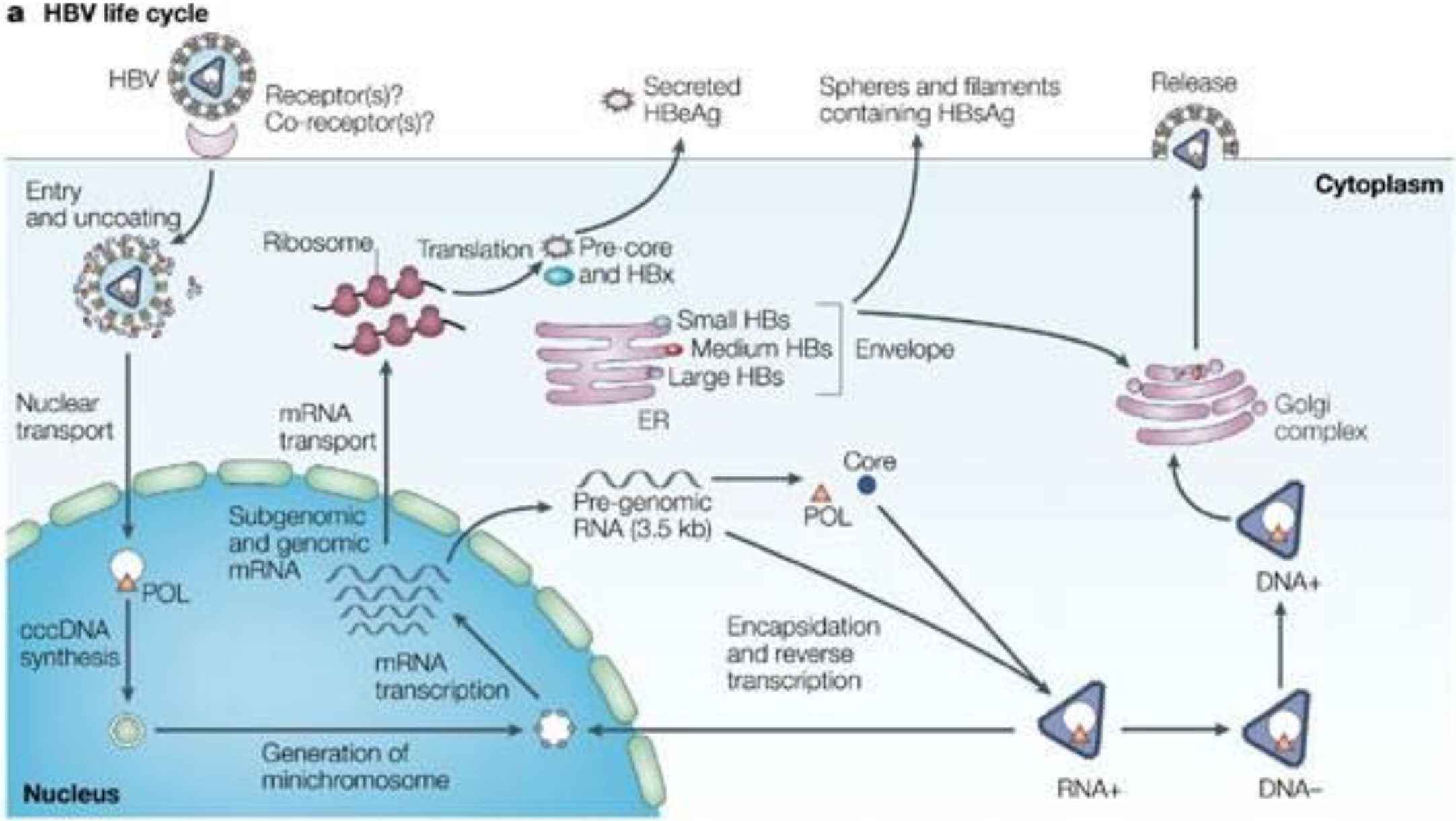
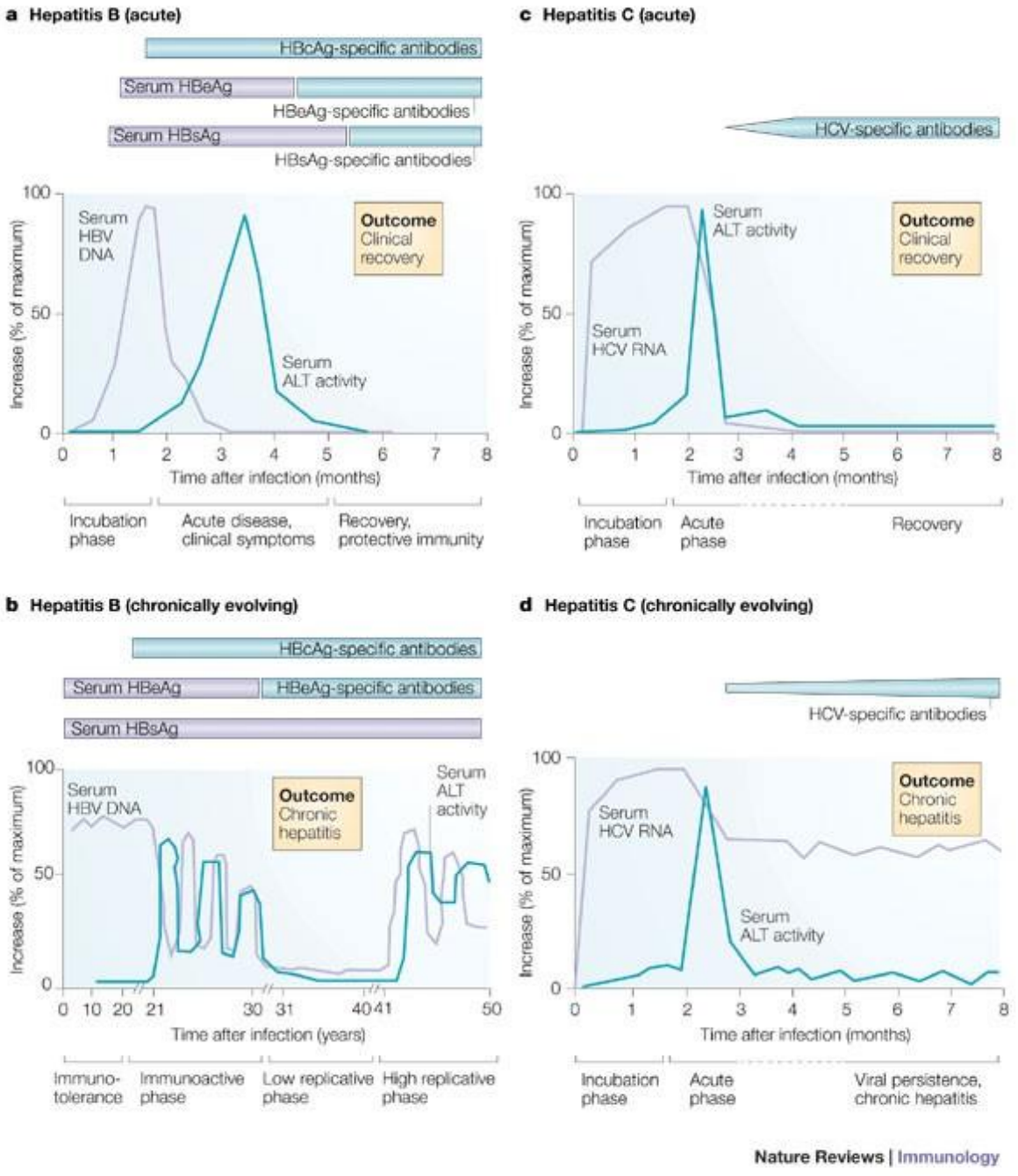
Table 2 | **Virology of HBV and HCV**

Viral features	HBV	HCV
Molecular virology		
Structure	42 nm; enveloped nucleocapsid; partially double-stranded DNA genome	50 nm; enveloped nucleocapsid; positive-stranded RNA genome
Family	Hepadnaviridae family	Flaviviridae family; hepacivirus genus
Receptor	Unknown; there are several candidate HBV-binding proteins	Unknown; the receptor complex probably includes the tetraspanin CD81 and as-yet-unknown hepatocyte-specific factors; there are several other candidate HCV-binding proteins
Replication strategy	Replication of HBV DNA occurs by reverse transcription of an RNA intermediate within cytoplasmic nucleocapsids	Replication occurs by synthesis of a genome-length minus-strand RNA intermediate within cytoplasmic replication complexes that form a perinuclear membranous web
Mutation rate	Low (1 in 100,000 bases per year)	High (1 in 1,000 bases per year)
Genotypes	8 genotypes (8% intergroup divergence)	6 main genotypes (20–35% overall sequence difference); more than 50 subtypes (10–25% difference); quasispecies in every infected patient
Integration into host chromosome	Yes	No
Viral kinetics		
Viral half-life	2–3 days	3 hours
Viral production	10^{10}–10^{12} virions per day	10^{12} virions per day

References are provided in the online version of this Table (see online supplementary information S1). HBV, hepatitis B virus; HCV, hepatitis C virus.


a HBV life cycle
HBV
Receptor(s)?
Co-receptor(s)?
Secreted
HBeAg
Spheres and filaments
containing HBsAg
Release
Cytoplasm
Entry
and uncoating
Ribosome
Translation
Pre-core
and HBx
Small HBs
Medium HBs
Large HBs
Envelope
ER
Golgi
complex
Nuclear
transport
mRNA
transport
Core
Pre-genomic
RNA (3.5 kb)
POL
Subgenomic
and genomic
mRNA
DNA+
POL
cccDNA
synthesis
Encapsidation
and reverse
transcription
mRNA
transcription
Generation of
minichromosome
Nucleus
RNA+
DNA–



- Each year, 2% of patients with chronic hepatitis B spontaneously clear free HBsAg and develop neutralizing HBsAg-specific antibodies[1], and HBV-specific T-cell responses have been detected in the blood just before seroconversion[116]. Accordingly, it has been shown that effective therapeutic reduction of HBV titres results in a transient restoration of HBV-specific $CD4^+$ and $CD8^+$ T-cell responses in the blood of patients with chronic hepatitis B[117,118,119]. Collectively, these findings indicate that immune-mediated clearance mechanisms can be spontaneously activated or induced, even in chronic hepatitis B.

Antibody Responses during Hepatitis B Viral Infection

Stanca M Ciupe [1,*], Ruy M Ribeiro [2], Alan S Perelson [2]

Editor: Roland R Regoes[3]

▸ Author information ▸ Article notes ▸ Copyright and License information

PMCID: PMC4117427 PMID: 25078553

$$\frac{dT}{dt} = rT(1-\frac{T+I}{T_m}) - \beta VT + \rho I,$$
$$\frac{dI}{dt} = \beta VT - \delta I - \rho I,$$
$$\frac{dV}{dt} = \pi I - cV,$$

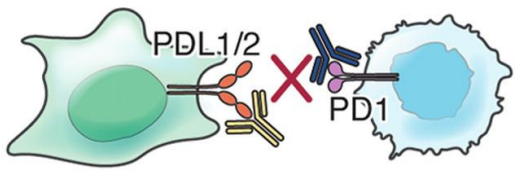
$$\frac{dT}{dt} = rT(1-\frac{T+I}{T_m}) - \beta VT,$$
$$\frac{dI}{dt} = \beta VT - \delta I,$$
$$\frac{dA}{dt} = p_A(1+\theta)V + r_A A(1-\frac{A}{A_m}) +$$
$$(1+\theta)k_m X - (1+\theta)k_p AV - d_A A,$$
$$\frac{dX}{dt} = -k_m X + k_p AV - c_{AV} X,$$
$$\frac{dV}{dt} = \pi I - cV + k_m X - k_p AV,$$

Adaptive immune modulation

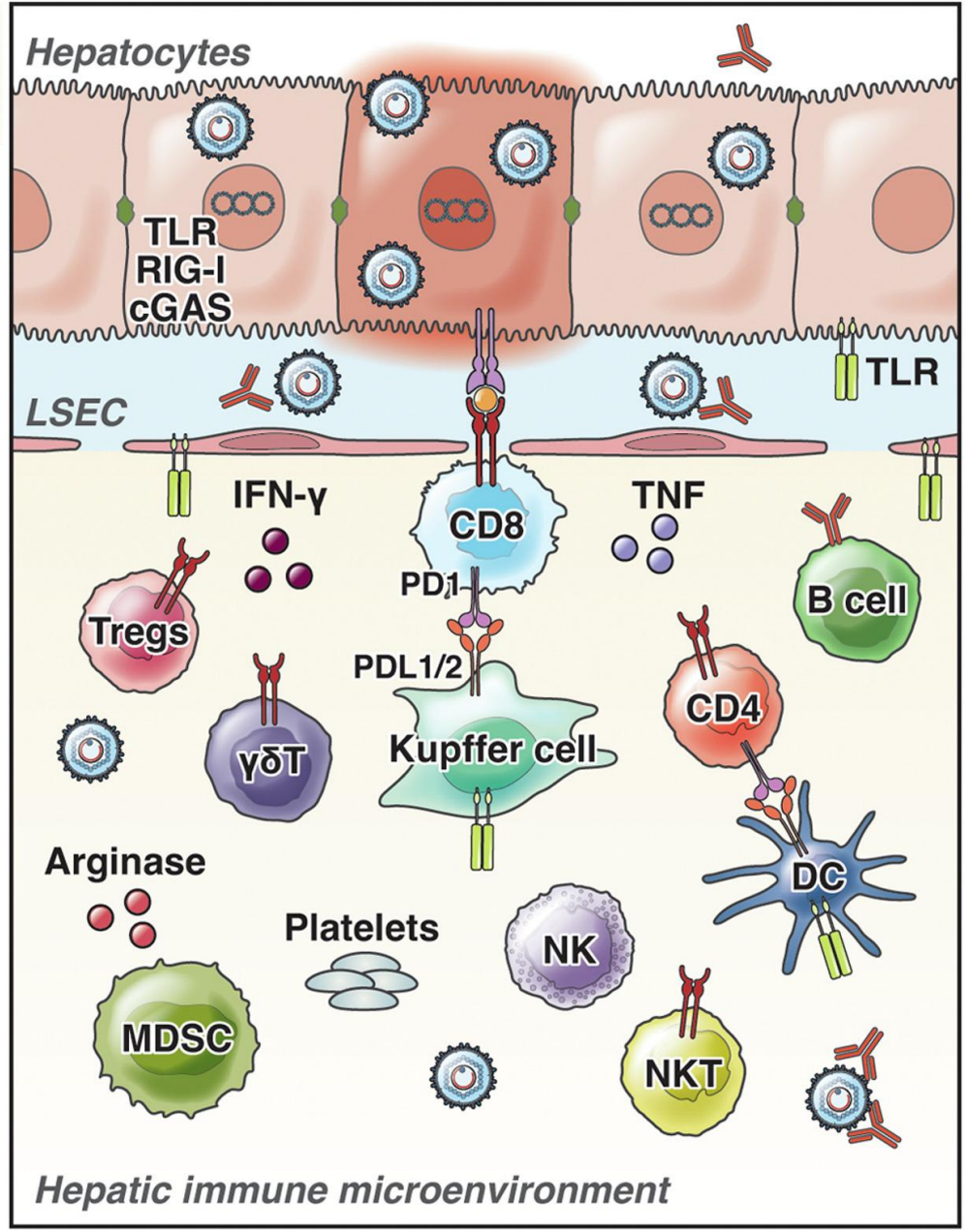
Anti-HBs

Therapeutic vaccine

Checkpoint inhibition
Anti-PD1/PDL1

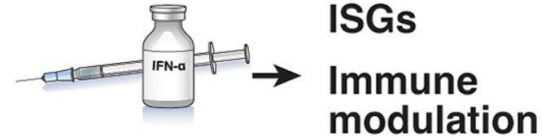


Engineered T-cells

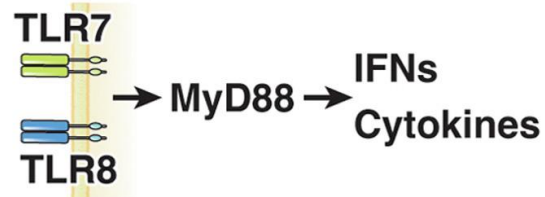


Innate immune modulation

IFN alpha



Toll-like receptor (TLR)
TLR7/8 agonists



Other intracellular pathways:

- Retinoic acid inducible gene-I (RIG-I)
- Stimulator of IFN gene (STING) agonists
- Lymphotoxin

Combinations

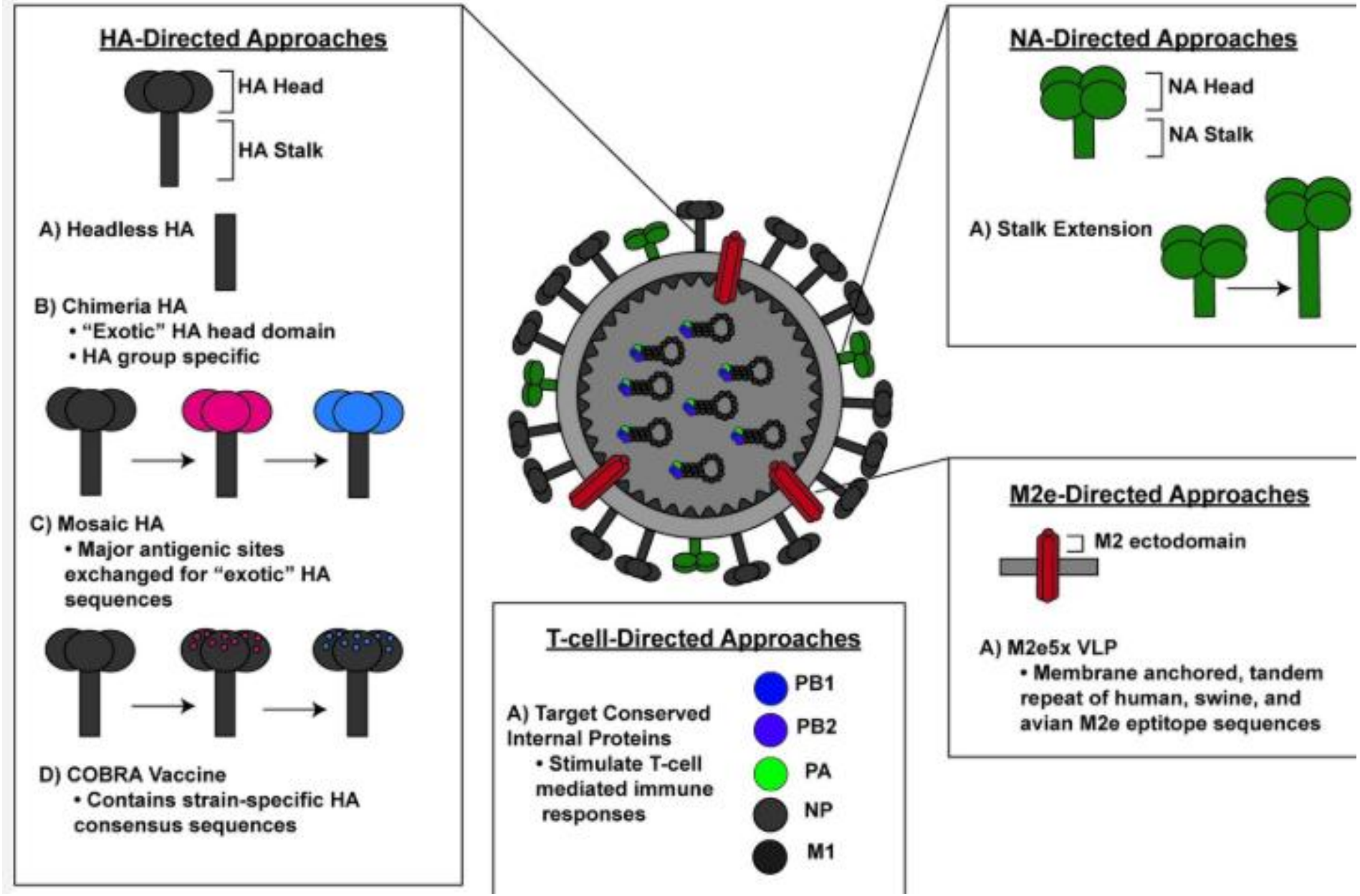
Nuc, immune modulation, vaccine

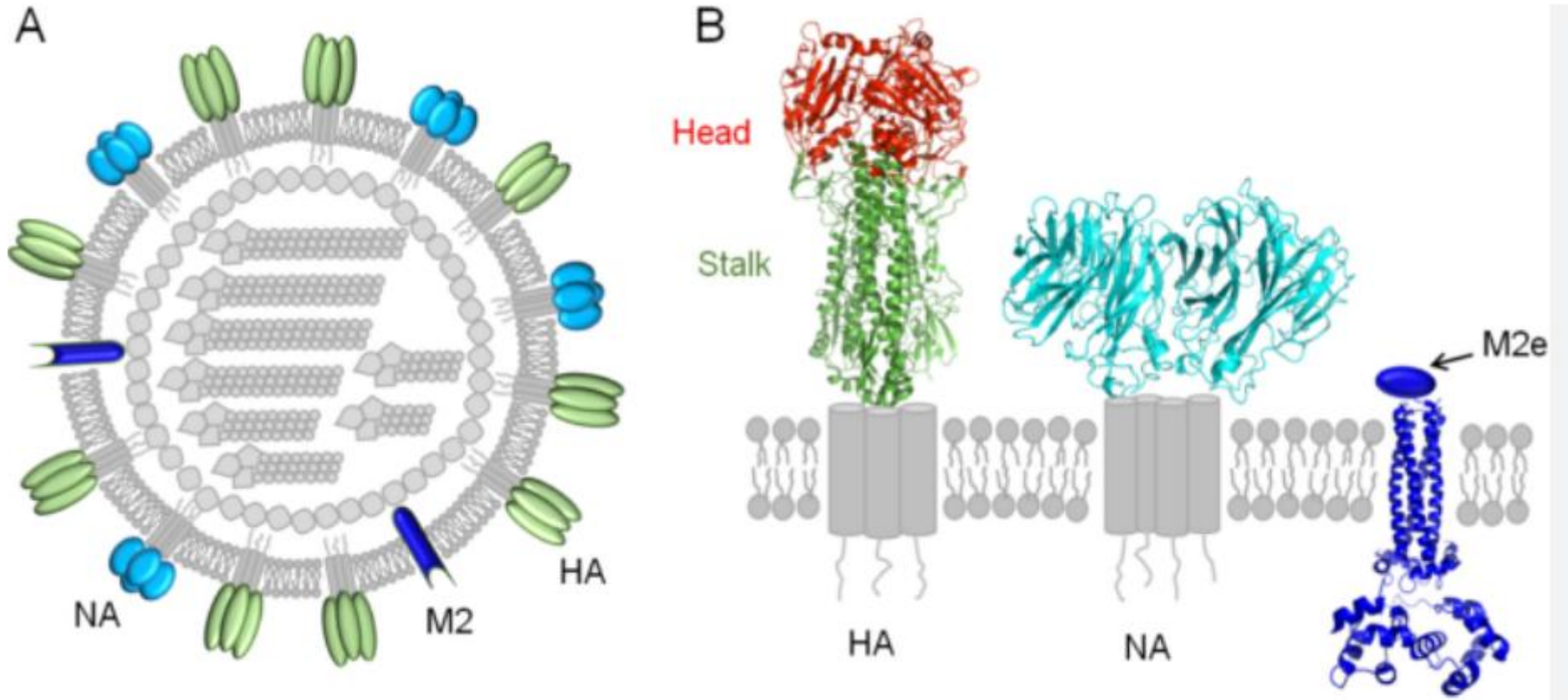
In this respect, it is notable that hepatocellular carcinoma might develop in the absence of cirrhosis in patients with chronic hepatitis B, but it almost always develops on the background of liver cirrhosis in patients with hepatitis C. This observation indicates a differential contribution of viral and host factors to hepatocarcinogenesis in hepatitis B and hepatitis C, which is reviewed in Refs 16,124.

A universal flu vaccine should

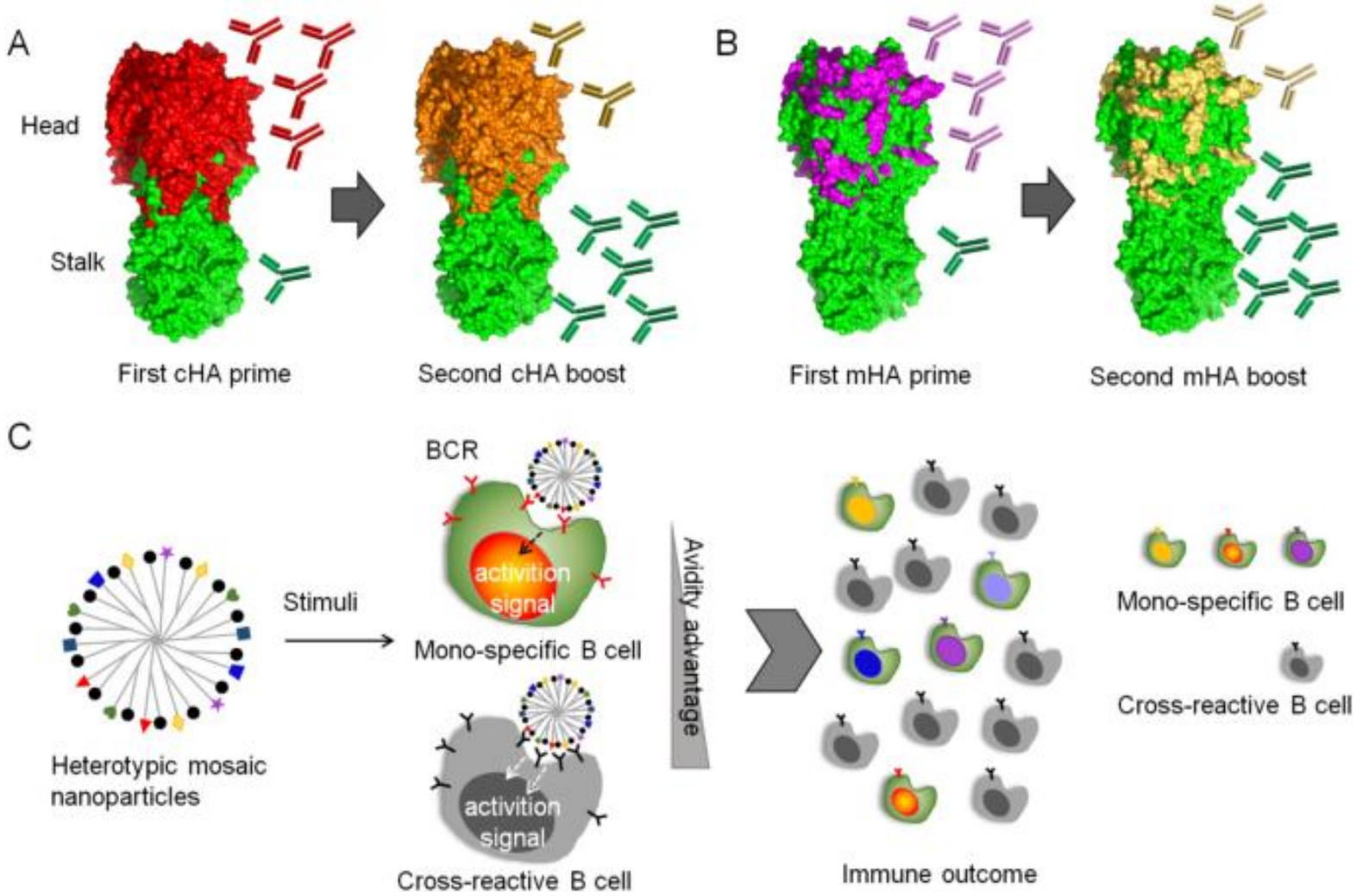
- Be at least 75% effective
- Protect against group I and II influenza A viruses
- Have durable protection that lasts at least 1 year
- Be suitable for all age groups

Universal Influenza Vaccine Approaches




A
NA
M2
HA
B
Head
Stalk
HA
NA
M2e

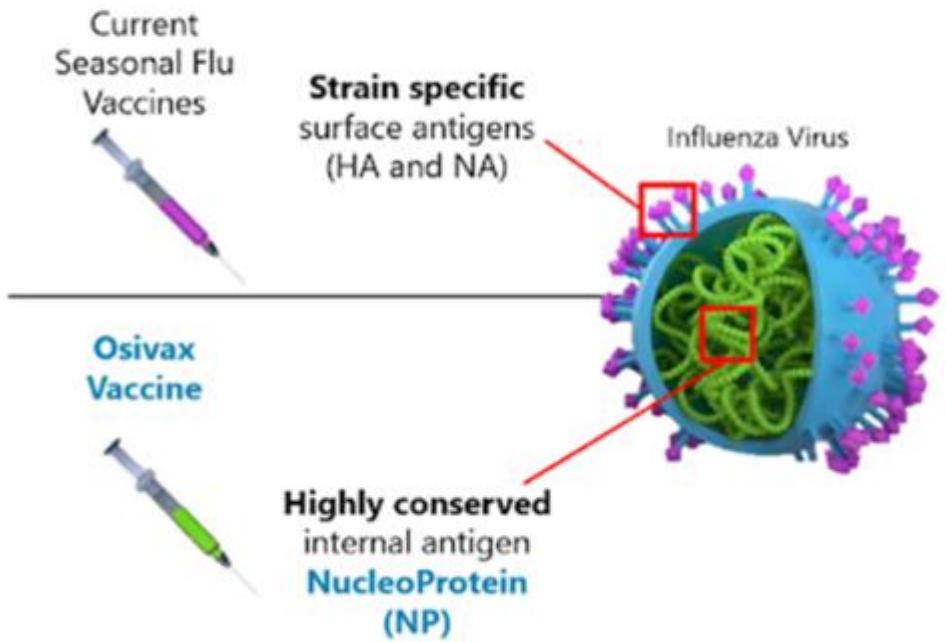
Universal flu vaccines



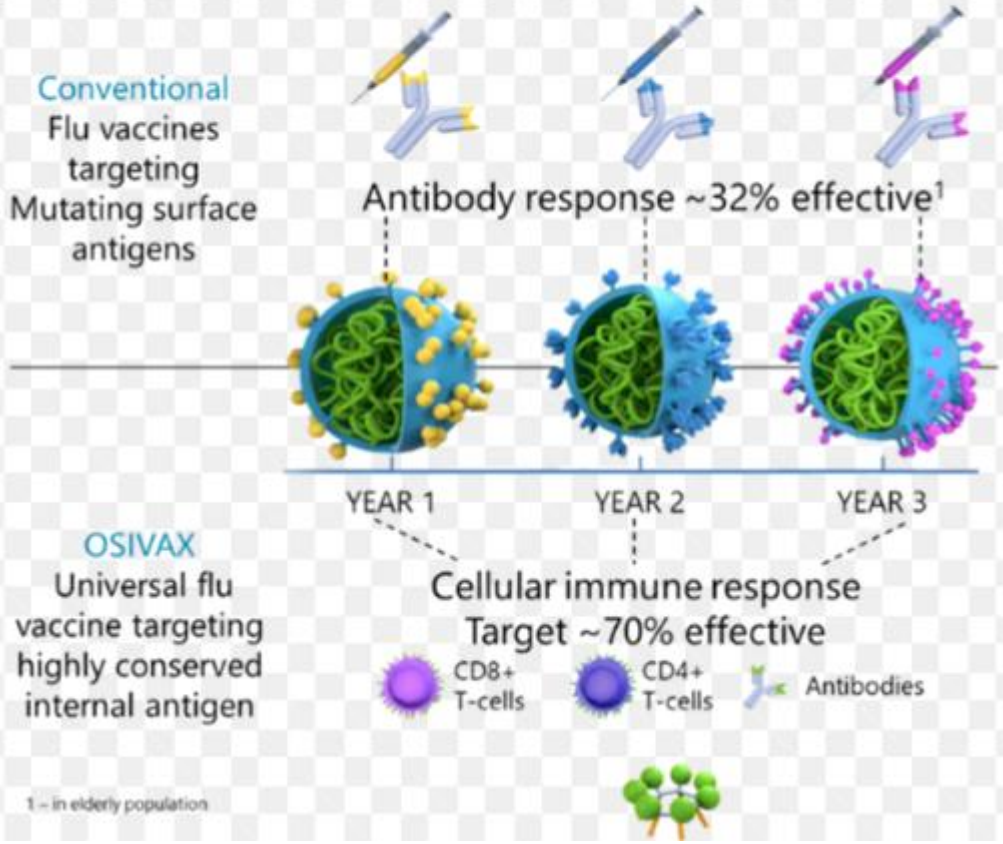
- **MHAA4549A Trial:** A Phase 2a healthy volunteer challenge study showed the monoclonal antibody was safe, well-tolerated, and did not cause antibody-dependent enhancement (ADE) of illness. However, follow-up outpatient trials revealed that the antibody alone did not significantly improve clinical outcomes. National Institutes of He... +2
- **CR6261 Trial:** In an H1N1 human challenge model, CR6261 proved safe but had no statistically significant effect on the duration or amount of viral RNA. National Institutes of Healt...
- **Viral Escape:** Studies found that strong stalk-binding antibody levels can sometimes encourage the virus to mutate, which allows the flu to escape the antibody's grasp. National Institutes of Healt...

- Conclusion: always bet on the virus

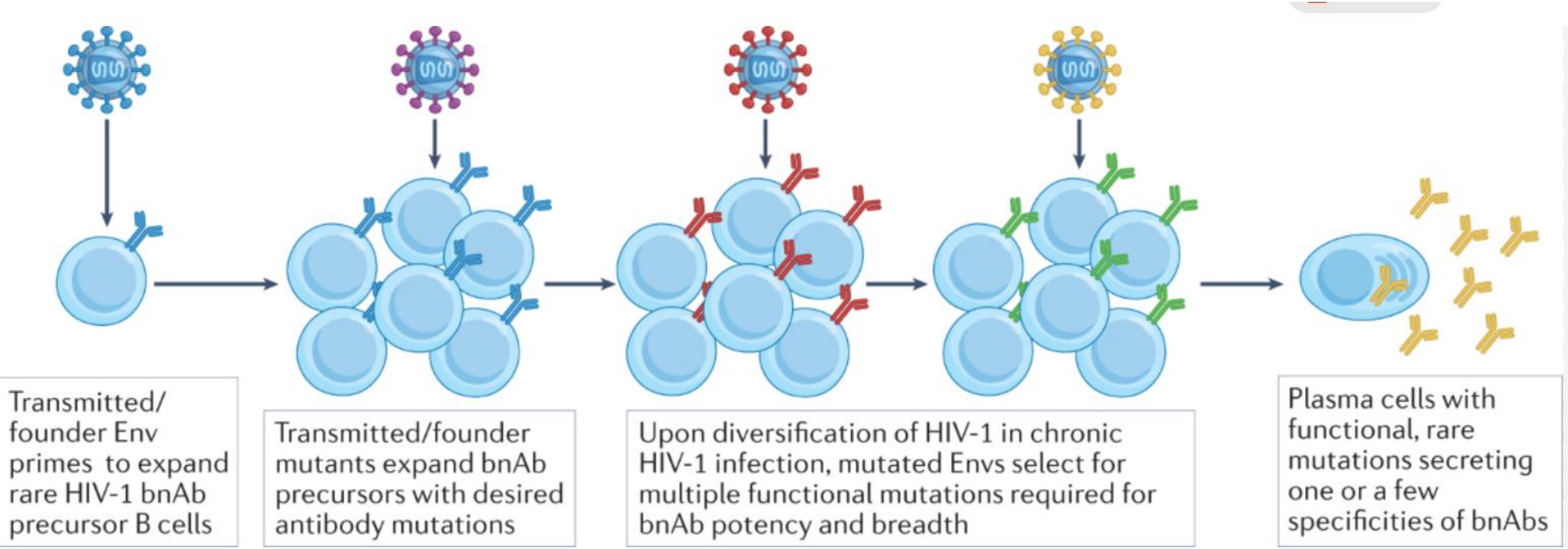
A – Osivax vaccine targets an internal, highly conserved antigen (the Nucleoprotein)

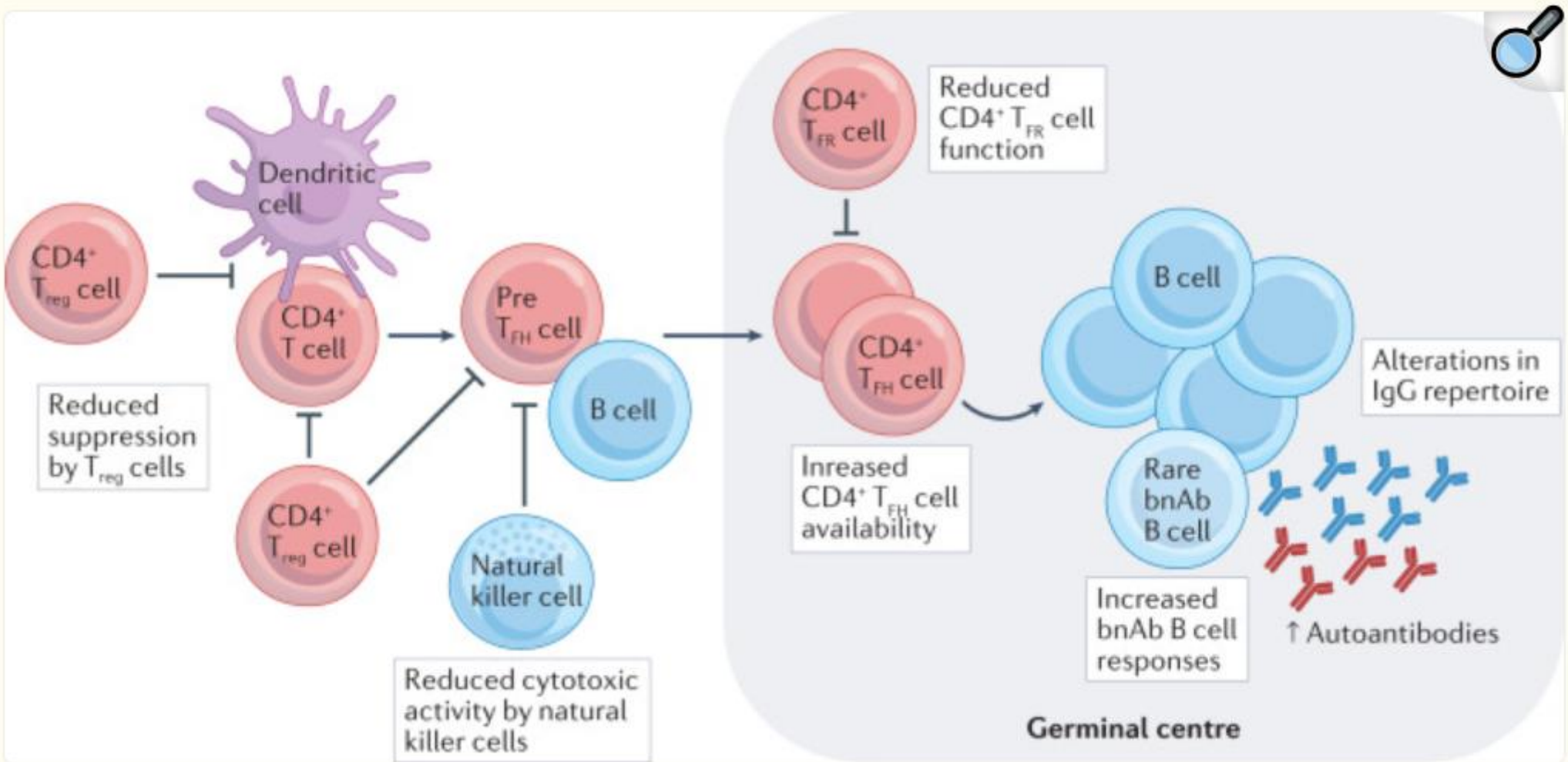


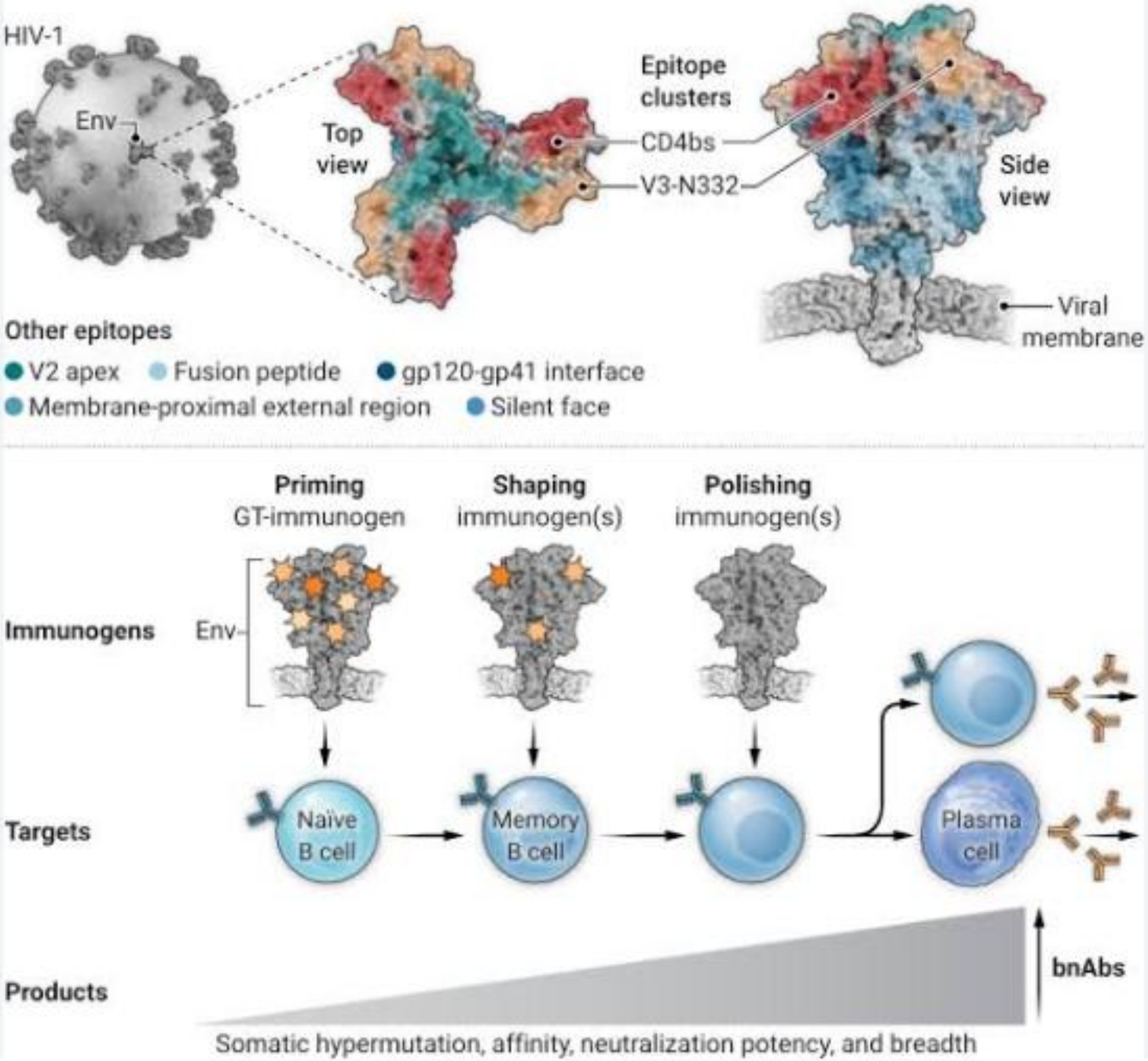
B – Osivax vaccine should trigger universal protection, with no change between seasons

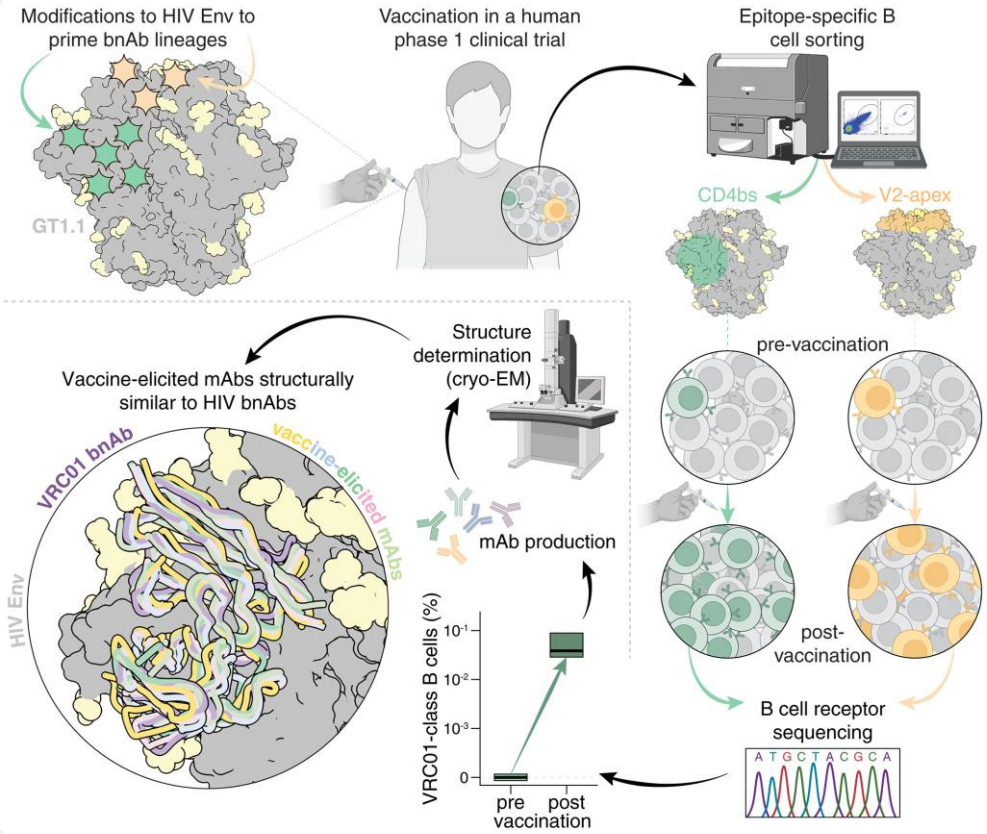


Disclosure: I have consulted for Osivax


Transmitted/ founder Env primes to expand rare HIV-1 bnAb precursor B cells
Transmitted/founder mutants expand bnAb precursors with desired antibody mutations
Upon diversification of HIV-1 in chronic HIV-1 infection, mutated Envs select for multiple functional mutations required for bnAb potency and breadth
Plasma cells with functional, rare mutations secreting one or a few specificities of bnAbs


Dendritic cell
CD4+ Treg cell
CD4+ T cell
Reduced suppression by Treg cells
Pre TFH cell
B cell
CD4+ Treg cell
Natural killer cell
Reduced cytotoxic activity by natural killer cells
CD4+ TFR cell
Reduced CD4+ TFR cell function
CD4+ TFH cell
Inreased CD4+ TFH cell availability
B cell
Rare bnAb B cell
Increased bnAb B cell responses
Alterations in IgG repertoire
↑ Autoantibodies
Germinal centre


HIV-1
Env
Top view
Epitope clusters
CD4bs
V3-N332
Side view
Viral membrane
Other epitopes
V2 apex
Fusion peptide
gp120-gp41 interface
Membrane-proximal external region
Silent face
Priming
GT-immunogen
Shaping
immunogen(s)
Polishing
immunogen(s)
Immunogens
Env
Targets
Naïve B cell
Memory B cell
Plasma cell
Products
bnAbs
Somatic hypermutation, affinity, neutralization potency, and breadth


Modifications to HIV Env to prime bnAb lineages
GT1.1
Vaccination in a human phase 1 clinical trial
Epitope-specific B cell sorting
CD4bs
V2-apex
pre-vaccination
post-vaccination
Structure determination (cryo-EM)
Vaccine-elicited mAbs structurally similar to HIV bnAbs
VRC01 bnAb
vaccine-elicited mAbs
HIV Env
mAb production
VRC01-class B cells (%)
pre vaccination
post vaccination
B cell receptor sequencing
A T G C T A C G C A

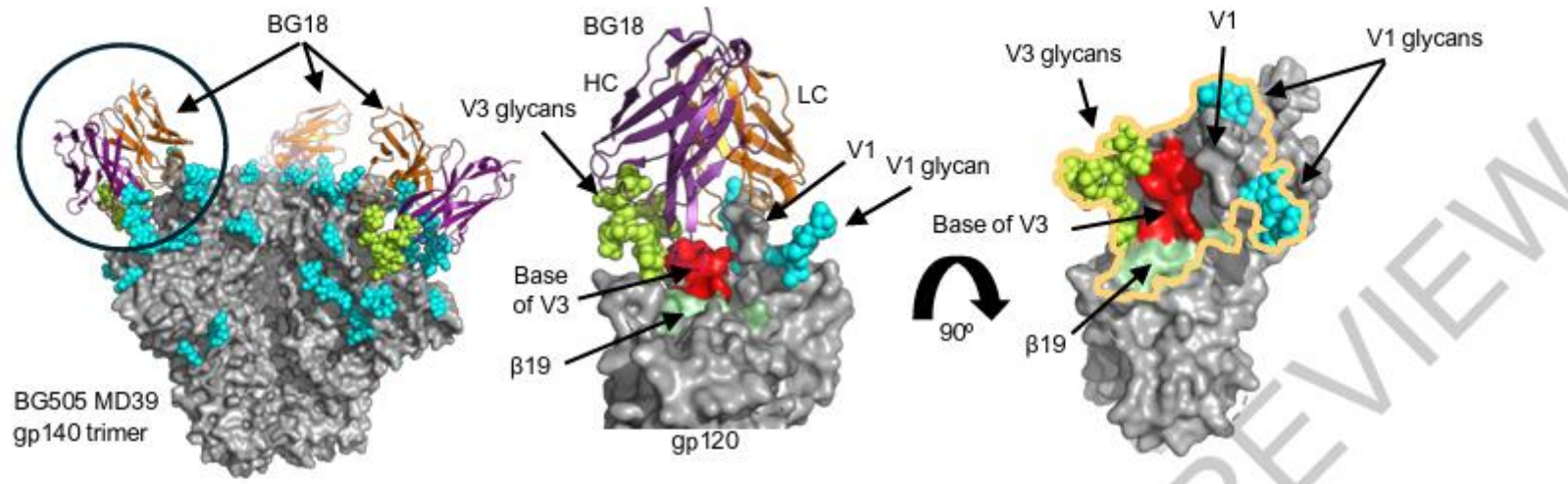
Article | Published: 30 June 2026

Vaccination elicits HIV broadly neutralizing antibodies in primates

Jon M. Steichen, Patrick J. Madden, Claudia T. Flynn, Swastik Phulera, Monolina Shil, Oleksandr Kalyuzhniy, Alessia Liguori, Carolyne Kifude, Leigh M. Sewall, Christopher A. Cottrell, Krystal M. Ma, Sabyasachi Baboo, Jolene K. Diedrich, Katherine McKenney, Allan C. deCamp, Diane G. Carnathan, Ivy Phung, Parham Ramezani-Rad, Ester Marina-Zárate, Brian Freeman, Zhenfei Xie, Jeong Hyun Lee, Troy Sincomb, Nicole Phelps, … William R. Schief + Show authors

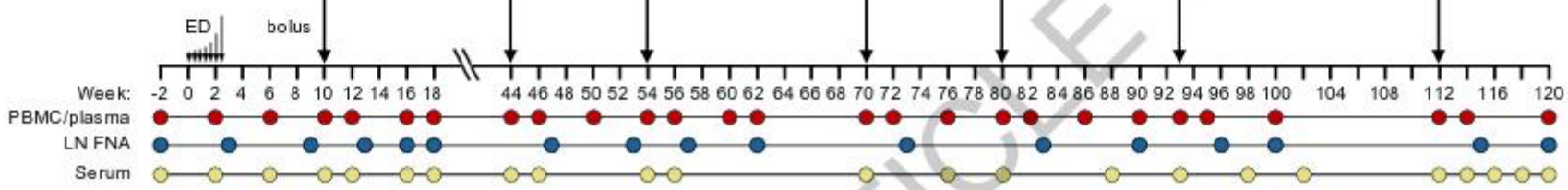
Nature (2026) | Cite this article

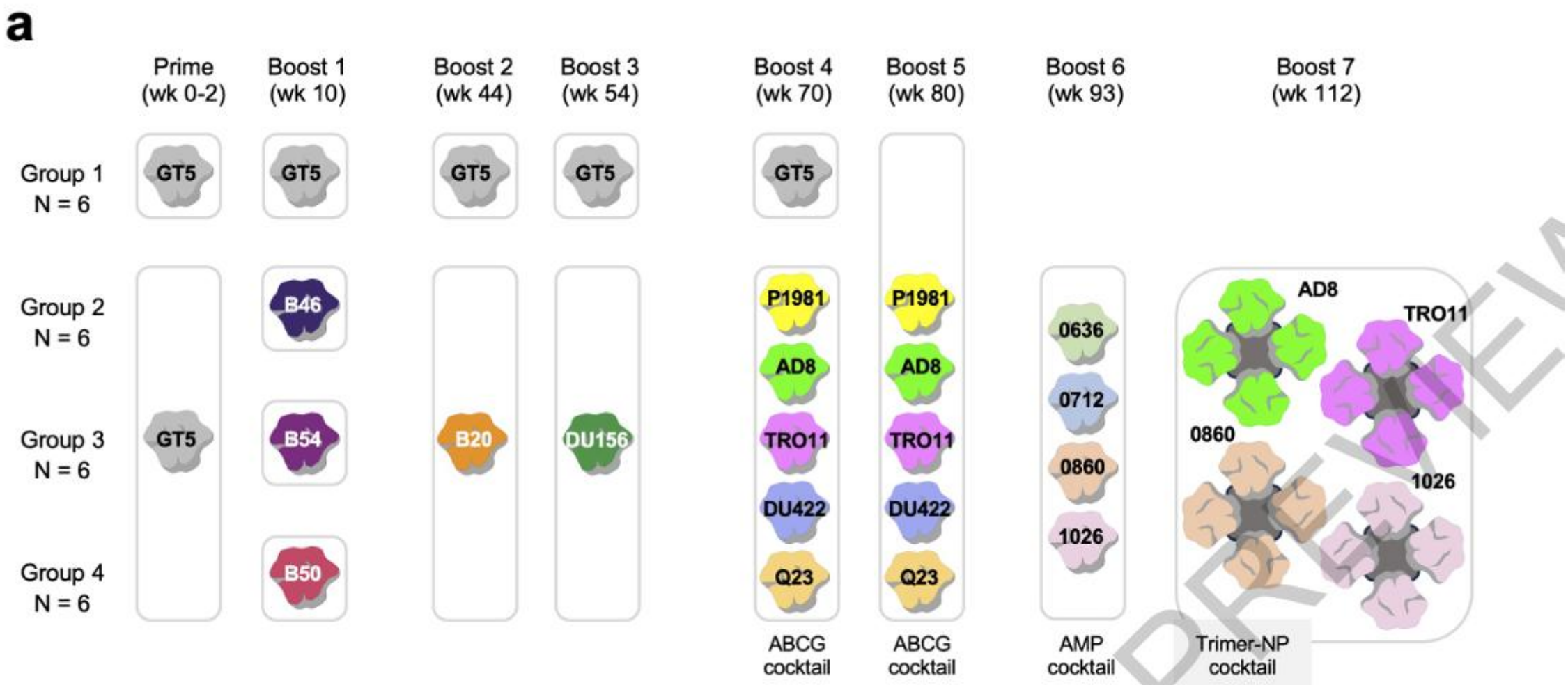
a

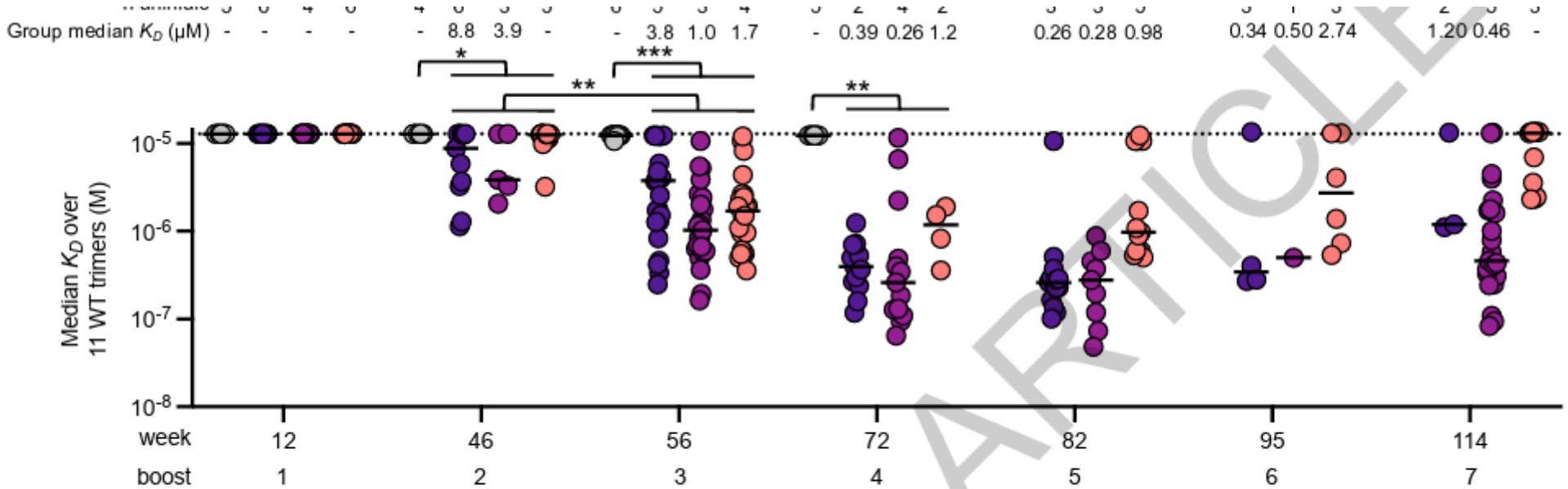


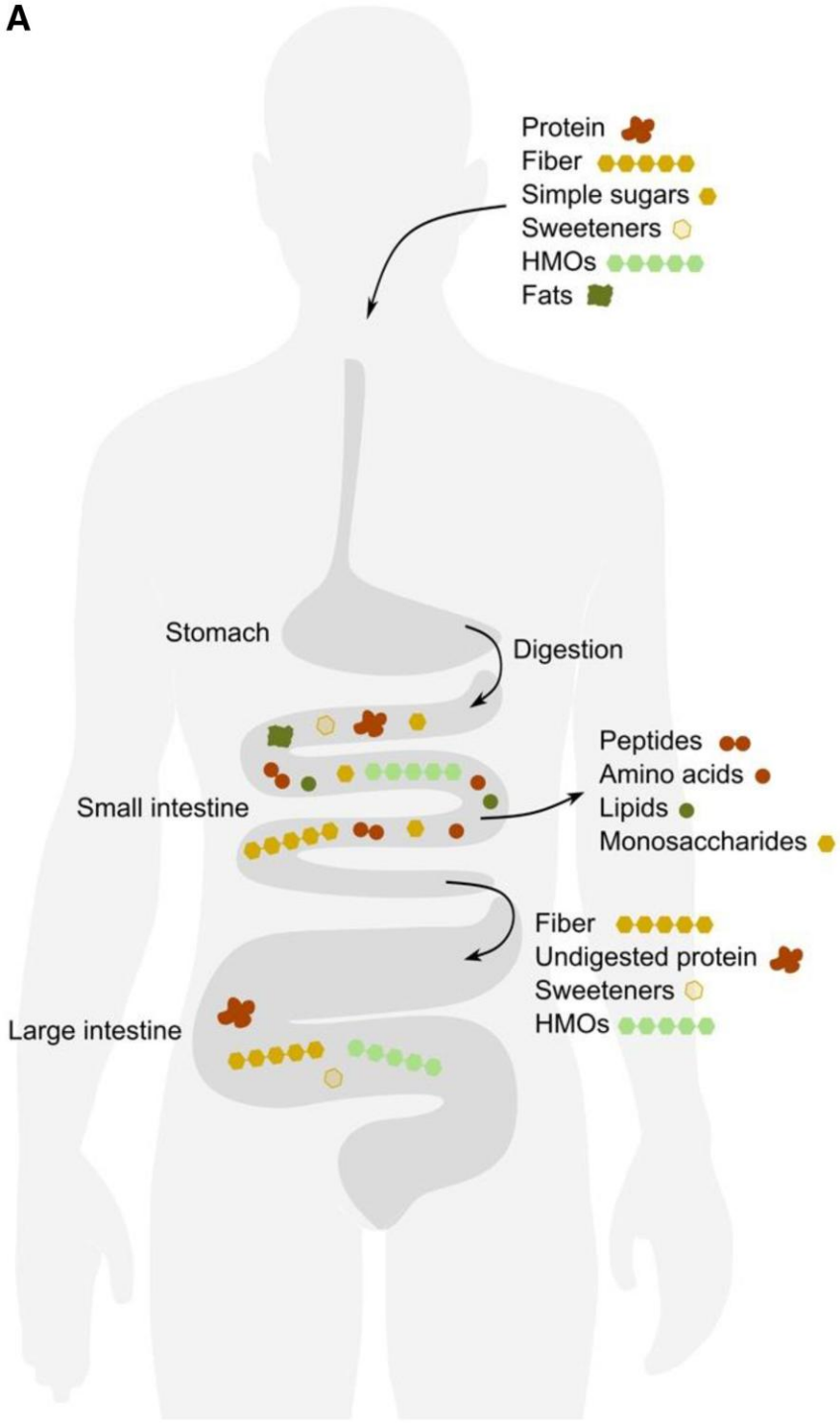
b

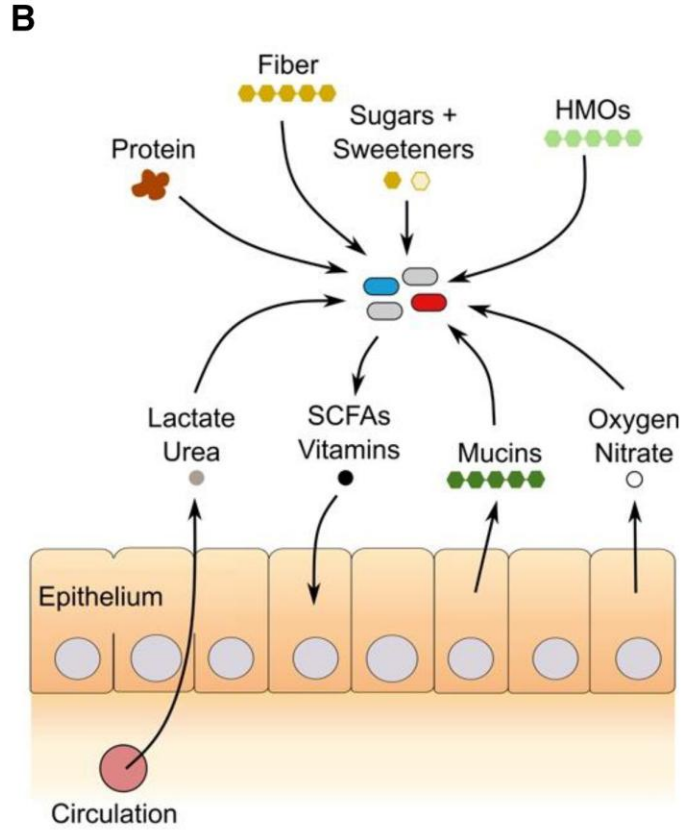
	N	Prime	Boost 1	Boost 2	Boost 3	Boost 4	Boost 5	Boost 6	Boost 7
Group 1	6	N332-GT5	N332-GT5	N332-GT5	N332-GT5	N332-GT5	ABCG Cocktail	none	none
Group 2	6	N332-GT5	B46	B20	DU156	ABCG Cocktail	ABCG Cocktail	AMP Cocktail	Trimer NP Cocktail
Group 3	6	N332-GT5	B54	B20	DU156	ABCG Cocktail	ABCG Cocktail	AMP Cocktail	Trimer NP Cocktail
Group 4	6	N332-GT5	B50	B20	DU156	ABCG Cocktail	ABCG Cocktail	AMP Cocktail	Trimer NP Cocktail

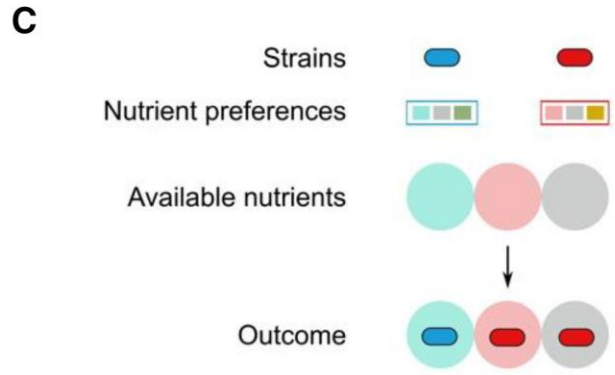



a
Prime (wk 0-2)
Boost 1 (wk 10)
Boost 2 (wk 44)
Boost 3 (wk 54)
Boost 4 (wk 70)
Boost 5 (wk 80)
Boost 6 (wk 93)
Boost 7 (wk 112)
Group 1 N = 6
Group 2 N = 6
Group 3 N = 6
Group 4 N = 6
GT5
B46
B54
B50
B20
DU156
P1981
AD8
TRO11
DU422
Q23
0636
0712
0860
1026
ABCG cocktail
ABCG cocktail
AMP cocktail
Trimer-NP cocktail


Group median K_D (μM) - - - - - 8.8 3.9 - - 3.8 1.0 1.7 - 0.39 0.26 1.2 0.26 0.28 0.98 0.34 0.50 2.74 1.20 0.46 -
*
**
***
**
Median K_D over 11 WT trimers (M)
10^{-5}
10^{-6}
10^{-7}
10^{-8}
week 12 46 56 72 82 95 114
boost 1 2 3 4 5 6 7


A
Protein
Fiber
Simple sugars
Sweeteners
HMOs
Fats
Stomach
Digestion
Small intestine
Peptides
Amino acids
Lipids
Monosaccharides
Fiber
Undigested protein
Sweeteners
HMOs
Large intestine


B
Fiber
Protein
Sugars +
Sweeteners
HMOs
Lactate
Urea
SCFAs
Vitamins
Mucins
Oxygen
Nitrate
Epithelium
Circulation

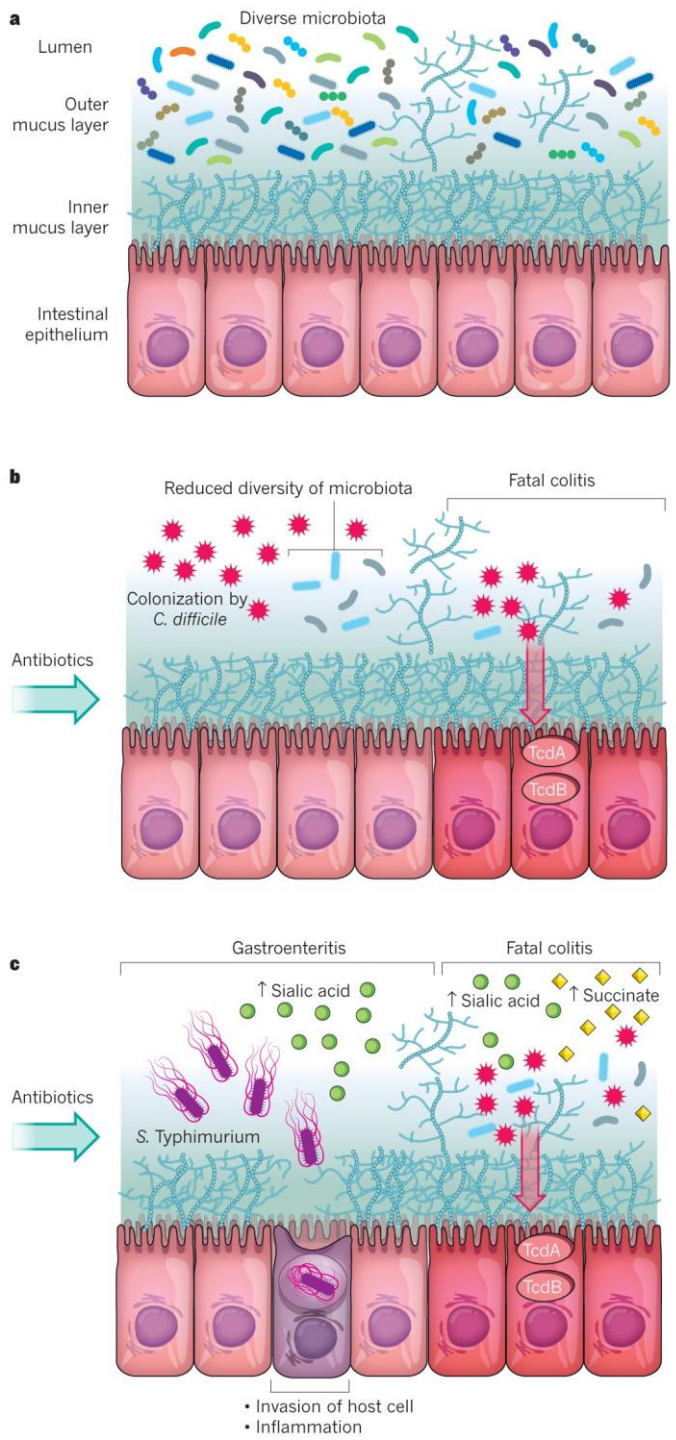

C
Strains
Nutrient preferences
Available nutrients
Outcome

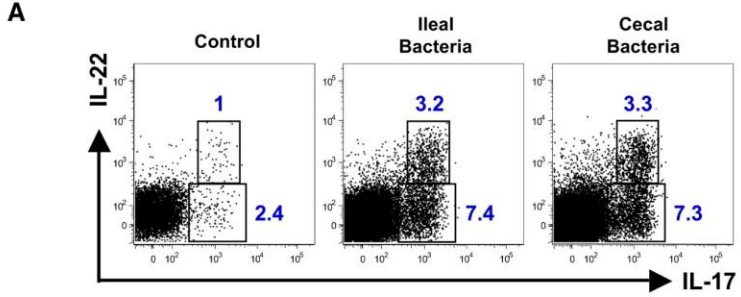
Review Article | Published: 06 July 2016

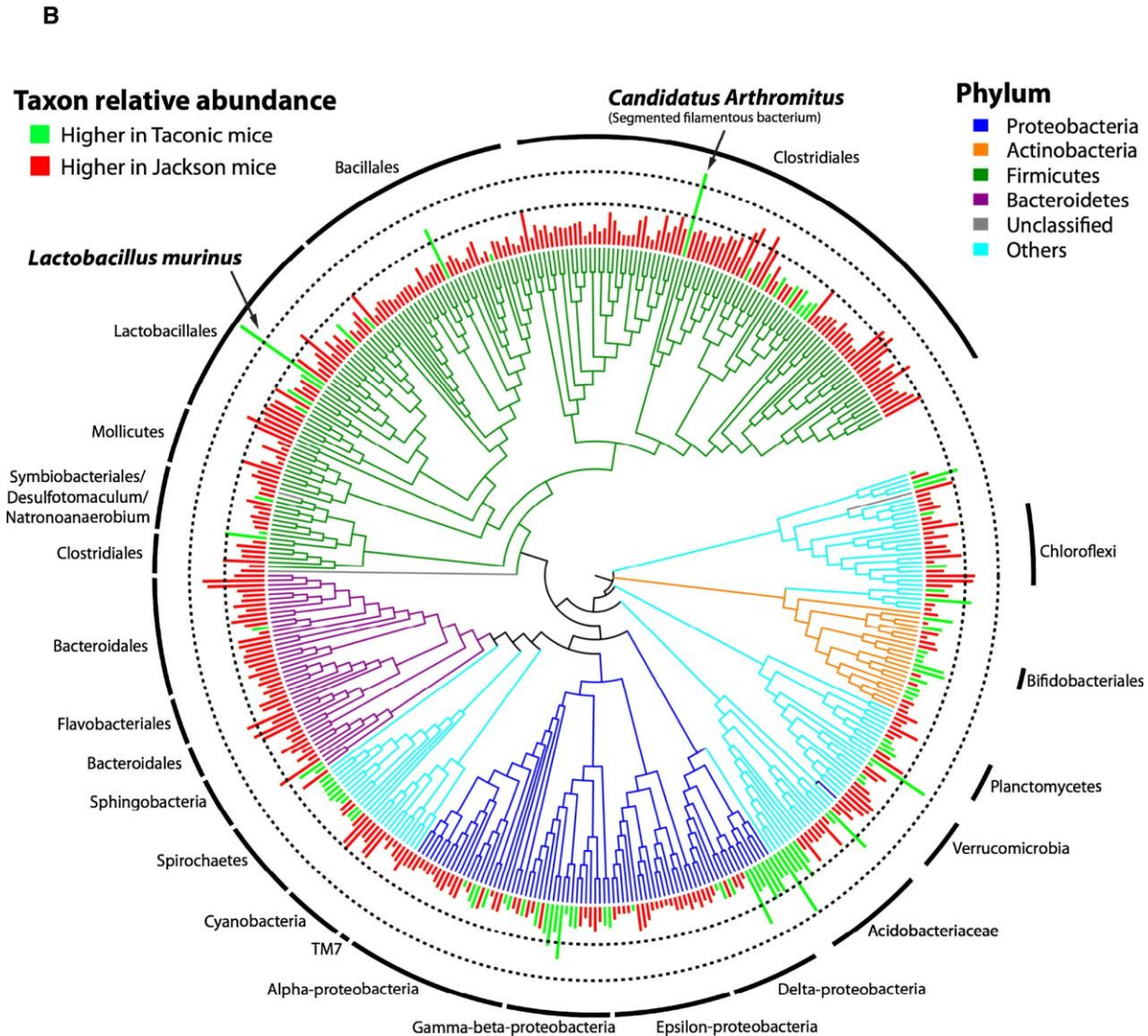
Interactions between the microbiota and pathogenic bacteria in the gut

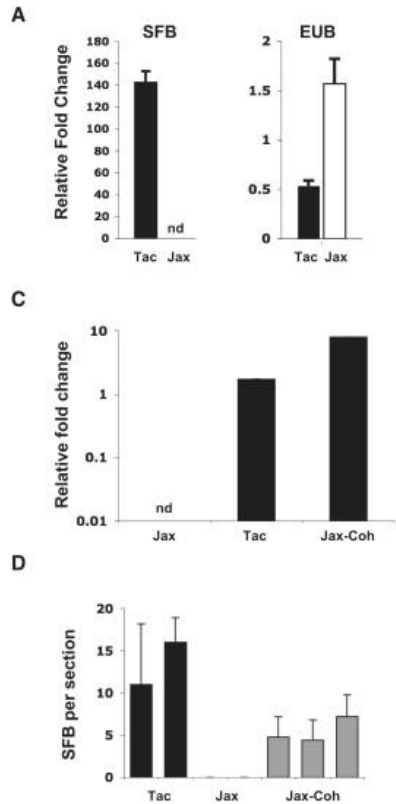
Andreas J. Bäumler & Vanessa Sperandio

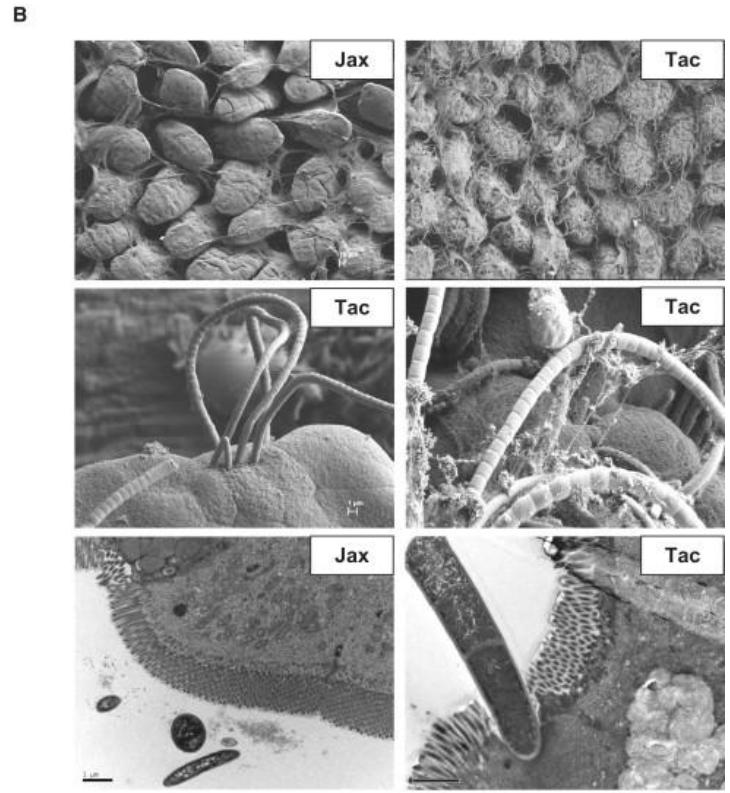
Nature **535**, 85–93 (2016) | Cite this article

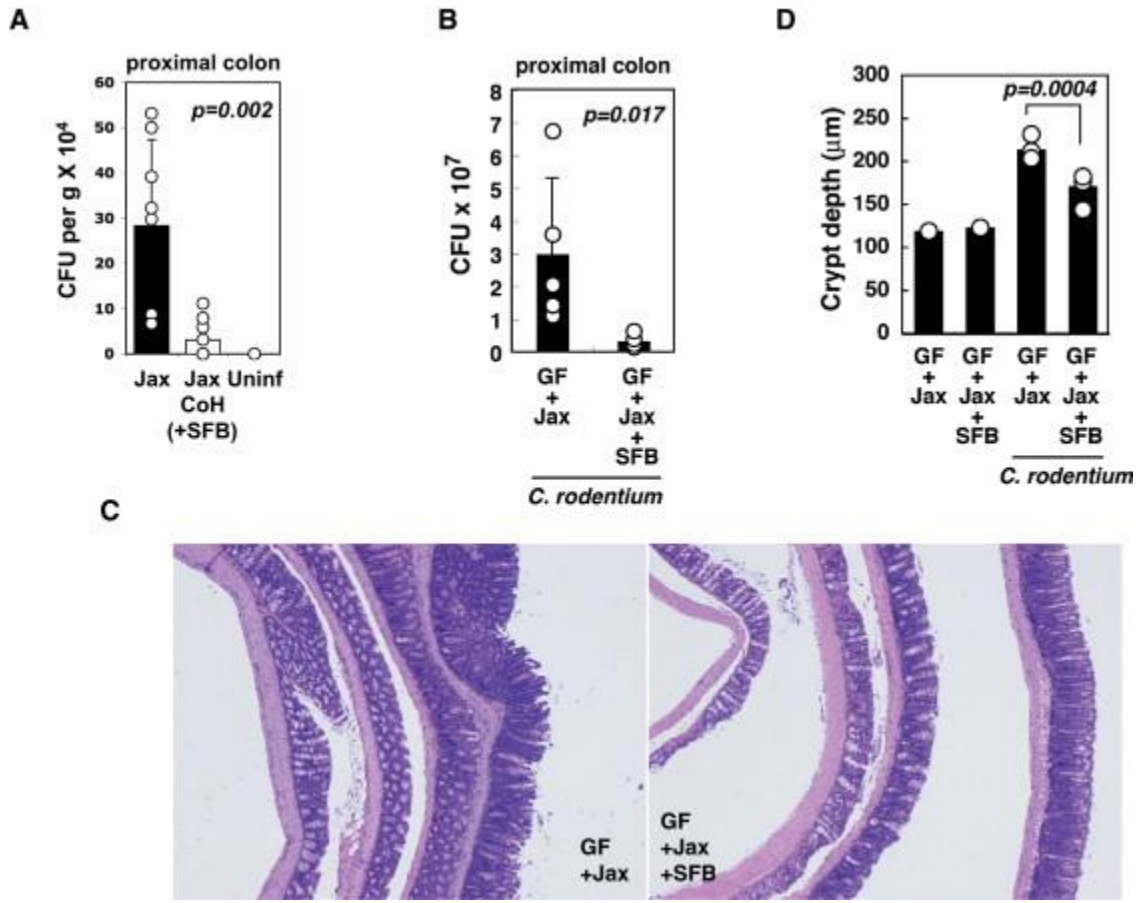

a
Diverse microbiota
Lumen
Outer mucus layer
Inner mucus layer
Intestinal epithelium
b
Reduced diversity of microbiota
Fatal colitis
Colonization by C. difficile
Antibiotics
TcdA
TcdB
c
Gastroenteritis
Fatal colitis
↑ Sialic acid
↑ Sialic acid
↑ Succinate
Antibiotics
S. Typhimurium
TcdA
TcdB
• Invasion of host cell
• Inflammation

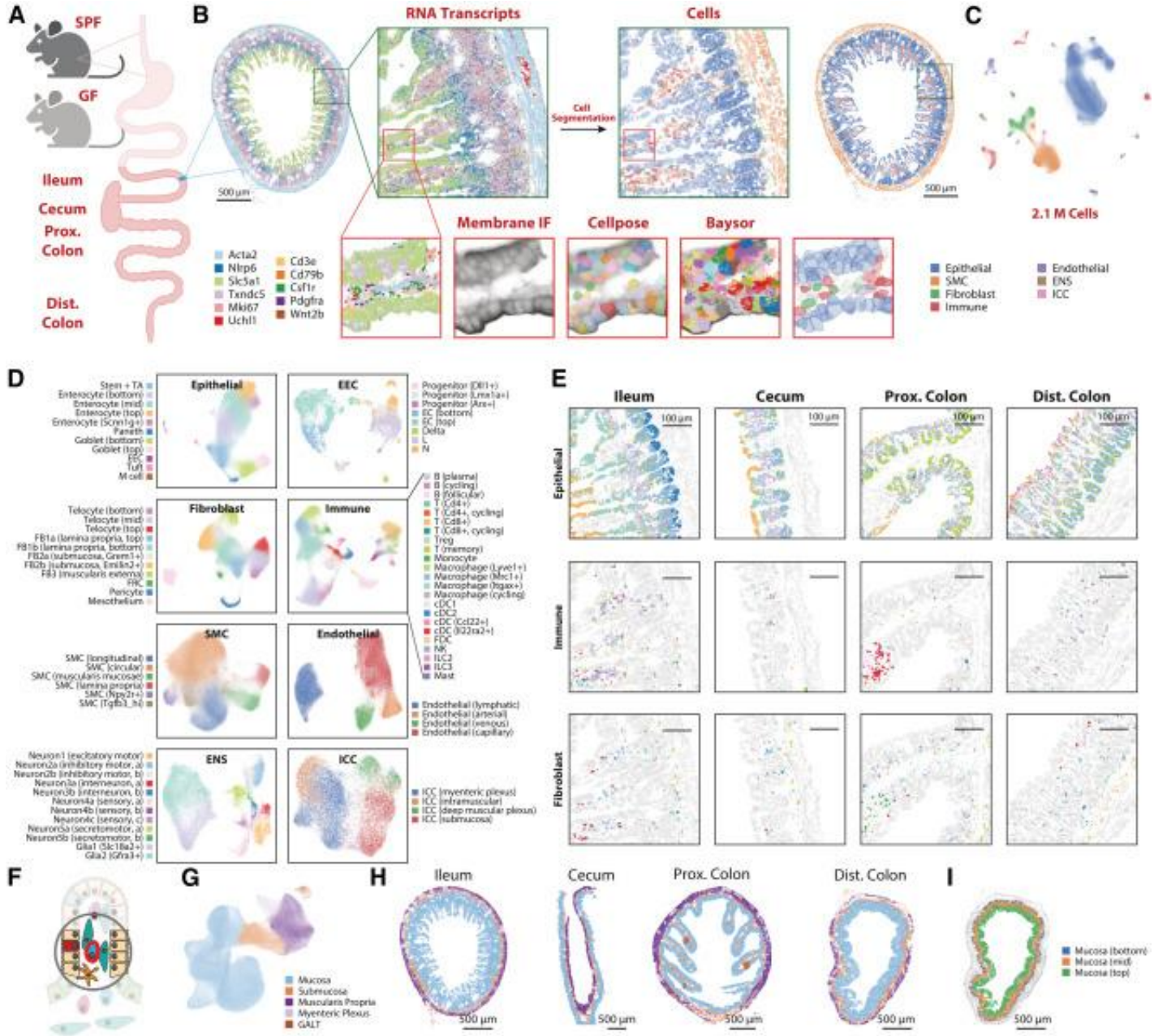

A
Control
Ileal Bacteria
Cecal Bacteria
IL-22
IL-17
1
2.4
3.2
7.4
3.3
7.3

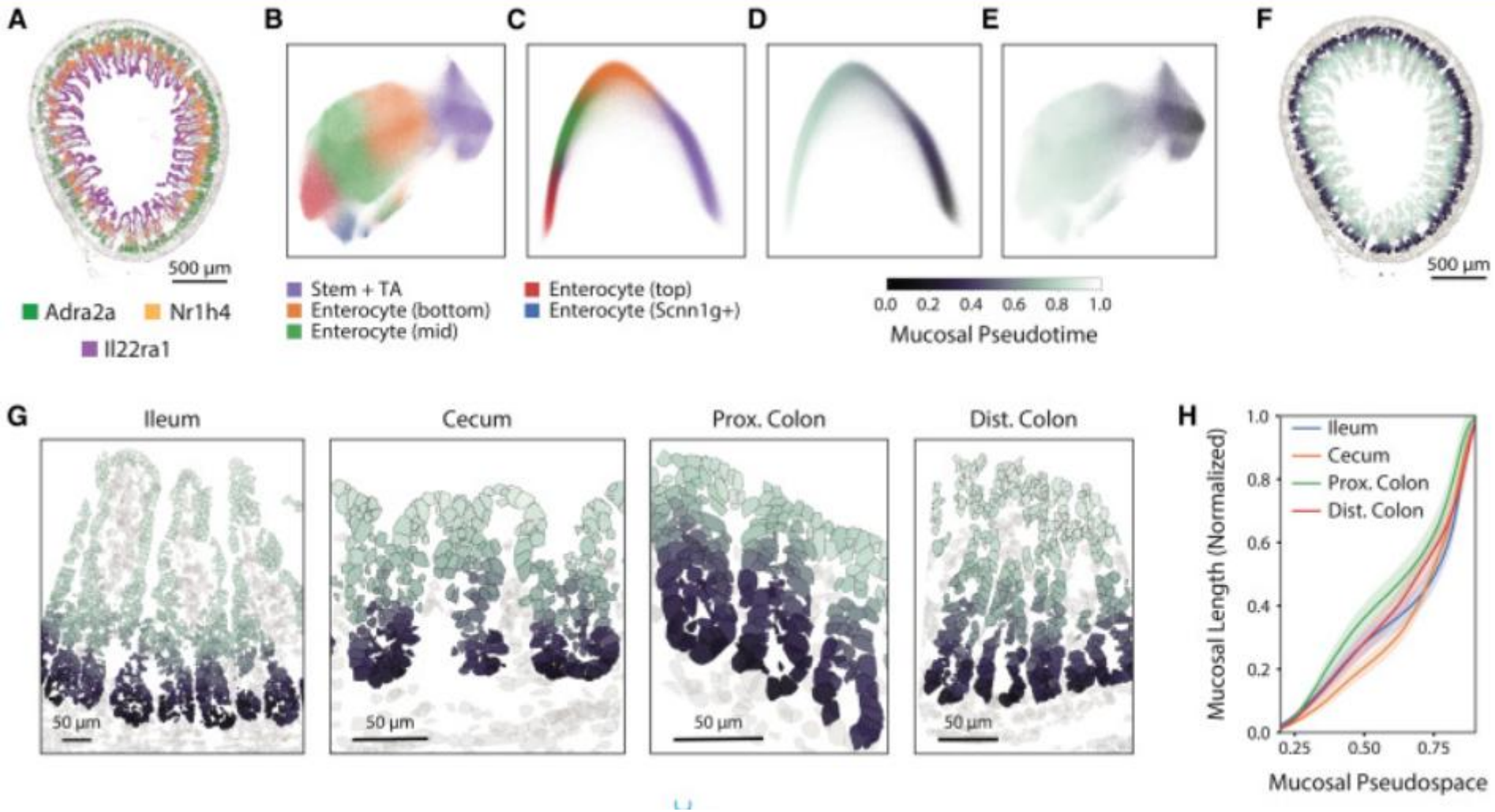

B
Taxon relative abundance
Higher in Taconic mice
Higher in Jackson mice
Candidatus Arthromitus
(Segmented filamentous bacterium)
Lactobacillus murinus
Phylum
Proteobacteria
Actinobacteria
Firmicutes
Bacteroidetes
Unclassified
Others
Bacillales
Clostridiales
Lactobacillales
Mollicutes
Symbiobacteriales/
Desulfotomaculum/
Natronoanaerobium
Clostridiales
Bacteroidales
Flavobacteriales
Bacteroidales
Sphingobacteria
Spirochaetes
Cyanobacteria
TM7
Alpha-proteobacteria
Gamma-beta-proteobacteria
Epsilon-proteobacteria
Delta-proteobacteria
Acidobacteriaceae
Verrucomicrobia
Planctomycetes
Bifidobacteriales
Chloroflexi


A
SFB
EUB
Relative Fold Change
nd
Tac Jax
Tac Jax
C
Relative fold change
nd
Jax
Tac
Jax-Coh
D
SFB per section
Tac
Jax
Jax-Coh


B
Jax
Tac
Tac
Tac
Jax
Tac


A
proximal colon
p=0.002
CFU per g X 10^4
60
50
40
30
20
10
0
Jax
Jax CoH (+SFB)
Uninf
B
proximal colon
p=0.017
CFU x 10^7
8
7
6
5
4
3
2
1
0
GF + Jax
GF + Jax + SFB
C. rodentium
D
p=0.0004
Crypt depth (μm)
300
250
200
150
100
50
0
GF + Jax
GF + Jax + SFB
GF + Jax
GF + Jax + SFB
C. rodentium
C
GF +Jax
GF +Jax +SFB


A
SPF
GF
Ileum
Cecum
Prox. Colon
Dist. Colon
B
RNA Transcripts
Cells
Cell Segmentation
500 µm
Membrane IF
Cellpose
Baysor
Acta2
Nkrp6
Slc5a1
Txndc5
Mki67
Uchl1
Cd3e
Cd79b
Csf1r
Pdgfra
Wnt2b
C
2.1 M Cells
Epithelial
SMC
Fibroblast
Immune
Endothelial
ENS
ICC
D
Epithelial
EEC
Fibroblast
Immune
SMC
Endothelial
ENS
ICC
E
Ileum
Cecum
Prox. Colon
Dist. Colon
100 µm
Epithelial
Immune
Fibroblast
F
G
Mucosa
Submucosa
Muscularis Propria
Myenteric Plexus
GALT
H
Ileum
Cecum
Prox. Colon
Dist. Colon
500 µm
I
Mucosa (bottom)
Mucosa (mid)
Mucosa (top)
500 µm


A
B
C
D
E
F
500 µm
Adra2a
Nr1h4
Il22ra1
Stem + TA
Enterocyte (bottom)
Enterocyte (mid)
Enterocyte (top)
Enterocyte (Scnn1g+)
0.0 0.2 0.4 0.6 0.8 1.0
Mucosal Pseudotime
500 µm
G
Ileum
Cecum
Prox. Colon
Dist. Colon
50 µm
50 µm
50 µm
50 µm
H
Mucosal Length (Normalized)
1.0
0.8
0.6
0.4
0.2
0.0
0.25
0.50
0.75
Mucosal Pseudospace
Ileum
Cecum
Prox. Colon
Dist. Colon

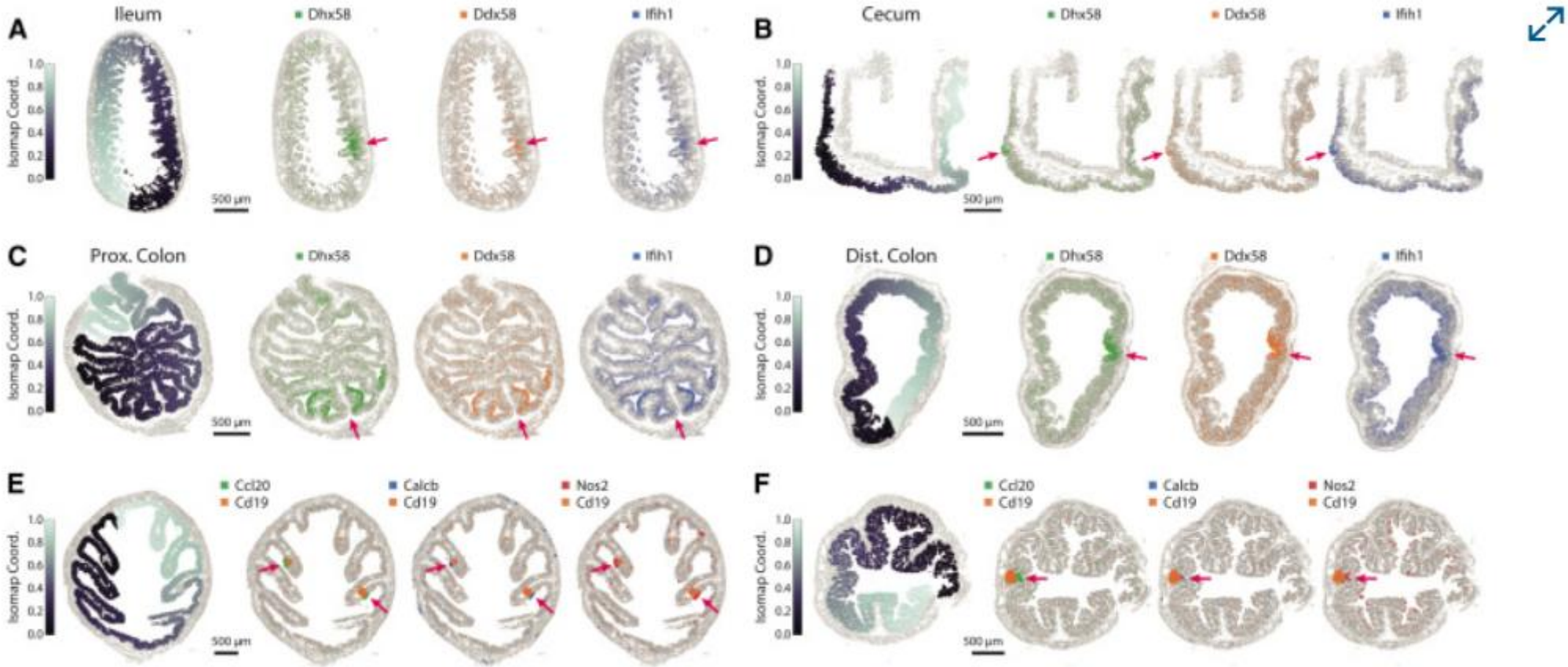
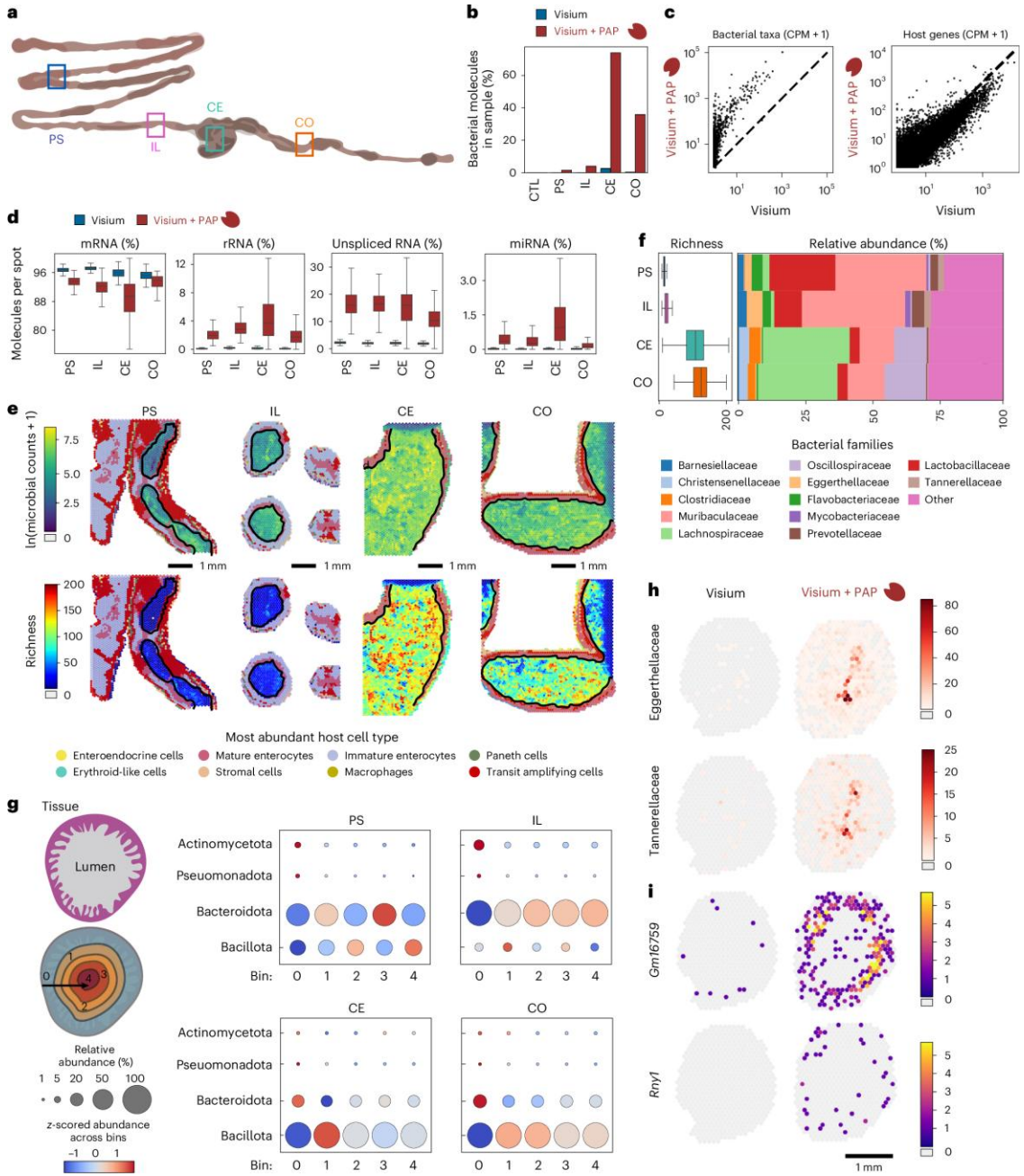


Figure 5 Spatially heterogeneous expression reveals ISG expression patches and follicle-associated epithelial states

a
PS
IL
CE
CO
b
Bacterial molecules


a
PS
IL
CE
CO
b
Visium
Visium + PAP
Bacterial molecules in sample (%)
CTL
PS
IL
CE
CO
c
Bacterial taxa (CPM + 1)
Host genes (CPM + 1)
Visium + PAP
Visium
d
Visium
Visium + PAP
mRNA (%)
rRNA (%)
Unspliced RNA (%)
miRNA (%)
Molecules per spot
e
PS
IL
CE
CO
ln(microbial counts + 1)
Richness
1 mm
Most abundant host cell type
Enteroendocrine cells
Mature enterocytes
Immature enterocytes
Paneth cells
Erythroid-like cells
Stromal cells
Macrophages
Transit amplifying cells
f
Richness
Relative abundance (%)
Bacterial families
Barnesiellaceae
Christensenellaceae
Clostridiaceae
Muribaculaceae
Lachnospiraceae
Oscillospiraceae
Eggerthellaceae
Flavobacteriaceae
Mycobacteriaceae
Prevotellaceae
Lactobacillaceae
Tannerellaceae
Other
g
Tissue
Lumen
Relative abundance (%)
z-scored abundance across bins
Actinomycetota
Pseuomonadota
Bacteroidota
Bacillota
Bin:
h
Visium
Visium + PAP
Eggerthellaceae
Tannerellaceae
i
Gm16759
Rny1
1 mm