Immunological mechanisms of vaccine-induced immune responses in older adults

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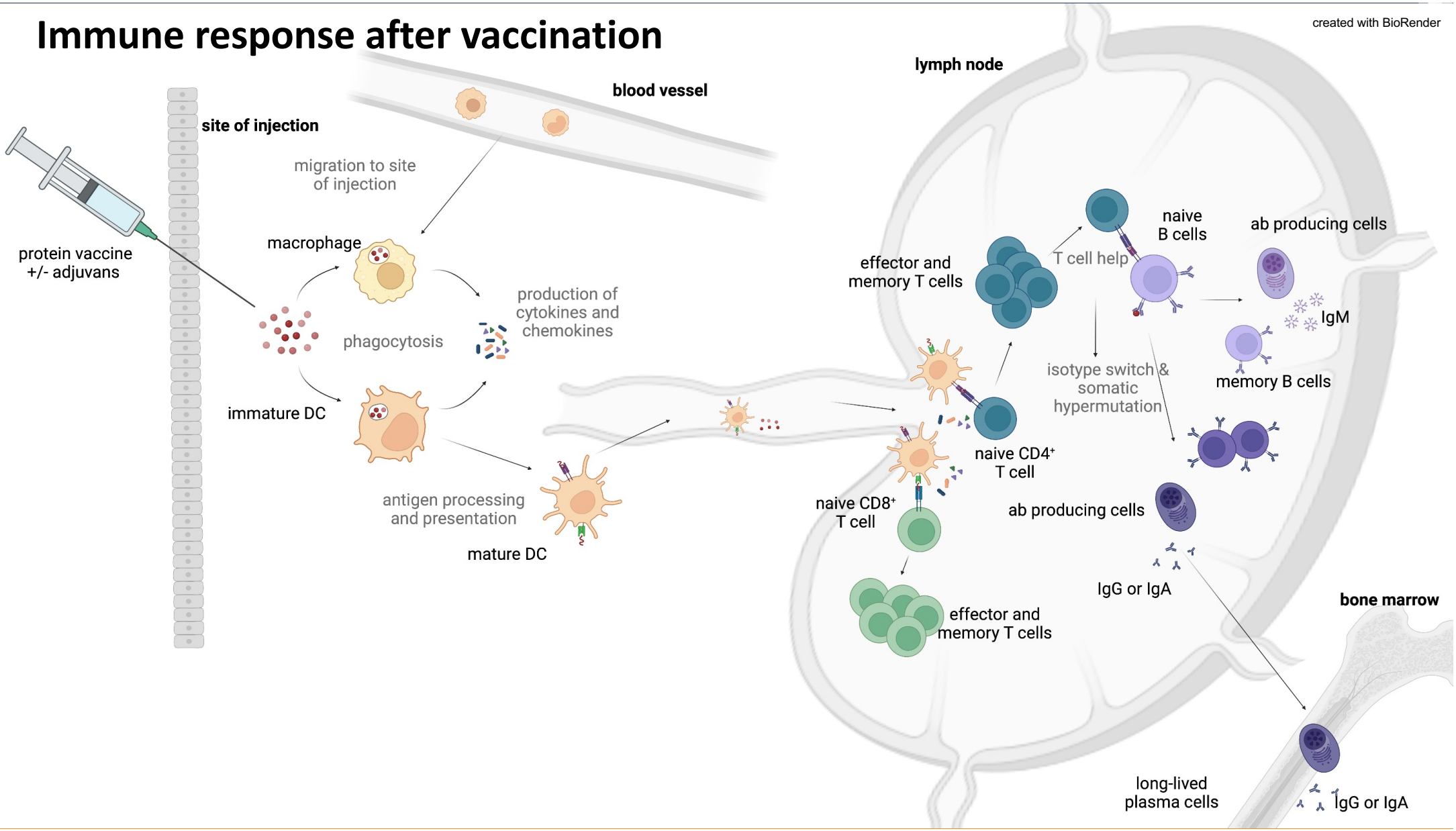
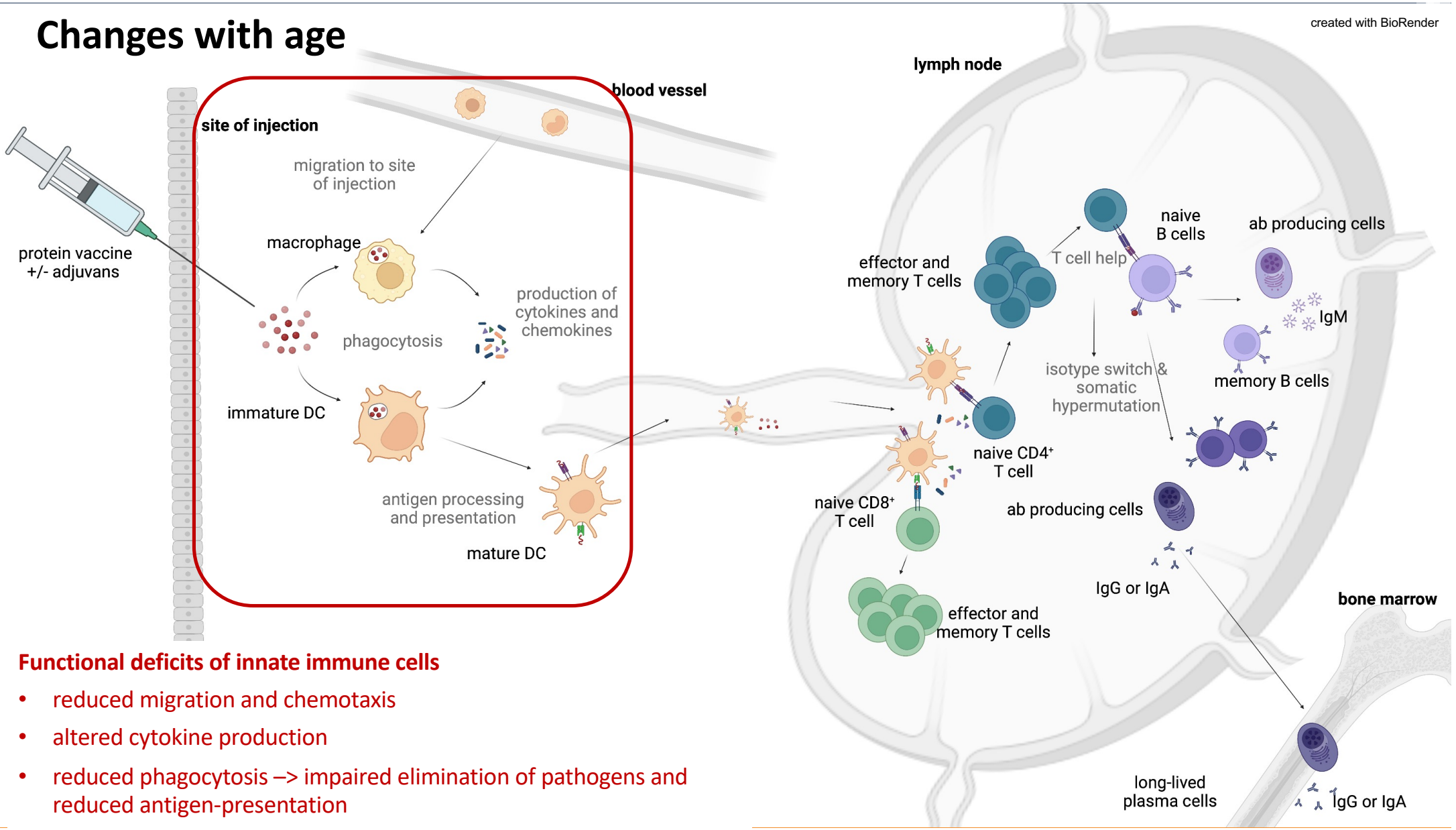
Universität Innsbruck, Austria

Immune response after vaccination



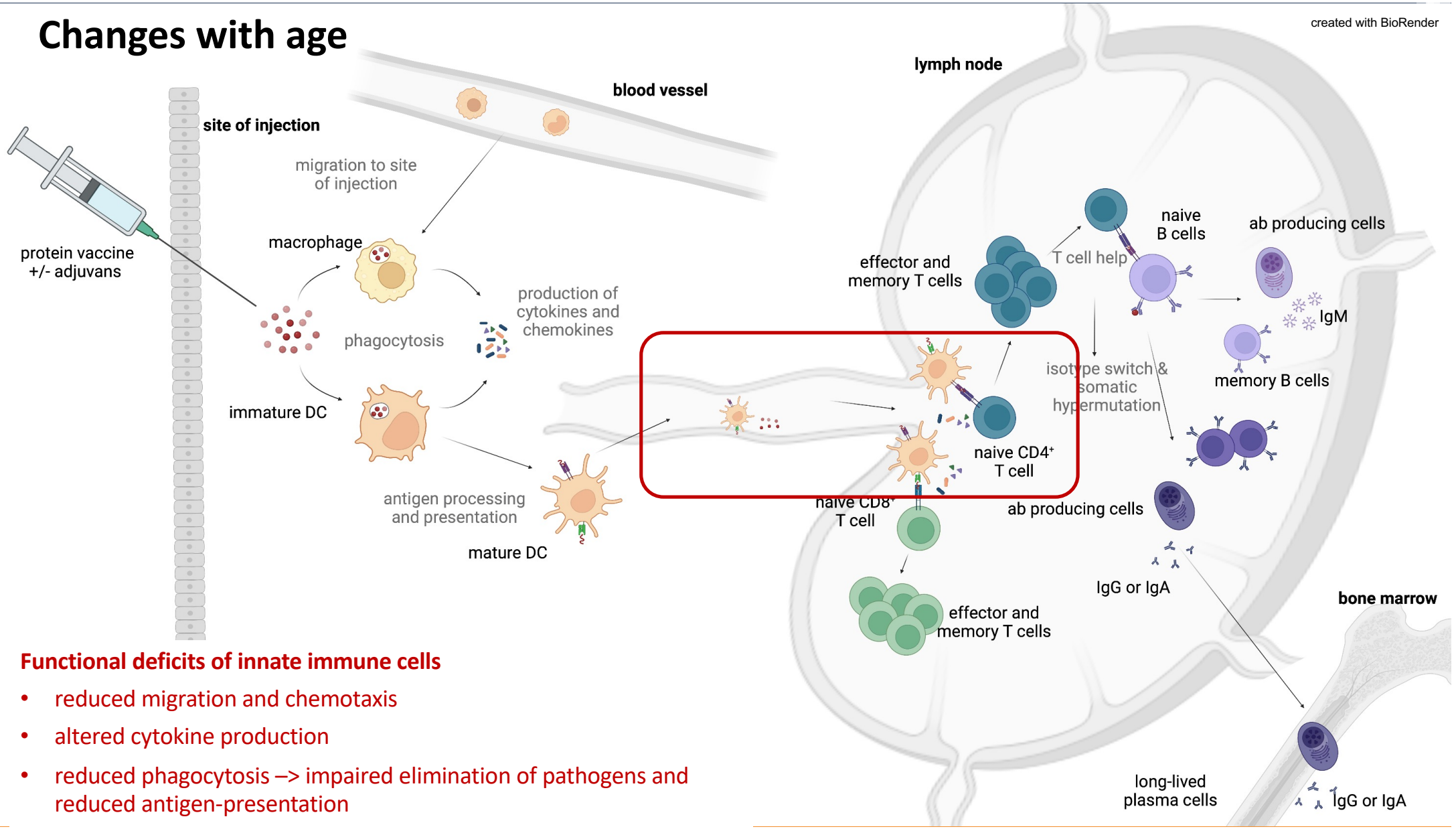
Changes with age



Functional deficits of innate immune cells

- reduced migration and chemotaxis
- altered cytokine production
- reduced phagocytosis –> impaired elimination of pathogens and reduced antigen-presentation

Changes with age



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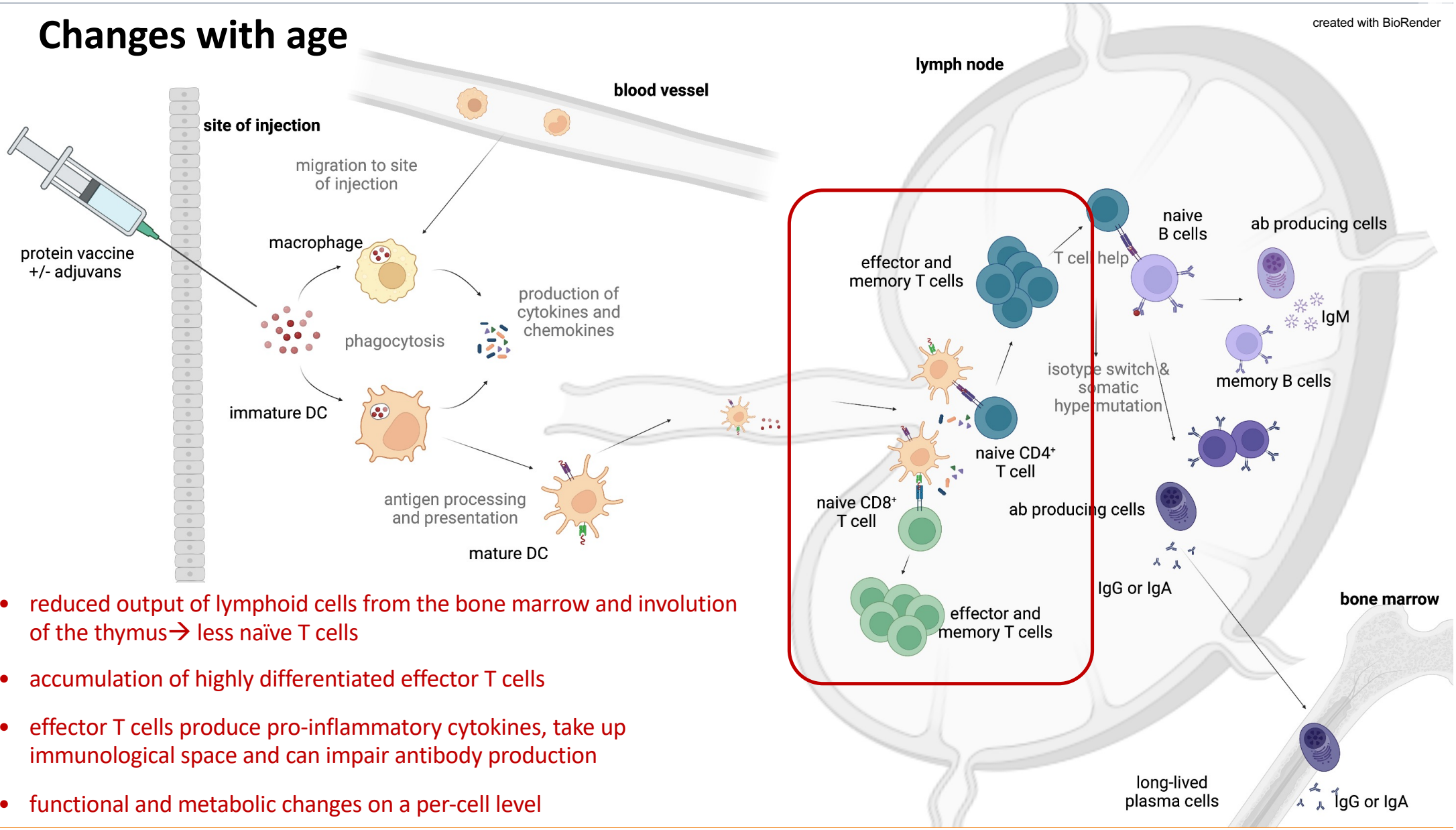
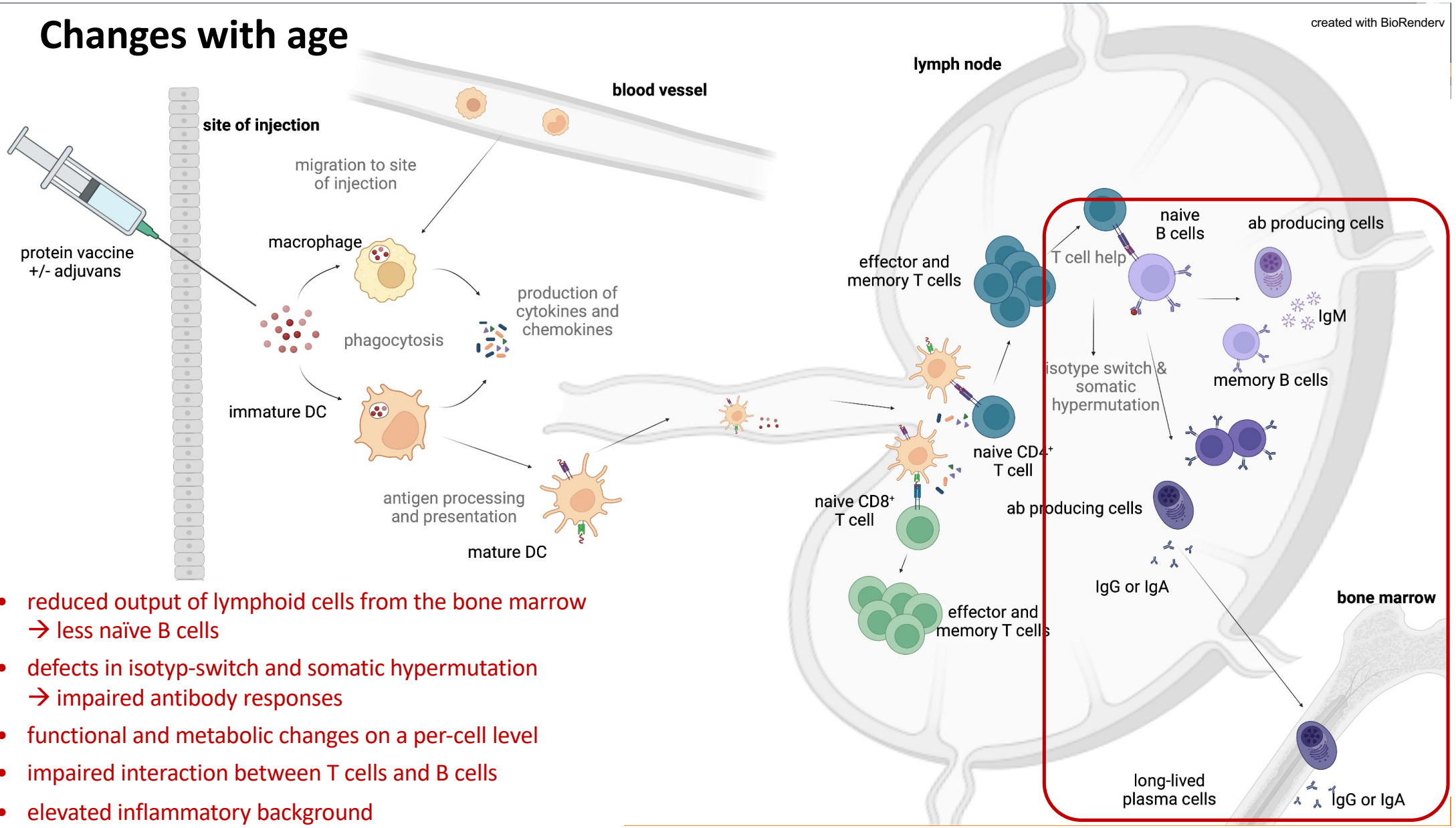


- reduced output of lymphoid cells from the bone marrow and involution of the thymus→ less naïve T cells
- accumulation of highly differentiated effector T cells
- effector T cells produce pro-inflammatory cytokines, take up immunological space and can impair antibody production
- functional and metabolic changes on a per-cell level

Changes with age

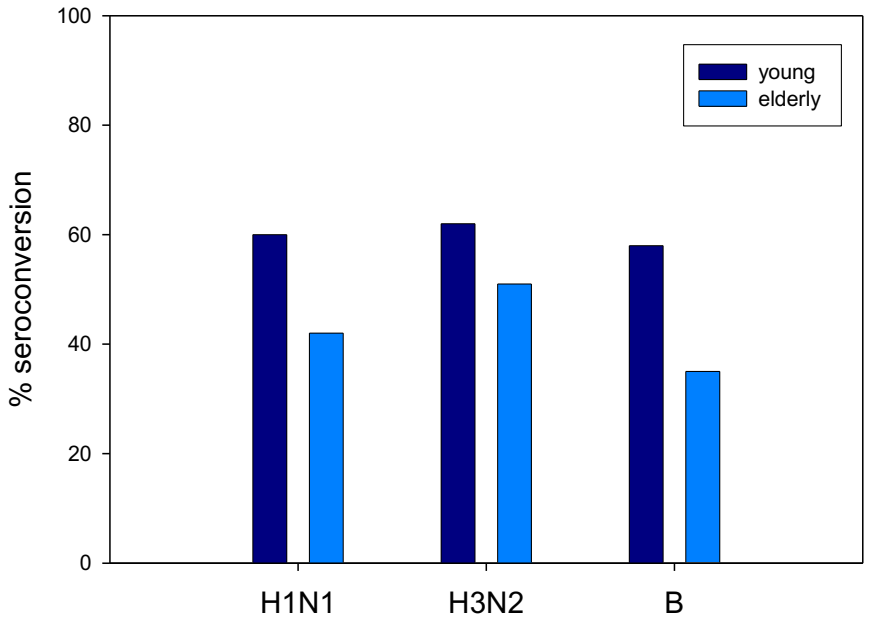


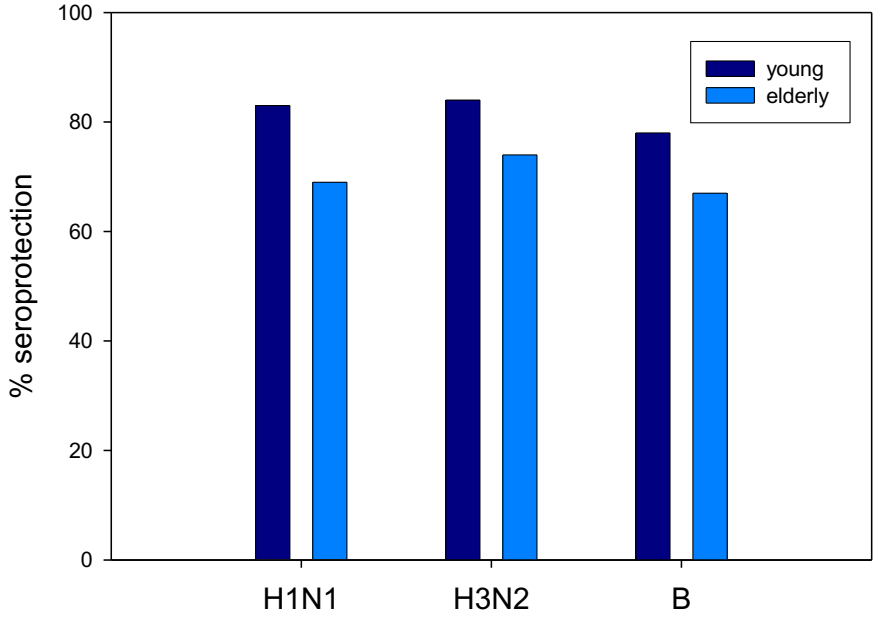
- reduced output of lymphoid cells from the bone marrow
  → less naïve B cells
- defects in isotyp-switch and somatic hypermutation
  → impaired antibody responses
- functional and metabolic changes on a per-cell level
- impaired interaction between T cells and B cells
- elevated inflammatory background

Strategies to improve vaccines for older adults

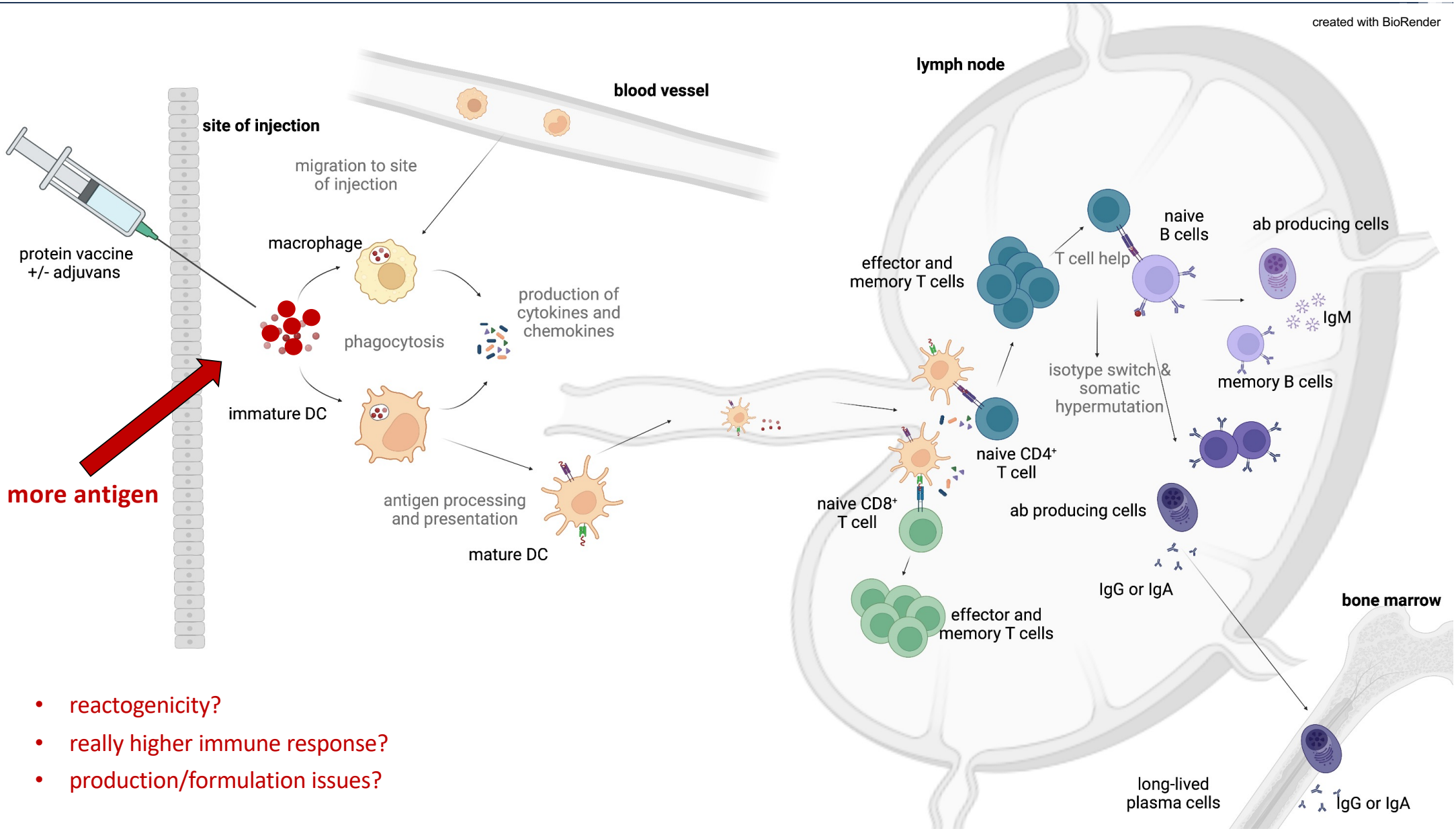
Standard Influenza vaccines are less immunogenic in older adults

meta-analysis of 31 studies (1986-2002)





data from: Goodwin et al., *Vaccine*, 2006



- reactogenicity?
- really higher immune response?
- production/formulation issues?

High-dose influenza vaccine: Randomized controlled trial (RCT)

Trivalent 60µg HA per strain instead of 15µg licensed in the US (2009/2010)

→ higher antibody levels, higher seroconversion

→ increased efficacy

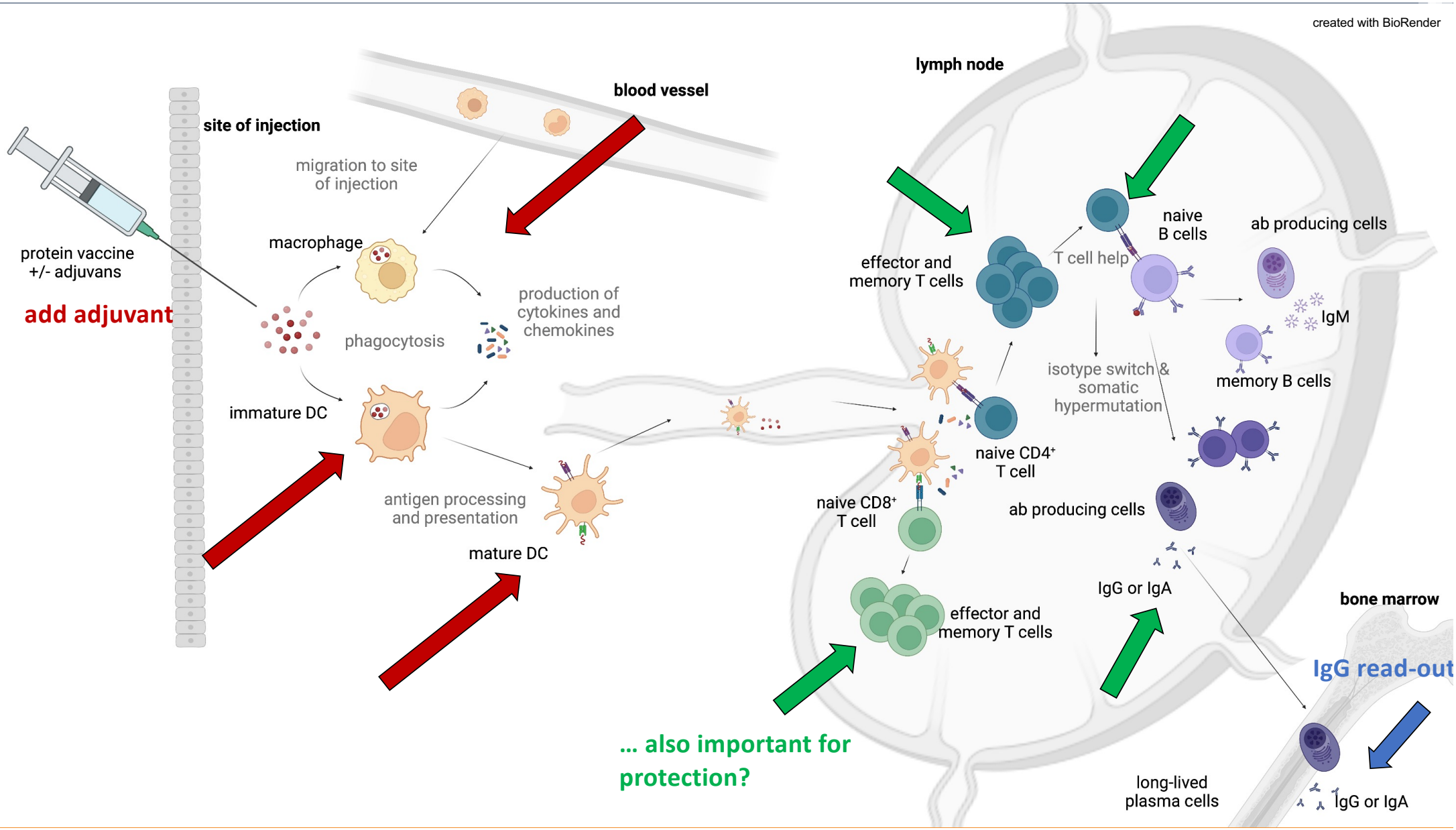
Efluelda in Europe since 2021
quadrivalent

randomized clinical trial: HD-TIV vs SD-TIV

Variable	Laboratory-Confirmed Influenza†		
	IIV3-HD (N = 15,990)	IIV3-SD (N = 15,993)	Relative Efficacy (95% CI)
	no. (%)		%
Protocol-defined influenza-like illness	228 (1.4)	301 (1.9)	24.2 (9.7 to 36.5)‡

→ Presentation 4.7

Falsey et al., *J Inf Dis,* 2009
DiazGranados et al., *NEJM, 2014*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lymph node
blood vessel
site of injection
migration to site of injection
protein vaccine +/- adjuvans
add adjuvant
macrophage
phagocytosis
production of cytokines and chemokines
immature DC
antigen processing and presentation
mature DC
effector and memory T cells
T cell help
naive B cells
ab producing cells
IgM
memory B cells
isotype switch & somatic hypermutation
naive CD4+ T cell
naive CD8+ T cell
ab producing cells
IgG or IgA
effector and memory T cells
bone marrow
IgG read-out
long-lived plasma cells
IgG or IgA
... also important for protection?

Approved vaccines with adjuvants used in older adults

MF59

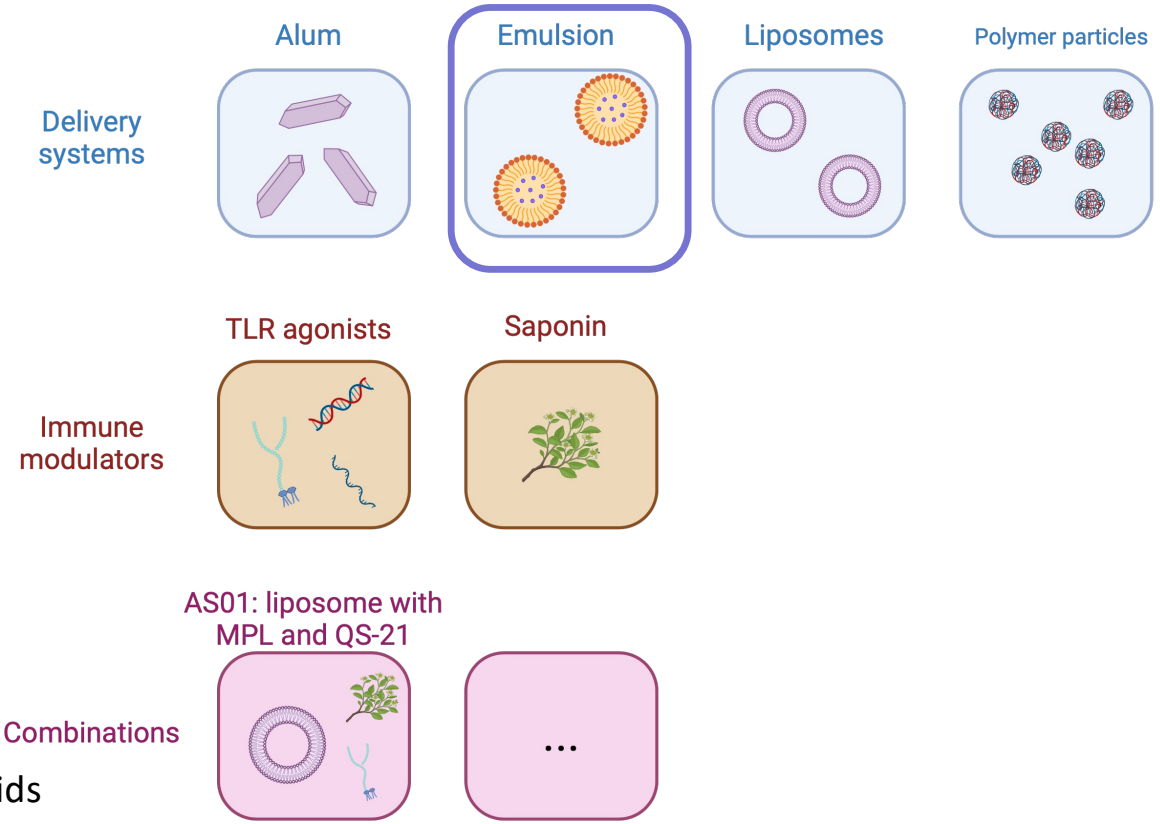
oil-in-water emulsion (squalene-based)
seasonal influenza (1997, Europe)

AS01

liposomes + QS21 + MPL
Herpes zoster (2017)
RSV (2023)

Matrix M

nanoparticles from saponins, cholesterol and phospholipids
COVID-19 (2022)



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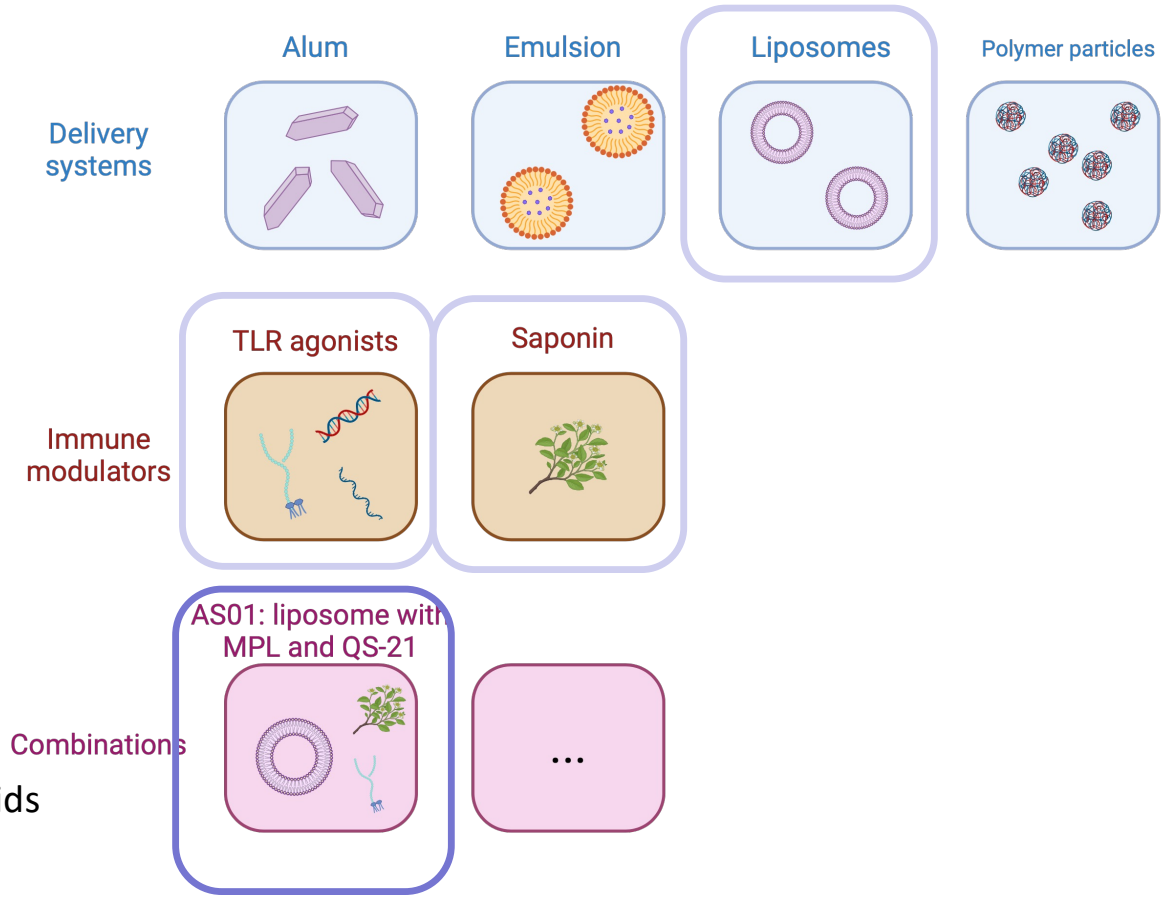

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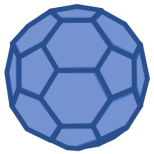
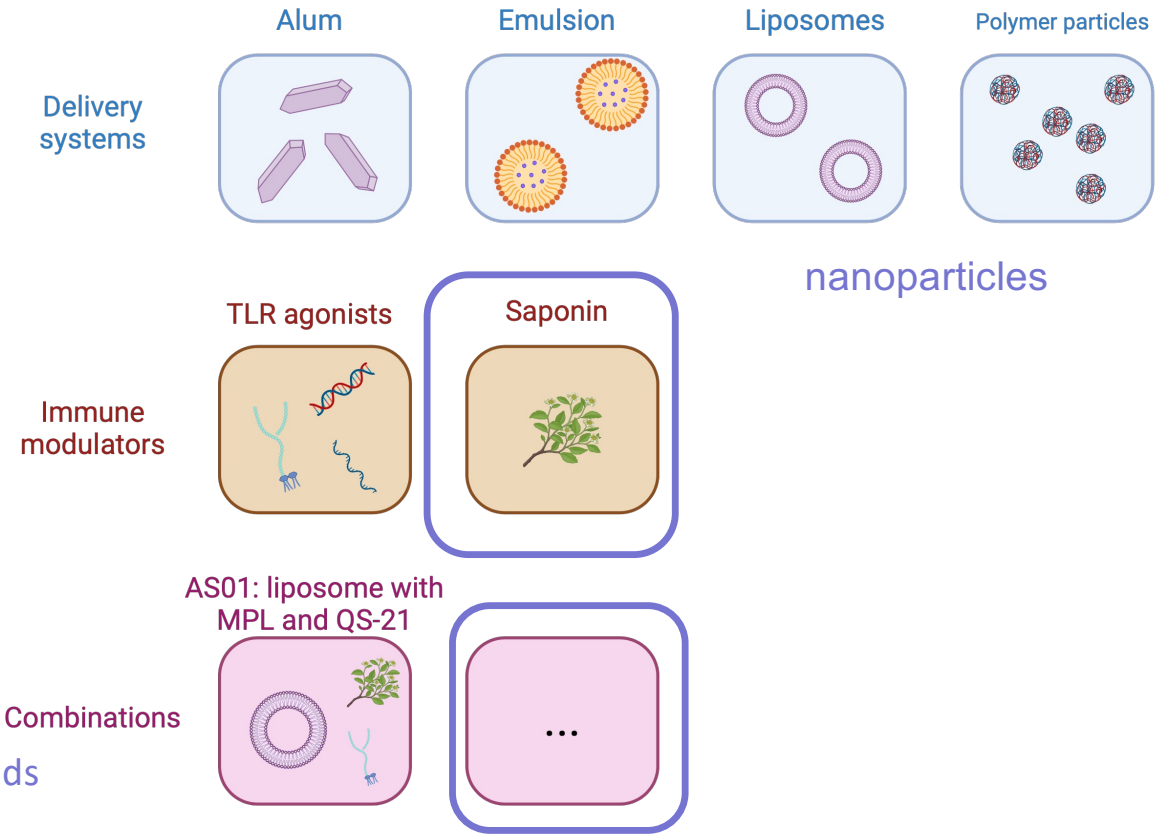


Chen, 2023



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Immunogenicity with or without adjuvant

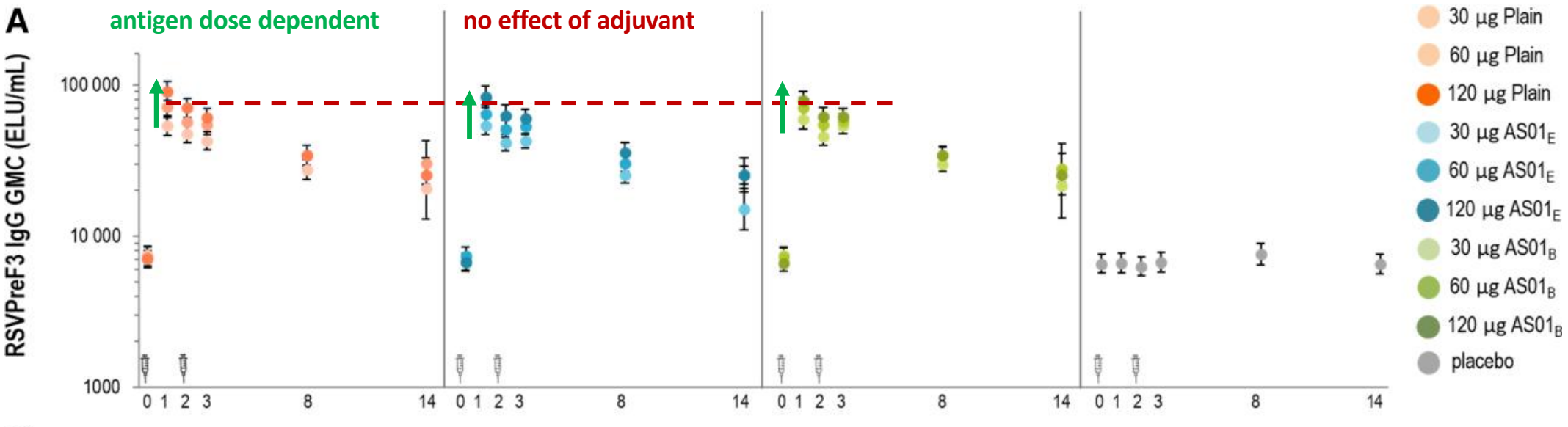
RSV preF + AS01

dose-response for antigen and adjuvant

two doses

60-80y

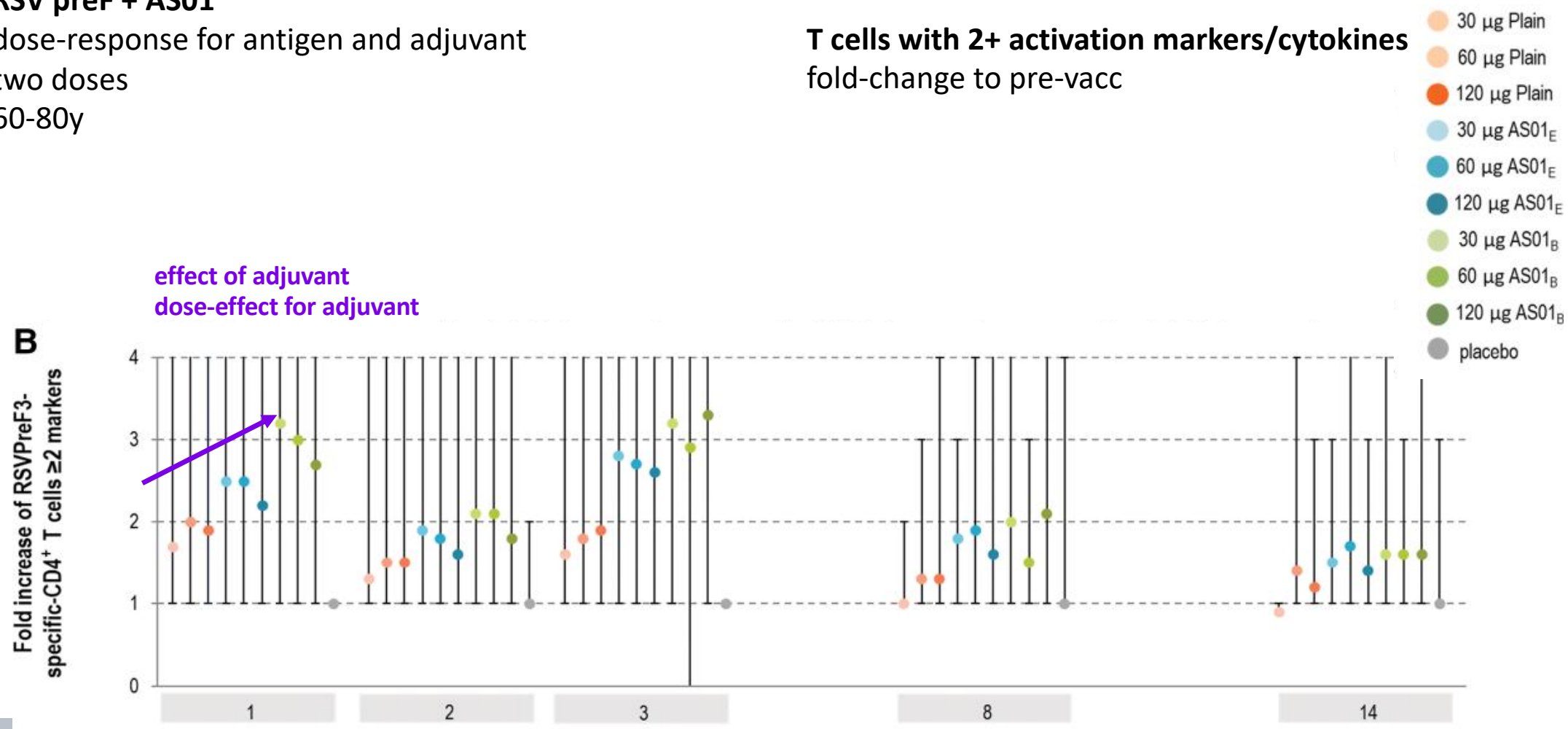
IgG antibody responses



Immunogenicity with or without adjuvant

RSV preF + AS01
dose-response for antigen and adjuvant
two doses
60-80y

T cells with 2+ activation markers/cytokines
fold-change to pre-vacc



Immunogenicity with or without adjuvant

Sars-CoV2 spike protein+ Matrix M

dose-response for antigen and adjuvant

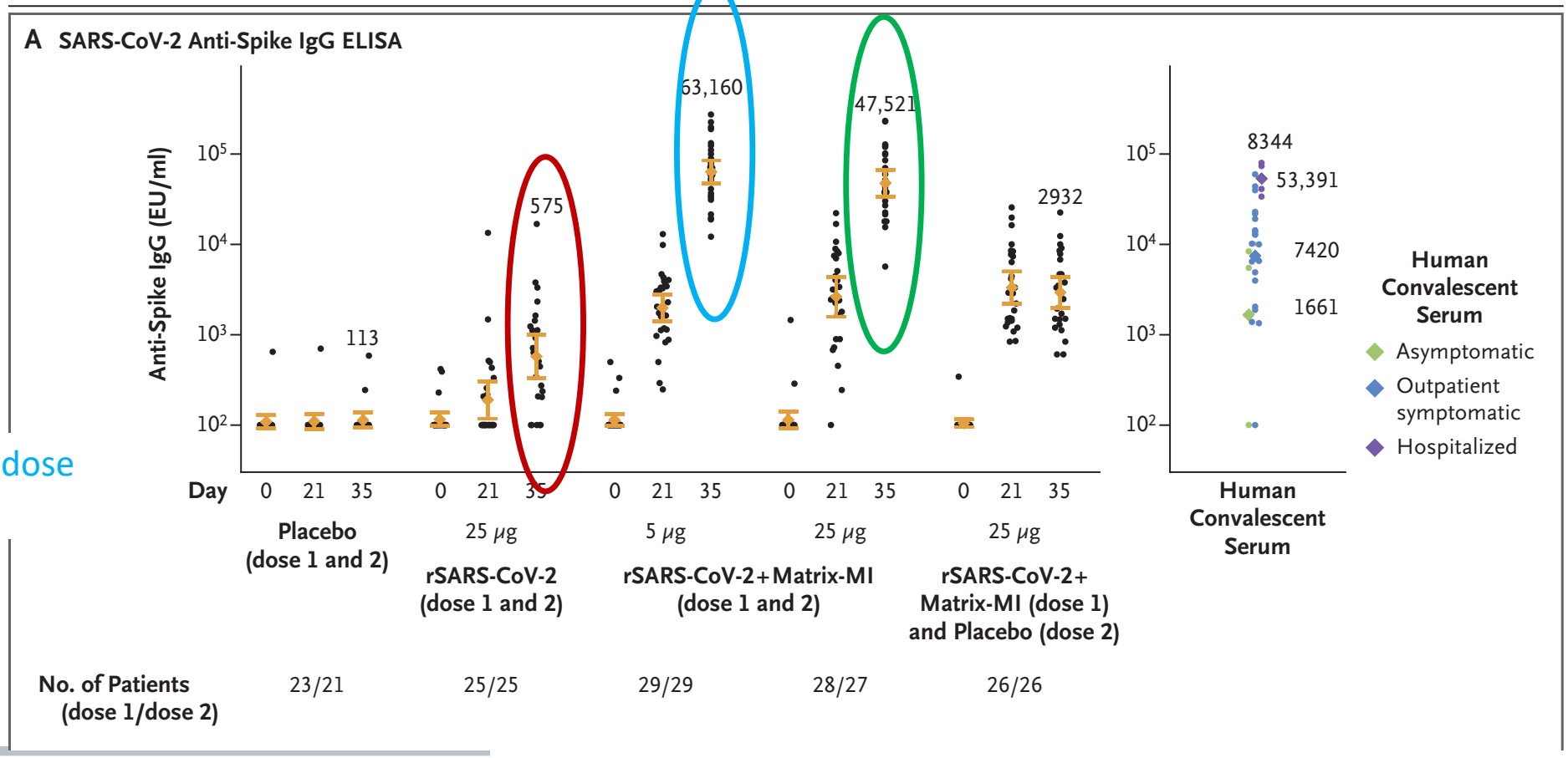
two doses

18-59y

no adjuvant

+ adjuvant

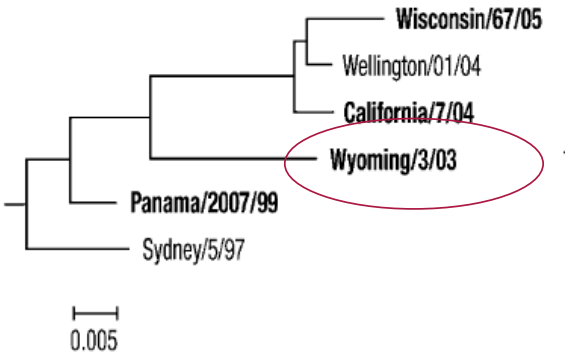
lower antigen dose + adjuvant



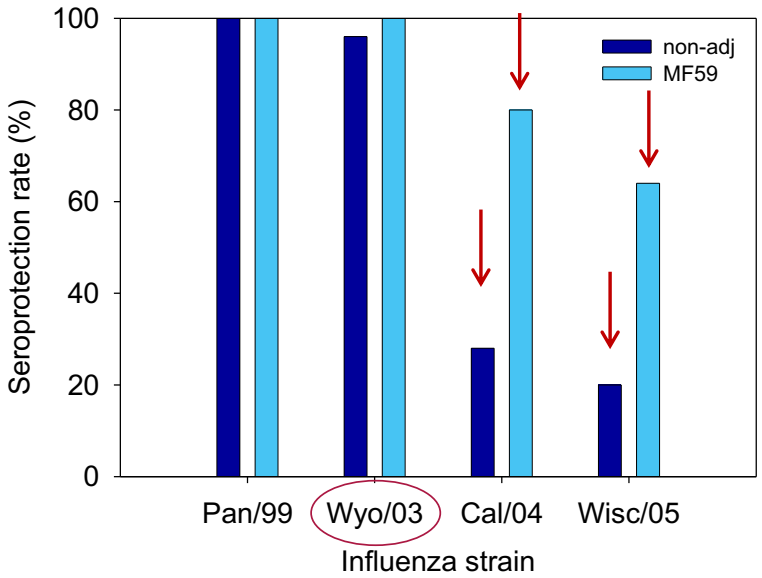
Induction of antibodies against drifted strains

seasonal influenza with or without MF59
>65y

(A)



seroprotection rates against drifted strains



Summary

- **Characteristic age-associated changes in all components of the immune system**

- **Higher antigen dose can lead to improved immunogenicity and protection**

- **Adjuvanted vaccines can achieve**
  - higher antibody levels
  - increased T cell responses
  - broader antibody repertoire
  - dose sparing
  - but optimal adjuvant – antigen combinations need to be developed

- **Other strategies to improve protection**
  - rejuvenate immune system / lower inflammatory processes before vaccination
  - alternative routes of administration: intradermal, mucosal…
  - universal / broader vaccines
  - optimal booster strategies
  - increased uptake!!

FEBS Youth Travel (YTF) grants and an IUBMB Transcontinental YTF grant are available for PhD students and young scientists

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Thank you!