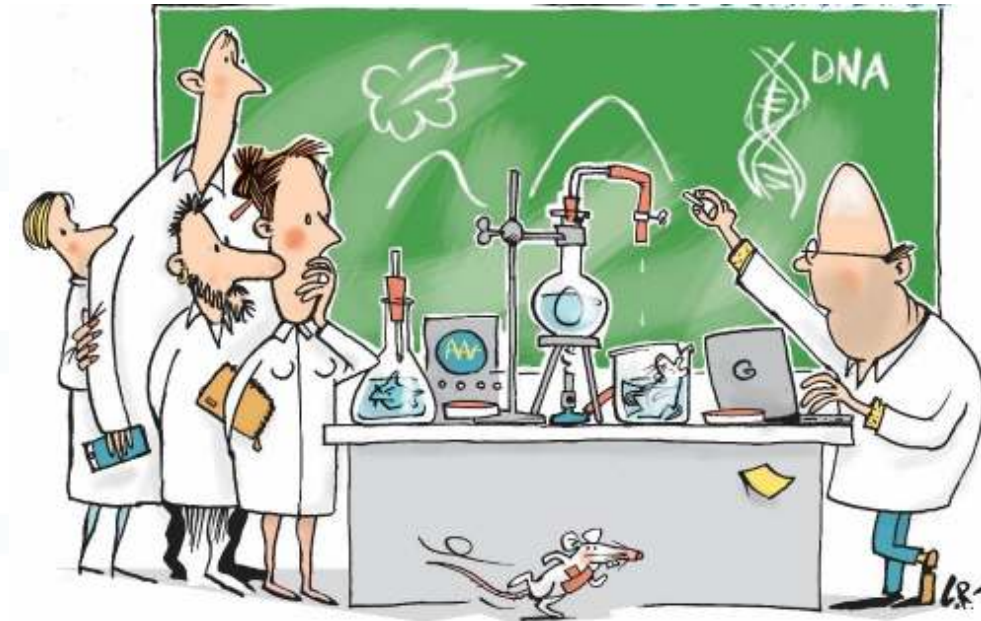




IMMUNITET VED PATTEGRISE

Gregers Jungersen
(ny) Sektion for Veterinær Vaccineforskning
SSI





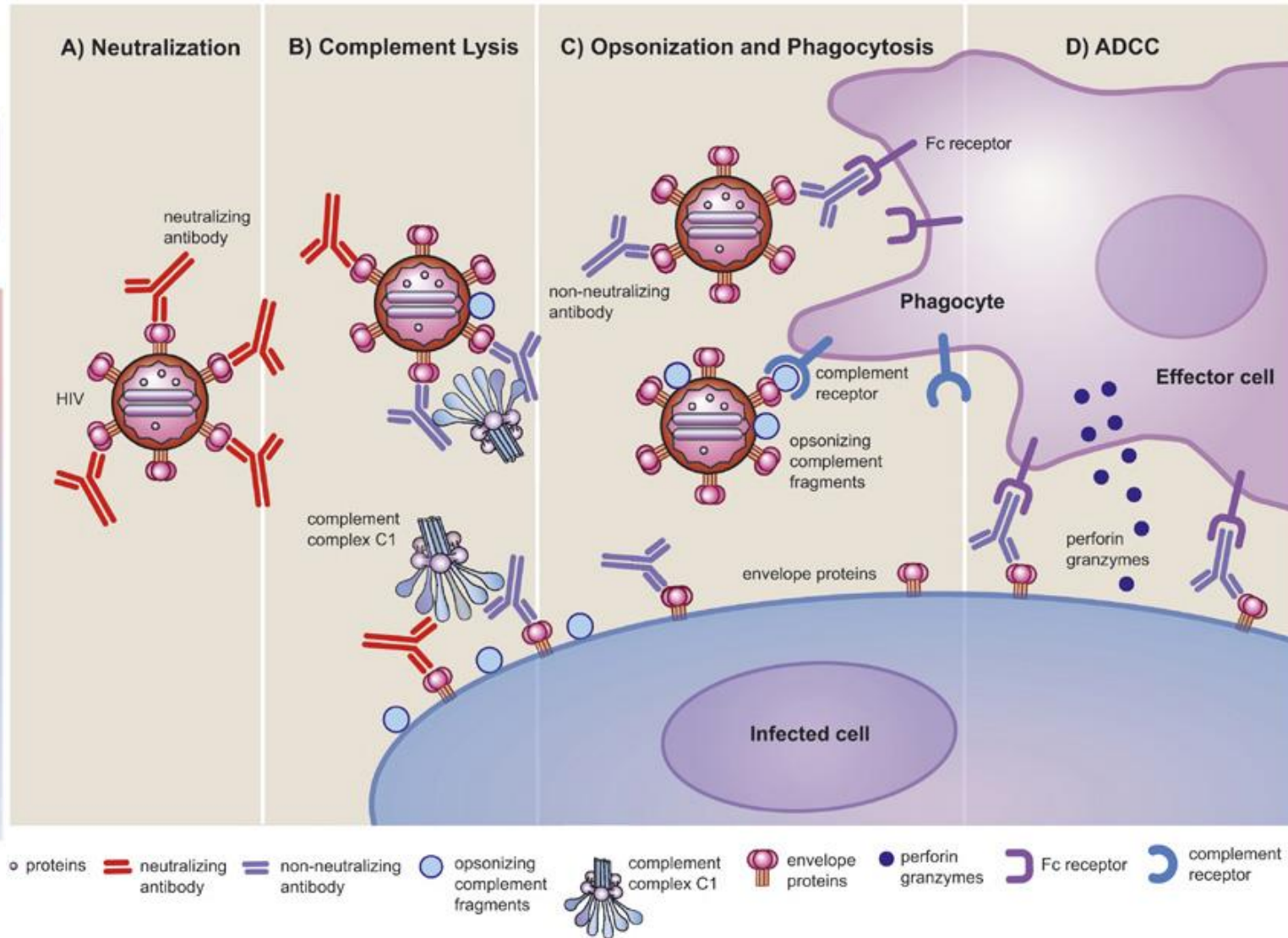
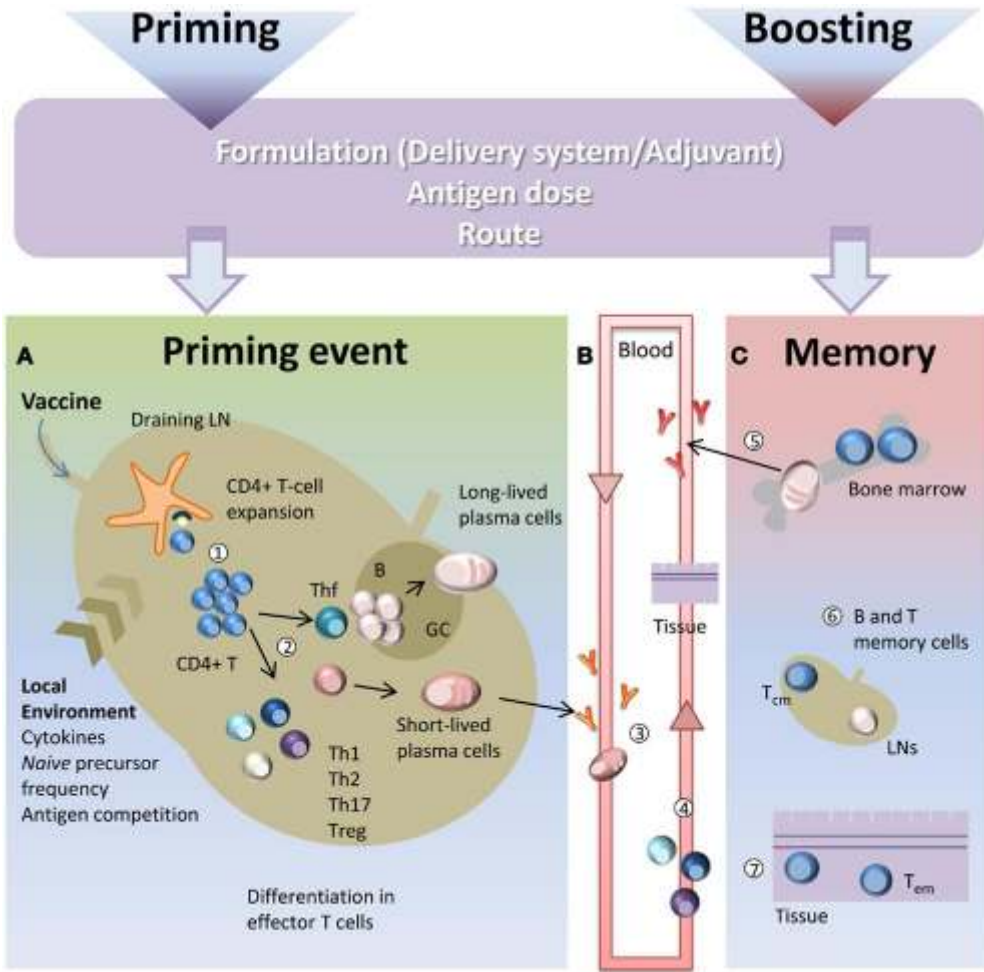
Råmælk

Sovaccination



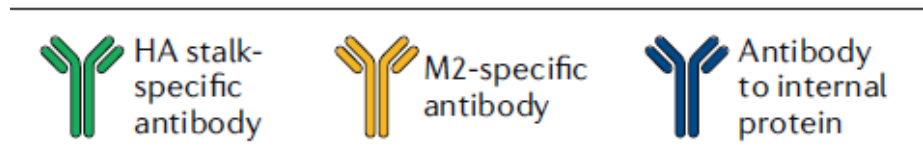
Fravænning

Opbygning af eget immunsvær



from M. Huber & A. Trkola (2007) *Journal of Internal Medicine*, 262(1)

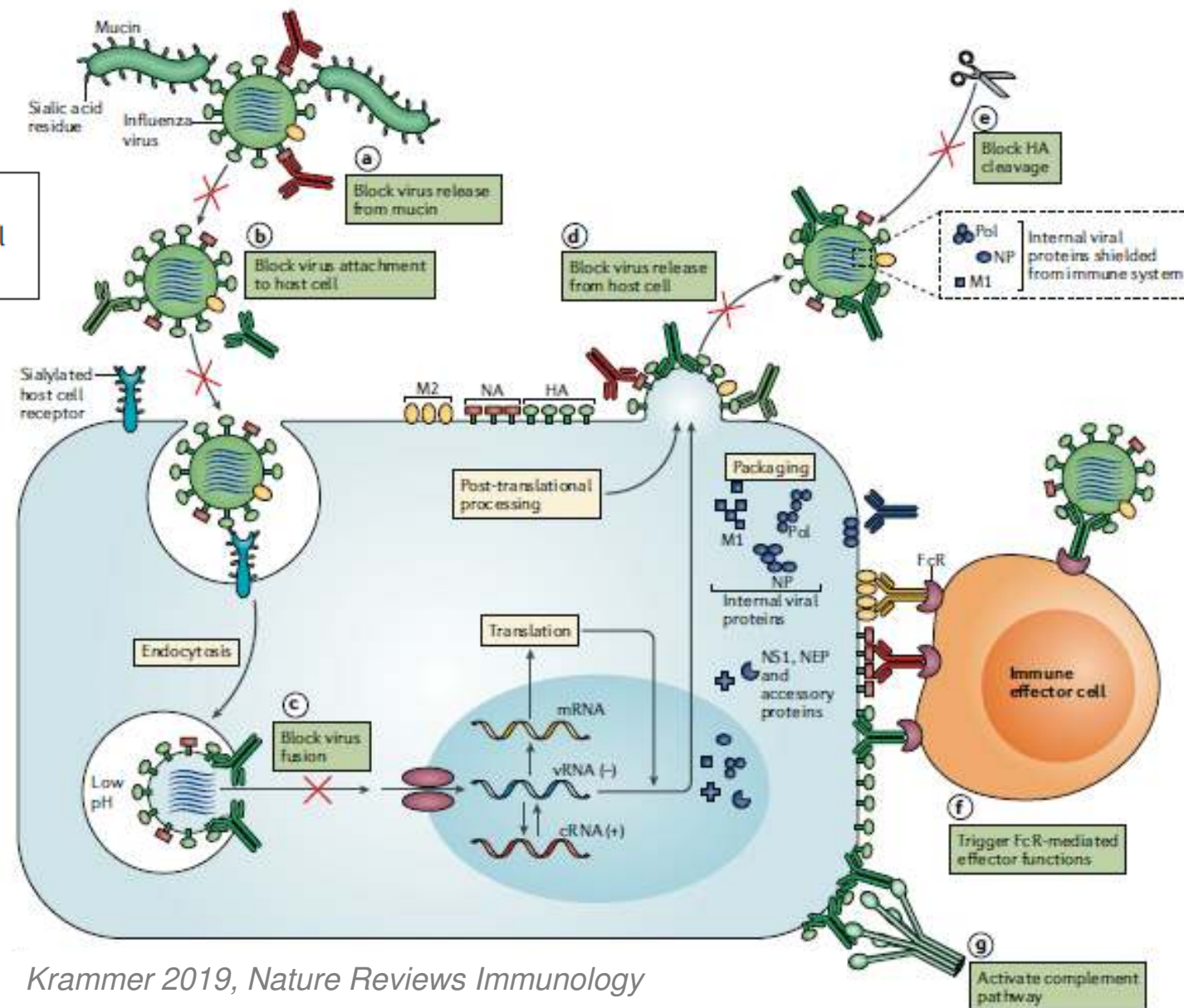
LOKAL OG SYSTEMISK BESKYTTELSE MOD INFLUENZA



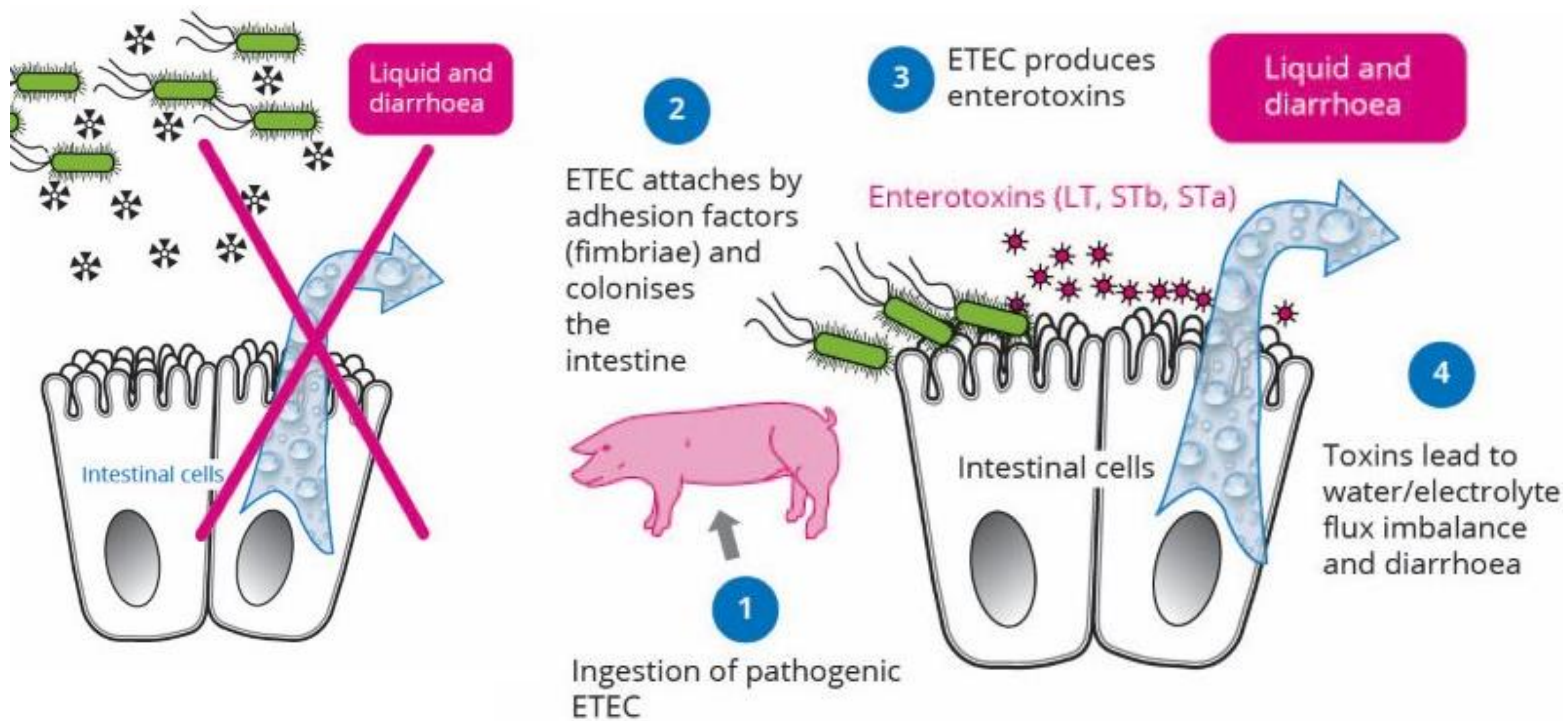
Antistoffer i mucus kan forhindre infektion

Antistoffer i serum kan standse infektion

T celler kan hjælpe ved nye varianter



Kræver immunitet på tarmoverfladen



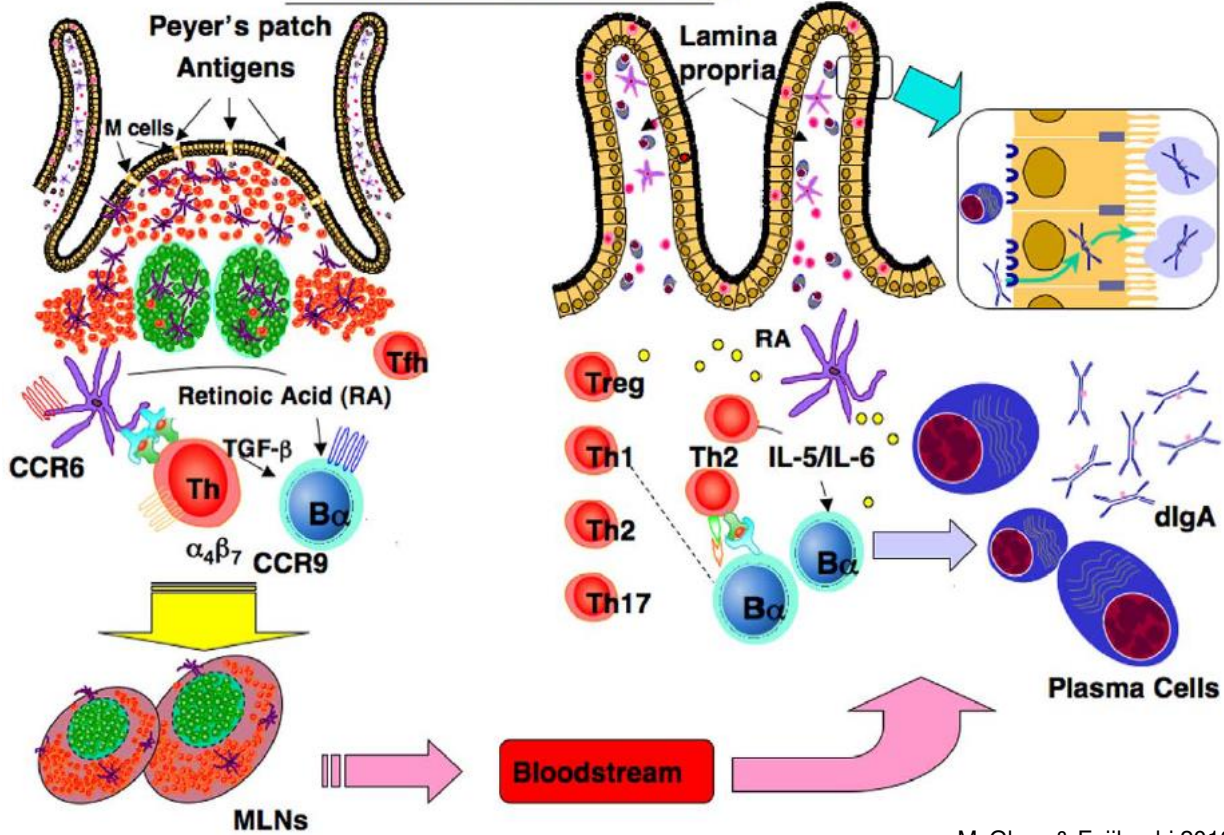
Function	IgG1	IgG2	IgG3	IgG4	IgA
Neutralization	+++	+++	+++	+++	+++
Opsonization	+++	*	++	+	+
Sensitization for killing by NK cells	++	-	++	-	-
Sensitization of mast cells	+	-	+	-	-
Activation of complement system	++	+	+++	-	+
Property	IgG1	IgG2	IgG3	IgG4	IgA
Transport across epithelium	-	-	-	-	+++ (dimer)

THE COMMON MUCOSAL IMMUNE SYSTEM

80 % af celler i immunsystemet er relateret til slimhinder.

A Mucosal Communication System

Inductive Versus Effector Sites

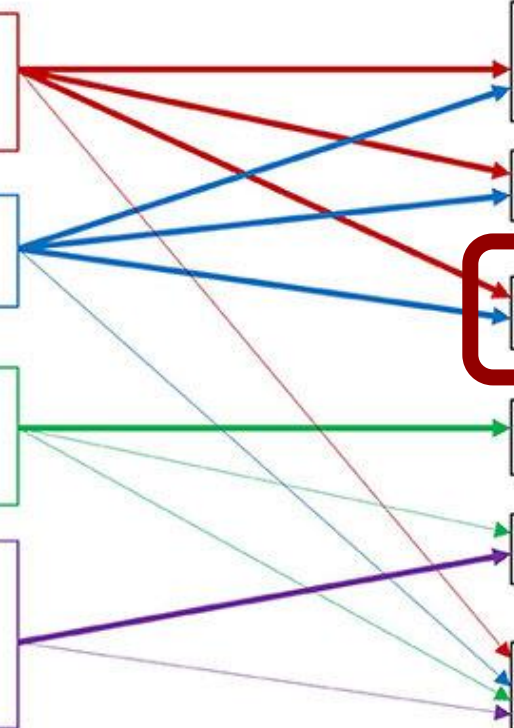
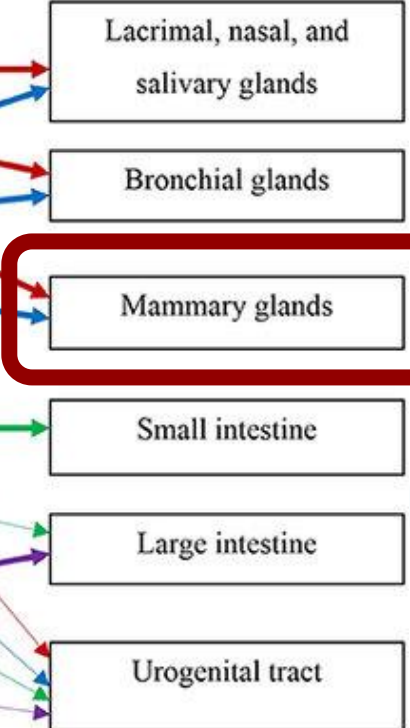


McGhee & Fujihashi 2012

Inductive MALT sites



Secretory effector sites



IgA ER SPECIALISERET TIL SLIMHINDER

SIgA generated by trans cytotosis of locally produced dimeric IgA

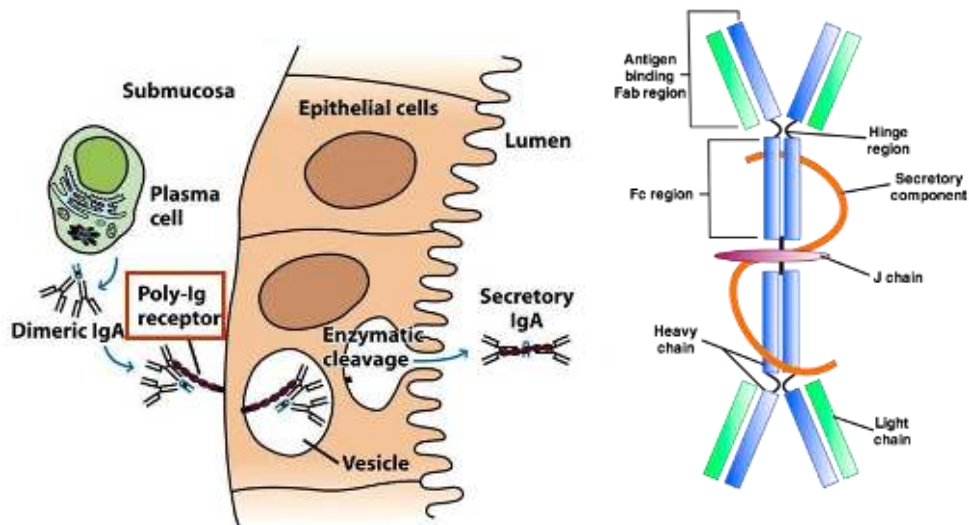
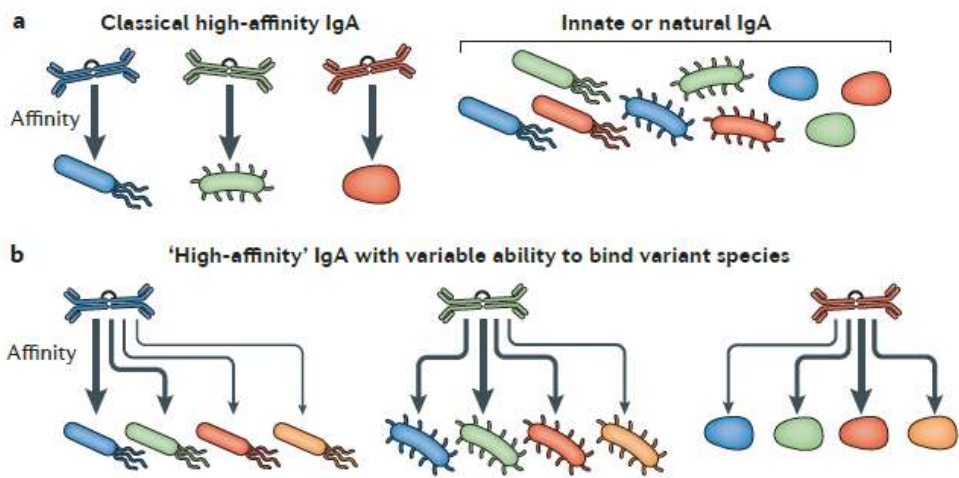
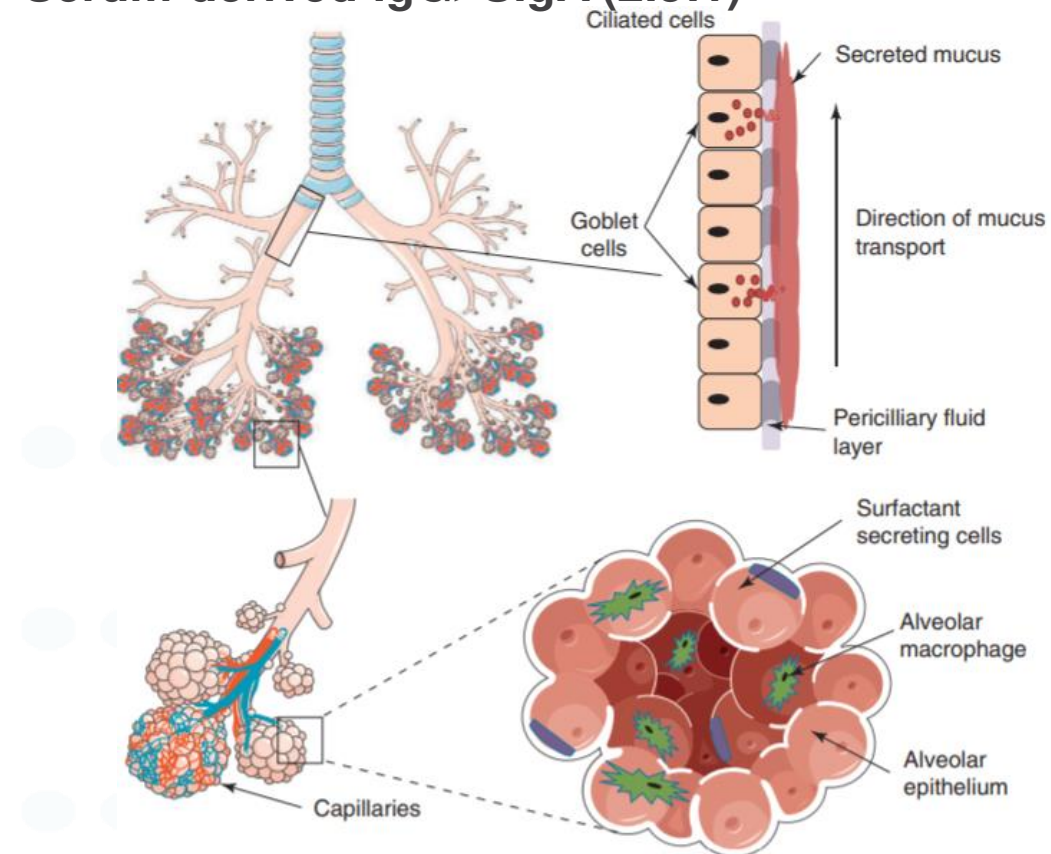


Figure 6-19b
Basic Immunology, Sixth Edition
© 2007 W.H. Freeman and Company

- ❖ Upper airways, trachea, bronchi:
 - local-produced **Secretory-IgA > IgG (3:1)**
- ❖ Bronchioles (<1 mm), Alveoli:
 - **Serum-derived IgG > SIgA (2.5:1)**



❖ So serum

- 35 mg/mL IgG
- 2 mg/mL IgA
- 7 mg/mL IgM

❖ Råmælk:

- 55-150 mg/mL IgG fra serum
- 8 mg/mL IgA fra serum
- 16 mg/mL lokalt produceret SIgA

❖ Somælk:

- 55% lokalt produceret SIgA
- 18% lokalt IgG
- 14% lokalt IgM
- Ca 10% IgG, IgA og IgM fra serum

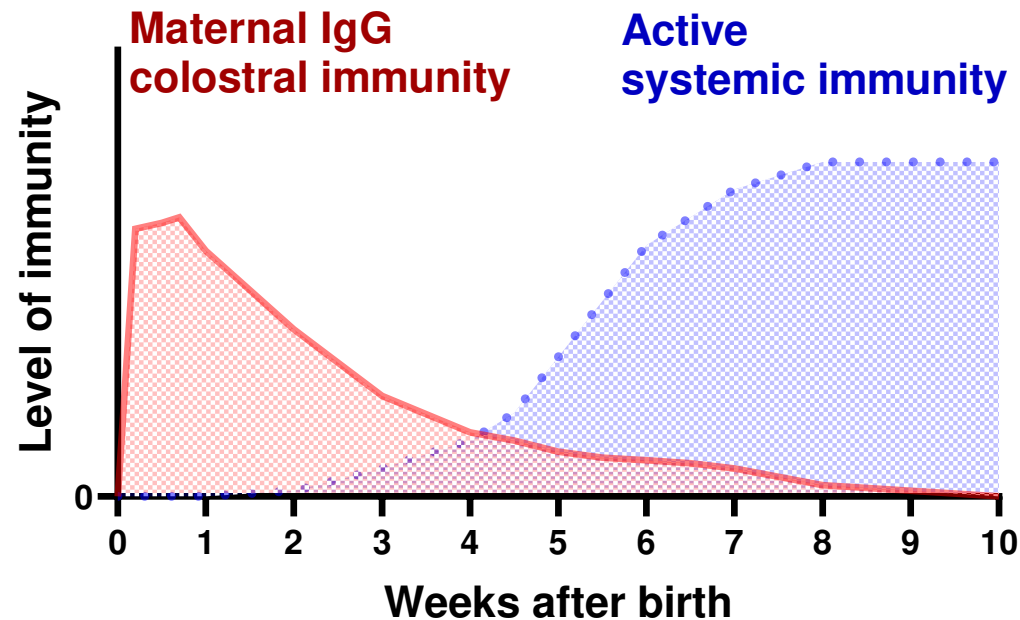
❖ Pattegrise serum

- IgG $T_{1/2}$ = 14 dage
- IgA $T_{1/2}$ = 3,5 dage
- IgM $T_{1/2}$ = 4,5 dage

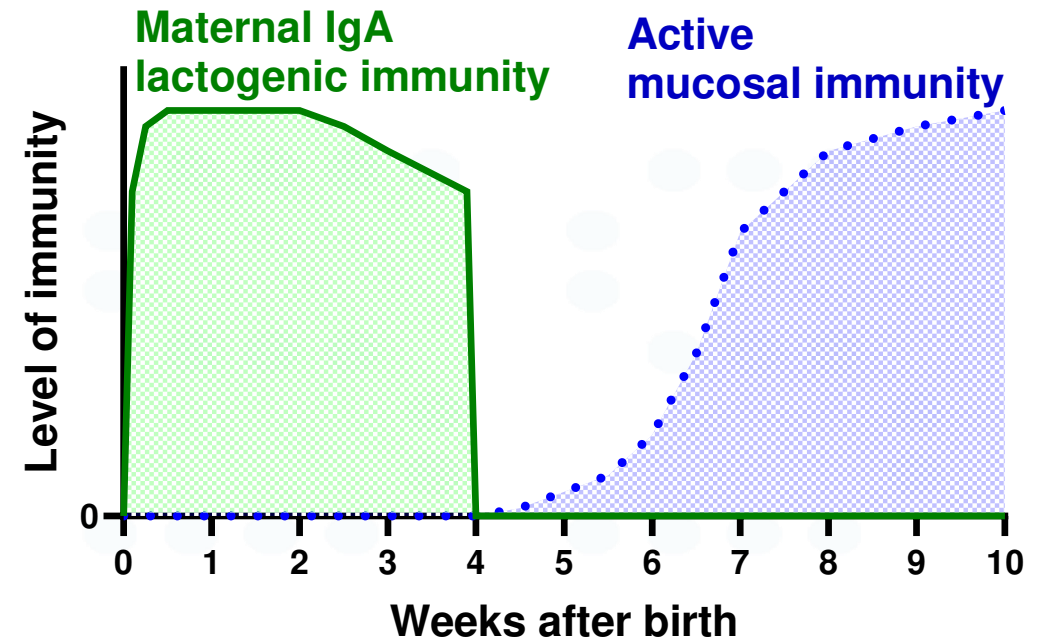


- ❖ Effekt af maternel immunitet på pattegriseimmunitet
 - Serum IgG fra råmælk forsvinder langsomt $T_{1/2} = 14$ dage
 - SIgA i mælk stopper momentant ved fravænning
 - Overførsel af immunceller fra so til pattegris
 - Svært at vurdere effekt
 - Har flytning af smågrise før kolostrum en effekt?

Systemic/Serum Immunity



Local Intestinal Immunity



❖ Vaccination af søer mindst to uger før faring!

- Tid til opbygning af immunitet
- Transfer af IgG til råmælk
- Undgå risiko for abort/tidlig fødsel

❖ To uger er...

- ...præcis **14 dage** for en forsker!
- ...**8 – 20 dage** for en landmand

❖ **OBS Mulig negativ påvirkning af vaccine til pattegrise/smågrise**

- Generelt, negativ effekt på antistoffer, ingen effekt på T celler
- I nogle (få) tilfælde kan MDA forstærke vaccine effekt

❖ Lokalt produceret SIgA i tarmen

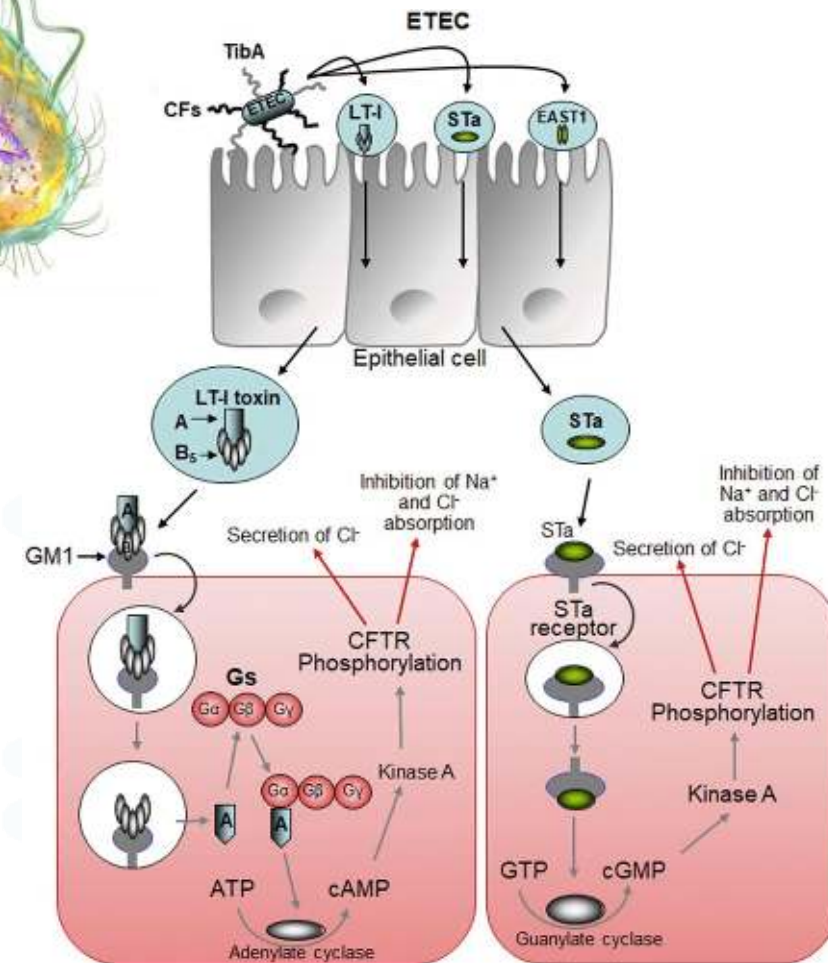
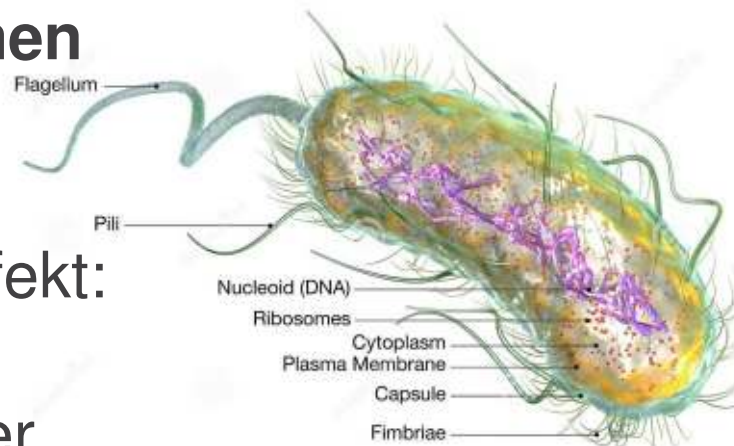
- Mælk IgA beskytter

❖ Bredt neutraliserende ETEC effekt:

- F4 og F18 adhæsions pili
- LT, STa, STb, (Stx2e) toksiner
- Rotavirus?

❖ Upåvirket af IgG i kolostrum/serum og IgA i somælk

❖ Effekt ved fravænning 3-4 uger gamle grise



DOSIS TIL STOR OG LILLE GRIS?

Mus – Pattegris – So ?

Levende eller dræbte vacciner?

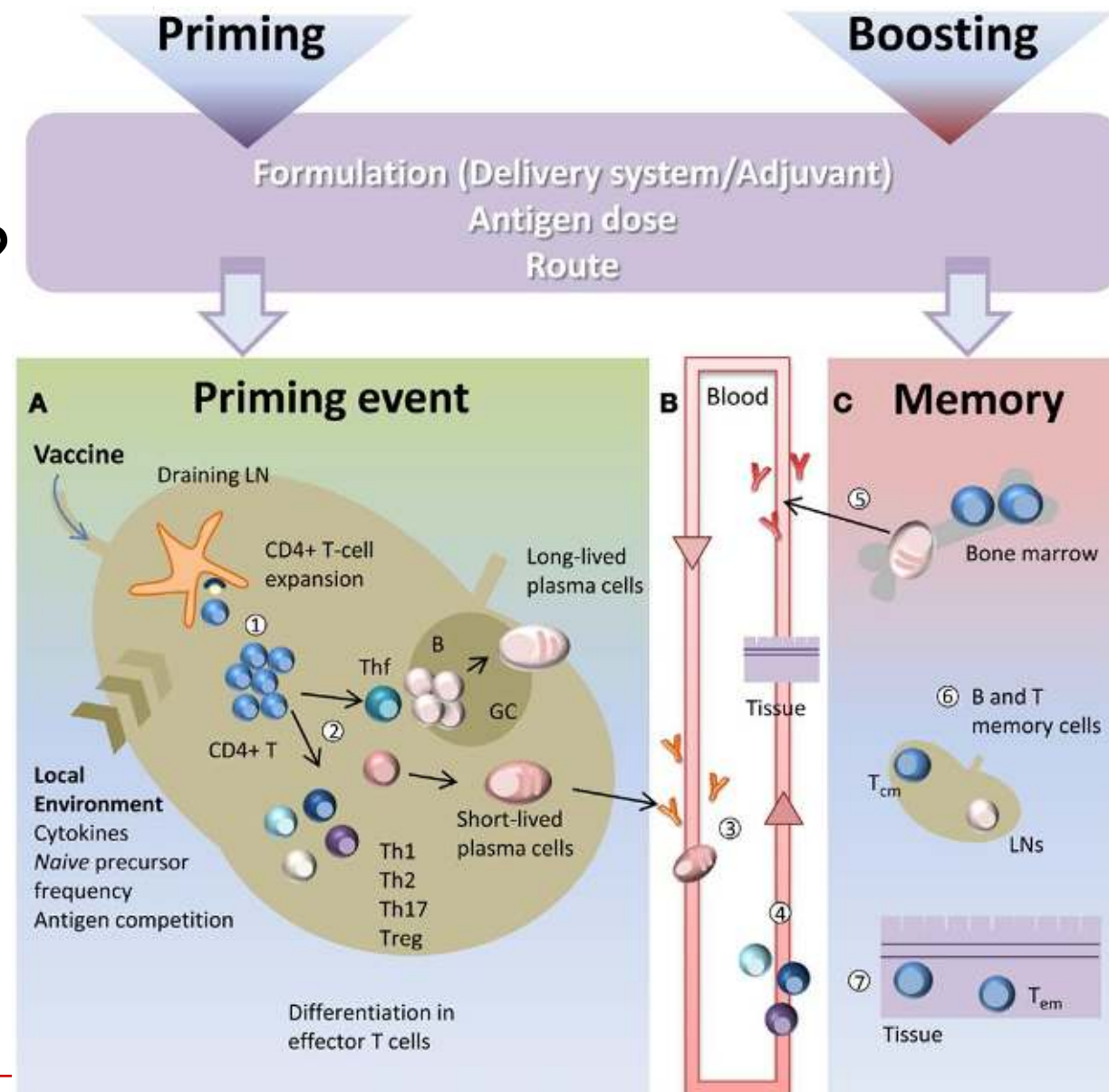
Typisk dosis til **mus**: 5 μg i 100 μL

Typisk dosis til **gris**: 50 μg i 1-2 mL

Mit svar:

Hvis man kan vise det virker, så virker det nok.

Man kan ikke gætte sig til om det virker



HVORDAN PÅVIRKES IMMUNSVAR AF ANTIGEN DOSIS?



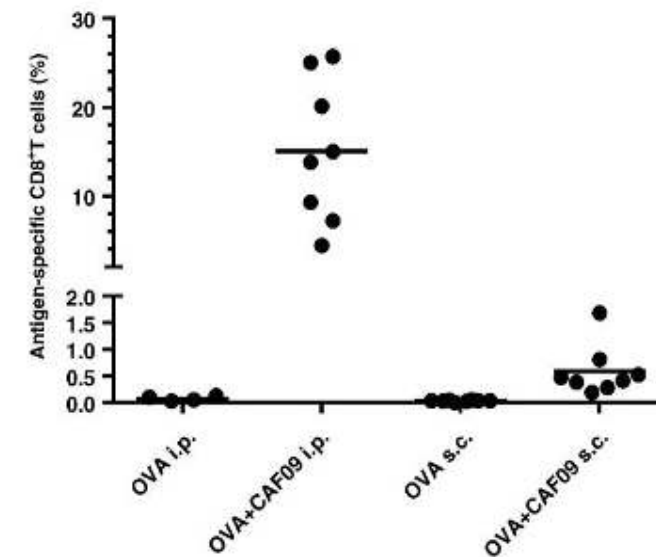
Göttingen minipigs
SLA-2*03:01

Tetanus Toxoid i tre doser

1 μ g

10 μ g

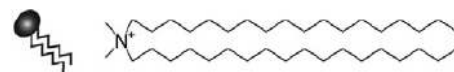
100 μ g



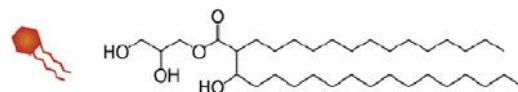
Schmidt et al, J Control Release, 2016

TLR3 stimulating adjuvant

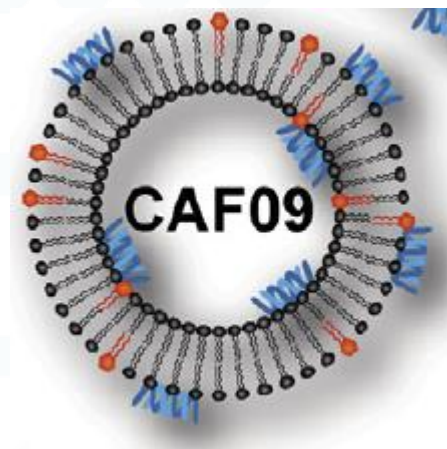
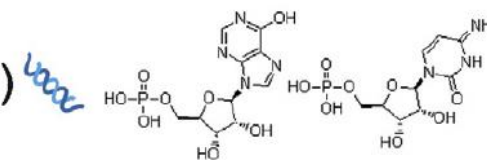
DDA



MMG



Poly(I:C)



Korsholm et al, Vaccine, 2014

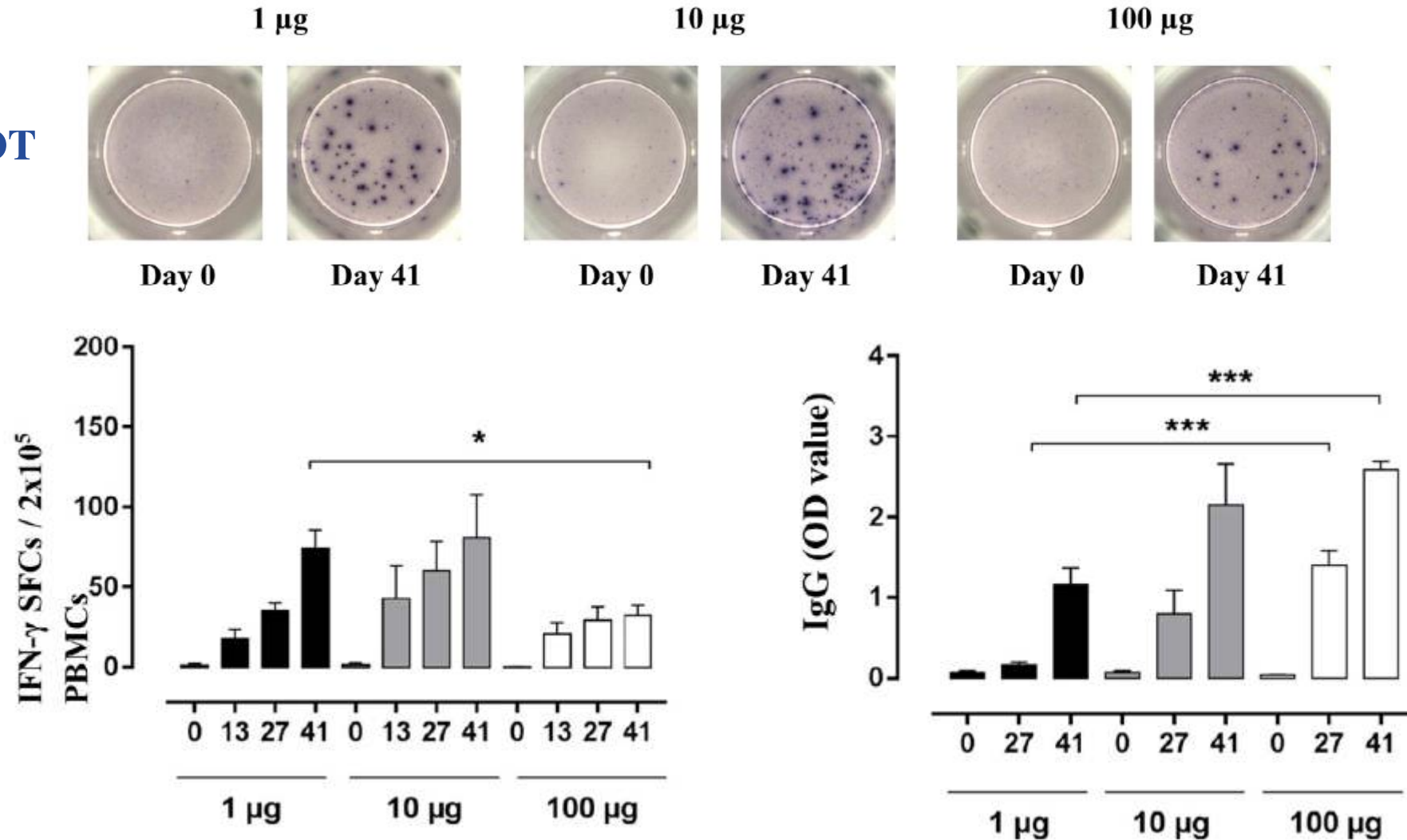


i.p. injektion

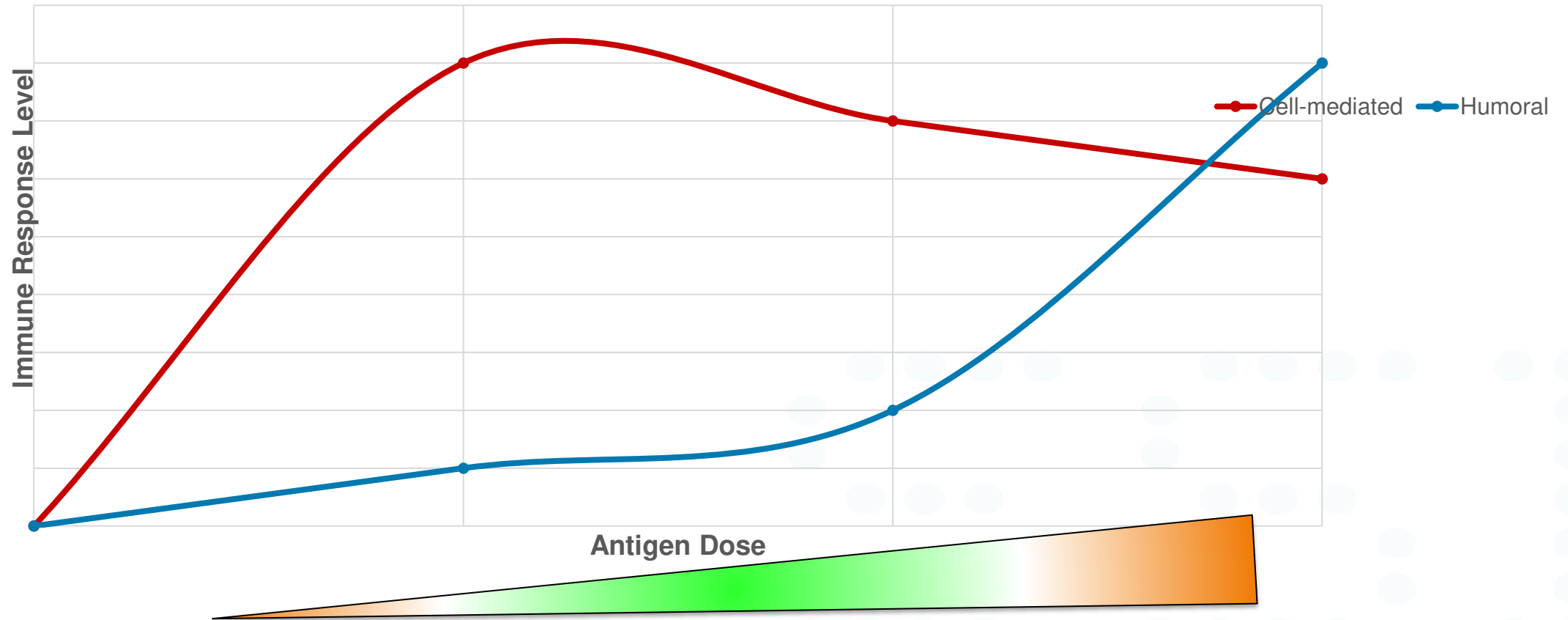
LAV DOSIS TT IMMUNISERING FREMMER CMI SVAR

N.H. Overgaard et al. / Vaccine 35 (2017) 5629–5636

IFN- γ ELISPOT



Model of Antigen Dose Effect on Immune Response



SKIFT AF VACCINEMÆRKE ?

- ❖ Antigener defineres på B- og T-celle niveau
- ❖ Hvis antigener er delt vil én vaccine booste den anden
- ❖ **Kun immunceller der genkender antigenet (epitopen) vil blive aktiveret**

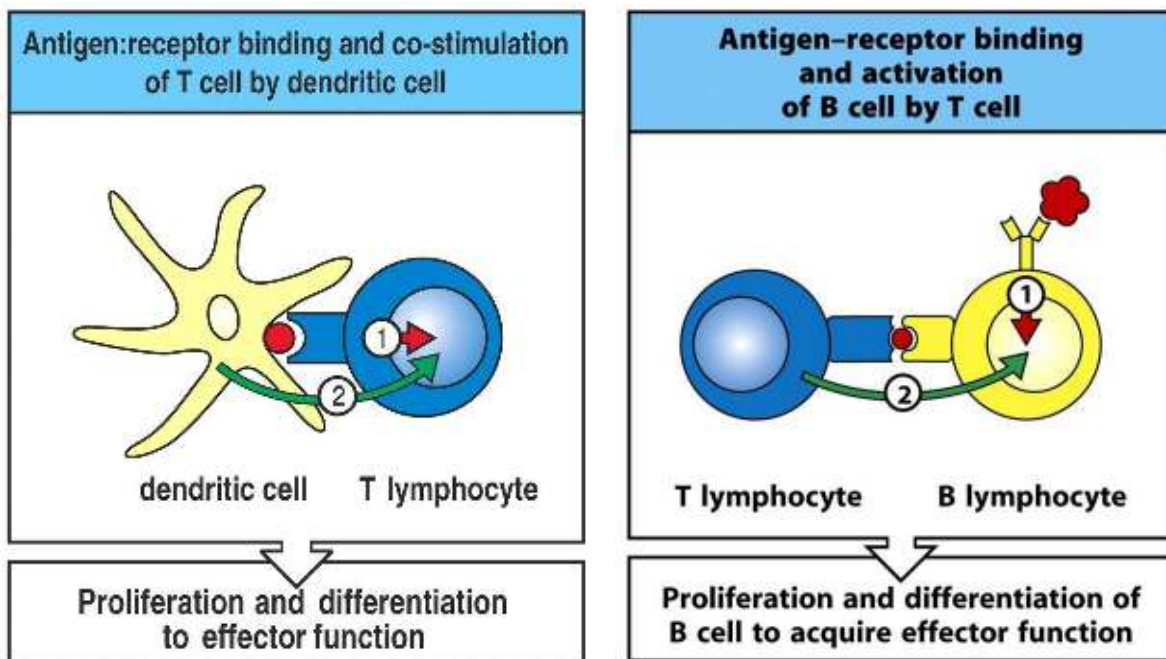
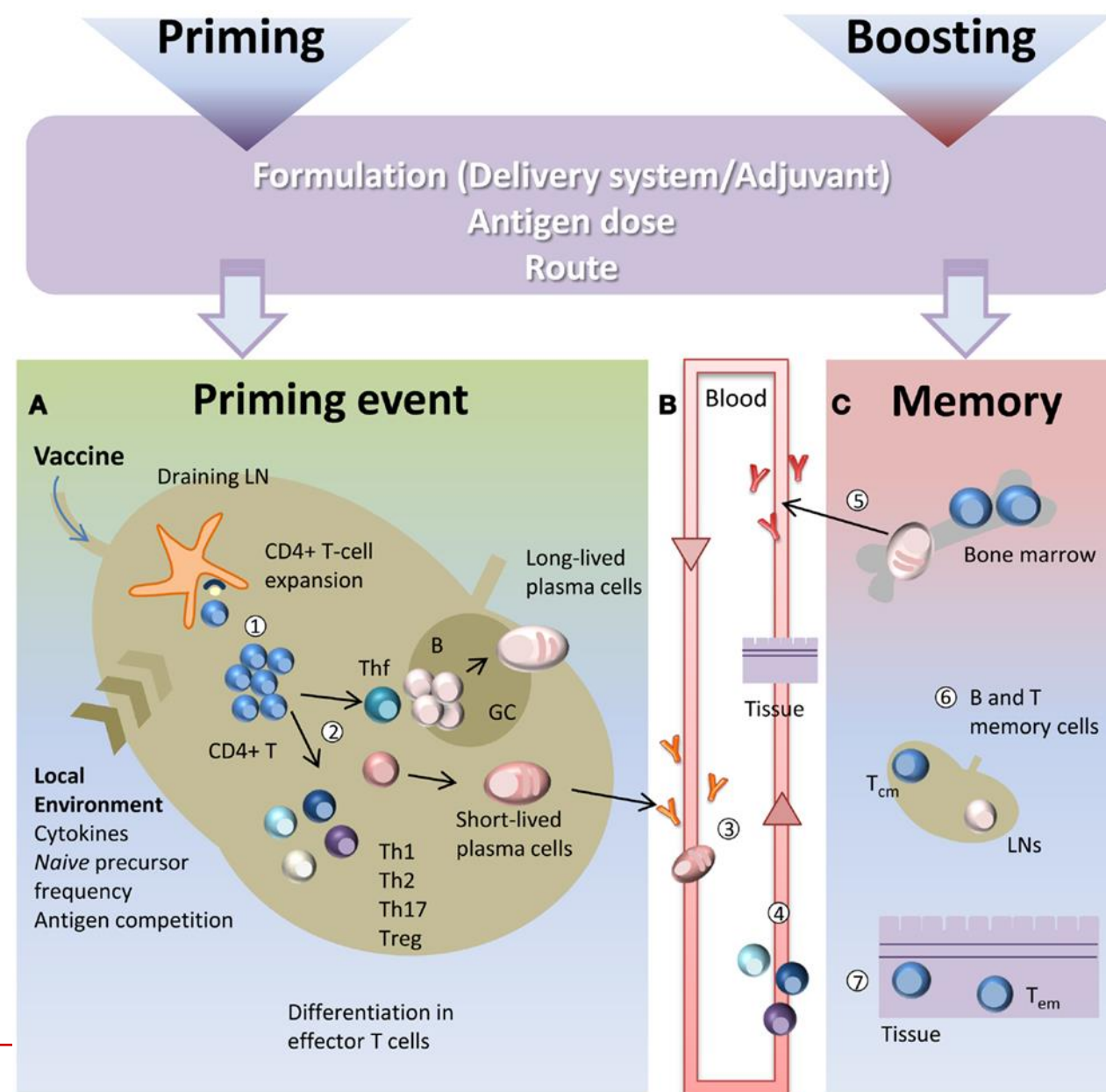


Figure 1-21 Immunobiology, 6/e. (© Garland Science 2005)



SKIFT AF VACCINEMÆRKE ?

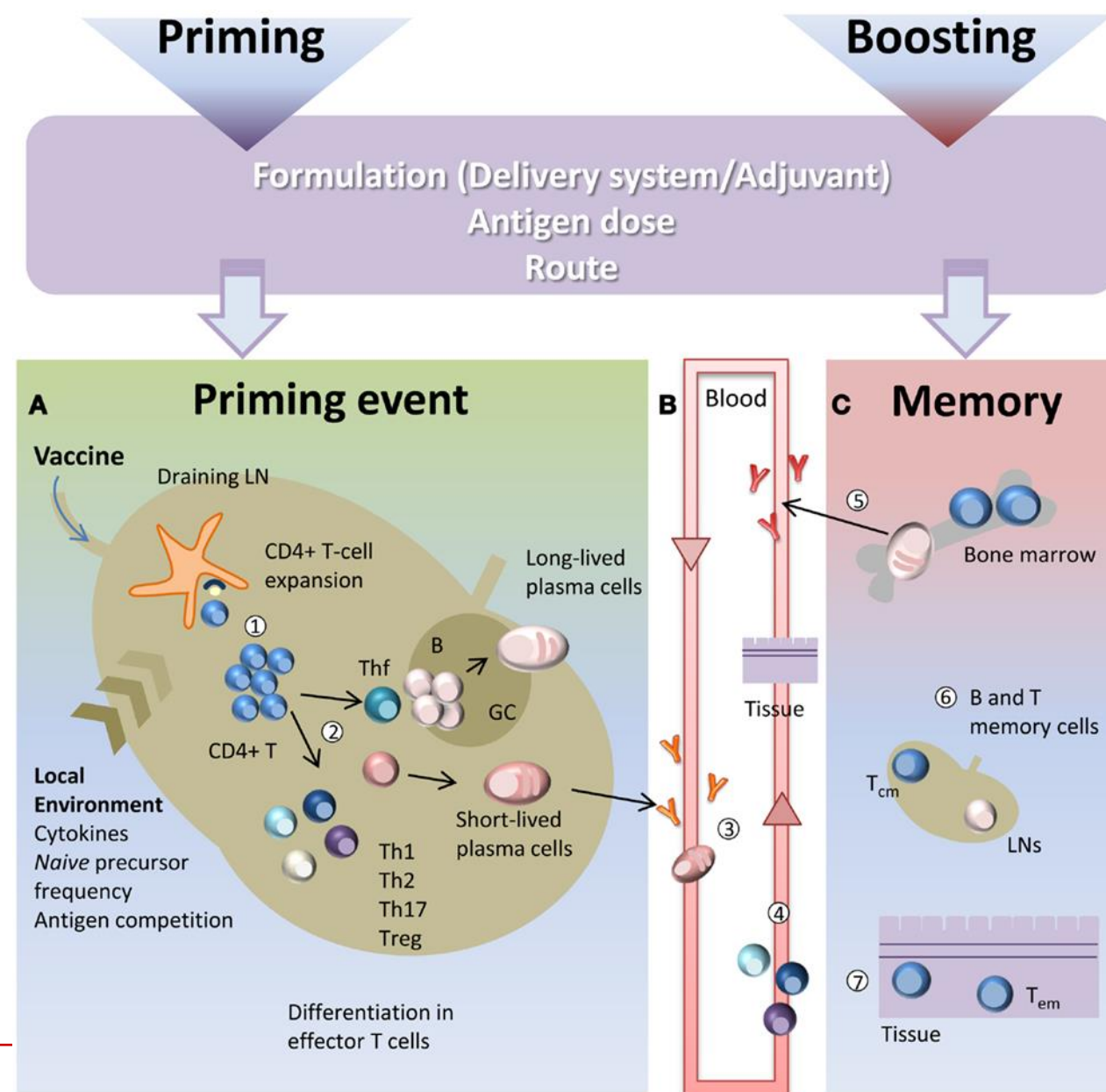
- ❖ Antigener defineres på B- og T-celle niveau
- ❖ Hvis antigener er delt vil én vaccine booste den anden
- ❖ **Kun immunceller der genkender antigenet (epitopen) vil blive aktiveret**

Mellem 10^{15} og 10^{20} mulige varianter of T celle receptor

ca 10^{12} T celler i kroppen (3×10^{13} celler i alt)

Mindst 10^6 forskellige T celle klonotyper

Beregnet $3,5 \times 10^{10}$ forskellige B celle antistoffer pr individ



TAK FOR INVITATIONEN OG INTERESSEN



grju@ssi.dk