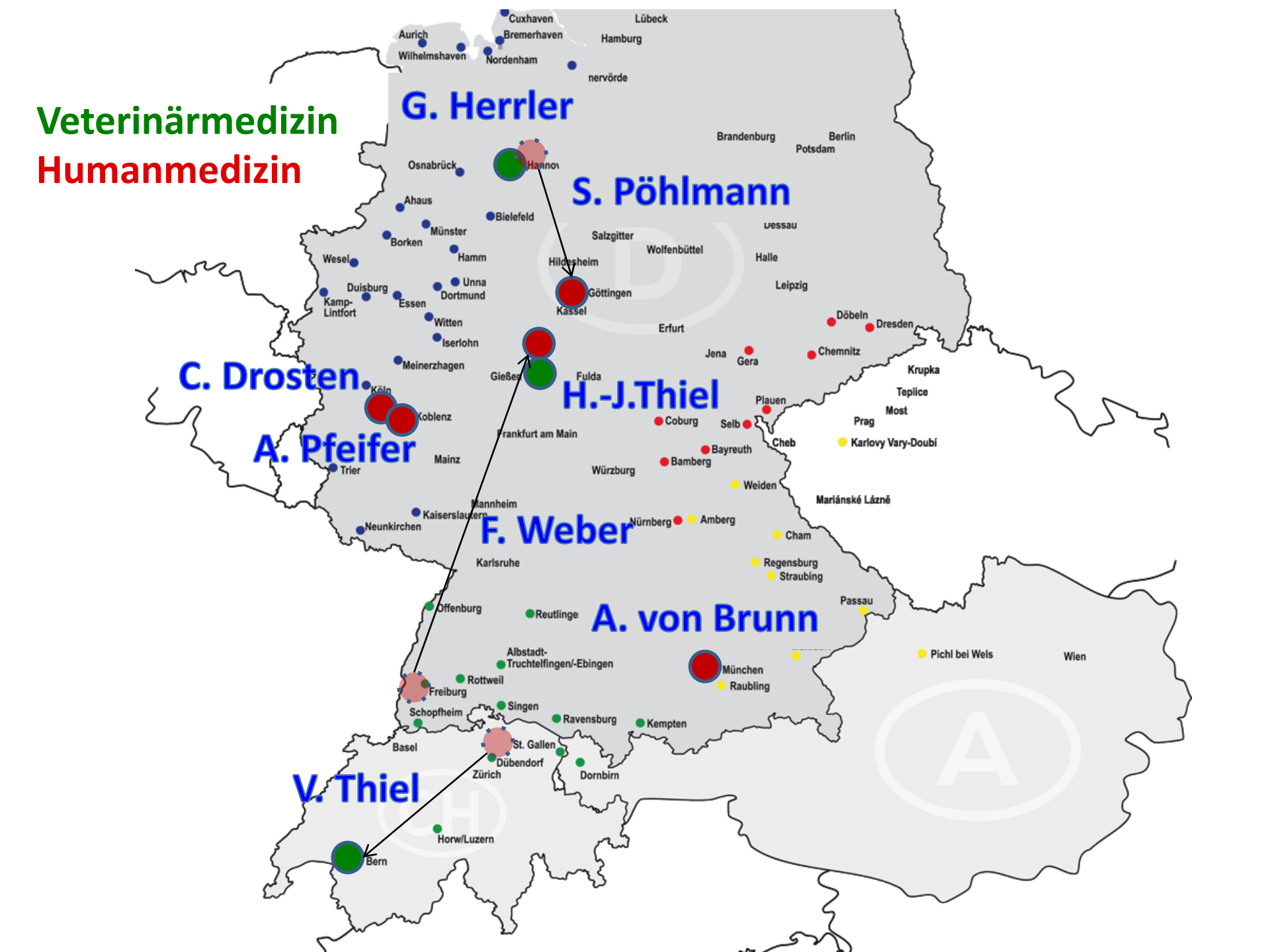
SARS-Verbund

SARS, 2003

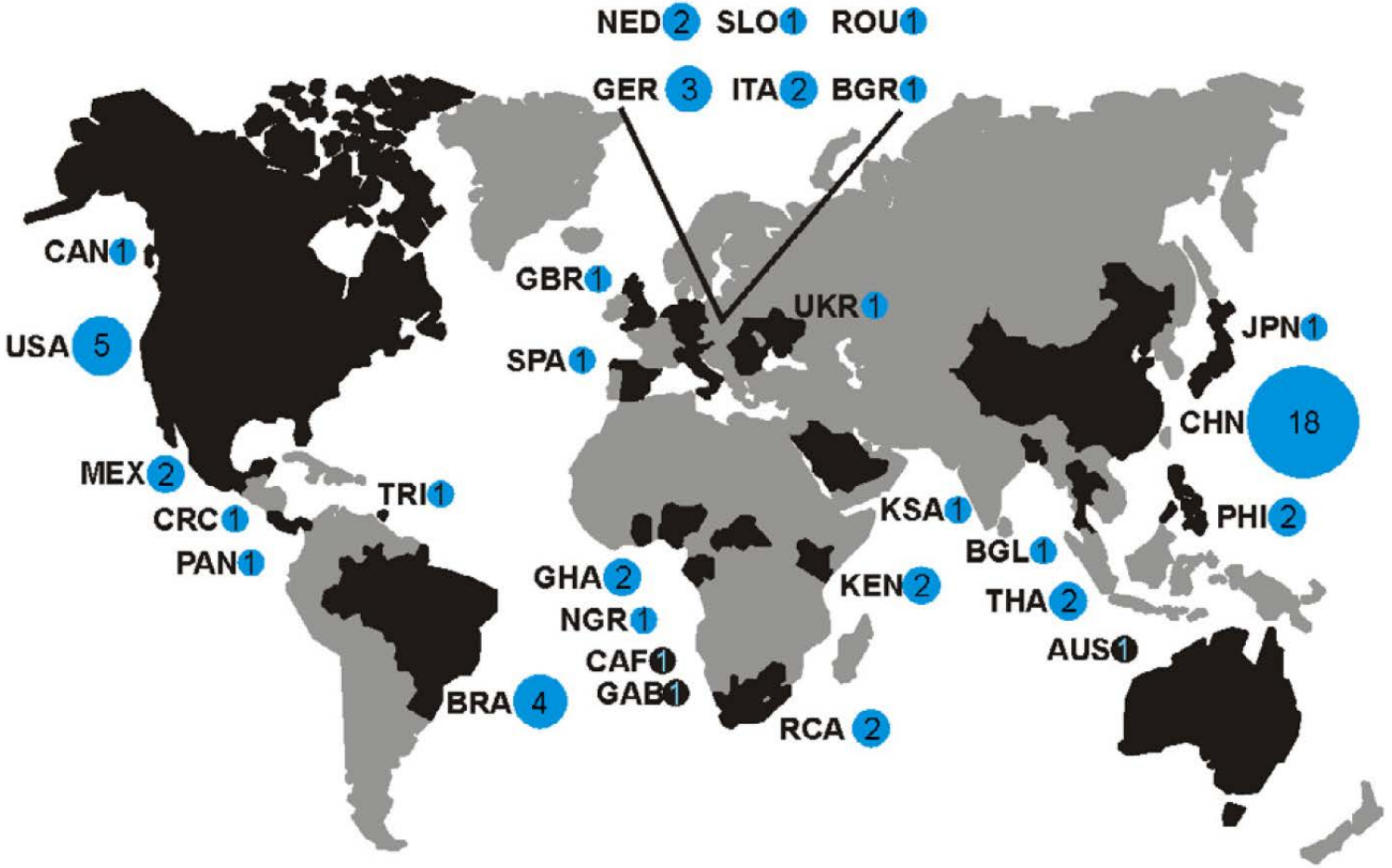
MERS, 2013

Coronavirus-Erkrankungen in der Veterinärmedizin

Name	Klinisches Bild	Virusbeschreibung
PEDV	Diarrhoe	1977
TGEV	Diarrhoe	1946
PRCV	Diarrhoe, Respirationstrakt-Infektion	1990
CCoV	Diarrhoe	1971
FIPV	Schwere systemische Infektion	1968
Bovine CoV	Diarrhoe, Respirationstrakt-Infektion	1972
MHV	Schwere systemische Infektion	1949
IBV	Respirationstrakt-Infektion	1941


Veterinärmedizin
Humanmedizin
G. Herrler
S. Pöhlmann
C. Drosten
H.-J.Thiel
A. Pfeifer
F. Weber
A. von Brunn
V. Thiel
Cuxhaven
Lübeck
Aurich
Bremerhaven
Hamburg
Wilhelmshaven
Nordenham
Brandenburg
Berlin
Potsdam
Osnabrück
Ahaus
Bielefeld
Münster
Borken
Hamm
Wesel
Salzgitter
Wolfenbüttel
Halle
Leipzig
Duisburg
Unna
Dortmund
Essen
Kamp-
Lintfort
Witten
Iserlohn
Kassel
Göttingen
Erfurt
Döbeln
Dresden
Chemnitz
Jena
Gera
Meinerzhagen
Köln
Gießen
Fulda
Krupka
Teplice
Most
Prag
Plauen
Koblenz
Coburg
Selb
Cheb
Karlovy Vary-Doubí
Frankfurt am Main
Bayreuth
Bamberg
Mainz
Würzburg
Trier
Weiden
Mariánské Lázně
Mannheim
Kaiserslautern
Neunkirchen
Nürnberg
Amberg
Cham
Karlsruhe
Regensburg
Straubing
Passau
Offenburg
Reutlingen
Albstadt-
Truchtelfingen/-Ebingen
Pichl bei Wels
Wien
München
Rottweil
Raubling
Freiburg
Singen
Schopfheim
Ravensburg
Kempten
Basel
St. Gallen
Dübendorf
Zürich
Dornbirn
Horw/Luzern
Bern

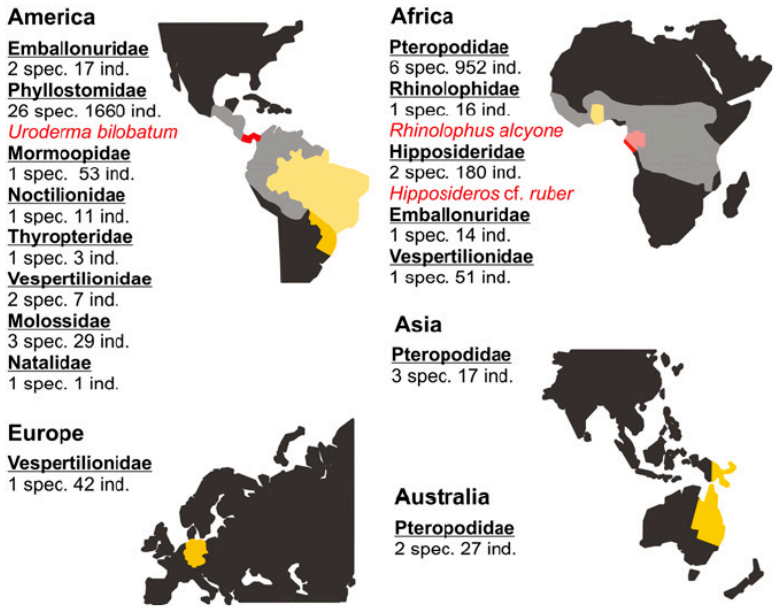
Weltweite Studien über Fledermaus-Coronaviren, 2013

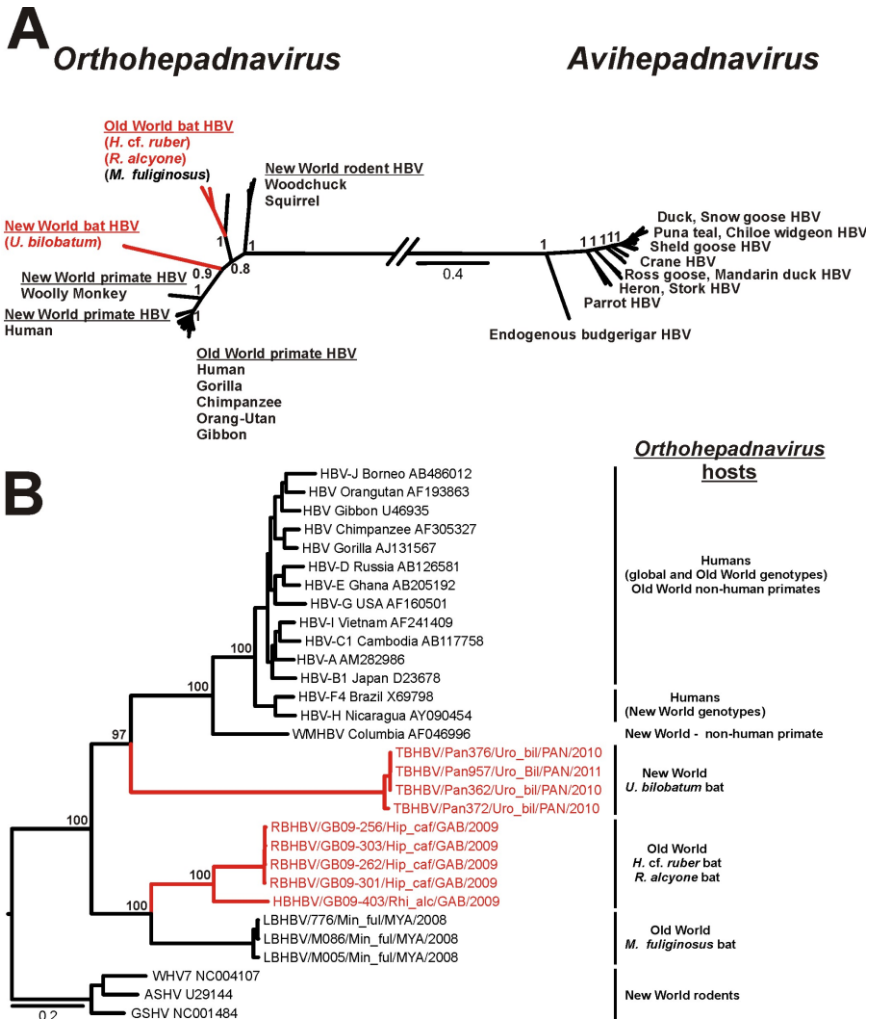


Drexler, AVR, 2013

Bats carry pathogenic hepadnaviruses antigenically related to hepatitis B virus and capable of infecting human hepatocytes

Jan Felix Drexler[a,1], Andreas Geipel[b,1], Alexander König[b], Victor M. Corman[a], Debby van Riel[c], Lonneke M. Leijten[c], Corinna M. Bremer[b], Andrea Rasche[a], Veronika M. Cottontail[d,e], Gael D. Maganga[f], Mathias Schlegel[g], Marcel A. Müller[a], Alexander Adam[h], Stefan M. Klose[d], Aroldo José Borges Carneiro[i], Andreas Stöcker[j], Carlos Roberto Franke[i], Florian Gloza-Rausch[a,k], Joachim Geyer[l], Augustina Annan[m], Yaw Adu-Sarkodie[n], Samuel Oppong[n], Tabea Binger[a], Peter Vallo[d,o], Marco Tschapka[d,e], Rainer G. Ulrich[g], Wolfram H. Gerlich[b], Eric Leroy[f,p], Thijs Kuiken[c], Dieter Glebe[b,1,2], and Christian Drosten[a,1,2]

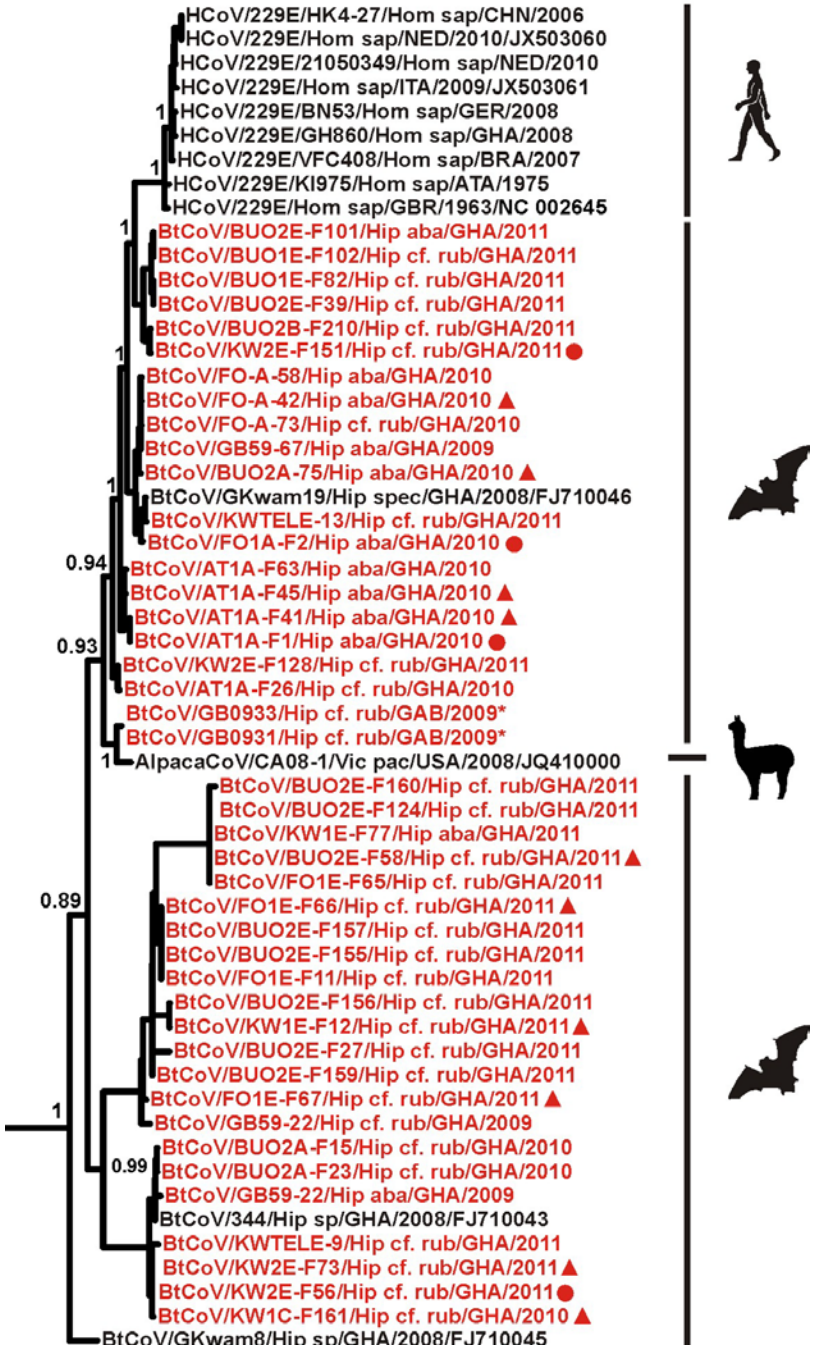




Drexler/Geipel, PNAS 2013

HCoV-229E

Prototypic human common cold CoV

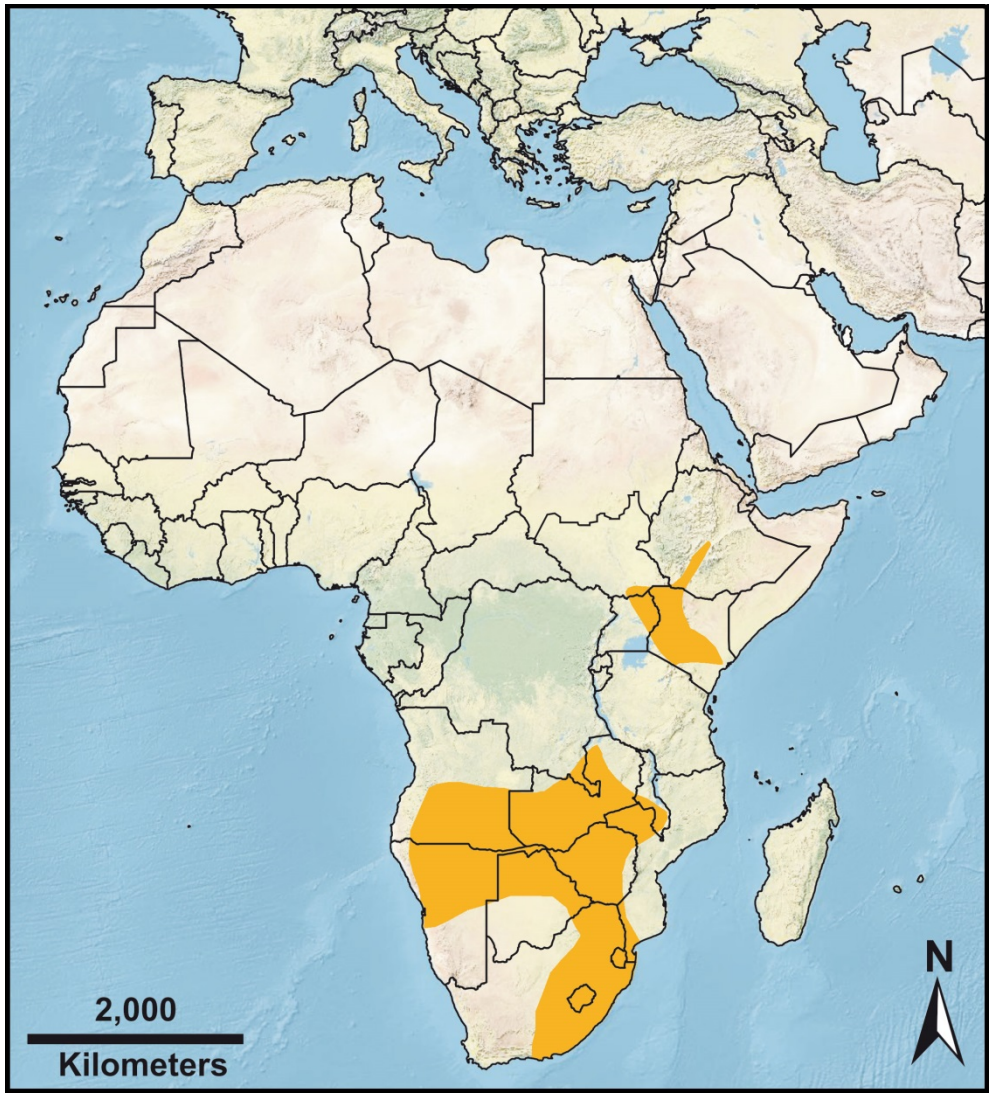


Unpub data

MERS-related CoV in *Neoromicia zuluensis* (Vespertilionidae)

Close Relative of Human Middle East Respiratory Syndrome Coronavirus in Bat, South Africa

recently described bat alphacoronaviruses from South Africa (*4*). The other positive specimen, termed PML/2011, was from an adult female *Neoromicia* cf. *zuluensis* bat sampled in 2011; the specimen yielded a novel betacoronavirus (GenBank accession no. KC869678). Online Technical Appen-



Ithete et al, EID, 2013

MERS-Coronavirus in Fledermäusen

Annan et al, EID 2013
Ithete et al, EID, 2013

MERS: Kamele als Zwischenwirt

THE LANCET Infectious Diseases

Middle East respiratory syndrome coronavirus neutralising serum antibodies in dromedary camels: a comparative serological study

Chantal B E M Reusken, Bart L Haagmans*, Marcel A Müller*, Carlos Gutierrez, Gert-Jan Godeke, Benjamin Meyer, Doreen Muth, V Stalin Raj, Laura Smits-De Vries, Victor M Corman, Jan-Felix Drexler, Saskia L Smits, Yasmin E El Tahir, Rita De Sousa, Janko van Beek, Norbert Nowotny, Kees van Maanen, Ezequiel Hidalgo-Hermoso, Berend-Jan Bosch, Peter Rottier, Albert Osterhaus, Christian Gortázar-Schmidt, Christian Drosten, Marion P G Koopmans*

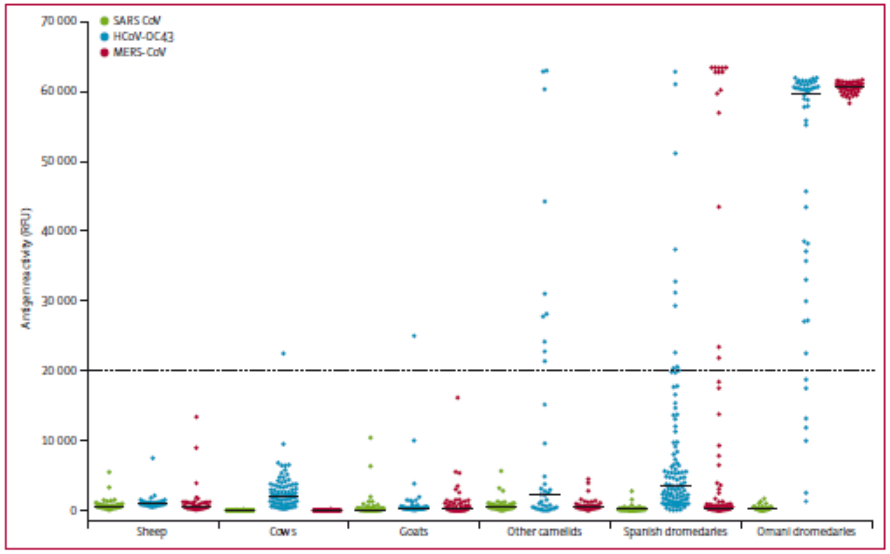


Figure 1: Reactivity of livestock sera with three coronavirus S1 antigens
Fluorescent intensities per antigen at a serum dilution of 1/20. Black lines indicate median. Dashed line is cutoff of the assay. RFU=relative fluorescence units. SARS-CoV=severe acute respiratory syndrome coronavirus. HCoV=human coronavirus. MERS-CoV=Middle East respiratory syndrome coronavirus.

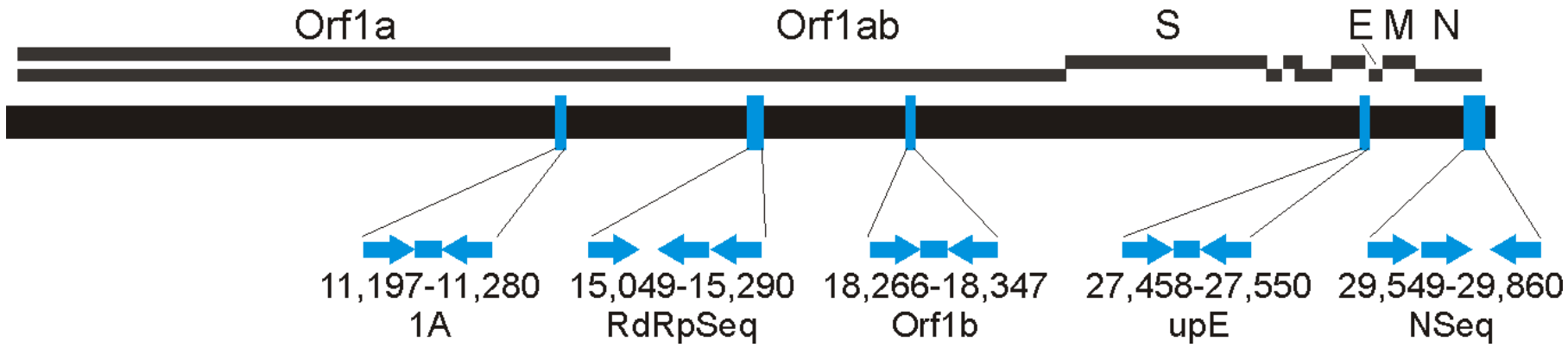
» recIFA und Neutralisationstest

» Neutralisierende Antikörper

- Kanarische Inseln: 14% (N=105)
- Oman: 100% (N=50)
- Emirate: >90% (N=651)
- Ägypten: 90% (N=310)
- Jordanien: 11/11

Kein Nachweis in anderen Nutztieren (Schafe, Ziegen, Rinder, Geflügel)

Reusken et al. Lancet ID 2013 Meyer et al. EID 2014, Perera et al., Eurosurveillance 2013, Reusken et al., Eurosurveillance 2013



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]

1. Institute of Virology, University of Bonn Medical Centre, Bonn, Germany
2. German Centre for Infection Research (DZIF), Germany
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

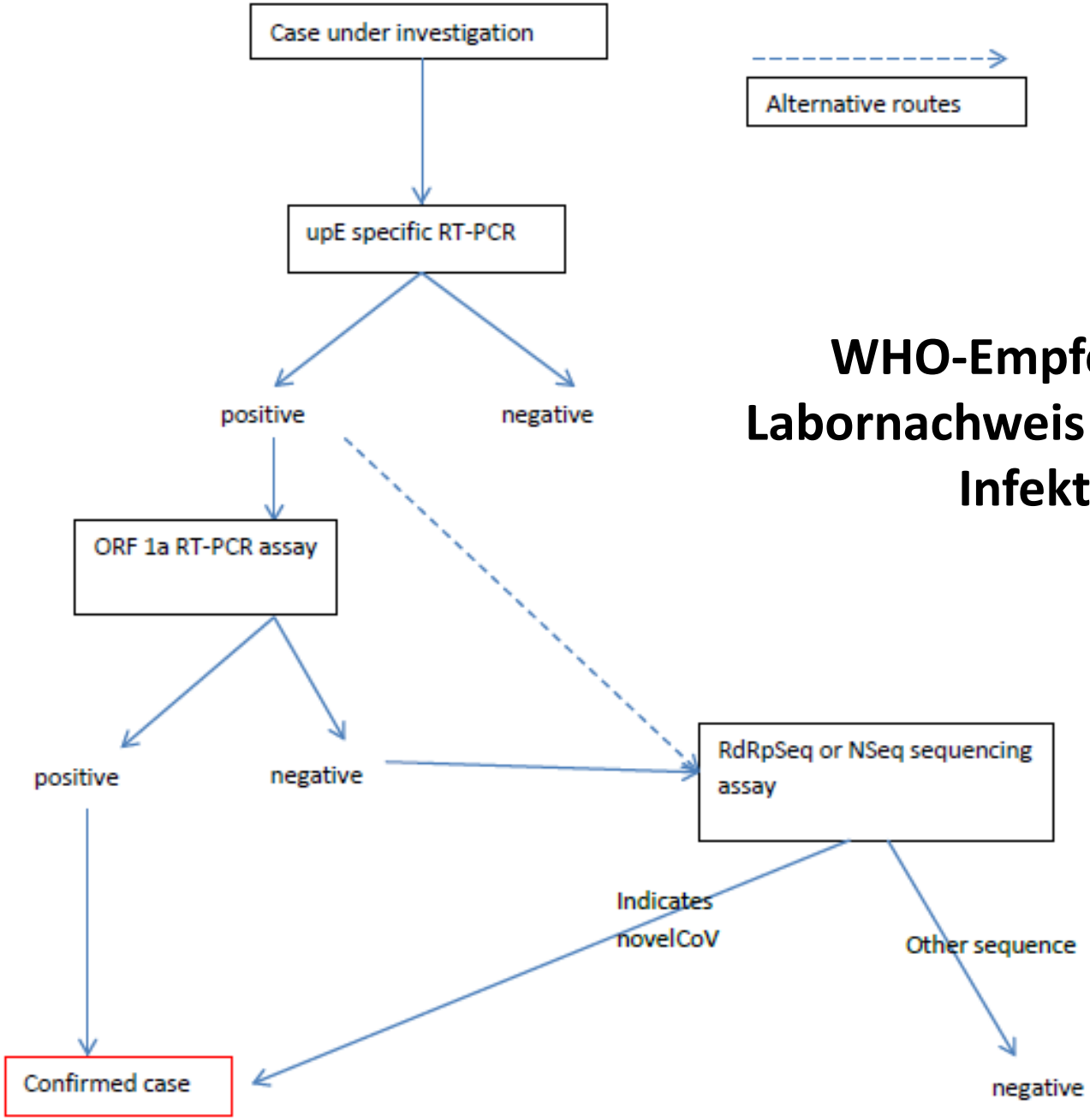
RAPID COMMUNICATIONS

Assays for laboratory confirmation of novel human coronavirus (hCoV-EMC) infections

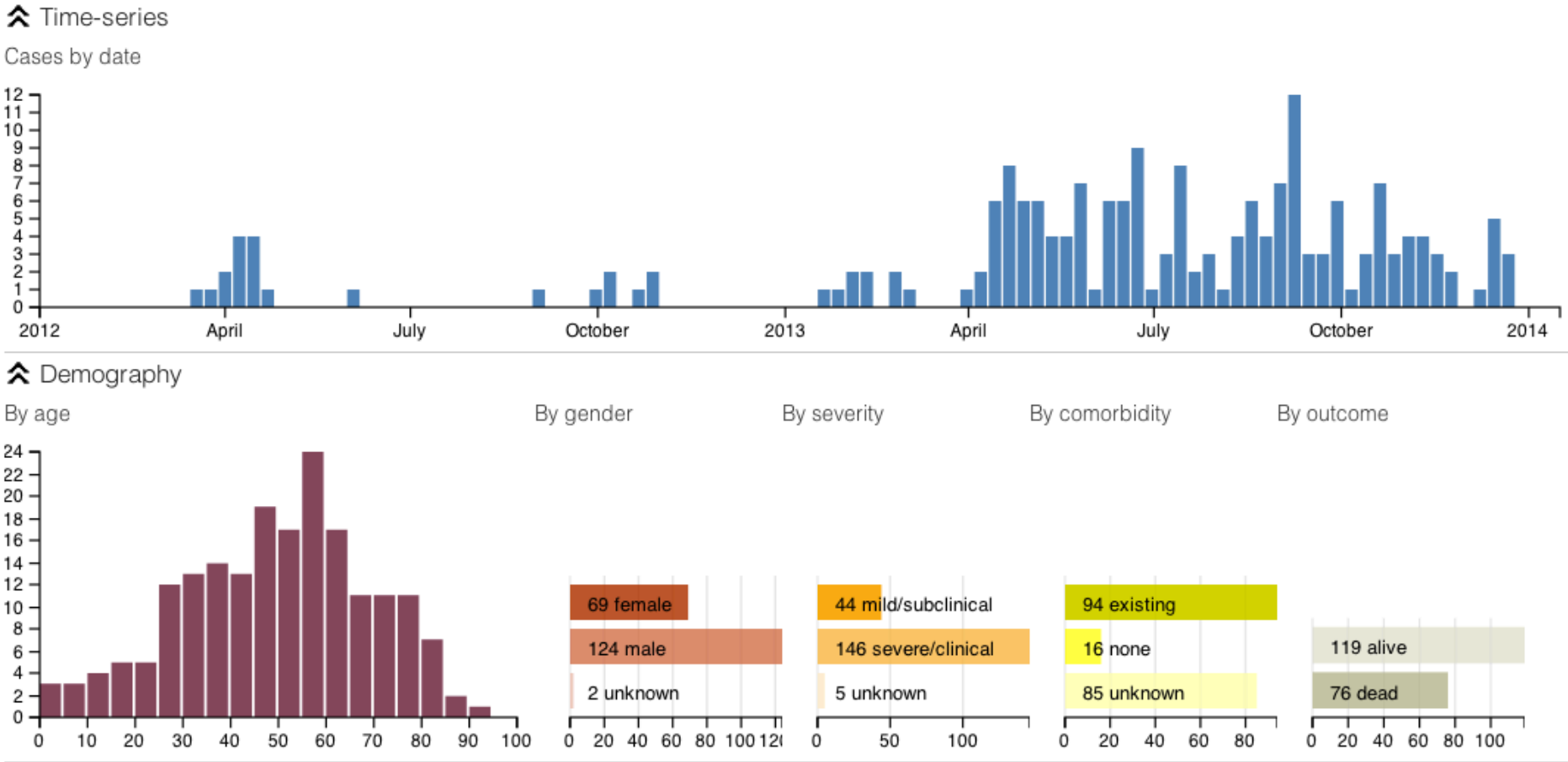
V M Corman[1,2], M A Müller[1,2], U Costabel[3], J Timm[4], T Binger[1], B Meyer[1], P Kreher[5], E Lattwein[6], M Eschbach-Bludau[1], A Nitsche[5], T Bleicker[1], O Landt[7], B Schweiger[5], J F Drexler[1], A D Osterhaus[8], B L Haagmans[8], U Dittmer[4], F Bonin[3], T Wolff[5], C Drosten (drosten@virology-bonn.de)[1]

1. Institute of Virology, University of Bonn Medical Centre, Bonn, Germany
2. These authors contributed equally to this work
3. Ruhrlandklinik, University of Duisburg-Essen, Essen, Germany
4. Institute of Virology, University of Duisburg-Essen, Essen, Germany
5. Robert Koch Institute, Berlin, Germany
6. Euroimmun AG, Lübeck, Germany
7. TibMolbiol, Berlin, Germany
8. Virosciences Laboratory, Erasmus MC, Rotterdam, the Netherlands

WHO-Empfehlung zum Labornachweis von MERS-CoV Infektionen



Bisherige Fälle von MERS-CoV Infektion



http://epidemic.bio.ed.ac.uk (A. Rambaut)

Direkter Nutzen für das Öffentliche Gesundheitswesen: Beispiel Essener MERS-Patient mit Umgebungsuntersuchung, RKI kann auf Labormethodik zurückgreifen

Contact investigation of a case of human novel coronavirus infection treated in a German hospital, October-November 2012

U Buchholz (buchholzu@rki.de)[1,2], MA Müller[3,2], A Nitsche[1,2], A Sanewski[4,2], N Wevering[2], T Bauer-Balci[5], F Bonin[5], C Drosten (drosten@virology-bonn.de)[3], B Schweiger[1], T Wolff[1], D Muth[3], B Meyer[3], S Buda[1], G Krause[6], L Schaade[1], W Haas[1]

1. Robert Koch Institute, Berlin, Germany
2. These authors contributed equally to this work
3. University Bonn, Department of Virology, Bonn, Germany
4. County health department of Essen, Essen, Germany
5. Ruhrland hospital, Essen, Germany
6. County health department Oberbergischer Kreis, Gummersbach, Germany

Citation style for this article:
Buchholz U, Müller MA, Nitsche A, Sanewski A, Wevering N, Bauer-Balci T, Bonin F, Drosten C, Schweiger B, Wolff T, Muth D, Meyer B, Buda S, Krause G, Schaade L, Haas W. Contact investigation of a case of human novel coronavirus infection treated in a German hospital, October-November 2012. Euro Surveill. 2013;18(8):pii=20406. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20406

Article submitted on 24 January 2013 / published on 21 February 2013

Direkter klinischer Nutzen, z.B. Fallmanagement des Münchener MERS-Falls

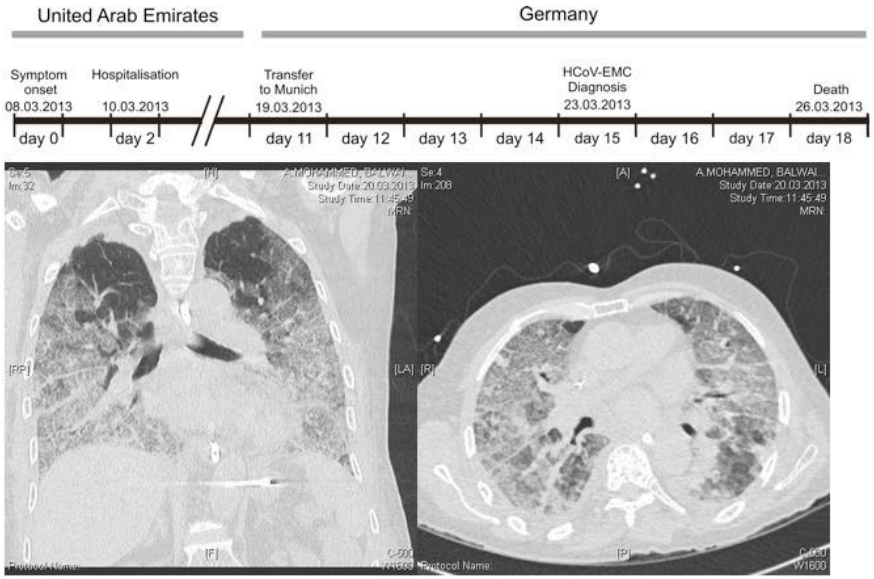
A case of infection with Middle East Respiratory Syndrome coronavirus: a description of clinical features and virological analysis

Christian Drosten, Michael Seilmaier, Victor M Corman, Wulf Hartmann, Gregor Scheible, Stefan Sack, Wolfgang Guggemos, Rene Kallies, Doreen Muth, Sandra Junglen, Marcel A Müller, Walter Haas, Hana Guberina, Tim Röhnisch, Monika Schmid-Wendtner, Souhaib Aldabbagh, Ulf Dittmer, Hermann Gold, Petra Graf, Frank Bonin, Andrew Rambaut, Clemens-Martin Wendtner

Summary

Background The Middle East Respiratory Syndrome coronavirus (MERS-CoV) is an emerging virus involved in

Published Online



Fast alle frühen Fundamentaldaten zum neuen MERS-CoV stammen aus dem Verbund

OBSERVATION

Human Coronavirus EMC Does Not Require the SARS-Coronavirus Receptor and Maintains Broad Replicative Capability in Mammalian Cell Lines

Marcel A. Müller,[a] V. Stalin Raj,[b] Doreen Muth,[a] Benjamin Meyer,[a] Stephan Kallies,[a] Saskia L. Smits,[b] Robert Wollny,[a] Theo M. Bestebroer,[b] Sabine Specht,[c] Tasnim Suliman,[a] Katrin Zimmermann,[d] Tabea Binger,[a] Isabella Eckerle,[a] Marco Tschapka,[e] Ali M. Zaki,[f] Albert D. M. E. Osterhaus,[b] Ron A. M. Fouchier,[b] Bart L. Haagmans,[b] and Christian Drosten[a]

JVI Journals.ASM.org

The Spike Protein of the Emerging Betacoronavirus EMC Uses a Novel Coronavirus Receptor for Entry, Can Be Activated by TMPRSS2, and Is Targeted by Neutralizing Antibodies

Stefanie Gierer,[a] Stephanie Bertram,[a] Franziska Kaup,[a] Florian Wrensch,[a] Adeline Heurich,[a] Annika Krämer-Kühl,[a] Kathrin Welsch,[a] Michael Winkler,[a] Benjamin Meyer,[b] Christian Drosten,[b] Ulf Dittmer,[c] Thomas von Hahn,[d,e] Graham Simmons,[f] Heike Hofmann,[a] Stefan Pöhlmann[a]

OBSERVATION

JVI Journals.ASM.org

Efficient Replication of the Novel Human Betacoronavirus EMC on Primary Human Epithelium Highlights Its Zoonotic Potential

Eveline Kindler,[a] Hulda R. Jónsdóttir,[a] Doreen Muth,[b] Ole J. Hamming,[c] Rune Hartmann,[c] Regulo Rodriguez,[d] Robert Geffers,[e] Ron A. M. Fouchier,[f] Christian Drosten,[b] Marcel A. Müller,[b] Ronald Dijkman,[a] Volker Thiel[a,g]

Human Cell Tropism and Innate Immune System Interactions of Human Respiratory Coronavirus EMC Compared to Those of Severe Acute Respiratory Syndrome Coronavirus

Florian Zielecki,[a] Michaela Weber,[a] Markus Eickmann,[a] Larissa Spiegelberg,[a] Ali Moh Zaki,[b] Mikhail Matrosovich,[a] Stephan Becker,[a] Friedemann Weber[a]

Institute for Virology, Philipps University Marburg, Marburg, Germany[a]; Virology Laboratory, Dr. Soliman Fakeeh Hospital, Jeddah, Saudi Arabia[b]

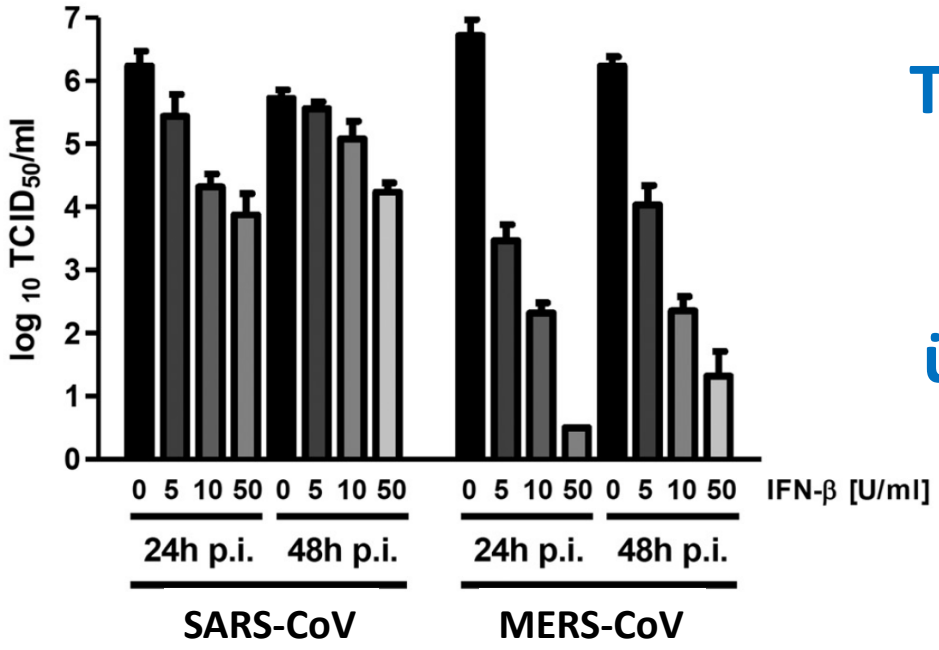
MERS-CoV ist deutlich empfindlicher gegen Interferon als SARS-CoV

Human Cell Tropism and Innate Immune System Interactions of Human Respiratory Coronavirus EMC Compared to Those of Severe Acute Respiratory Syndrome Coronavirus

Florian Zielecki,[a] Michaela Weber,[a] Markus Eickmann,[a] Larissa Spiegelberg,[a] Ali Moh Zaki,[b] Mikhail Matrosovich,[a] Stephan Becker,[a] Friedemann Weber[a]

Institute for Virology, Philipps University Marburg, Marburg, Germany[a]; Virology Laboratory, Dr. Soliman Fakeeh Hospital, Jeddah, Saudi Arabia[b]

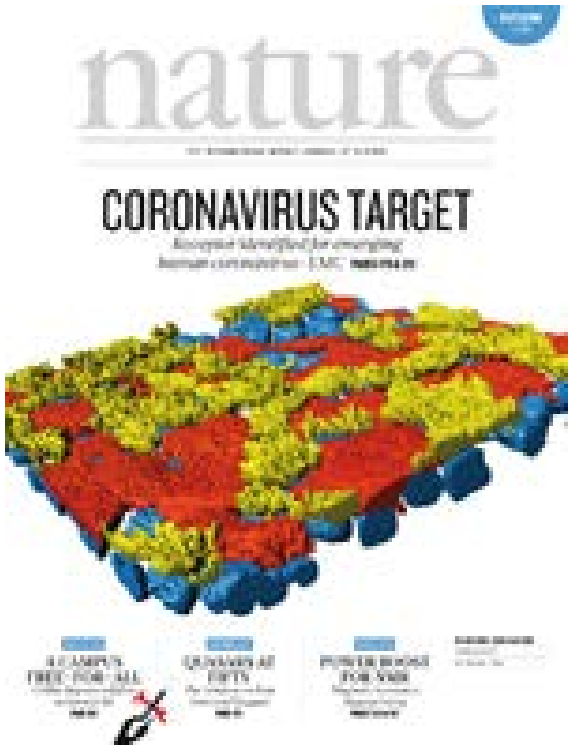
Replikation in Zellkultur unter Einfluß von Interferon



Trotz stärkerer Replikation und Zytopathogenität ist MERS-CoV nicht besser übertragbar als SARS-CoV

Zielecki et al., J.Virol. 2013

Internationale Vernetzung



Z.B. Identifikation des MERS-CoV Rezeptors (2 Gruppen aus dem Verbund beteiligt)

Neues anti-CoV Wirkprinzip

OPEN ACCESS Freely available online

PLoS PATHOGENS

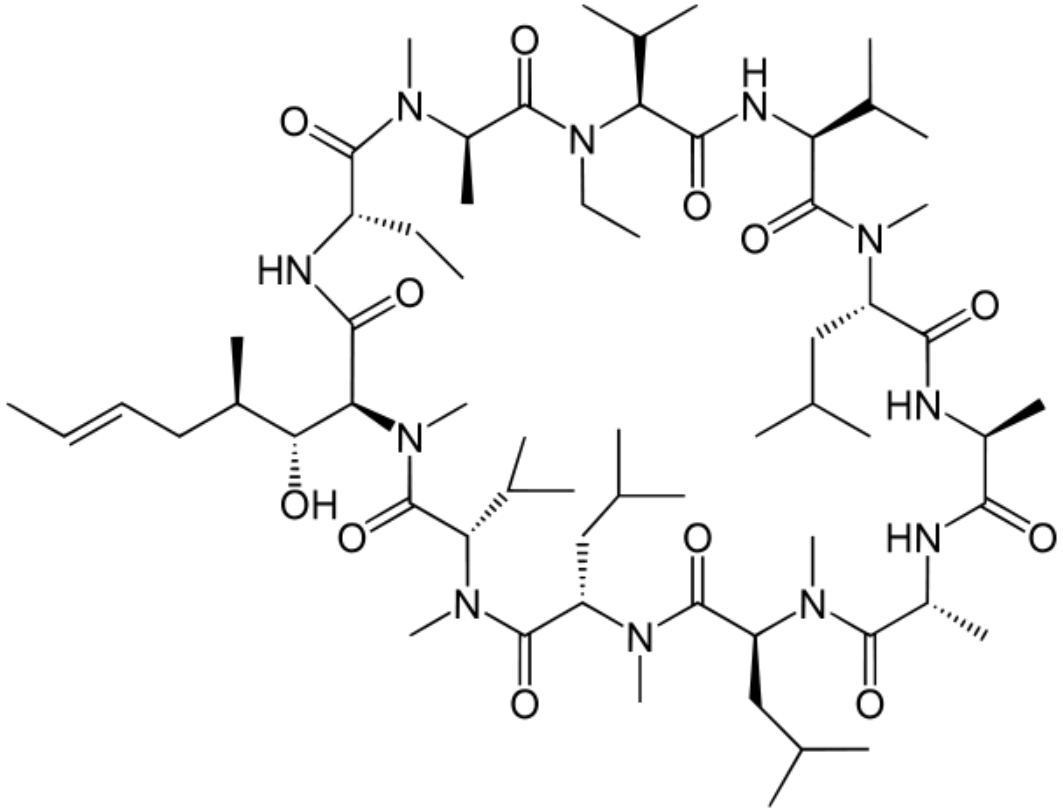
The SARS-Coronavirus-Host Interactome: Identification of Cyclophilins as Target for Pan-Coronavirus Inhibitors

Susanne Pfefferle[1,2☯], Julia Schöpf[3☯], Manfred Kögl[4☯], Caroline C. Friedel[5,6], Marcel A. Müller[2], Javier Carbajo-Lozoya[3], Thorsten Stellberger[3], Ekatarina von Dall'Armi[3], Petra Herzog[2], Stefan Kallies[2], Daniela Niemeyer[2], Vanessa Ditt[2], Thomas Kuri[7], Roland Züst[8], Ksenia Pumpor[9], Rolf Hilgenfeld[9], Frank Schwarz[4], Ralf Zimmer[5], Imke Steffen[10], Friedemann Weber[7,11], Volker Thiel[8], Georg Herrler[12], Heinz-Jürgen Thiel[13], Christel Schwegmann-Weßels[12], Stefan Pöhlmann[10], Jürgen Haas[3,14*], Christian Drosten[2*], Albrecht von Brunn[3*]

Große vernetzte Studie, alle Mitgliedslabore beteiligt

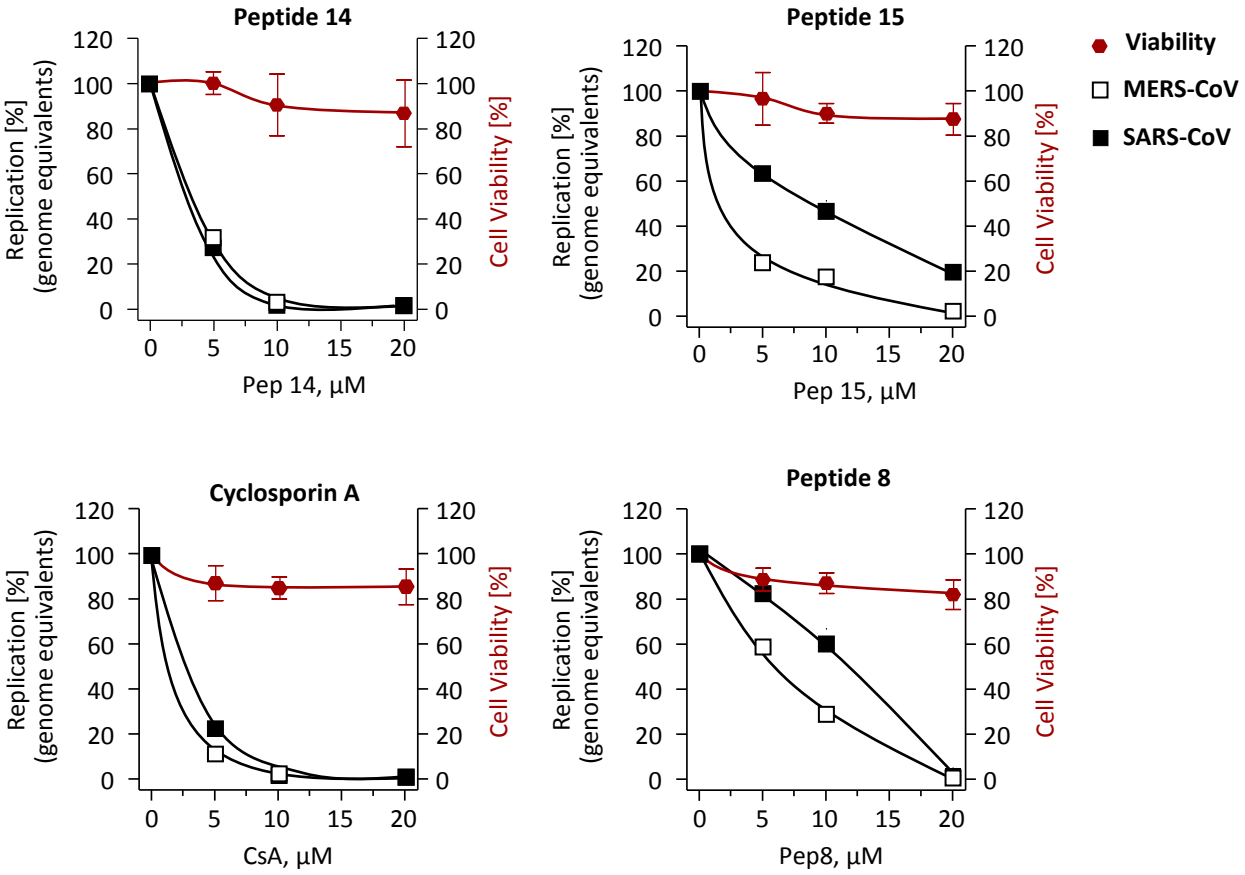
The Non-Immunosuppressive Cyclosporin DEBIO-025 Is a Potent Inhibitor of Hepatitis C Virus Replication *In Vitro*

Jan Paeshuyse,[1] Artur Kaul,[2] Erik De Clercq,[1] Brigitte Rosenwirth,[4] Jean-Maurice Dumont,[3] Pietro Scalfaro,[3] Ralf Bartenschlager,[2] and Johan Neyts[1]



Alisporivir (Novartis)

Ebenso aktiv gegen MERS-CoV

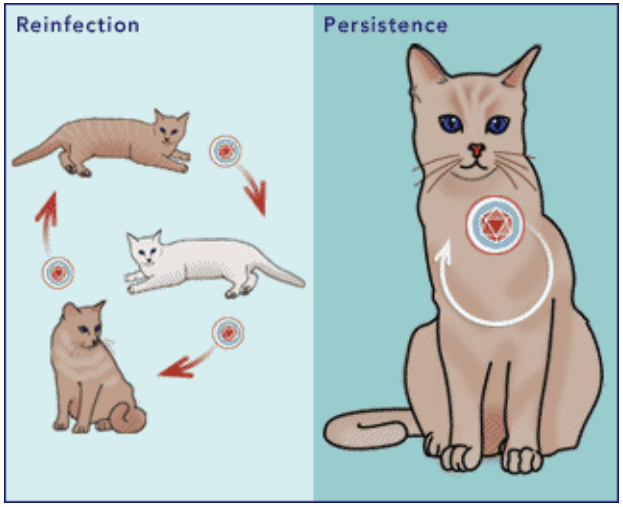


A. von Brunn, LMU München, unpublizierte Daten

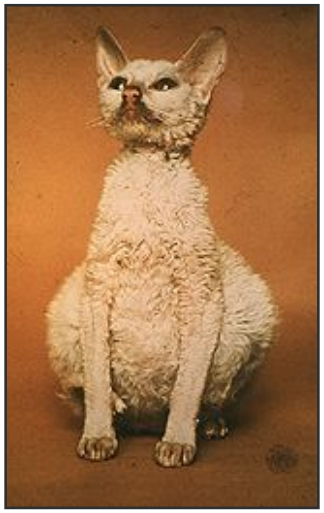
Feline infektiöse Peritonitis

-Verfügbares und hochrelevantes Tiermodell-

Feline enteric coronavirus (FECV)



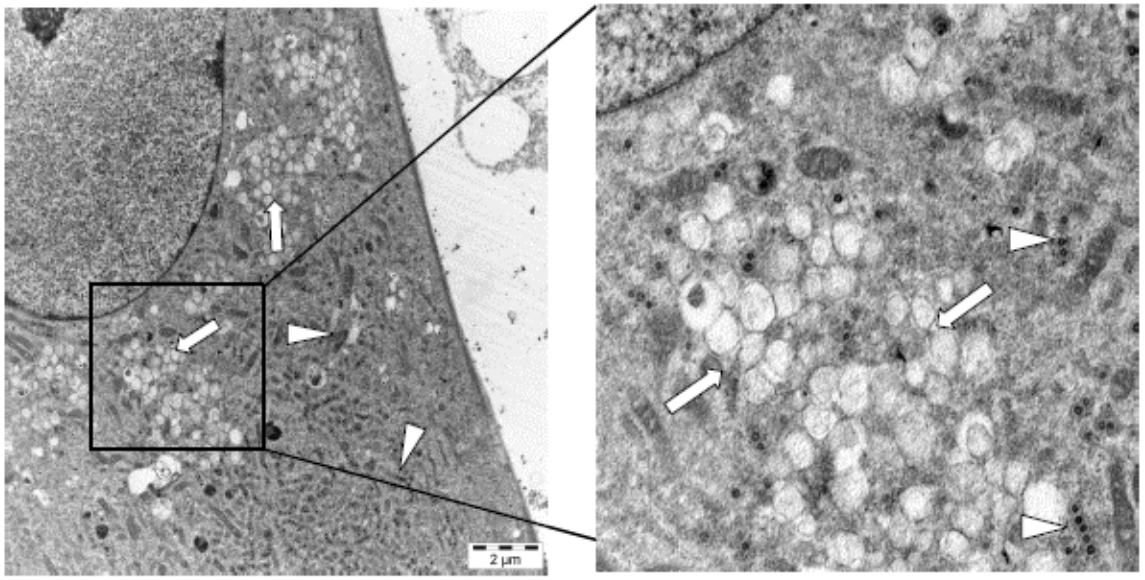
Feline infectious peritonitis virus (FIPV)



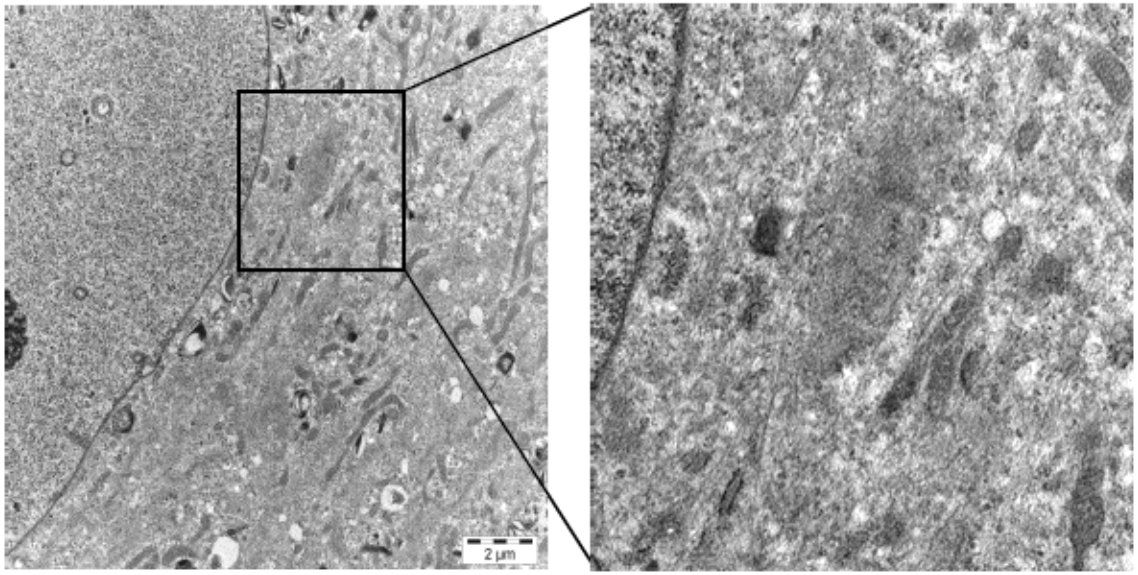
Translation in die Tiermedizin?

K22 treatment impairs DMV formation

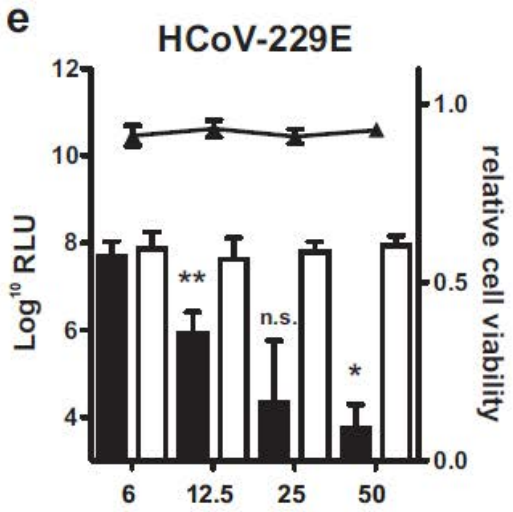
HCoV-229E

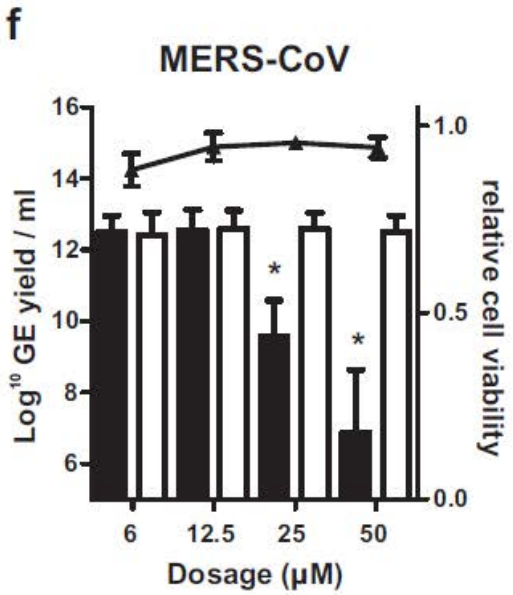


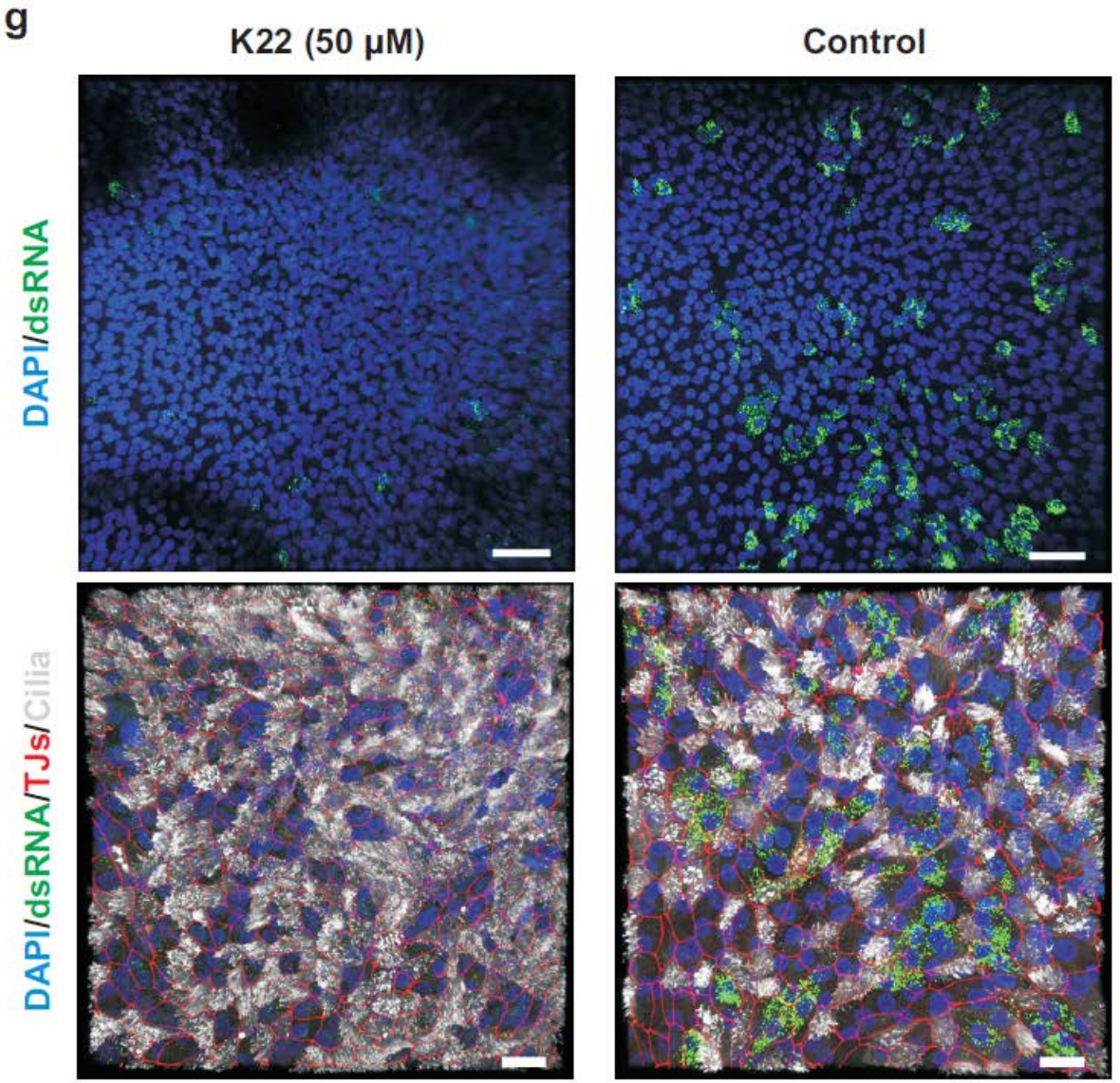
HCoV-229E + K22



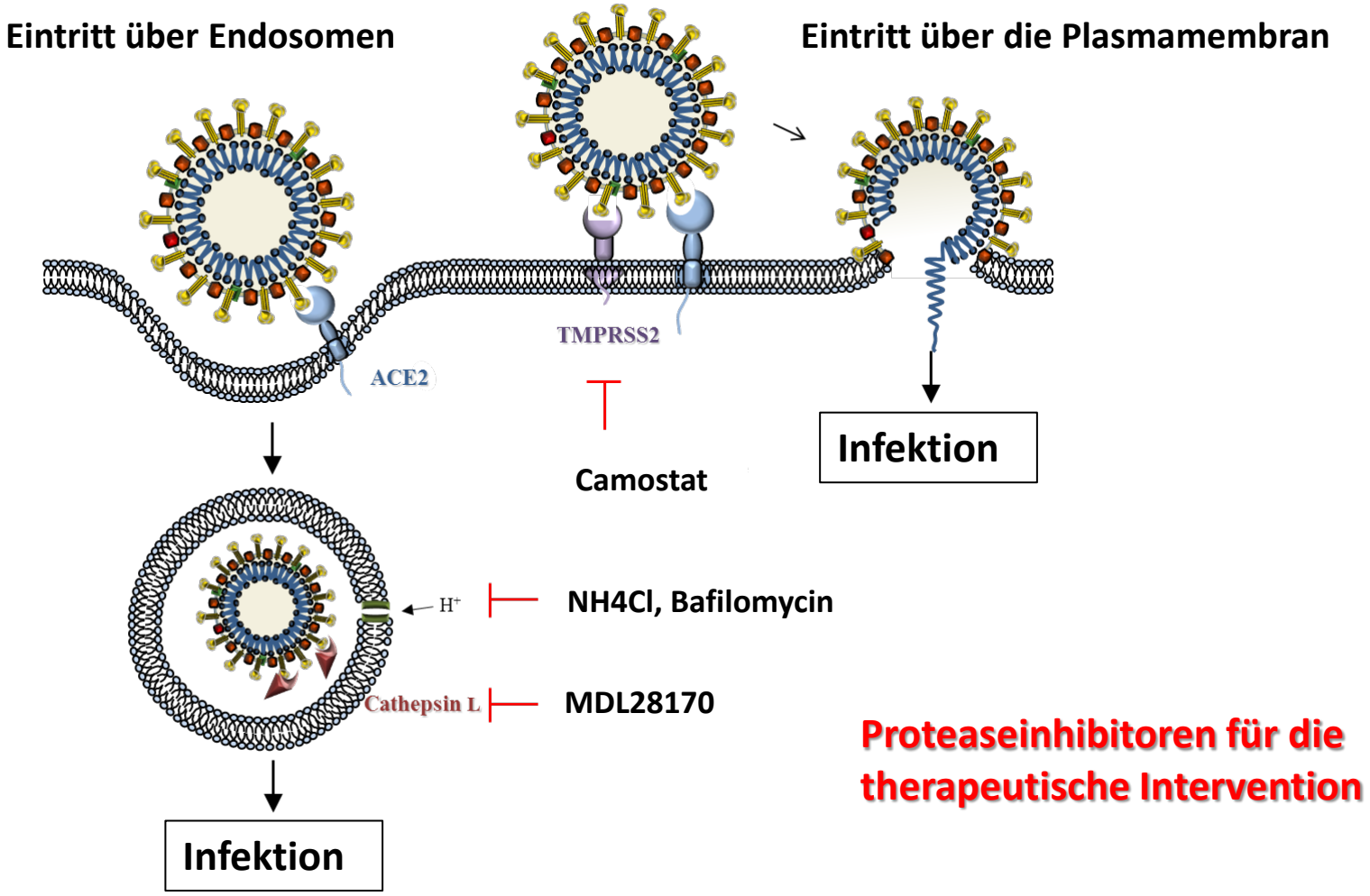
MERS-CoV inhibition in primary human airway epithelial cells







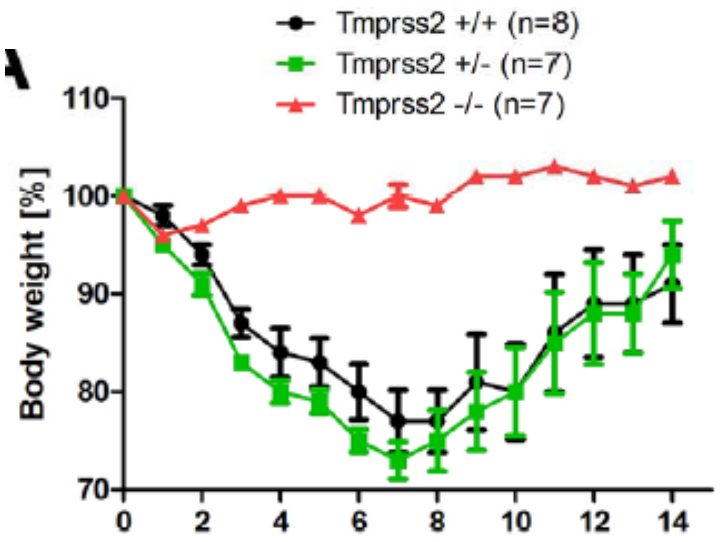
TMPRSS2 & Cathepsin L aktivieren Coronaviren: Neue Ansatzpunkte für die Therapieentwicklung



Proteaseinhibitoren für die therapeutische Intervention

Glowacka et al, 2011; Simmons et al, 2011; Bertram et al, J.Virol., 2011; Bertram et al, 2012; Gierer et al, 2013, Bertram et al, 2013, Simmons et al, 2013

TMPRSS2 ist essentiell für H1N1 Influenzaviren: Neues therapeutisches Target



TMPRSS2 *knock-out* schützt vor Ausbreitung und Pathogenese von H1N1 Influenzaviren

Hatesuer et al, PLOS Pathogens, 2013

MOLECULAR AND CELLULAR BIOLOGY, Feb. 2006, p. 965–975
0270-7306/06/$08.00+0 doi:10.1128/MCB.26.3.965–975.2006

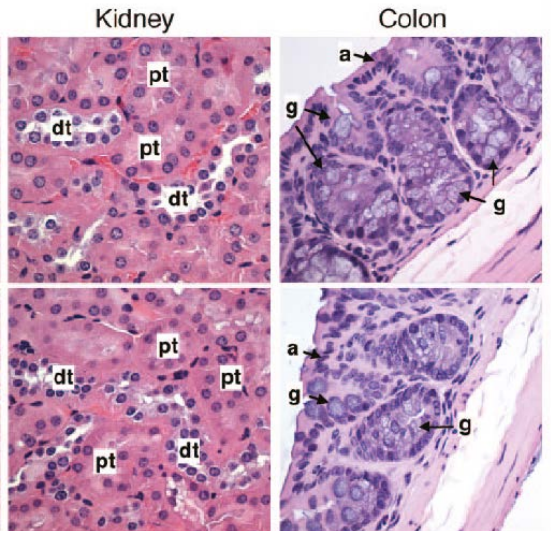
Vol. 26, No. 3

Phenotypic Analysis of Mice Lacking the *Tmprss2*-Encoded Protease

Tom S. Kim,[1] Cynthia Heinlein,[1] Robert C. Hackman,[2] and Peter S. Nelson[1]*

Division of Human Biology[1] and Division of Clinical Research,[2] Fred Hutchinson Cancer Research Center, Mailstop D4-100, 1100 Fairview Avenue North, Seattle, Washington 98109-1024

Received 12 September 2005/Returned for modification 21 October 2005/Accepted 4 November 2005

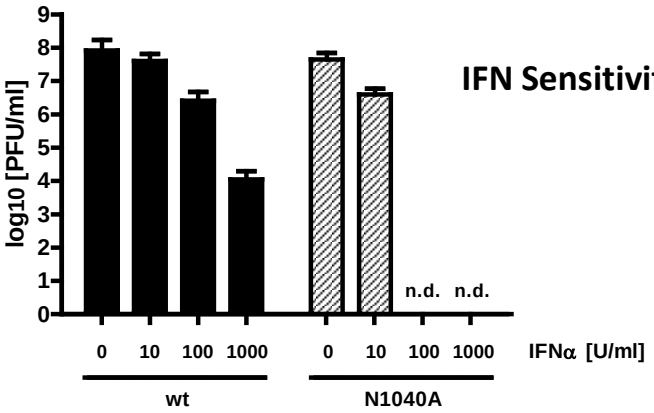


TMPRSS2 *knock-out* ohne Phänotyp in nicht-infizierten Tieren

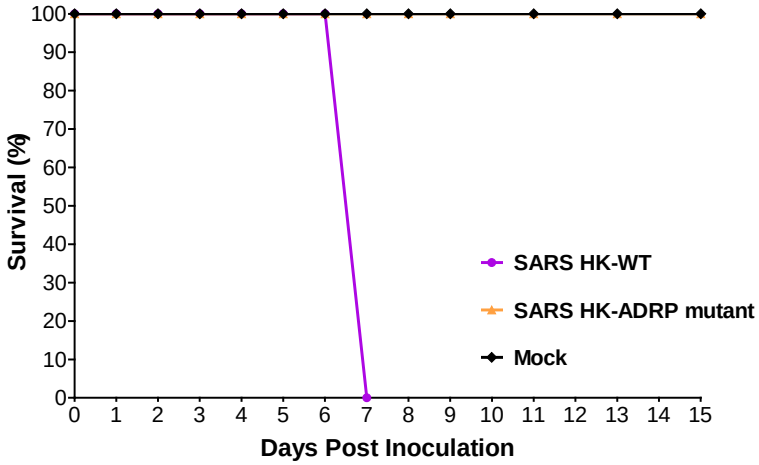
ADRP – Domäne als hocheffizienter Attenuierungsmarker, klarer Mechanismus über Interferon-Antagonismus, konserviert in allen CoV

The ADP-ribose-1″-monophosphatase domains of severe acute respiratory syndrome coronavirus and human coronavirus 229E mediate resistance to antiviral interferon responses

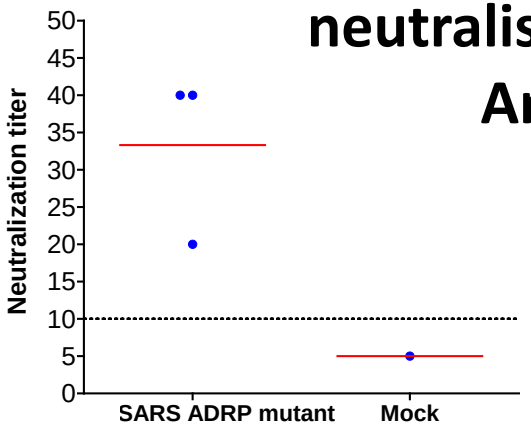
Thomas Kuri,[1]† Klara K. Eriksson,[2] Akos Putics,[3]‡ Roland Züst,[2] Eric J. Snijder,[4] Andrew D. Davidson,[5] Stuart G. Siddell,[5] Volker Thiel,[2] John Ziebuhr[6] and Friedemann Weber[1,7]



ADRP Defektmutante ist apathogen in ACE2-transgenen Mäusen



...bei klarer Induktion neutralisierender Antikörper

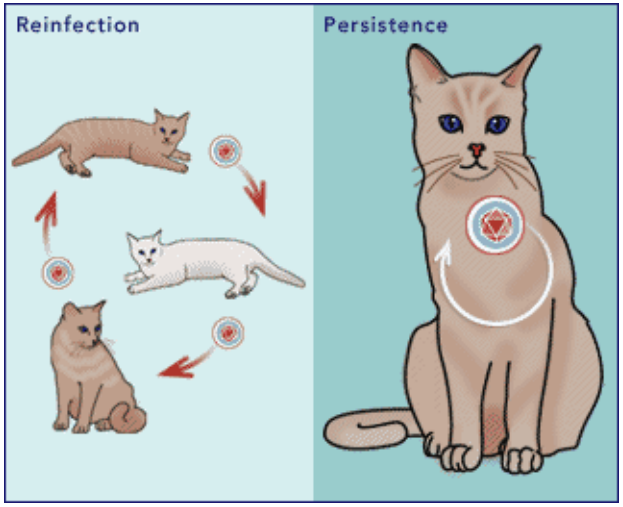


=> ADRP Defektmutanten als Lebendvakzinen

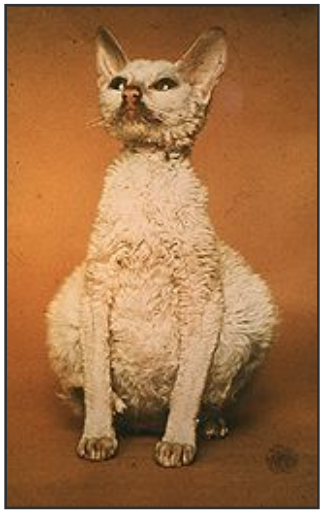
Feline infektiöse Peritonitis

-Verfügbares und hochrelevantes Tiermodell-

Feline enteric coronavirus (FECV)



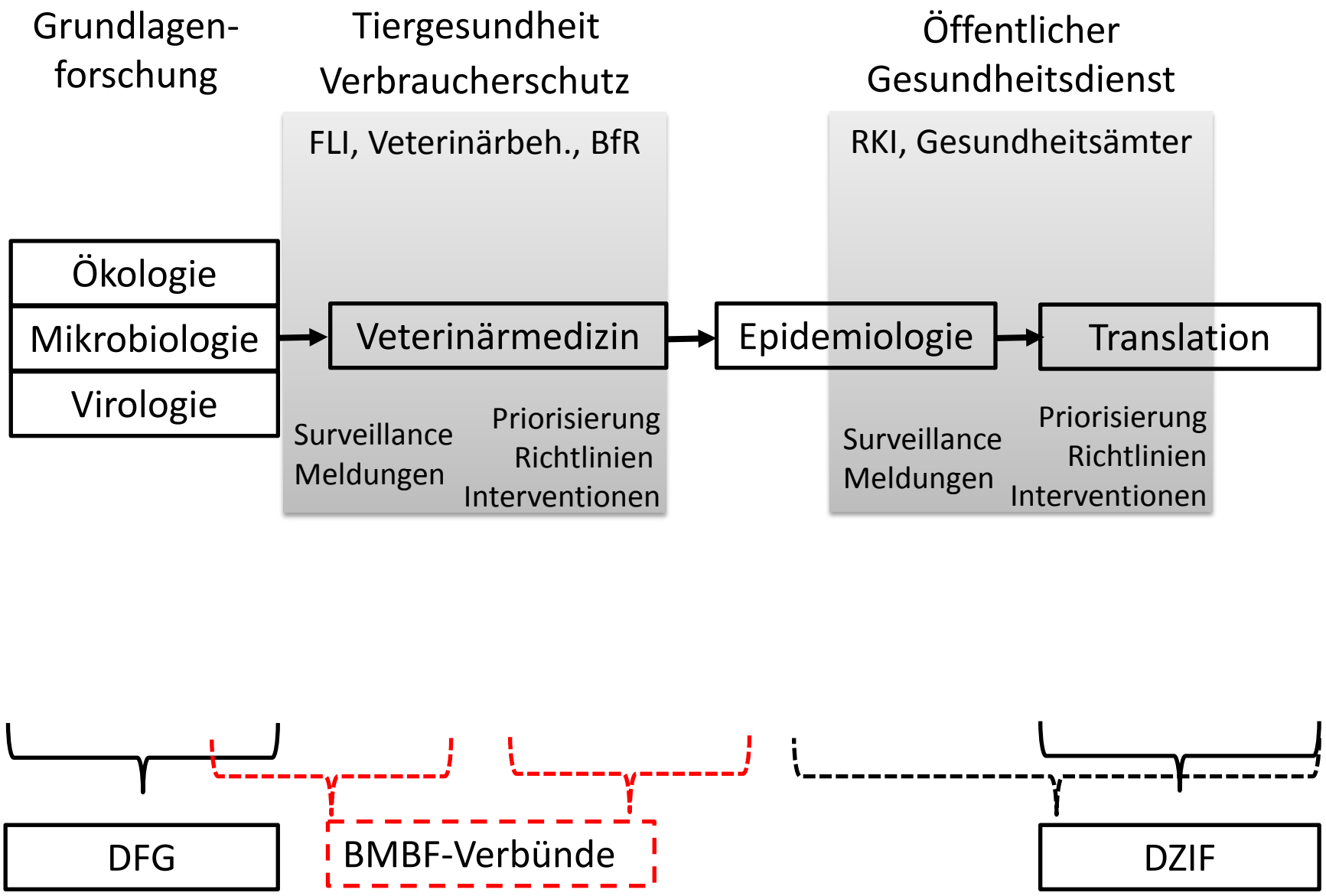
Feline infectious peritonitis virus (FIPV)



Translation in die Tiermedizin?

Output

- >100 Publikationen
- Erklärung der Herkunft von MERS-CoV
- WHO-empfohlener MERS-CoV Diagnostiktest
- 2 antivirale Ziele für alle CoV, inkl. MERS
- Antivirale Ziele über CoV hinaus (Flu)
- Attenuierungsmarker für Lebendvakzinen
- DFG-Schwerpunktprogramm


Grundlagen-
forschung
Tiergesundheit
Verbraucherschutz
Öffentlicher
Gesundheitsdienst
FLI, Veterinärbeh., BfR
RKI, Gesundheitsämter
Ökologie
Mikrobiologie
Virologie
Veterinärmedizin
Epidemiologie
Translation
Surveillance
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Priorisierung
Richtlinien
Interventionen
Surveillance
Meldungen
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Richtlinien
Interventionen
DFG
BMBF-Verbünde
DZIF