Erasmus MC

Viroscience lab
WHERE SKILLS MEET TO STUDY & PROTECT

Relevant knowledge of coronaviruses before the COVID-19 pandemic: virology and vaccines

Bart Haagmans, Viroscience department, Erasmus MC, Rotterdam

Coronaviruses

Coronaviruses are found in many different animal species and humans

- 4 human CoVs normally cause a common cold

  HCoV-NL63

  HCoV-229E

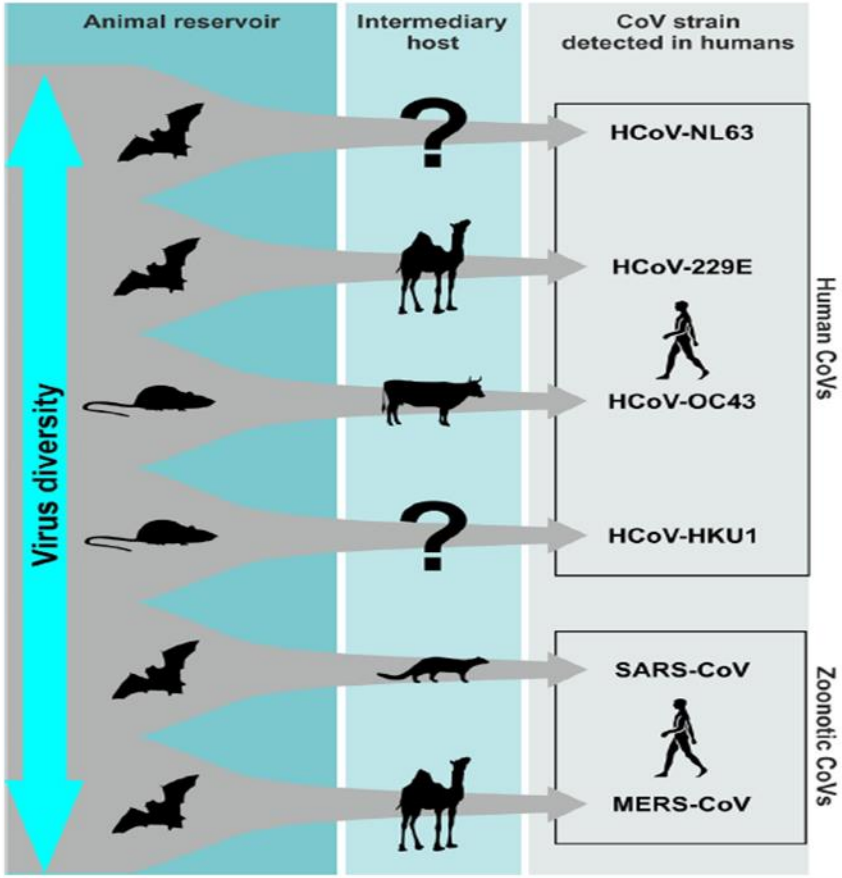
  HCoV-OC43

  HCoV-HKU-1

- 2 zoonotic CoVs cause severe respiratory infections

  SARS-CoV

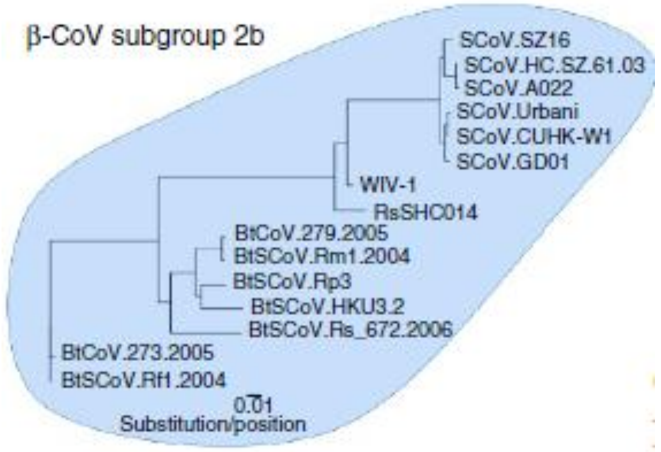
  MERS-CoV

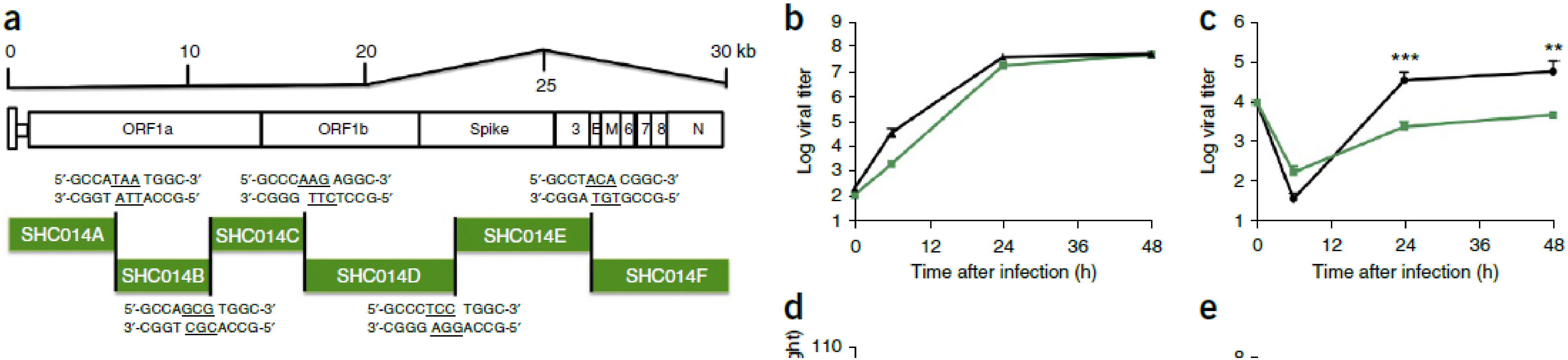


Corman et al., Adv Virus Res. 2018

A SARS-like cluster of circulating bat coronaviruses shows potential for human emergence

Vineet D Menachery[1], Boyd L Yount Jr[1], Kari Debbink[1,2], Sudhakar Agnihothram[3], Lisa E Gralinski[1], Jessica A Plante[1], Rachel L Graham[1], Trevor Scobey[1], Xing-Yi Ge[4], Eric F Donaldson[1], Scott H Randell[5,6], Antonio Lanzavecchia[7], Wayne A Marasco[8,9], Zhengli-Li Shi[4] & Ralph S Baric[1,2]



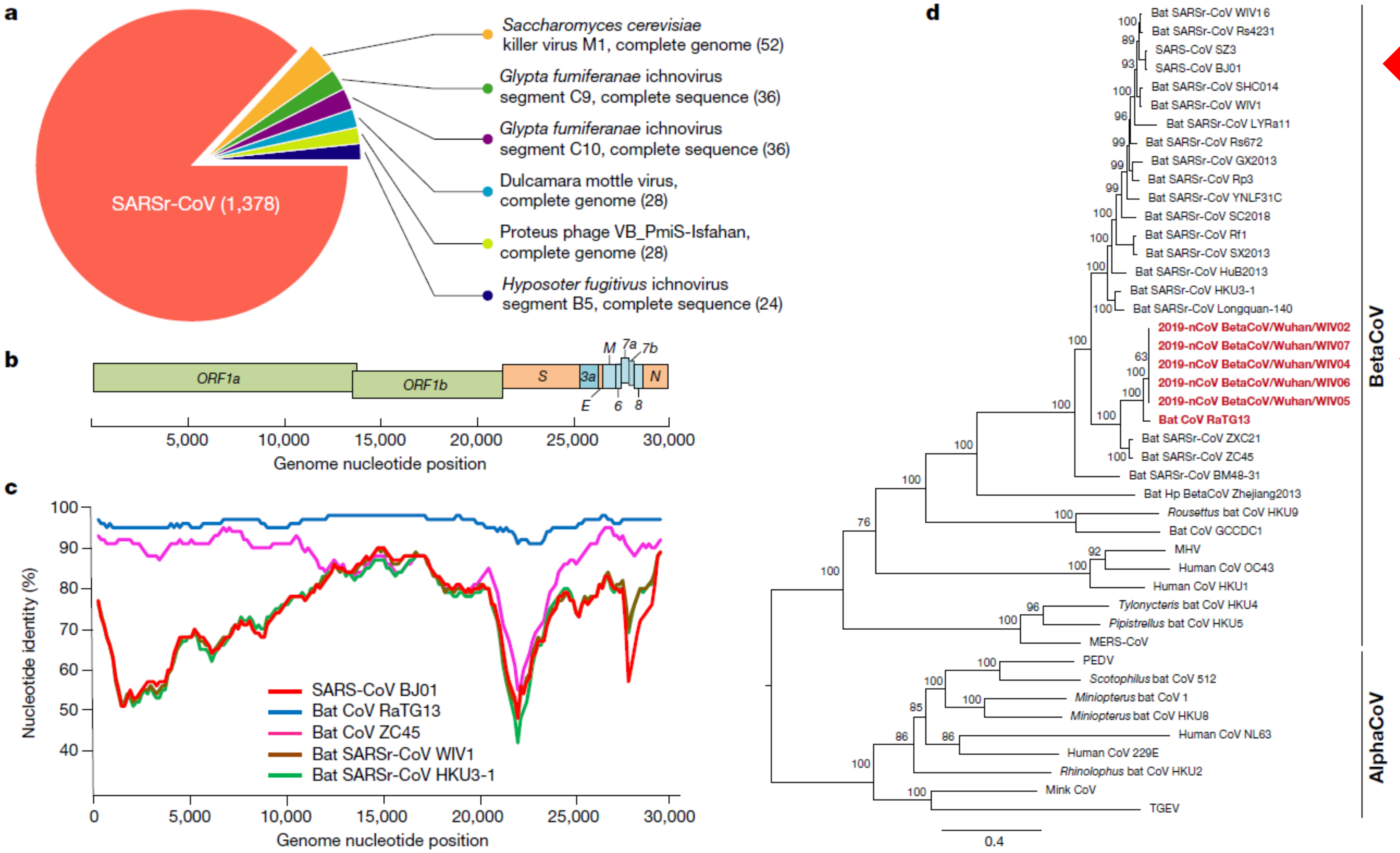


→ Bat CoV SHC014 replicates to similar titers compared to SARS-CoV

(Menachery et al., Nat Med 2015)

A pneumonia outbreak associated with a new coronavirus of probable bat origin

(Zhou, et al., Nature, 2020).



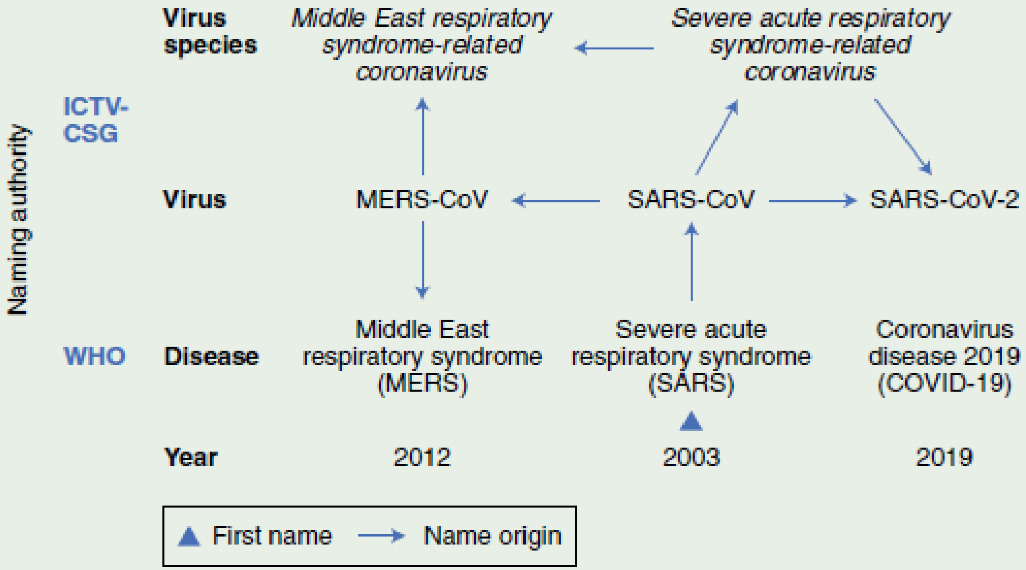
SARS-CoV

SARS-CoV- 2

CONSENSUS STATEMENT
https://doi.org/10.1038/s41564-020-0695-z
nature microbiology

The species *Severe acute respiratory syndrome-related coronavirus*: classifying 2019-nCoV and naming it SARS-CoV-2

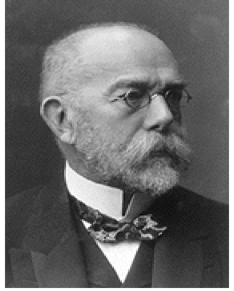
Coronaviridae Study Group of the International Committee on Taxonomy of Viruses*



History of coronavirus naming during the three zoonotic outbreaks in relation to virus taxonomy and diseases caused by these viruses. According to the current international classification of diseases[49], MERS and SARS are classified as 1D64 and 1D65, respectively.

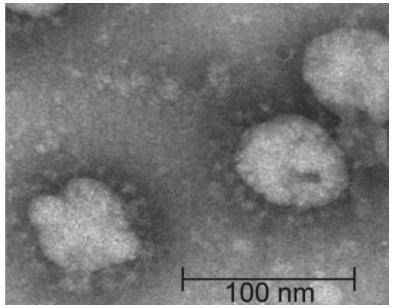
SARS

- Rivers' modified Koch's postulates -

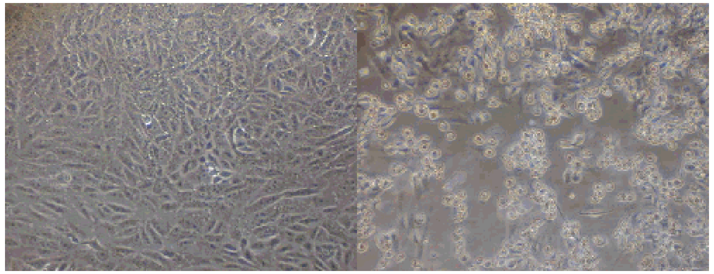


Fouchier et al., Nature 2003
Kuiken et al., Lancet 2003

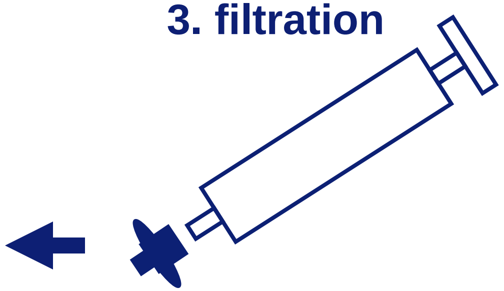
1. Virus isolation



2. Virus propagation

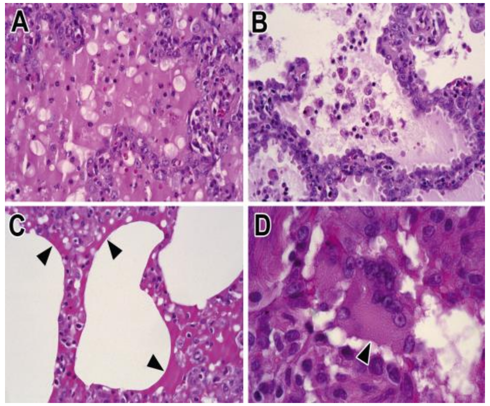


3. filtration

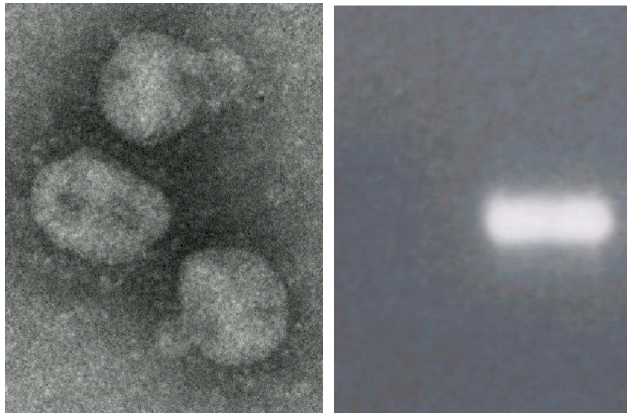


0.2 / 0.4 µM

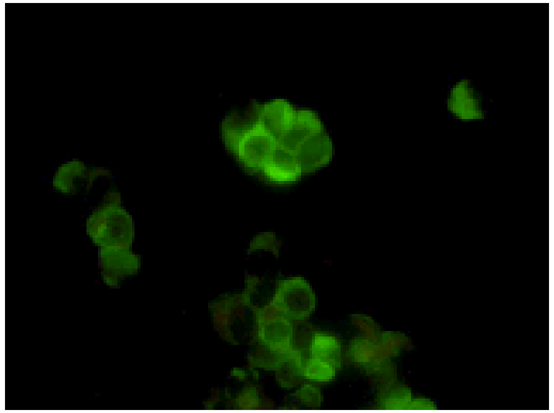
4. Disease in macaques



5. Re-isolation & PCR of virus

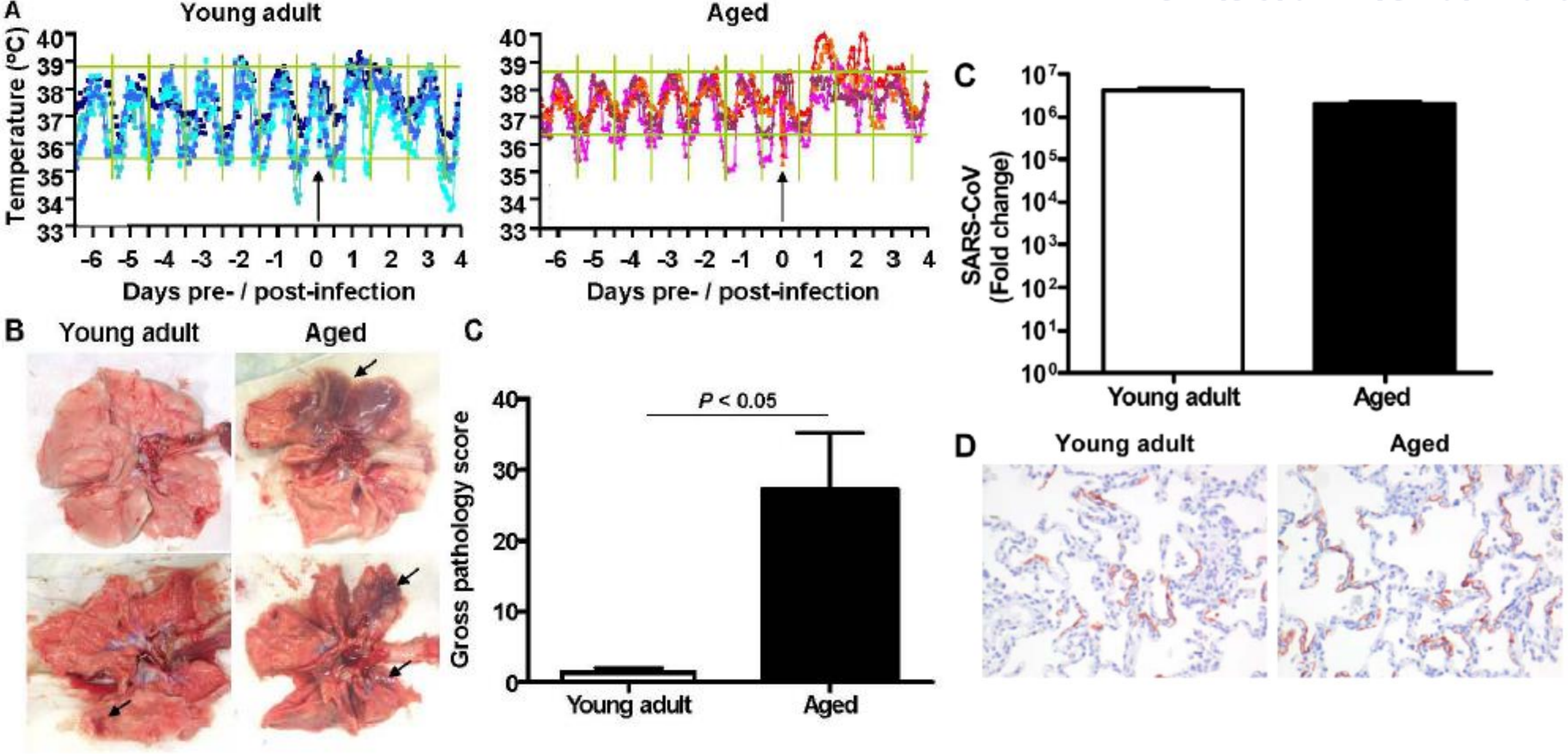


6. Specific immune response

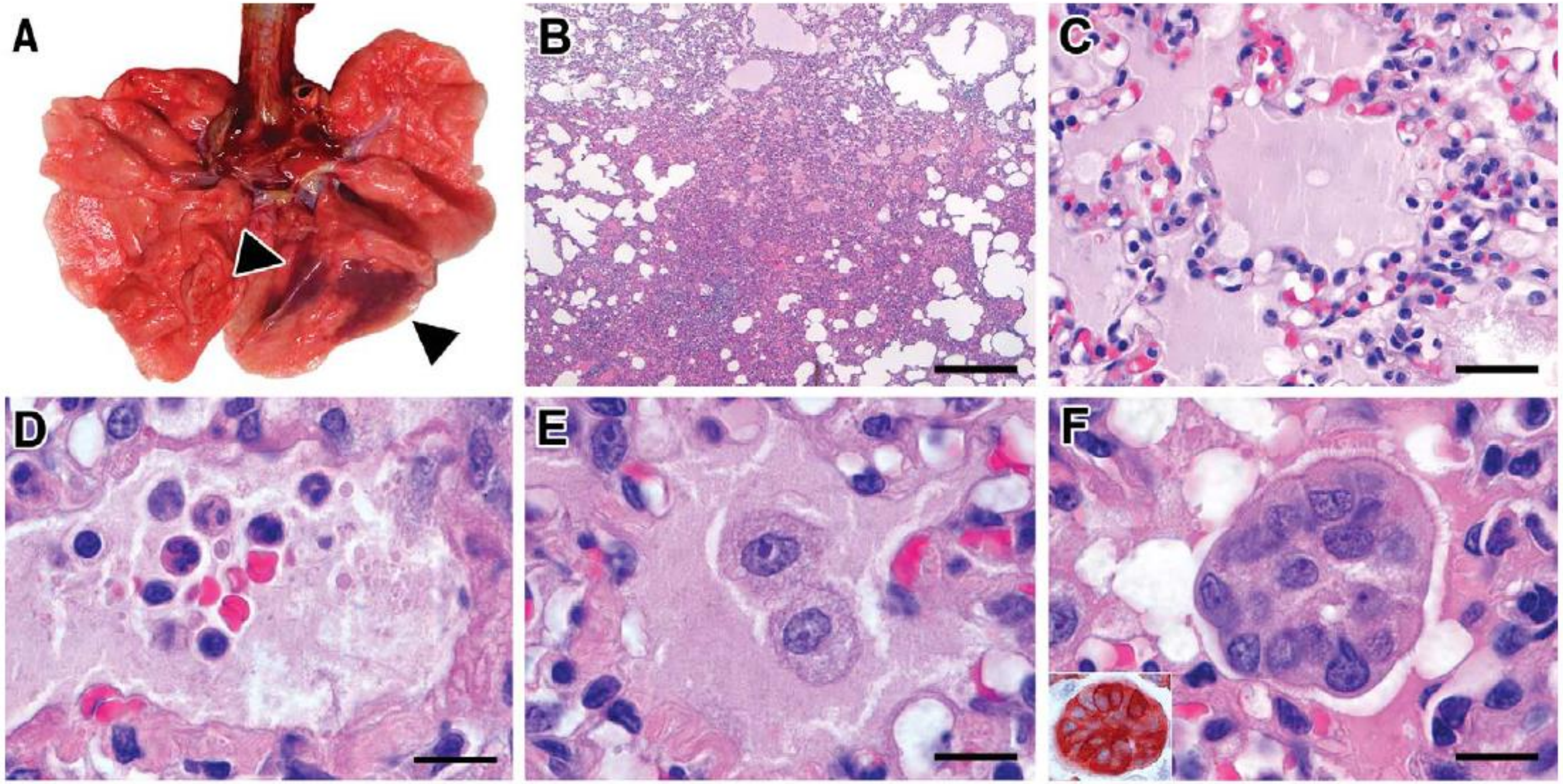


Gross pathology in SARS-CoV infected macaques aged macaques

Smits et al. Plos Path 2010



Comparative pathogenesis of COVID-19, MERS, and SARS in a nonhuman primate model *(Rockx et al., Science 2020)*



→ Similar lesions observed in SARS-CoV and SARS-CoV-2 infected NHP

RAPID COMMUNICATIONS

Detection of a novel human coronavirus by real-time reverse-transcription polymerase chain reaction

V M Corman[1,2], I Eckerle[1], T Bleicker[1], A Zaki[3], O Landt[4], M Eschbach-Bludau[1], S van Boheemen[5], R Gopal[6], M Ballhause[4], T M Bestebroer[5], D Muth[1], M A Müller[1], J F Drexler[1], M Zambon[6], A D Osterhaus[5], R M Fouchier[5], C Drosten (drosten@virology-bonn.de)[1]
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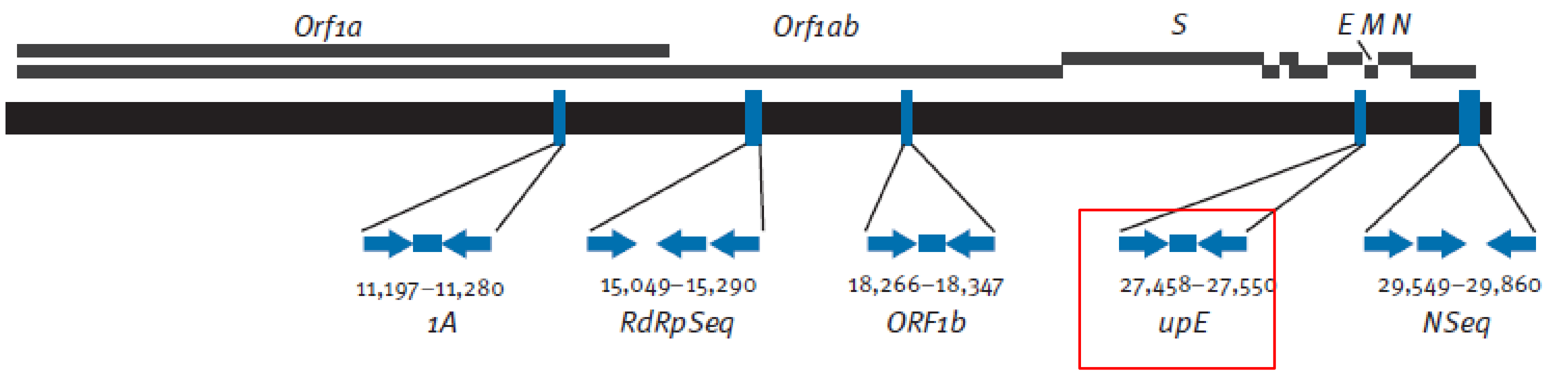
3. Virology Laboratory, Dr Soliman Fakeeh Hospital, Jeddah
4. TibMolbiol, Berlin, Germany
5. Department of Virology and Virosciences, Erasmus Medical Centre, Rotterdam, The Netherlands
6. Health Protection Agency (HPA), London, United Kingdom

Citation style for this article:
Corman VM, Eckerle I, Bleicker T, Zaki A, Landt O, Eschbach-Bludau M, van Boheemen S, Gopal R, Ballhause M, Bestebroer TM, Muth D, Müller MA, Drexler JF, Zambon M, Osterhaus AD, Fouchier RM, Drosten C. Detection of a novel human coronavirus by real-time reverse-transcription polymerase chain reaction. Euro Surveill. 2012;17(39):pii=20285. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20285

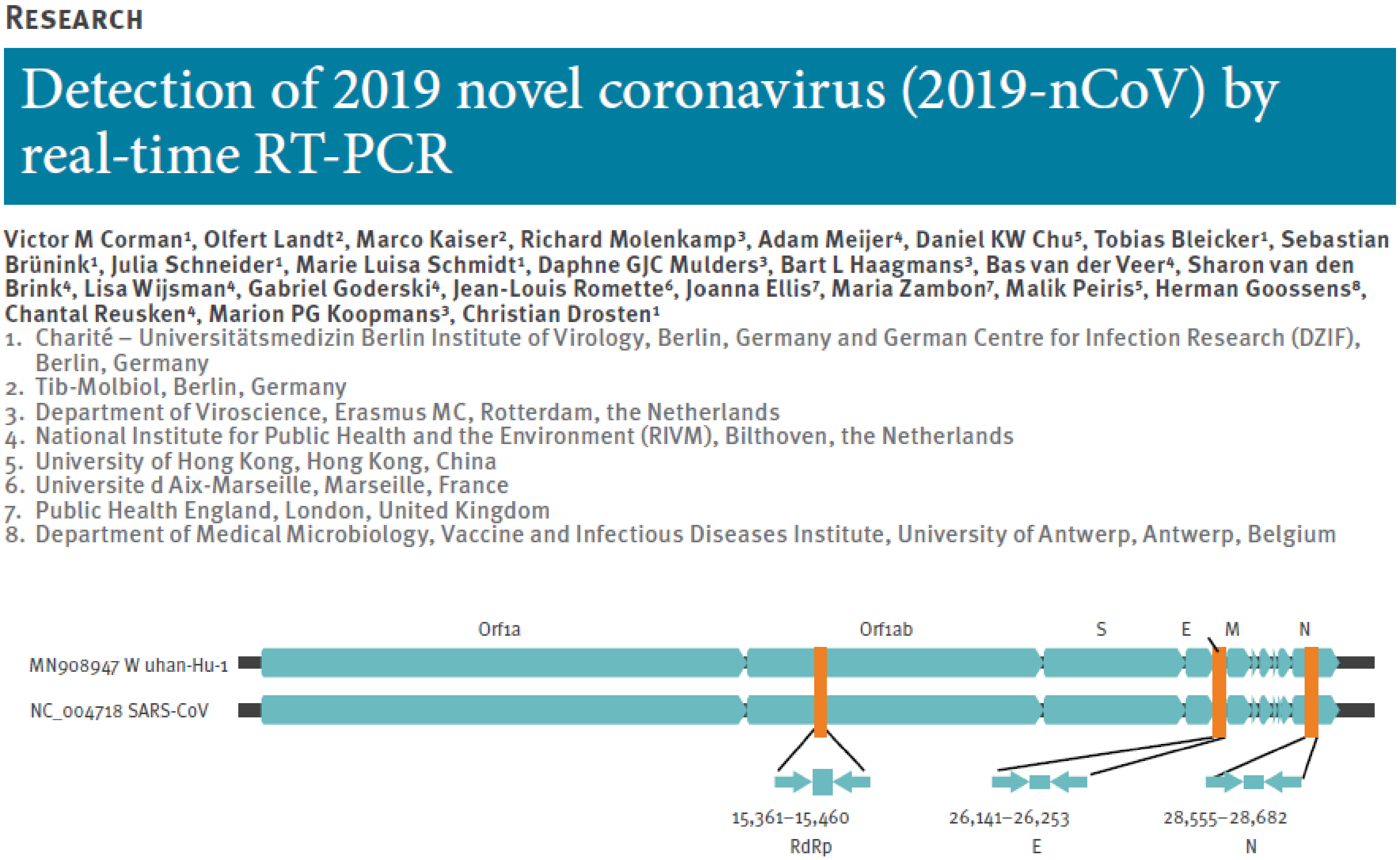
Article submitted on 27 September 2012 / published on 27 September 2012

RT-PCR target regions for screening, confirmation and sequencing of novel human coronavirus (hCoV-EMC)



MERS-CoV

→ RNA ctrls made available through the European Virus Archive platform



RESEARCH

Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR

Victor M Corman[1], Olfert Landt[2], Marco Kaiser[2], Richard Molenkamp[3], Adam Meijer[4], Daniel KW Chu[5], Tobias Bleicker[1], Sebastian Brünink[1], Julia Schneider[1], Marie Luisa Schmidt[1], Daphne GJC Mulders[3], Bart L Haagmans[3], Bas van der Veer[4], Sharon van den Brink[4], Lisa Wijsman[4], Gabriel Goderski[4], Jean-Louis Romette[6], Joanna Ellis[7], Maria Zambon[7], Malik Peiris[5], Herman Goossens[8], Chantal Reusken[4], Marion PG Koopmans[3], Christian Drosten[1]

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5. University of Hong Kong, Hong Kong, China
6. Universite d Aix-Marseille, Marseille, France
7. Public Health England, London, United Kingdom
8. Department of Medical Microbiology, Vaccine and Infectious Diseases Institute, University of Antwerp, Antwerp, Belgium

→ RNA ctrls made available through the European Virus Archive platform

Rapid communication

Laboratory readiness and response for novel coronavirus (2019-nCoV) in expert laboratories in 30 EU/EEA countries, January 2020

Chantal B.E.M. Reusken[1,2] , Eeva K. Broberg[3] , Bart Haagmans[2] , Adam Meijer[1] , Victor M. Corman[4,5] , Anna Papa[6] , Remi Charrel[7] , Christian Drosten[4,5] , Marion Koopmans[2] , Katrin Leitmeyer[3] , on behalf of EVD-LabNet and ERLI-Net[8]

1. Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, the Netherlands
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3. European Centre for Disease Prevention and Control, Solna, Sweden
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6. Department of Microbiology, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece
7. Unité des Virus Emergents (Aix-Marseille Univ-IRD 190-Inserm 1207-IHU Méditerranée Infection), Marseille, France
8. The participating members of EVD-LabNet and ERLI-Net are acknowledged at the end of the article

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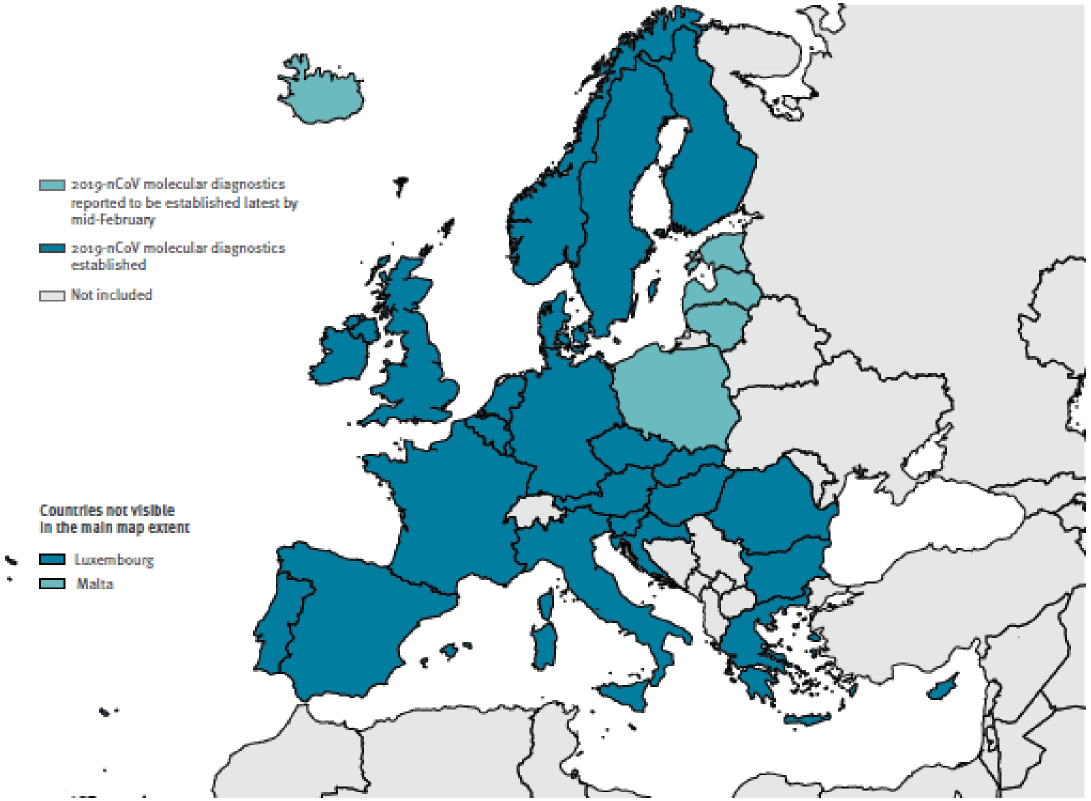
Citation style for this article:
Reusken Chantal B.E.M. , Broberg Eeva K. , Haagmans Bart , Meijer Adam , Corman Victor M. , Papa Anna , Charrel Remi , Drosten Christian , Koopmans Marion , Leitmeyer Katrin , on behalf of EVD-LabNet and ERLI-Net . Laboratory readiness and response for novel coronavirus (2019-nCoV) in expert laboratories in 30 EU/EEA countries, January 2020. Euro Surveill. 2020;25(6):pii=2000082. https://doi.org/10.2807/1560-7917.ES.2020.25.6.2000082

Article submitted on 03 Feb 2020 / accepted on 11 Feb 2020 / published on 11 Feb 2020

Diagnostics available 29 january →

Figure 2

Status of availability of molecular diagnostics for novel coronavirus (2019-nCoV) in EU/EEA countries as at 29 January 2020 (n = 46 laboratories)[a]



EU/EEA: European Union/European Economic Area; 2019-nCoV: 2019 novel coronavirus.

[a] One laboratory of the 47 included in the current study did not indicate when its molecular diagnostics would be available.

RAPID COMMUNICATION

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Letter to the editor: Plenty of coronaviruses but no SARS-CoV-2

Philippe Colson[1,2] , Bernard La Scola[1,2] , Vera Esteves-Vieira[1] , Laetitia Ninove[1,3] , Christine Zandotti[1,3] , Marie-Thérèse Jimeno[4] , Céline Gazin[1] , Marielle Bedotto[1] , Véronique Filosa[1] , Audrey Giraud-Gatineau[1,5,6] , Hervé Chaudet[1,5,6] , Philippe Brouqui[1,2] , Jean-Christophe Lagier[1,2] , Didier Raoult[1,2]

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2. Aix-Marseille University, Institut de Recherche pour le Développement (IRD), Assistance Publique - Hôpitaux de Marseille (AP-HM), Microbes Evolution Phylogeny and Infections (MEPHI), France
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5. Aix-Marseille University, Institut de Recherche pour le Développement (IRD), Assistance Publique - Hôpitaux de Marseille (AP-HM), Vecteurs – Infections Tropicales et Méditerranéennes (VITROME), Marseille, France
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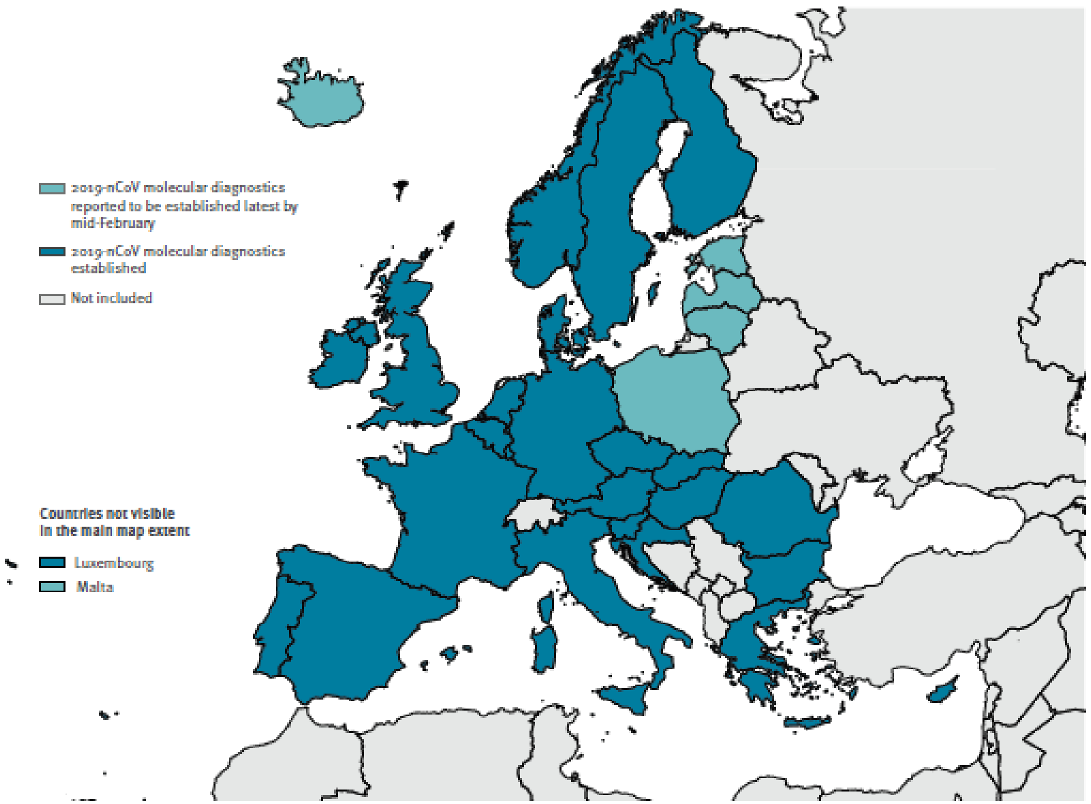
Citation style for this article:
Colson Philippe , La Scola Bernard , Esteves-Vieira Vera , Ninove Laetitia , Zandotti Christine , Jimeno Marie-Thérèse , Gazin Céline , Bedotto Marielle , Filosa Véronique , Giraud-Gatineau Audrey , Chaudet Hervé , Brouqui Philippe , Lagier Jean-Christophe , Raoult Didier . Letter to the editor: Plenty of coronaviruses but no SARS-CoV-2. Euro Surveill. 2020;25(8):pii=2000171. https://doi.org/10.2807/1560-7917.ES.2020.25.8.2000171

Article submitted on 21 Feb 2020 / accepted on 27 Feb 2020 / published on 27 Feb 2020

FIGURE 2

Status of availability of molecular diagnostics for novel coronavirus (2019-nCoV) in EU/EEA countries as at 29 January 2020 (n = 46 laboratories)[a]



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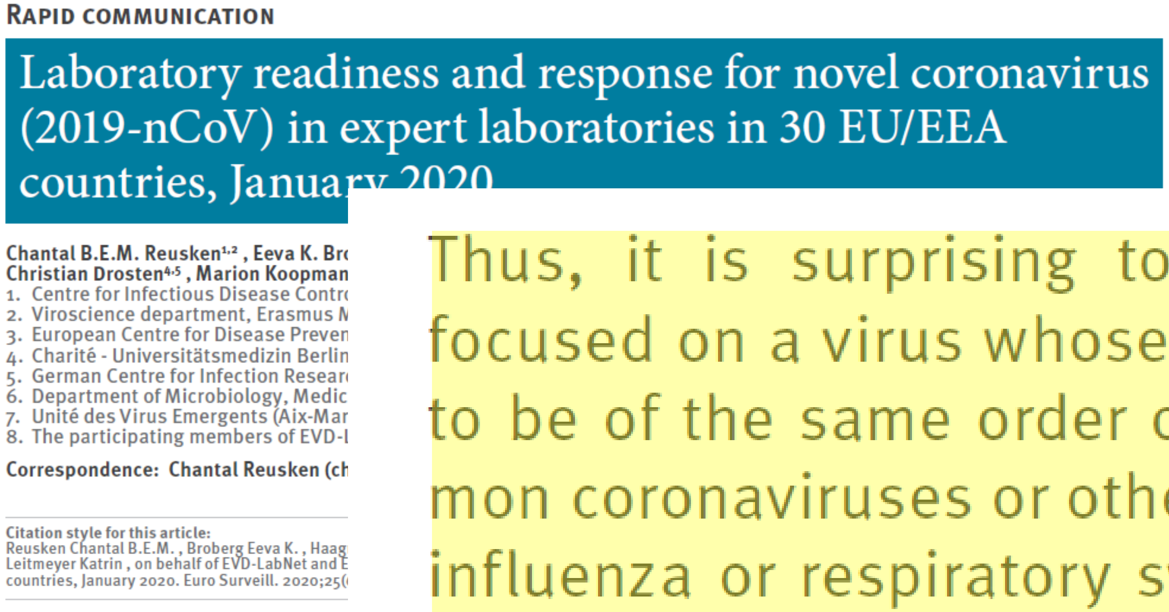

RAPID COMMUNICATION

Laboratory readiness and response for novel coronavirus (2019-nCoV) in expert laboratories in 30 EU/EEA countries, Januar

Chantal B.E.M. Reusken[1,2] , Eeva K. Br
Christian Drosten[4,5] , Marion Koopman
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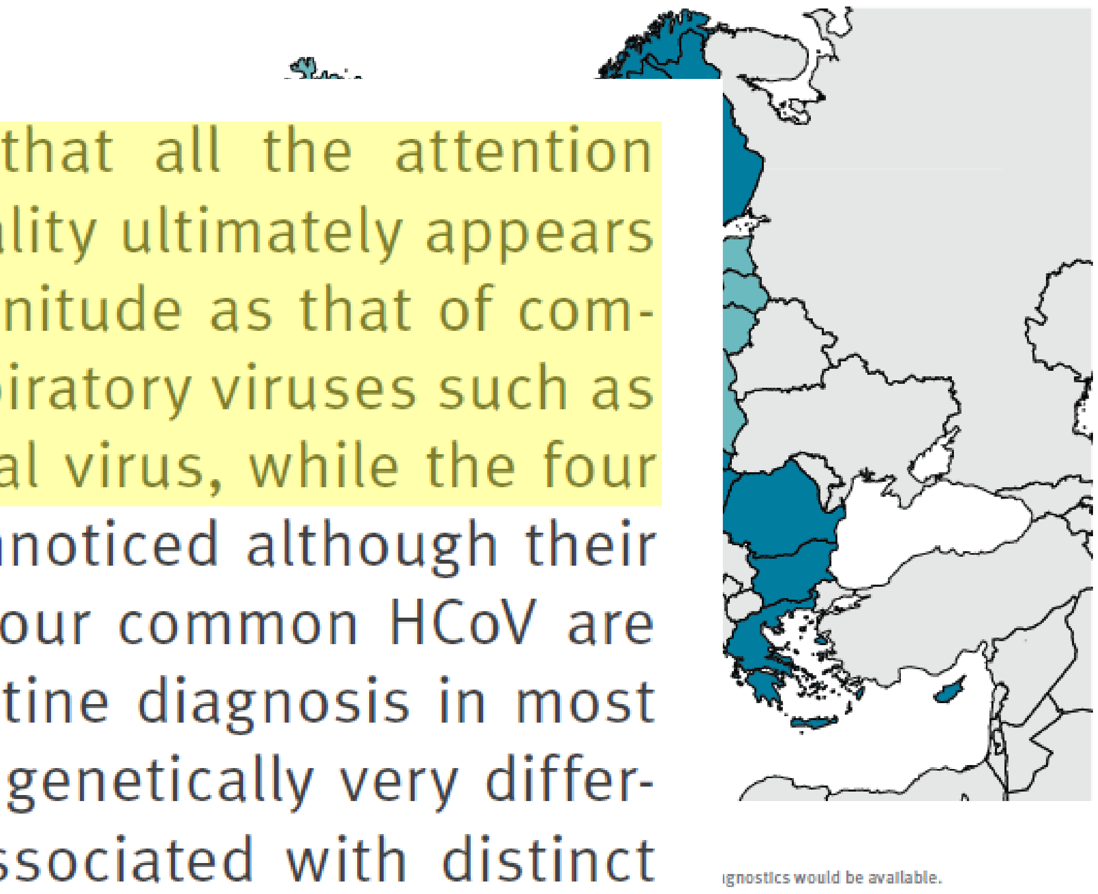

FIGURE 2
Status of availability of molecular diagnostics for novel coronavirus (2019-nCoV) in EU/EEA countries as at 29 January 2020 (n = 46 laboratories)[a]

gnostics would be available.

Thus, it is surprising to see that all the attention focused on a virus whose mortality ultimately appears to be of the same order of magnitude as that of common coronaviruses or other respiratory viruses such as influenza or respiratory syncytial virus, while the four common HCoV diagnosed go unnoticed although their incidence is high. In fact, the four common HCoV are often not even identified in routine diagnosis in most laboratories, although they are genetically very different from each other [7] and associated with distinct symptomatology [8].

Letter to the edi
SARS-CoV-2

Philippe Colson[1,2] , Bernard La Scola
Céline Gazin[1] , Marielle Bedotto[1] , Vé
Christophe Lagier[1,2] , Didier Raoult[1,2]
1. Institut Hospitalo-Universitaire (I
2. Aix-Marseille University, Institut d
HM), Microbes Evolution Phylogen
3. Unité des Virus Emergents (UVE),
4. Service de l'Information Médicale
5. Aix-Marseille University, Institut d
HM), Vecteurs – Infections Tropica
6. French Armed Forces Center for Ep

Correspondence: Didier Raoult (didie

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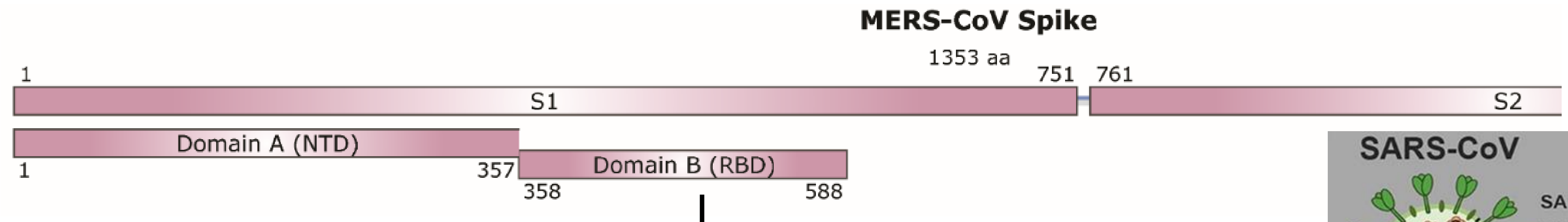
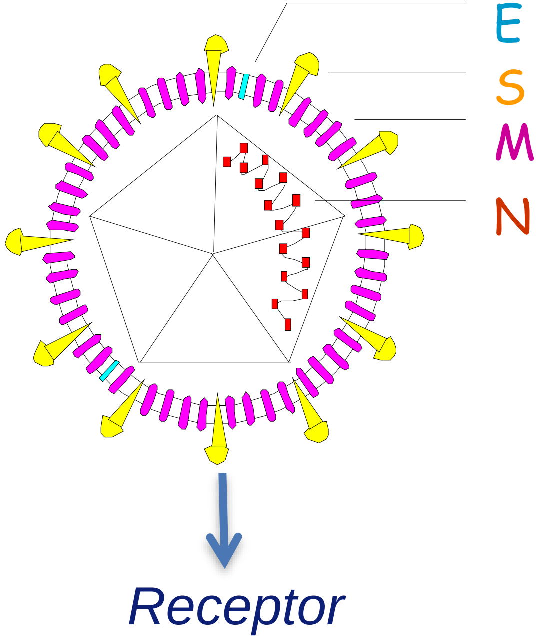
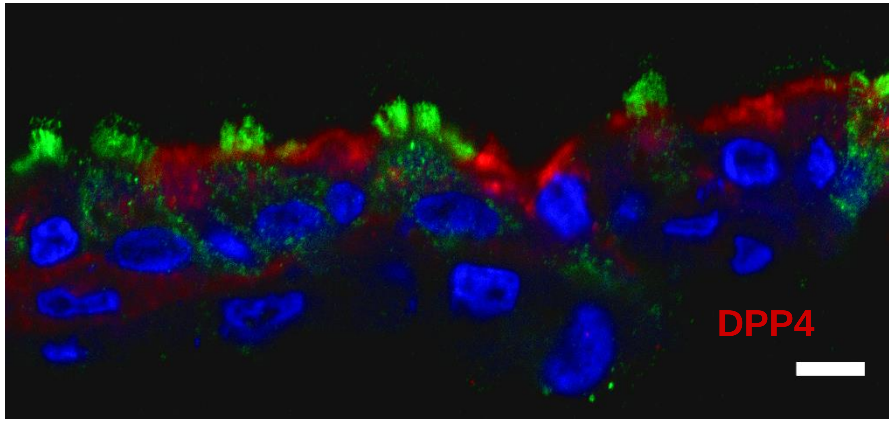
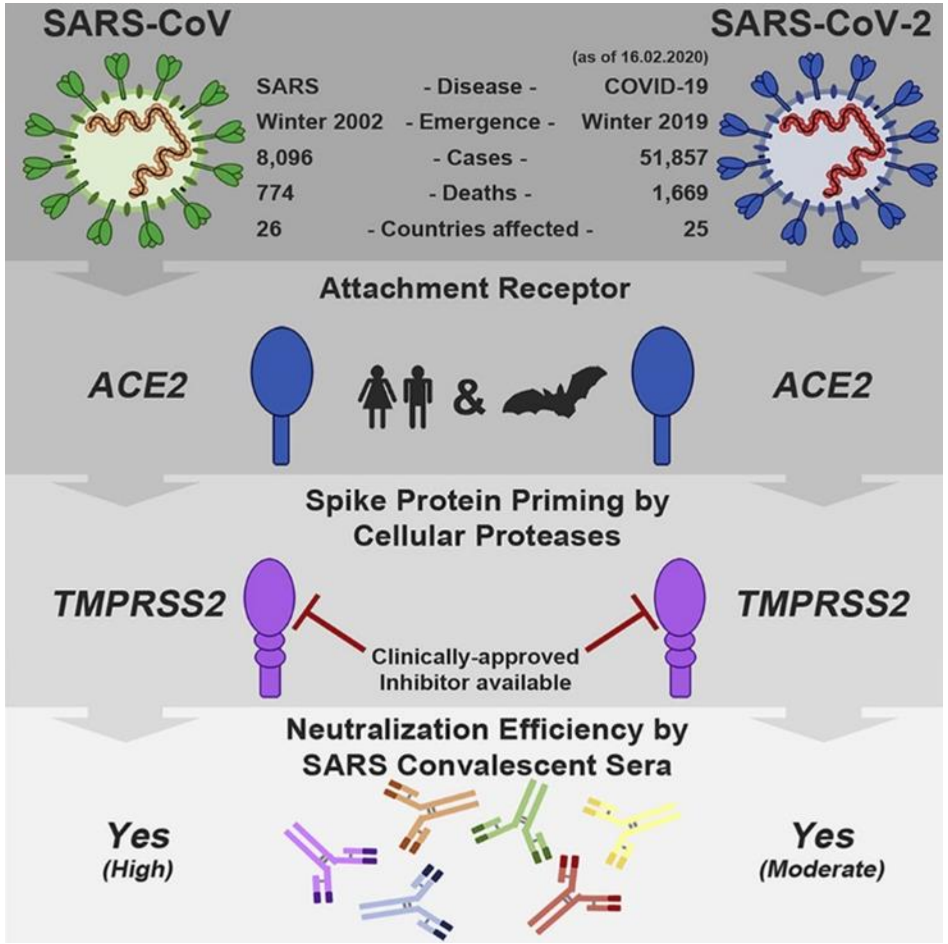
Spike protein: binding to receptor



S1^B (RBD) binds DPP4 (Raj et al., Nature 2013).

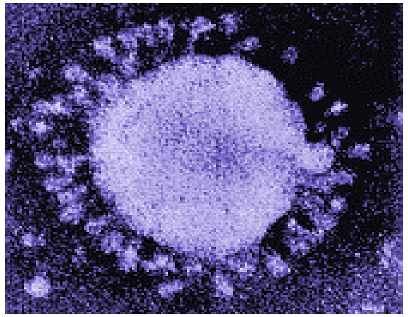


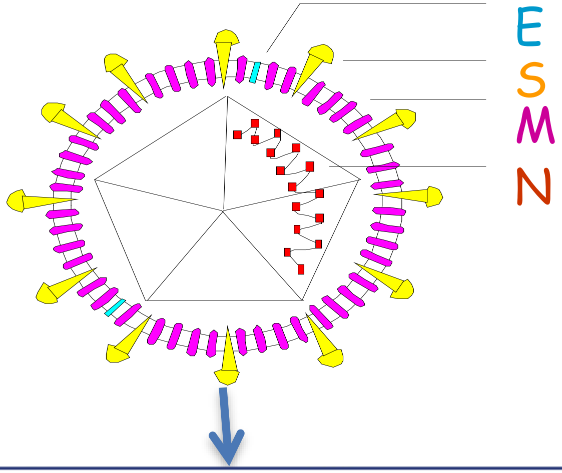




Li et al., Nature 2003 Hoffmann et al., Cell 2020

Use of coronavirus spike protein to detect virus specific antibodies

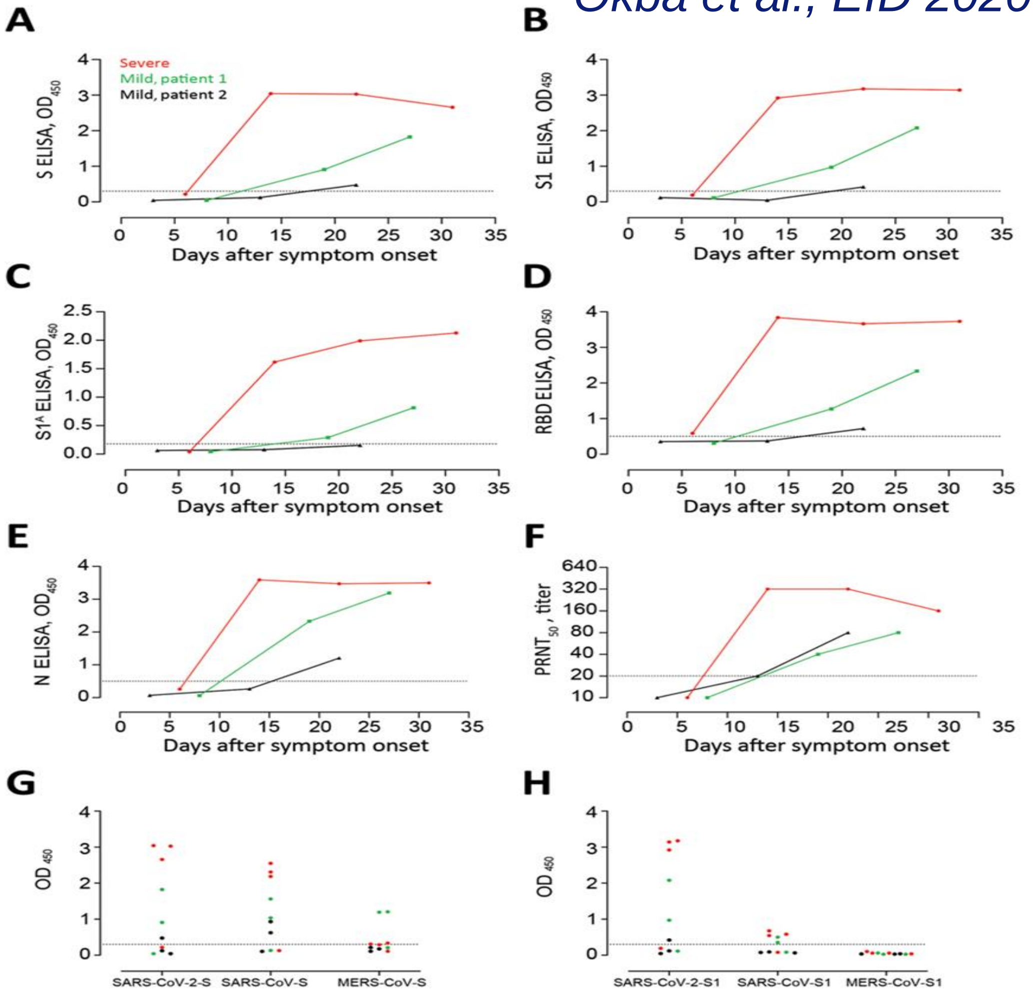




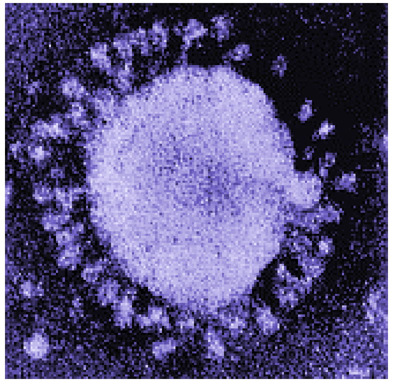
% AA pairwise identity to MERS-CoV				
		S1	S2	N
Alpha-CoV	229E	**5**	30	21
	NL63	**8**	31	22
Beta-CoV	OC43	**16**	43	29
	HKU1	**17**	42	28
	SARS	**15**	39	45

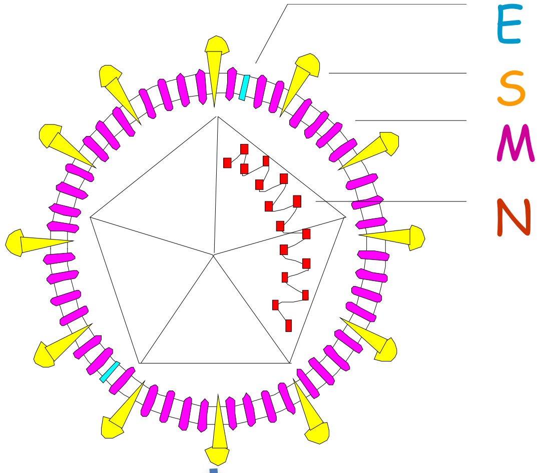
Sera from the first three French patients and German cluster in Bavaria

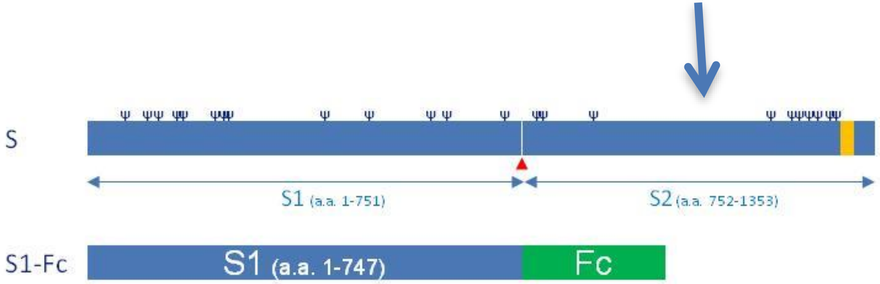
Okba et al., EID 2020



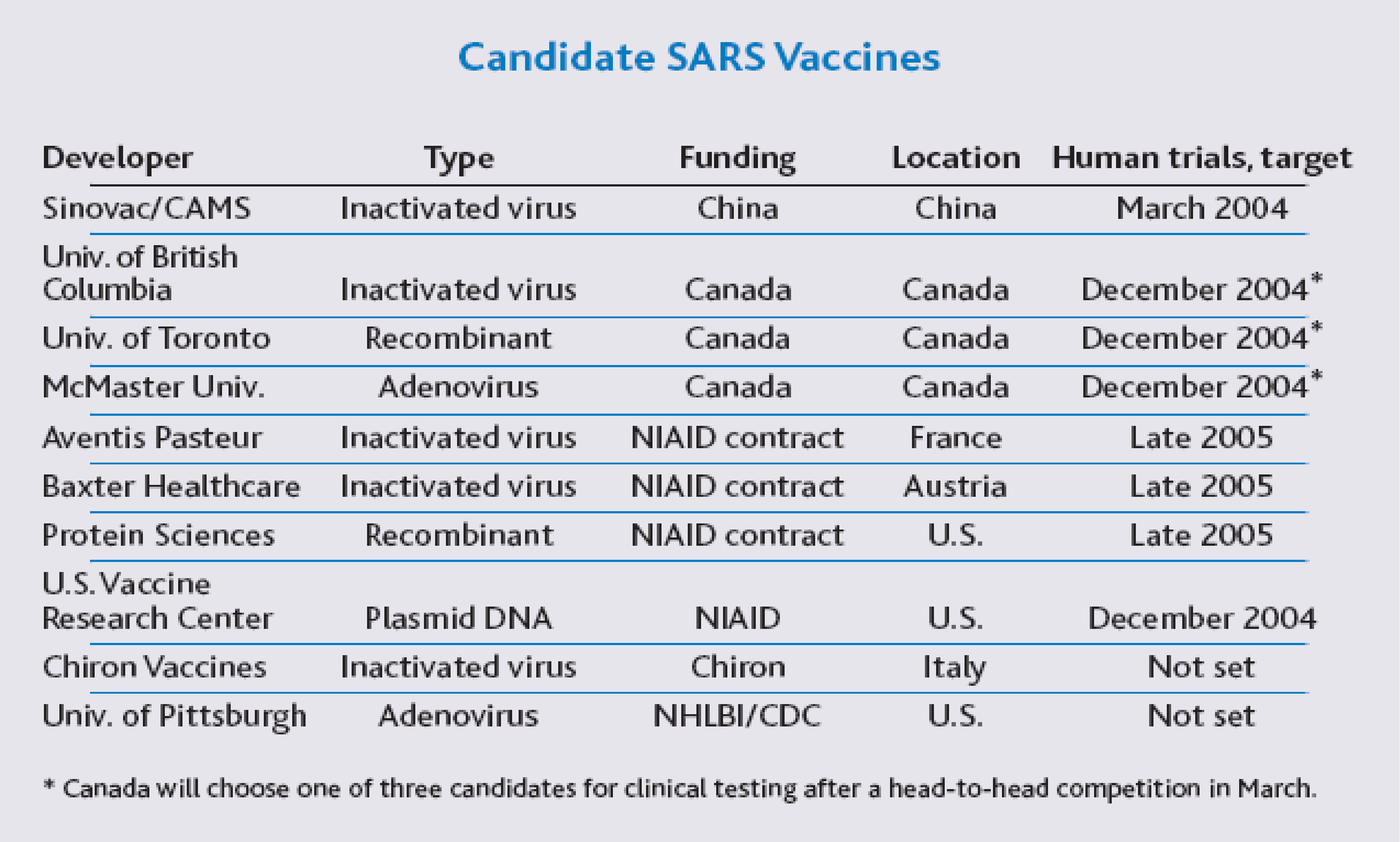
Use of coronavirus spike protein to induce virus neutralizing antibodies







Vaccines



Candidate SARS Vaccines

Developer	Type	Funding	Location	Human trials, target
Sinovac/CAMS	Inactivated virus	China	China	March 2004
Univ. of British Columbia	Inactivated virus	Canada	Canada	December 2004*
Univ. of Toronto	Recombinant	Canada	Canada	December 2004*
McMaster Univ.	Adenovirus	Canada	Canada	December 2004*
Aventis Pasteur	Inactivated virus	NIAID contract	France	Late 2005
Baxter Healthcare	Inactivated virus	NIAID contract	Austria	Late 2005
Protein Sciences	Recombinant	NIAID contract	U.S.	Late 2005
U.S. Vaccine Research Center	Plasmid DNA	NIAID	U.S.	December 2004
Chiron Vaccines	Inactivated virus	Chiron	Italy	Not set
Univ. of Pittsburgh	Adenovirus	NHLBI/CDC	U.S.	Not set

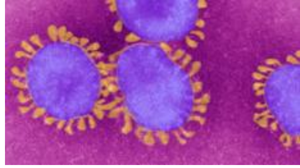
* Canada will choose one of three candidates for clinical testing after a head-to-head competition in March.

Marshall and Enserink (Science 2004)

MERS-CoV vaccine candidates

- Plasmid DNA vaccine (Innovio/GeneOne) → phase 1 data
- Plasmid DNA vaccine (NIAID, VRC)
- Virus like particles (Novavax)
- MVA vaccine (IDT, Sutter) → phase 1 data
- Adenovirus based vectors (Jenner Inst.) → phase 1 data
- Measles virus based vectors (Mühlebach)
- RBD vaccine (Jiang)

CEPI
New vaccines
for a safer world



Rapid identification and characterization of emerging coronaviruses

- Genetic characterization of viral genomes allows the development of PCR tests, antibody tests and vaccines.
- Earlier basic research on SARS-CoV and MERS-CoV was important in the early COVID-19 response

However rapid assessment of phenotypic characteristics such as pathogenicity, transmission, and antigenicity was more challenging.

→ Further basic virological research needed