

# Universal self-like peptide comprised within S2 fusion peptide

Source: <https://pubmed.ncbi.nlm.nih.gov/19439480/>

universal peptide      conserved flanking sequence

Group 2 SARS-CoV (TOR2)	<u>SFIEDLLFNKVT</u> LADAG-F 815	Group 1 HCoV-NL63 (Amsterdam)	<u>SALEDLLFSKV</u> VTSGLGTV 889
Sable Antelope CoV (US/OH1/03)	<u>SAIEDLLFSKV</u> KLSDVG-F 931	HCoV-229E	<u>SAIEDILFSK</u> LVTSGLGTV 708
Giraffe CoV (US/OH3-TC/2006)	<u>SAIEDLLFSKV</u> KLSDVG-F 926	PEDV (LZC)	<u>SVIEDLLFNK</u> VVTNGLGTV 910
Bovine CoV (R-AH187)	<u>SAIEDLLFSKV</u> KLSDVG-F 931	FIPV (79-1146)	<u>SAIEDLLFDK</u> VVTSGLGTV 980
HCoV-OC43 (ATCC VR-759)	<u>SAIEDLLFDK</u> VKLSDVG-F 929	TGEV (Pur476-MAD)	<u>SAIEDLLFDK</u> VVTSGLGTV 977
PHEV (VW572)	<u>SAIEDLLFDK</u> VKLSDVG-F 917	PRCoV (ISU-1)	<u>SAIEDLLFSK</u> VVTSGLGTV 750
Equine CoV (NC99)	<u>SAIEDLLFNK</u> VRLSDVG-F 931	Bat CoV (BTCov/273/05)	<u>SFIEDLLYNK</u> VTLADAG-F 801
HCoV-HKU1 (N19)	<u>SFFEDLLFDK</u> VKLSDVG-F 922	Group 3 IBV (M41)	<u>SFIEDLLF</u> FTSVESVGLP- 708
MHV (A59)	<u>SAIEDLLFDK</u> VKLSDVG-F 887	IBV (Bdttte)	<u>SVIEDLLF</u> TSVESVGLP-T 708
MHV-2	<u>SAIEDVLE</u> DKVKLSDVG-F 925		

MERS-CoV (2c EMC/ 2012)      **SAIEDLLF**-DKVTIADPG-Y<sub>905</sub>

SARS-CoV2      kpskr<sub>-816</sub>**sfiedllf**-nkvtladag<sub>832</sub>

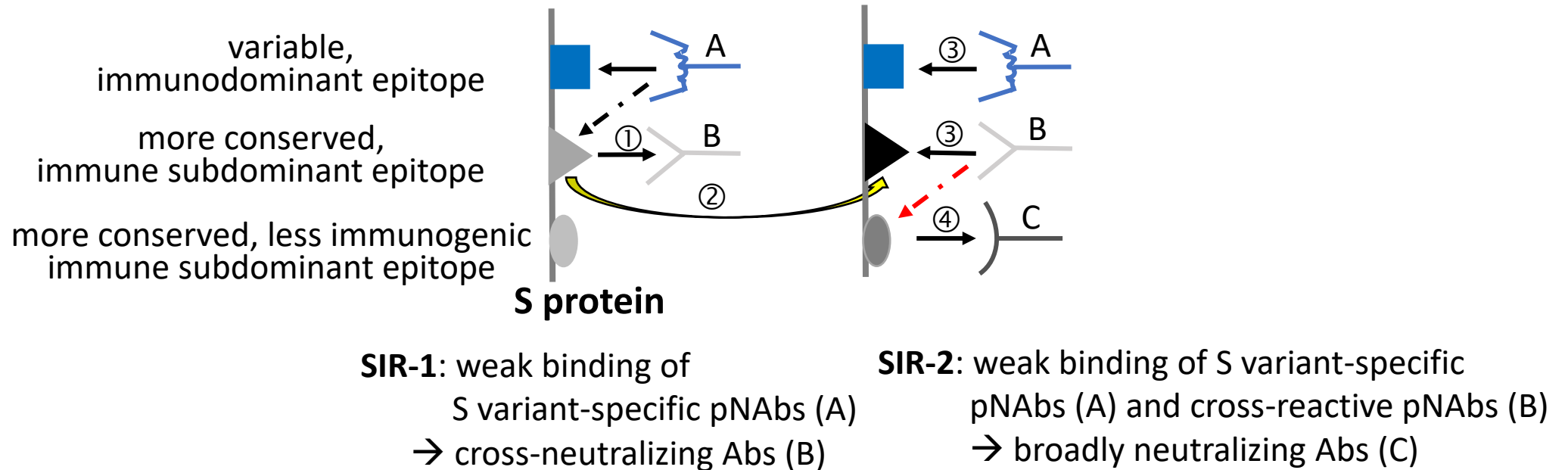
Conservation of S2 fusion peptide amongst Coronaviridae. Underlining indicates residues showing conserved properties. Virus abbreviations are as follows:

SARS-CoV (AAP13441); HCoV-NL63, human CoV NL63 (Amsterdam accession number AAS58177); HCoV-229E, human CoV 229E (AAG48592); HCoV-OC43, human CoV OC43 ATCC VR-759 (AAR01015); HCoV-HKU I, human CoV HKU I N19 (ABD75497); IBV (Bdttte), infectious bronchitis virus Beaudette strain (AA24433); IBV (M41), infectious bronchitis virus M41 strain (ABI26423); MHV-A59, MHV A59 (AAB86819); MHV-2, MHV 2 (AAF19386); PEDV, porcine epidemic diarrhea virus LZC (ABM64776); PRCoV, porcine CoV ISU-1 (ABG89317); PHEV, porcine hemagglutinating encephalomyelitis virus VW752 (AAY68297); bovine CoV, bovine CoV R-AH187 (ABP38295); sable antelope CoV, sable antelope CoV US/OH1/2003 (ABP38306); giraffe CoV, giraffe CoV US/OH3-TC/2006 (ABP38313); equine CoV, equine CoV NC99 (ABP87990); FIPV, feline infectious peritonitis virus WSU 79-1146 (YP239355); bat CoV, bat CoV 273/2005 (ABG47069); TGEV, transmissible gastroenteritis virus Purdue PUR46-MAD (NP058424).

According to Madu et al. (51)

# STERIC IMMUNE REFOCUSING (SIR)

Pre-existing Abs that bind with low affinity to immunodominant S-associated epitopes cause steric masking of these epitopes



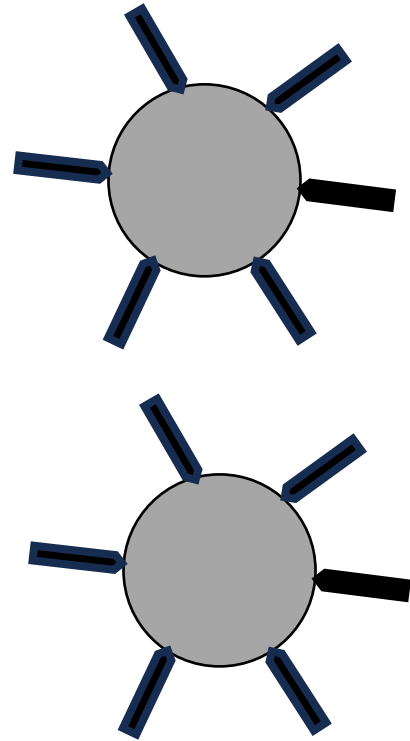
pNAb: Potentially neutralizing Ab

S: Spike protein

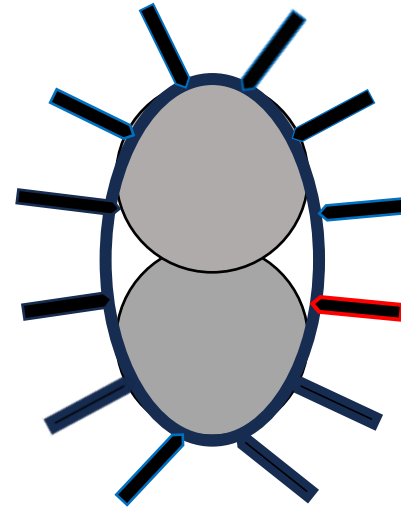
SIR: Steric immune refocusing

Broadly neutralizing Abs will quickly result in suboptimal immune pressure, allowing highly vaccinated populations to exert *large-scale immune selection pressure* on viral infectiousness.

# Low-affinity Abs stabilize viral complexes/ aggregates



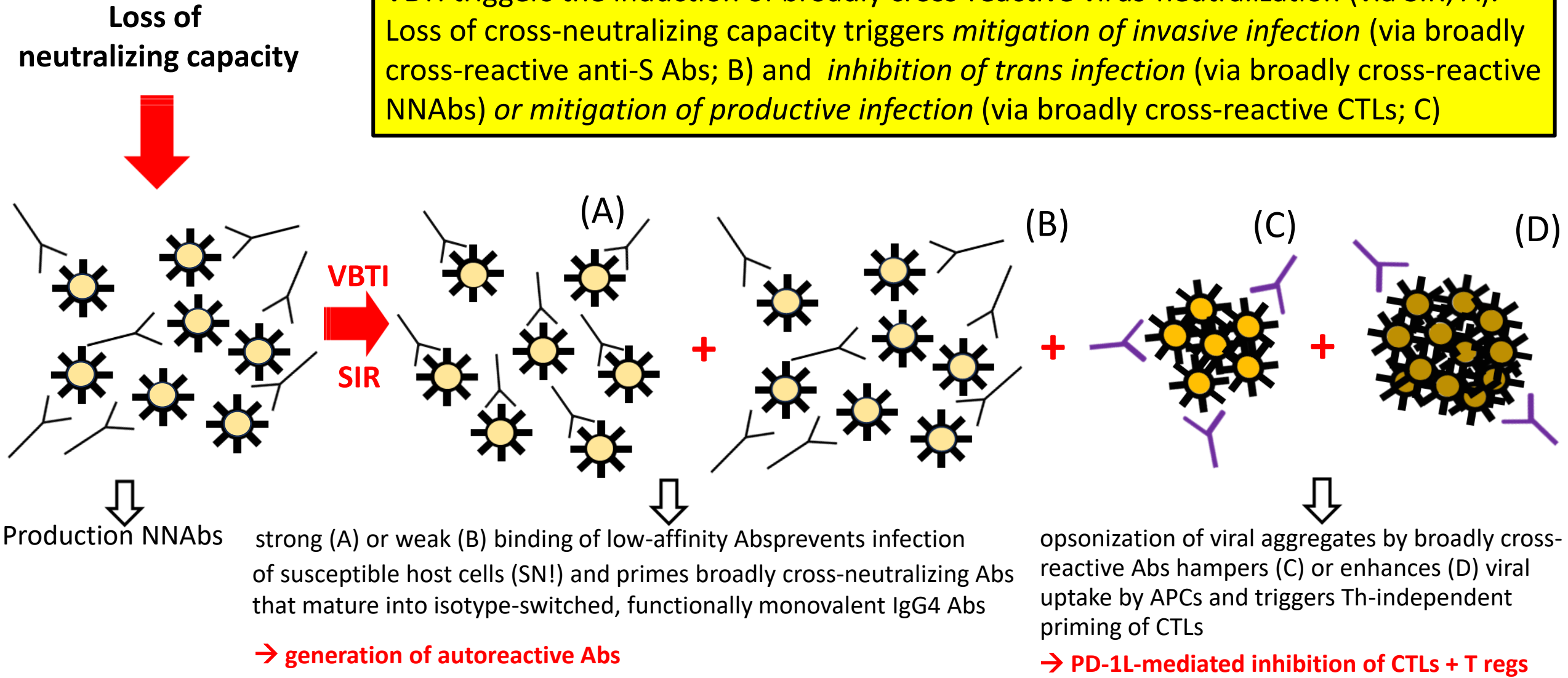
$$2 \times 6 = 12$$



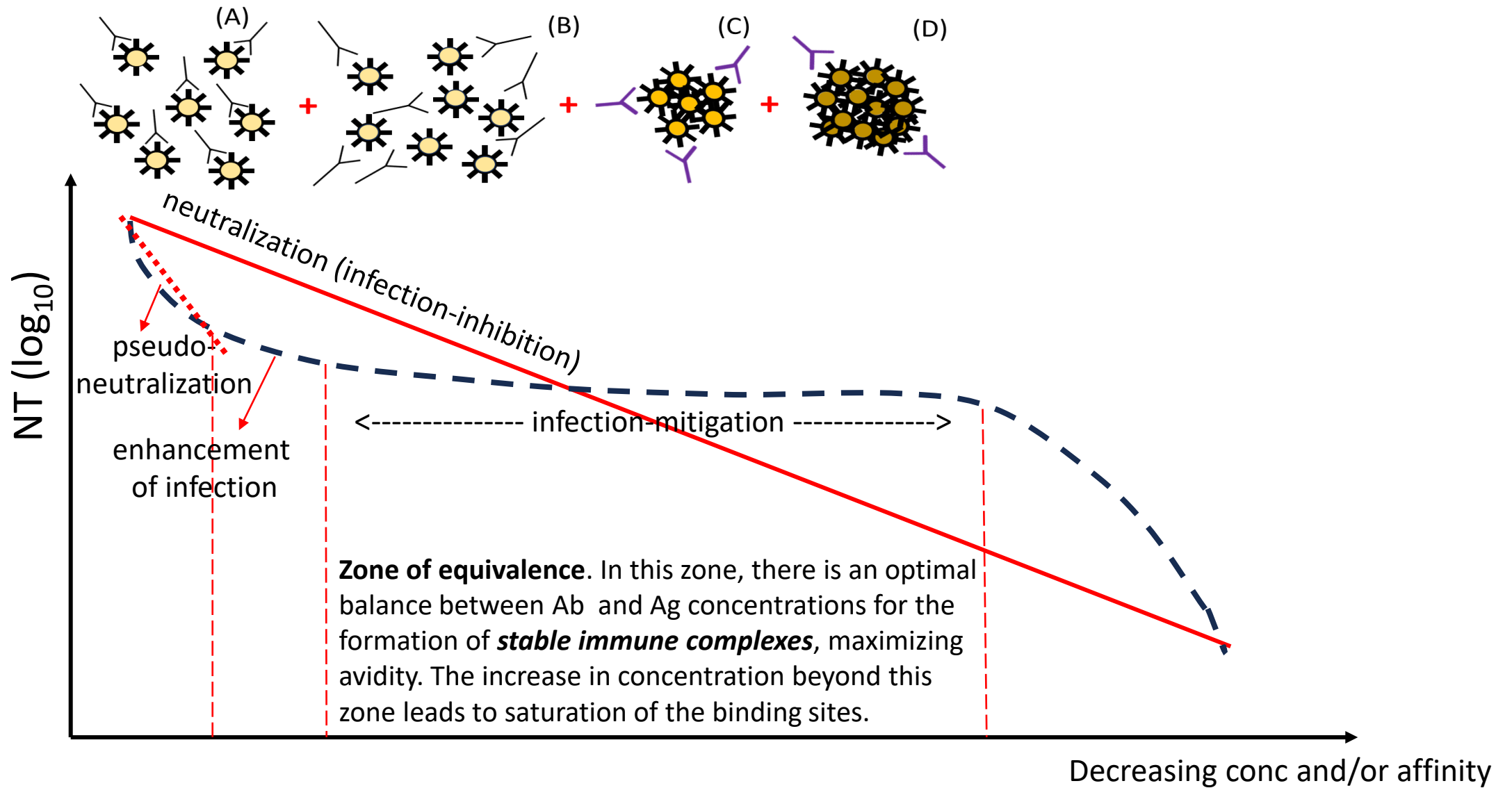
$$1 \times 12$$

Viral immune escape enables BTI whereas immune responses to BTI with Omicron and more infectious Omicron descendants enable (transient) protection from infection or *trans* infection, respectively

VBTI triggers the induction of broadly cross-reactive virus-neutralization (via SIR; A). Loss of cross-neutralizing capacity triggers *mitigation of invasive infection* (via broadly cross-reactive anti-S Abs; B) and *inhibition of trans infection* (via broadly cross-reactive NNAbs) or *mitigation of productive infection* (via broadly cross-reactive CTLs; C)



Avidity is a measure of the overall strength and stability of interactions between multiple binding sites on a bivalent or multivalent antibody (Ab) and its corresponding multivalent Ag



NNAb-dependent VBTI by Omicron (or newly emerged SC-2 variants)

Boosting of previously primed NAbs (OAS)

SIR: Priming of new cross S variant-reactive Abs

Re-exposure to Omicron (or newly emerged SC-2 variants/ updated C-19 booster vaccines)

Boosting of previously SIR-primed cross S variant-reactive Abs (RAS)

Short-lived inhibition of infection (SN)

→ Prolonged suboptimal inhibition of infection

Strongly diminished  
neutralizing capacity

Suboptimal immune pressure on viral infectiousness

New, more infectious immune escape variants

Production of polymeric NNABs

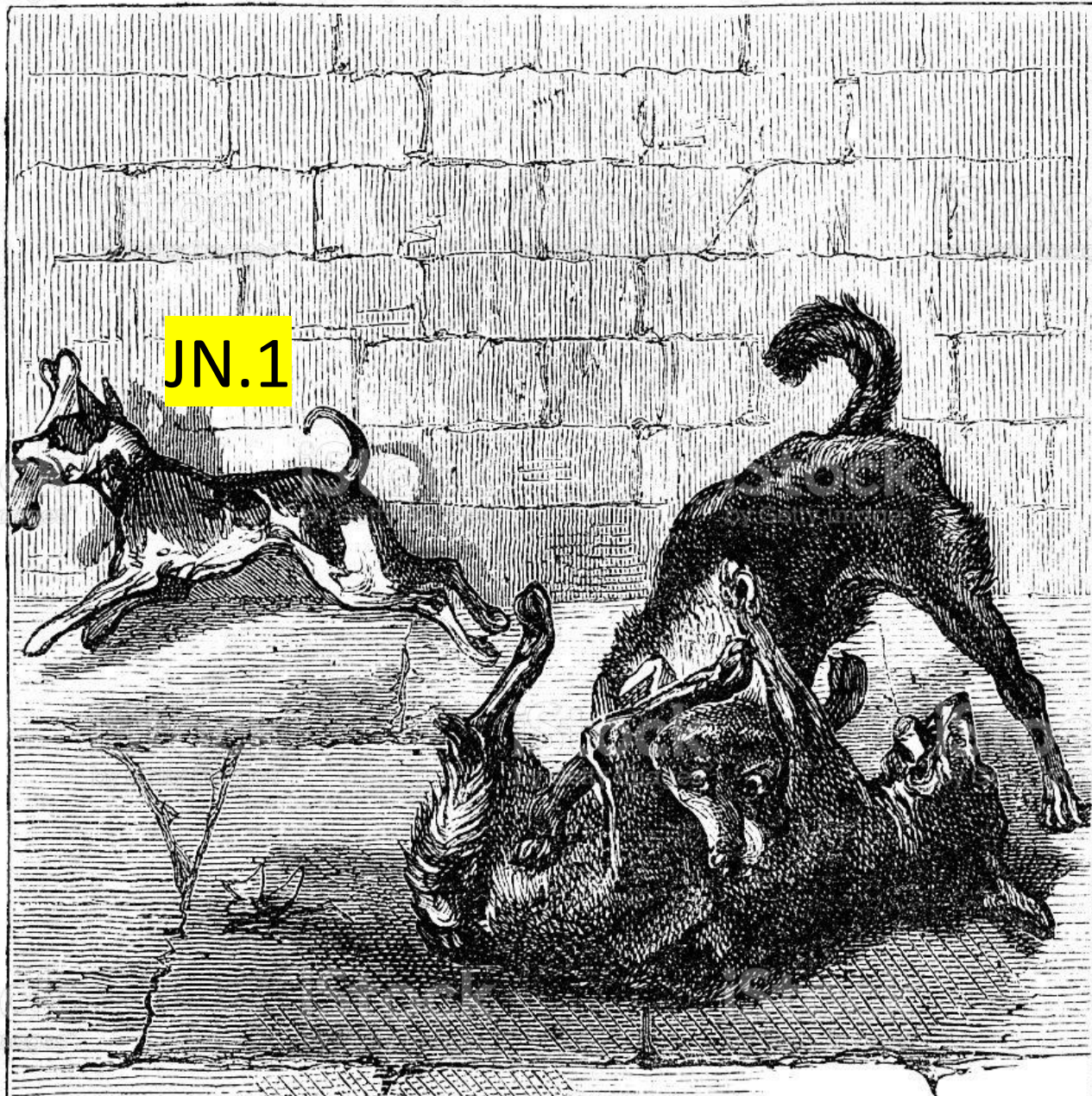
OAS: Original Antigenic Sin  
RAS: Refocused Antigenic Sin  
SN: Seroneutralization



BU slides



TWO DOGS FIGHT FOR A BONE, AND A THIRD  
RUNS AWAY WITH IT.



Wishing you Happy Holidays  
and all the best for 2024

WHEN  
YOU HAVE  
ELIMINATED THE  
IMPOSSIBLE

WHATEVER REMAINS

HOWEVER IMPROBABLE

MUST BE THE

TRUTH

SHERLOCK HOLMES



Geert Vanden Bossche, DVM, PhD

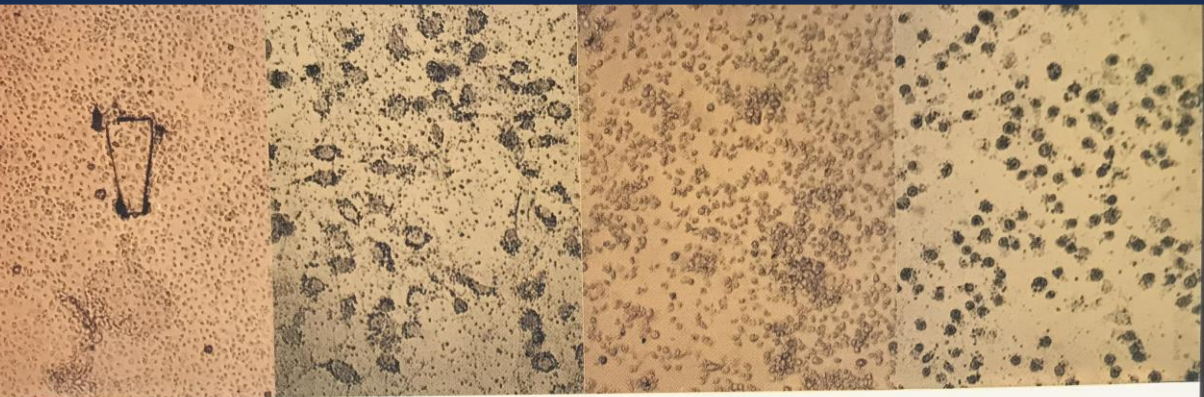
## The Inescapable Immune Escape Pandemic

Nobody Can Conceal The Science  
That Nature Is Now Desperate To Unveil

Society in highly vaccinated countries  
will be caught by surprise



With foreword by  
Dr. Robert Rennebohm, MD



Colloidal aspects of enteroviral infectivity  
in  
aqueous environments  
with special emphasis on poliovirus type 1

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HABILITATIONSSCHRIFT

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