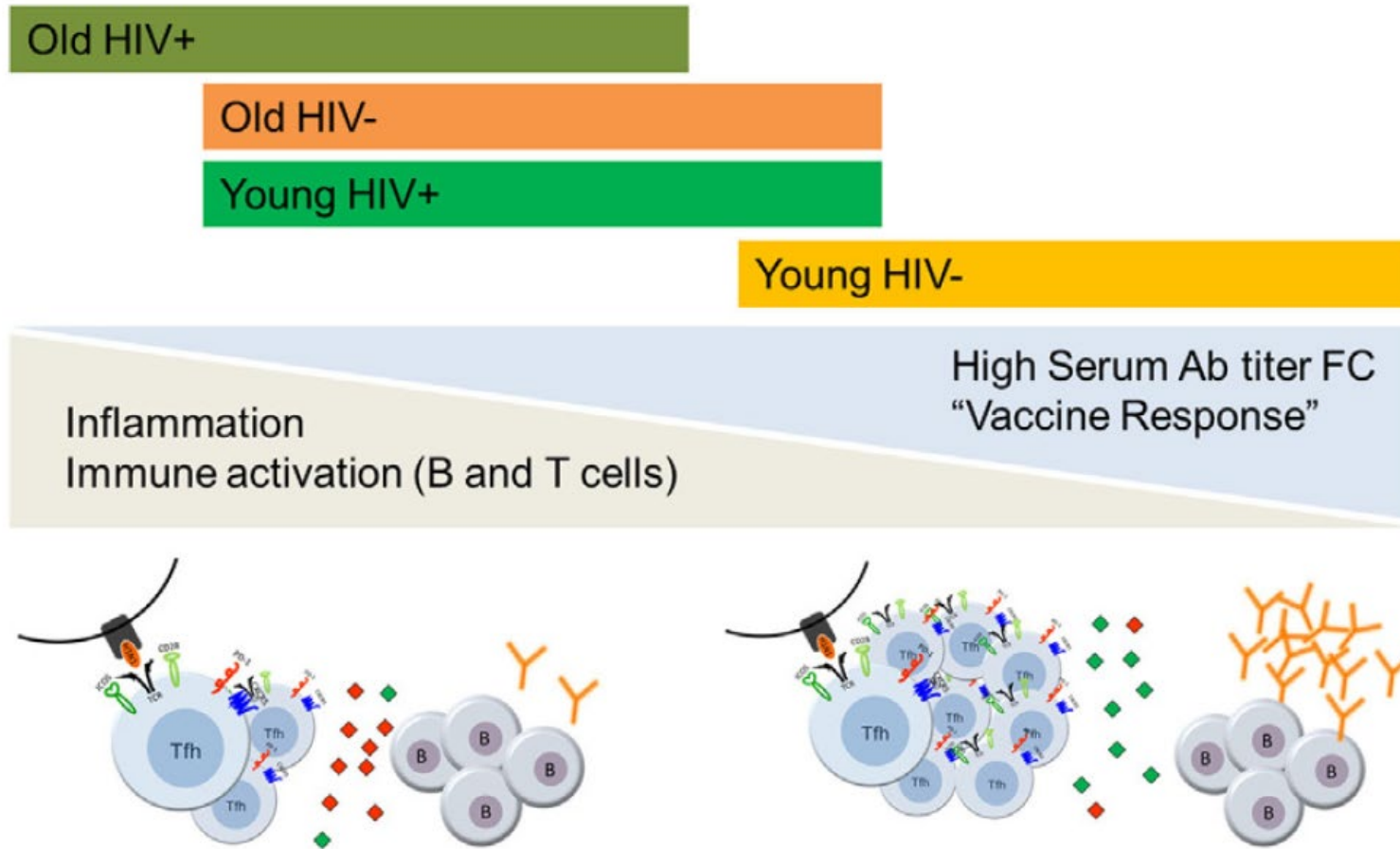
Immune dysfunction in HIV infected individuals despite ART



Premature ageing of the immune system due to chronic inflammation

- Partially restored by ART but not all (ex: dysbiosis)
- Increased premature comorbidities due to persisting inflammation (metabolic disorders, CVDs)
- Timing of ART implementation is critical to restore immune function (but some immune defects may still persist)

Defect in TFh and role in vaccine response



Impact on cellular response/memory?

Impact on Ab avidity?

Impact on quality of the antibody response in general....??

Impact of HIV infection on the different steps of the vaccine response

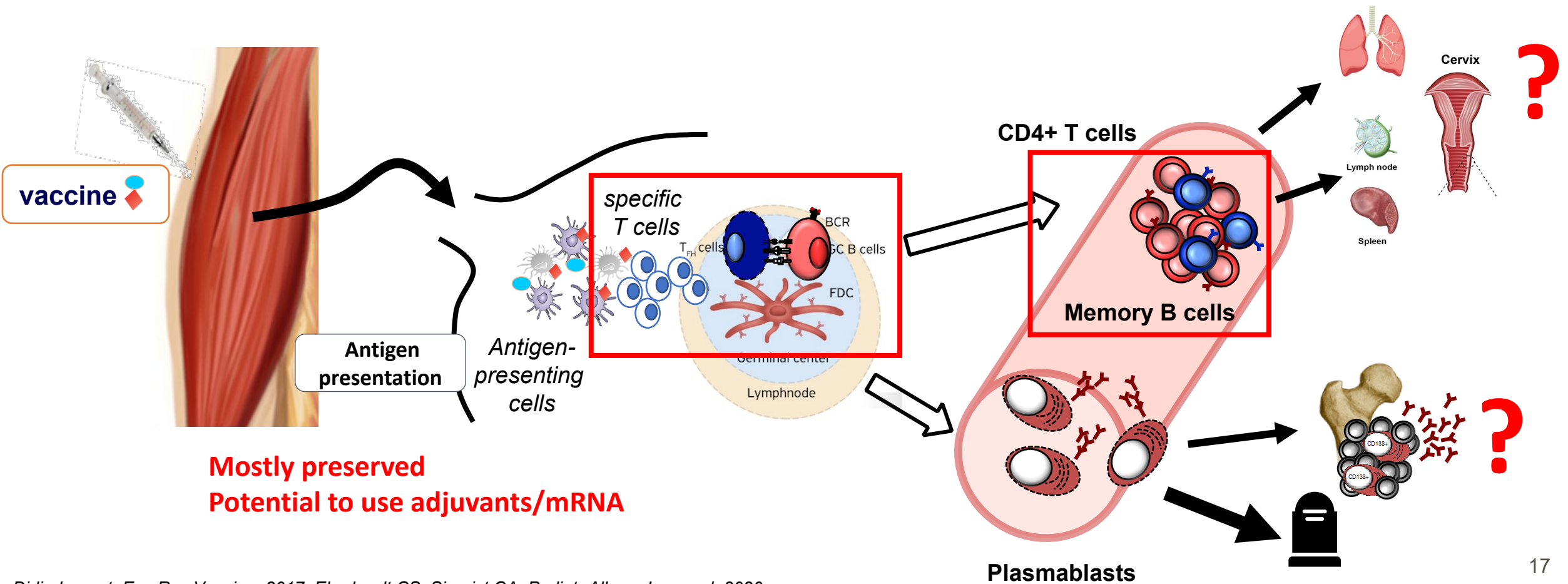
Transient innate response (0-72h)

Antigen-specific response (months/years)

Muscle

Draining lymph node

Tissues



Key considerations for vaccination of people with HIV

- Immune response to vaccine is generally good but quality and durability of the antibody and T cell response may be different from general population
- Some immune deficiency remains despite ART that may affect quality of the vaccine response
- Question regarding older people living with HIV -> combined immunosenescence and effect of chronic HIV infection



Pregnancy



Global Perspectives on Immunization During Pregnancy and Priorities for Future Research and Development: An International Consensus Statement

OPEN ACCESS

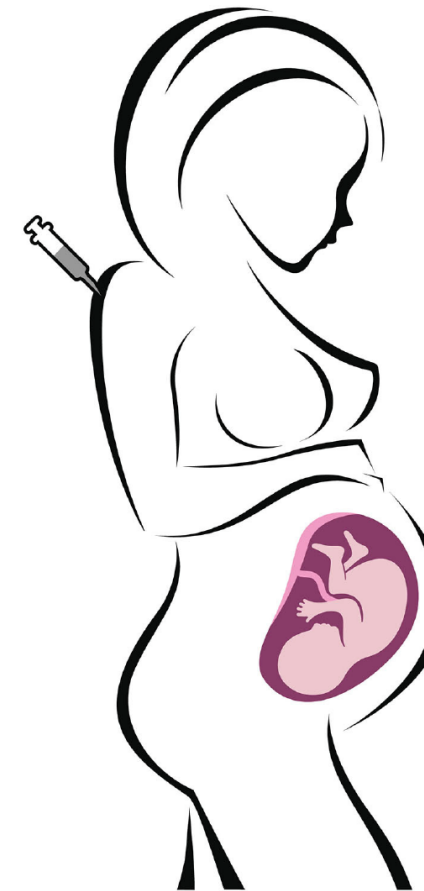
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MATERNAL ACCEPTANCE

- Perception of risk / severity of infection
- Access to vaccine provider
- Cost / health insurance

HEALTHCARE WORKER ACCEPTANCE

- Knowledge of recommendations
- Vaccine access and storage
- Reimbursement

MATERNAL IMMUNE RESPONSE TO VACCINATION

TRANSPLACENTAL TRANSFER OF VACCINE-SPECIFIC ANTIBODIES AND THEIR FUNCTION

INTERFERENCE WITH SUBSEQUENT INFANT IMMUNE RESPONSE TO VACCINATION

MATERNAL CLINICAL CONDITIONS

- Malaria, HIV infection, gestational hypertension, smoking

VACCINE SAFETY / ADVERSE EVENTS

TIMING OF IMMUNIZATION

- To achieve optimal immunity in mother and /or infant

GEOGRAPHICAL LOCATION

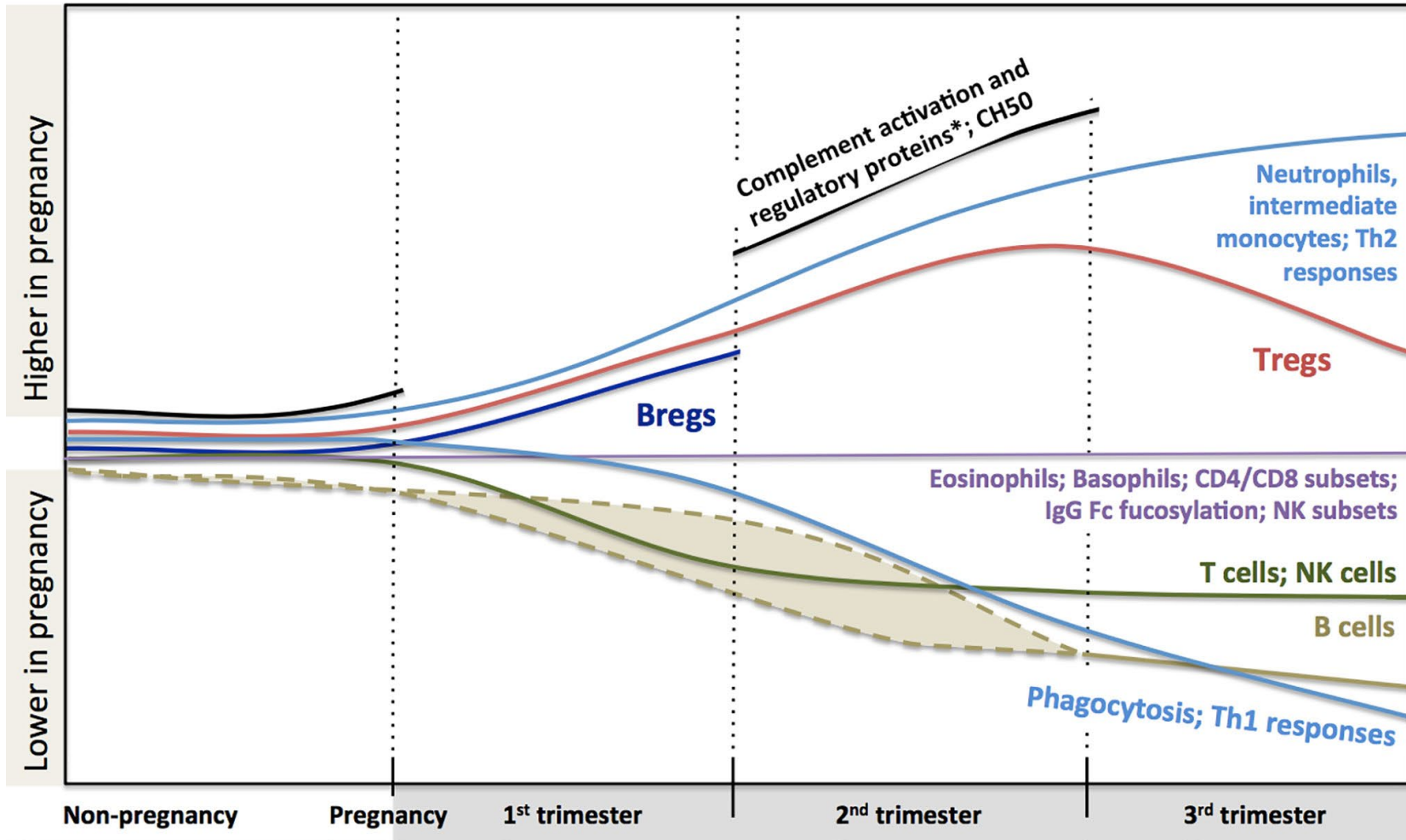
- Different circulating pathogen strains
- Different responses to vaccination
- Different local recommendations

SEASONALITY OF PATHOGENS TARGETED BY IMMUNIZATION

- Influenza, RSV

INDUCTION OF VACCINE-SPECIFIC ANTIBODIES IN BREAST MILK

Adaptation of the immune response during pregnancy and consequences for vaccine response



➔ Potential shift from Th1 to Th2 response
Reduced T cell function

But many immune functions are preserved!

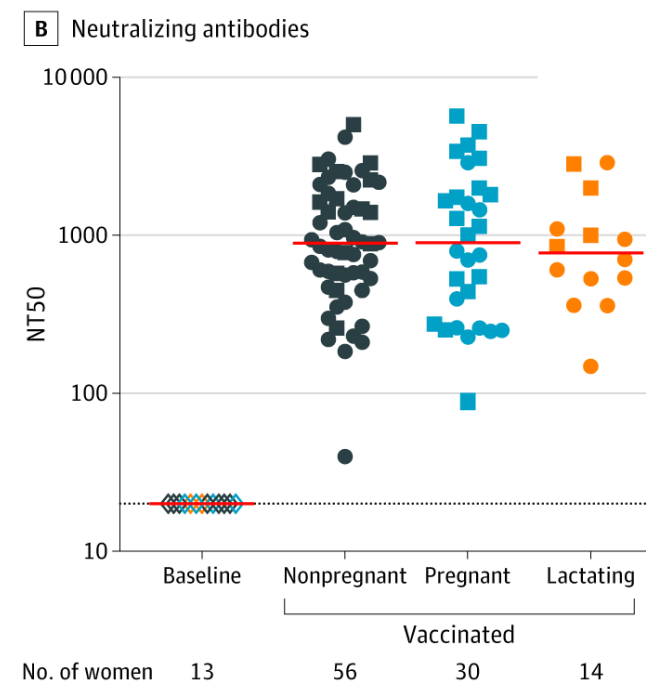
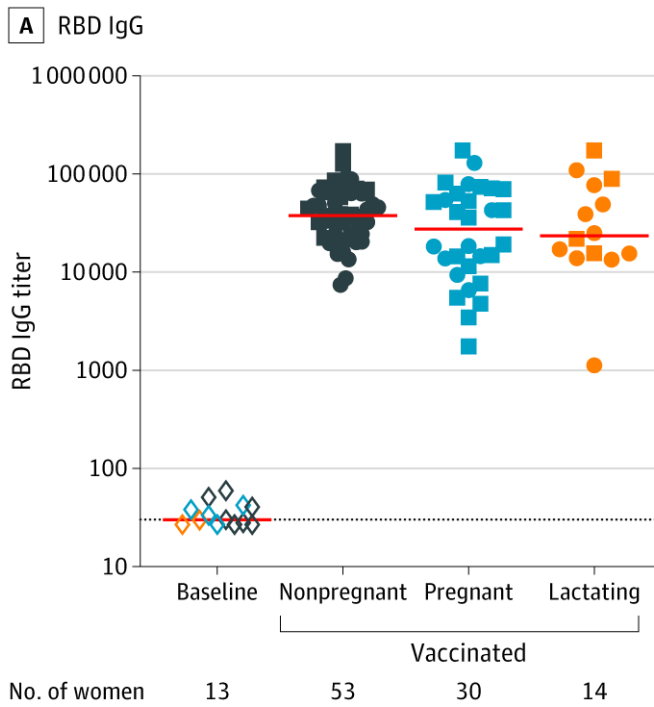
➔ Lower B cell counts and B cell function
↓
Reduced IgG levels

Robust immune response to COVID-19 mRNA vaccination in pregnant and lactating women

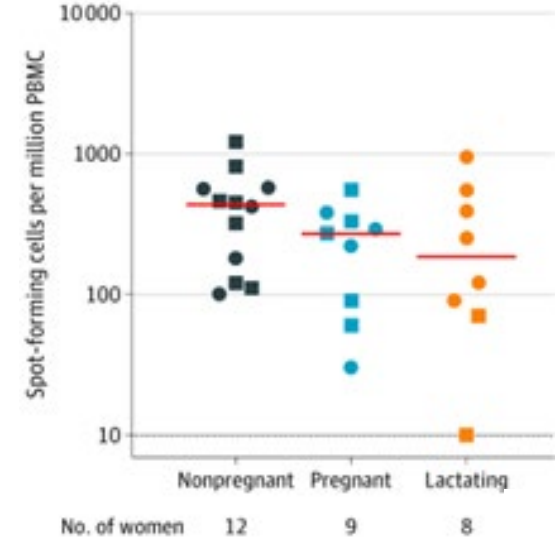
RBD-specific IgG

Neutralizing Ab

T cell response

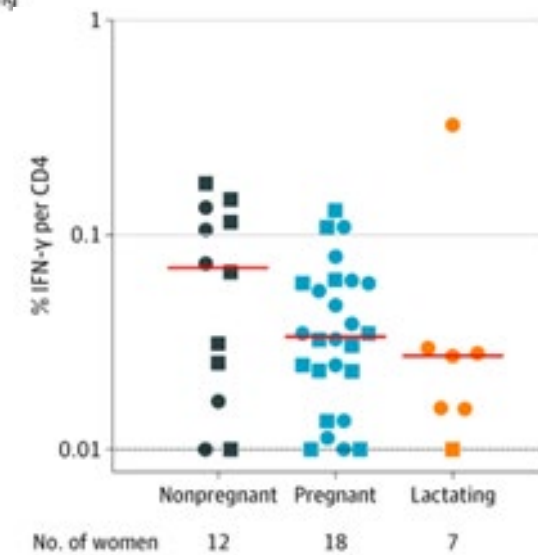


□ mRNA-1273 (Moderna)
○ BNT162b2 (Pfizer-BioNTech)



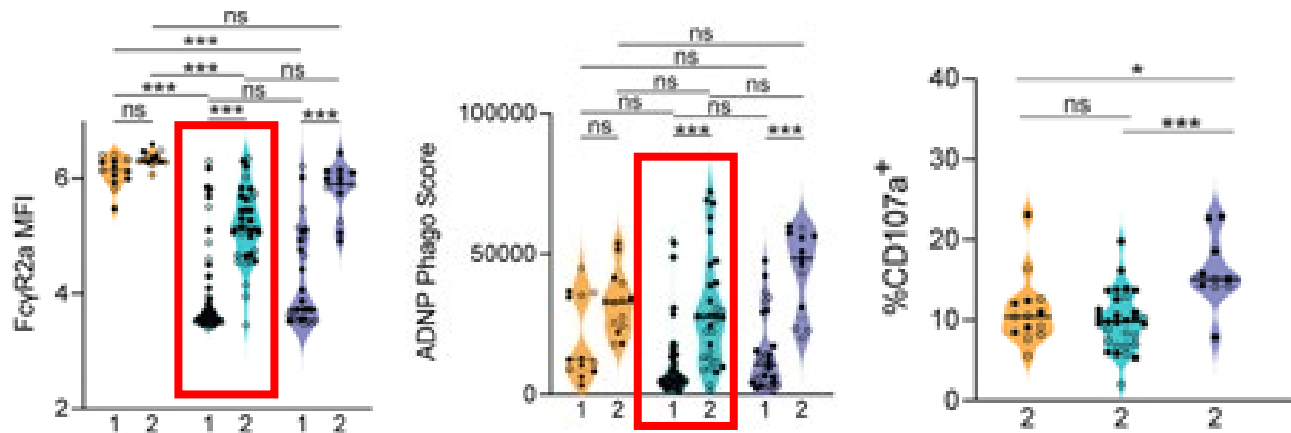
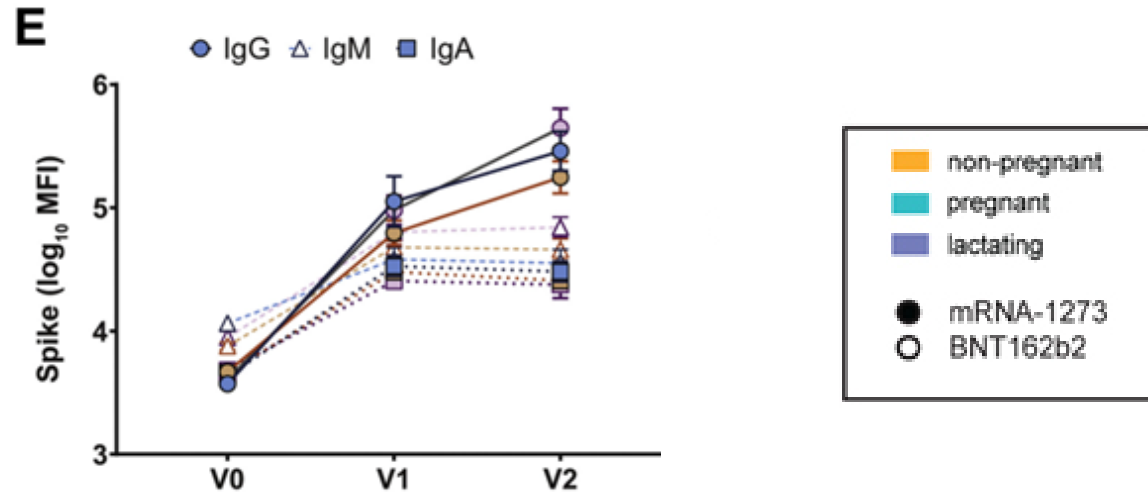
IFNγ ELISPOT

%IFNγ+ in CD4 T cells

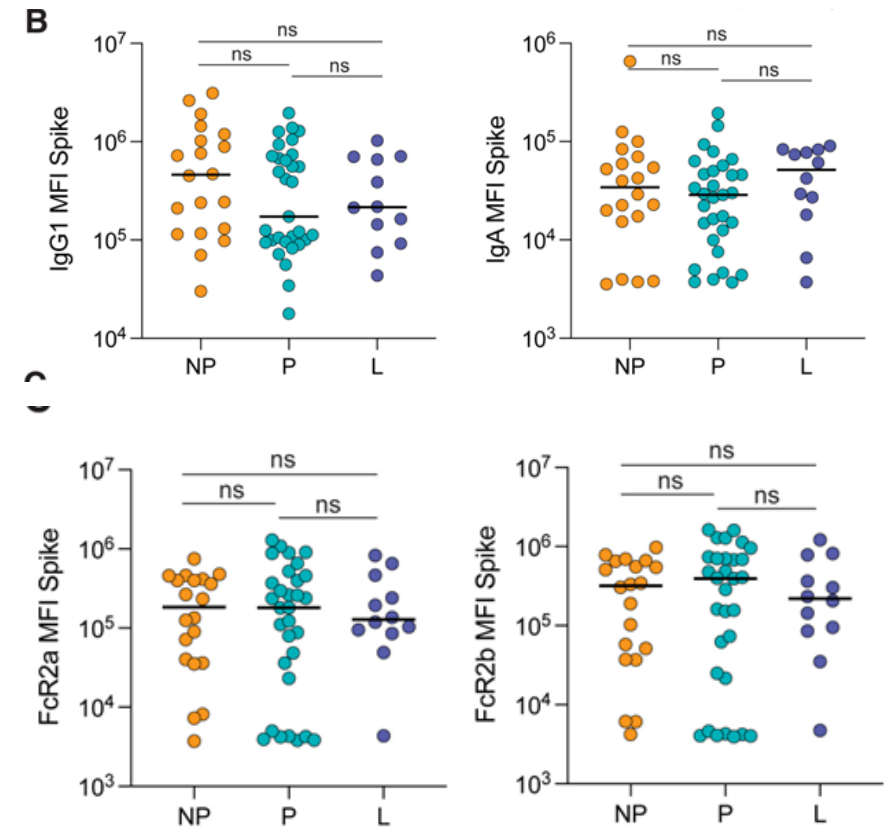


Difference in the quality of antibody response after primary response to mRNA vaccine

Primary vaccination



After booster (3rd trimester)



Booster dose increase antibody response to levels
And quality similar to non-pregnant individuals

Key considerations for vaccination of pregnant women

- Immune adaptation varies during pregnancy so timing of vaccination is to be considered to achieve optimal vaccine response
- Quality (isotype, function) rather than magnitude of antibody response may be impacted during pregnancy-> relevance to be confirmed
- Limited data on the impact on cellular responses to vaccines

Thanks