Role of broad mAbs to protect against panzoonotic enveloped RNA virus infections: from rabies, SARS, SARS-CoV-2 to influenzavirus

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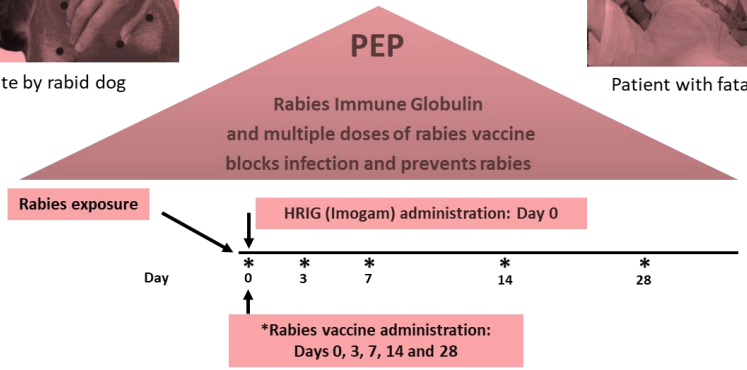
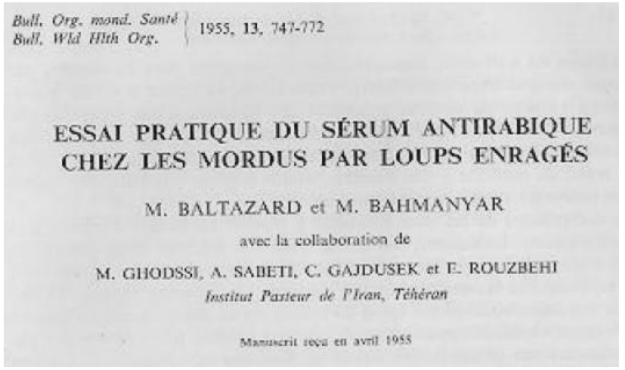
The rabies experience

Post-exposure prophylaxis 100% effective

Bite by rabid dog

Patient with fatal rabies





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ESSAI PRATIQUE DU SÉRUM ANTIRABIQUE CHEZ LES MORDUS PAR LOUPS ENRAGÉS

M. BALTAZARD et M. BAHMANYAR

avec la collaboration de

M. GHODSSI, A. SABETI, C. GAJDUSEK et E. ROUZBEHI

Institut Pasteur de l'Iran, Téhéran

Manuscrit reçu en avril 1955

TABLEAU II. RÉSULTATS DE L'ESSAI PRATIQUE

Série	Nombre de sujets	Nombre de sujets avec morsures graves	Localisation des morsures	Traitement	Mortalité
A	5	4	Tête	2 inoculations sérum + vaccin	0/5
B et sujet 28	7	7	Tête	1 inoculation sérum + vaccin	1/7
C	5	4	Tête	Vaccin seul	3/5
Sujet 27	1	1	Méninges	6 inoculations sérum + vaccin	0/1

The rabies experience: CR57/CR4098 cocktail

Escape from CR57

Rabies virus terrestrial mammals	SRIG	CR57
Arctic fox, AK	+	+
Coyote, TX	+	+
Cow/dog Sri Lanka	+	—
Dog/Coyote, TX	+	+
Dog, Argentina	+	+
Dog, China	+	+
Dog, China (RV342)	+	+
Dog, Gabon	+	+
Dog, Phillipines	+	+
Dog, Phillipines (231)	+	+
Dog, Sonora	+	+
Dog, Thailand	+	+
Dog, Tunesia	+	+
Gray fox, AZ	+	+
Gray fox, TX	+	+
Mongoose NY/PR	+	+
Raccoon SE US	+	+
Raccoon Dog, Russia	+	+
Skunk, CA	+	+
Skunk north central	+	+
Skunk south central	+	—
Wolf siberia	+	+

Rabies virus (Bat origin)	SRIG	CR57
Bat, *Desmodus rotundus*, Brazil	+	+
Bat, *Desmodus rotundus*, TN/MX	+	+
Bat, *Eptesicus fuscus*, PA	+	+
Bat, *Eptesicus fuscus-Myotis spp.*, CO	+	—
Bat, *Lasionycteris noctivagans*, WA	+	+
Bat, *Lasiurus borealis*, TN	+	+
Bat, *Lasiurus cinereus*, AZ	+	+
Bat, *Lasiurus cinereus*, NY	+	+
Bat, *Myotis spp.*, WA	+	+
Bat, *Pipistrellus hesperus*, CA	+	+
Bat, *Pipistrellus subflavus*, AL	+	+
Bat, *Tadarida brasiliensis*, AL	+	+

A second antibody is required to obtain full neutralization of all viruses

- No interference with vaccine
- Overlapping serum half-life in humans

CR4098 covers all escapes from CR57

Breadth of neutralization against street rabies viruses*					
Lyssavirus (source/strain)	**SRIG**	**CR57**	**CR4038**	**CR4098**	**CR4144**
CVS-11	+	+	+	+	+
Raccoon, SE, US	+	+	+	+	+
Gray fox, TX	+	+	+	+	+
Gray fox, AZ	+	+	+	+	+
Arctic fox, AK	+	+	+	+	+
Coyote, TX	+	+	+	+	+
Skunk, north central	+	+	+	+	+
Skunk, south central	+	-	+	+	+
Skunk, CA	+	+	+	+	+
Mongoose, NY/Puerto Rico	+	+	+	+	+
Dog, Argentina	+	+	+	+	+
Dog, Sonora	+	+	+	+	+
Dog, Gabon	+	+	+	+	+
Dog, Thailand	+	+	+	+	+
Bat, *Lasiurus borealis*, TN	+	+	-	+	-
Bat, *Eptesicus, fuscus-Myotis I spp.*, CO	+	-	+	+	+
Bat, *Myotis* spp., WA	+	+	-	+	+
Bat, *Lasiurus cinereus*, AZ	+	+	-	+	-
Bat, *Lasiurus cinereus*, NY	+	+	-	+	-
Bat, *Pipistrellus subflavus*, AL	+	+	+	+	+
Bat, *Tadarida brasiliensis*, AL	+	+	+	+	+
Bat, *Lasionycteris noctivagans*, WA	+	+	+	+	+
Bat, *Eptesicus fuscus*, PA	+	+	-	-	-
Bat, *Pipistrellus hesperus*, CA	+	+	-	-	-
Bat, *Desmodus rotundus*, TN/MX	+	+	+	+	+
Bat, *Desmodus rotundus*, Brazil	+	+	+	+	+

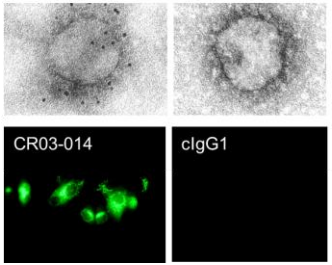
* Neutralizing activity was determined in a standard RFFIT. SRIG, standard rabies immunoglobulin, lot R3; +, neutralization; -, no neutralization; SE US, southeastern United States; MX, Mexico.

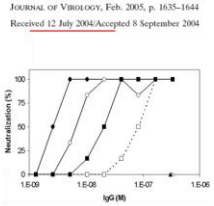
The SARS experience: CR3014/CR3022 cocktail

THE LANCET • Vol 363 • June 26, 2004 • www.thelancet.com

Antibodies Binding to the Spike and Nucleocapsid Proteins of Severe Acute Respiratory Syndrome Coronavirus

Edward N. van den Brink,[1] Jan ter Meulen,[1] Freek Cox,[1] Mandy A. C. Jongeneelen,[1] Alexandra Thijsse,[1] Mark Throsby,[1] Wilfred E. Marissen,[1] Pauline M. L. Rood,[1] Alexander B. H. Bakker,[1] Hans R. Gelderblom,[2] Byron E. Martina,[3] Albert D. M. E. Osterhaus,[3] Wolfgang Preiser,[4] Hans Wilhelm Doerr,[4] John de Kruif,[1] and Jaap Goudsmit[1]*





RESEARCH LETTERS

Human monoclonal antibody as prophylaxis for SARS coronavirus infection in ferrets

Jan ter Meulen, Alexander B H Bakker, Edward N van den Brink, Gerrit J Weverling, Byron E E Martina, Bart L Haagmans, Thijs Kuiken, John de Kruif, Wolfgang Preiser, Willy Spaan, Hans R Gelderblom, Jaap Goudsmit, Albert D M E Osterhaus

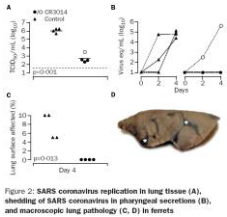


Figure 2: **SARS coronavirus replication in lung tissue (A), shedding of SARS coronavirus in pharyngeal secretions (B), and macroscopic lung pathology (C, D) in ferrets**

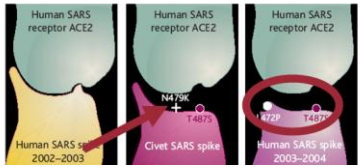
The SARS experience: CR3014/CR3022 cocktail

Distinct, non-overlapping coverage; synergy versus antagonism

STRUCTURAL BIOLOGY 16 SEPTEMBER 2005 VOL 309

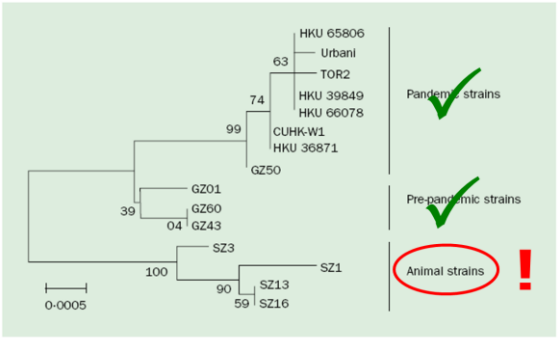
Adaptation of SARS Coronavirus to Humans

Kathryn V. Holmes



Severe acute respiratory syndrome coronavirus-like virus in Chinese horseshoe bats

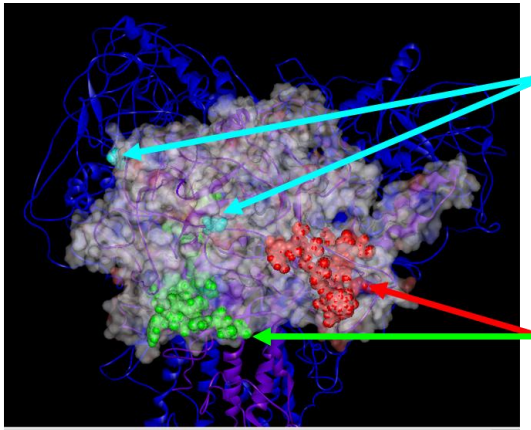
Susanna K. P. Lau*†‡§, Patrick C. Y. Woo*†‡§, Kenneth S. M. Li*, Yi Huang*, Hoi-Wah Tsoi*, Beatrice H. L. Wong*, Samson S. Y. Wong*†‡, Suet-Yi Leung¶, Kwok-Hung Chan*, and Kwok-Yung Yuen*†‡§‖



L L M Poon, Y Guan, J M Nicholls, K Y Yuen, and J S M Peiris
Lancet Infect Dis 2004; **4**: 663–71

Human Monoclonal Antibody Combination against SARS Coronavirus: Synergy and Coverage of Escape Mutants.

Jan ter Meulen[1*#], Edward N. van den Brink[1#], Leo L. M. Poon[2], Wilfred E. Marissen[1], Cynthia S. W. Leung[2], Freek Cox[1], Chung Y. Cheung[2], Arjen Q. Bakker[1], Johannes A. Bogaards[1], Els van Deventer[1], Wolfgang Preiser[3], Hans Wilhelm Doerr[3], Vincent T. Chow[4], John de Kruif[1], Joseph S.M. Peiris[2], Jaap Goudsmit[1]



CR3014

-residue 462

-residue 479

SARS CR3022

-residues 430-449

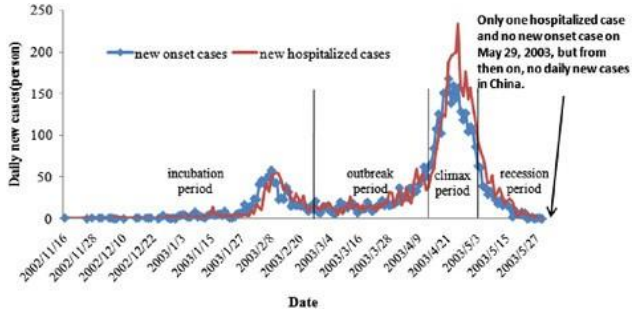
-residues 484-503

Model: Biochem Biophys Res Commun 2004, 325:1210-4

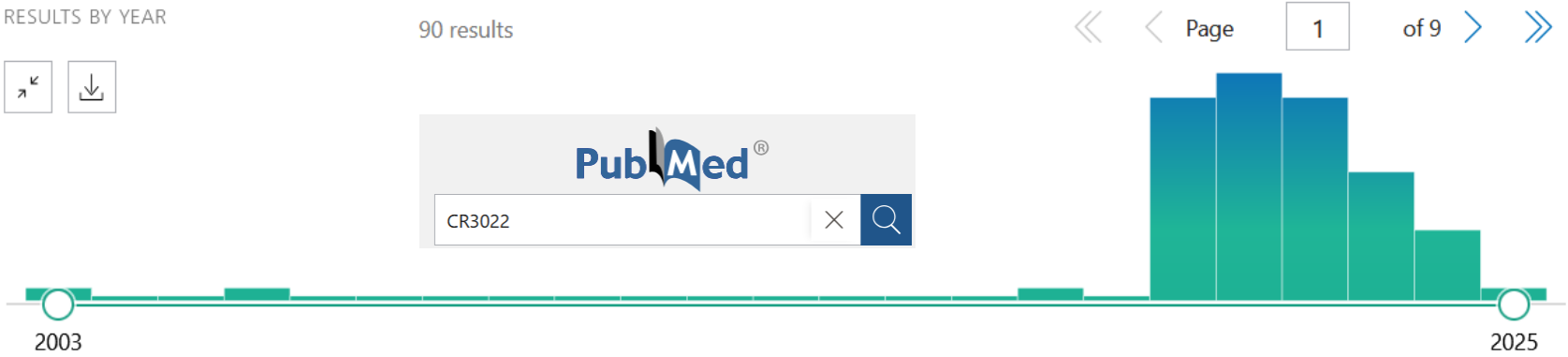
The SARS experience: the end of SARS was not the end of CR3022…

WHO declares SARS epidemic under control

BMJ 2003 ; 327 doi: https://doi.org/10.1136/sbmj.0307223a (Published 01 July 2003)
Cite this as: *BMJ* 2003;327:0307223a



CR3022 turned out to be cross-reactive with SARS-CoV-2: one of the first mAbs used for SARS-CoV-2 diagnostics and engineering

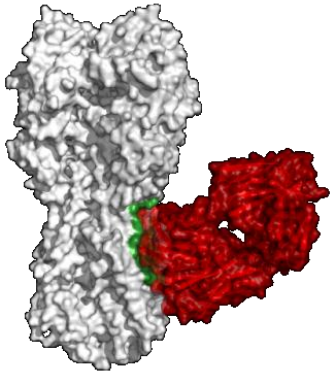


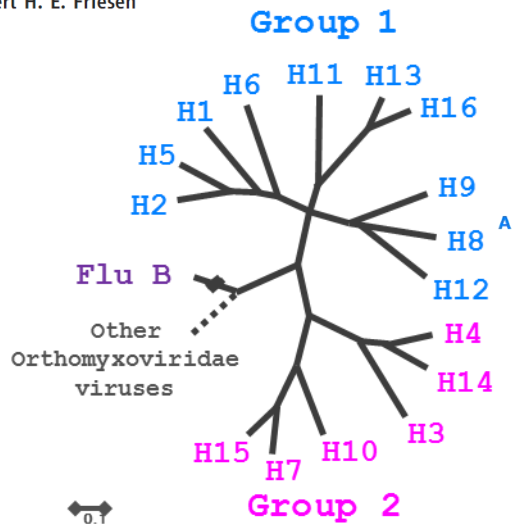
The influenza experience: discovery of the broadest monoclonal antibody to date

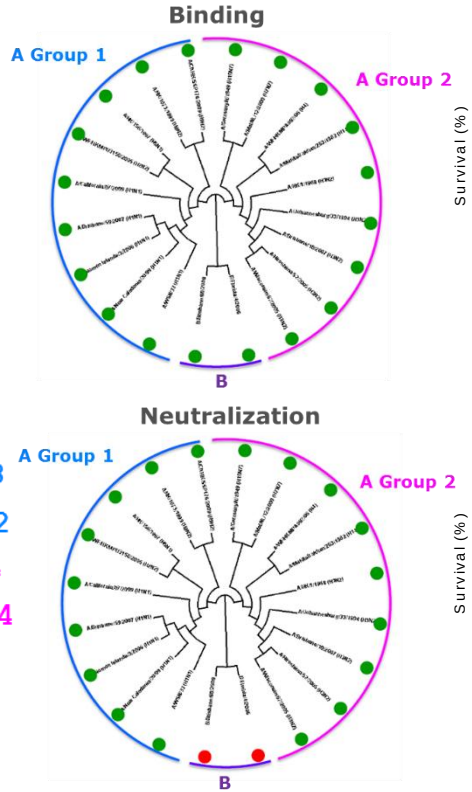
Highly Conserved Protective Epitopes on Influenza B Viruses

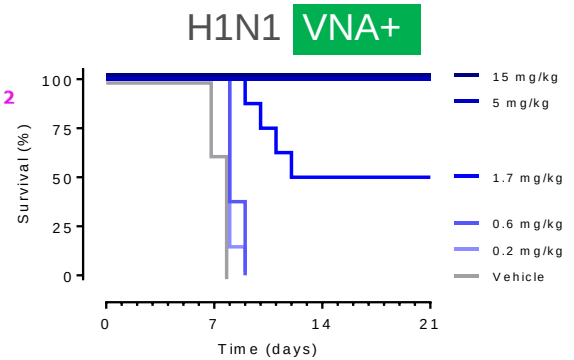
Cyrille Dreyfus,[1*] Nick S. Laursen,[1,2*] Ted Kwaks,[3] David Zuijdgeest,[3] Reza Khayat,[1] Damian C. Ekiert,[1†] Jeong Hyun Lee,[1] Zoltan Metlagel,[1‡] Miriam V. Bujny,[3] Mandy Jongeneelen,[3] Remko van der Vlugt,[3] Mohammed Lamrani,[3] Hans J. W. M. Korse,[3] Eric Geelen,[3] Özcan Sahin,[3] Martijn Sieuwerts,[3] Just P. J. Brakenhoff,[3] Ronald Vogels,[3] Olive T. W. Li,[4] Leo L. M. Poon,[4] Malik Peiris,[4] Wouter Koudstaal,[3] Andrew B. Ward,[1] Ian A. Wilson,[1,5§] Jaap Goudsmit,[3§] Robert H. E. Friesen[3]

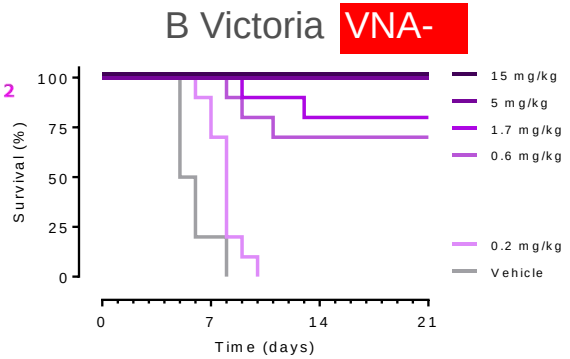
Science 2012





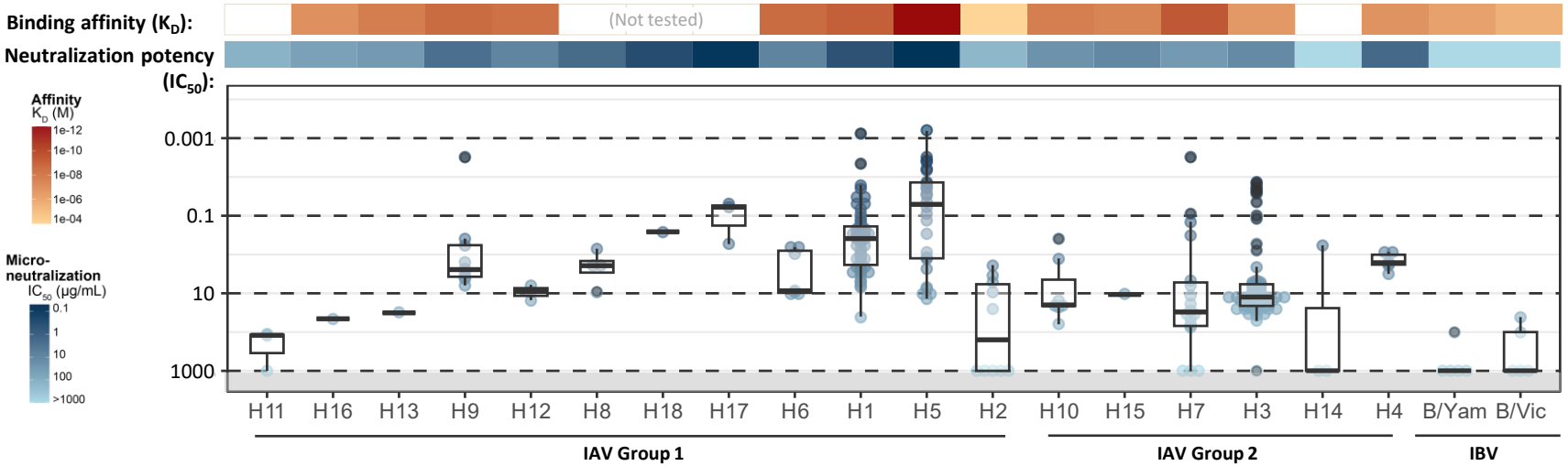






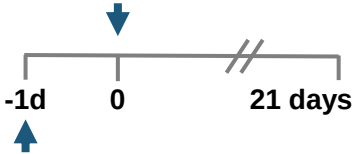
The influenza experience: discovery of the broadest monoclonal antibody to date

Binding all influenza A and B viruses, and providing neutralizing and non-neutralizing protection

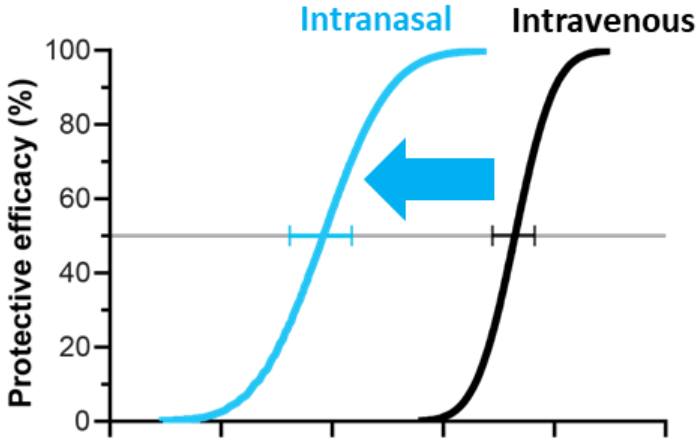


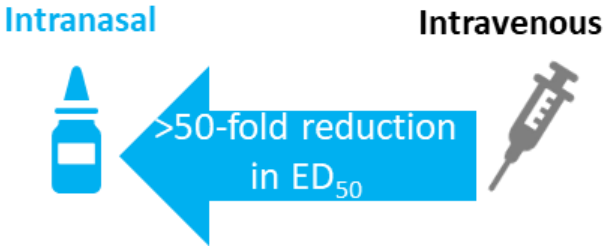
Solving the breadth-potency trade-off through administration route

Infect mice intranasally with **influenza H3N2**



Administer
CR9114 IV or IN



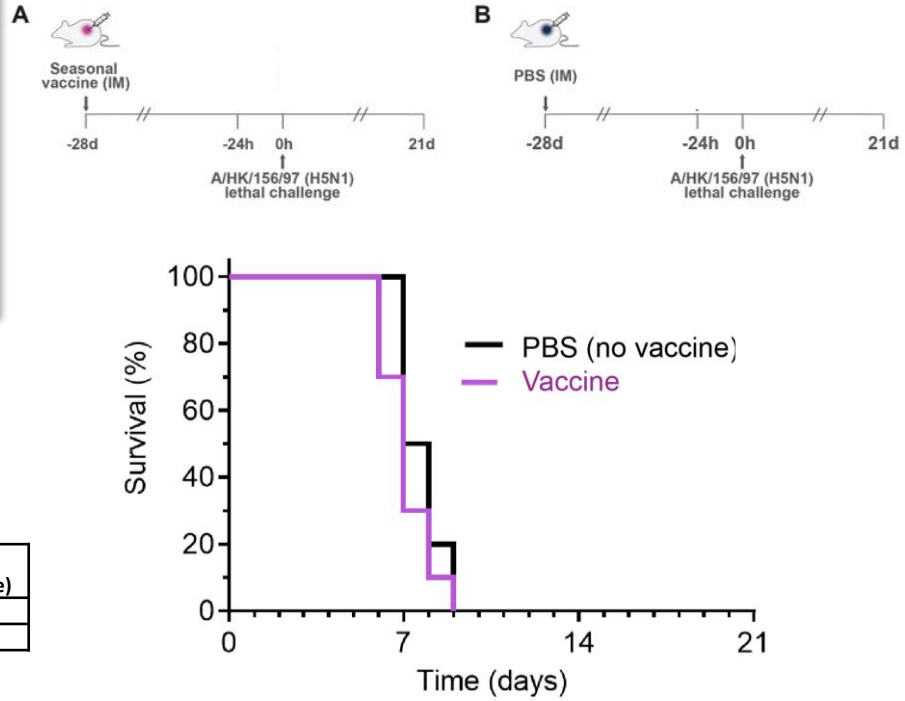


scientific reports

In press

OPEN Intranasal administration of a panreactive anti influenza antibody reveals Fc independent mode of protection

Active immunization with quadrivalent seasonal influenza vaccine does not protect mice against A(H5N1) infection



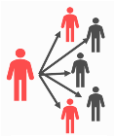
Seasonal quadrivalent influenza vaccine contains antigens from four viruses: H1, H3, B/Victoria, B/Yamagata

Mice	H1N1 (A/Victoria)	H3N2 (A/Cambodia)	B/Washington (Victoria lineage)	B/Phuket (Yamagata lineage)
Vaccinated	196	320	28	40
Unimmunized	≤ 5	≤ 5	≤ 5	≤ 5

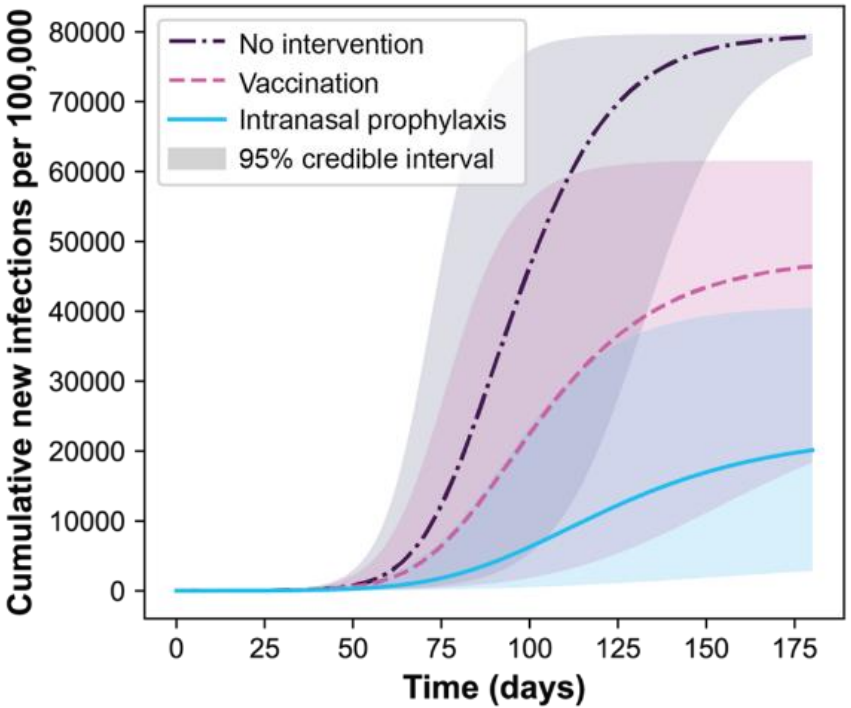
Geometric mean HI titers in pooled sera one day before challenge (27 days after immunization). Lower limit of detection = 5

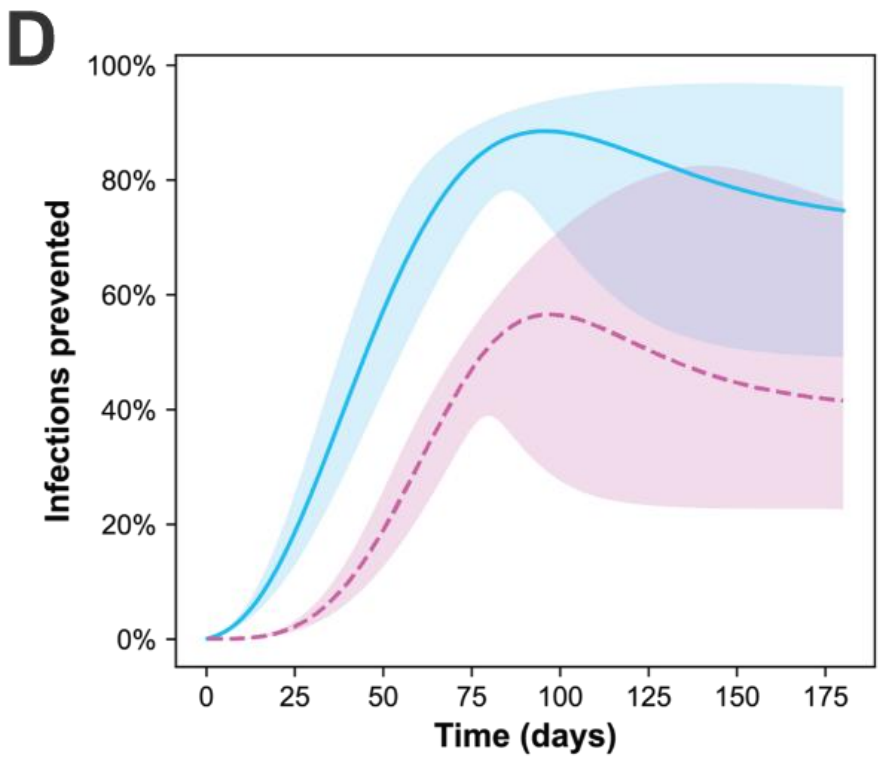
Even if H5N1 vaccine is stockpiled, time to roll-out and eliciting maximum titers is too long

Immediately effective intranasal bnAb of same efficacy would avert 35% more infections



$R_0 = 2$





Intranasal administration of CR9114 fully protects mice against A(H5N1) infection at low dosages

scientific reports

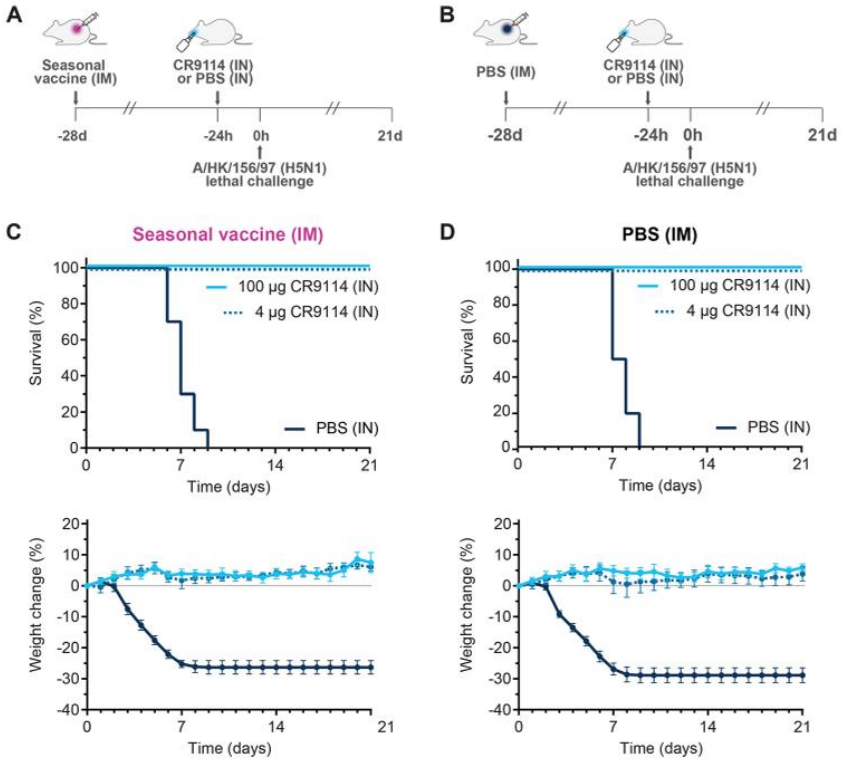
Check for updates

OPEN

A pan-influenza monoclonal antibody neutralizes H5 strains and prophylactically protects through intranasal administration

Anna L. Beukenhorst[1,2,3✉], Jacopo Fralliccardi[2], Keira L. Rice[2], Martin H. Koldijk[2], Joana C. Moreira de Mello[2], Jaco M. Klap[2], Christoforos Hadjichrysanthou[4], Clarissa M. Koch[2], Kelly A. S. da Costa[5], Nigel Temperton[5], Babette A. de Jong[2], Helene Vietsch[2], Bertjan Ziere[2], Boris Julg[2], Wouter Koudstaal[2] & Jaap Goudsmit[2,6]

Regardless of pre-existing immunity conferred by the quadrivalent influenza seasonal vaccine.



Towards proof-of-concept in humans

World's first publication on intranasal PK of monoclonal influenza antibody