paper-2020-nature\_medicine-proximal\_origin

You created this private channel on February 1st, 2020. This is the very beginning of the paper-2020-nature\_medicine-proximal\_origin channel.

I

Add description Add people Sendemailsto channel

February 1st,2020

Kristian Andersen 12:11

joined paper-2020-nature medicine-proximal origin Also Andrew Rambaut join

• Andrew Rambaut 12:13

Nice channeltitle

Kris

Kristian Andersen 12:13

Supersec too

Bat Wuhan.geneious Bat\_Wuhan\_SARS.geneiousZip Zip

February 1st2020

Pinned by you

Kris

Kristian Andersen 12 31

Post I

Ideas for analyses

Post

Structural analysis comparing nCoV/SARS/bat binding to bat/human ACE2

SRA searchturin site + neighbor

Likelihood o

of gaining furin site

Likelihoodof gaining restriction site

Conservation iin bbat viruses around restriction site

General conservation a

across RBD

Is RBO hyper mutated or is this what we would expect?

Examples of bywhich viruses pick uo furin sites

of mechanisms by

• Andrew Rambaut12.47

What are the coordinate of the RBD

Kristbn Andersen 12:48

22553 • 23140 inHu•l

(might bbe aslight jitter in 3' -needto doublecheck)

Ideasfor analyses

Private post shared in 1 place

Done editing

I •••

Share

Ideas for analyses

Structural analyses comparing nCoV/SARS/batbinding to bat/human ACE2

SRAsearch furin site neighbor

likelihood of gaining furin site

Likelihoodof gainingrestriction site

Conservation in tint vires around restriction site

Generalconservationacross RBO

Is RBO hyper mutated or

or is this what we would expect?

Examples of mechanisms bywhich viruses pick up furin sites

Structural modeling ACE2

inghumanACE2 vs Bat A

Ts/Tvf k-mer usageunusualin any way?

February 11st, 2020

Andrew Rambaut 12:50

Thanks

Kristian Andersen 13:17

The RBD is definitely heavily mutated,but I'mnot sure that's unexpected Ineed to compareacross the batviruses,

Screen Shot 2020-02-01 at 10.16.33.png

I

(this is protein)

And1'tiV Rambaut 13.U

•• Eddieis awjke. Send flim an invite to this sljck.

This is SARS and its dose rdatives:

REV0002899

Tile two bat ones areabout as far away as RaTG13 is from Wuhan February1st, 2020

image

Krlstian Andersen 13:28

I

Just invited Eddie

Eddie Holmes 13:30

joined

joined paper-2020-nature\_medicine-proximal\_origin.

Eddie Holmes 13:30

Morning

Andrew Rambaut 13:30

nCov vs RaTG13

Kris

13:30 February 1st, 2020

Kristian Andersen

The two bat ones .re about as far ;,,vay as RaTGt3 isfrom Wuhan

Help me interpret. so dis.tal\Ce betvteen SARS anti bat SARS--likeiSabout the same as between RaTG13 and Wuhan?

Morning £ddia. Gright:ind~:irly.

Do vou have those comparisons;.ist in protein swce?

• Andrew Rambaut 1H3

•• Wlage.1>ng •

I

,,.

Yes hold on a tick

r,I; EddieHolmM 13:33

,.....\_ That's a great comparison!

• Andrew R.ambaut 13'.33 februa-y ht. 2020 .,

·• .SARS:

nCov:

lroge.png •

I

So not wrtcolarly hewily mutated.

t1f!i1 Krlstlin Andcrs~n 13;3,

f.n Good!Theseareve,y simil.r-.What"st~ difference between SARS and that bat virus?

e Andrew Rambaut 13.36

•• 92.86% identity icross spike for nCoVvs ~t. 92.03" tor SAAS vs bat

So I do1'l't thillk the 'hypermutatfon• in R8S is a goer .

.'IJ Kri®n Andersen 13·37 J'cbtva,v 1,.t, 2020 .,

f:£1 Agreed

It's hyper mut.atod, however, th.at region in general is 1-Yipcr mutated • in other words. tflis is what we'd expect.

• Andrew Rom bout 13.37

·• Yes.

11!1

Kristian Andersen 13:38

e Andrew Rambaut !H8

•• 50 Clt";JvJge Site .}1)(1 ft:,ltiCtiO<l s'lles. lll01.1~b?

I

... Krls-thnAnd~r•M 1338

en I'm k>oking at cle:tvage site right oow • lemme sh.ue alignment

• ~teinaligrrncnt.gcnci:ous

For this I took -30 A.Asflanking th~ h.Jrin si:c in nCoVand proteii1blasted it • th('n downloaded (!V'Crythingthat omc tJP and aligr.ed everything. A lot of divecsity around that site in general

• Andrew ttamNut 13.~2

•• RaTG13 is identi~I except tor the 4 resicfuei11:Sertion.

REV0002900

a.wKristian Andersen 13:43 februa-y lSt. 2020 .,

~Yup

Wh~t does the regtOn .-round that site k)ok like in your previous atignments?

liflllill Krlstun Andersen 13:49

fl8 As tor the 8JmHI site. 1rs .t single syncnymous tr.m5't1on. Ti.e conse,vnloo downstre(ffl ot It ls tYPlc.JI tor other sequences hefe, so also not unexpected.

r, Eddi~ Holmos U.$1

~ Wh.1ttver h.ls hJPPened here, the virus bec.ame very quickly loaded for hurriln transmission.

~€).:>!:)

tiilllilKristun Andersen 13:St

mi9 so I U'liJlk we cansay tl'l.lt (1) hyper' mvtatk>J\ aod(2) r'~tr'l<tion Sile afe OOlh conSisttfl1 willl evolul1on.1,ytheofy. (3) furin sue i.speculi.lr' aod (for' ,iow) uoc-x.pected,but we have a lafte

;isc.ertainmentbias.

I

Yc-s • that could definitety be due to the RBD mutations + fi.rin

r"I Eddie Holmes 13:52

~ But they would al:50 be exactly what was expected by c:n,glnecrlni

• Andr,iw R.:aml»iut n~,

•• It will be irlterestin& to know wh.at Roil thinks. He is not going to want it to Ile a GOF escape.

~ Kristian Andersen 13:52

l!8 Questioo Is• evctutiof'l or el\gineeri,'lg, My J.'(Oblem is that both .-~ally rather plausible.

Yup

Ronwill liktly bush back ha'd • which isfine .

414;;;;;.lti&

... EddieHofmes USl

,..\_ Noway to prove. If it'5 cvolution~·ve misseda key compo:lent $Omewhert .. another host/earlier spread in humans

• Andrew Rombout 13,S3

• ■ ~or ~volution I guess we would pjSit a non•bat spe,cies Prior to humans in which the deav.121? site inserrlon occurred

ilfllil-KrisWn Andersen 13:54

Bl! I think the main thing still in my mind is th.,t the lab es1;ape versicn of this is so f riggin• likefy to have happened because thev were already dcing this type of work and the moleculiu data is fully

(Ot)Si:.lent Wlth lh:,t S<cn:,rio @i €) ,;> t:J

11:54 f!Of"evolution I gucu \W: would posit :i ncn b:it speclC$ prior to hum:ins in whkh the c.lc;iv:igc Siitc irv.crtion occurred

Yup. Need to try and figure out SRA S<'arches today

I

• Andrtw Ram.baut IJSS

• ■ spke?

would someone try tt'.cinstmon dcliberatdy? Sec wl\lt it docs? Why would you think it wculd wo<k in cor<Y1avin.,s

r,i Eddie Holmes 13;55

,.... And this lab escape story c:me from ochers ...Jcrc:my might cxplal'I. He asked me to k>okinto it I thougt\l ·ca1\'t be true' but..

Bob said tht instrtionwa$ the 1st thirthewould add.

• Andrew Rombout 13'16

4111111■ I.Jow would it be done in ~ l:,b?

How wooldvou decide wh~t to ~d?

£LUM.

r-. Eddie Holmes 13:S7

,-; MJkesit more fusogcnic so will increase virus titre.

11:s1 Just read th! Abstracc

t'OF.,.

•1~2.0•S0042682206000900•m.ain.pdf

POf

I

F11rwam,11p: or lhe-SAkS«w0n~IN'I spl.:c 5~1.:.0 fdu~

odl ""'111\,r;klllha dait:cMta!kt ,inot1u11rr

~•C 1.-;,.s-'-'wt.WII s.....,•

----·--...-..---,.,

---•-·--·-. ..-,·---·-

lliPlil Kristian Andcrstn 13;58

f8 Yeah.the fvrin site \VOUld be theflrst thing to add fo, sure. Bob dug into this a litcle more and some of the distant human coronavirusesdo have fuin·like sites. The one in rl:.oV is the optimal site

though

l"'I Eddie Holmes 13:S9

,-; Better get re~dy to c..11 in! ♦18¥1::984

REV0002901

ll'!il Kridian Andersen 13:59

~Y~.call.

Cheers

e Andrew Rambaut 13 S9

•• Stay on here in case we need to mesSJge .

....ai Kristfan Andersen 14:0t

~ Yup

11,WKristian Andersen 1,,13

f.B Just FYI -o-linked glycan also present in bat

tllfWKristian Andersen 14:19

!:I! Crap. don't know the context around Sthat make them gtycan sites. I might be wrong

I

The serines are the<e-in the bat

r'II Eddie Holmes 14:39

,....\_ Big ask!

ll!lil Kristian Andersen 14 39

II! Desttoy the-world based on seque-tlcc data. Yaycf nay?

~ Kristian Andersen 14:52

f8 Let's hop on .acall between the three of us afterwards?

41%4ilul&IG

r'lil Eddie Holmes 14:57

Febn1ary 1st. 2.020 "

,... Sure thing.

~ Kristian Andersen 14.58

rn I proPose San Diego.

Makes :sense what he"ssaying -but man. that's hard to pull off.

• Andrew Ramb.lut ts:01

•• v ...

~ Krinian Andersen 1s.01

r.\'!No

r-'I Eddie Holmes tS:01

~ CanVIC do a zoom?

~ Kristian Andersen 15:02

lit!I You too Andrew!

Yup. I II set up a zoom

• Andrew Rambaut 1s-02

•• Great.

There is a WHO research expert group meeting in GMC"va on the 12th Feb

lalll Kristian Andersen 1505

~ httpsc//zoom.us/j/9673242666

Call•

a

a

Zoom meeting

Ended at 4:()6 PM • lasted 101 weeks

M<eting ID, 967-324-2666

O people joined

Added bv Zoom

@Eddie Holmes • you hopping on?

I

111"111

Kristian Andersen 22:42

~ @Eddie Holmes and @Anclrew Rambaut • here's <1document I h.lve been working on trying to summJrize the dis-cussions. A little tric::ky to b.llance how muc:h to include versus not. so please feel

free to edit away as you sec fit. Maybe send this over to Jeremy and Tony Sunday?https://docs.googlc.com/docomcnt/d/1HOVH\laahY2wMwAij Mb-rllV3QomBai-DwROcn5060Ucdit?

usp•sh.iring

G ~tite 0otU11X'l'f ...

II

II

Summary

Googl<Ooc

F-ebruarv2nd. 2020 "

~ Kristian Andersen 0100

~ Dumping this hereas I need co think on this -it's kinda wcl,d. lool<lng at the Ts/Tv spectrum .

.,....

bat\_wuhan\_snps.xlsx a sars\_sars•like\_snps.xlsx a sars\_sars•like2\_snps.xlsx

Excel Spl't.:idsheel Extel Spre:llbheet ExcelSp'e:idshett

a I

a

a

snps.txt

PlainText

REV0002902

Febru:ary 2nd, 2020 .,

• Andrew Rambaut 04 lS

•• Hi Kristian,

lml.sstd this chismOf'ring othcf'Wiso I woukl h'°"chcldoff or. th(!r<!ptytoRon. I will tak! a look and let~ l<now.!edited)

Kristfan Andersen CYH4

Yeah. oo wor,'ic:sAndrew • I think your reply was g,cat. Both Ron and Chri.st'ian ate much too cooftictcd to think about this issue straight • to them the hypothesis of accidcl'ltal lab escape is so

unlikely aoCI f.Ol SOfOe1hio.g U-.ey wcuulo COMkte1,n,emain issue ;s that a,c<i<lentil escape is in fact l\igl\ly lilerv • it's 1\0l some rringe trieo('f. I absolutelY ag,-ee U\it we cao'tprove ooe way or the

other.but we never'Nill~ able to .. haw~cr. that doesn't rr..can that b-fdefault thcd.ata iso.mer¥:lymuch more suggestivc(lf a natural origin ascppos~ to e.g. passage. It is not• the furin

deavage site is ve:ry hard to explain.

I think my initial 1tternpt at writing up a surrmacyw;:ts ok. but I'm not happy with it -it's not reallygettin.g to the point. I'll rejig it tl!is morning. go dimbing. ard the, come back to it around n:)Qn PT.

Maybe Eddie c:anth~n seOOit Ovt< toJeremylatEt today· I don't think we should reply back on the cuireot lh,ead as he ~ffective}yshut down the discussion ther'e and I lhir\k wilJjust fead to a

Ylootint nutth •Christian ,md R.onm;ade itclearth.lt thevthink ;his i.sa cr.ackool theorv.

• Andrew Rambaut 10 29

•• ljus.t had a phone call fromMart<Peric:ilsatWHO who was asking meabou1 the HIV pape-r· the OG h~d rurg him and wanted to know if it \Vas true. Told Mark itwascomplete boUocks andwhyit

w,;1~. 8ut t"ittcr ill.going er~.

<Y€l~Q

rB Tony Fauci called me yesterday afternoon with the exact same Question and I gavehim the exact same answer.It's really disturbing we have to explain away that paper • it's complete and utter

I

bollocks My fearls that the likes of Chrisian and Ron puts the question that's being asked here into the same category-I'm pretty sure by now they think I'm a complete crackpot.

Robert Garry 10:48

■ was added to paper-2020-nature\_medicine-proximal\_origin by Kristian Andersen

Andrew Rambaut 11:10 February 2nd,2020

Ron hadme clocked as an anti-GOF fanatic already. Although my primary concern is that these experiments are done in Cat 3 labs.

Kristian Andersen 11:14

Interesting. I'm all for GOF experiments. I think they're really important however performing these in BSL·3 (or less) is just completely nuts! IMO it has to be performed at BSL·4 with exta

-

precautions.

•1have evolved a bit on this point. I used to think they're really important, but I'm actually not so sure anymore. I thought it was really important that we understood whether e.g..• avian influenza

could be transmissiblebetween humans• andimportantlywhich steps (and how many)would need to be involved -but honestly I'm not sure that type of knowledge isisat all actionable,while,of

course being exceptionally dangerous. It only takes one mistake .

Krlstian Andersen 11:15

@Andrew Rambaut to this comment I think we should write a parallel documentabout scenariosfor naturalorigins. The two things can be consideredcompletelyindependently". Yup,totally

agree. I'll take that whole section outof the document and write it alldifferently.Do you maybe want to take a stab on getting the other document started based on your pointsfrom the email?

Andrew Rambaut 11:16

Yesmy feeling is vouhave to consider the cost benefit for every experiment And do it safely.

Kristian Andersen 11:47 February 2nd, 2020

Reading through Ron's commentsagain I agree on pretty much everythinghe's saying -I come to the same conclusions. Where we differ is that he's looking for very specific evidence provingthat

this is unnatural (whichis understandable), but except for the most simple scenario where somebody plugged a gene into a preexisting backbone that would simply be impossible to prove.

Natural selection and accidental release are both plausible scenarios explaining the data anda priori should be equally weighed as possible explanations:The presence of furin a posteriori proves

me slightly more towards accidental release, but it's wellabovemy paygrade to call theshots on a final conclusion.

Andrew Rambaut 11:53

Given the shit show that would happen if anyone serious accused the Chinese of even accidental release my feeling is we should say that given there no evidence of a specifically engineered

virus we cannot possibly distinguish between natural evolution and escape sowe are content with ascribing it to natural processes.

.... Kristian Andersen 11:56

Yup.I totally agree that that's a very reasonable conclusion Although I hate when politics is injected into science -but it's impossible not to, especially given the circumstances. We should be

sensitive to that. (plus none of this matters at the moment)

Separately - having all of these discussions isreally critical to counteringAll the friggin' bullshit coming out and at the end of the day. that's probably the most important thingsthat'll come out of

this!

The latest being two novel viruses circulating .. https://www.biorxiv.org/content/10.1.101/2020.01.30.926477v1

(I'm starting to think that for outbreak research the bioRxiv really needs to start screening submissions -it's a slippery slope but it's justified at this stage

paper-2020-nature\_medidne-proximal\_origin

bR bioRxiv

Evolution and variation of 2019-novel coronavirus

Background:The current outbreak caused by novelcorornvirus (2019·nCoV) in China

has become a worldwideconcern. Asof 28 January2020 there were 4631

confirmed cases and 106 deaths, and 11 countries or regions were affected.

Methods: We downloaded the genomes of 2019-nCoVsand similar isolates from the

GlobalInitiative on Sharing Avian lnfluenzaDatabase (GISAIO and nucleotide

database of the National Center for Biotechnology Information (NCBI) Lasergene 7.0

and MEGA 6.0 softwareswere used to calculale genetic distancesof the sequences.

to construct phylogentic trees, and to align amino acid sequences. Bayesian

coalescent phylogenetic analysisimplementedin the BEAST softwarepackagewas

used to calculatethe m0eCular clock relatedcharacteristics such as the nucleotide

substitution rate and the most recent common ancestor (MRCA) of 201 2019-nCoVs.

Results: An isolate numbered EPI\\_ISL \\_ 403928 showed different phylogenetictrees

and genetic distances of the whole lengthgenome, the coding sequences (CDS}of

ployprotein (P) spike protein ($), and nucleoprotein (N) from other 2019-nCoVs.

There are22. 4, 2 variations in P, S, and N at the leveI of amino acid residues. The

nucleotide substitution ratesfrom high to low are 1.05x 10-2 (nucleotide

substitutions/site/year. with 95% HPDinterval being 6.27 x 10-4 to 2.72 x 10·2) for

N. l.34 > 10·3(5.10 x 10-4, 128 x 10-2) for S, 1.69 x 10-3(3.94 x 10-4,3.60x 10·

3) for P. l.65 x 10·3 (4.47 x 10-4, 324., 10·3) for the whole genome respectively.

REV0002903

At thisnucleotide substitution rate, the most recent commonancestor (tMRCA) of

2019•,~oVs appeared about 0.2S3•0.59"1year b<:foret~ epidemic. Co,-.clusio.'l: Our

analysis suggests thn at least two dfferent vir.il strains ol 2019-nCoV are invo\ted in

this outbreak th.lt n:ight OCQ.Jr a few months e.irlte, before it wasofficially reported.

ShowlCM.t.

T.lf'l30ttl2:>20

Robert Garry u1s

■ lhls new s«1uerce tf!II\_ISL.403928 e-sscntially rnutal'lons., 1,vtlatwewould say ls tht fuskm pe:pTIOC.althcugh

rus three ccnsecut1ve mars ~controverSlat."

Just ~ying• if I w.'lls goi,,g to do i;;.-,i.-. fu,~c-tionr'ese.:'llr'C:h -3t the YCr'y le.>st Sofn& 10 pour' g:isoo the

ol fund.On or' Joss of I misht mutotelhe fu5io,, peptid'e (d!,ht :.f-tet :.ddio,s the f11ln s.lte). So this 6

fire, Jeremy is absolutc,ly right this needs to be discussed in the light of day. And, ASAP. I

e Andrew Rambaut t~l25

•• EPI\_ISL\_403928 w~ one of the ones which orlgloolly had 50 SNPs wh.ch werest!quenclng rrrors. The lab then updated It (silently} and It Is now onty 1 SNP different from o:her Wuhan onn.

This mrxir i!>entirety .i,, i'rtiefact of th;(.

Robert Garry 13-:30

■ In thebioR.xiv pdf they say: "WN;n compared with the other 2019-nC<Ns. EPI\_ISl\_403928 h;:,s foor variations in S protein (TS721, G799V, FSOOCand N801K) and two variations n N proteb

(A414C aod 04151)." lean totally buy dlat tl.ats'sstit1 a, artfoct.

Here is the ali&ninent of 8a;G13 vs nUN.

fOF •

•LALIGN results B;t R>tG13" nCoV .pd!

POF

LALIG~

..,,,...,..cfwWllt.'>, .. '-'T.-nJ

IUl--l,,,-l°"""loo-1?1\_..\_.,!l,!CI

:=,i::::'!.;~q.r..:,;.;.;:-......

~ ~4•&•

•I-••-•• ............. \_.•,..••••••"•»··

I

Tt~ arevery similarSpike prottins except for Ule RBD th~ looks like it was human adapted :md the hsetdon of the PRRA. th.lt com:erts ~ site to M optirnal furin·flke cleavage silt aod

iiotentfaJlv<reates O•l!nked glyc .. n sites.

lo c;.on'll"Crt-1n low p.-.thogi;nl;ity 11vi,,nnu v ~o ., h:$h ~thosi;:ni~ityvin,,:; wh~t h.,ppcn, i:; the: inxrti<>n of two .:,rgi.ninc:i; • Own 2001.

2hles •

Alexander and Brown.pelf a 0Uan2007 LPAI vs HPAl.pdl

• POF PDF

Aleanderand Brown ttach ;hat: ~All the current evidence

indicates that HPAI viruses arise by mutation after

LPAI'Iiiruses of the HS or H7 subtype have been

intl'Oducedinto poultry. Sewral m~nism~ maybe

tl!'SJ)()(ISible

ror lflis mutation. Fo1 mos1 HPAI vin.6es. men;~

appears to have been spontaneous duplication of purine

triplets. wh.ch resulls il U~ insert-ioo of basic:am'no adds

at the HAOdcavacc s...lc.and thiisccms tooccurdoo toa

tranwiption enor by the polyma--:i$e complex (76)."'

This is what Andrew stated last night •it can happen in poullJy. Ek.Itits ~nd insertion of two amino acids not four at once.

I

H9 Ou viruses o~imitt a rnhirnal furin cleavage site to an optimal one .

•H9 and forin site.pdf

POF

A NlJ'ld Adi~..so.i M«h.ani.-n of AVJ.an lallut-nn, \'ioo H<JNJ by

Fuin

U:43 H7 viruses .iPPe3f to make rte¥/ potytnsic f\!rin lite de.wage sites by recombining in loogish stretchs of nucl(otides.

PDF • •H7 recombinationpdf

POf

Vlr~/;,~~':;~~~!j?~ l':i:~l\~~?u~nzl>

Outbreak, Chile

-.. -••-...\_,.,,.-..........\_\_\_ Cl.\_\_ '-9\_...,.

-1.-.,0..-.. --..-----c.-.,

.. \_.....,"""'1 ... \_....,,lt'-'-................. 4\_,

A very go0<1 review bY DrOS1eo.

I

REV0002904

•ORosten • sou,ce ofCdls.pdf

POI'

Hosts and Sources of Endemic

Human Coronaviruses

YlclorM.CorYN~,Ooiffft~••.o.ni.11~>"'••

CMiMi.iOroa"''"''

,\_, \_\_\_\_\_\_\_\_ ..\_\_\_\_\_

'""::.~...;::-.;.~~':.:!':;.."'.'\_..

y,....\_\_ ·

Robert Carry 1as1

■ Ne,w :inal~: SQme strains of mtJri1W:hepatitis viruses h3v€!a su,\_.er-optimal fura11-likedeav.a\_gesite (wilh pttdicted 0-liked glyca,1s).some just have-an optimal site and somt havt ,,o site at all.

Just b~sed oo tl-.espike ph..«>8efly thlsseenis lO have evolvedwith Ulespik.(> l)(Olein mofc « Jess but this ls out or my wheeOOust. No1 sufe if spite evoluUoo io MHV fOllows evctut'iOf'l,tMCRA c.-1c I

of other proteins but all .ue relevilnt questions gi'len the current issves beingdiscussed IMO

Wotd Oocurrent •

II

II

FtbrW,Y 2nd. 2020 .,

MHV spike evolution.doc:x

W~tdDocun,ent

And a nrst t>okac tne HKU·1 spik.e -1.saclose re1.at1vcor MHV.

Word Docurrent ...

And a first bok at the HKU· 1 spike -isa close rel.ative of MHV.

Febrtt.'lry2nd. 2020 .,

\Void o«utn;·nt •

II

II

HKU•lSpike.docx

w,,,J~'¢M

Rokrt Carry 1:J.SO

a Two pattens seen he~ (i think there isa third variant as wel~. There is an insert of three serines right next to the alreadysuper optimill flJrin ,ke cle.av;isebet-weeSl and $2. And, this cre(ltes

Jl(edicted o-tinkedgly<ans at andaround the site. Tt<lete is another mudn·like do1nainin 5i08 theJ)(ef\.6ion structure on thepdb batatnse. tHese presei\Ce cf this mucinlike domain e,q>ainswhy

the.1uthors we~ unsuccessful in determining the structure of the too of the trimer. but thev didn't kno.vwhv.

Robert Garry 1407

■ Bottom line on aI this analysis • mechanisms exist in flu as Arldre-H staied to make insertiom at the junction where the two ~ubunits are clea,.,ed • enh¥Kingvirutence and human infectivitv. CoV

.ip,»rtntlydo this .1$ wc-ll01 potcnNlly c:im do ttli$. Thi$ i$ .in imporbnt mc-.$.:a.gC#,om thi: di$Cu.s$ion :ind f"¢Cd to be t.1lkcd .ibout in light of the furin l1k¢ dc-.iv:igc $itc-being noticc-d.

Robert C.arry toll 10 f:'cb,u.;,,y 2nd, 2020 .,

■ I still don't know if the nCoVwas the r'tSultsor a defibtral~ ,nanipulalfo,1 or· nol. 11 riCo-, wasnol oogineered then RatG13 °'a very do~y related Sat virus ~nehow er,ded up ina situation in

11arurclike the poultrytanns for HS etc. as Andrew stated. That's very scary and perhaps e,Wne«cd \\Ot.Jldbe-better• at le~st that can be r~gulated so it doesn't happen again.

Robert Garry l◄

"l:it

■ So.

Of nCoV deve-lo~ that optimal furin cleavage site with the o•liri<ed glycan> (wh'ch I now suspect are important because they are prcscnt etsewhcre} then:

1. THe insertion mech.ani1msisdifferent tan flu HS in that it's looge<and doesn't just inVON'e purines.

2.The generation of the site fsdifferent than H7 and MHV ~cause it involve-san insertion, not jl.1$tmutating existing codo~.

a. the gener.-t1onor the turin site is cmterent u,.;1n H9 l>e<:.luse Ule 1nsert1on is a pertect 12 t1Jcteot1des. not a rather nofl•Speclhc recorrblnat1on.

Robert Carty 1◄ ~

■ It would beimDCl'tant IMOtogei a estimate on the timing on how long ago the MHC mutations .lfld the HKU-1 SSS insertion todc place.

ifMIKristian Andersen 1s04

fa Tl\ankS Bob. t11esc are really gOOd points. can you please sh.lre tfle sequcncts fretn y0ur analysis or the alig.rtment? I'llmet, take a clOs« fOOk.al over au diverg,ence. et·c.11001.edat these yesterday,

but I wasn't very5t.iccessful.at getting meanin.gful alignments.

As for the recent bioRliv paper • as Ardrev, stated, th.rt can be ignored • the S<:quenccis wroog Md that's where they're getting their sgnal.

Robert Garry 15 20

e KHU·l

I

REV0002905

~~(6).txt•

l >lcllDQ437619.1\_prot\_A3096198.l\_l (gene•S) [protein .. spike (l)'coprotdn) [protein\_td.,;.a096J98.l) [location"l .4071] (gbkey.,CDSJ

2 HLLllrllPT1LAVIGDFP,CTNFAINDKt:T7VPRIS£V'VVCW'SYGLGTWILOft.VVUITTILFlGYFPKS

GANFRDLSU:GtTVlS TUA'(it:l»F LSm~·t.001F Sk'VKN1'Kl YVNXTl YSE.FS T IVIGSVf INNS YT IWQ

.4 PtNGVLE 10:.SKGSSRtfES\.ttFOKSEP\.C TQ,IL RGTF

IT ACQYfHCE't'PHl L F« kN TYNVS VF HfVQE Y

MHV

>lcllttF618lS2.1\_prot\_ATNl7888.1\_) (prot•in&$-pik.i ilycoprouin] (prohin\_id1ATN37888.1) ( locatiOl'la-22720 . '26694] [&:bk•y&COS]

'I HLfVFlt.flPSCLGYIGDFRCIQlVHS.t.JGNNSAPSISTEMVSQC.ilGTYYVLORVVlNATLLl

l(iYYP

.a VDGSKfRNlALTGTHSYSlSWFQPPYLSQftflGIFAKVQNll(lSTPSG.AUYFPTIVIGSLFGVNSYTW

Here are the dustal 3lignments for t~ entire spike proteins.

,...,.

a

a

MHVclostalo-£20200202-150710 ... a HKU-1 clustalo-£20200202-1705 ...

PbinTcxt Plain Text

I

~ Kristian Andersen 1S:33

Febr\.l.l,Y 21'1d.2020 ...

ei\'!IThanks Bob -111t.ike a look

e And,ew Rambaut t3·1t

•• If you want to look here is a bunch of cleavage sites in high·path .wlJn influenza HS and H7.

Zip•

2 documents from H5Nl cleavage sites..geneiOU$

• z ..

llr.WKristian Andersen 18;34

~ Do we haw any location information on lhc bat SARS-likc viruses? I'm reading through papers and I foul'ld this particular sentence from one of Shi's papers interesting -•intcrcsringty, all the

SARSr•CoVsthat are capable of using human A.CE2 were found in R. sinicus in Yunnan Province•.

t bclic\lc RaTG13 is from Yunnan. which is about as far away from Wuhan as you can be and still be in China. What arc the chances of finding a viruses that arc 96% Identical given thatdlstarK:c?

Seems stromge given how m.1nv SARS-lik.e viruses we have in b.lts {which is what Eddie has been telling us tor ,1 while ... ). f.t6rtcd)

• Andrew Rambaut t8'.37

•• Ebola got from Middle Africa to West Africa in 10·20years.

~ Kri$lian Andersen 18.37

I

!B Yup. that's true

a:I Yup. that's t<ue

F~ruary 2nd. 2020 ~

• Andrew Rambaut 13 42

•• I personally think we should get away frorn all the strange coincidence stuff. I agree it smells really fishy but without a smoking gun it will not do us any good. The truth is never going to come out

(if escape is the truth). Would need to be irrefutable evidence. My position is that the natural evolution i:Sentirely plausible and we will have to le.ave it at that. Lab passaging might also genc<ate

this mubtion but we have no evidence that that happened.

Not that discussing it isn't fun.

~ Kristian Andersen HJ:48

r.r, Agreed. Howc\ter, I do think some of these points could be important • e.g., would it be Impossible to sec a bat virus 96% identical that far away? Answer to that. no-we might expect that.

Themain ('Or'lcern ('Oming up reading through all these papers is the kind of stuff that is being done -getting MERS•like-v1ruse:s

to infect humans. getting SARS•likc vin.iscs to Ciluse disease in mice

and infect humans. etc. Thern's a very st,ong focus on the spike p<0tcin f0< all of that work

But I do agree with vou -the mind can do amazing things and it's easyto get wcked in with confirmation bias.

One important thing I came across though -for the SAAS Gof studies they created a reverse genetics system for their bat virus on a whim. So Ron's and Christian's argument (which I found to be

the stronge$t) about that not being fea$ible is not true -they were alre~ c:reating those.

e Andrew Rambaut 19 19 8-fiiiji+

•• t think it would be good idea to layout these argumentsfo, limited dissemination. And quite frank\_lysowe can learn from rt even if it wasn't an escape• it easitycould have t-,...,. c-\_,,\_ n

i,W KrifflanAndersen 1928 ~rwrv2nd,2020 ~

~ Yeah. I'm conrncted -I honestly don't know if any of this i.nformatioo is useful without having read all the various papers. Personally. it's useful for co1ltext. but even though thet'e's some strange

research going on here. the<e's no smoking gun. Not quite 'Sure wh.lt such a gun would look like though.

Bob 5.aid it well though -I'd ~@fer this thing being a lab escape so we. h.ave l~s ,ea!.Onto believe oth@< coronas.night do this again in the future ·:.:.

What is useful is to summarize the main points considered ;md dis.cussed. I'll get ro<k on that doc:ument tomorrow· for now I still need to read more and al!iowant to take a closer look at the

alignments. Bottom line is that we can't pr'Ove whethet this is natutal 0t esc.)Pf? • leavingit to others to make that decision. but hopefully wecan ensure they're more infonnc<I,

• Andrew RamNut 19 31

•• I suggest we write this report erring on the side of extreme caution. Also I think the natural evolurionairy story may be a interesting one as well. Then \VC can give all the curious coincidences and

dodgy goings on to Ma,c Lipsitch to have fun with.

llf!IJ Kristian Andersen 19:31

Bi! Ag,eed.

• Andrew Rambaut 19'.32

•• tf nothing else • the fact that wearc discussing this shows how plausible it is.

irllil Kristbn Andersen 19:33

r.i'!I And yeah -would k>ve to go drnvn the natural sel«tion rabbit hole ~'

And yes. all of thi'S is highly useful and .absolutely required • taking a very close look at the dfffcrent scenarios. Gives some really good ammo to shoot do-..vnall the fringe theories .aod bad studies

going on as well.

I

REV0002906

ifillll Kristian Andersen 20-31 F-ebruary 2nd, 2020

v

In @Andrew RJmb3ut and @iRobert Garry take a k>ok al this alignment wMe reading these three papers:

https://jvi.asm.org/contenUearly/2020/01/23/JVl.00127-20

https:N\w1W.l'\cllture.com/;irtides/s41S79•018-0J 18·9 (section on "SARS·VNmutations that affec;.t human and civet receptor binding1.

https://jvi.asm.org/content/82/ S/ 227 4

This is very intere5ting • nCoV is loodedf0< binding human ACE2 receptor. Compared to the bats, 5/6 of the most critical contact residues are mutated in nCoV. Very interesting.

(key residues arc marked "mutated'" in Gc-ncious for lack of a better category, .. ) :rc1,ted

2""' •

a

a

spike\_alignmentfastJ spike\_alig:nment..geneiou.s

Plilintc:w.t • Zip

a..lilKristian Andersen 2046

fa One additional point to this• rC;>Sidue

472 in SARS (Ll converts from l > Fin tiswe culture incr'easing binding and infection (last papctj. It's an Fin nCoV, but an Lin the dos.cly rdatcd Mt viruses.

including RaTG13. HowN<!r. other bar CoVs do also somctfmes have F hc{c,

Selection or pass.,ge, this is very interesting• and adds to our understanding of why this is sprtading like it is.

~ Kristiin Andersen 22:2s

~ Two homology models to accomp.:1nythe struct\lral st1,.1tf1f you wont to have o look..

I

Model 1 is based oo 6acd.1.A and Model 2 6acg.1.A (cd>tcd)

February 2nd, 2020 "

a

a

modoll.pdb a modcl2.pdb

PlamT~xt Plain Text

....aKristian Andersen 22:35

lrJ One thing I 600 kind,cl funny here· all of this w0<k gettins bat samples w;;is supported by PREDICT.Soif they're not Jble to predict the pandemics they themselves c.1use. then I'd say their program

is in pretty bad shape ...

Sorry, had to get th.lt off my chest. Pandemic preparedness indeed . .a

F-tbn.1.ary3rd,2020 ,.,

e Andrew Rambaut ono

41111■ I was literally going to do this ,malysis today: https://twitter.comttrvrb/status/1224207999683547137

Thanks Trevor.

F'li Eddie Holmes 02~4

,-..; Trevor, bless. ros no idea about the functiooal properties of the mutations he is describin,g. Kristian, thanks for PREDICT stuff .. .1'11save that one for future use.

e Andrew Rambaut 02.;35

•• I guess all these mutations that enhance human infection <startto make it really unlikely that it adaptOO in humans.

PREDICT• perhaps they had planl'M?d a press conference predicting whk.h vitus would cause the next pandemic but then it escaped from the lab earty'?

I

... Eddie Holmes 02:39 Fdmmrylrd.2020"

,..... Jie Cui, who worked in the Wuhan lab and is on those p(lpers, used to be my postdoc. He's now in Shanghai. I y,ol'lCfer if I can have a have a chat with him'? Bottom line is th::it the Wuhan virus is

beautifully adapted to human tral\Smission but we have no trace of that evolutionary history in nature. Correct'?

• Andrew Ramb.aut0140

•• Yes.Butwe have de-cades of missing history.

F'li Eddie Holmes 04;()1

,--: Agreed. But it's exactly the evoluti0nary history you would want to make a human adapted virus so it woukt need to bt?in a spec~ that would behave the same as humans. For the summary I just

think we need to layout the features in the data and leave it open as to the cause. Just outline w·hat needs to be explained and leave it like that. Irrespective of what the answer is. and will likely

never know, these are realty important bits of biology.

This is what I told Kristian c1boot thc bc1t stuff: "'The-re a,e bat bctaCoVs from Hubel but they fall into different cladcs and ate oot from R. affinls. The Wuhan group seem to sample almost

excl1JSivelyin Yunnan, Must have loads in their freezers, So, it that sense it's no surprise that their virus is from Yunnan. BUT. if natural. what must mean is that there is a betaCoV from a bat from

Hubci that is >96.5% similar to 2019-nCoV ANO that there:must be an intermediate host that is even closer $till". Again, may all be natural. ButI .am struck by how differently this virus is be-1\aving

fromSARS.

• And.-ew R.ambaut 04-3:;,

•• I just heard there are two papers coming out in Nature today that use the nC,oV sequence lo predict host. I guess one is Daniel Strieke-l°'s one uslng a machine lea ming nonsense. Not sure what the

other is (presumably not the snakes paper). I wonder if they both say bat or do they have something better?

PerhapS this stuff is something we should wr'ite-a paper about to addn?$$ this not•a·bat thing..(ed1~e-d,

e Andrew Ramb.ilut (K43

•• Ha. Just got setit them (by media centre). One is yours Eddie. So not Daniels. And not really about hosts.

I

REV0002907

... Eddie Holme5 0-Ul F-dH'\l.ry 3rd. 2020 ...

,-..; No, it's our5 and the Wuhan Institute one. Ours is now em~rrassingly out of date.

No way Daniel can ect a p;!per into Natu,e saying that a bat-relc1ted corooavtrus has a bat host. Surety?

e Andrew Rambaut 0451

•• No. It was jun the way (he media person said it -she said one of them was about the host species and had been on biorxiv. I only agreed to k>ok at it because I was worried it was Daniels

nonsense.

Anyway. I don't think I will comrnem on these. They are fine. Well done.

F'li EddieHolmM 04:56

~ Wcifeng, who hctps George. is writing a paper on these 2 new bat CoVs he has sequencing. Hugely keen to know· how close these arc to 2019-nCoV but he has yet to tell me.

Or wha:t mutations they have.

e Andrew fbm~ut 04:S9

•• Do vou think we could write a paper on the ·pre•adiiptation· of nCoV to humans. Coold be(In inttrC1:ting e~mple of how the Predkt proje<:t is so flawed.

I guess they 'HOU Id just say we need to do even more sequencing to find these viruses.

r,i Eddie HolmH 05:0S

~ When the dust has settled a bit yes. Jon Cohen tssniffing,amund. Not about the I.Jbstuff but about all the cover-ups and 'Who knowwfl.JtW'hen. Very vexed thal the market was cleared. Soam I that

just smells bloody weird.

... Eddie Holmes OS:SS

,.....\_ Confidentially. just got this from Weifeng. Ones in red. Also Yunnan. H;;iven't got seqs bot can assume they have bat motifs .

•Simplot4 0203.pdf RAxML .. bip.artitions.c1In.S001 .. BGI ...

POf PDF

•

Robert Carry 08c39

■ https://\w.w,ncbi.nlm.nih,gov/pmc/articles/PMC6070550/

•>PubMed Central (PMC)

Evolution of high pathogenic.ity of HS avian influenza virus: hiiemagglutinin cleavage

site selection of ff!Vers.e•genetics mutants during passage in chickens

low pathogenic-ity avian influenza viruse-.;: {LPAIVs) are generally asymptomatic in

their narural avian hosts. LPAIVs can evolve into highl:y pathogenic forms. which c;in

affect avian and human populations with devastating conse<:iuence-s.

The switch to

highly ...

The major hangup I have is the polybasic cleavahe sile.

Oearly it can arise in Flu v Ha, but it's not really a .. natural~ process. HS, which is the one with the insertof the arginines required transmission from w;iterfowl to commercial poultry. In other words

it dis not occur in nature but only in a situation where intC.>tlse uansmission.

'"Thestability of the short motif suggests that p.:1thogf!nic:ity5Witc:hing may require specific conditions of intense selection pressure (svch as with high host den:;:ity) to boost se~on of the initial

mid-leogth HACS forms.•

e Andrew Rarnbaut 09.01

•• I agree, But for selection to work it needs variation. I.e., it needs the mutation to be thrown up occa~onally so that it can be selected for.

Robert Garry 09'.11

■ Yes indeed.

Conttibuting to my l\angop.

lb not two b.Jsic amino acids it's three plus the proline.

:.nd it's a perfect 12 base insertion -no mutations at all in lhc rest of 52 \.

So this n,ajor va,icition occurred without any other c.l\anges anywhere close til you go upstteam to the RBO • (nice wol'k K on the modcfing!).

For this to h.lve occurred in nature you have to posit the ex.ist.1nce of a Bat virus that is exactly like R.ltG13 .lnd nCov in all of S2 except that it has some variant of the polybasic cleavage domain.

Robert Garry ot.:z-s

■ Of course the hypothetic.JI virus wit~ the optimal furin-like site ,a;lso had to evolve a near perfect ROB that was a,s I( put it w.iis •Jock and loaded• to bind to hum.iin ACE.

~ Kristbn Andersen 11>13

!.r!IIII have some more analyses to look at late, today. Going to take a look at what happened to SARS.u it spread in humans vs what happened to it before. Preliminary, it seems like all cont.act residues

arc alraady mutated in nCoV, but rn.any/most of the oth<'rs that changed in humans during the SARS Cl)tdemic arc not. Not totally sure what to make of it. but that's both consistent with passage

and selection· but it probably tells us that we didn't have a bunch of missing chains in human:swhere it could haw picked up theACE2 mul.ations.

As to Trevor's al\31ysis. I looked at similar things a fow days .ago and saw the same• and got to the s.amc conclusion as this:

https://twltter.com/tf'Vfb/status/1224208100590096384?s .. 21

But the I realized . .actually no. not necesSJrily • unless it's highly obvious engineering those tYPes of analyses are no way near powered to detect a signal. Same for just looking at trees.

Robert Garry 10c1s

■ The full-length genome sequences had 99.8% homology to the human SCoV. which indicates that the human and animal SCoV·like viruses were closely related.

https:l/scief"Ke.s.ciel\Cet'l"lag.org/coott!'nl/302/5643/276

~ Science

Isolation and Characterization of Viruses Related to the SARS Coronavirus from

Animals in Southern Chil\3

A novel coronaviros (SCoV) Is the etiological agent of sC\lcrc acme respiratory

syndrome {SARSJ. SCoV·like viruses were isolated from Himalayan palm civets foulld

in a live-animal market in Guangdong, China. Evidence of virus infection was also

deteclOO in other a11imat.s (ioduding a raccooo dog. Nyctereutes procyonoides) and

in humans working at the s.Jme market. All the ,1nimal isolates retain a 29-mxleotide

seQuence tllat is not found in most human isolates. The detection of SCoV•like

viruses in small. live wikl mammals in a retail market indicates a route of interspecies

tra1lSmission.although the natural rC'Servoir is not known.

Oct 10tl\ 2003

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REV0002908

FeblU3JY3td, 2020 .,.

Robert Garry 1022

• Intilt ca,se of s.:1rs the isotation « ave<y(IQ>C progenitorvi1us from three pafl'n civt'ts. a raccoon d08;. and a O,inoe fe,ret badger happeoed quid:ly. Asimilarvirus wets circulating amongst sevctal

animJlsin the wild • Of they 311 got infected <,1tthe m3rkeL

Robert Garry 102,

■ fittps:K;our,...ls.plos.ocg/pl~thogens/artitfe?id•10.13711jour11Jl,ppJll006698 i thi1k this is ttie ~perycu want

~ jourM-l~.pbS.04'S

Discovery of a rich gene pool of bat SARS•relatedcoronaviruses provides new

iMig:htsinto th~ origin of SARS coronavirus

Author summ¥Y ln<re~sing evidence ~s been e.1thcred ro sovoort the ~t origin of

SARScorona virus (SARS-CoV) in the p~st decade. Ht.l\•,ever, ncoe of the currently

knownbat SARSr-CoVs is thOught to be the direct ancestor of SARS•CoV. Herein. we

report the identification of a d\rerse gro'-C) of bat SARSr·CoVs in a single <ave in

Yunnan, Chin.a Importantly, ;:1II of the buitfing l>locks of SARS•CoV genome, induding

the highly v,1ri,ble Sgene. ORJ8 :.nd ORf:3. cwld be found in the genomu of

difftrent SARSr·CoVstrain,s from this single kxatior\ Based on the analysis of full·

length genome sequences of the newly identified bJt SARSr-CoVs. Yle specu13teth.-lt

the dire-ctancititor of SA~•CoV m.rv ha\ll"ari~ ... Show more

lwllJIII tc>.:J1 FebruaryJ,d,2020vKrfstianAndorstn

Bf! Ye.ih, SARS seemed to ht1ve;, sign,iflcaitly more widespreJd reservoir • lateroo in the epidemic, 3dditional spillovers also OC<urrecl. ThJt may stiU be the c.-se with nCoV too. since it's a little early to

tell • no additional spilovers into humms for now though.

lotere,ungly, in u-.e:.Lruc.tu,e I·,ost specieS-,at.:, mi«, .. o(Jcivets are

paper on ncov 1rorn SafiC. they kX>k al coml).)\ibility of the ACE2 inte,Jclins mutd®os with J set 01 l)Otc,lti.ll ome, ,neOi..K.e)

ciut, and probably bats too. Ferrers is a maybe.

I think it might be HeI4 though/

Robert Garry 10,40

■ "I'm pretty >Ureby now they thinl I'm -11complete crad.pol."

Iihinle wQ'r• di~proving this hy1)0lhos.it. l.o,t of ,.d R;igs; .and no i1wont bo po«.itio to j)f'OY\IJ"M'tur:11" tt:1n,:rni11dot1 u,,til yo.1 find (QWr:il cfo<Qly rtbtod :inl~I viru(.0$ (>999Q. f 1>l'ttty suro w0<0 not

going to find theprogtnitorin ht.mans.

Obvio.is!y not possiblit to prove e-scape.

Robert Garry 1oso

■ Transmittinz a bat virus lik~ RatC13in Hela c:ellsand then asking your graduate studetlt to in~rt a fuM sit<' (she would havt-had to be taken literally not chanee 4 amino aicds but literaltv insert 4)

would get you there. II·s not crackpot to suagest this coukl have happened given the Gof research we know Is happening.

Robert Garry 1058

• for me proving •t1{1tur.,I" ev<>lution of the f-..-insite -.vouktrequi,e fin.ding sotl'le :inimot CoV "ith :i highly siniitior (identie.,I} S2:ind ~ever,i~I\ of the f\M'in site iMert • prefemlty .alle3S! o minim,11

deavage site R·X·X·R.

11WKristianAndersen 1t:St

!8 Yeah, !lgl'ecd on a.Uaccou,,u. I think we ca,,'t pl'OVe eithel' w&y, we Ol'lOnJy lav out whet we have learned al»ut the virus a,)d its cvolutbo. Makin& the de<l:sioo on what ~er\$ to bet~ mo)t likdy

~ena,io would have to be clone byottiers • we just netd to lay out the science. ArwJboy. is this virus irtcrc-sriog!

Robert Garry 13 53

■ tlttps:.Vwww.g10batt'1mcs.cr\1cootc-nt/lt76363.shtml

CB1lobaftimes.cn

Noc possible novel coronavirus engi\eered in I.lb: experts

The Claim that the r.ovel coron.-,virvs was engineered in a lab has been refuted

{350kB) •

l!ttps.,;k'www.(o,be-:>.ccm/site:s/vkt0<lato1stc-,/2020/02/02/oo•'-°'ooavUus•was•,1ot--ij@j @;&·pieu~·of•h'v•in•iVl3<.29tbec56cb

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ftttpJ/global.<hin1daity.com,cn/a/202002/02/WSSc36b2b7a31012821727432chtml

CD global.chinadaily.com.cn

Coronavirus conspiracydebunked byWuhan researcMr • Chinadaily.com.cn

A sdcntist fr0«i thcWu~n lnnitvte o( Virology of the Chinese Academy of Sc'c.nccs

hJsdebu,l<ed.t recerit conspiracy which tlJimed the novel coron.,virus WJ:S

manufactured and escaped from the insri:utt'smost adWnccd bloccmtainrnent facility.

(71 kB)•

I

REV0002909

~ Kristian Andersen 13:58 F-d>r\l.;iry

3rd. 2020 ...

la It's amazing that we actually have to counter the complete crackpot theory of HIV / SARS mutant virusC"S ...

Rob4!!rtGarry 13:59

■ Shi Zhcngli. a rC"Searcher from the institute. said on her social media oo Sunday the virus was the result of "nature punishing the uncivilized habits and customs of humans•, and she is willing to ~bet

my life that [the outbre;ik) has nothins to do with the l;ib.\*

Herc's a quote from inside the WIV.

I infor from thi'ii that ZhCilgli belieVC'ii that humans eating wild beasts is what lead to the current outb~ak..

Troe that the oCoV•HIV paper is just •complete crKkpot.•

How<!ver. I do think thal the credible scientists quoted are pefhaps overstating. No. not possible to go from SARS CoV to nCov by design.

Possible to go from RatG 13 or anQther 96% or better vin.is to something like nVN • yes.

r"I Eddie Holmes 14:2-"

,-..; I ;im disturbed by the fact that they cleared the fish m;irket so quiclcly. Surely, you'd at least take a sample from every animal in sight? And then they release these vague 'environmental s.1mpling'

resulls. What does that mean? At the very least a bloody big cock-up.

Robert Garry 14;29

■ Agreed. they found the 99.8% vin.i'Ses in the animal mark~t.

I

Big bloody cock-up for for sure -destroved any chance of llnding the intermediate animal or animals if they exjst at all. You have to wonder what the WIV sdentists were advising their governmenL

I'd have been screaming loudly to let me get in and sample everything with a lung.

And apparently at least one WIV scientist Zhengli believes that humans eating wild beasts is what lead to the current outbreak.

Robert ~rry 14:41 Fff>ruary3rd. 2020 "'

■ Aocf, precluding ask.ing the Question whether or not the market the type of environment were YoU cookl h.1veh.ld the intense selective p,essure required to generate .an optimal furin cleavage site,

Robert Garry 14A8

■ Note to self: coronavirus.cs $2 have one or two zinc binding dom.ains following the TM domain just like arenaVlrus.cs (except rcptareAavirv'i who stole their GP from filovirusesj.

r'II Eddie Holme:s !.S:35

,-; No way the selection could occur in lhc market. Too low a density of mammals: realty just small groups of 3·4 in cases..

Robert Garry 16:.18

■ That is what Ithought as weU. which begs the question where woukl you get intense enough transmission (like the pouHry farms for HS)to generate and pass on the furin site insertion?

• Andrew R.ambaut 17:09

•• That is the million dollar que5tion.

Although it may not be the $.Jme dynamic as poultry. It may just be an animal where the virus behaves very similarly to how it does in humans. Ferrets?

...ai Kristian Andersen 17:26

1.19I could believe ferrets. Baric's pape< atso suggest that the ACE2 mutations might be compatible with ferrets

Robert Garry 11::n

■ https://cn.wikipcdia.org/wild/Chinesc\_ferret-badger

tfl)l'Uil,Y ->ro.,lV,lU ...

\YI Wikipedia

Chinese ferret-badger

The Chinese ferrel-badger {Metog.c,te moschata). also known ~s the sm<1IHoothed

ferret-badger is a n"M!mber of the Mustelidae, and widely distributed in Southeast

Asia, It is listed as Least Concern on (he IUCN Red List and considered tolerant of

modified habitat.The Chinese ferret·badger is densely distributed mainly .:ic::ross areas

of Central to Southem China.

• Andrew Rambaut 17:33

I

4111■ https://cn.wikipcdia.org/wiki/Huanan\_Scafood\_Wholcsalc\_Mat1cet

\YI W1kipedla

Huanan Seafood Wholesale Market

The Huanan Seafood Wholesale M;irket (Chinese: ~$ffll1iP.~m'$). also known

as the Huanan SeMood Marktt is a live animal and seafood market in Jianghan Disttict.

Wuhan. Hutx,,; province. China. The market gained media attenlioo after the Workl

Health Organization was notified on 31 December 2019 of .an outb.-eak or pneumonia

in Wuhan. Of the initial 41 people hospitalised with p~monia who we<e idtntifted as

having Laboratory·conflrmcd 2019-nCoV infection by 2 January 2020. two-thirds mid

been exposed to the mar1c:et. The Ohlrket was closed on 1 January 2020 for sanitary

procedures and disinfection. 33 out of 585 animal spedm!fls taken from the mil'ket

showed evidence of 2019-nCoV.

Robert Garry 17::M

■ According to thcirt wiki arc in southern Chilla and hunted for their pelts, Test these people to seeif they have antibodies.

• Andrew Rambaut 17,34

•• Badger is a mustelid.

Robert Garry 17::Jj

• •33 out of 585 animal specimens taken from the mart<et show<."d evidence of 2019-nCoV.• Does anyone know what evidence -if seQuencc it should be out by now,

I

REV0002910

e Andrew Rambaut 17"9

•• Runny llOSes!

@:!)c.,

Robert ~rry t ?-40

■ C0t,1fdbe • ferreh with the t'lu look "'just'" like humans with the nu.

ltttps:.Vwww.naturc.oom/arti<lcsJ42S915a"Serologicaland virological studies ha\lC' indkated that Chinese ferret badgers (Mtfosalt mos<hota), masked palm civcts(Po.gt,no loMJta}and raccoon dogs

(Nyc;tcrcvtcs procyono;.le.s) c,n be infected v.-ith ~ vin.a, th.it is very ,imibr to SCV (ref. 31. Domcrti< (Alb Irving in th::cAmoy G;)rdcns .ip.irtmc;flt bl-o<k in I-long Kong, wh<:crc more th..in 100 rc,idcnt:i

contracttd SARS la.st .,ear. we~ also found to be infected v.ith SCV."

.. Nature

SARS vif\ls in(ectkm of ut..s a!ld fetreb

There is rt<YVIa choice of animal models for testing theraJX(.'s against the human virus.

" Nature

SARS virus infectiOn of cats and ferrets

There is now a choice of animal models for testing theraPcs against the human virus,

llifiMIKristian Andersen 17:46

la Barie has ttis intercstilg table with the coniact r~ichJts for the various spe<ies. I need to look at comp.ltibility of nCoV

:ic,cm)hot:020-02·0;,i,n 14-").11.png •

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..c. ti• ■

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J( J( 0 'I I(

-II ( 01>1

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...

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:.\_\_::!~!

\_.., KIO" 0111(

Robert G.ariy 1&1t

■ This is what that jnter.ction with s.ars v rbd looks like.

I

Fd>ruafY3rd. 2020 "

THe vellow sf)lieres are ACE 31. ;3, 38, 82 •nd 353.

THc red sphcresaroSARS V 472.479and 487

the pdb is 2AJF.

I

Possitic tomodd in nCoV•worth doing . ♦1581::¥1@

.,. Kri,-Nn Andernn 1&.20

ra Yeah, I'd ht interested in seting nCoVand RaTG13 binding toAC£2 from e.g., humans and bats. Night get toit later in lhcweck •definitely a fair bit of work to do ...

... EddieHolmes 18:28

~ The wiki into is wrong I bel~. According to the official newsagency re-port in EngliSh& Cl'incsc it 33 environment.al samplesthat tested PoSitivt, not anim~ls.An were from OM partitular part of

the market. Hard to kt1ow QJltc what this rreans.

Robert Garry 1&32

■ tilt~:Vse:.ience.stieneenag,o,g/conte"t/scii309/S742/18o4.full.()df

QG.t

Robert Garry t840

■ Not testing tM animals is definitety a crime against sdtnc:e, if not humanity.

REV0002911

........................ ........................

llf'!lilKristian Andersen 00-01 FttM'uary4th. 2020 "

f!a Alright, first attempt at creating the new summary. Please take a look and edit away. I closed access to the document. so @Eddie Holmes do VOtJhave a (new) gm.ail address I could share it with? I

suspect you mig:ht have a few opinions on this document .:

r,i Eddie Holmes 01-:N

,-.; Mygmail , I've edited the goog.le doc. Looks great. I think vou did right thing to makeit completely neutral scientiflcally. Good idea oot to mention all the other

anomalies .as this will rn.ake us look like loon$.. As it standsit is excellent basic science. which is a service in itself.

e Andrew Ramb.iut OLSO

.41111111

■ I agree. Excellent. Should Vff: add something .:ibout the possibility of these being adaptation to humans that have arisen post•zoonosis?

r'li Eddie Holmes 03'!,7

,-.; Y~. voocoukl potentially -:ldd a line saying that...although these ca-.;es ;;1r-eobvioosly missing.

One other thing that I've noticed I think. No more genomes coming out of \IVUhan. Correct?

r..• A A n

I

e Andrew R.arnb.aut 04.15 F"ebru.uy4th. 2020 ...

.41111111■ Yes. None since 4th Jan.

~ing0.Jl!M4)1"\8;"'

······••••••

ij

I

lj

r'lil Eddie Holmes 04:28

,-... E"itherGeorge is sitting on all the seq~ces because the CCOC are now completely in control. Of they've been told to stop generating the data. Either way, weird.

e Andrew Ramb.lut 04.59

.41111111■ Agreed. Interestingly Guangdong is happily sequencing away but t guessthe regions have autonomy.

e Andrew Rarnbaut 07.48

.41111111■ Hi all. I did a t>.tmore editing on the document to include a human .-dapution scenario that I think is important to raise (to coonter the 'OMG it is mutating' arguments). I also re-jigged it -so the

engineeringisnot one of the scenarios but is ru~ out explicitly.

~ Kristian Andersen 10, 12

f8 Excellent. Will go through again this morning.

Andrew, IN usknow if you need lcners of-support for this: https://mrc.ukri.org/funding/browsc/2019·ncov-rapid-respon-sc-call/2019-ncov-rapid-rc-sponse-call/

{l!ditectl

e Andrew R.ambaut 11 26

•• Everyone ~stalking about this but quite frankly I don't know what I would -spend the money on.

~ KrlstianAndersen 11:51

la Brer and pizza for the kmg nights in front of rhc computer?

r'li Eddie Holmes 15:37

,-.; Just think of how many spurious BLAST analyses you could do.

~ KristlanAndersen 15:59

~ To be fair. I just bought the man beer. so if he got the r»or'tl'y then maybe-he: could tcturn the favor and buy rne some beer for my blast ar..alyscs. Some very intctesting fCSults fr•otr1 blasting all the

nCoV ba-se-s individually· might be my best work to date.

Ffflrw,v 5th. 2020 "

e Andrew R.ambaut 02;28

41111■ I bet some of them match Ebola!

lr.!ilKristian Andersen 12:1S

la Hi @channel -had a Jock at the Pangolins and got excited about it. but docsn·t realty seem to change much In my analys.ls. It's true that one of the key residues (505) arc shared between rtCoV and

pan.go (and not bats). but the others are not. There are several other not-so-key residue-s that changed in SARS that are also marked in the alignment ifvoo want to take a Sook (the key ones .1re

labeled "Mut.ation• and the other not•so•key•but•changing on4;:s are labeled •stte:1. The not ~o key ones arc interesting bc<:ause they changed during the SARS epidemic and were involved in

various things. including immuoo selection· in nCoV these are very distinctly bat (and pango) but not hum.an. Screenshots and alignments attached· SARS Ubani is selected as the reference !.O

you'll see changes relative to that.

Eddie (and defmitely Bob .) I know you guys are Old Skool. but Gcneious realty is quite nice for viewing and annoial'ion (and creating!) alignments. Try it :: .

61\ies.

Alignment.png Key.pn.g •S proteins AA.g::eneious

I

1;; PNC -PNG z.,

•S prot~ins NT.geneious S proteins AA.fast4'.gz S proteins NT.~st-11.gz

T,> Glit;> G,ip

m m

REV0002912

Febrmiy Sth. 2020 ,.,

• Andrew Rambaut 12'19

•• Thisbid o1 looks like oonvcrgence to me (r(.oV shares with RaT13 as mvc:h as with the pangolins.\.

~ KrlHtan Andenen 12 2e

~ Agreed. Dowe know inyttfng about these P<1ngo sequene(S?Arri cell culture imolved-'? I w-s really hoping these guys'NOVld disprove the c:ell hypothesis by being (a) highlysimil.ar to nCoV.ancl (b)

11ot from ct.ltu~.

Robert Garry 1218

■ A2rtt. It's interestint that the Panaolh sewences were detected (and in dead arim3kl. Shows that there is a reStrvoirof ore-viouslyundetect~ drculation of Bat-like CoVs in mammals. But no

mo<e of a sinoking gun than RaTG13 as far as nO>V goes • not dose enough to be the progenitor nor locally dose enough to make a strong osc that it m~t SCfVt as a substrate to<a rccorrbinant

tllat leJ<I toncov.

ll,1il Kri«bn Andersen 12:30

rn Nope. Let's hope more sequences come out• would be so awesome to see ,m ~oV-like RBD <md turinsite, Would be critic.al evidence against cell culture hypothesis {which I'm stiU le;ming

towards).

Robert Garry 12 36

■ Definite lean for me too. Would buy Andrew a beer and Eddie a subscription to Ccncious. if Ron fouchier shares i:>reviou$.ly alluded to cell culture data showing cell culture pas~ produces a

I

furin site in a C<N.

Kristian Andersen t?-49

Mike Farzan said that the-v see futin sites in culture too. but I can't frnd any tapers on it! t'II Png him tomorrov, and a:sJdR01 day today ... ) (roiled)

RobertGarry nso

• Great • ask for data ....

Rebert Garry 1300

■ Ihope Fa:ian or Fovchie,h.,,e th6 dati. It would render the a.lreai:tv de;M;fbioengiooered scenario tot.tit-, Md completely dead.

g@7

It would Jlso mJ~e il strong ase tor the cell cultve/ac:x:ident.i1 esc.ipe modd,

tMil Kristian Andersen tS:57

f:ll Thi$ i1P<Cttv nifty,

hrti-.·//cov•elut' rv, gl:..:w: uk'#/c('f)l<'!t'f"n\rnt

Some of these m.,tations arc intu~ting • hJmanadaprlve mutations.. ..

~ Kristian Andersen 17.141

e£I Eddie's recent tree

II

II

FiX>fromiOS

POf

I

e Andrew Rambaut 18..-<II

•• For your amusement: https://ja,mestyonsweier.com/2020/02/02/moderatetr·strong-confirmation·of ·a·labo,atory•oritn-of •2019-ncm/

mjameslyon:swe.iler.com

Mode.rate-ly Strong Confirmation of a La.boratOJY Origin of 2019·nCoV

James Lyons·Weilet. PhD 2·2·2020Dr. f'llar'CWathe1et ccmmeoled that he wa~

p\lllled about my ~port of a )f)ikc protein gene homok>gou~ to part of the pShJttle·SN

vec;tor, given that spike gtyc;oproteins. ..

Feb ?tld, 2020(2781<8)•

I

Sec if you c.an work oot what he has done ~re. ♦l'iMl::I \ES

REV0002913

F'II Eddie Holmes 19:0S

,--; Kristian. 1 confused here. In the figure that I sent you· which is from the paper that Tommy Lam is writfng • the pango and nCoV seem to sh.arc a lot of the key sites.. But lhi.s ls not \Nhat you,

alignment shows, Correct? Does this include the pango sequence I sent you the other day? I don't think we are comparing the same things here. No cetl culture involved.

r,i Eddie Holmes 19:21

,-; I h.:ive Geoeious but I'm too old to deal with things that go out frame.

tl9iil Kristbn Andersen 19 S.l

lil!!I Let me look into this a little closer lomorrow. The online p.1ngo sequence hcls a tot of missing b.1ses, hence it w.lSn't included in the previous alignment. But JS I'm eyeballing it at the moment. I can

s~ it lining up better. I'll take a look tomOf'row .

... Eddie Holm~ 20:11

,...... Thanks. I'll get word more info from Tommy shortly• try andWQl'k out which $CC!ucncclO relate-$ to which virus in the tre-e. It ~ems that Pll and P2S w<!re scq1,1cnced by differentgroups(the one

on the SRA Is P1Land th.al from Tommy ls P2S). I think they are both have very slmflar RBDs to humans.

February 6th. 2020 ...

~ Kristian Andersen 01:<lO

I

~ :. See-ifyou can work out what he has done here,

I can't figure it out ... tell me

~~ 2rt-Plits Last~y3'V("arsat:o

... Eddie Holmes 02:0J

,-..; Tommy says that the key seqs are P376, P377 and P378, trom the SRA. and 'OurPangolin v2'. He merged them for some amfyses as they are very similar.

Pango madness. (1). The more divergent cluster in the tree arc from Guangxi. These-do not have 2019-nCoV like RBOs.The cluster closer to 2019·nCoV a,e from Guangdong (seq IDs a.bol/C), They

arevery similar to 2019-nCoV in RBO,sharing most of the key residues. Closer than RaTG13. Indeed, comSXJtatiofl.;,I docking analyses (Rosetta) shO\.vs thctt the pangolin ROB have similar high

binding .tffinity as 2019•nCoV ROB to human ACE2 {2). The-two Guangdong vir'UStS we~ ~qutnced by diffettnt gr0ups at diff ettnt times. No human cell culturt evolve. (3). The similarity betwttt"I

the RBD of the Guangdon.g pangolins and 2019-nCoV is onty at nonsvnonymous sites. No movement in a tree of synonymous srtes. So,convergeocc?How is all this explained? Remarkable that we

h3ve two clusters of panso viruses that are closely ret,1ted to 2019-nCoV but th.'lt differ so profoom:lly in the R8O.

e Andrew R.ambaut 09 ~

Al■ @Kristian do you mve a genome alignment of everything in Geneious with annotations?

I mean all the bJt SARS-r and the l).l!"lgolins?

I think I am going to go to the Wl-1O meeting ln Geneva ne.xt week (I was invited by the modelling group t am on). But it might be-good to see what crops up about all this.

ti,y KristianAndersen 11)()4

fa On my ageod.a today so I'll have that in a few hours

• Andrew Rambaut 10:08

I

•• Thanks. I feel I need to do a deep dive into it all but my current data sets are a mess.

~ Kristian Andersen 10-16

&1!11Agreed

Just remember• the P<)ngos are only Sand some very incomplete (which concerns me a bit • the one-5 th.lt are complete don't look like nCoV in the RBD, the ones that are incomplete do. I'm

worried about data quality here. but 111 look into it)

e Andrew R.tmbaut t0:24

•• l>erhaps @Eddie Holmes can pe-r'Suadc them to $,C(lucnce full genomes with some urgcney?

®~

Wlil Kristian Andersen 13.0S

~ I can't for the life of me get ,1 good alignment with those .additional pengos included ... They seem vc-ry low quality. I'll cootinuc ... For now. here are spike protein aligrvTicnts containing the bat.

pcngo. and some select human vin.ises. Changed the annotations to be more logi,cal too.

,.....

~ ali~nmcnt\_spike\_nt.fasta.gz

laGz:4p •

alignment\_spike\_nt.geneious

Zip

r'lil

,-;

Eddie Holmes 1s:16

There are whole genomes. I just sem vou S to make it easier, which clearly failed. I'll see if I c.in get all the seQuence data. I

Tr;mslat~ this

$.ele<:ted\_ROO-whole.fas

..,

>2e 19· nCoV \_E PI 482124 ISetacov /WUha.n/WI V04/ 2019( 2)

2 AAT TTTGGTGAAGTTTT'TAACGCCACCAGAftTG T1 TA TGCTTGGAACAGGAAGAGAA TTGCTGA rec-, Al AT AA r TCCGCA. AAG 1'GTT TCT

AJ f ACAAACTTGTGCCCT ff fGCA TCAGCAACTGTG TI A TTCTG TCA'IJTTCCAClTTT ATGGAG1'GccrAC lAAA1 TA

AATGATCICTGCTT1'ACTAATGTCTATGCAGATTCATlTGTAATTAGAGGIGATG.AAGTCAGACAAATCGCTCCAGGGC.AAACTGGAAA<iATTGCTGATTATAATTATAAATTAt.C/113ATGATTTTACAGGCTGCGTTATAGCTTGGAATTCTAACAATCTTGATlCTAAIJ

GTTGGIGGTAATTATAATTACC.TGT4TMATTGTTTAGGMGTC1'MTCTCAMCtTTTTGAGAGAGATATTTCAACTGMATCTATCMNCCC-GlAGCJ\CACCTTGTMTGGTGTTGAAGGTllTAATTGTTW.TTTCC:TTTACAATCATATGGTTTCCMCCCa=.crMT

GGTG T f(>(jTT ACCAACC,\ A6 T .\GT TTC TT

T .\CA4AGT AC TTT C TTTTG,AAC. T ACATC,CA(.C~GCAA.CTG

3 ,EPI4821l1 I8ftaCoY/bat/Vunnan/Ra TGl)/2013 I2813•87• 24( 2)

-1 MT A TTACAAACTT TGGTGAAC>TTTTTAACGCCACCACA CA6TT1 A TG<TTGG,IJ;C,¼AAAGAGAA tGTGTTGCTGA TA.lAT AA TT CC.ACTTCAT AAATGTT CCTACTMATT A

A TGTCCTTT TTCGCAT TT AGCAAC TT ,\CTCTGTCC T TTCTACCTTT A T<iGAGTGTCT

r'li Eddie Holmes 15:35

,-... Our Pangolin • Guangdong. GXP • Guang,d

~ Kristian Andersen 15:4~

fl!I Herc we go • I cleaned It up. Seems like we might have oursclves a pangolin recombinant ...

,\_.

I

alignment\_spike\_aa.geneiou:. r.. ~lignment\_spike\_aa.htsta.gz

• Z,p laGi1p

REV0002914

AJicnmmt.pne .. Ftbru.1iry 6th. 2020 ..,

~ Kristbn Andersen 1S:◄7 ra renamed the channel from -~•wuhan\_engincering• to •projcct•wuhan\_pangolin•

r-1 Edd.leHolmes 1S:!i0

,,....\_ Thanks! Take a look at those key sites.

~ Kristian Andersen 1s:s2

r.rJ Yeah-those are ttie ones in purple in the alignment above. Very similar. Still concerned about data Quality though as the sequences perfectly split on whether they're similar or not based on quality

• however, I assume that's b¢causl? they're from different groups. so we might C!xp(!Ct that

• Andrew Rambaut 16:09

•• I can't decide if RaT13 has a recombination with QHR63300.1 or nCoV with P377

• Andrew Rambaut 16 42

...

Ndlo ~,~in. i·• p;lrt of°"" u• tO\'edn; the liuh:in ,corcnW1NIL H.a;iplly for N, l ,..:is Ofl ~ extended fhh!nc t1"1p when it itar'tcd, io ! 111h~~ 11.11nyof tM inithl ~torte~. i!tlt 1'10t<Il'•

o.t,ck. ~M tr-yltt& to bi-h•lpfol.

t'• tryiric to chcl: o..it .t r"tl'IQr-th.tt"" tditor 1ot frc-, SOI.II'-(. --th,t th• US .JOY'"""'""t h tryine to stri01.1s))' inYHtiC•U th.fl pouibility thlt th nCoV ,~ lklt of th• W\INl'l

,11 COV1!1""n-:ient

Virus libor-.JtOI")' r.it~r th~l'I Oll't of ,11 wt Hr·bt.

And, if it vas -· would ther-e be ilin.)' wy to tell? (I M.ln, l usuu th• bb h,n ,11 l,11,rce libr,11,ry of c:orcn,11viruses, sonoe of wtitc:h Ulllt fro■ ani11,:1l ;,1~l•s. tf ,11l.:al>t•ch cot infected with

Ofle, I iti&init it would!'l't l>e VOl'Y dlff1t.-ent froi. OU that a r.tltt Nrlcet wro,..•r picked up ff"()■ th• s~ a!'li"al.)

Is ther'lt nythinc 1n th• s•(l'l.l•nces posted so hr tltilt suuuu tM virus h~s ~on r.-inl~bted by I\I.IM.n h~ds in ~ny VolYl (S.ql.l9fl<H fro■ 1nother v1Ns 1n,e1"1:•0, ddet1ons thn see. unllkel)'

to <KC:UI"b ri1m,1r1, ¥l)'t-Mn& lih th~tn

I

Th~s Donald Kc.Neil

• Andrew R.ambaut 10:49

•• I am thinking of just replying and saying lhal •1 sec nothing in the genome lhat would make me believe it has been gcmct'ically manipulated in a lab."' Seem reasonable? I don't want to say I won't say

anything.

RobertGany l&SO

• NYT serious • McNeil verv credible by like everv reporter can be mislead.

but by like every reporter

That's a good hon~st response.

WHO can't have its -special mrg fast enough.

• Andrew R.amb.aut 11:2,t

•• BcfO<C I could reply ...

Sil'l<e J lllt"Ote th•t, llic-h1rd (bright •~liil'lkl to H that the v1P"uS h 96.2 f)el"(e!'lt 10.l'ltiUl to bit ((M"01MY1rus ltiTG13, 11tuc-h~ S•id WU c-ollec.ted b)' Wuh,114lristltuu of virology in ,11 cave in

Y\lnMn 1n 200}, •ncl ttlH has bfen stor.d .tt th• instttvt, 11nc, thffl.

Riehl l'IOW, idtt1 tM ~nihble Nu, h• uys. tl'l•r• h no W)' to tell. 8ut ht l)Oinu out that S,,.flS got into N,W,i"' t.ti. first tiM in 2ee2 fro■~ Chet, ltld th HCOt'ld, third and f.cM.irt.h

tl••s frCNI labornory •ccidftlts in 2tel.

Oo you •&rH with th•t an.dyih?

I

♦SEMI::+!..&

REV0002915

fd>ruaiy6th. 2020 "

My reply:

I hcl\-. lOOi<.♦d •t th♦ C•!'oOf!t •1'16 t"-"• h ~Ulif'll I un Ht thclt woulc -,l(f • think tti•t it ti•$ bttn gtntdolly •,t.1tlP1,1hteC1.1M RclrGU vir1,1$ h inttt4 56$ idendol b11t t~,lt h •ct\lcllly

qunt oht.aint ill RWi vil"Us teNli. Tht VlNJS H••s tQ t>e e11Qlvtn1 •t ;bout clt • rate u abcut e. u: P'@t yur (and thclt is a reascn,tily avtNJt r-.at.t to, •n IINA virus) so tl'ln wci.ld be •t hut

49 ytar; of evolvUon to P,ve ;:r,4" diffcN:-'ICC. So Rat~U h not ;:r, due rd,Uvt to ~h• virv~ th,t jiap•d into lwa;MH to c.auH ttlh tpidttic.

a.Ill Kristun Anderstn 18 10

la Ijust got tlvee ell\Qils from him~ welt ..

;.r ,:r

r-'i Eddie Holme, 10;•1

~ I think the pangolin data is dean, although I will chcckcowragc lewis. Key thing• done by two groups a few months apart. Doyou think the simifar of the RBO to the Wuhan Sna<e Flu vinn is

recombination o, con\'etgence? So halt! to tell.

c.tn·t belle'Je \hat the ICTV (UCI not preprint their papet.

◄l'ii§l::4HU

Robert Garry 18S9

■ W~ should problibly put soine ~Hort into fieurineout th~ responses to the$t' QutMtions.

Andrew's response is <redible omd correct. but is not going to ~tisfy all the repone<s.

e Andrew Rambaut 19:'(IJ

•• Trve but I 3m happy if I am quoted .ts •t le.l$t a semi-sane voice.

li'IJillil 1,::02

Kristi.in Andeuc:n

f!a In just goin.c to stick to wh.it we knov., • reservoir• bJ!s ~nd defmitetv nothing to do with previous lab strain

e Andrew Rambaut 1t•2

411

■ More questions I,om Oon,;,ld:

Robert Garry 1902

■ I think t-h.3t you would ,ec dc.3r ,ig,nol$ of rccombin.:,tion Ot tn0$.3X:ism,but I'm lc0$t qu-,lif'tcd to judg:e this .

I

e Andrew Ram~ot J9i12

411111

■ Leave a bit of CRISPRtn your genome by accident? ♦IHMl::l·-914

Robert Garry 1903

■ 5onctic m,3.nipul.ation loavo ,i3na1uros in a virusN0

e Andrtw Ramb3ut 19;03

•• Exact!{. TM is what I said. CRISPR just cuts the DNA/RNA

Robert Garry tto<

■ No • YoU ccvld p1,1t th,e h.lrin site in very cle;,nly.

e Andrew Rambaut 19:-04

•• Yes. Bvt Id dn't 5.lYthJt.

Robert Garry 190S

■ No• it would not pick up the c.ell ONA

• Andrew Ramb3ut 19-%

•• Hereiswhat I replied:

! • not .t hi, v.!.rologht but •

Febru:uy 6th. 2020 '"'

n,.,,.. h ~t cotnc t~ ~ slc<1n11res of th,at type • ,tt viNs c•~ is v•ry <~•ct 111d e>u~MOl.ls btu will disrupt it. Also tM ce,o.M h ltHA so Mo\ is n.ot CQ1f\Cto be il'lserod. c1USPt h

bad<.ally 11s•d to Cf,ltON.A(()It' flltA) .at vfl"),' $04CUic k>otlion$ S.11)'CM.IO!\ ~d biti 1n Of" l'fOh« t....\_. tut ...,t 'IOU would ~ 1n h tll♦ u .. blt (l'f)ft .anot►♦I' v1r1,1s(I .9., O♦l'l'l.aos s~p in .a

a•n• ff'Off,nothtr viru, • •lthCll&h 1t wovU pr'o»bh' b9 • rd•ttd vir1,1$).

lit!\*" re-pllotlna in th•Y Qtt rt"<O!llbi11•wit, othtt' vir1.1su th•t .,... donly reht-4 bvt. h h lik• ~inc ('f9hctd 111hllUk♦ (uU♦d l!Molop.i, f'tcollbln•tion). e.>dc.aUy it h f'fpbditi °"'

,t.-.\ck of e,en,or,e ...,u, ,e11Ktly \ke •-atrf/1;-ch o-f t•• otti@r V-i!'U\_. (dthot.cf, h •II)' ,ont'!ljn cliH,erenctf in the e11•ct .\_.q....,.<e). Thi• h e"•<tly ttiot ,\_ u can hf#f>t" in n•t1,1re wh,,tn • k01t h

infe<tt-d wl.th tl.-o diffel"fflt vil"\lscu cf tlw:I so•• ty.,-• thay un genet.)tct aouiu. gcnoocs. The ~ diffel"fflt thlt t'IIIO v1ru~s .," the bu Hlutly the resu:ting vlna •,..t!l '9110f'k·.

> Or un it i•piy thn tt·s been circubthg 1n t!UNu for 48 yurs, w1thcut uusing notiuble sy«ptoes, Wt p!d:ed up sc«e scrt: of viniltn<e Nt.lt1'3f'I N!<ently? (rd !$ th;it likdyl)

Vft')' ul'lltk!ly~ r thlrt: (both b1ts), • )l.lffl froa • ~-hunan anJ•al 1S .u<I' .Of'♦ pl~usJble as \ilt kl\Olilth♦ v1~Sf1 •re out tiler. and tt ~s h~pp,t"led bttor.. SAits was U&:hlJ p,t~el'Uc wt\~ 1t

]U~ fra-~Mt:•U•

REV0002916

Ftbn.l.,ry6th.2020,.,

Robert Garry 1909

■ Youun also synthesize bitsof the genes dcnovowithpcrl«.t precision then add them bad: in withoUl a t,;x:c.

Ancl, occellent r~ponse-s Andrew. You're doing much better than I wolkl.

e And~~m~vt i,.u

•• True (but you are still going to get the sequence from somewhere~ unk'Ss it is very short).

Robert Garry 1924

■ Im thinlcingmos:ly about ttlc PRRAtogencrate the ftltin sile. RC1ativelycasy toctop 12 bases in.

The pro line b the hans·up • why add th<1t? Makes me think the ccll culture pa$sa,s;C sccnarioi$ p0$$ibklprob.lbly •s$uming this h<1s in fact been observed before by F<1n<1nand fo1Khier.

• Andrew fbmb3ut 19-54

I

•• Yes. I am Qllite convinced it has been put there byevolution(whcthCf natural selection or artificial).

I haven't got the paper yet. Killing me.

Uf Kf'I.Sl1anA11det$ell

Oh boy ... what'sthe m'lmc??

And foe Don• I gotta say,he pretty muchnailedit. Let's not tell him

~ell it) i l),)l)tl· 2020-1'1,UUfC tnedlcii'lc·S)r!llti,n.il otigin Feb dth, 2020

Apparently the manuscript i5still being fma1ised. It ,.v;ube preprinted and sent to the WHO at the same time

A Eddie: Hotm<:~

can't believe that Ute IClV did not prep(i1\t their pai,e(.

Posad In i l)):>e:r•202l>n.1turt\_m«tk•N?-Pl'QXlmal.on,lntth. 2020

kb

Robert Garry 11~d

• l'vel<nownOon for 30v~rs. First time my work l'n3dethe front page of NVTimes. I sa,whim;1t T,op Med meeting a, few morths ago. V~sma,rt rn;in • don'tqoiteknowwher he is goi~ to go with

this• curioos as to the high in the USC is.

tlis source. It would be prudent to continue to pre·think res1)0flses.

ldo like Wuhan SlklkeOu virus fct thel\ameBTW.

I

loo bW thEY dldn't test tvnle cocton !Mge.

Then it could be Wuh~n Turtlo F111 virus WTFV

G½)@;

r'W Eddie HofmM 1':49

,,....\_ Nailedit.

AOOrew• U1a1\ks! Important typo.

~ Kristian Andersen 20.28

&\9 My drafted reotv to Doo. I'll chew on it a bit more. but (emme koow if y0u have any suD?esttOos..

n,•• cocxl \o ht.or ,...\_ ,-, .,.,. Y•• l of w .. ,. •• ,.\_.,. o..r C"'ut (c,.,...,.. .. tj;q,nt, •bovt zii.. •""' ,1>oh. 1t'• .,. i"t•,.•"ti"f .\_,...tiO" Y°""'rc •~ki..."'f• lut t.',. •\*"•id l •ifh\ n9t be thoot b•ot

~rscn to ,nswr, u "• att 110stly lookina at "'"at's roina on d,rina th• 9c,id.-ic (not befol"e). Hostly, unless tfl• viN.s us , roll:, obvious r.cOllblnant virus, I'n not lluit• sur-9 llhat •

•irw> (,'<lft c .. lt,,,-e ¥> •" t,ne.....,.dhu t.ou wo.,H lool Uk• • I th.ll\lc tl.,.y'" 9'M1b•bly be itdhti~guhhblc.

l. A lot c,( t~ (OilSjlil'<J()' tl•f'Ql'h> ....... t,:1lklflg .oOO..t lt1h tlelfl& .. 1\t@r'" 1.ot, >ll"illl'I th<l't had p,'•lll(kl>))' t.,f'(l,fl p,"Wu<~ (N•t ........ ~lClflt pap,ot<") Q<' J,(a@ flol!>oi'~(~C,lr,••t. ll'l'.)I! ~ .,,. ..

<lt'.-OStNrtf.-oly f.lla -wt would hJiV♦ been ablt' to ouUy i:1<k tn.,t UJ tf that ~Nt t"t.e c.'li.e, ~VOi' it h not.

I

2. n-. virus is highly r'tLlhd to t>.t SAllS·lih con,,,.-virus•~ sow on vitfl strong rvit-erce sty th.11 th• r•urvoti-ho•t 1S also• b4t. lihly tMr• w-u •" -'ll!llifyt•g. ho,t involv+d ~fo~ tflit

V1t'1.1$ Cot lfltO /11,1,1\•M, 01": we, ®fl't >M lcllOWl(IUt lt ■lCl'tt l)t,. 1·• nre tl'ert'S • lot Of 11WUt1CilUOfl$ l('lng on •a.o•tH1f1 tfl.tt f!)(,)(t quUUOf'I,

3. A$ ~ Nnt1on, wt <♦n ch•rly Ht fro,,. ttl♦ i♦queeo d~• prod\lcec $oO hr ttl•t th, 1ntt"OC11J<tlonuto tt4> hUl\ltl popuht1Qn v.s a s1ngl• ev♦nt. ThJs cou!d Uttllfl' bt froa • $lng\_ht 1nf♦Clitd

ho5t to • ~inglt mll!l..n, or a s.Nll da5tcr of h)$t5 :nto a $.Nll duster-cf ~ple. 'lh• vtrn Ms thtn be-m $p,.:idin& flun..n to hurwn ever 5inn.

Robert Garry 20.31

■ PIich per~ rcspons~-As I'm suf'() y¢u'II know 9,r"~ht is tho ai.•vwho think$ Yoshi ~nd tho of GO!= rosoi«t-r( 1hovld be locked 1.1p'Mth tho key thrown :.w.-ty. A liH-lo kno~cdg:~ boi~ tho most (fane;i,

ous thing, I suspect Ebight (i'm working with a bit of historitJI eXPerieocel i► goirtt to fi..a,t-outsay this isfor sure a 13bescape•not:unlike the unde<belly a,tide. Reporters aSde I do not think Jnyof

thisi:Sgoing awa·,.

~ Kristian Andersen 20.37

!a Aer~d • this'll amplrfyt::Nerthc-~xt couple of W('eks. I just wish there was a way to condusively say one or thC>o;her. but withooi th3t inte,mcdiate host or W!ry earlier cases.. thM!'s just no tcUire

I

IMO. Which all means it's back to ()S)inions• aod hoocs-tly, for this type of qucs-tion I don't tlilnk opinions arc helpful• u,kss they have somcdam!l strong science bchil'ld 1he-m.

Robert Garry 2040

■ -So. he 31'S~ed, it could h.l)ve ente,ed hum::ir.s froM the-cove in Y1..nMn or 01\0there.3ve.or o ...vetm:il'ket. Or-.oltern:.tivtly. it couldh:iveesuped into o humo11 from thebb"

Threehypothew.s here.

1. not likely a OOtvirus right into a hi.ma,,-couklhavehappcn long ago but not so likely.

2.We:t market •<:kmaybe an intennediatc host. I think pangolin virusei s.equeoces still too far af1eld but cou\j be patt of an animal circulation that ge,,erate-d the virus.

3. l~b passage I'm open to i:llld c;in't di$C::Ount Either furin sles have been generated Q.' they havf;n't. If they have I'm suspicioos ol 1.1b

• thilt just bcciuse I don't know the data 1nd few others <10.

ocape. but nol concluslve <videt\oCe. If fu,'ln sites have 1'10l b~n ~netued on eel cultvfe passive, then we!'~ looldng at eitll<t a long circula~o ot a very i,,tens.e clrculedo,, in eilhet h1.11nanso,

~nimals.

REV0002917

The,e Jre obviously other ix>ssib1ities including lab pJSsage combined with some ill considered GOF rese.trch.

r, Eddie Holmes 20:51

,...\_ Yes, its going to blow.HefKe why JeranyvQnts is thiric.ing ibout putting sometllng ollt. H(:flce the toned d:>wn versico I ius'l sen: him

Robert Ga<ry '2.0:Sl

■ The public sp.1teis not the pl3ee to discuss this, which WHO sh<luld be aw~e of [re.1li;iing th.lt in itself will pour gas on che fire].

r-w[ddit:Holmc.-s 20:SI

,...-; I agret Bob. Very tricky.

e Andrew Rambaut 21'.'03

•• Reme1nber when durin;: the swi.ne flu outbre;:ikAdrian Gibbs suggested it Wis .J lab escape? C3used J huge shit sflow.

lll!ill Krbdan Andeuen 21:0-1

~ AOOreN·it's2amm;:in...

Adrian Gibbs

Ge-e. I just googkd that • what a shit show(and I'm not quite surehow the l'c<:k he coukl get to that condumn!

~ Eddie Holmes 21:J?

~ He's an arse. Unfortu~tt-ly, alocal arst-.

Robert Garry 2309

■ lttps:Uwww.vox,om/llJI\Jre•perfect/2019 /3/20/18260Q69/de.;dly-p.1thogens-,,;cope•l;,b•smalt,ox•bkd•nu

VOX

How deadly patho,:en.c; have escaped the I.ab -over and over again

Research i1llo dangerousvirustS and bacreria isil'nJ)O(tant but for the dt?adlies!

~tllOgens. it·s not ctear the beoer1ts arc wOf'th tl'IC r1sk.s.

I

M;,r 20th. 2019 (S7 k8) •

Agree that the Gibbs rtooscnse was just thal. But $.lylrg it can't ~er happen and should be diml'Sscd out of handis also irrcsponsble. 0McN sakl three timei SAR$V escaped lab • this article says

six times.

• Andrew Rambaut 06·32

•• tittp://virologicJI.QfC/Utacking•rumon'Of•a·suspicious·origin·of·ncov2019/384

Q Virologkal

Tadding Rumors of a Suspicious O,tin of nCoV2019

I h.r,e been privately dealing with rumors and inquiries, foclJSed on the RRAR

potential furin c&e.rvase site. that nCoV2019 may ha.,e a suspicious oriiin as an

eng neertd. taboratory•gtnerat~ virus either xddentally or deUberatetyreleast:din

the area ot the worian searooo andanimal market. The pubncaoonot the highly

simlar RiTG13 seqt.tenceabo~lt a week ago has tueled this type of Sl>CQ.llation.As I

havt told people privately. I see no evidence at all to support suc-h adaim. In sharp

co~a ...

Fd>Tch.2020

Robert G;irry oe:l8

■ Bill Gallaher did the alignment with Ra!Gt3 yesterday afternoon Jnd emailed meabou; 4prn literally unde<the tide "Oh cr(lp." His initial thought \\laS l:iowe.,pon.I told him I c;outdnot Qlk about

it. butth.:i,t '0th.er$." h:d notlcc-d .:ind ~row::itkinson t. Homu!;lh~vothe.,writt~n lhii p~l. But~ii,a:, !l:n"Otl guy hcblkc.-d hin'liolf tx.ck f,om tho btOwo:>,:onthins. To hi$. c-tcdit ho pickodup on

thewtirdness of the Pf'Oline and something that I hadn't noticed. that being that the insert is "out of fume.• N-ot sure that virologicalwas ever intended for this type of discourse.

1till woncl~1ing if the 99% (or m<n} Wuhan pangolin flu virus has the-furin site or somtthtng Ilk~it. Also vt-ry curiousabut the O·link~ glycais.

Robert Garry 0930

■ littps·//www nrdc org/(">q)(>rti/cllv•p,eppcr/nrdc•.md•.,\_1ic,1:,suc;, ti'ump idministr.iition~prot«r•p.iingofins

I

REV0002918

" NRDC

Febru;uy 7th, 2020 ..,.

NRDC and Allies Sue Trump Admininrnion to Protect Pangolins

The illegal ·wildlife trade is pushing pangolin.s toward extinction. The-administtation

must use the Endang<.>1ed

Species Act to save them.(221 kB)•

Two weeks ago the Tn,1mp ;idmin was sued (o stop importation ot pangolin parts into the US.

09:31 Soroo: good info in this arridc.

rnter'Cstedin which species of paniotin has the-99% virus,

The Suncb pangoUn ctpparently carrying two fairly divergent lineages and different lineage from the 99% virus.

Also ro,-.sick!< that US imports meat and scales. so not infectious.

Robert Garry u>.07

■ To the point of the live .anim.-.t trade. With so milny different isolates does seem likety this is resident in p;mgolins, but. ..

Is there a bat virus or viruses also doscr and seeding parigotins and perhaps other animals? Or Is the pangolin sustaining this virus in It's 0""1l popuf.ation? Not sure the situation with SARS·CoV-1

provides definitive guidance on this.

wJeremywants us to publish our rcoort somewhere. Thoughts?~

Ithink it's really importanl to get the pangolin sequence first (Iassume they haven't sharedthe FASTAfile yet).

0 &;

The implicatioosof a 99% ~milarity and a 99.8% s.imilarity ar'C pretty pt0foundand at leastwould dramatically alter the discussion.

pretty profoundly different

Robttt Garry t0:57

■ I suppose could start revising the white paper with the expectation that the 99% pangolin sequencewilt appear in the near term.

I

• Andrew Rambaut 11:20

•• It all dependson the furin site • a pangolin with turin insertion woukl kill the passaging theory (whatever the distaoce). Without an insert, the closer it is the more likely the passaging theory

becomes.

GJ)rg;

F'II Eddie Holmes 17:53

~ SARS•CoV•2 is a good choice. Completely agree about the pangolin+ furin insertion thooty. l thiok we haveto wail fot this. Woukt be daft to have a paper out th('re saying that passage is possible

and they then show the pangolinhas the insertion.

~ Kristian Andersen 17·55

r;a logically SARS-CoV-2isgood. but I do have to wonder what the Chlnc-sc will think about that name given all the stigma around ~SARs•.I'm not su,c they want another one of those, so definitely

important they're consultant (I'd be ok.-y with not getting all l.S billion of themon boord though ... ),

Somepotential fun for the weekend -alignment of relevant ACE2 re-ceptors. I was trying to get a sense of how similarpangolin ACE2s.were to hurnan aOO whether replicationin that host could

~ad to a receptor that's quite finely tuned to the humanreceptor. Not very clear chat that's the case.but I'll play around with thi5 a bit. Manis javinica • pango

2'11n.

ACE2Receptors.geneious ~ ACE2.pn,g

• z .. PNG

r'II EddieHolmes 18:11

I

"""1 China will HATEit. Tommyreckons he has data th?it sho'ws that the pangovirvs will do well with ACE2.

c::v

rt

F~ruary 8th, 2020 .,.

r'I EddieHolm~ 00:34

,....\_ Some news from on the ground in ChiN: they have samplesf<omWuhan for sequencing but becausethecity is scaled they cc1n'tget themout for NGS.Makes sense. Keepto yourself.

• Andrew Ramb.aut0J·l4

.a■ The civet (Paguma) has that bit from residue 41 onwardthat is reallysimilar to the the primates.

Robert Garry 08-09

■ o they reallywanl to publishfusl in Chine:se?Any change of getting Nature/Jeremyinvolvedwith the Southern Ag University woho have lhe 99% paogolin s.equel\Ce?Offer thetn a Nature pa~r

(heck. offer them the cove<) in exchange for the sequence. we·11 review .1nd"help• them edit. the put thewhite paper up as an editorial. D

Sooy keep hitting return

Dothey really want to publish first in Chinese? Any chance of getting N;)ture/Jeremy involved with the Southern AgUniversity with the 999' pangolin ~Quence? Offer them a Nature paper {hell,

offer them the covN) in exchange for the ~quenc@. W@'ll reviewand1lelp• them edit. th@ put the white paper up as an editorial.

e Andrew IQmb.lut 08 30

•• ~Y is.aware of the importanct'c' of the pang99. I think we should get our report into apa~r ready format (wt'c'need a fowdet.:1ils.and numbers). Eddie has also tried to contact theauthorS as

wcU. A co-publication may be a good idea -Nature would probably accept a bilck•to-ba<:k pair· or our report could be a commentary.

Qucsrion from Patrick Vallance and kfcmy -docs the cxSStcnceof the glycansites be used to s.aythey evotvcd in the presenceof an immune system?

Even if chey did ic wouldn't rule out a se<ial passaging in animalslike Ron's HSNl paper. I guess?(«-tcdl

REV0002919

Robert G.arry OS43 Fi?bru.aiy8th. 2020 "'

■ I'd ,av the ('Xi.stanceof thoc:-g;IYt:ans is ~ettv strore C!'Vidctlccof evolution in the presence of an immune system. I don't ,hink it is random chance since the g.l)onsaf)P<:'., in other bc:tac:oronavinncs

that "evolve" a fuin site,eg MHV and HKUl. MHV and HKU1 alro simo.lt;ine<:>ust( a variable .:trd sometimes large patch ot O•linked atvcans at the to? of the prdusicn {virion) form of the

evr:J:ve

spike. Seems pretty dtar this is immure b.ased setection all around tom~.

Yes serial p;,s~ge in anim3f-s wo'-'<.I do the SJme thins, There are i couple Po1SSage ., chicken p.1pers • the furill siteappe.rs insteps.

of H5Nl

Hopefully the pangolin 9996 CoVshov.s up with a furin site if not as And,cw said passage becomes more likely.

If this is eoinz high profile we need to add a few things.

A diagram outlining the three scenarios wiU-. cartoons of bats and pangolins. Don't ma~ the tell culture pas1age scientist look asi,in (bvt maybe resemble an Ego guy). Could even have a

bioweapon sc:.enirio \'liith a big X.

Maybe some sort of diagram of the overalJ scikemodd • Kristian made a pdb. and so dd I so can do this pointingg out the hlrin sii:e and o gl'ycan if this sounds like a possibilitv.

• Andrew Rambaut 01:J;)l

•• I hav<: created a copv of thcteJ)O(I to tum into S<>mctt,;ng publisroblc: https:Udocs.googl<>.com/documtnt/d/14Hl2ltdEvXQSXB8DC2KwH>Stl(flyMdKWdMZGXXbd2z8/c &) €) .:, !J

01:s2 W~ need a cartOl'l pkture of Peter Oaszak to use in all tht 6gures.

I don't think we should go anywhere near biowe.ipons • exdJding lab constructs is sufficient.

I

It might be a good idea to nailtht Lyons-Weiler stuff without ment'ioning it ex,plid.ly • Le., saythen?: is ro evidenc~ of inserrioos or recombinat'10n rrom ou,er k00!/\1' viruses (inc:ludng SARS). The

entire r£oV genome is descended from .a put..ative conimon anceitor with R~TGU.

Robort Garry OCI51 l=eb~ry 8th. 2020 "'

■ Stating theobviws: When !ht p;angoUn99% sequence com!'S we•re{a.nd nobody better) are going to ha~ to evahate whether this jumped straight into people. We kno\\l the number of mutations

from the SARS·CoV-1 market animals to people. ls this in tl'c same range 0<docs the Jxibgolin virus have too marry mutations (incuding °'not the furin or r'l'VJCin)

to be the immediate progenitor?

Will need lo includer>erhilD'iin adi.1gram..

Rob<>rtG.>tty 0903

■ dose enough?

I

• Andrew Ramb>ut 09"4

•• Tlla1 will (SQ.Not lmpl}ing anything al>Out nef¥1oos gctngs on.

J.8tQ<>d.I W3S thinking of doing :1quicli: an:alysis to esriinate the due of the common ;1,nc:esto,with R.3TG13b,ufXI on :atc.)SOMblc range> of r)tes. We could then reverse th.:at:ind give the ex,cctC!d

11umberof substitutions for a recent common ancesto, • although I am not $Ure v.e knQw how rewntty ;i nCoV•pang99 MRCA would need to be. l" divergence would inpty about S years back in

tim~ (m.inimum • given currtnt ncov rate estimatts). Sul we wouldn't txpttl UC'ffi it was ba>iCallyin \'\'uh.an market.

to gtt t'l $i! errsr:12,

RObert Garry ouo

■ Perfect

Robert Garry 09-11

■ I could see the o:her p,:insoin sequences f-.ictoring in 3$ well. If tt-ey are closer in the RBD • Jnd as Kristian is teaching us they're petty damn close. and pans99 is closer elsewhere ex.cept in the

bindi~ domain thre yOtt cruld havl? a recombinant. Stlould be "'str.1iJl:htfOf'Ward"' comes..

ot not to rule thii out once p,:•u·ut99

Yeah• big dtterrce in implic:atioris between 99.0and 99.89'. If I h.id to guess I'd SJY ;sc1oser to the fonneror else we'd be hearin&howpang9? w.asne~rly 100%simil¥,

e Andrew Rambaut 09'.32

•• Esrim~tes of the date of common ancestor of nCoV and 8aTG13 .1ssuming a rate of le·3 (left) and0.5e-3 (ri.ght)

I

9S% credible inltMIS:

rate le·3: 1982.'271. 1997.564

mte 0Se·3: 1947.6461, l97&.0608

So basi~llv not more tec.cntlythan 1997

e Andrtw Rambaut 0?:43

411111@Robe-rt to Jeremy. He asks if it is OK to forward that to the whole group? looitcd)

■ Garry • I forwarded y()tlf' reply about the g1'{can.s

Robert Gany ot.SS

■ sure!

Robert Garry 12.◄2

■ ,;nyonewant totakeas~batTonyFauc:i

squestion?

•■221. ..ma..2

I

REV0002920

• AndrewRambaut 12,)S Fd>ru.ary8th.2020"

•• I S,1A!$iLileWnJ)fe a1\5'ftt:r' i~ oo • tllete is no cliffe<e,x.ebetweeo a •l.ftl.l'itl infect100 .lllCI a w~s;.ise<ii,,recuon.You could argut the lf.ln:,,ini:,5iQo 001,ueoeck mig,I,t be latgt<?

--;:::\_ \_\_\_\_\_\_\_\_

Rob4trt G.:.rry HOl

■ Well •I alreadysentan answer• not incompatiblewithwha1vou're sa.,;ng • n thelabwu canovercomethebottfeneck.

Great Cooking figure!

Robert Garry 1321

■ ~ttos:Vwww.blxcomin,w</wood·S1429400

BBC • ac:toal reporting• at k!ast they 1.6U3lly try • we h;1ve very little of that ett in the VS.

Robert Garry 14M

■ Comment$• as predic:ted • by RonFoochieruponthe email

r1I Eddie Holme~ 1S:J2

,-\_ Crap comment$.-.basic.ally ju$t s.wingit c:an't be lrue.

AliLII.J$!5&L

• AndrewRambaut t>:43 r.ebrwry8th.2020 ..

•• Ye:s.Conflating the absence of ~en(e (passaging)with actual e-1idence against (engineering.).

Argument<!boutttle «ner viruses Is racue

RolM:rt C3rry 15

◄

7

■ Ag<e<!d

IIPIIJKristian Andersen 15:53

~ Super frustralin,g conmM!nb. To Ron·s "As f:ir a~I arn aw-.are, no labC>rdtory ha~ \VOJkcd on pa½aging the pangolin·origiJ1 virus. lht! bat ·CoV RaTG 13. or aoc:nhe: <.losetyrdatetl virus or ha:J accbs to it

11riorto the outbreak"• not only has this been done. it"s spetifically being done in Wuhan. In BSL·2. Th,1t in itself means that we can't just dis,niss a lab theory off hand bvsa-ving "not c:,<>ssibfe".

That

would be very foolhardy.

~ Krlstun Andersen 1604

f!ll The furin link keeps bug.gins: me too• I can't find any good refereocec; on it in the published litP.rature for CoVs. When I asked Mike. he fnked to this p;.lper. v.tlich doesn't realv describe it either:

httpdjvi.asm.org/coot•nt/79/22/14451?ijkoy•709••Sd•9513<,80f42db103•cl9b539..Slcc350b&ktytyp,2•tf\_ipS<,csh>

~ Joumal ofVlrology

M111ine1CoromvinK with::iin £xtqndii,d Mod Sbngct ~e1-c; Mqp::iir::iin S.1lbto::1ic. ::iin fnhy

Receptor

Ont( a relatively few mutations In its spike pro~ein a!IO\v the murine coronavirus to

swi:ch from a murintNestric:ted tropism to an ext~ed host range by being

pass.)3edin vitro. Ole SI.X'.'hvirus that W8 Sludied had acquired two putative-heparan

sulfate-binding ,itc, while pn:·)erving another lite in the turin·cleav,ge motif. The

,adaptatfonof the virus through the useof heparan sulfate as an attachmcnt/ert.ry

recepto,was demonstfated by ir,creased hepa,in binding as wtll as by inhibition of

infection chro4.1gh tre3trn<'nt of ce-lJsand the virus with hep.irinue :ird hep.3rin.

respecti~ty.

Nov I 5th. 2005

Robert Garry 1606

■ Kristian yoo wereon the NASHv1 call I think• who wasit Uut volunte(fed that furin sites appeal' if you passage ON in culture?

• Andrew Rambaut 16:19

•• @Kristian With 1esp&;t to this •

As to publhhinc thh doc...nt !n, journ,1 1 t ,a cu,,..ntly not in f,vor-cf dohg so. l tMH•-,. th,1t publhhin& sOMthing that h optn.ended co,ild b1clcfit• illt thh ~uge. I tM.nk it',

iltJ)Ort;)nt th.it i.~ try to g.,tficr .additiOl"l.>l o-vidm<e • 1ndudini .,..,.,itinc or the ;,.>~olin viN~ uquen<U a.rd further :.c,-utini:e die hr!.n dC!,>,\':l,ie site ;)n~ O,link~ ityuu • befoN

I

!>'lblhhtnc. that Wil)' .... c~ (tio,.fvlly) COM cul Nltl SOl!le Stf'O~ (<lfduilve 'lUUl'itl!ts tNl illr-t bastd Ort lhll bht <1,u ... hav• access to. l (lo,'t t'.\lnk.,. .,.. lMl"t )'•t.

What do ycu think we should do?

~n.i.>ory 8th. 2020 ,.,

What do you think we should do?

ll9il KristianAndersen 16:21

ra We should all just st.ay on Slack. that's what we should do • ind ll:)t use email ':.: Chec:k myothe-e-mai1 . I deflni~ely think we should move towards publication and crtate a ~parate docume-nt

tocused on that. but I think it's too ea11y at the moment

Otw • ~ry nrons cornmcnh from A+E here• it's unbclievi'!~ how conllktcd Roni,-.

Robert Garry 1630

■ We nQ.w ha•te (and we will get more) the pangolin data{Edd"e hasl we think we can tie :his up even righter wth th? next iteration and make a conclusive state-mern which will then be the go to

scientific~tatC(nl'1ll lOrCfCt to.

£ddic.il\d lh.ivejutt c:omc off a~Uwith th~ N.1tion:ilAc~cmy¢1Mcdicincin the US who the White Mo°'c ~ a,ked top,,-oducc a ccponon this;.

Movirc fast • dOf'l't think we should necessaritv waiton the NAM to &« something out tllere if pango99seois av.lilable.

lwlWIKristbn Andersen 16◄0

~ NASEM is use-less• they'll Nve ecactty zero. .. Too political an organization.

~ KrisrtanAndersen 17:52

Ila So he a.RteG? "I do ooc understand Andrews argunent" Tht sequence data clearly and uriambigoouslyrules out ~Y form of lab constfUCt orCOP.ineeril't8of the virus. ". Molecular biologists like

mysel' can ;enerote perfect c:opies of viruses without le.rving 3 tQce. egthe 8JmHI site. The arguments for ;,nd 3g3insl p;:isSJging ;;Mld tngineerio.g ;:,re the S(llne if YoUask me."

.:::.

I

Robert Garry 1610

• Nature and passaging in cells or .inimals will generate unpredictable cMng~. thou we might make some rather ge"lcralizcd guesses as 10 what mav pop-up.

REV0002921

Robert Garry 1s 1 s

■ Engineeringwould not be ~tecYble bV modem methods o, course. Yciu could wth enough cash wnth?size the entire genome. SARS·CoV 2.0 isnl engineered. The furin site with the siroline is too

fonky.The RBO i$too different from ""-hat k or at least was at the timeout there. I also don't rtallv sec pass.age in lab .nimals. Which leav~ nature or passage in cell cellular.

cells.

Robert Garry 1829

■ P.-ngo'l9 might provkfe the.inswer, lfl h.lsthe turln site. u not. trs the three cho.cesoutuned In the wlllte p:iper,

r'I; Eddie Holmes 18.33

r-"a Things are movi" so Quickly th,11 I'm havi°' trol.ble keeping up. I wilt see whJt I t..1n today. The ChinJ CDC will be put more seQuences on line today (hopefully). i11cluding 3 environmental sampies

which I aswmc meansthe fish market. Maybe huge. I'm ho,ing to get the first, but ketp an eye en GISAIO.

~~

r"W EddicMolmC$ it,◄?

,...\_ C.-azy politics in Chi1\a They want to p.,blish in a Chinese jO'Jff'lalbecause they art worried aboutctitic6m. This is fall out from tht NEJM paper. Also. we re31v 1..eed to see if the pangodata is as

good as they cfairn. Indeed, it is actually 'up to 993'' rather than '99%'. Tl\at fooled me. It soU'lds like they ha\'e rnetagenomes confirmed by PCR of the ~nimals. It might take i little while for thisto

come out. So.no need to w~t fot it.

• Andrew Rambaut UH6

•• Upto 9'9%isno good.There is a 342 bp stretch of RaTG13 ~h(ltisidenticalto nCoV. Sigh.

I

Robert Garry 1as, February8th.2020 .,

■ Sc:i~1qe by p,re>>C:Ol'lfiereo« b ~ ni;ve:r•, good th,e hype.

If they ::.re worried ::.bcut critkis.11'1 then m::.ybc tNs sde-nce thing&. not for them (tell th,u to my gr:id studenn; all the rime).

OK• maybt tht frshmarketsampltsv.•illhold th~keyW the-ycome • sll:>uld ~ in the range of 99.8%. MaybtPlease let\ hop! fora ttanspartnt definition of 'environmtnt.al:'

ifllJ Kri$Thln Ander$en 21:11

e.s Guvs. one thing !hat ~curs: to methat is not currenttv mentioned it'I tM d()('Ument0c' Nnail tonversatfons • let's rot forget that what we're ct>sen«I is completefy unprecedented as far as I know.

Ncvcrbcfo•e l\ac;:. zoonori( vi,uc; jumped into hun:.nsand ,orc3!.I thrtJugh the 001)1.11:.tion tCQuirc futthc, inquiry .as the vin.1~ it; obvio(.lc;fy

like wildftrc with thit; lcir\d of soccd Thie. in itself w<M.1ld

tiighJy c.ipal>le of 'living· in the human popubtion.

Ftbruary9th.2020...

• Andrew Rambaut OS:!6

• • Swine Ou 2009 cid thoush.

• Andrew Rambaut 0613

•• I thoug\_ht vou might be .:unused bvmvcommentson the IClV ,oron.1virus stvdv srouo's nC<Nn.1ming ome, Youwill be able to deduce whJt the ~oer ~id from ow ccmments:

I ~l'lotu1Uy t>tlitve tl'ln tht •tt•t to cbuify vtruus in i lli•l"•1ch1ol U.>u1t,Ot"y•n•l~s to tl'IU of lult•r-fOtU h • fuUlt ·usk of Shyp•11,1s• that a •xpe:ndiflC tht tlM al'ld e11ercyof

w.ay too ~Y llit0loghu. 'liN.tHS art inh-ert11tlt r•slnant to tllh scrt of UXO'IOW, t,y thdr Yff'Y nat\lr♦ .nd diversitv and tlw Nneflts of such a U<Or'IOIW/ar• far fr-oa clor t:> 11♦.

That bdn,: uid, con,btent and d♦finitive bbeUi.ni: of pJrticuhr dl$HU' ca11$in.g .apnt$ h .ss•nthl for efh,;tl11♦ cONtmiotlon. t -rtronily of the vitw that $1RS•C<Y•2 h a on;h,ent

rntff for the cu·rcnt flua;in outt,.n;i,C n~. Con$htcnt with the nu,ini of prev!ot1i. tii~•ntc virui.u i.u<h ai HlV•I, HlV•2, lllflJHn!ll 8 llnd tnfluen:a C (•lthe-.-,i lnflue..,:i1 Ah t:<f'C coepHcatcd).

I

Th•n •r• virtUO thrt •nttred th• hu .. n p)pUbtion llnd tlie MM .. ,.. •nign.•d to viNIH~ that ... de1cendlf'lh of the~• :ocnoti< •v•nts (•lthou-1, NlV•l ~d KlV•2 c~rht •ultiple :ootlotk

JCZJJ ..

I Im• quite a few f"turvations about tl'lt ai»lyih tllt allt'IOrs 'lave itrfol'Md (Se. bd0'.4) b\lt \lltitNtely J ti.11,vt th•t thtil' ul.t1•.iit cordus.icn u1.n SAAS·C0\1·2is a \_.,. of th•'"°"' of

viruM"s t~t .,.. bbtlhd s.MSl"•C9" is SOU'ld.

Ulti,utely SAltS•COY•l s.Nm 11kt a reuon.Olt n,\_ fro. 1 scientific point of v!.ew (: tMrk 1 .!gt,t ~av• FNhrr♦d •SAAS•COV•I' so that it doesn't sound ~he so nuch like a 'se,qu•h').

Th• di«us,ion of •quuhp,Cies' 1s a dhtucti<HI. QllH1Sptdts h illl tnteresti~a ••thf!Mtical todtl that h used to ticpl<ll"f SOM thtoretical ~vioul" of Npidly ..,olvinJ viroses Mil it h

... t~ly Silll)lhtlc at\d ~ il'l8d@QUJ1f di'Cl'1ti1:l0ft Of tl'I v1\I\O @l'Olvt,~ry fll"(J,(Uf,.,\_ It! tut1Cllltt' ttl@ teii!fll tNt V1,..o, l'!<'OVlatton, •""' ·c~1,ntvf' h 4 •h~ ..n•Mt11e of tM -.dtl. '""

th• p.trposts of this pap,er I wovld s~u:est ...ot 09tnitt& this un-of•WOrt'IS ¥Id st.ply state that ,iNs poP\lbtions within ,111ind1v14u-al tiost ♦xtlil)it Virhtton.

PaiNolht p,atristl< dinance is not an .adtq.iatt ,,ttri< fol" rtbttclntu bec.ause of tht r~ic evolution of il>.Avirusu. il1iA \'in;ses ac<!.W'IIJhtt P?O .at the r;i,te of .a~t e.ll per )'tiil'. rhis "'"'

O,.at •-lf .a vt~uc lud dl.-.ctly 6-u..-ded ff'Ofl t~• po,p;,li,,thn of vir,..,u that c.autd SM.~ in ::i-., -\_.1c, •,o;pe<' • HO of n l•ut 1.'1C. tn♦ntt.ally th• ..,thoN (•NI pt'♦c,.,n.tbly t.\_. %(:TV

in gfntr<d) haw tot tt.Mwlvts into a cil'(.ul•rlty wl!tr• thty bdld 9hylogtni

♦) &t'ldthtrt GHSurt p.ilrbU< diSunos off tht p!Yflog•lli•~ ir!d tl'IM ••k• phylogtntti< infertnc.s fl"O■ tht

p,•t.-htic <:Jtn•M••·

ln fj,.,,.. 40 th♦ ...,thor• \_.\_ \*'729)4 •nd ~7n9J3 H clff♦ rebtivo to ,1,1t,.(...,·2 b..t t.h.tf.♦ •~ •ct,..•Uy rec--.in•nt• .-,d f9" .\_\_ of tt.e •-• •~ \_.\_ c-14,,,er to t.h♦ l♦t of "'i"'•••

around SAIIS•CoV.ltlh Cllln be 5-e♦n in fig It of lholl et •l (2'028) tlllltu•.q. Thh piper dso c:ocribcs llllW(h cloHr SAASl"•CO\' '.R.JfiU' vhich $fflll<I, not to be recOf'Dinant with f'e$pect to> SAR$•(oV•

2 ··"' 1) • COl»!H'.Cl'>l diH .... ,.c: •• ,, ..ui tM .... ,1 ... g•n-.

"t1t$ t, • QOOI" •~1• M'<♦..,)C It 1) e<-t1.1•U)' o c-1 vin1), it..U vlrn.e) lft>cllt'Ct •) l'le:-11.${Wffle:ther it. hu-) or ,.\_h) •.re <IC)(Cf'.ld♦II fNM • ,\_n •n<e)toc' thn ••> 1n ,c\_h, "C•IJ'I• tllh

I

w.a$n't kn0tt n tl111e f1f n;r,Nnc.

£111?.tJI!££EL

Robert Garry 08 56

~ldty 9th. 2020 .,

• Nlcclydon~!

fl!I! Git Keyboard~ U9:4/

liill @Kri<tian: /gifs owned (120 kB) •

..-..I Kristian Andcrstn 0950

~ They rc.-.llyshould gct$omcbodywith phylogenetic knowlc-4gc in th.at5roup, .. I h.,d., long discvssion with $Orne of them .tbout p.1tristic dist.irn:e • cnti,cly 1.1nfruitful...

Ro~rt G,3,ry t001

• httPS:Hwww.ncb.nlmJ1ih.gov/plbmed/2691628~

REV0002922

It) ncbi.nlm.nih.gov

Molccu1or epidemiology and cvolution...,ry hi.:itoric:i of hum.tn conmavinn OC43 .:ind

Ht<Ut amongi:,atients 'Nlth ui:ipe.r respiratoty tract infections in KuaL • PubMed •

NCBI

Viral J. 2016 Feb 25:13:3.1. doi: 10.1186Js1298S-016-0488•4 Research Support.

Non•U.S. Gov't (13 kB)•

tttps.:Vwww.ncbt.nlm.nih.gov/prrc/artkles/PMC4476415/

•

e) PubMedC.entral(PMq

Genetic drift of human coronavirus OC43 spike gene during adaptive evolution

Corona vi-uses (Co¼) continuously threaten human tie;iJth. However. to date, the

evolutionary med,anisms that govern ~ Slt~n pe,sistence-in human Pol)olat'ions

he,~ not bee11 fully u~~tood. In thb .,ti,dy. we clwrac;tc-rizcd the evolution of the

major anrlgen·spikc ·

Februaiy9th.2020"

l!tc!X,•k\vww.nc-1) nlm.nlh.gov/pubm•d/21849456

•> ncbi.nlm,nih.g-ov

Molecular epidemiology of human coron1virus OC43 reveaJs tvolution of different

genotypes over time ;and rcx:ont omergonc:,q of ;a novc,I gQl'lotypo due to ... • P1,1t,Mod •

NCBI

JVirol. 2011 r<ov:85(21~11325·37.doi: 10.1128/JVl.05512·11. Ep<Jb 2011A>Jg17.

ResearchSur,oort. Non•U.S. Gov't 113 k81 •

Robert Garry 1014

■ Bttoming matt convincedth.:atSARS..C<0V·2

furin site and O·linktd glycans has prttedenc:e in ottitr beta,ccrol\aliiruses. MHV. HKU1 and 0:::43. Variable S1/S2 deavaGe sites an:t variable O·

linked glyc.:ins. Also pe:rrincnt is the adaptive cvdutioo of the RBD in these vin.ises. Also rcxombination. The vatiablc S1/S2 dcavagc sites and 0-tinkcd glycans seen in othC'f subgtoup A virus. but

~ Se3'Stnot yet in the b suba:ro1>p containing SA RS-Co Vs ~nd t@fated l»t viru.es.

Robert ~nv UH

■ A few new romments on the em.1,il chains. Six minutes apart.

https:Vabc;,ew~.go.com/Po!itics/while•house~asks•scientists•invtstigat~Ofigins•coronavirus/stoflt'"?id=68807304ABC

News' Chief Medic.al Co,respandent Of'.Jennifc, Ashton asked the director of

the N..1tiorulInstitute of Allersy :.nd lnfecrious D:Se.:ise about concerns th.it uem from midntomurion on line that the novel coron:win.it c.ou~ tuve been engineered o, delibe-r;:i.te'y released

lhert•s ;:itw;:iysth.it concern," Or, Antttoc,y F.tuci said. 'And one of the things that people Jre doing right now is very carefully lool¢n,g ot sequences to Steir tllere's even any poss.ibiJity much less

likclihOOCIthat that'$ going on. And you could ultimately determine that. So peopJt are looking at «,but right now, the focus 1s Oil what are wegoing to aoatoul what we ha•,c.•

@ABCHcws

White House isks tcienti$ts to investigate oriiins of coroll.lvirus

The White Hous.e asked sctentists and mtdkal expcrt:S to rcs.eirch the origins of the

th•outht•.:tk. tB:9 k8) ..

nowl eor0rUv.ru<. in p.:'ltt to eauntor mic;irlforl'IUrion:.bout

I think Fauci 1,a~ the corre<t answ·er rep.arding enRinttrirlP. or deliberate-rcle.tse, You need to loot. It follows and makes sense that you also look at accident.ti release as a possibility (somcthin?,

I

BTW,hat happer,ed with SARS·CoV•I SEVERAL time,

canme conspiratorial (OK that horse left the barn), but I think there may be some haflway t~k gO:ngon at Erasmus.

...aKristian Andersen 15:39

Pl! ldidn, realize beth Ron and Mat:on are at Etasm1JS

... IRtctcsting.She makes some good points though that lagtctoo.

GOOdcomments from Tony in that artkle • tv-¢r the politician.

REV0002923

Robert ~rry 1 SS7

■ MPGK: -And I would leave •1ab escape~for the dtSWssion. becziu:se putting that in the public domain as a hypothesis in my vie"\•, will be reacf as ·see. they also thought so·

1. Its already in the public domain as a hypothesis. so we really would be the ones ·putting it out there."

2. not Mldrcssing a<:c.identil release would~ worse than mentioning it, since then it looks like a cover-up.

~ Kristian Andersen 16.01

~ Agreed• this isa1re.-dyout there in full force so it'd be very important to discuss. Can't just sweep that under the rug.

Robert ~rry 16·0S

■ 3. Ac.c.identa1releaw of SARs•CoV-1. happened several times as <K:knowledged by WHO~ not mentioning this as a possibilty or worse burying it in the small print might m;)ke some people on the

ttam less uncomfo,...ble. bot IMO WO<Jld blow-back b;gge, than Mt confronting;, head-on and offe, eve,y reason why;, d;dn't happen ot at least may not have happened he<,. Really need tho,.

I

Pango up to "99" or ·cnvironmcntaJ" sequences. I am starting to fear that there may be something wrong or they may not come soon or 'NO<Seat all.

would NOT wovld be the ones "putting it out I here."

• Andrew Rambaut 16:09

.a■ I h<1vc seen the 'environmc-ntal' ~uences (I hope this is OK to mention it Eddie?)· they are identical to the Wuhan backbone. 8ut who knows what they are.

Robert Garry 16:1'1

■ Hmmm • if by identkal you mean 100% like a lot of the SARS·CoV·2 sequences. my first guess would be it probably means they did not come directly from anvanimaL

Robert ~l'l"Y 16aJ

■ http-s://wwwnc .cdc.gov/cid/articlc/l l/12/04-1293 . .1rticle

D Emerging lnfttdous Diseases Journal

SARS·CoV lnfedion in ,1 Restaur;mt from Palm Civet

Epidemiologic investig;itions ,;howed that 2 of 4 patients with severe <K:ute respiratOtY

syndrome {SARS) identif1ed in the winter of 2003-2004 wece a wa ... (132 kB} ..

EMERGING

INFECTIOUS

DISEASES

,,.. .,\_, "'""'1"'"" "'\_ I

o,j....,,..\_

http,s://www.ncbi.nlm.nih.gov/pubmcd/1S980414 Febru.lry9th. 2020 "

•>ncbl.n1m..nih.gov

ldcntit\cation of two critical amino acid residues of the severe acute respiratory

syndrome corONvirus spike protein for its variation in zoooolic ... -PubMed -NCBI

J s;oi Ch"'1. 2005 Aug 19:280(33):29588·95. Ep,,b2005 Jun 24. Rcs,arch Suppo,t.

t-lon·U.S.Govt (13 kB)•

I

htlps://www.rlCbi.nlm.nih.gov/pubmed/15695S82

I) ncbi.nlm.nih.gov F~:iry9th. 2020"

Cross-host evolution of severe acute respiratory syndrorno cotonaviros in palm civet

and hum:m. • PubMed -NCBI

P,oc Natl Ac.ad Sd USA. 2005 F<b 15;!02{7):2430•5. Ep,,b2005 ,ob 4. Resean:h

Support.Non-U.S. Gov'I: Resear'Ch Suppotl. U.S. Gov'l P.H.S. (13 kB)•

hnps://www.ocbLnlm.nih.gov/pul>med/15347429 This one ime,csring!

I

REV0002924

•>ncbi.nlm.nih.gov

MutatiOflal dynamk, of the SARS coron.wiru~ in cell culture and h!Jl'Ncn population,

isolatedin 2003. • PubMed • NCBI

BMC lnfKt Dis. 2004 S•p 6;4:32. Rt~an:h SupPorl Non•U.S. Gov't (13 kB)•

Robert Garry 16:34

■ https:.Vsc.1cocc.sc1cncanag.org/cootcnt/SGiJcatty/2003/09/04/socncc.1087139Jull.pdf iffrom an animal source. Yes Indeed wouJd re good to kl'IO\Y

ldcnticalsccrrs u~xpc«cd how the

environment was samofed.

I

• Andrew Rambaut 1 H8

•• Something that Richard Ncllcr noticed• a mutation in ORFS where tht cluster sti::klngoot with Many of the recent ca:s::-:s

matchc~ RaTG13 (amino add S) where as the so-called Wuhan outbtcak

sequences ti;we :i l:

It?

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There is al!O a synony100usSNP111

ORF lab that sho,vs the sameP3lttrn:

Februaiy 9th. 2020 "

.. Id¥''")' ..

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Februarv9th.2020..,.

This suggests .-differo,t rooting of the tree:

-,3ge\_png •

fFf I-'··~

lf ·-·-/-·..~··

·= -·--.. ..........

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I

Jcttli .£

REV0002925

Robert Garry 18.18

■ Very interesting ;;md important. More evidenc;;e that the market W35 not the point source from which the outbreak spr.mg?

e Andrew Rambaut 18:23

.a■ Need to seewhat the p.Jngo!in looks like!

Robert Garry 1&30

■ Oh yeah • the suspense ls killing me ... .l suppose that's what beer is for.

F-.i Eddit!! Holme:$ 18:37

,-. Apologies. but I'm not going to be able to t.1ke part in these discussions much for a while because this storm has caused havoc. I've had no power for 24 hours and it might be another 24. It's .1 re.al

mess. Need to do a d~an l.lP-A few things though: (i) what arc we cloing about this p.:iper thing? I just can't get to it at the moment: (ii) the environmental 5eqs are spectacularty uninformative.

r>retty shocking ir this is the b~t they have: (iii) how do y0u interpret the-altem.ative rooting? I can't ""°tk out the localities in the top dade.

96,000 houses without pow·er. Al.». I live in the worst affe(:ted area. I only came into work to charge my devices.

Robert G.any t8:4t

■ Nothing to .apologize about -sorry for the mess, the distraction .1nd the headaches.

• Andrew Rambaut 18"43

... This is the BEAST tree:

lm.lge.png •

Enforcing this root in BEAST doesn't really change things much. Rate 8.7e•4 (2.4e•4, 1.4C!'•3), TMRCA2019·11·29 (2019·10.20, 2019·12·20). Expooential growth rate actually goes up~ equivalent

of a doubting time of 6.5 days.

Only one Wuhan seciuence in the top clade but quite a few of the export$ in tl\at clade came from Wuhan.

You might think the bottom cl;xle are from the martcet (hum;;n me<fi.ited spread?). top from prior circulating viruses.

I

Robert Garry 1&:<16

■ Waiting on pango up to 99. I was hOl)ing the environmentJI samples would he1p, but the results made me uncomfortable. Afraid Pango99 might not be any more infOJm.itive either. I think Kristian

was going to t.akca stab at pc1pcr. Th~ guidarlCc from the cmai1 tca.m not a.II that helpful either so fa.r.

February 9th. 2020 .,.

Robert Garry 18-"M

■ Waiting o,, parlgo up to 99. I was hoping the envlronme11tal samples would help, but the result.s made me uncomfortable. Afraid Pango99 might not be any mote infOl'mative eitl)e(. I think t<ristian

was going to take a stab at paipcr. The guidance from the email team not all that helpful either so far.

r"i Eddie HolmH 19:00

,....\_ Andrew. can I pass this info back to China CDC? Hopefully might loosen them to send more data.

• Andrew Ramb.aut l9·SS

.a■ Of course!

Nick lofnan and I were looking at the genomes that went up vestercby(9 of tllem?). Some of them h;ive weird errors in them (rows of 4 SNPS and things). We don't realty know what is causin.g

these erro,s.

P'II £ddie Holmes 20:07

~ Thanks.

~ Krlfffan Andersen 22;12

f!.£1@Andrew Rambaut did you take a look at the environmental samples? They look Wuham to me. but not particularly bas31 to the rest .. Tells us nothing. I'm a little suspicious of these, ..

tlf'lil Kristian Andersen 22:31

!a Rooting of this\_tree in general is~ird. Keeping the origin in Wuhan and taking RaTG:1J"l£f!{? it tocks to me as if WH04 (406801) is the most l()$ical ,oot. but the RTT on that tree is

hoPCtcss. Multiple closely space intros? :!.Ceditedl !!''~!~

REV0002926

ft,\_bruary 10th. 2020 w

Robert Garry 0'1.17

■ I have some Questions about 1his EM.

Wll~l)nR; •

t-e,t>ruary llJtll, :J.tTlU w

http:Nwww.chioadaify,com.cn/a/202002/07 /WS5e3d1daca310128217275d93.htn11

CD chlnadaily.com.cn

Pangolin could be comnavltus Intermediate host: Study • Chinadaily.c0tn.cn

The p.Jngolin might be a potential intermediate host of the novel coronavi,us, as

genome sequences ol lhe disease strain separated from the aniffl(IIS were 99 percent

identical to thos.efound in infe-c:ted people. a study h.as dis.covered. (102 kB} •

From aoorhcr artide-: ~bruary 10th, 2020

w

GUANGZHOU, Feb. 7 (Xinhua) --lbe genome sequence of the novel corooavirus strain separated from pangolins was 99 percent identical to that from 1nfec.ted people, indicating pangolins ~Y be

an intermediate host of the virus, a study has found.

The study was Scdby the South China Agricultural University. According to Liu Vahong. president of the univcrsity.the researchteam analyzed more than 1.000 mctagcnomc samplcs of wild

animals ilnd found pangolins -'S the most likely intermedii:lte host

Molecular biological detection revealed that the P0$itivc rate of Bctacoronavirus in p,an.golins was 70 percent. Researchers further isolated the virus and observed its $tructurc with an electron

microscope. They found that the genome sequence of the coron3Virus strain was 99 pctccot identical to those in infected people.

AssumingthrSan a«uratc accountthe resC?arch~rsdid mctagCt"lomic:studies of 1000 wild animal samples. ThM th~ gtmomcs,ar"M:t

.assembled analyzedthern.

Here'swhat keep me up last night:

THEN the "Researchersfunhc, Isolated lhc v"irus and observed Its slfucture with an electron microscope."'

So• they grew it in cell c:ulturc. Those picture looks to me like growth in cultured cells• probablyVc-ro. You can't ge-t EM picture-s out of animal tissues like this. Furthcrmore the virus is g,owing

pretty damn well in those cells.

Rob@rt Garry 09:41

■ This doesn't happen overnight. This likely means that the mctagcnomic s:tudy etc happC1'l a while back. My BIGGEST Question how far back. The first I heard of pangolin scquenc~ on Virological

about 10 days ago. My second BIG question· if they g.rewit in culture as they said howmuch did the virus ch.Jnge on p.JSSJSe?

They surety did not grow the virus in pangolin cells, Gentlemen

please walk me-back on wh-ere my mind is wondedng ....

• Andrew Jbmbaut 1003

•• 99% is not close enough.

, I

~ Kristian Andersen 10,08

&I'! Those Guangdong sequeoces do look mighty basal though ·:.:

I think the likelihood of them Quickly throwing these into culture to 'snap' some EM pktures is pretty high. Doesn't me.an much though -getting EM ;md sequences within a couple of weeks is

pretty r'eason.ible if vou kl\OW exactly 1,\lhat to do !these folks had a p.ape-r on pango se:<iuenc!s l.lst ~.ir, so I assume th~y do).

Robert Garry 10;21

■ https:Uwww.rKbi.nlm.nih.gov/pmc/arric:les/PMC6893680/flgure/viruS('S

11 00979-fOOS/

•>PubMedCentral (PMC)

Viral Meta,genomics RevealedSendai Virus and Coronavirus Infection of Malayan

Pangolins (Manis j;wanica)

Pangolins are endangered animals in urgent need of ptotection. ldentifyin& and

cataloguing the viruses carried by pangolins is a logical approach to evaluate the

range of potential pathogens Jnd help with conservation. This study provKles insight

into ..

THis one?

Seems like different group in Guangclong than South China Ag but maybe they came together.

I

REV0002927

Fig S tindaa me-is The phybgcnetic treeof Conronavi'us from Malayan p.a~olina Ftbru:i,v 10th. 2020,.,

The study t:l!sign was apprcwed by the e,thics committee fot animal e.xpedrntnts at the Guangdong Institute of Applied 8iologica1 ReSOtrees (refortrxe number: GIABR20170720. 20 Jlly 2017) and

followc:-d b$ic principle$ outlil'\Cd by this oon'lmihoo.

Robert Garry 10.35

■ Still need the pango99 sequence with or without fu,insitc -the O·glycans may be a distractio,, (tOOugh interesting questions).

~ Kristian Andersen 10.JS

~Yuo

~ 'environmenc-a.l' -I'm not convinced they're actuall)' (!nvhonmcntal.

sampleswere entirely minformati•,c

Robert ~rry 103'1

■ Probably not• wh.at • they swabbed crates of live animals and recovered seq,ience-s?

"9?'6 i:snotdo)C enough.'"

Robort Carry tOS~

■ Agreed+ jump to humans. some hJman circulation then to SARS·Cov·

but what about adaption of Pangolin99 to Vero by passage followed by an accide<1taJ 2 HowSongwould this path take to

gener,lte SARs•C.OV-2?

Robert Garry ion

■ "I think the liketihood of them ql.ickly throv.in.g these into t\llture to 'snap' some EM pictvres k pretty Mgh. Doesn't rnet1n muc;h t.hou.gh-getting EM ;,rd sec:μenceswithin a couple of week$ is

p<etty reaso,,able if y0u k1')()Wexactly what lo do(these folks had a paper on pal'\&O last year. so I assume thty dol"

se<1,uence-s

I

Robert Garry 1111

■ The Wildlife gr()(Jp in Guangdong has been doingmet.J&enomics on p;ti,golN\arwJothre wild anim;3Js this sincemid-2017. Doesn't seem too hr fetched to think they st.arted workir\g with Sooth

Cl'lina Ag Univeoity somcv,he<e .ilong the way or that SCAU dt?d::lcdto get into a"race• pre-outl:reak. My bet would b? thai the SCAU started culturing viruses from the samplts they got pangoln

sequences out or pre-outbreak not ane:r. po-haps even several years t»ck. lhc nm case was announood Mi<l·OCcc-mbO' • Sll'C • they could Mvc gcare<I up. got re.al serous and done some CCII

culture work and EM .1tter that until the press confereoce la>tweek. but l"mguessing it's been longer.

RobertGarry UH

■ ~rtps;.V\w,w.scicncedirect.com/scicnce/article/Pi/S0166354220300528?\lia%30ihub

L s<.ie-~direct.ccm

The spike glycoprotein of the new coronavirus 2019•nC<N contains a furin·like

clt?avagesite absent in CoVof the same clade

In 2019. ;3 new coron.avfr11s h:.s emef'@.ed

(2019-rCoV) infecting 1--kim.a.r.s n WLh:.n.

China. Its genome ha.lsbeen sequenced and the gen(>mic; information promptl...

Koopsman :,.assed this to the ern.1il gr0up. Not 1 g.re1t .1nalvsis IJVO. but i guess this m.;kes it somehow more •real"

...i Kristun Andersen 16:27

IJ!I They're ck.vty thinkin3 along th~ lines of escape in th.lt article too ...

Toe virus that was supposa1lv initially transmitted from an animal teservoir to human (pcssibtv via an am1>lif)'i1la: h:>sl)tut human•to~hu-nantransmi!.sicn has b~ r<:ported I .. r

I

.,.ve identified zi peculil1rfurin·like cle,wage iite in the Spike protein of the 2019-nCov•

Robert ~rry 1706

■ I think if they would have compared to RaTC13 escape mi.ght have been even more explicitty impled.

Kristian Andersen 17;S2

.h.1stadding Bob's link here 1inc;e this is a pretty critiC<ll reference. httpsJ/www.ncb,i.nlm.nih.gov/P'.tbme:l/31801868

•>ncbl.nlm.nih.gov

Trypsin treatment oolocks barrier for zoonoti< bat coron.aviruses infection. • PubMed

·NCBI

J Virol. 2019 Dec 4.pii: JVl.01774-19.oo: 10.1128/JVl.01774-19. [Epubaheodof

print) (13 k8) •

I

REV0002928

Pofyp..-otein

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1.~£~

Pofyp..-otein

-·•-

1.~£~

Robert Garry 16:75

• Probably + or as we've said lhc mind can play tricks and one of those tricks is denial. SARS·CoV♦ 1 escaped from Chinese labs 2. 3 or 6 times ldc~nding on your source) AFTER the outbreak that

killed 100Ei of people infected w.asover. Yes. Wuhan mJybe Betting too much ol the attention+ could be anywhere. We koow two groups in Guangdon.g were doiog metageoomics and grcr.ving CoV

from pangotins perhaps for years. Escape via a custodian or resca.,.chers could happen from a lab and vouwould PROBABLY never know it.

Robert Garry 13.49

• The virus nowhas an offidal, though tentative, name

China's National Health Commission announced Saturday that it had lcntativcly named the ¥irus ~new coronavirus pncumonla.· In English. it will be referred to as •novel coronavirus pneumonia• or

"NCP" for sho<t,

NCPV? 0.. is a battle brewing with ICTV?

ft NBC News

Coronavirus updates: Death toll hits 811. surpasses SARS deaths

As conftnned cases reach more than 37,100 in mainland China. here is the latest YQU

need to know. 173 kB) •

I

~ Kristian Andersen 18 Si'

I.a IMO China should h.ave-the-right to name this thing• howeve-r, NCPis pte-ttyd.am terrible-...

Robert Garry 19:44

■ Leaves very little room ton.arnc th~ next CoVdiseasc th.ait u«si-'C) r·o,,, eu,,,~e,~ e-merges,.

,e, e leb i., PJe,tt, Ctneli111t1 Another novel is paradoxk.i.l.

r"II Eddie Holmes 21:22

,.....\_ Trying to catch•up ... they've said we-·rc not going to have power for a week.

I

r'II Eddie Holmes 22:43

..... A bit more on the pangolins..Adon't for a second think that this virus out of a tab inGuangdong. I believe the authors in their explanation as it fits with my own work on pangolins. There is now a

lot of interest in pangolins beuuse of trafficking. Indeed, independently I have a different paper on pangolin viruses that has identined a novel pestivirus and coltivirus:

PDF •

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Figure 4,pdf

POF

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VP2

PO, •

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Figu.,.e S.pdf

POF

·-~-'"'"~-...-,,... ....,\_\_\_ \_ -"-•,.,--

-···-~ --T-b ...,,,.,\_ ...----···---·-------

At war~. I think they have got ove-r•excited with the-ir results and cl.aimed too much. TheImplication is that their pan&olin Virus ls doser to NCP th.an the one we have-from Guangdong but we-ne-ed

to sec the data. Unfortunately. they may nol publish this any rime soon because they have faced huge criricism in China, I think mainly from admitting that pangoiins a,e illegally trafficked into

China which Jppareotty ycu Jre not meant to sav.Very Chemobyl, About to edit the doc .

.....aKristian Andersen 22-49

!ii! Thanks Ecl,clie for sharing. Not quite wre what those pangolin viruses are though? And yes, I'm worried they have overclaimed too ... Kinda bummed that the 'environmental' samples didn't shO\'I

.anything at all.

As for document+ realistic.ally I'm g04ng to have,1 very hard rime doing anything on it this week since I'm off Thursday > Sunday and have a compressed week. Come next week I'm back in business I

though • plos I wmho;Wesome time Wednesday and first p.3rt Thursc;Lw this week.. Qi i,£J .. ,J(L.£

REV0002929

... Eddie Holmes 23:44

,-; Th.anks. Very hard to drop everything to keep doing this stuff. I've edit the doc a bit. Hopefully more like a paper now. Those trees I sent were for pestiviruses and coltiviruses. Only rclevant in

sense thaL look. trafficked pangolins contain viruses.

G:v(l;)

F'lil Eddie Holmes 23:51

~ I've had a bash at the paper version of the text If people want to take a look that would be great. Should not be too onerous.

f.ebruary 11th, 2020 .,

~ Kristian Andersen rots

~ Will try to find some rime tomotrow.

Running a pretty interesting an~ysis cit the moment. One of the hallm;trk features of SARS was that the spike protein adapted to the human ACE2 receptor + immune system early on in the

eptdcmic. Th<!-question is, how d~ that compare to nO>V? Calculating dN/dS across the full spike protcin from earty SARS sequences we gtt a dN/dS of 1.82. For nCoV that drops to 0.29 • whic;h

isJi lot lower. Hypothesis being that the spike P<Otein of nCoV might already be adapted to a human receptor. Of the handful of nonsynonymous mutations we do observe in nCoV, none of them

are involved in receptor binding.

I

Not yet done with this anal'ysis, but pretty interesting.

Calculating dN/dS for SARS in the middle of the ~idemic. it drops to 0.44 • so still higher than 'early' nCoV.

• Andrew Rambaut 02.-os

•• Heading over to WHO now. Will keep yoo informed here if anything interesting crops up, Hope to have a few miootes to chat with Jeremy too.

r"li Eddie Holmes 0,1;37

,....\_ Have fun at WHO.Ask Dastwatabout th.at Guinea Ebola seq. Anyone who wants to edit the papcrvcrsion of the doc plc.tse go ahead. Should not take a whole more. Bob -there is a bit for you.

• Andrew Rambaut 04,s2

•• Had a quick chat with Christian Orostcn. He is strongly of the opinion that the virus has adapted in humans. He thinks it has been circulating in some part of Chio.afor a while.

r"li Eddie Holmes 05:28

,,..... Evidence?

Then why the ~nimal maricet ;ind the po-sitive environ!TH;!ntal snmp~s?

At lea'5t that's one of our possibilities. If hc''5 right I'd bet Gu.angdong.

• Andrew Rambaut os.43

•■ NOC'll''iden<:C,

The animal market could just acted as a stntincl site in the surveillan,ce system (i.e., a cluner of h2h that got flagged because they all work there).

And environmental samples are what exactly?

I agree about Guangdong, though (might explain the tooting, above). However, this divergent still isot very long ago.

I

Robert Garry 07. 58

■ can someone send me a link to the googlc doc? I only have the link to the old version. I gucss.

Robert Garry 08.26

■ Sorry • got it...

~ Kristian Andersen 09.55.

~ I don't think Christian is right· docsn·t make sense when we look ~t the TM RCA and very limited diversity in the earlier samples. Sure. we may have:missed transmission chc1ins that died out. but

that would have beoo peculiar.

Gunngdong does seem like a viable root of the tree thoogh • the rooting rtill has me majorty confused.

~IJ!I3~ics LastrcptyJ..,-cars.:ig0

Robert Garry 10..28

■ hltP'S;Nwww.sciencedirect.rom/science/artic.le/pii/S006S352718300010Ma%3Dihub

E sderlc@direct.com

Hosts ;md Sources of EllOemic Human Coronaviruses

The four endemic human c:oronaviruses HCoV•229E, •NL63, •OC43, and -HKUl

c-0ntribure a considerable share of upper and lower respiratory tract infection ...

•

Here is Christian's thinking of this conge(lled into a very nice p<1per.

Other human pathogenic CoVs circulated before being discovered.''The emergence of HCoV-OC43 in humans was proposed to be linked to a host-swilching event around the year 1890, a rime

th;it coincides with a p.:1ndemicof respiratory disease recorded in humans (Vijgen et al., 200S, 2006).

L sctcnccdlrectcom

Hosts and Sources of Endcmk Human Coronavlruses

The four endemic human coronaviruses HCoV-229E. -NL63, ·OC43. and -HKU1

contribute a considerable share: of upper and lower re-spiri!tory tract infection ...

.E sc.iencedirect.com

Hosts and Sourt:e-sof Endemic Human Coronaviruse:s

The four endemic human coronaviruses HCoV•229E, ·NL63. -0C43, and ·HKUl

contribute a considerable share of upper and lower respiratory tr3ct infection ...

Robert Garry 1Ck36

■ Agnostic: approach wor1cs • give the pluses and minuses of each scenario.

REV0002930

Robert Garry 10:so

■ •calculating dN/dS aero~ the full Sl}ike protein from early SARS sequences we get a dN/dS of 1.82. For nC.oV that drops to 0.29 + which is a lot lower.•

Can you calculate dN/dS for the pangolin spike scqucoccs? They arc prcny divergent

Gre.at everybody comes up with different n;imes. l"m st.arting to like 'WTFV more and more ...

w!il Kristian Andersen 12.-00

~ Can you cakulate dN/dS for the pangolin spikesequences? Th(!yarc pretty divcrgCflt

Yeah. that could be done. but the scQuences arc a tittJe sketchy so I'm not quite surewhat we'll find.

Robert Garry 12 38

■ ASfora new figure is there som~ wavto for lack of a better word dtJmb doi.-m a hgure like this from 8arit?

My fear is that most readers eyes will gJazc over at the sequence alig.nmcm and maybe worse a c.rysta1 structure.

IIJ13.g1t.Pnlj: •

,\_ ==-::: ··• :. :

• Andrew Rambaut 14.26

•• Going to chat with Jeremy tomorrow momi"S-I am beginning to be more convinced about the mid•point fOOt. I think that me.ans a long prc•detection period in Wuhan (possibly outside). Basiulty

once you ,~ the market as the origi1t all be:b ate off\_

ai'lil Kristian Andersen 14·34

P.c!Ye-ah.I think that~s an inte<esUngpossibility too Andrl'\v • and the ,oot isdefinitely challe-ngir,g.T11ingis..given what we're seeir-.gon the cruise ships. in the hospitals and communities.clearly this

thing spread<; ext,emefy caiily between humans -so as you say, it's highly plausible that while the market wai were it w<1s dcte,cted {and potentially amplified) it's not because of an animal re<;ervoir

there. it's because of e>etended hurmn•to•hum..··tntransmission. If you look at the environment;il snmples they nlso look lilceJ),lrient s;imples • which woold be consi~ent in Sl.Jdia scenario.

e Andrew Rambaut 14..46

•• That is my thought. I suspect the surveill.:1ncesystem picked it op because it was a market~ this is essentially an avian infltJenza surveillance system. But it mavhavejust been spreadwithin the

market.

REV0002931

llf!il KristianAndersen 1504

~ If we drop some of the earlier assumptions (e.g , market limited H2H, people infected from animals, etc.). all of this would fall more into place. We know that H2H tran-smissioo likely wasn't limited.

which puls a dent in the market hypothesis anyw;ry. With those. a midpoint root becomes an entirely p(ausib!e scenario and would explain the data a lot better. Now. @Andrew Rambaut hoo,v docs

this influen<e TMRCA estimates? My knowledge is too limiting here• but what would the 'root'TMRCA .\Ctually correspond to? Pr<'sumably, with significant undctcc-ted circulation and a midpoint

rooted tr~. the trnc TMRCAcould be signiftc.antly furthe< back in time?

~ l~y 3.,ellrsa,go

Robert Carry 15 12

■ Agree• the r'r\arkct could be a red herring, Octcc.-tion bias. Fr-om the Party PoilrrotPaper: The Guangdong Wildlife Rcswc Center rcc:civcd 21 livc Malayan pangolins from the Anti·'Smuggling

Customs Bureau on 24 March 2019; most individuals. inchJding adults and subadulls. YtCfC in poor health. and their bodies we<c covered with skin eruptions. All these Malay.In pangolins \'/CIC

rescuedby the Gu<mgdong Wildlife Rescue Center. however. 16 died after extensive rescue efforts. Most of the dead pangolins h.ad ,a swollen lung which contained a frothy liquid, as well as the

symptom of pulmonary 6brosis. c11nd in the minority of the dead ones, we observed hcpatomegiit1y and splenomcgalv. We collected 21 orpn samptC$of lung, lymph, and spleen with obvious

I

symptoms frof'n 11 dead Mat.aya.n pangotins to uncover the vitus divetsity and molecular epidemiology of potent'1al etiologies of vituse-s basedon a vital met:agenomic nudy. This study will be

beneficial to pangclin disease research .and subsequent rescue operation. So. people infected from animals likely happening but when?

lllliil Kristian Andenen lS;tJ

!.C! For .1111 know, people could have infected ~ pangotins.nor the other way ... :)

Robert Garry tS:15

■ l"m glad you said that not me.Something happened to turn the progenitor of from a viru

Somcthing happened to turn the progenitor of COVIS-19Vfrom a virus spreading at a low le~I to one that spreads more easily. My bet would beon the furin site.

Robert Carry 1s 33

■ how does this inflUCn((! TM RCA ~ti mates is the big <tucstion.

e Andr-ew JQm~ut lS 34

•• I ran BEAST a few days ago enforcing the 'alternative' rooting. for constant size the root is 2019· 11 ·30 [2019·11 ·08. 2019· 12• 17). For ex.ponc-ntial growth 2019· 11 ·29 [2019-10-20, 2019· 12·

20). I will ta·y re running it today.

So not that much.

~ Kristian Andersen 1S42

In Hmmm, yeah, that's pretty much exactly the s<1me.I wonder if ther-e could have been undet«ted tran$1Tli5$iongoing on for a lot longer ~'ln that (.and currently fully uns.ampJed~ but W'ithout e.g .. a

time at which the cleavage site was picked up. and nol entry into lhc human popularioo.

--~-·-----·~~~-~----·--~,~---~

-·~--··-·--··-··-·--·-I

t think I could buy that and would explain away everything;

1. Rooting being so difficult

2. Furin de.1vage site since we have seen these in other hum.ln betaCoVs

3. Recent TM RCA

4. HumcJOoptimized RBD

S. low dN/dS because of 'pre' adaptation

Does this even make sensegiveo the data? !ed1rcdl

1~

February 11th. 2020 ...

Robert Garry 1S:S7

■ Thumbs up • I'll give the l.ay response.

RobertGarry 16.lS

■ Need to work 1 ·S above into the paper.

Robert Garry l&?l

■ Also need to include assumptio,ns that am or prob.:ibtyam be dropped from KG.A 2:04post !market, limited H2H. people infected from nnim.11$). Not sure can n.ile out the last one {but agnostic].

SARS•CoV-1pretty much full-blown was in civets and caused disease st'rai,ght into people.

Robert G.11rry 16;30

■ But SAR.S•Cov•1 did adapt it seems• dN/dS of 1.82 fOf'SAR.S•COV•ldropping to .44 vs .26 for SAR.S•CoV•2 suggests to me human•to•hurnan of SARS•CoV2 for some time.

Robert Garry 16;40

■ \*Undetected transmission going on for a tot longer than that (and cutrently fully unsamp~). but without e.g .. .a function.al fudn site. Then once that was pk.ked up some additional u~etec:ted

C.lSCS that we're starting to sec rraccs of in our dala before going boom." I'm going to call that the Andersen Hypothesis. ls there another hypothesis that fits the data better?

iflt.l KristbnAndersen 1HJ7

!ta Furin acquisition hypothesis

Makes sense to me• but need input from the Grand Wizards of Phylogeny

I

BotSARS·Cov-1 did adapt it $eems • dN/dS of 1.82 for SARS-CoV•1 droppin.g to .44 vs .26 for SARS•CoV-2 soggEsts to me human•to·human of SARS--CoV2 for some time

SARS-1 ,-nost certainly adapted during lhc epidemic.· primarily earty on and ,nost/a k>t of thal happcoi,,g: outsklc the RBO. This doesn't appear to be happening for SARS-2. so ccrt.:1in1y consisteflt

with a pre-circulation hypothesis.

~bru.lrv 11th, 2020 ...

RobertG.arrv 11.13

■ The precede-nee for a betacoronavirus that does not change much when it jumps species is Beta<:oVt. Seems that is pretty much pan•tropk • very similar viruses in a variety of species including

cows, dogs, giraffes. water buffalo. vak1 etc. Yes • per Saric JV optimal furin 1ite plus predicted 0-gfycans as a bonus. Not sutc about the RBD but these arc very similar vi~cs overall.

Robert Garry 17:20

■ The receptor tor thcsc viruses is sialic acid.

RobertGarry 17:32

■ Human to human p<e-circulat'lon hypothesis looking good? Pre-cire:ulation in animal:S then animal-to-human. follO\YCd by human-to-homan (like SARS·Cov·1)1ooking not so good?

Robert Garry 17::Je

• Can you now distinguish P"C·circutation in animals. then circulation in Ve<o cells. folloW1:'d by human-to-human? I think it might be possible to nearly eliminate chis one too with some addirionat

thought/input.

Robt!rtGarry 1&00

■ https;://\W1W.sc.ieocedirect.oom/sc:ience/artic.te/pti/S2211124718311483?via"30ihub -bottom line it took multiple passages to adapt to the receotor.

Here one cell culture passage paper

I sclenudlrect.com

Ad.11ptiveEvolution of M ERS·CoV to Species V,ui.ation in DPP4

REV0002932

Micxttc East R('Sl)iratory Syndrome Coromvirus {MERS·CoV) lil,;cty o,iginatcd in bats

and passed to humans through dromed.1rv C3mels; h::>we"-er. the genetic ... {8S kB) •

l!nps:.Vwww.nc.b.nlm.mh.gov/pfY'C/artK:leS/PMC2495oO/

x e) PubMcd Central {PMC}

Generation of seal ilfluenza virus variants pathogenic fOJchickens, because ot

hemagglutinin cleavage site changes.

lnfl11cnz.1V'trusNscal/Mass/1/8O (H7N7;w.1s 3dap1cd to grow in lvOCKcclls and

c;hidcen embr),o cells (CEC) in the absenc;e of eKogenoos prote.se. Thebiologic;al

prot>tr~ of the virus variants obtained coincided with intrace(lular activation of tht

hcrnagg:lutinin, ..

~ Kristbn Andersen 1804

fr'3 I don't think any of these can be eliminated or co..1flnned at this stage, but a coupk-of thing~

1. A~ <U•ta seems to be (())Sb tent with u,e pre-cPcubt1on llypome:i.is po:std atx,ve

2. O·linked glycans ~lid tow dN/dS l'Ot so consistent with passage in cell culturt • fulin cleavage site and optimal human ACE2 RSO very consis~nt

3. low dN/dS and optimal huMc'ln ACE2 RSD not so consistent with passage in animal model • furin deavage site very consistcrw.

4. 1.,c;wdN/dS, lurin cloa-ngo 5ilo, ond optimal humon ACE2 RBO not so consi$ttnt w·th direct spillover• c-pi dot> consistent

fllt res>lv3 .,~ars aao

Robert Garry 1804

■ Ukcw:SCmany many i:;0ssagcs in chick embryo cells to generate a polybasic cleavage in flu v. You can do it by ctJf culture passagebut you rca'ly need to be trying to do C.

Robert Garry 18.11

■ A&ree' Grand W,,,.ardsol Pnyloeenv need to poke hok-s. if there .ire any. Need to firm up precedence of undetected ci,culaOOn in hununs p1ior to emef'lence of Ht<Ul. OC43. Nl63. Z29E •

Drosttn re"iew has scme ot this.

C..nyoumake~ figure of the dN/dS dat;:i? Does this hold througl'K>ut the geoomeor just spike?

e Andrew Rambaut t8·t8

•• Th.it MERS p.ioer • why do oeovle thirik MERS is ;:id.;iuted a fTI)(lth in hum.ins No Jd-1ptations get b.-..;k into the

to hu~ns? It has never tmn-.mitted fOf more th.in ..11:>out th;:it arise in hufn.lnsWQ\11d

camels. It is a camel virus. It is adaipted to amrk and just happens to replicate in hum.;ns.

I

I am not cowinced about d.N/dS either• where do you get~ dN/dS forSARS of 182? Across thewhofe genome?

Sound:Sartifactua.l to me.

Robert Garry 1a,o

■ Agrtt· bad prtmise. but th~ tritd passagin&MERS CoV inc:ell culture and ctwas pretty hard tog-et the virus to adapt• th.at was my pcint.

e Andrew Rambaut 18 21

•• Fair e-r..ough. t just have Ilea.rd he-re ~le talkingabOut MERSa:sa human virus.

Robert Garry 102'2.

■ MERS•CoVanothe-rone that should bek>okcd atfordN/dS.

~ Kristian Andersen t&◄

S

Ff!brwf'/ 11th. 202(! ..,

la Yeah, aon'tget the M£RS stuff~ dQcsn·t make sense.

For SARS/nCoV tm i;poci6c.,tly lookif"IS i'.lt the 5pit:Gprotoin(tor now) • oomi»ring SARSoi'.lrtyif'I the>04.ltbrq,1k to in tho middle of it, For SARSthis Ns boond-<lOGby other$ as WGII

https:.v'www.ncb.nlm.nih.gov/pl.bmedl147S216S

•>ncbt.nlm.nlh.gov

Molecular avolutiol"I of th<lSARSc:oronavirus dul'ins th-a course of the SARSepidemic

in China. • Pvb-Med • NCBI

Science. 2004 Mar l2;303(5664):1666•9. £pub 2004 Jan 29. (13 kBI •

I

REV0002933

r"9 Eddie Holmes 20:06 F<tbrua 11ti\ 202<1 .;

~ Sot,y.necd to e::ilehul).Hod to teoeh a do$~! One:. yoot. Yes. MC.RS i:HI c-.omelvirus. ,-,..,.c,. '!',c. ..,.,. ., ..... .,..oFfe soyil is II botvin.i,s.Anywoy. lh:ave uoublewith lhehuman p~•odoptt1tion ide.,:{i) I

don't sec wry the market is analogous to AIV strtening unless Arorewknows somethiog l don't. I think the best SJJrveiUance takei place in ti.e hoipital>: (ii) the main reason why fvc be-cfl to

Wuhan a fewtimes is to t<;l~ p.art in ttiis big hmgw.:ishstudy (BA!J sttJdy we ha~ going on. We hwe meta•transaiptomic dat;s of ...6()0 people repo,tin.g to Wuhan Central Hospit;il wi1h

re-soitator"Ydiseasta. Wi! have the:t rull meta•transc.riotome-s but it is t~~in:eM a2e to analvse because the d.ata set is so bie. I'm e<>ne toalt.a(h the ,a,w virus d.at.3 here (keeo to yourself) I think

these are from 2018 but I !Yvc to check. There arcCoVs but nothing new.I need to double-check with my Mang OOt he is about best in wortd about this, The cens in y.!llow are confirmed. the

°'thers per lane re flea fnde-.•hoppln.g. Obv1ous1y, not r;onclustve, t>ut a representative sample that the \irus was not there ,hen. 1 suppose we need to g(t this publshed ASAP?

1'.xt.t!I Si,,t1ad1l'lttt •

II

II

20191008\_'-'rus\_,uml'T'lclrv.xlsx

E>a:elSp«,d\_,

0,,,., .. ~.\_,,. ..... '11.ot~..\_\_ .. --...

l~s«,,ISZ!M O»MJ:otM 1-..0 6

os.11,1\_,. l6,Sll641,I >l

o~, :1m•l4 ),>

·~ ~M'(,;I

II~ Ml11)1(11, 0~ JIJJO:UI 1~

U~ SOIUIW

·--I

==~I~~ ;!

....\_ --05'1~ I~ .. ) II

-~ Sfr>>-11(0(

,s. .. ,»i l«-164.JII U

°"'"'°""SWOM

l~ S«:iCUT 1J0-3'S,,O ~CQ ..

1'-'>41W1 WOWDSN 1•m11• •1~n, ,..

•~ ~JIIU 14ll2t7U M141Ce U

•~ s«mCICl

".........~..:.: ! :~:.,: ~~~::!!! :

u,...... ~oms 14JiOl5MX :n11o11u w

11,.\_, s,tlOtl,1 1\*1'0U 1,ISN,O~ )t

Ftbru.·w121h, 2020 •

e Andrew Rambaut OH1?

•• About om.ail&:• no prol>lcm with l;m b9ns on it. Hi&:qu95tion hOf"q,.,

Do we think tM furin in~rtion could have «curred one: AA at a time? Se~ms unl'kelv a-syou have to insert .1whol(' codon at a tiM. And if I reme,mber for A'N sometirres tht-actual iMertion is

ftom dscwhcre in thcvirusgcnome(rot su·eabout this• it has been awhile since I looked at this).

With respect to the prc•Deccmbcr circulation • I don't think we can S3f th.at it was more than a month or two and in that time the numbers would be very small. If 2 months with a dolble. time of 6

<l.)yswe hove obout 1000 people. Out th.:>tpre•:s'-Jppose:st.he exponE:t'ltital i,awth r~te we see now which ptesum:>btyi:sthe r'~ull or the rurinsiL

Istill ran't see it circulating long enough with stutterin: ch;l'ns of transmission for it to evol11e the fur in site bnd i.d,atever elsPJ ;ind then take off. This stuff can't happen eac.ilv or It would h;we

happened in SARS

~ KristianAndersen 0204

fa All I know is my h~.~d hurt<t ...

Furin $ite p-obably could be step by step• incre.a$ing its abilty to be deJved little by little. Codons come ;md so sometines in RNA viruses, so I wouldn't be that surprised (e; .• we have seen it in

Lass.a and Ebola. but rot Zika and West Nild.

I

Did you e)Q'llotc routi~ more? I tried masking so,nc sites in carti« safll)lcs that .re suspect and also rail bc:ist wi:hout time information undc< a couple of diffctC1'1t models. Creates sotnC

he:iutitoll'y midpoint rooted trees.

r"W Eddie Holmes 03:24

~ I've added Lln to the Google dot$. I'll edit .a draft now ind hopefulJyhecanidd some wise wo<ds.

• Andrew Rambaut OJ:31

•• Had a chat with Jeremy thrs morning. Really not mlKh more to say,

r, Eddie Holme:s 03:32

,...\_ You mean for the doc?

a Andrtw Rambaut 03:33

•• Just that he still thinks it is important 10 get a matter·of·fact paP(r oot the-re.

~ EddleHolmH 03:36

,..\_ Yes. tct's just flllish it.

Much as I think it is dumb, we net<! to use COV10·19. The IClV arc a bunch of twats.

Plus Jeremy is WHO linked

• AndrewRambaut 03•7

•■ Problel'n is t~t COV10-19 is thedise.:.se. We co.Jd swt to collitCOV10·19-CoVlf wew.'.llr'ltto troll lCTV

I <lm cbing an up,to•date BEASTanaJy;;iswhich we could use to discuss timhg of TM RCA. Will then use ther;ite we get there to estim•te diver&.ence to RaTG13. Will be ;i minimum d;ite htJ1 we

could make that deaf.

C.an we use GISAIO data? Wovld need the adm. tab~ but there is also the bit about at:empting collaboration (tor all submitters?).

W, Eddie Holmes 03:SS

I

,..... Shil. vou're right. so coofusng, I think ilddi~ GISAIO 03ta i:s;:i good idea. TJb~ cJn go online.

a Andrew Rambaut 04·.49

•• Needs Quitt a lot of work but w~t about\_. figure like this?

REV0002934

e Andrew Rambaut OS:14

•• The aml.no .icld allgnmem Insets could Include a tew more bats and SARS aindyou coukt let .-.e know {t?Krlsttan) whkh you want and V'lhlch residues to show. I am happy to un•Genelou.s It.

Perh:irx, a ,lidingwindow ,irnll:iri(y plct .ilors the top to ,hoY.ih,c,w unrecombin:i.n.t it l$?

P.Eddie Holmes OS;22

r'W Eddie Holmes OS:56

I

,-; Bk>ody obvious wtien vou think .bout it: https://www,express.co.uk/news/wocktf1240664/c0<onJvirus·news·btest-chin.a--origin-meteocite-.scientists·l-.e31th·waming·deJth·tolJ.latest

[J Exp.-..u.co.uk

Coronavirus cam(!, from METEORITE which hit China last yea,-bombshtll sc.ientist

claim

THE deadlV Q;l(On,)Vlrus which has f.'.illed more lh<m 1.000 people glob,1tlvcame trom a

rnetcorit~ which hit Chini last year, sdentists have sensationally c.laimed.

Feblltl\.ro20~58k8)"'

I

e Andrew Rambaut 06 10

Al

■ ui:ikc,s.p:,c-~-nu

Robert Garry 0753

■ At least gives an alternative tMCRA • not quite ready to add another scenarb.

Robert G•rrv oeoo

■ from blcxarder .-.ct b<own ,ef

All the current evidenu~ indic.ates th•t HPAI viruses arise by mutition ;after LPAI viruses of the HS or H7 subtype h~e been introduced into poultry. Sever.iii mechanisms m.av be responsible for this

mutation. Formost HPAI viruses. there appe,ars to have been .spontaneous duplication of purine triplets, which re.wtt.s in the insertion of basic:amino acids a, the HAO de.avage site, ,;1nd this seems

to ocOJtdue to a tramctiption e<ror by me ~lymerase,-coo-.,tex (76). Mowe-,er. aspoiltted OUl t>yPeraueet 31. (76). ll'li$ iSclearly oot me onty n)e(l\anism by-.vhich HPAI virt.-.ses a,1se. ~s some

appear to result from nucleotide subs11h1ti01rather than insertio!\, while others have insertions withoot repeating nucleotides. Tl"e Chk 2002 (107) and the Gan.ada 2004 (75) H7N3 HPAI •1iruses I

tiave emecged as the result of an entirely different mec:h.imism anti shoN distinct and unusual cte.r,age site amino acid s,eque'lCes. They appear to h;we arisen as a result of recombination with other

ienes(lhe f'lucle<>pcoteing~oe a,~ matri.x geoe. ,-espe<tirtly). resulti,l.8 h, an i,,sertioo at lhec.leavage s·te of 11 a,nk.o acids for the Chic vifus and sevt,, amno adds for lheCaoadian vifu.s.

I thinl! Kristian ison to somethinc with the dN/dS but morean.al\/Sis needed.

Cell.2015 ,\in 18:161(7):1516·26.doi: 10.1016/i.ccll.2015.06.007.

Ftbrua,y 12th. 2020 "

I) ncbi.nlm.nih...gov

El><lla Vtn.is Es,idcmiOlogy, rransmlsslon, and Evolution during Seveft Months In Sierra

Leone .• PubMed • NCBI

Cell. 2015 Jun 18:161(7):1516·26. doi: 10.1016/j.c,ll.20!5.06.007. RcS<:atCh

Support.

N.1.11.. Ei,:tramural; R~arch Support. Non·U.S. Gov't: Rcr.carcti Support. U.S. Gov't,

Non-P.H.S.(13kB}·

I

I lik,e An(lr,ew's now fle,.1re too.

Robert Carry 09'18

■ Spe3kingol figures• of whi<:h weneed sevet~I. some pethaps the mott tecMkal like the detailed alignments ca,,be SLC)plement-al.

I started 45 minlltes tVld did not finish a pango c.-irtoon • a "scenario" diagram MIGHT he US(ful or it might betot;Jlly unhelpful • p,,1rtk:ularlysince the main t•rgets for this piece a1e not all

vitologjst~/~volul"ion.:,ry biolosist.s .

.,.pna ..

e Andrew Rambaut 09:..;

•• Great.A quick sketch of Peter O to be oor 'hum:u1' would be good.

I

(coinc:denbl similarity, of cotu'S(!,)

REV0002935

Robert Garry 1009

• Do you thiti< so.nclhitlg like thi~ is too much coil'C:idc,'ICc?

il,~png •

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:C···-.·,·

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. "'

' . '.... --·~--. ·,

: .... ~

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I

Kris-tun Andersen 13;3,4

Ilike Andrew's figure a lot • so yes, let's have somethif"€ like that. I agree with Bobthat havin.ga schematic ot.1tlining the variousscenarioswould be critical M well• here's one I gee. started on for a

Ulk I'm sivillt; loter todoy. Wouldn't be this one for the ix,per. but could~ O-'~ storlins point?

tr.)ASf'l'l6~ion.ip1t •

'Mar""t' hypothesis • • •

C C? ·-· 1'

~

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,➔....,➔ •••

--•••J,

·-·

'Pre-clrculallon' nypothesls • • •

c c? c? ·-· 1'

~ ➔ ~➔•••

➔••• I

..... ....,·-· ·-·

·---J..

·-·

I think it's important weinvtstigate the dN/dS difference more in•dcptn as itcou:ld provide criticaJ clues that we currently don't tuve • if the spike protein evotvesgreattv after CoV jumps into

flum.ins but -.ve don't observe that in rCoV. th8f"I th;,t'svet'yfmport.,nt infor~tion WOtth indudin,. I h3W! reac;hed out to Andrew, so hopefully I c;-.n wrestJe him ;,w3y for 3 few minute, to discuss

Final point • now would probably be .1 good time to re.x:h ou-t to CIJre to make sure lNt this is of interest to them and ;ilso get asenseof wh3t specific things they might want OOdressed. Oo y',111

want me torebch out to het?

I'll get on the document too. but I'm l)r'lneddown at the moment• I'll have time possiblyl.ater today, but otherwise tomouowAM.1'11 then be gone until SundayA!\11 (w'ilh n.ointemet • I'llbein the

middle of the dcsert...i (< Jitt'(f)

Robert Garry 13"18

■ Yc-.:i• ping O-,rc: • 5i~ hc-r;, little: b.,Y;kgrot.md .ibout the cm.ii group.

Robert Garry 16?6

■ What about these?

~..c,ng•

i I

Robert C.af'l'Y t4s.t9

■ I don't know ;ibout this one.

it\3gepng •

I

REV0002936

F<bn,,,y12t~2020 • @ €) ¢ Q

... Eddie Holmes U:S8

,...\_ Kristi<l'l,ifyov could re.,ch out to Oare that wouldbe gnmd She's had way .oo many emails from me. Jeremy said that he would speak to M;1gd;,. I don't thirit we s~ld have a pciure of the

pangolin a5 an lnle,rmedlate host. Might be them, but I bet these Co½ will be round In a whole range of animals. I don't think we want to come down to hea~ly on the side d pangollns for row. I

would just puttifl: a bloody great question rrt.ark there.Of use a generic rodtnt scrt of thing.

t!JKristtan Andersen tsot

... Eddie Holmes 18:07

,-...,: Why h:l$ thQ n:u'lle or lh-c vnd i,, the P.:.f)Ot'boen<:h:)r"cd lx»c::kto 2019-,..COVwho., thot is~ out-of-d:,te, I ('.h.)~ed thcn1 :rill t~ SARS-Cd.1-2 :rind oow it h::iosb«.-o C~"8e6 b:)c::k.

..... Kristun Andersen :t8i1.0

f.a I thillk Ian 1"light bf:?respoosible ... k>oking at the yef'Sion histo(y. We should stick to SARS·CCW-2I think?

Emaikd Cl.ite• will k?t(all know what she Sly$.. If Ws .i no. Science would li~.ely be into-ested and Cell would take it for sure.

Robert Garry 1&20

■ Change chc:nge to generic rodent withqvestion mark

~-91'18'"'

I

Or ch.an.cc any other .161)CCt as ~II.

even ·Peter Alb§ .Ji&!&

r"I Eddie Holmes 18:33 ftbrw,y 12th. 2020 "

,..\_ Yes: {1) gef'leric rode11lwith?; {2)we need to us~ SARS-CoV•2. Assooo as l.:n as inishtd I'll do a,.::,ther gJobal r,nd•aOO•l'epl.xe.

Robert Garry 18-'4S

■ Other edits corrections suggestions ,wkome.

~fine ...

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<I' (!?-' .

........ !ii

-'":' -1

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ii

~ e @iii -.-ii•

,-+ \_,,. + +

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ii

ftbl'UM( 12th. 2020 ,.,

Robert Garry 19 28

■ Could do sometting like thtse d~grarr.,sforSARS·CoV·1 and MERS·CoV for the supplemental file. Gocd contrast...

Robert Garry 201s

■ M~ybe ch3A2e o~neeCoVs l0 "~mar ~ptation to human rcc('ptor' Maytx, ctv.necrcccptor to ACE·2?

r"I EddieHolmes 2M0

~ Dooc more on the text Looksgood.

~ Kristi.an Andersen 22.:23

Ill I'm wioed • but will bke a eood dose look a'\d J)(Ovide edits first lhi112 tomorrow .

... EddieHolmes 22:2:6

,....\_ Get some rttt!

e Andrew Rambaut 04·24

.a

■ I'll be.abJe to get on it today.

r"I Eddie Holme» o-.as

~ Thatwouldbegreat.

Robert ~rry 0942

■ 11ttps:K\WIW.nc;:bl.nlm.nih.gov/pibmed/1740219S

I

Ftbl'U3f'f 13th. 2020 ,.,

REV0002937

Ftbruar, 13th. 202() ..,

t) ncbi.nlm.nih.gov

(Study on tlw! dyn.:tll'lk p,cv:.lcnce of «!RIM :.t'llibody 33.:1iMt scve,.. :1eute rcs:pir.1tory

syndrome coronavirus in em.pk)yees from wild anim31 marl<et in Gu~. • PubMed •

NCBI

Zhonthl.D Liu Xin2 Bina Xue Za Zhi. 2006 No\1:27(11):950·2. Enelish Abstract

(13k8) •

I

~ Kristian Andersen 09 49

~ Clar~ got back to mewith a •Yes please!•. She sugg~ted this was prob.bly a •Perspectwe•

FtbruafY 13th. 2020 ..,

m l!I El ...

., ...

y,.,.\_,.,k ..... ~"-c•

,,.\_...,,. ,-u ...........

'-'k.b,,t-0

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DISClUMElt TH-J ••Nit•

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-,.,O,W~41\0!UllOl'lgiN.

hlfndt01~ • ,ou hM

-~....\_..... "'\_....,\_

NOffl'litlt~.,,.,~llffOffl\_\_,,.,....

\_,.~ \_\_

I

e And,.,.Rambaut 09l2

•• 1 was thinking that something aklflg tre unes o, a perspectl\e as we are bast:auy wmhestsire 1nramat10n.

lr.!IIA Kristbn Anders~n 10.'Y.l

Ila Yup. agreed. I'll take a look as wen shortly

Robert Garry 1021 Ftbrua,v 13:th. 2020 ..,

■ That's good news.

11W KrisrtanAnclersen JHl

~ A couple of guidelines for the PctSi>CCrivc format• it's similar to a Review. but we have mote flcxibilitY in te<ms of content aM length (can/should be short): https;.1www.naturc.com/n.aturclfor·

ilUthors/otr1er·s'-Os

Main thing• 200word syncpsls .ind we can include a fait number of figures. so we might consider having maybe three?

~ Nn.turc

Other types o1 submissions I Nature

Ott-er types ol submissions

kbtUMV 13th. 2020 •

Robert Gar,y 12-29

■ Was thinking of something fike this for the ~;uoolement. esoeci;illv if Kristfan devdoos some convincina. dN/dS di'lt.i c;omo:iring SARS-CoV• 1 ;md -2 mavbe other vi<uses.

~.png•

Al$0 I ptob.:ibfy h:)1/(.\n't aptutcd the bc,st now for the ~riOu$ tecn:,tiOi: bu throw·ng th1s out fot <liseusslon :'Ind m:.ybc lc:,tnlog somcthif'\8,.

I

We might want to go with other •gene-ic'" "humans· ~tsome point. @IZ\i#i:: J§b-$

REV0002938

.... Eddie Holmes 1S:13 Ftbruar, 13th. 202() ..,

~ Jetemy ha.s connected my Y\'lth ,.....agda. So. It might be worth at leas-l siendlng her an ur~ml.shed draft Ju~t so ~hean .see w'hat we are ddng. If we can craGk thl:s loday that would be gra'ld.

lrlall<rifflanAnder<t1n 1S1$11

e.£1 I thinksinct aa,tis on it the<e might not bt a need at U1is stage?We had a long« chat about dN/dS and sorne phylo figure$• f1gu,eswill be helpful. but the dN/dS needssarte more thou&ht. so

we'll told off on that fornow and keep digging through those anatvses.

~Edde Holmes <a.-, you pltase let Ma.gda 1-:,-.ow thal we already talked to Oare?

r,I: £ddio Holm0ce H,76

~ Will do. Pel'SO<laltv, I oot sure I'd bother with dn/ds.

tlf'6IKristi~n Andersen 1s.21

fa Normally I'd agree with you. but <ould provide a <riti<al Gluc in this parti<;ular Gase will cXJ)lain later •~ ,

GutfOI'oow. not aoinato bt part of it.so allaood.

Robert Garry 1610

■ lncre3re variat"wn is Sl)ike was a thiog duting the sprea::I into Ko,ea • ll"ey were worried a neutt.lli?atton resist<mtmutant.

trttps:.Vwv,w.nc;t,i.nlm.nih.gov/prrc/articles/PMC4696701/

.) PubM~ ~ntr.\l (PMC)

Variations in Spike Glycq,rotein Gene of MERS~CoV,South Korea, 2015

An outbreakof tiosocomial inftctions with MK!dle East,espit.lt<>ry sy1~rome

ooron.wirus0<wrr<'d in South Kore, in May 2015. Soikeg\_lvcO(lroteh genes of virus

strains from South Kore.1wereclosely rebted to those of strains froin Riyadh. SJ1•:

Arabia...

-Si\ih:Hfl@

10;13 THi.s paper may not bt very good· you·re vvaybetter than me to judge, but k .seems that changes in spke occur on introduction p.lSsageln humans.

t':13 tittP5:VWWWfl<.GdG..aov/«ald..'orticlo/22/1/15•10SS\_;1rticJQ'

D EmergingInfectious Diseases Joum.al

Variations in Spike Clycoprotein Gene ofMERS~CoV,South Korea, 2015

An oulb~k of 1\050<:om\31iofectlOns with Middle E3sl respiroto,y -syrw:fr0rne

coron.avirusoccurredin South Korea in May 2015. Spike glvcOJ1roteheencso ..

(132 k8) •

EMERGING

INFECTIOUS

DISEASES

A""·R,.;,,,db!""T~,n ....... 0.,0,•••

.;ilso on passage in vcro cells.

Be saf~ in Vie desert Kristian. Watch out for snalles • can't ~ too cattfuJ with all the co.mn&•,iru!tS o::irert ...

~ €7 ♦f&i~~&~~

... EddieHolmH 18:40

Febru:uv 13tl\ 2020 ..,

..-,; Jerem•t has spoken to Magda. She gets it.

FtblUl'NV14th. 202() ..,

..... Eddie Holmes 04:48

~ Oeor (ckfie t,nd Je,emy.

M;inythanks for the oll yeslerd;w. Jeremy. and for this emal. Edd;e. I have lorw;irded 'f()Ur message lo Clare so close the IOOP: as indK.ated to Jeremvaverthe phone yesterday I lind this very

intere-sting and important: we win discuss in the tditorial office .andOn will follow up with you directly. Eddie.

Th.Jnkyou lg.tin.

Magdatcna

Robert Garry 1 S44

■ Useful~ perhaps for the supplemental file?

., •. png •

REV0002939

... EddleHolmt:S 22:.c..;

,..... Tile paper i~conin.e together. Howcvtr ... Zhang is hinting that they ha\lC sonething big. He won't tell me until it is conftmed. Cold warlcV('IS of paraoo'ta,, Gi\'<'n that wewere discussing re-analysing

(inc:. "iith PC~ tho o00 prG•o..itbro.-,k 8AL r~spirotory &ampl$, from W1,,h.,n I \.YOndcr if h,c M ~ hit? 01>,,iov5'y. this willbc;i husc but ol~ lil<Qt( r,cndcr our p,.ap(I< poin0oS5 $in<:o it VI-OuklI)«)~ ono

tiypot,'t,esis.Alternatively.he!may just have (fontified a related virus in scaly fcrrel or somctting.. I II let you know as soon as I do. Sut I think we stv.>uld just hold off until I knc:,w wh.at is going on.

Ftbrua,y 1Stl\ 2020 ..,

RoMrt Garrv 08.11

■ Agree that the J»pcr k progre-ssingnicely.I think all the bases are cove:red. I can't really think of V1tlat Zh.angcoukl come up \vith short of finding exact SARS CoV·2i:na wild animal (pangolin?},

which is doubtfVI. Unless there issome ex,ensive htscQJYor 1he BAL 5(11nple,; evefl finding SARS Cov· 2 In a pat1enc would n0t (llsdnguish the cwo hypotheses. Fhl(!lng SARS CoV~2In 5·10 w0t.Jld

sirow provt the cryptic circulation hypothesis. btit I doubt tl'tis possibilty. Ht might also find a polybasie•le,$SSARS Cdl/·2. which would be kindacool.unli~ly but I tllnk that eMancts not moots

the paper. lOWSthcre a possibility he could add extra helpful bu: likely not dcfinlivc data. I think we should push this out ASAP.

e Andrew Rambaut. 0818

•• Eatltet human sa-npJcs wit hoot oolybasic insert • crvotic transmi$Sion folkwlcd by adaotation • hypothesis 2.

P.tngolin or marketan 1m;il with with polybJsic insert • hypothesis 1

Pangollnor market anlmal very close to SCoV2 butwlthoot potybaslclnsctt -no nforriation about hypothe'Sls 1 or 2 but perhapsmakes lab passaging more llkely(.llttle rime for anything else).

Eatlict huma,n sanplcswith pofybasic hscrt,., C()1)tic transt1ission. market probably not imJX)ftant. but no adaptation to produce epidO"nic .. no irlormationabouI hypothcsts

Robert Garry 08:33

• I veiymuch ag,ce cxctpt foc ·E.rlicr human samples without pot,,t)ask: insert • ayptic transmissoo foUowcd by aoaprarton .. hypothesis 2." Make 2 more m:c!y but not dc-flnitivc. we won't know

whe<e the person got the progenitor • from another h1Jman or frcm eating/exPOSure to wild anim.11. Also no way to know if it took off °'wasa "stutter" • all predicted in the text.

a And~ R.lmbaut ous

•• I think if wesee human casts without aninse,t then it pretty much PUlS us into hypotliesjs 2 country. lhe alternative is that the tumans with and without the insert are independent ;umps

'book~n(ling' the acqvisition o! the inyirt in the non•hum~n host • thi-. s~ prert.y uriil,c,ely

Robert Garry 0843

■ Agree• much more likely. bat I think you wtered From purely geek perspective would love to actually see a polybasic•less

this nicety with the "paradox" d:SCUSSion. SAR$CoV• 2.

e Andrew Rambaut 11 ,;7

• ■ 5till a bit of c-ltarin,g and tidying to go. Happy to have-thoughts 011 this...

Robert Carry 1:J2S

■ 661 ccdipigagi caSyqtqTns prmrSvasq

Is the nombering cor~ct fo, residues? I've been using QHR63290.2

e Andrew Rambaut 13.31

•• I-Imm. The numlw:ring i$ from th~ :)lignm,cnl

I can adjust the residue numbcrin2 for the inS<:ts but probably best to use SARS·CoV·2 numbcrin2?

REV0002940

F-tbru.irv 1Stl\ 2020 "'

Robert Garry 1334

■ Ok • Wt CO<lh,1)t(l (0t • , ~wily P\ll lhe dllli00 ~kl (lurllbef!, 01 th1: i(l(,livi(l1,1;)I (~i(lues r,oot ...,llJ b~k Of e,:.n;h io~vi(Ju~I )l:(tl.lefliCt', Set:fn!> to be (t&lll in u,e text. Also 1'(111lcJYbejv:.l Pvt;) IXIA

.iround the residues $673, 1678, and S686. It's t~ insertion of tt-cproline th.atput$ a l:ink Jun the sequence and ~ads to tht pr~ckrioo of 0-linked glytans. Other betacoronavir\.6C'S likc HKU1 s~

diagran at 2:44 ycstctday have a somtwhat diffo-cnt solution'°' a sttoog tum 0ots of scrinc:s) but a S, T. Prich regions is a requirement for mucin-likc domans of 01hcr virus GP

Using the SAR$ CoV•2 numbering wor'<S just fine as weU since its 5673, T678, and S686 in the text-just need to that say in the legend.

Just to be dcar·ycs I

'd us• tho SARS·CoV•l nuttbtring.

• Andr,w Rambaut 13 38

··•

The other thing I could do K to coloorthc rtsiducs so that they arc onecolour if they matc-.hSARS·CoV-2 (I hate typing that}:md a different ooc if thcydon't{i.c .. oot h.we <CSiduc-spccific colours).

Robert Garry 13·'10

■ Also I wa:> se>ing to say put h S1 aod S2. but you're rast!

• Andrew Rambaut 13·"1

•• Ar'e you happy with tl"f'!othe< labels?

Robert Garry 1344

■ Y~ • 1:1~1 'S:'lre Jooking fine :,nd I think this is:, big uP9":>de for lhe-in-text figure-.rd stH keepttnd ~rt»p~ even exp:,nd the: :itignowmt f\gure$ lor the s~pletne1H~ file.

As for the c:ifforcnt colors l'rn thewrong one to ask· color t:4ind ~ the colors arc notvcrvcolor blhd fref'ldtv(not a big deal in this case of coul"S(!)• what I can pick out thav~m a bit ar'bitr.irv an:t

not really group .1CCordlng to chemically similar amino acids Y,W and F shculd be same or similM for cxaml)lc. I t"iink putting the boxes around ttc ldC'ltical tcsklucs li<c youdid is the best

appro..cll. @Si:i§f::

fb/@-

FtbNMV lStl\ 2020 "'

•• Eddie is coJ1>ur blind too (I remembe< from the Ebola i»Per).

Robert Garry t3:S7

• AndrewR.ambaut 1H1,

■ Shovld be S1 o,nd $2 )Ubunit. The coron.lvirolosi,bi 11ke to \l$C N·tcrmn.JI d()n'l.lin (NTO) .>ncl C·tcrmin.il dom.>in (CTO) for the tW'Op;.'.lrb of-$1 thill ~n be R~.

• AndrewRamb:u,,t 13~7

•■ OK.

Robert Garry 1400

■ Lookir,,g grc.,t • might pvt ";pikc"in the toplin,c b;.,t I don't have ,trongfccfing forthi~

I might have to look into Gcneioos.

I see you had spike in a~ took out • your choic~

e Andrew Rambaut t4-<18

-. I dkMl me.in to delete it. Wlll put il bacik

I

Hereis the (Illustrator edit;'!ble) PDF vetsion

PDF •

f'-e1>ruarrl)tl\ .lU:.N ..

•frgure.pdf I

P01'

Robert C&rry !◄ 17

■ Looksdeanand to the point to me• exccllet1tW<lrk!

... EddieHolmes 14:58

,-...,; Right. lcfS onty make miniJNI changes to th snow. l"H get a nna1 vC<'SIOO as a t.ormal word ooc. Submit a~ soon as wo cal\. Figure IOOkS

today• ~maps tncn tor drcu1at1on great.

I ,cnt clo,c to tht fin~ dr:if1 to Jcremy.:,nd he lo,-cd it. Cot ~me comment, b:ic:k from him ~nd ,omconc cl,e .:,tWcllcome th.>t I will intorpor-atc. L.>vric C.:,rrett ~, b¢-en on Twitt::-r ...

Also in the O;iily ExPrtSS

• Andrtw Rambaut tS:OS

•• Was it about the METEORITE?

REV0002941

Ftbru.vv 15th. 202() ..,

... EddieHolme:sH:U

~ Follow the Garrett tflread. They are directly excusing T1Jn who I know well rod is.l gre~t guy, StJCll BS. Theyooly did animal dissections in the Wuh30 lab.

• Andrew Rambaut 1s.11

•• So b:,,i~Uy this~ a MW K~n.:ariQ • dirW inio,;ti,on from a b;-it (hc;wQV¢1" it h-ppc~d). Mow¢ver, th.lt dQ~n•t ~kc; $¢n'° bccavl.<l ~$ for as~ <;an$◊e: b,."it; don't h."IVO(lither tho RBO mtJt.,,tion$ Of

the furi,, site-.

Robert Garry 15:28

■ We make all the key points." Agreed • evel')-one will not like-It.BUT. cvttyth'ng had to be coosidctcd, p.1rticutarly given the unfortunate coincideocc of the locatia, of the Vv\.than lab 3f'ld the •

excusethe pun • batsftit c<.uv ,xess and conspira:-;y bk,ggen.

'-inliktly tobc a direct intecrion from a bat.' Yeah direct statement to that effect would be good.

Robert Garry 1 S:37

■ Bats have distinct ACE· 2. There is no txample of tfansmissi<H1 of aoy bat Cd/ dir«tty to hur'nans.

Robert Garry 16.0S

■ Either way good but • just re.ading th:.t Express ;utide though tall<lng .about the l»ts ...

r"'i' EddieHolme:s tU7

~ Ok. Fair poin. l'lladd.

r'9 Eddie Holmes U:56

,...\_ Arl\13'ty. I think there <eroloeic.alevidence of bat CoV<. in horn,,o,c;(Yunn:in)As <;u(h. (l(l)b.abfyw~r rw:,tto i;t:tte there-isno direct tmnsff'r to hutn3ns.

I

Robert Garry 1813

• Ok Eddie agree • love those sc-rologica1 somesort of comJ)'chCt'lsivc

studies but nC<'d mete data. I think .ii the bases arc covered. S~ould probably COn'IJ)OSC acknowledgment section. starti~ with

invc:stig3lOI$ that posted $CQV$nteG (romo,?). th$ virologk.il comribvtort. who frfftv $h;mxl insights. t;ono0$pts ond d.ihl (n .. mo ,orno?), and Jaromy .>ndtho en,.,il iquod (n.arnos?).

W.. Edd it: Holme,s 18:59

,-; No we really need to?The 01,ly unpublished data wecite is i reference to Andrew's dating analysis from Virologicil. We don't actually p-esent anything specinc. Seems like o,erloU to list evuvone

who has depositecl a sequence. Perhapi Jus1;i generic statement!

Robert C.:.,rry 19()$

■ I was ,nostly thinking 11:>outthe Chinese sequencers who wtre ca,ceroed ::ibout getting credit then ported ;,nywl!(. Seems flee people went out ofthe way to th¥1k them. but not necessa')'

anymore • as tor the-«hers goes without sayingI think. .. A ~nerit statement would be gOOd-• lor treelv sha,ed insights. concepts and data.

• Andrew Rambaut 1•.14

• ■ wt

We arc citing papers for the SeQUC!nccs use (pang din is a bit d.ibious I g1.1css).

f.tbruary 16th.2020 ..,

Robert Garry 17 S2

■ tiups:/lwww.washingtonpost.com/poldcs/2020J'02/t6/tom•cotton•coronavirus<onst,iracy/

., Washington Post

Tom Cotton keeps re-pe:.tin1 a coronavfrus cOflspir.acv th.ory th:.t was :.Ire.adv

debunked

Experu say lt'W!re·sno cvdence the virus is man~ma<1eana it's ·l'ligl'ltyunlikely" it is tl)e

result of an accident at a I.ab. (127 kB)•

I

..\_. Kristian Andersen 23:39

fa Some data to show thlt SARS•CoV•2does indeed bind strongerto human ACE2 reccp1or: https.://\vww.bioo:iv.org/co~ent/10.110t/2020.02.11.944462v1

Oh, and stJucture ...

bit btoRxl''+'

Cryo•EM Structure of the 2019-nCoV Spike in the Prefusion Confo,mation

The outbreak of a novel bctacoronavirus !201 9•nCc") rc~ents a pandemic threat

th.3t h.:.s boof'I dacl3rcd 3 public. hc.:.lth cmcrgC!f'\Cy of intcm3tion.:.I concern. The CoV

spike (S) "vc®rotein isJ key brget lo, ufgenUy ne«led \\JCtines, thef3peutic

antibodies, and diagnos-ti~s. To ladJtatc medical couitermea:sll"c (MCM)

dcvcloomcnt we dcrermincd a 3.S A-resdution c,yo•EM structure cl the 2019-nCoV

S trimer il the prefusion conform3ti:)n. The predom'nJnt state of the trimer hJ:S one

of tl'te three nxeptc:,-•blndlng clomalns (R80s) rotam:I up In a rtceptor--a«essltfE'

coriotmation. We iso show l)ophyskal and structu"al C'Vldcncc that the 2019-nCoV

S bnds ACE2 with fligher affinity tmn SARS·CoVS. Addit .. Show more

Ftbf'U,,l,V17th. 202() ..,

I

REV0002942

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"'::';,,i

~: ~·

/

,.

"'::';,,i

~: ~·

/

Robert Garry 08"16

ttbrua,y 17th. 2020 "

• Thlslsftomthc sup file

iN~png •

A

o.c-•-t

o.r---•1

----J

Those arc ~bably the o·linked glyc.ans • tl-ey W1?re iust gu,essing what that density is.

e AndrewRambaut 08'8

•• Are tl~e mtibody (tCCCS:,it,lc?

I

Robert G;a,rry M'I~

■ Th.It's the trimer so yes• right on the outside.

e Andrew Rambaut 08-'9 f:ebru::uv 17th. 202() •

•• Cool.

Rob9rt G..lrry Otl $2

■ It's •onty" a3.5 angstrom structure wllch i-sgood for ctyO. But leaves a k)t to modcUng and imagination TH«e are > 20 n-linl:ed g)ycans

THe o-linked ones probJblyk>nger <md less structured, but the f.actthJt thJI density is ther1? is asvou 5.'lid pretty cool .

..J Kristun Andersen 0916

t.i9 Cool. Any 1ns,ghts a-s to wh;it th.11 cle.av.1ge site rrwghtdo?

.... Kristun Andersen 09:38

la Just skimmed through the rnanu"SCriptand will read more closely ~ter today• probably best to wait witll edits (if a-ly) until wehear back from Cla~. I 00 noticemt name is misspelled though ':.:

Af.c,hew, c;;orrt:c.."l«f vll;:'r:,qn.it Qn tlu!Vin;,logi-ci,I

Robert G;a,rry 1014

■ They haven't posted their coordinates yet. I'm goes.sing s.tiU refming the models v.tiich takes computer time. Tiley dkS modify the ~AAR site to PGSAS,but this wo1,1ld leave tile Olinkages. At the

veryStaStVihat tM-y&abtle<las gtyc.ansat 717 aM 801 likelyaren't • t~are tOOl'ligt\up.

G:!)~

Roh.rt C~rry lCY.l1

■ I think that is the Engl:s.hspeUingof ..Andersen."-noturtyouknow.

The version on vrolog.cal is pretty good • .k;Yemy is asking for it • make;s a mudi strooger case against l)ivoengineering.

Whilevou were dodging rattlers did you come to any insights re dN/clS????

• Andrtw Rambaut 10.3)

ttbruary 17th. 2020 ..,

411111

■ Tile versionon theGoogleOoc:: is out of date. I arn just going to 6x the figure.

~ Kristian Andersen 1c><10

~ I'm gonna spike Eddie's drin1t for pulling fhis out <>fGoogle and inio Wc,,<d • .

Finally~ up and pJOperty read through the whole thing it's very good and ba1anccd IMO. I'm.sure:we'll have <hancie to provide updates.~

Will"'-Ofk on dN/dS tod.w •lot's io•wh.oro that bk•s us.

Robert Garry 1040

■ There is a SARsthat Should be SAR.S. Sony not to pickup on the 5vs6thing.

Robert Garry 1046

■ "Will work on dN/dS today• let's see where that takes us." I think that it could be VERY important.e~n dccisi~. But ttie curr<-nt versiM will be prettv understandable by thC' policy oeoole who I

dm most coocerned about .rt the mo!YY.!nl. The structure/bi11ding kinetic paper c.a~ at ;ust lhe fight time. MUCH stronger ai'guimnt a~inst bioweapo11.whch is ,ust what is needed now to

counter the t-ox News crOWd and otllefs. There are plenty of tono.v-up man11sc.r1ixs ..

where di"l/dS. pofybaSlc and O-Unked Sites across the C<N family. etc could go.

1111111 10.~3

KristianAnde,sen

~ i:>tally agree• ,min issue is that it'll pl.ti us more in a research direction as opposed to perspectivt so it could get tric.ky. But I'll work on it and write up a Virologic.al post probabfytornorrowor

Wednesda~•·we can l;hen ~ where this takes u~

As forf())( News· Tom conon lstrendngv,:tr, COVID·19 o~ the Twitters atthe mom<s"lt.I gotta say• the tuvisn't totaltywroog. "'lth0u8h, of course, me reasoo whytoc-y·redoi,'t this has nothing I

to do with the virus and everything to do ~h they Ch na comment.lry, so obviO\ISty wroog).

• And,\_ Ram bout 11'°9

Ftbruary 17th. 2020 •

.a

■ ~oplt are oickir'@up on the tact that we don't rule out animal passaging.

1itnaeeon1 •

•=

--.,~lboth,Or)ltllil~

--b..nlll'll/"IO.-,~N

~M!flflll'C!IIO•not~I\

...... ,.....,.~

~..-.:1 .. ~ttoh

~"!OJrtli:M:lr:INf'lflf

";,\_.,\_-=----

-

o:: I

·=-.~-=-==-=

REV0002943

Ftbru.vv 17th. 202() "

~ Kristian Andersen 1111

la Ye.ah, unsorptisirg. There is no que:sticn that thi-sil be picked I.IP with "'top scientists con side, this could have come from the lab". lhis w.lS my main cone.em with this 'backfiring' basedon our

provi.o..,1:v•sion,; ""4,,e,ath• condu<ions ~o too opcin ondod • I feel ii, th" cu,,..,nt v.-~ionV#i do OVOJylhirtJ 1'W)AA.iblo lo 1>ro1)Qrtydi~u~< (tl,li:trythins, but y«, :u thi< SbQe VII" unrortun:iotqly jud

Ccln't rule out a potential acddental infecrio1'1 from the lab.

Robert G.arry 11'44

■ No. we ca.n't and shoUd not because that wookl have precipitated the cries of COVER UP. No doabt Tulane would have been l>ccn im~icatcd.

Robert~rry 11 SO

■ Whatcouldand~hould be doneinmyopinion is 10 havesolleont • gtt SenCotton orsomoonc from his s~ff plus some credible-scientists•togo to China and inspect the labs artWlllan •maybe

ilso tl:e ones in Guangoong too. Theywlll Md that th,:y .are set 1..p to <!lssea dead anlmals and sequence • l'V)t much ei..e ;mo certainly not a program th~t cculd have bloenglneered SARS·CoV•2

ftom scratch. look for a ONA s.,nthe1iztr.

• Andrew Sbmb.:liut tH9

•• Is there a new pangolin sequence on GISAIO? can't c.~c.krght now but someone mentioned it O'l lwitter.

llflllKristianAndersen 1201

~ For some n:a:sonthe platfonnwcn't load fo1 me. Will chcckagainin a bit

~ Krid'l:.nAndorHn J'H6

I

la Four new stquenccs.

lip •

pango.geneioos

...

First glance• they're quite different. Doing some alignments righl now

Robert Garry 12 20

■ PARA most import;mt. Guess I need to get geneious.

WIiiKris-tun Andersen 1222

la Bob. you ddmitely need Geoetous -CCJmmitto it.

No turin am:I the-se are ~mllu to the prevk>us pangos • Le .• not the elusive 99% and tile R60 Is not similar to human.

!I~ •

nlignmcnt\_$pike\_;1.1\_p.,nso.genciou$ .i,lisnment\_$pikc\_nt\_p-,ngo.sendot1-,

II ,.,

• ?Ip

e Andrew Rambaut: 12:s1

•• Peter Bogn~r h,:a-!.just \ent me anothef one .. hare on

Don't share just yet -will be upon Gisaid shortty ...

EP1 ISL 410544.fosta •

>6etaCoV/p.angol in/t'.D/P2S/2019I Ef>I.,l SL\_ 4l 9S,4'

TTAt.1ATCTGTGTG;CTGTCACTCGGCTOCATG(TTI\G!GCAC.1CACGt:iGTArAATT~fAA!TAATTACT~CGTTGA

CAGG.\C.ACG¼TA."-'TCGTCTATCTTCT«t~NMltfffltmNNIINN~NNNfM».tMmGCATACCTAG

.. ~TTT~<;fCC~TG,fG,A((l';~TM(ATWGMC:CTTC.T<C<T<;nnc.v.c~A<ACGTCCAACTCN;,T

Thenew~golin hJsgot NNNsover the cleavJse site!

~pns ..

\_\_\_\_\_ ...,,\_,

\_\_,\_\_....,.

I

OK nc--w one isn't much use eith('I'. Qi#\faJ,i. hi&

ll!ialKristtan Andersen 1301

la Yeah.they have done 1ha1 bef0<e • filled in with N. I'm prcny sure that's beousc they ali1.ned to SARS·CoV·2 and just filled in. I'm confident those bases don't exist in these icoomes

• Andrew Rambaut 1110

• ■ Yeah. Not the sm:>king gun.

What do ycu reckon about Jeremy's mtUe5t to t.lce down the v1rologlcal post and wait for a press conference. ThJt 1$not gong to work. Butyou are cccresp:;,ndlrg.

~ Kri,tian Ander5tn 1:i.19

!a Here's my thinking:

1. Vrolo»"cal post staysup

2. I get .l holdof Oare and my institution to coordin..ite

3. No press release <Itthis stage • for one, I can't beause itwovkl be against institutional policies

4. Pres!, re~ase wilt not hetp at tlli!, ~ge

Kristian Andornn 13.2-4

And 5. -no pre-print at thtS stag~.Myhandsare tied on above u.ntil I get a hold ofmy institution, but 5.is mypreftre-O(t -thoughtt on this part?

RobertG.lrry 13 28

■ Idon·I really sec the dlffetcncc btwn preprint and the posrlrg onvlro'°glcal.

Rob@rt Carry 13 30

■ I' t1·1· gUee.gl tlst-slt • ,!ftle~lest eio l:1 Ucc tllco ·,t etleJ<el eb e1·c1cc.W;iitltakethisbackVERYbadide,1.

REV0002944

~ Kristian Andersen 13

◄0 ttbruary 17tl\ 2020 "

~ Preprint (bioRxM becomes more otflcial • Lt .. at that stage we·re deflnitctyact1ng on bd\atf <:Aou, inst1tut1ons. we need to gtt all our ducks in a ,o.v here ano then pusti f0l"W3fd.

1,hoUd ,-oy (since I wu hiding in the dc,crt.,) • I think till ot thi, w-"' done correctly. Out there's o need to sl~ down here • let', mokc w<e .ill chMgc, ;,re inc~tcd, fin:il venion\_, prcp~red,

ii,e-ss •ele~ Greilted. and everyth,ing pushed out as fu\31 pee,, reviewed JX.Jblkarlon. l',n hopeful a11 of thfS can happen within a few days.

@Andrew Rambaut how far apart are the Word and CioogSeDoc versions? Any w~y to make the GOO<: c;vrrent? Mvc;h easier to keep it there and I'll make sure evwything is 6naliz.ed when the time

comes.

Robert Carry t:345

■ Another consideration• Clare knew about the-structure pa~r immediately • maybe she's followi~ this VERY closely, but anotherposs.-bitlty is th3l that JXIPN"was submitted to Nutur~. Ir so. she

may h.lve both papers on the fast·track. Just speculation,

.,..a Kristian Andersen l"';•:.?

la I'm already getting ml.Atiple medi,1 requests INYT • not Oon\_ • and Bloombe!g bel\g the biggest). This i;: as expected, but we need to have a response ready. Thoughts about this?

Toe~dite the sdenc.eand for comp.letetransparer.cy,wehavt madeour findin,gs ovdlobJeto the pubic as tapidly as pl>SSibk. 8esi1esthosepoints already teiterated on oor Vir°'°3kol post, we ore unnf»e to

/Vrthcr comment on ow study at t,.ispomtirl time.asit l.scuffMtly belns reviewed byothcrsciendsrs to cr1s1.•re occuracy.Grvtltthe impo,ta11ct of th?.se{lr>diftSJ..

we~rld tllor ,t 6 cridcol thot our study is

\'ettedbvotherscientistsond oor (lnd;ngs sho11kf thtreforr be consid1red ,;reliminO'fVunorwblishedina oeer reviewed iotimd.

\Yethank you for your intttestond we vlll beltot>P'Yro touch bosewith yo.io.am.it reviewed. Weare hopefuJ this will be very SOOfl

onct the paper hos been vttted and pttt . .edtl'd}

{We uc;ed a very similar response for our 'Zika Cuba' pfl)er. which was also somewhat contr~rs.ial. This line of res.p,onse worlced out pretty well).

I

F-tbrwry 17tl\ 2020 ,.,

Robert ~rry 14.'17'

■ Pitch perfect...

Robert G.arry 1◄ :;a

■ I just used a version of this ,oo ...

C!:] Gi

e Andrew Rambaut 1$1:12

•• Y~. That is good

~ KridbnAndcrscn 1S0-4

Ira Aod(e"N • lt!a.nks for bfowing up Twitter. Great stuff.

e Andrew Rambaut !5'.(15

• ■ It has been quite posld~ so far. Oul rmybe the crazle,; are liaven't gol out cl bed In thtll" parenls' basemenL

~ Kris-tbnAnd•run ,s09

113 A lot of good diswssions going on and so far pretty rcasonab&c. l'I just stay in the background for now• no needt:>rei~tewhat's already on thcvirologicaJ post

Should have the Googe Doc upd.,ted shortJy • ca is slov,in,g dov,.n progress. For 1he kwe of GOO, let's please keep this our version .

...\_. Kris-tun Andersen 1.S:20

Pl! As we aet tflis wrapped up (hopefully). let rre just share some SEAL and Napoleonic wiWOm. Not Quite sure who s.a.id v.haL

Dress me sbwty. Iam In a h.irry.

Slow is smooth, and smooth is fast.

I

Slow is smooth, and smooth is fast.

f.tbruatV 17th. 2020 ,.,

iflll Kristian Andersen 15:53

rJ9 @chanf'lcl Google Doc is f'lOW O\I master document • please use that and not the Word vcrsion. No more desert vips for me so I can ~ndlc SYbmissioM. cu. @Andrew Rambaut left a COffi'I\Cf'lt

for you in the legend.

t. Finnedbyyw

tTttl)):k'c.k>c!I.SOOgk:.Wtn./documCl'lt/d/14Hl21tdEyXQSX880C2KwHx.SfKff)'MdKWdMZGXxbd2.dS/Cdtl

G SuiWOocUTJC'Jlt •

TheProximal Oriain of HCoV• 19

• Gooclelloc

Robert Garry 16.¢2

■ I think th~t·s an crlifact, but good thought • probably not needed now.

r"WEddie Holmes H:08

~ The new pangolin sequences are all from my paper with Tommy. No cleavage site. The P<'!(>Cfwas sent to bi~xiv a week ago but has d~P()e)l'ed. It has been revised and that revision w111be

I

.-.I Kristbn Andersen 1&20 rn -@Edde Holmes • anymore insights on the 'Zhang Scoop•?

Robert Garry 16:21

■ So SARS•CoV-2 i'i fmavbel ioing, to hit Naturewith several O.'loers and the cover~1:1ZikaV? Hooill(: th.it's true •WQIJldbe extra fine. very approori.ite and a sieht to see!

r'W Eddie Holmes Io:22

,,..\_ Not ex3ctfy .. bvtl've heard they've h3d a lot of bat SillTples in the lab,\_

0 @

r"I [ddleHotmes H:J?

,-. Seems like Twitter are reascn;1b.Jy interested in oor pap;:.r?

...aKrlstun Andersen 1616

~--I

Already got the iitert'lt of ~eral major ne\'O outlets too· rno:,t importantly NYT. For now. let's j.J:,t s·tick to the party line above with oo further comment> for now(the ones I hcl'Y'Cgotten back to

with t"3t response h..ave betn nice/ undefstanding • including, 3gain. NYT).

REV0002945

.!ii Kristian Andersen 17:07

Fcbl"l.l,#,ry

17th. 2020 .,

ra £m..1lfrom~c.kforG,-1.11! •

http://virologtul.org/t/the-proximal-origin-of-sars-cov-2/398 Feb 17th, 2020

From Dave O'Connor (No content}

Some comments from Dave O'Connor -Just FYI

Robert Garry 17:36

■ Thoughtful. I get the la.st comment about renaming lhe passage SKt'fon. but it's not tiealty paralJel cor\Struction that way.

• Andrew Rambaut ta·t0

•• Interestingly, BetaCoV/pangolin/Guangdoflg/P2S/20191EPI\_ISL\_ to go up on GISAIO) is very close to the 'pangolin on1ioo' sequence we used in the paper

41054412019 (one of the last 2 p.angolins

from the mctagcnomk datas.ct. It is ac.tualty Quite complementary in that they are both missing bits in different ptac.es. Not exac.tly the same though.

r"I Eddie Holmes 18:34

,-; Indeed. This is all <kscribed in our paper, This is a scale sample that is completely separate from the previous Guangdong pan.golin. Hopefully bioRxiv will ~ sorted very soon.

Robert Carry 09.46

■ Well r~ived for ,sure -and >18.000 re,l(fs in less than 24 hours.

REV0002946

.-~or--, ,011, ,ev,ev

~ Kristian Andersen 1 S:37

l!.I! Sooy Andrtw and Bob that you C!i.df)'[ quite make ttiC CU( to be a ~Top Ep~iOl~iSC Hilatfous ·,.I.

f.ll"frtrniOS-.

In ,1 p.ipc-r past('d:oolbe scicntlfk:

onlintfon;11,\'itolc:.glt~IOI:

~,lhtt<CW'nltou-\llbo

indudt lop t'picl,tnwklgbt W. l,t11

l,ipldtfromCOlumlUVn.~1'$1fy.

l'.dwa'd llohntt. from ttw

Unlwnl1yod$¥dixy,and~n

Andea.tnofkrlw,~Uidfflt'w

«~c1\ldalgtn!tk'

I

dueslndkwlf 1h.-tJw

co1omvin.a.~

QW~l.Wf:SIIOt(1'f',lltdln,

l,1bontory.

I

•

Febrwry 18tl\ 2020 "

e AndrewRambaut 1ss,

•• I dc;m't think Y<H>get th.·n~obri,qui;t, Kri:,ti;:m (o< Cddic). You i1r<: jwt n 'x.icnti$t'.

~ Kri$1Un Andersen t',·S7

rn Th.lt's just like vour opinion. man.

I ,h;nk you mignt be right •~

Robert Garry 17 14

■ It's all fmc -I'm just aoin&to keep ofu22ina alona be-st I can ...

An,d yeah li'Sl got the top billin.g and a ritJe. Eddie and Kristi.;n were sort.ii afterthoughts. Oh well ...

• Andrew Rambaut INS

•• We have OtJr firsi cit;;ation in the Lancet https://lhww.thelancet.com/pb•assets/1..t'ncetJpdfs/SOl40673620:»4169.pdf

R.obert Garry 100,

■ Must hJVe been added in proof I guess.

e Andrew Rambaut 18:11

•• I signed the petition too.

You know tt\3t •top cpldcmblogi!t' Is <C>Ckl'ley rhyming sbng for '<all my p<oetologl.st'?

., I (a;

I

February18th.2020 "

e Andrew Rambaut 18s2

•• I think this is'pango99'

t1"1\_l>L\_410tl1,tinw ..

~-.,., o\l /p.,i.,,,ol l "/Q1fl.tWf(,l\8/l/2~23 ItPt \_JSt.\_ 4lG72l

CACGC.AGJATAATTMTAOCTAATTACTGTCGTTGACAC-GACACGA6JAACTC6JCTA"CJTCTGCAOOCTGCTTACCGT

J TTCGTCCGTGTTGCAGCCc.a.TCATLJri.GCAiTA.CCTAoGGT1TCGT«GGG1'GTGAC<GAA.lrGGTMGATOOAGAOCCTT<lTC

.fi CCT6STTTCAACuAl'".w\.VCACACGTCCAACTCJ.GtTT«.CTG1HTACAGGTrC6C6.ICGTGCTC61".!r,CGTOO(TTT00

Robert G.any 18.S2

■ ls.igned it too,b.Jt I'm fearful l'meoi"9to sbrt getringr~s.ts to don.ate to GVP

L treptv 3yearsag,o

• Andrew~rnbaut HH:\ Ftbru:uv 18th. 202() "

•• Pang.o99(it that is what it is)doesn't have the furin site.

IINgepng .

When they say 'up to 99%' they mean an avct'agc og 90%

imi,'f!.pns ..

kl.ctY/H"G ..

=~~--;;...,=n"',z;;-.,.;c-===~~-~;j

,:j),OU)O,◄

I

REV0002947

F-tbru.irv18tl\ 2020"'

~ Kristian Andersen 18S6

ra Hmmm

\\/hat's the RBO like?

Also. thiswas picked uo in Guanedonain J.ll'lu.:tryof this vear? Th~ more oonaos«iuen:t-s I se~ ttie less lik~lvI fird that they art i'\ttrmedia~ • I think they're-just OM of m.-.ny aninalswith SARS·

like CoVs

• Andrew Rambaut 19.«l

•■

2it>"'

SARS-CoV·2\_B;,TC13\_P;,ngdin.gcndous

• z..

I thinlc they are oickint it up i'lt m.1rken or stagingare;is?

Very likein MERS in camels•k>tsof really shott rccorrbinatioos.

Suggestslotsof coinfoctions

But bclsically the same as the pa~otinonline in RBD

liPlillKrlstfan Andcrstn 19<W

~ Yeah. basiolly lookslike a t:etterseQuenced version of the "pangolin oAline" sequence. lnterestini with the RBO fo, sore.

• Andrtw Rambaut: 1?.!0S

•• lgoor~ • th.it 'MlS Ns

I

lifllil Kristi.an Andersen 19()5

llJ Yup

Lookshig,-hJvsimH;irtome

• Andrew Rambaut 1•~s

•• ""'1<'••e.

wi.l Kristtan Andersen 1906

fla Que-st-on is· did thc:y recently realize that pangolin, orry o,v, and then grtw them in the lab to sec if they could infect human cells? This is quite a high J)f00abi1ity event.

Cl♦~rly nont of l~$e ~ngolin s«iu♦ne♦$ v.'Q-ret-~ $-OVr't♦ th<M.1gh

TheRBD isvery intrig1,1ing• if it'snot ~b. then defmitdy rec.ombinotion (Jlsohigh probability event)

Robert Garry 1908

■ The NTO oi S different than SARS·CoV•2. but yes the RBDthereaften,ery similar except the PRRA. Ard yes thJtlooks like~ CoVthat could infect people.Bot re<.ombinJntwith wl\itt?

Wlil Kristian Andersen 1909

r4'! Recornbinantscan be inytting really• could be OOt and pango. just all pango. pa~o and interme<iate. etc.

I

Cou1deven be human and i:,ango.

a Andrew Rambaut 19-10

•• Yes. But bo!h thepangolin and the SARS2 lnt?agt will have dive.-g:~ since the recombination.

It coulU ha"'! Jt.HTC)e(I either way as well.

~ KristitnAndorHn 19.1~

fno.,fini<cly

Robert: Gany 19-16

■ 00 we,~ to~J<l a line o, tw'01Jb0ut ,ecombif~tiOoto the pap,tr • atk:ast put lhe wo,GI ioa-s a pote.)l1;:if?

lr1alKrls-thnAnde..sen t9-2j

Pn Yeah,we p,obJb\r should. let's wJit until we hear b.lck from Nature bef0<e doing any twe.iks though • I talked to Clare this mornirrg and I'm hopirg end of this week.

Rob<>rtGarry 1918

• De~:. on who lhey:.cnt it t.o • the: twittering 11.1:.b«-n <:.lo~.-tc.>9?% fpo:,itive)th.on the: p,,n.goln :..e<iuenc;e, A few diehi,rd:. mi5ht object tc.>even whiffms .it thcpo:;:;bilityof .i bb e:;:;;:,pe,but I

didn't g~t the sense from the public reactions that that was offensive to most. Clcar1ystating no t.oengineering seemsto bethe take home, plus that it is well done and needed.

~ Kristian Andersen 19,37

~ I thinlc there ace two camps in the intecpcet•tion of the paper. {l)Glefintely didn't c:omefrom the lab, (2) mer s.ai(Ithey can't n.,teoot it c.;1mefrom the l,;1b so rt:definitelycame from the!ab.

:. I

Ftb,w,y 18tl\ 2020 "'

e Andrew Raml>aut 20'08

•• New p;mgolin is •t lea~t a much betterseQueflce. See the recombinations in spike nicet,,:

Just the RBO:

,,,,

-..I: Kris-tun Andersen 2012

~ Yup. pretty cool to see. Since thilt 'online' sequence wi.'15kincb stitched together, rm 3lso happy to see ,1 higher qu.11ity seQUelCe for thi$

e AndrewRambaut 20;14

•• Yes. I ;,m Jtso strooglymoving towards the idea that these poor bJst..1rds orebeccming infected in the Ive .inim.,I chain from some other animal (ferret-badgers).

Robert Garcy 21 12

■ Maybe a couple of animals • hen<e the several lineages?

Me thete ftally that l'MJW dffotenees at tht s·end? Cl' is that sequ-endng error?

I

REV0002948

llfllJ KristbnAndcnen 2n8

'8 Ithink thars prol),lblvreal

Vou have Ccnclous now Bob -cheek the aUgnr'l'\Cnt#:.,

Robert Garry 2122

■ Geneiousison myofflcedesktop· but if I was thereI'd be Uasti~ theS' end of Pango90k>okingforamatch.

liW KristianAndersen 21:27

819 •No sig;niflc:.nt simil:u,ty found• . Mmmm

RaTG13vs nCoVandpangovsnCoV.Sigdip in si-nilaritybetweenl)ilngoandnCd./in the 5' end cl (he spike.Interesting.Couldbe recombinJrionbreakpoint.

RobertGarry 21.33

■ Hmmrn • ttPt's uoe><pected Did '{OU run ;) proteinbl3st?

~ Kristi.anAndersen 21'.S9

rl!I Here's• tblostx:https:Qblost.ncbi.nlm.nill.gov/81ostcgi?CMO•G<t&RI0•4T8H83NH014

RobertGarry2206

■ So vou ran the blasbc:oo the 5' sequence and nothing?Tlut's very strange?

IM.I KrlstunAndcrsen 22:10

Im No.the tbl.istx h~shiU.to variOU$Co'A (viJ the link Jbove}•includingHKVs.TheblJstndidn't return Jnvthirg.

.... EddieHolme:s23:08

~ Th,ere<1re<1few oointsto note: (i) the<e<1re2 line.l\_gesof 0.1ngoCoVs.smuggledinto differentorovinces(Guang-xi& Gu.lngdc:ng).th.itt<1reBOTHcbse to SARS·CoV·2.If therewerejustuught in

thechain.why the geographicalseparction?Thatseemsnon-randomto me.Why both viruseslikeSARS•CoV•2?;!ii) hemto explainsimilarityto SARS•CoV·2in the RSD?In the RSOthe pango

CoYs,uc the ck>~St rriali~ to SARS·CoV·2.If it is recombination.wflal Is ,~nbining with what? lnttrcstingly. if you c.loanRODu-eeon~'Yflonymou~~ite~only thIw the JX,n.goCu½,aremoc-e

<lista1"Kto RaTG13again.So.I don't th:ilk voucanexcludeconverge-nee.But what is driving that?Verydearly.therearemoreanimalsirl'IOtvedin this oot it isvervllard 10 wo:k out what is moving

I

towh;it.

G::v0

.•·-•--· -····-·-·

r-'I EddieHolmes 23:11

,....\_ Thenew pan.20 ,.;,usi:Salmostidtntic.alto curs.TM-vtot.allyo~r·hvped in that prf?SSrelease-.Mindvou.Universitiesalwavsover•l'lvpethesethin~

PDF •

• ~g\_wSCAU.pdf

-•-•4•<

••.·--\_...,\_, \_\_ \_

ft,,,. .. \_\_ \_

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ij=·==

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i-'! ...•·=------•--

e Andrew Rambaut 01·SS Ftbruarf 1911\2020 ..,

•• Morni\a.

~ KristianAndersen Ot:S9

~ 'nlghl

e Andrew Rambaut 0200

•• Lookat thea1ignm.entI postedabove.

il'lage.png ,..

llflll KristianAndersen 0201

!,i9 Ve.ah... true • recombination.

• Andr~ s:lamb.aut ()?-01

•• Youc.:inseethens• end.Bul alsothatRaTGt3 hasa patchr:Jdiffe,~'ICfsin U~ RBD.ltlooks lik~il hada rtte>rnbinationin?

Twothings• needto look if th;it recombinationin S'spikeextendsinto 3' ORFlab. Secondk>okif the R80 patc:llin R"TG13tSalsovisibfein the n.ics.

WllilKristun Andersen 0204

PJ!I Thisiswhatvoueuvs~inMERS?

I

REV0002949

e Andrtw Rambaut02,oe

.. ■ Tl'liS soft or thing • extensive ,eeom1>inalion but often or quite ShO<tregi0c1s,NO\"lhe,e near is di..-Cl'SCas this..

if1i1Kristian Andersen 0110 ra Probaibly vast maiority of times it doc'Sn't. I think the ooly reasonable explanation is that the,c is a fuck ton cl CoVs c.irwlati~ in abunchof different animals in some i»rts of China /edted)

Do we know if anybody haseverdonep.:1ssive surveillince h .any of these 'wet' marSc.ets? cirtulam.g. You kllOIN. simi13rto wh3t GVP

Would be intefesting to know if one would find .allsorts of Cr:JJs

h.-.s S($8«tcd doing.... I don't knc,..v if ;w,y of these fig\11(1< ;.ro ac:c:urato. bl1t I think 1 ~w 1~ infoctivityr-'t~ in «)f'r'I('.' of th<t c.;.ptwod p)ngoll'ls • th«1t's vcrt w,ry ti.gh.

{which.if true. probably also means tl\it they'rereservoirsand n« merelyintermediatesl

~ Eddie Holmes 03:2~

,....\_ I still don't quite totally see RBD recombination into the part;olin sequence. I see it the bit Yklereis divergent. but where does it acquire the human seQJen.ce?

r,: fddie Holmes 03:36

~ I'm not doubting that there'srecombif\ltiOr\ Ob\lious. But I need see v.here it makesthe hullan and ptf'lgoliriseQ\tCfKt so close in the RBO?

e Andrew Rambaut 04<12

•• Iplan(Odo a more dei.aited analysis tcday. Wm ix,st here.

r"I Eddie Holmes Ol:0:)

r--; Or areyou ~ying that the RaTG13 RBD h.ls reco-nbintd out? Couldn't that tittle duster of mutations just be receptor adJptation?

rtOl'Uilfy 1'1tf\ ,lV~ "

•

• Andrew Rambaut 04:06

• ■ Needto look in the svnonymous.

rlllllll[ddieHolmei 04,1)6

,... PDF•

Fi;ure3\_2020·02· 18-6'm.pdf

• POt

·--~ ":,:".:'

~~E ;r,

e Andrew Rambaut 04:06

•• Eitherw~y ;his hiooened <1while back and ltierc ;.re overt..-,'Cd mut.;itions.

r'I' EdditHolmts OU>7

~ Hercarc Tommy's trees fonhc RBD

I

~ Eddie Holmes 0&:12

~ Here's a r°'-!gh amino )cid ttee of the RBD. Pretty striking.

POF-•

• :,ecte<I\_R8D\_whole\_wSCAU\_ .. \_phyml.pdf

••-v-•-----•"

'

-

·-·~·-•-""-...~......... , ..,..

L--

-------------·--

For the RBO I can't qute choose between l'Kombinali:)n orcoovergcrce. o, both?

I

H.l>i'WIYl'ftl\ lV:.Ni ..,

• And~ Ram.baut °"·4'

41111

■ In;i good way?

e Andrew Rambaut 04,14

•• It deflnlteCylooks llke the nucleotides lollov; the aminoa<:ld$:

-

I will add in all of Tommy's mes .ind a fewootaroups and keep k>okiOR.

Inall but 1 or the 6 key .-esidues. the pangofn andthe huma1,vfrus use the same codon.The e.xceptionis a NT t(ansvei-sio,,In the third position.

Robert Garry osos

■ The Guangdong Wikflffe Rescue Center rec,ived 21 lfve Malayan pangoJins from the Anti•smuggl ng Customs Bureau en 24 Marcil 2019; most individuals.including acl.llts and subadults. were in

J)OOf health.<md their bodies were covered with 1kin eruptions.All these Malayan pangolinswere rescued by the GuangdongWildlife Rescue Center. however. 16dicd after cxtel"6ivo rescue

Eff orth Most of the de.;d pangoCins had 3 swollen lung which cortained ;, frothy liquid.as well as the symptcm of pulmonary fibrosis, a~ in the minority of ttie de1d ones. we observed

hcp:itomet;11ly:ind ,plc-nomeg.,ly. We collected 21 or.&,ln \_,.\_-.,nplc,of lunt;, lymph. ~nd ,;>lccn with obvicu, ,yrnptom, from 11 dc:ad Mo~y:i.n ~flS<llin, to uncover the viru, dN'Cnity Md moltcubr

tptdcmiology of potential etiologies of viruses based on a vi'al meta.genomicstudy. This study will be beneficial to pangolJn disease r~arch and ~bscquem ,c-scucopecatiCf'I.Oncor scvcra

members of the Coronoviri<het.amilieswere identifled in 2 out of the 11 M.p!Otlicoindividu31s(individual 07 alld08).

From th~ Jnfl partot wu~io pap~r. I dOfl'l think in curnmt rd li:,t but ~bably ~hould tie.

REV0002950

Robert Garry 10.21 F<'brwry19th. 202<1 .,,

■ q,ikq protqin (8;.f SAstS•lik,o eoron~vimi)

Sequence IO:AV1'78042.11eng1h:

12◄

SNumberof Matches: 1

Robert Garry t~

■ This Bal SARS•lil-:e co,ona,,1i,-us is& MUCH dose,match to f)&1'8-o90o,SARS~COV•2i11 the 11•te<ll'li1)aldotnain {NTO) of Sf}lke. Then the ,im'il¥ity drops way off i,\ the R0O/CTO. If you•re looki1\g to,

a reoombin,1nt it might be one like this.

e AndrewRambal.t 10;37

• ■ Yes.Beforets.arc:;i3came oot Uut wa1 the 'clos~r. It was actually wtl.at cal.6eCIme 'SNke. p.,per to proposeSARS·COV·z wu a ,ecomblnant (tney mixed upwhK:11one wastile rccom~nant).

Robert C~ny to.◄:.

■ Act\Jatvmt' Bat matches pango90 betterthan SARS·CoV· 2 • I mistYPed that abo\'e.

just in th¢ NTO

Still don't know where the NTD of SARS·Cdv'·2 C.Jmefrom

Robert Garry 11:38

■ RatG13

So.moyb~ bal·SL--COVZXC21 + RalG13 = Pango 90. Paingo 90-+ R.atG13 = SARS·CoV•2.Sorry to be slow to catch up if this isll'w.?sc-enario,

Ff.bru~,y 19th, 202(1 .,,

Robert Gatry I3:S2

■ tttps:,Vscience.S<ienc<mog.org/c0<1tent/scile0tlyl2020/02/I

9/soence.abb2507.full.p<lf

1t9i1Kristbn Andersen 1504

In I didn't real'Ze Jeremy signed this:

ittpS:Kwww.th•~nc•tcom{Journals/1,ncet/art!ci./PIIIOt40-6736(20)30418·9/hilltex1#back•bib1

Prettyinterestiog. Also. coverage in Science:

ltttJ)S:Vwww.sciencem.la.ort/ntws/2<:fl0/02/scientists·stl'OnRtv•tondtmn•rumors•and-conspirac•,-theories•about•orQ!:1n•corona\'uiss

I think it'$ <bngctOU$ to SCJ»t.-itcthc origins into cithet you f::i)bC!li<.>-.,c MC lin~.

it'$ C!N'ircly .utuf'31. 01 (b) it's:) c:cnspit'lcy. It's:) ~ry

-• Science IAAAS

Scientists 'strong1ycondemn' 1umo1s and conspiracy theories about origin of

coron:ivirus outbre,~k

A statement in The Lanett ass.ails misinformatil>naOOut the possibilitY 1h2t COVJ0· 19

Qlme fro!ll a lab in Wuhan, China

Feb 19th. 2000 (273 kBi •

.,1111; tS:3SKristbn Andersen

1,,£1 @chjnnel • anybody else beingasked follow up qvestions from Don McNeil? He's asking some very difficul1 to hindlequestions wanting to ·cKJd coior· to his stocy. I'm wort:ing with our

tom,n,.mk:,tiot'1$ on h6w to r~pcnd {or noL}.

Screen Shot 1020·02-19 ;it 12 34.t7~ng •

£HMI..L&IJL

e Andrew Rambaut tS:38

•• I suggest Mt goingdcmn thc1troute. JltSt brush it off as, beire happy co talkc1boutthe ~iencc but the-mrrarivc in·10lvesothtr people.

F"'I EddieHolmes 1$:59

,-; Justdon't talk aboutit all. I'm nolon2cr talkin2 tojourMlists.

Or doing social mt?dia for that matter.

WMI:Kristian Andersen 16.20 ra I think I have a WifVto <:teat with it. Will draft and share

lgno,ing could furthc,cscalatc . ..-.tiich I hav~ to be w:ry cardut itbout

But to b<'t~ar • he ~n•t coot-acttd a!'IVor vou?

REV0002951

Robert Garry 1631

■ noconlbct

tubne's pr a btt ;antsy but at~

lirllilKristian Andersen 16:!!11

~ Okay.hc<c's what I'm 1hinkhg..Th.isIs playire oo hisprevious emails ard !no\Jdcshumorto dcRcct the fact that I'm dismissinghim• soycs. the St'l'lilcyt.K:cis vcrydcfibtratc\_, Can'tign0<c him and

(.;)n't jvn Si<IC him the $Cientific story • th.at wot.1ld only le<>d to fofow up quotion.. I'm hopins th;)t by inc;h,t<li~g "extrcmc-ly bv)Y" 111ill.so be ;,1blc to dcfl«t <CQVC:$hfor ~ c;,111 .ind <>bo 5ivC$ me o

get out of jailcard for ignoringa po.tentialrtqueSt...

HiDofl.

Notiorol seturity? Whitt House?Spooks?J wi~, my(ife ,m tool txci!irl8.tut I un(Ot'tunotelr doo't huvt onythjng to odd here• my exisltMt iSll'treolry in 1tthnicolor, so I'mjust Iotustd on I.M sdtrn:e :·J.

t1Y'113 of thevitvs. As w<:cvtlinc;,, our •Pr<X<imo1Ori3i11

Sp«ificolfy. we hcN(; bc>:11 to vnd«stondthe 6mins.ori.,f"I. ond rronsmissiM of SARS CIN2"post en Virclo3k<Jl. thedo tois coroistcrlt with o Mtvrol

scenario and inco.1sistentwith a scenario invo.Vinsony type of deJibEYote bk,.~pon.

aeneti< engineeri~. i~dinso

Our post on Viro~icof is currcnllyMdcr peerreview Otldwe'resltll t,?ttina feedback from oJot of peope to oosurethat on« poblisi.etf.t~ scientifkmess:ise"ill be os dear os posslb'e. In (>O(0lld. we're

t,11(,.UrielyOUsyMltkit)800 ,,rxe IOy·lutlSVO.StmocetM finclv<JiflS FAQ$) (110(wt IK,lf)t will ,~rμ Cl<A'ify itltJJOt(UIH Qt~Hon.s ol)w( (hf vitl.40tl(I tl}t(leml<: to (ht gt.rlef(ll pvl)lie, weo,e ln)J)itl8 lh0( "" Of (hi> Wi11

bt (lnolized within the next coople of wttks, $0 happy to loop b!1ck Yith you onct alto( that ;s c0n:tplete.

Best of Jvckwifh the stQtY atd pJeoseJetme kn01,v ii I am help outwith Orff of the sci.en ti lieQuesffons.

Oh. ond yes· rm t>ocJcout of the dtsert the b:>15'really "'eren't t.hot zreor~.

Cheers.

Kristim

\_\_and I should add • I really fucking wished my lift wasn't ti-is exciting~. 68i@j J§j@i

11

ROJU.'lr'f lYII\ il.Vil.\J "'

~ Eddie Holmes 16:47

,-.. Your call. 1\-c had a nlrtlbcrof joumos contact meabout this and I've just sa"dthing llke:'So<ty.I am too busywith other m.ittcrs to comment'.Or Ijust l\avc-n't re-plied. Our paper says cvcry1hing

yov n-eed to k.now. Wl-ry :;.,y omythins d:.c?

He is eoina: to tell his ~toty whatever yoo do. I'd ktto ',(Kit dsl3nce.

llfilMIKristian Andersen l6·S2

Ira Yeah, that's what I haw be«i tetling a bunchof otherjoumalists too• or simply just ignoring them. Don's a Ihle different s.inte I have been talking to him a ru1nb«of t'mes over the Ian fev-.•weeks

snd h~ knows me from the past (J'K:'s writt('n about a few of our studi("s}. My worry is that ignoring him -or totalty dismssing him will j.Jst lead to further questions that will be h.ard("rto address.

One main problem I have too is that my name is on e.g., theNASEM &etter andotller 'dhci.al' thinp: looking atthis• so I need to beable to deflect potential t'vtureenquiriesthat could directty

involvt/narne mt.

r,a Eddie Holmes u:,c

,..\_ Actuaty,hadid anail m~ a coupleof days aio asking for the pangolinpaper. I told him to wait for it to (Omc out. I think ;ournos: .,,,iting stories on things postedon bioRxivi~dangerous and I'm

refusing to discuss them.

111111Kristian Andersen 16:59

~ Aarecd. I do think it's i'nPOrt.ilnt ttiat oeer rMew is c.omotettd oororewide disSCl'flirUtfon • esoedally if the took: is comroversial O have dealt with this afew times,.. atwayS been tile oarty line •

l!appyto discuss when published).

... EddieHolmM U:04

,-: I agree. H.l.s to 80 throuch peer f('View. I :..mvervconcerncd th.)t IN() now in a ntMS cyde driV'C'nbvpreprints;md Twitt«. I undersbnd why it is h3ppening, but I re.1lfy don't like. l'in not takire p.11'1.

G::i)&

Robert Garry 1717

■ If this paper gets accepted we will haveto clgfee to an embargo until aspecified d.lte. I think we'reactually in a de f.Kto emt»rgo now not wishing to P\!t an impOfta.nt paper in an impo1antjourral

Jtrid<.

That's plan 8.

• Andrtw Rambaut 1n1

Al

■ I suggest you just send him the email you had before aboot waiting f0t peer review befo.te fun her comment.As ~u know the goyyou could quote the emailarw:Isaythis is t~ email we are ~ending

out in response to media requests andvou don't w.-.nt to m.1ke eiceptions because it is wh3t we .ill aireed.

~ Kristian Andersen 18·22

pa Ran some more selection stuff • here are the rwrnbers. Onlv thing ooe can m1lly s.1y is that il looks li)(e the SARS spike protein w,1s pos$ibly 1,1nder positive sdectiOC'le.arly in the epidemic and th.lt's

not ,ometl-wng we ,cc with SARS·CoV 2. I hod c)lpected dN/dS to be lower for ORJ:1, bvt h-ereSARS•CoV•2is actuollyhi,gher.

Not realtvs1Jrewean condude ~nvthing from these ... h's somewhat intrigUng t~t the soike from SARS·C<W·2 doesn1.tooe.tr to be ullder selection <n all though• doessuggestsome sort of o-recirculation

to me

Selectli>!'I.~ ..

ORF1 Spike

SARS-CoV-2 0.91 0.29

SARS, earty 0.81 1.82

SARS, middle 0.68 0.44

SARS, late 0.32 0.51

F,I Eddie Holmes 1t,i4

,....\_ lllterening. In yoor 'SA.RS earty' data set how many secondarytransmissionsare tM-re? Similarto SARS-CoV•2? Dn you add o~ of the endemic h·.unan CoVsinto the mix?

~ EddieHolmes lt:30

~ P.5. Agree with Andrew's suggestion.

i,9ill Kristian Andorscn 19 :12

ra The phases are defined based on the molccvla, e9i paper in Science:

The e.arly phase isdefined.J&the period from the first emerieoce of SARS to the first documented superspreaderevent (I thiik Nov 02 > J3n 03). The middle oh-™? ,eters to the ensuing events up

to the first clusta of SARS cases In a h:ltel In Hong Kong O think Feb 00 > Mar 03)). Cases following th!$ duStcr fell Into 1hc late phase (Apf-onwa,,ds).

Good question about endemic hum:m CoVs • I h.wen't look at those. but I should ed1te4J

Doo't have g,ood numbers co SARS. but translatingthose dates into numbers I thiok it's something like -150 for eattv. --1500fonniddle. and then the rest

REV0002952

... EddieHofmes 02:16

~ Thanksfor-that.

However ttis ou1bre-,k/epidemk/p;uldemk goes it has been bloody good f« Virologiol.ora. Amlling number-of views for the proximal orians pi«e. ~o:1,t«IJ

e Andrew Ramba!A OS:S.3

• ■ I thought I better shate an «nail that I think is really to all of us:

~ltf?'PnR,..

0

\_\_\_ ..,\_\_\_\_ \_

-·------, ..\_\_

\_\_\_\_\_ ....,...\_..

\_\_\_\_ .\_\_..\_\_\_ \_

Robert Garry 06:27

■ -11 lookS like the SAl'{S splke protein was po~lblyunder positive selection e(lly In the «>IClemlC

Robert Garry 0040

■ Shouldbe possible to look more closely at that• not easily. Map the mutatioM on the S 30 structure. I'd expcctidaptariontoshow upor get fucd at the R8Dand in the hdes in the glyc:anshiekl

[:.ka epitopes]. Might have to do it by 1i,,eages" to see what got fixed in a certai,, tfansmission chain. It may~ more f'31'1dot'l"I

earlyOf'I.

e Andrew Rambaut 06 -tS

•• Hey Bob, 'Mlat v,,ould vou think the effect d a df?letion just befo~ the furin site tin a hJman SARS•CoV• 2 virus). lhe pup le in this flgu~. Would this be a viablespike protein? I ca1't tel you whier!

this ccmcs from just row.

Wt:~Pni ,..

• Andrew Rambavt 06;S7

• ■ Possitly the deletion ii alsothe polyb.isic residu(S as well:

b~~-png •

Robert Garry 0706 Ftbru:uv 20th. 202() ..

■ 1t would be very interesting for sure, Viat>Je yes.The PRRA created an longer loop where the furin or tur1n·likc-enzyme has to chp. If you soorten the loc:,p and remove one ifnot more of the O·

finked glyc.ms you're b.lck to SOfllethirg thilt structurt'ltly is vrobabtv like RJTG13. Looking ~t the seQue~es around 51/S2 in other CoVs there's .18Qod bit of variJtion including insertiolls and

deletions at the end o! Sl or in the deavagt site thems.efvf,$ witlln avir'us (like HKUl orMHV). Also its possible to ch~e {1:nockout)the cleavage site altogether and get a well-fold~d protein as

they did to get the c-ryostructure in the nC'Y'I:scie11Cc-po1pcr.

Robort ~rry OH,

■ l'C'Sl)O(lding si1e there at all. If

to newmessage • curiouser and curiouser IAliccl. But al,so still vilblc fd get unless you knock out the last R in tht PRRAR in which case you don't have any c.lcavagc

the virus in this case fSstill viable thefl rt·s u~ing .i cleavage .site f\lf'lherdown, Those e>0st but this would be~ preuy btg variiltion on the theme.

I'd gu~ss

• Andrew Rambaut 07·13

•• lntcrc1ting. Thanks.

What a.rettie residues would I be lookflg fot for another cleavage site?

Robert Garry 07;32

■ R oos,iblv K most likelv

I

• AndrewRamb.lut 07.19

•• One last qvestion • could this be somuhingthat passaging nVero-£6 cells could induce?

Robert Garry 08 2-1

■ if th¢VwCn:p~ginsinVcro eek then thcv no doubt u,cdttyp$in tocplit !ht! c:~11$. It'$ ~rd to w~.c off ,1.II the t"Y!Xin C)nd in factyo,u don·tw;inttoif you•rcsro111.ing;iviru,like l'l'\0$1fluvc 1h;it

don't have a furin site.So ytS i Sl.l)pose if you passages a virus with a furin site a lot yoo might ~ntcr-selccr. to a try,xin site or maybe cve-n aoother ~av-ate sitt attoicther in ctU cufture. CoVs do

tiave ,:1seccod de..tv;i:sesites· th.>t is KR in inost viruses rigJ!t before one of die ftiSK>n peptides.There's .1lsosome alternatives f01virusesthat aroo't "activated· alld don't tuse ilt chesurface

(catha,psin)but RO the endocvtk route. Lot of seciuence behvero the Sl/S2 runction and lhe S' sile-.

wash off

e Andrew Rambaut 09:38

.a

■ Bask.allya coU.1boratorhasfoundthisdeletton in about 5°" of the reads from asample, I guessitis possiblethat it is .1cell .1dapt.1tion(removmgthe gtycansitesas well}. I may get back to-,oo on

thisif thev want to t.ake it further. ft>dit 11

Robert Qmy 0939

■ lntere>ting • Happy to weigll in a> needed!

Robert Garry 1000

■ You'd probably get different perh:1ps cpposite tEMiUlts with a rapid forced 1>3wige vs a meandering slow pa5S.1ge.

Growi'l.g virus stocks ~nd avoidi~ generation of iltcroal deletions akadcfo<tiV<! interfering partidcs is so~thing of an att form.

I

https:Klink.sprin,:o,.com/thopte,/I0.1007'42F978•1-4684•1280.2\_23

REV0002953

• Sprif'1'.Crlfok

Ocfective Interfering P~rtides of Coronavin.1.s

Oeftttive interferi1'lg {Dl)particles are vi~I deletion mutants. whichcanoot replicate

by themsetves and require homologous standard viruses io provide helper fuflctions

f0<

theirreplk.ation. DL

We t\we. however. detected the gen,en-ition of ooron.nlirusOI p;Jrtides dvrin: high•mllltipli:itv D.lS$~ges of the JHM strain of MHV in tissue colture (N..-.kino et at.1984:i). These OJ o.1rticles

contain a sing.le-stranded RNA g!!nom~ of roughly 5.2 x 106 mol«ularweight wtich isslighlly smaller than lhc genome of the standard viru1 (M.W. 5.4 x 106). Olgonuc:lcotide 6ngerprinting

~UIJic:s::.ho wed tl't.'lt u,e RNA or JHM 01 b miss.i~ scvt<al 1.-arge RNaseTl •rcf>i::.t.r-,t~rionudco(tdcs. Y111ichrcpr(~c,,t scvcrc1J<Siff~fent reg.ioos on the ~and;)'d viral ~<:nomc (Makino ct al.. 1984.t

1984b). This observation suggests that the corol\lvir~ 01 p..1rtk:les .areunique since the 01 genomes ol other viruses usually exhibit more extensi,-e deletions."'

\_,... Krlsdan Andersen 1009

18 lntereiting with th.atdeletion. I shovlds.,'lythat Mike F3rz;:inmentioned that any deletioos .iround this site would be J red flagfor him th.at the furin site had initial'v come abovtw·th (T/C) p,BS3ge•

and ti-en wth slower Dassa1e in humans. mlltht be modified Much too early to S<Nan"tthin2. but will be intcrcstirn::: to seeif there's more 'mcssini about' with this site.

• Andrew fbmbaut 1010

41111

■ They will be sequencing some more samples unckr similar conditions tomorrow.

I

0G1

Robert Garry 1013

■ lndttd • that PRRAiostrtion is tM most ptrplexin,g aspt-ct of tht enti~ geoo~. It's like-ly "out•of•fran,e• actualty. but seeming inserted like a scalpel into a ,-try constant reiion. If that region is or

can be put under somt selection prc-ssurewould be good to know.

e AndrewRambaut 10-20

41111

■ This whole thing is doingmy brainin. I literally swivel day by dJY ihinking it isa I.al>esc;,peor natu-.il.

.... Kristi.an Andcrst:n 1c►.2s

~ Haha. my brain h:ts been a badly c.alibroted MC MC. I'm hopilg it'll start comerging ot 50C'Oe

point-..

Robert Garry 1026

■ All of our brains ~re ina bit of trouble• hopefuUyyou•ncton't get rear·ended anytime soon ...

~0

Hopefulty-'sowe hearsomething positive from Clare SOON· thffl we'll all likely be facing the lab escape 0<natural question head·on arw:I should have a consistef'lt respon~.

(;]) 0

...aKristian Andersen 12:36

e8 (m.,il f'Qm Sl.ac-kfQf Cn\ili •

Occisk>ne>nNature submission 2020~02-02583 Feb 20th, 2020

From c.thomas@n3ture.com (No content}

It's a no al Naturt • which doesn't entirely surpriseme. Thefre suggestion going with Olt)ef N.lture joumals and (~hl O()wt think we sh:iukl coostder Uvee different options:

l. Nature Medicine

2. Cell

3. Science

~h:IJ

I fool prottyeonfidont .11XM.i:#1 <"nd.f1, b,vtnot (ll.1ite Sl.lro~bo-.Jt 11'3 (but tw, most im~ct) I know C;ironno could <Jofinitcly roieh (k.lt

w<N.•1d thi¢r6)s<>

Also. the re<1iewtrsraiseSO'lles:oodpoints th.lt we netd to consider. UnfortunJtely the pon:olinsdon't help cl.lrify thestoryJnd reviewer #2 (who's the one influencing the decision) is wron~ on

those points. Most imp0rt.antly • we unfortunate~ can't refute the lab origin hypothesil. and it is vrh.at it is.

I have SOlllf othl:f busine-ssI need to attend to this morning. so let's wait unril @Eddte Holmes wakes up and then come up with game plan.

.1

ROben Garry lJ.16

■ ·Nature Medicine~re ilterested ii publishing it either as .a Comment aCorrespondellce."This is m«e positive than the other two. SUre;iddress the conctms .nd publish in Nature Medicine.

Of

I

Essen:iallyth~ sarn~ Impact Factor as Cell.

Quickerit seems~it<' )

QUlU: ...Jti!!L

REV0002954

e Andrew Rambaut 13:19

•• My re.cling of that comment is N,tMed would take th~ rt"Vicw,-a, they are •nd we can just -1dd~) thc:m.

Robort c~nv t'l to

■ ASforthecomme-nts: • for;heo--glycan wecouldshowsome of the additionald.ala on the predicted sites in other CoVs -this is convincing to me.but perhaps not to a skeptic. If not th.at just

f,Jrther tone down the comments re the O•glyQins with more qualifiers..

R.obert Garry 13.2)

■ \*Alsosfate <:le.irty th..lt this site isonlypredttted so far ;.ind that eXl)eriment.il evidence for its biok>gical tunc.tion and its potential impact on pathoeenesis .1re required." well the site is there•

wMtt-er it is used or not tec-hnic.1:llynot tstabtishtd, but a good tett sirKe it's ustd forothef Covsand appa,rentlyknoding il out •II0wtd the S tobe stable tnuff to giyt a 3A structure. Confused

thougl\ wh:lt tjhc rcviciwcr w~nts ut to do wh,'\t ~ ~IR.'!.'ldy ct:itcd cx.'lctly?

I don't think review 2 got it at all• ma.,t>con purpose.

The paperW.lS to e><Plorethe possibilities ol the proxim;11origin • not to refute the bioweapon scenario.

• Andrew Rambaut 13,Z7

•• C<>u1(1a:,.k CIJfe to (ecQOS,i(le,1

R.o~rt ~rry 11.28

■ That's another pbn • He/She set up a straw man that oor paper was to refute SARS·CoV·2 as a biowe~n then shot it down.

•

• Andrew Rambaut tU9 Ftbru.i,v 20th. 202() "'

•• But more import3nUythis revfewer feels. and we ~ree. th<1tthe Perspective would Quid<lvbecome outdated when more scientific.d.>ta are published (for example on polenti3t reservoir hosts).

Thii is the irnporbnt bit to :1ddre!shc-'CIon• tho p:)ngolinsdo not solve the is~. f«1,t;:d>

DIt~y lye,"rs:igo

Robert Garry 13:29

■ Agreeing with Andrew that NatMed would t,)kC it.

None of the pango sequences are the smoking gt1n that s-ys this virusit.Jmped right into a ptrson "'It i1 not dear wtiy the aUlhors rush with .l speculative pe-:spccrive if their central hYJ)Othesiscan

be wppo,ted by their own data. ?lease explain.." Actualfy th6 is r.Jther frea.kin,e insultina: to QY the least...

~ Kristun Andersen 13:32

ra replied to a thre.d: But more import,3ntly tflis reviewe-feels, and we agree, th3t the Penpective wouJd quickly become outdated when more Kientific dat~ are publi$1ed {for e:,cample oo po ten ..

Ye-,, th;, i, key3nd I ~dre~d ttbin myrc-;>lyb:ick toC~re(ol$0tO $CC if th¢y'drecon$id~r)

Sc.rccnShot1020-02•20at 10.31.17 AM.prg •

o-::-·---:=:-::.:=-~--~-..

·----::· .. :=.:..:

------·--·-·

::.

The only potcntfal doof still open with Nature wQ.lld be fof Eddie and Jere.my to get a hold d Magda. Reviewer 2 in gc-ncral doesn't understand \111\at'sgoing on (he/she doesn't understand that's

tven .i theety In the 1',fst place) aoo no. ~ly. the ~ngos oo,nserve ttlts. I get asensethat N.iture ml gilt be a llttk gun shy tllOugtl • hence. we·e1 nee<I10 go au the way to the top.

I

Robert Garry 13:,o

■ Good Idea • let Jeremy knO\V and give him the rationale wtw Reviewer 2 was full of it.

e Andrew Rambaut 13:37

•• Perhapsproduce the rebuttals?

If we eod up going Na!Med they will wa,u rebutuls foi-these feferee:> comme,,ts.

Robert Garry 13:37

■ Yes• Gonna havt to do that arrvway.

~ Kristian Andersen 1339

119 Let m~ set up 3 Goosle Doc l!lnd ,h:ire

Robert Carry 1340

■ Ytah good plan • shoUd not actuallyt•ke long ...

~ Krlstun Andersen 13'14

rl!i Sha,od a GooglQ Ooc with '/illl: hrtp$:lc:IOC$~0oglc.c;orn/d<Kumcnt/d/1vS~lql.filo$1Op02VWl>CKIQ3i!rrncoW?dcfl.nq4vhQ/odit#

G Stw:Oocu--nent •

l!!!S Nature rebuttal

Iii GoogleDoc

I need to ht.Kt out for an hour Of so .

I

... Eddie Holmes 13:S8

,..... Iforwarded to Jeremy. Reviewer 12 is clearo/ of the FoochiEr min\lset. I'm very surprisedat Nat1Jre here .. rejecting it t~ recommending another Nature jovmal. Mightw;int to remind them of the

43K vie~ on Virologk;i,I My wo,ry ;i,bout tr;i,ndflrring to N)turo Medidno ;i,t th;i,t th,oywill w;i,nt th• t·od hugoly nduc.d for;i, Co,nmMlt-/Comt(pol\do-neo <o:&n Al(o I think wo <.hould<.tick to

our gu,s about the m,ess.ag~ and not tone it down just to get it published. I'm pfetty sure Cel would take it. . .they arc desp,efate to get in on the act.

... EddieHolmH U:23

,-..,: From Jcrcniy: I would give them• rintfil"$t.

If r~ally a no. then Natur~ Medicine -bestis the auicl«-st way now

w'WIKristian Andersen 14.26

~ Agreed on appfoach. EddtC".doyou want tog\_ivcMagda a ring?

e Andrew Rambaut J4 u

•• Iatf~ that we s.l'lould not shorten it (if .anvthin:a wt ma.y n~ to .add a few set'ltMCes.

F-. Eddie Holmes 1S:19

.... I'm a(jually in New Zealand at the moncnt and given travel and time differences I won't be able to her until Monday hEr timt. No1 sure somtone else can to:norrow? Apologies. ~rh.aps \VC should

Robert Garry l SA6

I

■ I've put in my two pef'1ntC'Sdr'3ftin,g responses lo all tho pcints. As :ilwavs no sacred text or anv pfoblc1'nS what.soc-IC<witJ1wholcsaJc dddions Of edits. ?least do tMt. lhcrc afc scvcall fCfcrC<lccs

and cl>angc:1 that will need to be made to the manu:script bvt not too cnel'Ot.l~.

Ye.:ah• no s.hort~nma.

REV0002955

11YKridun Andqr1-cin 19·11

lal Sorry. dealing wi!h gr.i11tthings today. but I'll get on this tomorrow.

For next steps, here's wh(lt I'm pfQPQSing:

1. fhish up 1ebuttal and {ll)OSt edits)

2. Eddtewm email Magda with the rebutt~ requc-sting a call (I think this should be Eddie• I don't have eoo11gh gravitas with her}

3. f"nish final edits to m(lnuscript over the weekend

4. PbnA:rout•b~kto l\btu,..; Pl;i,1'18: bounc•o\l\trto N#uro Mtdkin.-: Pbn C: m•h> conU(t Sl'i ~rd get thi( rltoC.n

Y.iyornay?

Robert Garry 19·-4S

■ Yay

Robert Garry 2035

■ but b • no shortening

0 Q I

Ftbtu~ry21st2020"

Robert Garry 1047

■ lets hope tf'lat tv'<1gda will over•rulc the rejec.tion based on aflawed revi-t?w #2.

If not:

Here are the typ"-S of articles in N;iturt Me<l:Revi!w

A Review isan authoritati'IC. balanced and scholarly survey of recent dtvclopments in a research licld. The requirement for Nlance nc«I no1 prcvtnt a\lthon ffo,.. p<oposing a S1Xcihc viewpoint,

but if there are controversies in the tidd, the 3Vthors must tre.tt them in an even-handed WJ'f. Re-,iews are rormt111y3,000.4.000 wordi, and ilh.1strations are strongtv encouraged.As o sviddine.

Revit-ws aUow ul) to 100 rcferen(ts. vtith t.xcepti::>ns PoSSiblein sptt"ial c.a.ses. Citation~ should be seltctive and. in the cast of partic.ularty imporUnt studie-s (s 10% of all the rcferenct~}. we

f!r\COU'!I~ :authOl'ot.to provide <hc>rt :.ooot.:ationot. t'!xpbhing v.ihy ttlc!:<i :am ltr.yeonc:riburiortt:. Th<:> scope of .:aReview <hould h<lbro.Id CC'lough th.:at it i< not domin:it&t by rhc v.o(k of ::as.i11gl(!

laboratory, ;md p.1rticularly not by the auth0rs· own work,

Reviews indude rcccm?d/accepted dares.Reviewsare always peer rC'V\ewed to ensure tactual ac<ur;,cy, appropriate citations andschOlarrv balance.

Commentary

Commentary is a Ve<Y flexible fonnat: Commentaries may be on policy, science and society or puretv sdefltific issues. The main criteria are that they should be of in.mediate interest to a broad

tea<,k,Qhip .t•'Kl:.hould be written i11IJll IIC.CC:))ible.n<)n•lC1;h11ical )lyle. TI1eirl,ength ~ t'(l>icttlly 1·4 ~!Se:,.,.-lth(.)\lgh :.<,me, n1~ be lqng<,-. 8«au>e the content i) v~1i11hk:.the f:;N-m(lti) 11!>0 lle11ible.

Comment.:.riesdonot nom"G:ly conloi;; piin-1;;ry research data. a:u-,ough the;, mavi)(es.ent ·sooolog:k:Jr 03ta ffundin,& t~nds. demc:Graphics. bibliogrophk: d3t3. etcJ. As 3 guldelir.e,Commentar'{

allow up to 30 referen::~ and artkle titles are omitted from the referenct list.

Commentaries troy be pcerrcviC'NCdn the editors•dis<:rc~r>n.

Perspective

Petsptcrtve is a new tor mat for scholarly reviews and discu~ionsot the primary ,ese;itch literature that are too t«hnkal for a Co,,mentary but do not meet the aiteria for a Re~-either

because the scooe is too narrow. or beuuse the authcr is ~dvocating ~ controversial POSition or asoeo.,l,3tivehvcx>thesis0< discu>s.ingwork pri~ritv from coe group. Two revie-M adYOC.3ting

I

opposite sides in a research controversy arc normally publiS,\ed as Perspectives. The text should not normally excccd 3000 WOfds.As a guideline. Perspxtive-s allow up to SO references.

Pcr:§Cpcctivcs arc always p~r reviewed and Include rccclvcd/acccptcd diltcs.

Qii\Mi ..I&:.&

Our piece -1(:toallv ootenti.UV fits all tlYee.

I'm not opposed in any way to Kristian hitting up Cell 0UM!t • optk>n C.

• Andrew Rambaut 10:s.1

• ■ Pcfsl)Ktive seems the best ht.

Robert Garry o.o&

■ Yeah • we definitely want the petr rem-led stamp.

<:ii©,;, t:l :

~ Kristian Ander$en 1.<:13 ra @channel • updated the rewttat witl"l some edits and comments.Andrew I Bob· had.1 rewsptciflc q~stklns to, the two or yoo.1·m taking the lab out for lunch 10, th! next coup~ othours and

then I'll get back to this aft«• wtcaneasi1yfinish thlsup today. Hopif"IP. to flni-shup reviS4ons to the paper ttiis ahe<n()()n as well.

Rcb<Jttal:https:/1docs.googie.com/do<wnent/d/lv5FqAlqlf?lo5fOp02VWIXKIQ3arm:oW2ddlnq4VtQ/cdit#

Papoc https://docs.googlc.oom/docurrent/d/14Hl2ltdEyXQSXBBOC2KwHxSrKf!yMcJ<WdMZGXx1xl1z8/cdit\*

kditedl

455 .. ; ,;,;;

II

II

Nature rcbutt.11

GoogleOoc

•

e Andrew Rambaut: too

•■ l~gc from iOS •

,.,.cm::m

.,...roei< G, Ar1c;l•B<>A

♦Ara"'~S•riov,

q,.,c~N)i,

Oot:i ,~ k.illQU ¥1<1clogso, on•,~.\_• thtffl

Itek? IIOWl'mydoo)• tO

Mu~plC lW>'!tl'-'Ctn'l/)(4,f~(Vw,9S

Robert Garry 1◄

'416

■ Cats viere definitely infected with SARS•Cov~t

I

REV0002956

https:Kwww."3tufe.com/attklesJ425915a

-Nature

SARS virus infection of cats and ferrets

There is nowa choice of animalmode-ls fof testing therap;cs against the human virus.

~ Kristi.anAndersen 14•47

ei'9 Come on Andrew b..-e.'.lkher/hi-s he.lrt!

Robert Garry 14 48

■ Apparently (and this com~ from a pretty gt<>d sourct)cats in Ch na art con,ing d:>wr\with the illness in droves and arebeing round«! up ard txttrminattd.

e AndreYI Ramb;tut 14 $3

.a

■ Wt: thou Id :add th~t to our p~pr::r.

Robert Garry tS09

■ I don't disagree. So. add the phrase: "inc.ludilg wild and domestic animals· somewhctt in tht text? Covers another ban albeit a r.uhef unlikl!'ly o~. If my S()(Jrte is cOC'l'eCtpcoplt will go crazv if

they thjnk that cats arc going to get infected. pass on the di.sca:i-Cand possiblydie. Krbtian for one is "fond" of cats.

·~

... Kristian Andcrstn 1s2s

la Whattver 'YOUdo• DO NOT pass on this information to my wife! I think she's more scc1redof the cats dying of this than me ...

Ro~rt Garry 1s2a

■

Agreed• normywife.1ndd.>ught'CN°s -~amcck>;d,M

Qii\tti ...StU..L I

• Andrew Rambaut 1S:?9

l='d>,v;-try 21st. 2020 .,

•• I have two cats. I like ooeof theoi.

r, Eddie Holmes 1S:36

~ I'll ao over the rebuttal today. Aeree with th~ pbn above. Ext.ellent OP(IO(lunitvto ouree c.ats from th~ planet: ~ a nee1 .a bioconttol for th~ in Australia ard this may be just th~ tickEt.

Robert Garry 16-43

■ ~1tps:Vdocs.google.co1ntdocumenVd/l4Hl21td[yXQSXBODC2KwHxS<1<ff~MdKWdMZGXxbd228/edi<#

Is this the tlnk to the paper you·re using?

lwllJIII t6•:.

Kristian Andorstn

Bf! Yes, sorry • wroog: link Jbove

Robert Garry 16"16

■ NO pu:,blem!

~ Krls-tf~nAndersen 1.71S

l!i'llOne point tor @RobeitGarry • Its SARS·CoV. nc< SARS-COV·1 ·~.Yeah.logic.

Robert Garry 1111

• Ok. noted. ICTVrealy shoul(I gel its iKt together. {f"<Hl'"<Sl

... £ddleHolmes 1":~6

I

~ I've given therebutt.ilanedit. Seems good.I view it JSiJ sort ol kgal jl.dgemenl.50 it needstobewritten inti bJfancedomd neutral tone.

But. .. the last point about being out•of-datei.:s a fc1ir oneandisnaggingat meas well. I think th,;1tsome new bat viruses are on the way. Whatwoukf we do if t.heyalmeout quickfyhad the furin

deav.age she? H)'pothetical I strt-ss.

~ Kristian Andersen 1752

~ A bat with a furin c:lea-.-agcsite still doesn't ,uJc out a lab scenario. hO'v'Jev<?r,it would defmittly mtan that the s.iteitself wasn't gained in the ab. My opinion isthat the ,ucreat ma!n reason to even

consi<IC, Ulc labsce:n.rioisbccause: ot the rutingtc, but again. seeing it in bats wou1on·t rule it oot (bu! I would n'l<I much less fcasoo to speculate on 11).

Do you h:i'\11: re.:.son to believe there's o b.,t virus with the Ivrin site? If vcs. then I think we should wait • bccw,c white rt wouldn't involicbte .:inything th:it we're '-lying. it'd be very import.on!

;ickfitional infomarion

... Eddie Holmes 18:13

,-: I sugg~t wt wait a few da~. I hear ,u111blirlg).Nol s.m~ yt!t. Vine~ Rac:anieUo bast:ally rel)t!'clled our pa pee lttp:/twww.virOl<:gy.M/2020/02(20/pangollns•antHhc•origfn-of•sars<ov•2·

coron.ivirus/

8 virology.ws

Pangollns and the origin of SAR.S•CrN·2coronavirus

A (O(On:wims felated to SARS·CoV·2 has been isolated from Malayan pangolins

illegally imported into Guangdong province. but it is not the prtcu,sor of SARS·CoV·2.

Robert Garry 1$ IS

■ Iroalty c.an·, ,co ~nyth.ng coming out that would refute ;ill the sctnarios wo l)<opos.od or cv-<none of tticn d•finiti'loly \.lnloss somtonc ;sol;:it,., SAAS CoV-2 fully realized in somo wild anim,3l

I

... Eddie HolmM 18:18

~ can you just humour me to, a few days?

Ro~rt G.arry 1sn

■ Yes ofcours.c absolutdy! I was gOfngto add tho'-l&h •· if some "rrollyimport.:int 3ddition.31informition•camc outwo could add a note n proof .

... Eddit Holmes 18:21

~ Agreed. We cc1nprobabfv still send back to Nature on Monday.

Robert Garry 1a22

■ VR is:~ very eood guy. s:upcrb s:dentis:t 3nd communic~tor. but that's 3 pre-tty d0$~ ~raphr:Jt«-.

... EddieHolme:s l8:2S

,-; Almost cut·and-paste!

Robert Garry 18-'26

■ I'm .'IC1u:itty rooting fot $0~ nnimat vi,u-..(b.·u, pMgO,in. <nmcthing cl<~ hopc:-fulty not one of Kri<bn'~ c;at<)10 h~w.1-' polyb.l$ic site.

llflllJKristian Andersen 18:3-4

E£I I think we're All rooting for some animal virus here • would makt the 10CSsagcso much ea~r!

REV0002957

llfllJ Kristian Andersen 21:05

t..c!Just in case people think it's difficult to mJke a CoV reverse genetics clooe from sc.ratch • these guys did it in a week ... (just approved this paper for the bioRxiv. so please keep confidential for now).

2 l,)eol •

Screen Shot 2020·02·21 at 6.04.0 ... a BIORXIV•2020-9S9817vl•TMel.pdf

PNC PO,

Februart 22nd. 2020 ..,

• Andrew Rambaut 04:1S

•• I think VR's piece is supposed to be a summary of our paper. It cites it with a link at the beginning. But it could have made that clearer.

Robert Garry ou1

■ https://www.politioo.com/news/2020/02/21/coronavitus•lrump-while•house•116650

IJ POLITICO

White House fears coronavin.,s could sl\ape Tn..tmp's 2020 fortunes

Though Trump in public has downplayed the virus. prtvatefy he has voiced his own

anxieties. (180 kB)•

Robert Garry 09;30

• Reviewer #2 pretty muc.h got it all wrong· Nature should reconsider. Andrew did a great job upgrading the lab origin response.

Robert Carry 10;14

• Kristfao • what do you think of starting a google fo, the rebuttal letter? One page. Seems the 3 major points arl! 11 parlgolin SQQgive no def answer, 2} lab escape and 3) new data· if it cor~s at all •

not a show-stower.

Robert Garry 1Ck23

■ Just a brief intro letter that points the eds to the key points in the c.urrent resoonsc and not so subtte that reviewer #2 clearly was biased and got it all wrong .

....aKristian Andersen 1303

!ii! Just created a document. but no text yet. Also shared the whole Google folder with y'all so it"s easier to access these individual documents.

https:l/docs.google.com/document/d/1TQoMX8u\_Qiumfellwl06TU.VKPBefsv34tj08fLE6o/edit

Waiting to hear from Eddie whilt's up in China before next steps.

CSuite Oocum1,>nt •

a

a

Nature rebuttal k:-ttcr

Googll' Doc

Robert Garry 13~56

• We need to give Clare several reasons to reconsider.

https:/lwww.bbc.com/n,ews/world•asia-S 1596665

" SSC News fl'brwty 22nd, 2020 .,

Coronavirus cases double in one day in South Korea

The PM describes the situation as grave <1s th~ total number of confirmed infections

fise-sto 433. (114 kB)•

One reason to reconsider is that thi'5 epidemic is looking more and more like a pandemic.

r'li Eddie Holme:s 18:44

,..... I'll hopefully be able to update on any new data tomor10w. Pretty obvious it was going pandemic. I think Nature have just bought RC'Vic-.vc,#2's argument that we just going to fan the flamesby

adding speculation.

r1I Eddie Holmes 19:<li

~ IVe just done some edits on the original version of the rebuttal in Google docs. Looks pretty good to me.

I

REV0002958

Robert Garry 19 s 1 Hbruarr 22nd. 2020 ..,

■ Yeah· damn good ·I agree about the "'ran the names by adding specutadon.' It would not surprise me that the revlewerwrott-a VERY strong private cOMmer,,: to theed tor that effect to scare the

hell out her .. Ag.in r~c~rv#2 wroJli about everything. SOK• v'cws and proOObtv 10s of thot1sands of rwtcts and retwccts • I did not detect fa:med flames • OA the conttary.

r"9 EddieHolmes 1':S4

,-.-; Agtccd. No doubt th.at the private comments to the Editor we<e \'Cry strong.

Robert Carry 1,-::is

• Yeah ltope-fully sl\c buys the counter-arguments

e Andrew Rambaut 2018

•• Bee,\ trying to gtt myneaCIround me ,ecombinatton. Hefe is tneover'rie-w. Going to dig imo spike next to Steii I tall Sine1oon the seque1\Ct01acquistton ol tN: RBDresict.Jes.

--------------

~ EddieHolmes ».-.1

I

~ \!J ~ ,J :

,....\_ Nicely done. Very messy in 1he S protein though. What do you thrlk atout Tommy's synonymous tree-sin tht R80? The pangolin ¥irus is not the closest to SARS•CoV ... bit very close in amino a,id

tre,es as here. too too)

wft.('"I~ RBO wllffl' wSC AU .u ohyml rme •

SCAUi$ obvic>ul-\t tho Soutl'I Chin ... Uri on•

•

••

Andrew ~mbaut »~7

Yes. For RBO the SCAU pangolin is cJosest (this is nucleotide).

~png,..

But I think this is beca,.,se ttiereisa re<:OO"lbin:mt ltdct in RBD i,, RaTG13{th;it comes f,oo, elsewhere}oushine:it away from SARS2.

If I dip out 202 rocleotidesin the RBO th.ltspanthe 6contact sites I get R;::::TG13asdosestagain

AISQif I just m.sk those sites with Ne;in ttie RaTG13.

irl•..png"'

--\_-·---\_-:

r"W fddieHolmes 21:06

,...\_ lo me it looks like the pangolin amino acid sequence in the RBO isdose, to SARS-CoV·2 than expected given thcSr over-all level of drYergen<e.

e Andrew Rambaut 21:10

•• iir'l.,~png.,.

u:;

.=

• Andrew Rombaut 2116

411

■ So in the first half of the RBO (up until the blue bar). RaTG13 is 7.9% divergent from SARS2 at the nudc<>tidc levd, and the pan:gOlinis 13.5% divergent

Inthe second ha'f (i.e .. the blue ba(}.RaTG13is 22%di'lerg,ent and pa~olt1\ is 12.6% (i.e .. slightly less divergent).

For Amino Ac.t il is similar· 1st half. RaTGl3-SARS2: 2.8%. Pongo•SARS2: 3.7%. 2nd ~~If. RaTG!3·SARS2: 19.5%. Pango•SAAS2: 2.3%

Soit the PNlgolin stays rot1ghly the same divcrgmce m RaTG13 shoots up,

Jeezilis 2.30.'.lm.Going to be-ct.

r--1: EddieHolmes 21:31

,....\_ Thanks. Yes. ao t6 bed.

Robert G.rry 22<>1

■ yes, many tl'lanki!

REV0002959

f-ebru.,ry 23rd, 2020 v

Robert Garry 09:05

■ I can't contrlb1,Jte much here. but one consistent observation ever the ye(lrs is th~t virus fL.1sion prQteill$~a ·modv1;u" ;ipprooch. swapping in and 01.1t varioos <:omponents. If -you're splitting the

spike protein up for comPc1risoos at the tlUC aod ptotein levels and if there's not another more rationale way to pick the $plits, it might make sense Ito me) to do it according to the "modules: This

alignment shows the •modules" in spike: https://www.naturc.com/articles/naturc17200/figur~/10. The orange "variable loop• tSthe receptor binding domain for CoVs that have a protein

receptor like ACE-2. For CoVs that use sialic acid receptors the binding is in the NTD. MERS CoV might use both cl,1sses ot receptors (siJlic ueid and a protein). For some CoVs like HKU1 (in the

pointed 10 alignment) there is a .. moclufa(' insertion in the v.1riable loop of ,1 proline, serine, threonine rich region ak.1 a mucin-like domain. (edrtedl

Robert Garry 09.14

■ Apropos to that wh3t you've labeled the ·trac.r appears to me to be essentially the "'variable loop" that is a module frequently swapped in and out of CoV spikes. (l'Cfil<-<0

Robert Garry 09-.2-1

■ Our friend R.llph wrote about it:

hnps://www.ncbLntm.nih.gov/pmc/arricles/PMC2838128/

I) PubMed Cent,al (PMC)

Recombination, Reservoir5, and the Modular Spike: Mechanisms of Corooavirus

Cross-Species Trans.miss.ion

Over the past 30 years. several ctoss-species transnlission events. as well as cha,lges

in virus tropism. have mediated significant animal and hum.-.n disea"Ses.. Most notable

is severe :icute tt-:spiratory syndrome (SARS), a tower re$piratory tract disease of ...

Robert G~rrv 10:48

■ htt~://wwwnc.cdc.gov/eid/art:ide/t9/7/12·1094\_ar'ticle

D-Emerging Infectious Diseases Joum.al

Mutation in Spike Protein CleaVcJge Site and Pathogeoesi<,; of Feline Coronavirus

Feline ooronavlruses (F'CoV) exist as 2 biotypes.: feline enteric coronavin.1s {F'ECV) and

feline infectious peritonitis virus {FlPV). fECV causes subc:lin ... (132 kB)-.

EMERGING

INFECTIOUS

DISEASES

A,\_..........\_ JOlndJrocQlguniildJ'ritl Oiw:N .,Ills

Probably need to reference this.

e Andrew Rambaut n<>J

•• Th.1nks Bob! That looks like an excellent way to try to dig down in to this (better than my sQuinting at the alignment and trying to see where the break-points are). Opens up all SOfts of interesting

questions about where do they get these modules fr'om? ISit just hornologOU$ recombination from othcf-coror~vifuscs?

I

Also with respe4;t to cats -weren't you saying that there were Qe~ c,1ts evetYWhere in Woh.ln?

ffit-c;ul",..n\ und•r$t•nding i$ U,•t F111V -11ri$H duri"i-in Yivo inf-t<tion f~ • &@Attic; '",rt.lion of Ft:CV (8~H). A IOflg•s.t•ndini hypothui$ i5 th•\ FI? YiNHS ,u·ht-fl'Ofl inurn~l 9'111t•tion of

~demic F(CVs (12), ti.flictt h bitlbved to O((llf' i,n .:,PPl"Oxim;iotttly lX-SI of e-nter-ic infff.tions, ruultin,g in th-e ,11blltty of tho v1N$ to !.nhct blood !IOnO(ytU and ti·uue IUCl"OJlhillO$. Ttte

r-.ultint productive infection of theH u1lh, • h.11lln.ilrk of FIP, en.11blH sysu■lc spr.-d ,nd NsulU In NCrophag• act1vat:1o,,, with c«icoait:iltlt: i..une•..diated .-v•nts leading t:o death. fo

dat .. , UM! prethit .uhti«I or nuUtlOni th4l Uu1e ii sblft 1n ,Cd,/ biotyp• ha~ "'>t biten tdintUied.

Robert Garry 11:14

■ Ye-s indeed -could be coincidence. but if SARS-CoV-2 is in fact infecting cats in Wuhan (and that's no( a bad bet since SARS-CoV docs effectively infect c:-ats in the lab and cats wctc definitely

infected during a early SARS cluster in an apJrtment buildin.s) then the pofybasic site misht ;ive the virus a leg up in pathology.

yes • homologous recombination from other coronavkuscs 'oVOOJd

be mv bet.

Robert Garry 1t.27

• If cacs are infected, I suppose one might ask the question did poop,Seinfect the cats or was it the other way around?

• Andrew Rambaut 11 ·27

I

•• Just an,,ott1ling up lh<! spike l'Cgions in the <'llignmcnt now. One qui<:k think I noticed in the figure above Is the S2' cleavt1ge site just before the fusion peptide. If the S1/S2 cleavage site w3$

knocked oot by a deletion. would this one take C1Ver?In SARS-CoV-2 it looks like this:

im~.1)1'18: ..

TCAAA~CCAAG AGAGGTCA

S K P S K R S

REV0002960

Robert Garry l 1.34

■ I think than: a di'stinct possbility. rd look for a c.athe¢n cteavage site as wetl. fe<ftedl

'1ttP5:Vwww.ncb.nlm.nih,sov/pn-c./arti<:lg5/PMC2519682/

•>PubMed Central (PMC)

Cathepsin l functionally C~ea\·~ the Seve:re.Acute Re'Spi'ato,y Syndrome

Corontwiru.s Oass IFusion Protein Vpstrnrn of R.flth(tr than Adjacent to the fi>sion

Peptide

Uf'llike other' class I viral fus.Oo ptoteins. spike ptoteins on severe acute (espiratoty

sy(f•omccoronaviros virions .l~ und{".aved.As we .ind others ~ve dc-mOllstraied.

infection by this virus depends on cathepsin proteases present in endosom;il

coirpartments ...

Ntr:,s.//www.ncb.nlm.nih.gov/prrc/art'il;:les/PMC6226446/

I

•>PubMed Central (PMC)

Functional analySisof J)4'Xential cleavage sites in the MERS.·coronavirus !,pike

protein

The Mkklle Eastrespiratory syndrome-rel.lted coron.,virus (MERS•CoV) can cause

sevtre disease and has l).lndemic potential. Thtttfore. devclopment of antiviral

sttatcgic, Is at1 lrnport:,nl task The .etivtirion of the viral spike protein (S} by host cdl

pro:eas~ ...

• Andrew Rambaut 11su

•• OK.As yougue:ss.ed • that tit I bbelled'ttact'wh~h I got byeyeballingthe ali\_gnrrent iswitlln 2 nucs at oneend and 6nuc:s~t tht other tot.ting the 'variable loop'in that paper.above. So th.at

looks like :twinn~r.

I guess the pangolin/human lineage could have got it from somewhere else but given in the rest ofthe genome, RaTCU is cbsest it woukt mean the Pangoln lineage a,d the one leadl'lg to SARS•

<:.oV-2wou(t ha,,c to get it SC1)aratcly.

Robert Garry 11SO

W Gte:i.tP€!th:i.ps:::i multi~tcp pro<:4'?Uto g~t to SARS,CoV-2?

• Andrew Rambaut !7:tS

•• tittp://www.mictobe.tv/twiv/twi\'·S88/ ( frctl'I iniriute 42)

• mlcrobe.tv

TWiV 588: Coronavin,s update• Save the J>,il~olin! I This Week in Virology

The T'WiV team returns this week to SARS•CoV·2019 co,ierage to rtvicwthe latest ~pi

curves..the fatality rate. furin dea-vagesltc and recept0< bindingdomain in the ipike

gJycoprotein, related CoV r~<Wered from p.1nsofins. evidence th.it the virus did not

esca~ from a laboratory. and many more q~stions scnt in by listemrs.

Robert Garry t 7.33

■ Is it possible to mak-e mo~rdoine a Podust • o..is this just a hobby" I'm l'KX judtine,.just clflous.

• Andrew Rimbaut 1737

•• lhavewondercdthat.l thirk rt is just ahobby. 8ut they are 2.5 hours '°"g. I don't know who has time to listen.

Robert Garry 1a3s

■ ttttpc;·Jlq1. com/180S4?2/W11han.-virQloSY•l.ib•vruble--t:o~qvrll-china•«)f'On;ivin.1s•conspir;;ici(":/

E1Quartz

Why a Chinese virology lab is unable to quell the coronavirus conspiracy theories

:.routid it

The episode shows how Chin.J's public has an decre~sing level of trust in the

government since the outbreak of tf'le coron.avirus. say e>q>Crt$. (98 kB) ...

Some jourll.)ts. such as Natvre. h;,ve appended notes to older stories ~t the Wuhan lab c:.111ing 4unvelifled."the conspi'Jcy theories Jbout the a3b

.,, N2iture Nfl.W't I:, Comlll'l•nt

Insidetht Chine-se lab Poised to study worid'smost dang&r0us pathogeos

Max1mu-n-securitvbiolab is part of plan to buil::I network of 8SL·4 hc:.d1tits across

China.

Wow • not s.ure Nature is correct on tt1is.

11'1"1•-9ng ...

,...., 1110cn1neseio•-10 s,wy-1<!ll most

dangerous pa,mgons

\_.\_.-.,. \_,\_\_\_\_\_\_ \_

\_ \_,

\_\_ .,,\_\_\_\_\_\_\_\_\_\_\_\_\_\_ ..\_

..,. \_\_\_ \_\_ • \_\_\_\_ \_\_

.,. ,..\_11111) \_

\_\_ ..\_\_ \_

I

Robert G.arry 1858

■ Nature seems tobc getting some bad~dvicc did rcvitwer n shikc again?

♦1'14il·\21G

REV0002961

~brwry 24th. 2020 .,

e Andrew R.ambaut 10:13

41111111

■ @Robert Garry Quick Question -would Vero-E6 cells have furin JVJi1able?

~ Kristian Andersen Ht.27 m I bel"""' they do.

Robert ~rry 10,33

■ Yes they do • heres the data.

~-~"B ..

c:11lJ.)T c:IC....-l

n:i~

=

"''

~'t~ ... ~# 0~ .;,\_-t'

,('If"

C.-<#\_ ... \_ .... \_\_\_\_ ..,c\_\_ \_

-------ilUl'c...1--m

-•-".-"' \_\_\_\_

...,.\_

-----~·-.,...,.,.\_

------...---....

-----IIIWI( \_\_\_ ..,.... ... \_.\_

---·-.....---·-~

I

https://www.r\atur~.com/articles/s41598-018·34859 w

,. Scientific Reports f.cbru.iry 24th, 2020 .,

Functional analysis of potential cleavage sites in the MERS--coronaviru

Functional .malysis of potential de.av-age sites in the MERS•coronavtn.is spike protein

• Andrew Jbmbaut t0·33

41111111■ But perhaps not as lung epithelium ce-lls?

Oh! Snap.

An order of mag less.

So might select against using furin cleavage site

Perhaps less than an order

~ Kristbn Andersen 1~37

r.l! Doubt iL.. Beingable-to use furin is a neat trick

• Andrew R.arnb.aut10:38

·• OK.

Just thinking about this deletion of the cleavage site we arc see-ingin a sample (at aboot 40% frequency),

-...I Kristian Andersen 1039

~ One-thing funn usage might do though• ma.kc the-virus lc$s stable. So changing temperatures in T/C etc. coukl probably me-ss aroond with it's usage of furin.

The loss vou're seeing· any sense if that specitlc to culture or whether i~ in the patient?

• Andrew R.arnbaut 10.47

41111■ Thai is what we arc crying to work out. One hypothesis I was thinking of is that the<e is another population of viruses that has .arisen targeting other cells in the body? Perhaps less furiny.

Robert Garry 1os1

■ Very possible. Would really like to g<'t some site directed mutants going on that furin site -then explore tissue tropi~. Pretty sure Barie arld Yoshi a.re burning the mldnitc oil gcttins those cxps

doue. Putting those mutants into animals very much needed. Tulane primJte center hJs the virus ~md is working with a consortium to establish the Jnima1s (NHPs. ferrets etc· maybe ~ts).

Tulane has Chad Roy th.at may be one of the few people that can credibly do an aerosol challenge.

BTW· Just got an invite fmrn Amy Maxmen of Nature to p;irticipate in a panel at a jourr\alists' mc(!ting in Austin end of At>ril.

Someone should tell Nature thilt the fish m;>ritet probably did not start the outbreak .

.-..I Kristian Andersen 10-56

1;&1!11

All very p\;>usible.

We now have the rcve<sc genetics system, so I'm sure Orostcn and folks arc on that as wcU.

Andrew. one thing to chc-ck • if the~ arc grown in culture, please have the doubJc.chcck the temperature in their incubator. If it's a few degrees higher than exl)(?(tcd, then I think w<! have a likely

mech.tnism.

Amy reached out to me as well • turned it down. but Bob. th.1t's your old stomping ground. so you shouki go.

~-2res,lies Ulstreply3~ars.Jt:O

Robert Garry lOS9

I

■ They arc just contributing to the conspirac.y theories that WIV built and released SARS-CoV-2.

THat was my guess. ~\*jfaj

@jifo-H::

Robert G.lny 11:07

■ Old white guy -hope they get some women.

e Andrew IQmbaut 11.11

•• Ask them fof' the panel list (can also chec:k for crazie-5)

Robert Garry 11:21

■ wm do• I think sirKe Kristian broke Amy's heart she is scrambli11g ...

r"li Eddie Holmes 14:41

...... See attached. STRICTLY confidential as I am not meant to SCl'ld it out. Yunnan bat from March 2019. Highly recombinant b1Jt close-st to SARS·COV•2 in one region. Still different in the R80 but the

other thing is ob,.,ious... Discuss.

REV0002962

PDF •

•FiJ.2·0224now.pdf

"°"

Robert G.arry u 44

■ Holy O'.:lP • that's am;i{ing..

I

~ Krls-tbn Andersen t4◄

S

fa No potybaslC a mechaniSm. wait Ulnl lt'S OU1!«bted)

Site. HOWEVER. this P<CW10C'S Tnls IS cr1001 {0 MVC out and plug In • len

Ro~rt Carry 1

◄~

■ We:lt· it is a logicai proge<1itor 0< at least a substrate for recombin~rion •just R for trypsin or maybe it relics on Catl • also deletes two of the three P<cdictcd O·linkcd S or T residues (and the

sequence is not predicted to be O·gvl<osyfii.ed (I just <hec.ked) .

.,.. Krlstfan Andersen 1soo

fa Agreed. Here's e·1ide1Ke showing that the virus likes to 'mes& around' in this part of the genome (in animals}. so ttut provides a template for OOw all of this happened in animals • <ritical bit cf

information

Robert Garry lS:<>4

■ I don'tsee how it gets us any doser to discriminating between anv of the m:>delS-There stilt needed to he recombin;ition an:I evolution in eithe<an animal. nnimals. hu11anc; or all of the above. It

d~s not rUe oul or in lab passage.If h's being posted fast yes lets wait• bul if its going: to bi"an detenninate amo..mtoftime IY\a)be get ourp.lper out Nature or Naturt Med. Add a 1l0tein p(oof if

it cornes oul SOOl)Cr than1a1er• (lthernise I think \·te antklpate that there arclikdv intt-rme<liatesbetv.ec,, knownbat .ind p,:mgOfn vtruses and SARS·C.OV·2 or maybe &Cid this to me <liscussiOn as

apersoMI oommunic.ition if poS$ible .

...aKris-tun Andersen 1sos

!!I! I think this tends pretty strong support for an anim.tl origin ct the 'conhtsing' features of the virus.so I think it's illl)Ort.'nt to ·nclude

ta,lil KristianAndersen 15·t9

119 Non(! of thi~ di!:.p-ovos ::iccidc-1\l:tll::ibinfection. howcv~r. it ~ows Wt 311 the tlCJM C!II\ occur in n:aturc -hC!i'ICCthe ro.1~ to own co,uider ::i bb link it docre3i.cd. Sir-.o&we luve ~uch :i minlscufo

sampli"lg of the animal rcseNoir seeing just small parts of the stcp•by·stcp mccl\anism is important •tome this d.na shows that bc<ause. YC.lh, it shows that the virus likes to •mess aroond' \'1ith

this put of the genome. I think thJt's important knowledge.

~Edde Holmes • what's the putHcation str.itcgy for this paper? Ican )CC it's fo,mattcd for Nature. but will there be a bioRxiv?

Robfft C:my 1S 20

■ BTW• what is la~ted the e<tenlcll subdom~in is the Vlriable domain Andrew W.lS djsc.ussin.s in the recombination subthread above.

e Andrew Rambaut 1s 22

·• Hi. Ju)t wo1king my way lh10ut;h thi,.\_

Robert C,arry 1'i7'.l

■ "the reason to e\len coosi<kt a lab link is decreased" • yeah good point. Don't think it necessarily points to adirect animal jump likeSA.RSor MERS or a rather exttnded hist(lry in humans.

If you happen to be working on cne of those standup d~k things,.I suggest sitting dov-,n.

-l)n.,,,V 4,.1\_1'\ 4V4V •

~ Kristian Ander5en 15:21

l'J9 M.ikC$ it rnuch mo!"¢ likely the fol furin $itc could h:wt: be-en ;icquirt:d very c,.i,rlyi'l hum:in$ or potentbfty in 11n intcrm¢diatt: l\ou • in~t~ of foming fJly de novo it'$ more :.kin to wh.at h:ippcn$

with f'\J.These are critical points that I think need tobe 1nade de:.r in thecom016'taf"V· aodcan'I be add(?din 'i1\ proof (given how important theme:ssag~is. it needs to be as clear and sofidas

siossil:Aefrom the get go IMO}.

Robert Garry 1:1s10

■ Andrew's deep scqueocing result with sometimes (40%) deletions in the S1iS2 jlllCtiOA alsooonfirm that the messing iround is common.

Wlil;Kristian Andersen 1 S:3-4

!'ta Yup.good point

r'W EddieHolmes lS:36

~ SO<ry,haven'l got time to respood now. Will talk later.

~ Kristi11n Andersen 15.36

r.£1 Yeah, no worries Edd~

{nothirtg on bioRxiv • it.1st cflecked)

Speakingof all of u,is here's a pressrek?astdraft (in e.xpe,c!arion of a futurt pubkation .... ). If foils have time to take a look and ll(ovide edits a1ld preferably some quotes. then U1at'd be a~.

WOHi Ootuff"-'llt •

REV0002963

Anderstf'I Coronavirus N.11ture 2010 Press Rdease ...

Wl)t'(fC>oa#ncnt

The C0\110·19 co,-aYlf\'5 eplleml( ~s a "\*'"~lorigllF\

M:ledkU ~v· l.

The,.to'e!SNIIS-Oil't'l<-~~11'1the(ltydW......,.\_C..,,.,

':.: ..~-::.:::::.o.:~~O:'!'!..~~-~

.C( ......... ,.,.,... .. ~ttdt,.-,IM"°".,.11(1(

TI-.•"""'~d,...\_\_..e\_.U..\_,,$.NISCd'N"'4..,.\_.....,

..,.\_...\_\_ .. ,\_111«11',c..,... .. ,n'""'6911'1•--•07o,oll>,

mw~

.... EddieHolm~ tS:37

,....\_ One thing though: it iscummtly being Sanger ~ucnrecf for conhrmation.

e Andrew Rambaut t~.&O

•• The 6gurc looks quite f.:lmili:ir.

Robert Garrv 1 s.<12

■ Nice job on the PR• however. you could have more activclybo"owcd from the R.ll'\Ca:nicllo piece• I mean. just to be fair.

Ftbrwr, 24tl\ 2020 "'

Robert G.lrry 1603

■ '"it needs to be as clca, and soltd as poislblc from the g,ct go IMO' Surely. aoo the points you ouUlncd above shoi.Jtd be lncotporatcd. Makes the ple<:c cvc-n mong IMO. This flgurc loob pretty

mature to me and the impC~tions arc not likely to change U"llcss San~ somchcr...-doubtful. t·in all for .starting to update ourpCCc dear and sclid aspossblc based on

hlls in the gaps. whi:h S<X?-ms

the re,iev1s 3nd ,he new inlo. Then we can see ,·,hat OOyit is.when we think lhe ~ info might become public an.d go from there.

Robert Garry 1612

■ 'The figure looks Quite f ami iJr.'" lhat's simply sinrere flattery.

-ir folks haw ti~ to take a look and ixovide edits and preftrably somt q\_uo!es.then that'd be awesome.'"<:ao you plact OI') the google or do you,vant t1S to tdit the old fashioned way?

e Andrew Rambaut 16'.16

• ■ Botti .ingnments start ano stop at exacuy u~ samete.skfue•s my r1gurt an.a I picked trl::>SC complttety arbitt.1:l'ity.

• Andrew R.am~ut 16 ,:1

•• I am not su,e that the new RmYN02l»t se<μcnas add aoything to lht story oll'\et than bats can have insertions ·o the St/S2 cleavage sire. In the RBO it is basic.1lty idtntic.il to the ZC45/ZXC21

which are the recombinant ones !in brov-m i11 the ligurt below}:

Ftbruar, 2◄

tl\ 202() "'

Robert Carry 1~-33

■ Dowt know tMnudeotidesequence there• th..-·s clearty c11optimal align~H .it lheami,,o acid level but how did tht sequenceal'ise at t~ nucleotide k!vfl. If ~oo compare RaTG13 to nCoV-19

the PRRA results from a sing.le insertion of 12 nut. BUT it's out of frame from the coding seq,uence of RatG13. IOWS not a sinpfe 12 nuc insertion directly encodi,,g PRRA. I'm gl.l:!ssing somethi"3

like tlis • a sinele insertion even1 rer,bcin.e 24 nuc with 18nuc. Comparin.aRm'IN02 to one of the bat CoVs. Possib~1 ( '1'frtN't)

Robert Garry 1101

■ l'he ell e, pos~i'bTts in c , st ekgie.'li:: oeleet'dt 6cletieu. Ol • this likefydictn't hap,pen.t~-d tcd}

• Andrew Rambaut 17:23

•• You c.;n go from the furin SfQ~1encein SARS2 to the RinYN02 c;.ite using only deletionc;.:

~pnJ •

lfMTTCTCCT--GC-GGCACGT---GTAGCTAGTOJN S P --A-A R --• V A S C

TA.A TTCTCCTCGGCGGGCACGT AGTGTAGCTAGTC1

NSPRRARSVASI

But it (l(.,:,Cnd'!I> Ott what CO(J()1IS a'<: bC"11g u.SC."(I.

Robert C:.rry in-1

■ lntc-rcsting!

• Andrew Rambaut 17:33

• • There are some other solt.1tions but always with 3 deletions.

REV0002964

e Andrew Rambaut 1',3S

•• Y~. >o 4 deletion>.fr-1C'd)

Robert G.srry 1eo1

■ Coincidence that YoUSFOt'I deletion ~bove took out QTQT(N)? Maybe apreferred site for recombination?

I

e Andrew Rambaut 1838

•• Ooh, lnlete'$ting. Too ffluch intcrrnk«I $t\.lff soing Oil,

.,. EddieMolmes HhV,

@i€l¢!J:

,...\_ The vi'us is actuc1Uy the closest to SARS·CoV· 2 in soine parts of the genome. although not hugelyc.lose. Very complex series of recombinatic:o evmts. Obviously, the key thing is the insertion but I

think that is huge in the current context. Clearly shows this Is In Nature. Here are the nuclcorldes. 'Nhcn did you do your alignment Andrew?

Oe.::iv;iie~te 20200220l71S2long ...

Nudeotide pie attached

In 'nature• snaU case. Not sure about publOtion strategyyeL .. soon I tope. As usual. much pg1itics.

• Andr<!w R.ambaut 19:01

•• Mvalignm<lltabovc is just a mock up• I did'l't know what tt)enucJcotide-s were.

So beca~t! it has those two As in U1ert!', my pure deletion ~elution d~n·t work.

So you ne(}d 2 tnn$ition; and three: ddcti011$ (or in;.e-rtion$) to so bct-.,-ccn the:;.c.

I am not convinced these are related inserts. Oeoends on the background in the rest of spike.

I still think that all it tells you is t.Mre ar-e some oot viruses with an insertion ,n this site.

r'9 Eddie Holmes 210$

~ Yes.but I tl"ink that is a,nerorlY'IQJS·au given tha: 99%01 tht Ia1>esupe idea fmmgeoomicswasthecl!avage site insertion and ~~not seen t.l\is inanvother bat virus. ldon·t lhinkwe \VOUICI

havewritte11 the samepaperwitfl this inforrnatio,. I also think it may be a different insertion but it me.1nsthese inserrions are happcntl\g in nature.

I

r'II Eddie Holmes 23-40

,..\_ A bit more:(i) se4ucnce confirmed by Sanger:(ii) bats collected May• Jutv 2019. so ,..6 months prior: (iii}in most of the virus genome it is the close-st to ~RS·CoV· 2 although not in S: {i\l} some vcrv

wide ran2ine recombir.atioo events: (v) essentially supports what Ref 112saY§ ("'WOO knows nowmany out ot thousands undi'icov«ed bat ancestors also acciuired well a motif. the sam~in& bias in

descriptioos of rtmote bat '-lirusesis dramatic~). That it is a differErlt insertion is n~t the Point in rnybook. V«y Sltonglyargues a\_g:iinstlab.

97.29'identity in lab.

FtbtUilry 2Stl\ 2020 ,.,

tllllil Kristtan Andersen 0000

mi!I Idon't think tl'lts data necessarily arguts against accl<lmtal 1ntect10ntre.tease. hOY,evcr.It soows sometrlin& very Import.1nt • hscrtsons at this site can h.lppen 1nn.c.ure,making the necCI to rt.ach tor

a noo-natl.lral explanation much dimill4,hed. This is new important knowledge that woukf need tobe introduted in our commentary and lends significantly stronger support 10 the 'natur.;11'scenariOs

we·,e describing.. I say we have to wait to, this to come out • at a minimum on the bioRxiv. It doesn't go against (or prove/disprove) the scenarios we·re descrlbi,,g. however. is wry irnporta,u

knowledge for a reader to know.

@Edd~ Holmes • wh~'s ye.or ta~e on how we h..-idte this? I think we should w.lit until this k out. update, tht commentary. and thtn out that b.3ckin vi;, Natu~/NahJte Mt<f with som~ sianlficandv

stronger conclusions about this being 'n,aturat Tho\lgtts?

r-. Eddie Holmes 00:53

,-...i: I'm nc,Nvery $tron.gty in fovourof;:, n;:,tvr.,lorigin, Thcc:ompc)f'lent bib of the"'ITT.ls ;)re more or IC$$ there in a tiny$ilmplcofwildliM:. Ph,1:;th<:rci$ more to come (Uli$i$not Zh;:,ng'$d.,t.,).1 don't $CC

why we nc«I a 14b origin on these dat.l. I agree ....,,e ha,-t>to hold ~k for bi<:1Rxiv.Hopdully something will be submitted this wed .. I'm actua ly at a !Tt(?eting with Clare next week..

... EddieHolmes 01:10

~ Rhhiolophusmolayanus

Kristian Andersen 01-31

I

Sounds gocd • I too think we should wait until this is out and then we can do a quick tum•around -I think wc"II still haw a pJper to put:tish bvthen and in fact, I tMnk it'll be even stronger as it'll

tiavc 1nuch le>> d an open toding (a~u. it <k>Csn't .. any 'rnystuics' to cxt'3in -we sec the OJ)tfrnited RBD in pa,golin> aoo part of the

rule OUl tab inkction/rcl.:-asc. t1owt>ver. there i$ now oo 101\~cr

farin site in bats (wtiich is p:etty cool!}. Generallyspea~ing. 1 also don't think we w,:,1ntto rush, It vou can please gnb Clare when You see her, then th,1t'<I be great.

@Ro~rt Gany and @Andrew Rambaut • thoughts? fafted)

• Andrew Rambaut 02<18 ~bru.v, 2Sth. 20~ "'

•• Iwa-satwaysin f.1vourof the pre•adaP1ed ju-np from animali hypothesis but now it is ~usible that thacwa-sdirectly from bats.

F, EddieHolmes 03:04

r-"a Agreed. I oromist to &et this oushcd out ASAP. I need to talk to Jeremy in a itt5e while.

Clare wants to talk about stuff so this will c~ar1ybe oo the ~er-.da .

... Eddie Holmes 03:30

~ Jettm•t agr~swIU"I thi.splan. I'll get thtbatpaper sorte<JASAP. lbiey'h'.lnt toe.all the humanvirusHCOV•19 I,

• Andrew R.1,mb.,ut0$.4.$

•• Here ismy spike re-combinationdiagram. Cle-arly shows how RaTG13jumps out in the RBD \-ariable loop reg.kin.

recombinaOO"Il\~.pn;g ...

"r--· -----

L-=;===-....:\_\_

I

-{ -L

~ '-{.

REV0002965

~bn,wy 25th. 2020 ,,

r'li Eddie Holme,$ 03:49

~ Beautiful. So. the human and Guangdong pangolin-.. inherited their very similar RBD seQuence-s the host specie-s

from a common .11nce-stor. of which is ooknown?

• Andrew Rambaut OJ 52

Al■ 11-.c-most parsimonious is that human, RaTG13 and .lt least one of the pangolins had a common ancestor with the ACE2·Iiking RBO and then RaTG13 lost it. Makes it likely that the RBD residues

were in a bat as well as the p,ingolin. What does the new bat have?

r"I Eddie Holmes 03:S4

,-..-; Very different R80, Ontv one of the 6 residues shared with the humJn virus . .lnd a different one to R.lTG13. Should be in that figure I sent.

I

• Andrew Rambaut 03:S4

Al

■ Oh yes,it was. Sorry.

r-'I Eddie Holme.$ 03:ss

,-..-; I wonder if the human and pangolin viruses are derived from a non-bat host.

• Andrew Rambaut O:kS6

All■ Dunno. Some convoluted shit going on here.

I wonder ifthe-pangolins are a ted helling he-re and are just picking up bat viruses lefHight•c.entre. Not certain.

• Andrew Rambaut 04.02

•• So the new virus would ~ in with the two btewn lal>cUed ones at the bottom of the dtag\_ram in the RBO (ZC4S and ZXC21).

r,i Eddie Holmes. 04:06 Febrwry 25th, 2020 ...

,...... Some convoluted shit -will use that the paper. Seems important to me that the bats are aO diffc<ent in the RBD. Sub-optimal? As for the p.an.golins what has always struck me is that both the

Gunng,ci and G1J;ifl$clong pangos are in the $ARS•CoV-2•Iike lineage....but ther(! are londs of bat CoVs w whywo1Jkl they both hnve distinct lineages thnt <}re dose to SARS•CoV-2? I tMnk we have

sucha shit sample we can't tell. I dunno either.

• Andrew Rambaut OS'.'00

•• OK. To return to the paper• so arc we going to:

1)Rc-nuanc.c it to c~icitly lower oor bet on the lab passaging scenario on the basis that both cleavage site insertions and the full RBD exist in nature. This leaves just having the sourr:c vi~ in the

lab and someone being infected with it which is just an alternative human exposure hypothesis without any evidence.

2)l.o\vcr our odds on the pre:-<:irculation in humans bec.tusc of reasons above. and lack of evidence of CMCS.

3) ..

!JIJ ~ 9replles ~strepfy3ve;>t'$:180

I

r'II Eddie Holmes os:01

,-....; Yes, that's it. Minor editing.

f.cbrwrv25th, 2020 "

Robert Garry 05:24

■ Think we nttd to have another term to use other than insertion. Compared to the other bat CoVs there is a net lost of three nucs. 5 amino acids inserted six deleted. likely a singtc "sm.alr

homologous recombination event or series of mutations and deletions, The recombin.:1tion could happen "'faster." The mutations and deletions that's just "nature~ aka unsampted diversity.

Robert Garry OS:30

■ Andrew's QTQTN 409f. deletion suggests the Sl/$2 site is prone to the deletions• th.Jt's ;ipp11rent in other CoVs. but yes not previously seen in bat CoVs so significant.

r-1 Eddie Holmes O!io:3~

,.....,-; Ne,ct of kin baboon pe,h,11ps.

Robert Garry 0!i:36

■ Maybe the term is "insertioo/cletetion" or maybe just "mot.ltion: Au v can get polybasic: site via small recombination events, point mutations or six nuc ins.ertion. ~cclitl."dl

P'li Eddie Holmes OS:36

,--; Bad< on tomorrow from me.

Robert Garry OS:'12

■ All good Eddie Jnd thanks for the upcfJtes! Paper will gel a signillcant upgrade. Not sure about the baboons.

Robttt Carry OS.SO

■ CJe.1rtythere Jre l.1rger sc.11e recombination events going on as welJ. I think Andrew's beautiful recombination figure adds a lot of weight/signi6cance -maybe enough to pU5hIt to N.1ture itself

r-athcr than NatMed (not a bad joumal either).

I

REV0002966

Robert Garry OS 56

■ Andrew R~Ttb.lut [4:00 AMI

OK. To retl.l"n tothepapef • so are wegoii)J to:

1)Re-nuance it to e)(J)lic.1tlylower our bet on the lab P'Ssaging scenario on the basis th:tt both cJe.:,vage site insertions ,md ttte full RBD exist in narure. This leaves just h.avinsthe source virus in the

lab and someone bein, infected with it which is just an alternative human exposure hypothesis withoo1 any evidence.

2)LowerOU!'odds on the J)fe--ticculaUooin human:sbecause of reasoos abO\'e,at1dlackof e"idence of cases.

3) ...

EddieHolmesl<:01AMI

Yes. ttmt's i<.Minor edting .

.a, Andrtw Fbmba11t

OK To retutn to tht paptr • so are we&oingto:

1) Re•nu,,nceit to e<oliciilv lowet ourbet on the lab oos~.eingsc:en•rioon the b-elsis

that both cleavage site i~rtions ard the full R80 exist in natvre. This leaves just

having U-e ~ouce viru~ fn lhe lab and ~orneom! l>clrts inf«tt!d with ii.which r..~t an

I

alternativehumane<posurehwothesis Yiithout any evidence.

2) Lower our odds on the pre•cira1lation n hurn.'tns because of reasons above. and lade

of ev~nce of c:is~.

3) ..

Po\t,d in i p.-~r-2020-Ntvn-~ICll'W-Pf'Ol(imM Qflgin r...,;,lSth. 2no ¼!wfflb<\.,I~

A Eddie Holme:.

Yes. that's iL Niner editi~.

Posud.\_i~21)20naturt\_mc<lc.w-.c•pro)(lmal.~ ~lSth.~)20 \ilcwmm.ag<

Robert Gar,y 0603

■ Asrqqwith 1), This will m;iko Nmure Qt,r;qv1;,nh.ippi(>r I think• SOY9$-1Q0 n4.1.>nc;(> TI,q ~sponsq toR'iV 11 l~st (11JqdionbQ.comqs. rolov.int.

I

RobertGarry 06-10

■ It nec.assar)' to examine the lab h•;pothesis, but wedid and it's not nccessar;· to invokt lab ~cape and the ~nts leading to nCov-19 all could have and in all likelihood did occur in nature. ·-n most

of thcviru.sgcnomc it {RmYN02) is the closest to SARS~CoV2 although r'IOt ir'I S" 'Seems importMt to ,ne th.It the bats arc ~I different in lht RBO." (eJi-.ed)

• Andrew Rambaut 06;13

• ■ We are also prOVing the point of the edito, that the findings can become ou1 of dateas new data isadded. Need ro think how to respondto that.

Robert Garry 06.17

■ I W3S just going to s-3y though that st-ill no "str1oking g...--." TM analysis hO,ds up evoo with another close-f' b:it R.mYN02.

• Andrew Rambaut 06:!9

•• Yes.We just need to come up with a good response. Something like th6 is our bcn undctstanding and it is l.rllikcl'I to changt substantially. The only thi\.g that would st-tttc the m.attcr isthe direct

Jlf"Ogcnilot (which b pn:tly 1,1nlikdy ), And Ut..tl wouldn"t inv.-id-1t-=:wr ill'l<>ly~·;:i• jV>l 1.0t1r.nn which i:. t;Qf"n;:cl.

Robert c~,ry Ol.'1

■ YES!

RobertGarry 06.29

• I think we C<ln $aythatwe arc not likel'/ goirg to find the direct progenitor in a bat. The R80is too much different.

Robert G3rry 0643

■ Batviruses arc percolating in paf'6olins.. likely othef animals and probably ht.mansfthe seropositives) too. I couldbe COflVirKtd otherwise. but I doo't think we haveenooghOOta to say werethe

(llrect progenitor arose. In tAC back of my mlnd Is the fact that ,he vfn.t:s lsn't changing""-lch ;tt ;tll, untfke SARS·COV. This to me suggests some pre•clrc;uIarlon In humam and argoes ;tganst a SARS•

like civet to human dir!ct tmnsmissiort

e Andrew Rambaut06·-'S

•• Justathought, y,flat about pigs?

RObel'l Garry 06A6

■ Yeah • would not rule out domestic animals • even fcr2' (ats.

• Andrew Rambaut 06"6

•• We stfl ha\lC tMpa.radox • it tMvirusishurnM adapttd, it should havt startM circulating as soon as itarost. But\"re don't ~~anvg~~tic v.1rian':$thatarehkelyOlderthanAutumn 2019

• Andrew Rambaul 06 S3

• ■ Pangolin CO\I gtnomt came up on gtnbank:

~ttr>s:i/www,ncbi.nlm.nih.gov/nuccore/MT084071.l

Seems closely ref;ited to tht Gu.31'Sd0t1a/1n020

Missing chunks though. Just saysthis virus was c,rculating in tll'ly 2019(edrdl

Robert Garry 0700

■ I gues~ al this fnome,)t (subject to c.h,i'ulge} I ,n lear,ing 10 a S(Cnario where a 98 or9'9%rcco,nbi1\ant arose in soine animal with a tuman•lik-c ACE-2. The la,t e.ha9'&c in an aninal $XObablywas in the

St/S2junction maybe a minimal furin site that alowcd better cittul<IOOn in humans w1'c,c the fi.1)3I pdybasic site was set and~ got to 100% nCoY·19. I'm not too much bothered somucti by the

lick ol detection of ,1 dose,v;ni.Ylt in "omens. OC43, NL63 etc orcolated prob fCJr de<:3desbefore they were detected.

Bon om llnc tor me • ttle scenarios in tl'le cuffcnt Clratt don't change. except 1.1b escape unncccssasy (wt said this: but ca, be turthtf nuanced) • the ncv,data rcnncs the aoolysJs consldttably

sharper. ~uticulJrly re recombil'\:.ltion.which is ;1 major upgrade.

Yes • parado)(still in full foccc.

REV0002967

Robert Garry 07:40 ~bruary 2Sth. 2020 "'

■ The mainargumcflt against the lab escape is that to get to nCoV-19 in Vero cells you would have needed to 6rst have the 99%virus from a non-bat c1nimal then blind pass.it a 100 times or more.

This is what we wrote. Did not happen. Jost as likety to go the other way like Andrew's 40% deletion mutant Mixing b..'ltaod anim;il virusc-s in wlture to try to generote a recombinant? No one

would do that Thoseare-the "exp@rimrots• that go on in nature millions or m~ times as frequenlly as any lab activiti~.

• Andrew Rambaut 07 46

•• The only thing that is left in lhe 'cOf'lspirMy' side of things is that a researcher became infected through handling. sampftng bats or culturing bat virus.es [I.e., the exact one ttiat became nCoV). But

we don't (and cannot) acktress the actual nature of tile-zoonoric cvem from an evoluri00.1ry/genomic event -so we -shouldn't even mention it

(;30

Robert ~rry 07:49

■ Agree-and as in the l.l-st response to Rev#l the potential lab exposures pale in number to natural exposures.

So agreei1\g: with Eddie lhal •minor"' edits needed. The edits need to be sharl'.l and concise ~r Kristian. Must addfess the new dat'.t kills our atgur'l'\ents (it didn't and won't). Bigg~t upgrade needs to

be a ne\V disc~sion of recombination IMO. (~itcdl

fa replied to a thread: OK. To return to the paper· so are we going to: ...

~---I

Yes. I agree with this· mentioo it (becauseit must). but then shoot it down. Th.'lt'll be the most powerlul w;,y of countering this.

I'm still favoting a pre-circulation scenario and I believe the furin site could have-bec-n fully formed in humans.. The main reasons I still thlnk this is a real possibility• midpoint root of tree-and dN/dS

being incredible low f0<the s.pik.c (this. is holding up in bigge< c1nalyscs. but still trying to finish those up ... .}.

I consider a ptt•circulation scenario uncontroversial.

.......--, .......

\_,,,\_..,

lfl.lillKrittfan Andersen 09;40

&Cl The last change in an animal probably was in the S1/S2 junc.tion maybe .a minimal fur1n site that allowed better circulation in humans where the final potyb.}sic site was set and we got to 100%

nCoV•l9

Yup. I agree with this sccnarK> too -seems very plausible to me (TMRCA becomes bottleneck. not introduction: alld helps explain midpoint}.

I do wonder if we could throw in a dN/dS • it's consistent with the prc•circulation scenario. BUT also consistent with e.g., circulation in pigs. Uncontroversial and lends strong support to natural

scenarios (tissue culture wouldn't do thal).

Oh. ;md one last paint• this virus rsalso nowhCoV-19 to me• SARS-CoV-2is dead.,

Robert G.arry 10:12

■ ·we could throw in a dN/dS· I think would depend on the data. If it k>oks convincing we should consider it. Andrew's beautiful figure hints at the same thing.

Robert Garry 10-11

■ "SAR:S•CoV•2is ~<M:r yeah WHO and ICTV need to reconsider. But is hCoV-19 the infamoos viros X?I'd say no (but open to coont~rsJ· too similar t=ixonomic.ally to SARS•CoV,which is obvio~rslv

what ICTV focused on.

~ Kristian Andersen 11>22

~ WHO has never used SARS•CoV•2 -they'"re refoSi"& tocalt it that. If the Chinese would like to call it hCoV•19. then I think that should be the name• not what a group of white dudes decided in

Europe...

REV0002968

• Andrew Ram~vt 13:~S

...

(lJI ,) vhh to Sll"'0Ct.1MI, 6Wonc0Qflt {lf'CVino. h~t yto,)t, th• Gu,,)NJbn ,nd su(f troa CICGOF UV It (,Utd '•dlit),' o--.viously ust,O (Qt-,)ttNOltd l>rttdil\l of tl't,t Mtod0tt$\y ·•Nl-tl)•I>,..~

P-'l'llolin.

ITttps:Vwww.theg,uar6.1n.ccm/envirorment/2020/febf25/coron.ivirus·cloi-Utes·reveal•vast-scale-of-chinas·secretive·wildlife-farm-indJstry

c&the Guardian

Con:,n.:,viru, clo,u~s ~:ii vMt $C41eof China•, ~cretive wildlife brm indu,by

Peacocks.po«upillCS and pangolins among spocics bred on almost 20.000 fatms

closed inwakeofvirus

~c."b24th. 2020ft5S kOI •

I

ihope some one is sampling those animls • would be~ gOOO place to genetate dWersiiY in covs.

lagret \atwe s>IOUldus nCoV·19. Willd.OSO from I On.

REV0002969

Febrwr, 26th. 2020 .,

e Andrew Rambaut 1=

•• I h;ive added a plot ot distances to the bottQm of th!$. The bars m'ltch the dots on the trees

tN:On-.bl""tforl-~o,,c•

----··--

......... ... ...

J,,\_ ·•-

I

◄l'IIU,Hii@

...aKristi.1n Andersen 10:14

PJ9 Th,s looks gteat! Which part cont.1,ns the RBO ancl the: key rc:s,duc:s?

• AndrM Rambaut 10 ro

• ■ '1ar..aijcloop

If we useil we c~n tf'y to standardise the Lwo f1gtJres.

a,'MI Kristian Andersen 1024 rn I think we should def1nite4yuse it -but yeah. we'd probably need to stlf\Cbrdi.!e the two to n.ake it easie:r to follow. Lo...e this ooe it very nketv illustratc--s th£! natural sten.ario (!l(Otainina the RBO!

More 'credit' from TWtV~ .. http:hwww.mic:robc.tv/twievo/twicvo-S2/

• microbe.IV

TWIEVO 52: V1rustvolution by land and by seaand by O:,V I Tills Week In £vdudon

Ncl> andVincfflt e><amintSARS-CoV♦2 from an evolutiONry vCwpcint, e><amining

whcctthe spik(' gtycopiotein sequence informs us about the origin of the \'irus.

Nice tittle ~ure they have there

Robert Garry t056

■ Lookss:treat• minor tweak: should be N·te<minal domain.

/2 l (i;i

Robert Garry 1101

■ Yeah • GREAT

Robert G.!lrry 1108

■ ~n thisbe summ.:triied as: 1) RaTG 13 is d<J$est to nCoV• 19 (need to harmoniie) in S except for tne vari;ible 'oop, where closest i$ pangoG1.-1,;mgdong1/2020. Sugg~ts recornbim,tion. 2) Spike

also appears to be a hots.pot for rttOn"tlination ir, the p3ngoviruses. OJtskft of spike cllld the variable domah is AATG13 stiR close-s.t tonC0\'•19 or is this hCov•19 in al the gene~?

e Andrew Ram.baut 11"-2

•• Yes. But I think the kev ooirt is tl-..at the RaTG13 has had a rew variable looo reaion come inOt's 2,2oetic: disbnoo iumos uo. whereas tht oani:otin stavs the same). I think we can inf et from that lhlt

the RaTG13 line;,ge had the good RBD resiQJes pior to this recombinJt:ion event.

So wee.an Infer that ttic ACE2 lildng RBOw.lS in bats.

Robert Garry 12 20

■ So.1} ,ccombination in the variable loop to optimize an at ready pretty good human-likt RBO in a RaTG13·Jilo! virus foUowcd by 2) inscrtion/dclction/rcxomt.nation/mutation [stil gtasping for a

\!etb) ill the S1/52 junction geoerJted the progeritor to nCoV-19. Does this awesome .tnaly$iS provide clues asto what species l Of 2 took ploce in? Seems 1 or 2 coo1d potEt'ltialty have been in

pa1'3o!ins. ~oothtr aoiinal or hun'\anS.. Evc-1\ if 1 and 2 both took place in at1i,nalssomepre-Wuh,!u)cireulatiOf\ mayhave been rcqur.-ed if'l hu1Y1&ns LO tock in the optfrnal potyl).).sie site.(~ tc-d)

Robert Garry 14:37

■ Should SARS•Cov go on this second figure? h's on the first one.

~ Eddie HolmM 11:57

~ I haV<l to sa·f that I disagree with this. I think we shoold stick to tho origiMI plan for this arride a.s much &s possible and not try to l>e too d-c:uik·d ~boot what we think happcncd (o..g..~kh bits in

which hosb) and I don't think we should use And'ev./s figure in this piece. I $3Y this beQuse I cer1i.1in ttiat the picture is.going to change rapidly JS new data <0me out and I am IOJthed to make any

strong conclusions ~n the samplt isso small. Forexample, I don't think~ firmly conclude that the hCoV•19 RBD came from a bat. I strongly believe there was another intc-rmc,diate host

some•whe<e.In addition. the ,,ew b3t Vrtus is actwlly d:)sest lo hCoV• 19 in 20t<b of U~ aenome. Also. it outs me in 3 vtfV difficult oos.ition 3S it mtans th;:it I am on o.apef'S th'Jt wit be publis'lled

around the same time making almost contradictory statements. So.if )OU w,mt to go into detail SJYing which bit ct sequence camt from where then I fed th.at 111 need to remove my n.ame. I

I

nonestiy dcn't we need to oo this~ 1 tMk weJust evi'IUclte the d3ta In support ot the v;.clou:s hypgthesg and Jeave It like this

REV0002970

Ftbruary 26th. 202() ..,

■ I Gskcd th.lt question this morning.: "'Outsid(I of spike .lM! tht V.lri,blo domain is RATG13 still dos~st to nCov-19 or is this hCov•19 in .:al tho JOrM,S?" So-e as how the •,xw b.:a1virvs is actu.:allyc.Jo~st

to hCoV•19in 20Kbol the genome" does considernblycomplicate things• so I see your point Ed6e.

~ Eddie Holmes 18:31

~ ll':. clost:St in t;,b (97.2'6>, Slill oot ma1:.ive ~iose.out Closer. LOtsor fecombio,,1tiooelsewhere. I just <IOO.l lhiok vtt o~ to 1XOS)O)eaoy\hiog too 1a;,ecU:c.

R.o~C:my 1U1

■ I'm su·e we can come up with the optimum approach to modify/upgrade and upcbte this piece th>t has atre.dy hid somuch positive impact and get it out ASAP.

f.tbrwry 27tl\ 2020 ..,

e Andrew Rambaut 09.27

•• Pcrsol)311yldon'tsee how Mothe-rbatthat isa b't closer dun RaTGt3in lab changesinvth'ngwe are-saying he<e.But I agreeit is likely there isan inte<me<liateanimal between bat andht.rnan. I

<10tn,nio<J<JoevrJy o, me omer at>oul the 1eco,lCIfigure.

The only thing thot Is turrcntty unpublshcd :ind th3t wa n~ for this is the <:k!:w,gc site in~ri in 3 b::u.

But the window of opporru,itv for publishing thn in the formit is in is 'lanishing ciuickJv.

,J\t <iii

Robert Garry 09'48

■ lagret • v1indowc:losing.Maybe update thef1gwith the newvirus• cha1lgethe narn<?to either hCoV·19 or HCoV•19 (i:,-ickor\e) • make the ninorll>ut clear and concise] mOdihcabOns(tl'le:ntion

recombination as a oossibilitv.blAwithout detail). I'dsav S<nd back to Clare and see if she'll reconsider or Ptrhaps fa-stt'r settd to fllatMed.As more sewenct data comes andthe oict-u-e on

recombin;ition clarifles there will obvi()\JSIYbe a need to address ,noredefm.t:ively in a filturerub

Robert Garry 09SS Ftbrua,y 27th. 202() ..,

• ~nCoV•19

I'm not pidcv

~ Kristun Andersen 10:34

I.a I'mnot too wO<Tiooabout not beingabk?to publi>h this • yes, it's getting to be of decreasing interest as focus mO\-es to p(lndemic control. OOt it's still of interest. Here're my diovghts.:

1. If lht-3~dil-1on:ilf,gur~ brio~ in too mu(h 'r.:i'N' d:.t:i/:,n:itysis U1:iol (Ould be cootro-.,cri:i:.I, then yes. we pt0b3bly shouldn'l indudc for:, C()(l'lr'l'ICnt:,ry

2. I will focus on reshaping/ flrishing the manuscript Monday/Tuesdiy, assuming the half.furindata will be-publishedshonly{ish)

3. 111reac:hout to Sri at Cell to sell the story toner• that way wedon't deal with the reviewers .andCell is fllOre ikelyto take it

4. We eitherreference toa nev,,Studt sho\.Yi11,2 out a,wtime soontooint to <llher,·iruses that 'fwin stuff h3ooe"" all the time. a-nd

haU•tuf'in t,om Eddie's fl,21.te.OR (if that isn't ,2oin2 tobe sa:vin2

we p,edict we'll see the samt hert ...: That wavwecan hcepthe message strong. without act1.0lly citing the study• if the study comes oot in the meantime, then wt'II throw a citation in. In

ntlthercase wm v,'\;' discussh detail the ;icql.llsitsonor the site sin<er~II be tor the p<inary pape, .

... Eddit:Holme> U;JI

,.....\_ Things havt been a littfe delayedwith d1c blt paper ... theydone somere-sequencing,.Doesn't change anything but it is slowtr. I ag,ee wiU1 the window is closing. Why not jun sendto Nature

Medicinetoday~ is?That will the fastest.

Robert Garry lS 17

■ I'vebeen editing per the r('Views. No changes in stone •yada yada and a few references tohsert,but IMO not too bad as is .

.... EddleHolmt-s ts:20

r-; SorryKrisNn. dtdn·trt.ad Ol)C ofyo,1..rr rncss.iges. Cc-II is fine. They'll take it. Vr:ry keen for stuff. I ttink v.emove away from Nature (straJiht) as that will take longer. I'm againstthe additional figure

for re;isons above. But we 5houk:I do this in the next 4-8 hou-s I think. I suspect tte new bat paper will be submitted oo the same time•fines. I think it's HCoV-19. Perh.1ps.

Robert Garry 1s:n

■ lputhCov·l9blAeasytocl"1nge.>II.

I

(ddic • do you mean submit to Cc-IIovc-rNatu,c Medicine?I'm line cithcf wayjus1want to be the fastest.

r, Eddie Holmes lS:24

,....\_ 11st use the-name the Lanett paper.

Robert Garry 15·24

8 Yeah then HCoV·19

I 1rle<1 not to he 100bt\ltal w1th thechanges bt.Jt :;ome were needed. please e(lit the edits...

r-1, Eddie Molmes U:2S

r"'a Notsi..re .ibout the f~est. Will N,ilture Me<!icinew.>nta review? If not• them. KrisliJn • should v.-e ask Sri?

...aKristun Andcrstn 15;30

pa I ley folk,. Sorry, in c.01t,hm1 ,necting, loday (at UCLA)and tomorrow· drivhg batk f«:m LAX tonight. I'll be:able lo fmd a Gcuplc of pockct5 of time. ,o let me u,c ttw.t to tir,t write Nature Med to

see what they'd need• if ful re-review. thefi let's go with Cell. Otherw$e, Set's tryNawe Med fiNt • seems tke m;>St folks leaning th;it way

Robert Garry lS'3S

■ lactvilty think the rev,sionis not in ooclsh;-ipe but does neoo some he"p with t:ransitions;ioc, the new refererw:es.1'11stop 001it needs sever~ passes by the rest otthe team. Not alon.gproc;ess.

KristiM jus1 fcmcmbcr • write drunk bJt edit sob::cr • I need a b«r or two.

Should notnttda fullreovi<"wat NatMed • all points oi the priOr'r~ewaddressed • mostly •i thfllk.

"" Eddie Holmes lSAS

I

,-.. Nat\lre Medicine then. I'll go over the nevi version of tt'ie p,'lJM?r ttis morning.

REV0002971

Robert Garry tS so

■ RaTG13 but not RmYN02 in the fif:urecorrcct? Docs NOT tt"ally change text that much. Jf RmYN02 is in then scnu:-ncc about a .. hilt" furin site need to be adcf.cd. :RmYN02 not realty needed and if

the paper appe:'11'$ during proof covld potencially add a note. f!XSitcSI

... Eddie Holmes tS:Y.

,-...-; Le~we ~mYN02 out completely ror now.

Robert Carry tHS

■ Works for the p..~r ;:ind for me!

WMIKristbn Andersen t8JS

~ we111e.aveO\JlRrnYN02.l1)Sleadol direcUyl)Ointlng to it. we'll make it clear that ~tuH like tris happens an the time aocJ Ulat "we'd eXJ>«t to s.ee animals I-.arb01i1lg o:/1/$ with simil:Ir i1lsert'lofls as

research is ongoilg" • and then add ;i few more ~ints to e.g., furin in human CoVs;:md Ru. Will make us look \vic;ked sm~irt v.hen the RmYN0'2 paper c;c;mesout too .... lnft .. tfl

Robert Garry 1842

■ Yeah • pape' still needs some "wi:ked smart'' edits based in all the new publC. not public. etc info. but I have grea: confidence that it can be done without too much effort. Letme know it you need

somemor~ oertin~nt ~~rences.

~ Kristian Andersen t8SO

eB Ifyou can pleaseadd PMIOswher'c yo.i think they might be rcb3nt, tl'tcnthat'd be helpful • I can then go through and inclu:Se as I edit. Agan, I'm unfortunately totally tied up with m~ting.s so

this will bk~ mc:lwhlk-. but I ~d to get In th~I'~.

n: EddieHofme:s n:22 ftbn,Ll'H"f27tl\ 202() "'

~ Bob. rvc rc'Nrittro the pango bit. st111 ricedS pollsf'llng thougri.

Robert C3rry 19.31

■ Nice job Eddic!Kristi.an • PNIDS arc.added let me know if you need MOrc. EddicaddOO his wicked sinart cdits.ar:d l'insureAndrtwand yourself will do.as IA'CII.Slnificant upgradeftorn the last

\'ersion. ~ve to admit that the referee's ch31len~s spurred us to a greater height.

w'MIKristian Andersen 19.3'1

t'n Iwrote to J~o from N;:itureMed bvt got .>nauto replys;:iying he's out until r,ext week. If I don't hear bJck by tomorrow I'll email 5'i to ga\Jge her interest.

Robert Garry 19AS

■ Maybe sc,nd Clare the revised paper and the rebuttal just as a professional curtc-sy. Thank hu-and tell her it°) a big upgrade a,d th.at the editors and reviewers helped a lot.

I

... EddleHolmes 21:16

,....\_ Sounos goed. Ill be seeing Clme on Monday, perhilps even on $\Jn(lay 11n -n,i,oe),

Febrw,v 28tl\ 2020 ..,

~ KristianAndersen 00:19

~ Heard back from Nature Med • vt(y positive tesoonse.Hoping 10 fu\d some time tomorrow~ I C,h) send it over to hin'II:

a Andrew Rambaut Ot S6

•• OK. I am ui:,.I wi I take a look at it now.

REV0002972

Ftbtu."lcy28th. 202<1 ,.,

• Andrew Rarnb,a;ut nns

•• The<eis a.nother Pcln,&0lin genome on GISAIO, Doesn't add ,mvthfng to our story.

~png,..

=

...\_\_\_\_\_\_\_

\_

... Eddie Holmes 02:26

..---; NOl)e. can be igoored.

• Andrew ftam~ut OZ t9

I

•• Willgtt thef1shorigins nuhand the labodgin coospiracy loons to,gethergiw,, th!labit comes from.

Robert Garry 08 52

■ tTttps:,Vwww.washingtonex.mincr.com/waShington•sccrcts/fauci

chinesc•Gat•fCastS•li'1kCd--to•virus

W:ad1inaton E.,c.amlner

Fauc-i:Chinese ~t 'feasts'linkedto virus

At® U.S. medical official on Thursday sad the coronavirus could have spread n Chil\3

thrQ(.lgh cat fe.asts.

Feb ?8th. 2'J20{123 k8I"'

• Andrew fbmb.!iut 1MS

•• I think Pence may have kidnapped Fau:i's children.

@)~ I

• Andrew Rambaut 13,02

•• "Faucidesc«b~ the science behhd the coronavirus..sayingit ju.mped from a bat to a 'dvic cat' served at feasts in China and then humans.•

A civk cat i~ono that Ives in a town.

r"I Eddie Holmes U:38

~ Goneovc-<the text ind-ctailagain and it looks tab.Just the refs to add. I'm happy for this to go.

Canalsoconfirm that lhefeis no hint of HCoV•19 in our603 lungwash samples from Wuhan in 2017•2018.

,<iJ

~ €) ¢ Q

-"' Kristian Andersen 16:~(I,

~ I'm still stuck In mcctfogs • all fucking week. My bstmectiniof the week MJ cndat4pm and then finally l'1/havetimc. I'll gtt it done ~d then bounce over to Nature Mcdlci~tomorrow.

BTW• Eddie. don't know if vousaw this? httpS://www.scmp.comitcch/big•t~ch/article'30S2624/more•60•<cnt~chin~se•companes~still~teltcominutiog•amid

coronavirus

REV0002973

, South China Morning Post

Woricers at 60 per cent of Chinese firms still telecommuting undef-lockdown

More than 60 per cent of companies in major ChillCSI!!' cities have nol reopened offices

since the LuMr New Year holiday, allowing employees to work remotely from home.

Fri, 27th. 2020 (238 k8) •

Reference to show that lhc furin site is functional in hCoV: https:Hwww.ccltcom/pb-asscts/journals/rcscarch/ccll/Ccll 50092-8674!20}30262-2.pdf

•

r'li Eddie Holmes 17:SS

..... Oh, good reference -we should cite that. I'm in very regul.-r contact with people in China -they .;re doing {me.People .Jre out and .Jbout on the streeti .JS normal in Shanghai, I'm hoping th.;t things

might start to ~Im down a bit when pcopl~ don't start dt0pping dead in the ~nsiblc streets of northem Europe. TheKorean numbers look the best mc,.asurcd to me• CFR is -0.5%.. Clearly a

massive underestimation of cases in Hubei.

~ Kristian Andersen 20.02

@Eddie Holme-s • do you l\clw, a v~ion of out previous submission with line numbers?

... Eddie Holmes 20:26

~ No. I can't sec that we ever had one.

llrW Kristian Andersen 20;21

~ I don't think we did -I think it might be in the NaturE! system ... AJI good -I managed to f1.gu,eit out. Do we have a high resolution ve<sior\ of @Andrew Rambaut updated figure? (Mited)

~~-= I

~ Have checked: the Oil(' I submitted did not have line numbers. I don't ha'll'ea version of the figure that says 'HCoV-19' .

...al Kristian Andersen 23:<13

II! Will fmi-sh this tomorrow morning. Some funky bits that reQuircd rewriting and a number of missing refer enc.cs. Should be sorted out now. so should be comp~tc<I soon. @Andrew Rambaut one

comment for voo. and can yo,u ~e-a~ also share a high resolution version of the most up•to•date Fig\_ 1?

REV0002974

f.tbrua,v 29tl\ 2020 ..

... Eddie Holmes 00:!6

,-.; 111read through ag.,in Shortly.

My t-•bnd:uin is not up to tn..1eh,but .'lpp:..rcntly this .'IN!v,is wsgc,u th;,,t o~k origin.'lted in 1he US (node H38). https://mp.wehdn.qq.com/s/JW\_ ◄

~2grSU14f'lVl34$Tqw

Clllfa~~'l'tt

lli~liitfflfiliJl.9.ILll!?lj>JSl,:.;g.i8:i:cil!:t7"Jlffl"

<l>@A, 'f'lll!Wr-JUHAAl'H2!

~ Krfstfan Andersen 00.17

!a Damn • must ha,,c bctn the Democrats.

... EddieHolme$ 00:is

~ A ploy by Bernie to ~how the value of l'lcatth care.

ti'!IIIKris-thn Andersen 00-20

&£I Can't deny it being a good example ... "'!.

e Andrew Rambaut 03 25

•• Here Is thehlg\_h•res versk>nwlth HCoV• 19 h U1e labcb.. In tile Google Drive folder too. (oc:ht('d}

PDF •

.,

'::!:8'.= .;-::~:'!:..-:-:....J~ .. !~:"

... EddieHolmes 03:$7

~ Ve,y mi,-.ol'edit.s ,nbde and so,ne mino, ,-eff:f'e,,ce is sun to f,x..All good to n~.

Robert Garry 1WS

■ Odd<:

A«ident;a,I retease from 3 la) -0.0019'

Gcncticallycngi11ce<cd andtcleascd by a Trump minion -0.00000001,£

I

Gencdcallyenglnee..-ed and<eleased bv a Bernie minion .. 0.0000000(X)0001'6

Ftb~f'f 29th, 2020 ..

Robert Carry t S·27

■ Decent iobon this m.,nuscript. Still think NJture ismissing out an opportunity. 8vtwillbe happy to see it come04Jt in NJtMed.

Robert Garry 1s.io

■ "So ycu're telling me there'$ a ch•nce•

tlttps://www.binc.comtllideos./sea,ch?

q•so-ti%27.,.,•got.. •chance&&view•detail&mid•7CEFE6FF4482BBC195A87CEFE6fF44828BC195A8&r,smid•F30C2A2557AA88EFE3FlF30C2A2557AA8BEFE3Fl&FORM•VOQVAP

~@

1lfllllKristi.an Andersen t6:l6

l'9 Ok;.y @channel,! went through thewholem;inuscript.:wid lthinl: it looks good. I luve:a few things to.:.ttend to. but will send it CWC< to.Jo.ol;i.tertod.:ay.:.fterl tuved011e a fin.ii i»ss. lfvou h.;rve

any additional ch.loges,edits..or comments, please feel free to go through the document one more time.

~ Kristian Andersen t6.12

PJ9 N.atvre (NC'W$} publi$hc-!> thi$? http$://www..,,,.,ture.wm/-,rtide$/~1S86·020-00S40~~

~ Nature

Mystery deeptns over animal soorce of coronavirus

Pc1<1gOlin~

arc• prime .suspect.but a slew of go'W:tic analyses Ns yet to lilki ot<Yldusi~

proof. (65 kB) •

Robert Garry 16 lS

■ Hmmm • new, dep-,rt,nenl different from t.ht ~ :,,<;ieneedep,ut.ment'.>Al$0 mioor detail but re~llly CoV) don't have ONA.

"Three.-simibr comparison studi~ were posted on bioRxiv I.ist wrek. Cne of those papen. -by .an intem.ation.:a,I rese.41rchgrcup. posted oo 18 Feb'u;i,ry-found2 th.it cororuviruses in frozen cell

samples from illegally trafficked pangolins sl\ared between 85.596 and 92.49' ol their ONA >Aith thevirus fovnd in hvmans."

~ Nature

Mydery ck3opens C:W9' ;inimal J;QlU"CO oF coron:ivirus

I

REV0002975

Pt1ngolinj are .ll prime sus.pe<;.t, but a s.1ew of genetic ;matvses. h3s yet to find CQnCfusive

proof. (65 kB) •

Nature should publish our paper to fully inform the mystery.

ttY Kristian Andersen 16·'20

1,1!1@Eddie Holm~ • ate you seeing Clate this wec:!kend?

~---I

~ Talked to Eddie. Hc-11 sec Clare tomorrow or Mooday. We'll send it to Nature Med later today a.odthen Eddie will give Clare a full run·down • if there's a chance they still want it in Nature, then they

'4ln pull it p.xk from Nature Med. I don"t really care too much -this'll get a big .1udienceanyw;ry,

• Andrew Rambaut 16:!i.3

•• Soond5all good to me.

GrcatwOfk.

Rob@rt Garry 17:30

■ ditto!

PDF •

a :;ProximalOriginofHCoV-19.pdf

11,. ,.,.v~.to,ipo,.fK(...,..,,

....... i..~.---.--.,1~,r,t-c.-...• .. --....1<,.,,,f

~ •·:\_:7.,;\_.~~•,;\_-o~.,.,.', ..,..--... ,-.r~~:,mv..,\_

.,;::::..~~:-..-c;;::-=~~;,~~: -..==----' -~..

..., ... ..,...., ..... \_ ................. &,., ..

,...;::-\_-\_7:..\_~~:T"'-·----....

\_';>\_ ... \_,..

'l .......... .,M'X,

~\_...\_.,,\_ ....

-

~~~-~";t1,.-·

-•""'--"'•-.....-i--•-JOMICOW,O.!'lln\_,<"ll"'°'........... ........, \_\_\_\_ .,,......,., .... ~.

.......... a-•J \_\_\_\_

I

REV0002976

REV0002977

REV0002978

REV0002979

March bl 2020 ..,

REV0002980

• Andrew Rambaut 03 20

•• The nev, bat \/4rusesare up on G1SAID

Robert ~rry 06i>3

w'.lillKrlstlan Andersen 22:24

~ Some updated numbers on dN/dS. It's interesting that there's no positive selection in the S ... Also inclvdecl some com~risons to Tommy's d.1t.lset • he had a la(8ef and a smalfer one. Gel similar

results for SARS u$ing thos,e~s the ones I have previously used.

REV0002981

Interesting for this too is the-fact that ORFl in HCoV does have a prett; hi&h dN/dS • similar to SARS cirty. It's almost as if tile spike protein is adapted to human. but the rest of the virus isn't.

Could be wme crnty l!>:i-<e«>1nllntil-kr1 event.

I'm hC¥>ing to get ;21ch~nc.e 10 loolc .21t l.21t«in tt.e week to see ii .21nything h.21s this d;i,t:au~t it a couple c.f weeks old.

the now bigger HCoVd.21t.21s~t changed Screen

Shot ?020·03·02 a1 7.21.03 PM png "'

ORF1 Spike

HCoV-19 0.91 0.29

SARS,earty 0.81 L82

SARS, middle 0.66 0.44

SARS, lalo 0.32 0.51

I

SARS, Tommy\_big 0.54 0.90

SARS. Tommy\_small 0.48 0,85

SARS, VIPR 0.62 0.82

MERS, VIPR 0.32 0.38

HKU1, ViPR 0.11 0.29

M.atcb 3rd. 2020

r'I Eddie Holmes 00:2'1

,,..\_ Loads mote Chi~e gtnotnes c.«niog,. I'm oot qLitc wl)cn. b.it they arccoining.

~ treplv 3 mrs 3go

Maren.sra.1.u,tv"

.,. Eddie Holmes 00:45

,-. I don't think Oare is here. There are other f\ature people and tlley think she may "lave c.anccllcd due to the a:iandonic.

11!111 OUM

Krlsllan Anclerstn

1:.1:1 Fuuuk

Robert Gairry 05..20

■ i'd send Clare the revised paper/response ~ ffe:the,-know we submitted to Nat Med.

• Andrew Rambavt OSti

•• Ye-ah. Maybe witfl a cheeky 'you c.an srilt ha,•e it if Yo\•want it' at the end.

tlM.II Kristian Anderst:n 1s-to

ti! Joao trom Nature: Me<! wat¥s u:sto cut to -Z200words and up to 30re:terences. we currenttvhave -JOOOwordsalld 60 references. Y;Jr/0< nay?

• Andr'1W Jt:.mb3ut 1S,29

M~rt.h 3rd, 2020 .,

•• 800words?

I~ that an acceptance?

~ Kristian Andersen 15:31

!'9 Not ;in ;ic:ctp~n(II> • b1.1t eel~ An.d yc~h. wt'd nood to Ct.it 800 WOf'dS-which prol>;\bly wouldrl't bo too turd

RE: Interest in "Proximal Oria:ins of hCoV• 19"? Mar 3rd. 2020

Ftom.Joao Moottiro (Nocontt'!nt)

Robert G.lrrv t6S1

■ Yes th.,t's fine. Should NOT be too hard to cut.(Nit«!)

0&

F"I Eddie Holmes 11:38

~ I say yay. VVeneed it out. I can easi1y hke a look bter today.

• Andrew Rambaut lNO

• ■ I will go oVf;r it now with suggestions on • see wh.lt I can find to trim.

e Andrew Rambaiut 19':10

•• OK. Got 2/3s of the way through. Not c;ure how much it s..1-...es nnvthing\_ too f,,r.

but feel free to re~t voofeel~

I

REV0002982

Oh. And someone else is going to have to prune references.

r"I Eddif:! Holmes 20;10

,-..; l'Usecwhat I can do shortly.

F'II Eddie Holmes 21:12

,-.\_ l'Vcgivcn it a good hack following Andrew's edits -now down to 2304 WOfds. Pretty close. I'll leave someone clS<:! to deal with the references -I've cut a few,

~ Kristian Andersen 2u1

eiC!Thanks guys. I'll get on 1t first thing tomo<row morning and shave off the last amount off-at and cut down the references.

li!liiilKristian Andersen 22"2"4

~ I do f,nd these bits peculiar ...

For the, first pan, SARS•likc virus('$ rcptic:atc ilt very low lc,vels in tissue culture. but rc,quirc trypsin for efficient replication. Prolonged culturing would therefore, c:l'C'atc an enormous selc,ction

pressure for the acquisition of a furin site. This papc< shows that me furin silc is fulty functional.

Forth(! S(!c;:ondpart, it's kinda unusual that the virus doesn't pick up any mutarlol\$ after culturing (Dave O'Connor told me the same) • typically viruses pick up mutations pretty quic::kly in tissue

culture.{cd tcd)

Sc,een Shot 2020-03·00 .at 7.18.~ PM png •

W.--.!!',.....\_ • ......\_.\_..\_......,,.,,..,\_....\_,....,..

.....,...,,,~c:--~~--.si..,~ .............. .,.

tillalll~lt,l,I)~\_.,...,...\_ \_\_ .....,\_.,...,. .... ..

-....,..\_KM.ffA!-r... ... porw1--.,j.\_-,

-«'6oot"""11lJ rl,rll.\&-•lAIISC.VI--•\_...

... \_\_\_\_,, \_\_\_ ...... \_\_\_ ~c.-.•i-, ..... -

\_...,. \_ \_.,\_,, \_\_ , \_\_ bA-~..V:i \_\_\_ \_

\_\_\_\_\_\_\_\_\_\_ .,...,...\_.......,.... .... ""Jiiiiliil

.. ~-~---~1,. ... s..,,as.c.v-,wns.c.vw

This is from the rcce?nt btOR.xivpaper on the? first US patient: htips://www.biootiv.org/contcnt/10.1101/2020.03.02.97293Sv1Ju1t.pdf

M.)rch 4th. 2020 .,

• Andrew R.ambaut 03.5.8

•• There are some parallel changes going on in OR Flab:

https://ne?xtstrain.org/ncov?c-gt•ORF1a\_3606&m•div

REV0002983

o rt Garry 16..56

REV0002984

It lool<s good.

One reference to update.

Krlstfan Andersen 16:58

need to c~!m down first r:.: . Will sen(! it backwithin me h«1r.

ll,al Kristi11n Andersen HI,.$<,

r.13Any COis to declare? @Robert Garry?(can't have the full VHFC one· nowanon,prof1tJ

:. fj 6 ~ies La~trtl)ly3ye,ars...go

• Andrtw Rambaut t8:S6

41111

■ .,:,ge.-o,ng •

~~-f!O-d~(}«:,Nt9'

·---~

Those dirty C;:mJdiJnS

...

Robert Garry 19 11

■ Ii UliS itl'M)Uier fe)SOfl \0 pusll hatCI to iet lt.>se l1afli.lfl samples?

a.1111Kristian Andersen 19'.18

~ Oneshouklwonder why this is rhe top trending atic;leon N,.ture Medicine ... I think our P3Pef might be timely.

SCtetonShot 1020·03•04 at 4.1 s 28 P¼ png "'

-

ti,.J Kristun Andersen 21.21

~ 800 • C<1n't c.-11 it MCoV,j9,. Pr-edic;t.,.bly vnf<>rt\1n;i.tely ..\_.. Also pinaed Cl.'lre with <1C:oY8ffl~il • just in (..Se,.

Robert Garry 21'-'IS

■ No problem• I guess they b.1Ikedon Wuh;mTurtle Flu Virus~ well?

..,. Eddie Holmes 2b'6

~ Sony. I w,uout .1II d~. Now io UX wait to esc.ape the war !One. Th:iinl:s for pusting :iii this stuff through. Tocl.arify. Nature say it has to be SARS-CoV-2? The Quote .about the 8.a\':iiri.anch.ap... what

was from the Technology Rtview? I can·tat(CSS that II so, that isjust appalling.

r-1 EddieHolmes 21:S2

~ U>n't 'Hf; v,e 'the virv, formi;rly known ;:1::;'SAAS<:ov-i·?

(;;]) €i

REV0002985

~ Kristian Andersen 22i}l

~ Y~ah, MIT Technology Rcv;cw. Less than optimal.

Fddie. I'm sure you 5-ilW the email to Clare· once you havt! rca<I between the lines. let's wait until the mornin.g to push the Nature tvlediciO(!button s,o she has a ch.:,nce to mspQnd

M.irch 5th. 2020 ...

wlJiilKristian Andersen 11.29

f:a Manuscript has been transferred over to Nature Medicine.

\I' I @J

Robert Garry 141'I

■ https://www.nature.co,n/artk1es/s41S64-020-0695·z

I

Nature Microbiology

The species Seve<e acute respiratory syndrome·relatcd coronavirus cl

The present ootbr~ak of a coronavirus•as.sociated acute respiratory disease called

coronavirtJ!i. disease 19 (COVtD-19) is the third documented s.pillovcr of an animal

corol"i3virus to ™,1mansin only two decades that has rC$ulted in a major epidemic.

The C0tonavhidae Study Gr'oup (CSG) of the lnternati()n.)I Committee 0n Taxonomy

of Viruses. w·hich is responsible for developing the classification of viruses and taxon

nomencbture of the fnmily C0<onaviridae. has assessed the placement of the human

pathogen, tcntativcty r\amed 2019-rt;oV, within th¢ Coronaviridae. Based on

phylogeny, ta)(OOomy and established ptactice. the-CSG recognizes this virus as

fom,in,g ;:i s.ister clade to the prototype human and b..ll ... Show more

I

It's officially a bad name now.

• Andrew Rambaut t4·23

411■ At least they have ct\anged their naming suggc-srion to put the da(e at the end.

~ Kristian Andersen 14:26

fa We can all blame Andrew ~

REV0002986

e Andrew Rambaut 14 2a

•• I plan to refer to it as COVID-19-CoV from this point onwards..

WWKrl~nAndersen 15:41

rl!I Again-shoukt have stuck with snake flu virus ... (or Cotona flu virus as Trump calls it -not a b.:1d name).

• And..-ew Rambaut t6c07

•• Ac.cepte<l!

llf'-MIKristian Andersen 16,06

f:a Yup. That was fast...

Andrew. by popul3r dem;md. we need a ·how not to read a phylogenetic tree· ·:.:. (I'm only half joking· having .some ex:amples of -b~ phyloger,etics" woukl actually be super helpful.

Unfortunately. would r'C(luirc some actu<d !'Cal work ... )

Robert Garry 17JJ9

■ Kristian • there's a press release correct.

I

Should send to Jeremy • maybe the entire email group.

Are there other CoV papers in the April issue?

··~·~........-.......ti!IJ KristbnAndersen 1n1

Pl! Yes. theres a P"eSS release • should get that bn.lshed up. Let me know 1fvou ~ve any suggested changes or some Quotes to OOd!

https://andersenlab.slack.com/fl~/UOHFUE9E3/FU20M7A2W/ande<Sen\_c.oronc1virus.nature\_2020\_press\_re1ease~draft\_3.docx

Word Documcn1 •

Andersen Coronavirus Nature 2020 Press Release ...

• Word[)o(wnoot

..,...\_n COt9,,,,..,\_,,Nfll,lf'I ~-..\_. • ..\_.,. Ortlt 2-H-?O

n.. COVIO•lt <OIOl'IWl.-vs •ll'ld,tll\lC h.a, a ,..-tun,I Mglfl,

,<leftt\luuy· 1

""'"-SN'l$.(..,...z~\_......,..,.1JM1~1nt1,•0tr""'WUtlon.(11,,.

lh!,.\_-• ..,,...WoC"•<........,.•W-0-~COt,11D-lt~-"''....

.. ~.,....\_n,cll(,,<...-«~.,,uw..-....t\_,n ..... 1,..oouGn.

¥<~ .. -....~ .......,..,t\_,.,1P\_...,\_1u

TM•\_,.~,sot....-~e~t;oata,,..,,-5AAS<~ar,\_

.......... ~..., .......... ~"" ......... .,.-0. .... -.. 0<)''I'

.ct't-1'1<!:~

I

• Andrew Rambaut 17:16

•• Can you te•on:ler the .iuthor list to put the one who dfd nothing .atthe~.

(in the press release I mean. obvioo:sly)

W!rilKristian Andersen 17,19

la It's currentiy alphabetical. but 1·m happy to toss Ian at the end '...!'

Letme edit this some. clet1n it up and post ;i new version

e Andrew Rambaut 11-20

•• Holmes comes before Lipkin in the alphabet.

Btlt yc-:s, In these li:sts. Ian comes last

~ Kristian Andersen 11-22

~ Gee man. it's necessary to tcacil me the alphabet now?! It's all downhill from here. IIguess I can't blame this on the fact that I'm Danish?]

~ Kristian Andersen 17:56

!i£I @Andrew Rambaut -do you have a ttcc/alignment with only local cases? I'm 1rying to get a sense of# clusters in different countric-s and it's really hard because alt the sequences arc mixed

between kx:al and travcl. E.g.., does South Korea have-a bunch of diffe-~nt chains? Or are many of those-travel•related?

.£ l!i 2 rc~itt l.'.lst rcpfy 3 y,tars :igo

~ Kristian Andc"en 18-07

f!.ii1!IAlrighty, here·s a clean version. Please let me know if you have c1ny edits • quotes woo1d be great too (I attributed one in the end to Andrew).

I

Word0<)(.u~t .

M.ir<:h Sth. 2020 .,

Andersefl Coronavirus Nature 2020 Press Release ...

• Word Document

-1'ofnC-Hr.<1.-l,lt'l~-~~---$f>ril!Ol'lJ

n.. COYIO•l'J coron,wlnn a11>1dvr.lc Ms a 11.-blnl or1glrl,

scie,.tt.tsuy

::==::eC::::•~=~:;":::::'-.W.::,!!:::•

----MIOll-~Ktl'lf;~Ol---l,,l,on,KCIOfl:ll,,4

--~wt>hlne!l-,.lollll4Jlul'l•1N«vr~

n.e.~ ..of~~Mql,lt.fffoatahffiS-lAS<f/""2w,4NolKK

vlr\_...,.,...\_o .. nc.1!>,.tt,oi~•.,-""•--o<J°"

toltle,.,,Me,o:,,

r,i Eddie Holmes lj:33

,.....\_ I have 124 new scciuence-s from Wuhan (I need to get the sampling date info) and Mang sent me the attached tree. I don't koow which a,ethe new sequence-.; and it only contains the GenB.ank

sequences (none from GISAIO). 8UT is says th.:,t they are not allowed to publish the p;iper d~ie to govt. restrictions.

REV0002987

'Wuhan.of ... March 51h. 2020 ..

·°'"~

-~,,.....-·

•Ow.--~

~ KrfstianAndcrsen tH•

mi'!IIAll the 'c.hina' ones are new in this tree?

I

F,11 Eddie Holmes 20:04

~ Not St.Ire. China will be r'W!Wones+ those on CJcnBank (not .sure how many a,c on Gc-oBank). I'll try to get more details. This is being repressed. Fuck knows why.

~ Kristian Andersen 2005

~ W~11.I have noticed that the US (CDC) also doesn't appear to be pushing out sequence data anymore ...

Something vtrvwron,g is going on in the US {and Chin.1?) at the moment -suppression of information

... Eddie Holme.s 20:08

,......\_ What is going on. t will pass on the dit.a wh~n l get it

W'.liil Kristian Anderstm 20:10

Ii'! Sounds good.

It's so weird man· I cJn't even get numbers of infections in this country from the US CDC ... I hJd some side-convers.otions with 3 few people there· something is definitely going on.

F'lli Eddie Holmes 20:22

,...... Looking at the d.Jt..1 new. H01,-.,ever.

M.Jngsent I think that 95% of the Chinese sequences Jfe there are no associated SJmpling dates. Let me get those and I'll pass it oo.

Gc.t

....aKristian Andersen 21 SS

ri19 Would be great to get some date information • 1 wonder if they have some of the earlier oises which would defmite,ly be helpful

... Eddie Holmes 22:10

I

..-; rnget that as soon as I can.

March 6th. 2020 "'

r"lli Eddie Holmes 00.36

,...... Got this f mm Ming (in Guangzhou) about whal they can write about ""We can say the evolutionaty stories or m~ic-al s:tOo~. but not epi stories (espe<:ialty 1)0t the origin r,om WuhM): be Her us

and Wuhan". Good job Trevor doc-sn't work there.

i,y Krinian Andersen oc►..ci'

&Cl Damn. That's weird -I wonder why? The rooting of the-tree has been iffy. so I wonder if it could be related to that (e.g., root not actually in Wuhan).

•-·-better US and Wuhan•~ huh?

r"I Eddie Holmes 00:56

,....\_ There was paper'• on ChiiuR.xiv? -suggesting a US orig.in. That was very PoPulcirin Bcijing.. t think we dis.cussed it eirtier.

• Andrew Rambaut 02 18

•• The root is almost certainty on the branch between the two dadcs. It is ac-tvillvthc thing the S/llinccigc paper got right.

Their are two sites that are the same as the R.lTG13genome in the top clade but mutate in the bottom (one is non-synonymous SIU. So more parsimonious if the top clclde is basal and the bigger

bottom clade (which conuiins most of the initial Wuhan genomes) acquired the two mutations.

We have 42 ge<iomes from Guangdong going up on GISAID soon {a c.oll.aborator of Oli). Charles Chiu ha-sjust sent a bunch from California and is planning to not preprint and send to NEJM so he

can h.Jck off.

r-111 Eddie Holmes 0-1;,01

,...... Thanks for darifyin.g rooting {I'll vse that line in an Australian sefnil'\ar). Perhaps Trevor will 00 soml? inappropriate anal vsis on the Californian s~m::es to piss off Charles.

e Andrew Rambaut 04:06

•• That is probably why he won't pre-print it (cl.aims it is bEcause NEJ M told him not to).

REV0002988

Robert Garry 10:17

■ www.rorelgnaffairs.com/artlcles/unlted·:tla~es/2020--03·05/us•chlocse•dlstrust•lnvltlng•dangerous•caona,>Arus•coosplracy

Our N.,tMed pie-co stil r('lev~ntt

bttps:Vwww.vox.com/2020/3/4/21156607/how•djd1:hc·coronavirus·P,Ct·started·china·wl!hat1·lab

Vox

The conspiracy theories about the origins of the corona'!Arus, debunked

There's a ,umcir thec()(Oflavirus started in a CtlilleS-e bb. And a sde11tiflc <OMen:susl

didn't.

MM 4th, 2Cl0 (1)7 k0) •

MentiOfls Vince ..

Robert Garry 1036

I

M.lrch 6th, 2020 v

Constdet the oossibility of wriri.n1: a letter to NYTimcs e>r W8'Post reOritiM • could even mention rcsoons.lblc c:>i

REV0002989

• Andrew Ramb.aut 12,30

•• Jian Lu from Peking University has just requested a Virological account so they un respond to the critique.

tiW Kri$tbn Andersen 12:40

In HJha, what's there to s.av?But sure -they should have that chance

r,i Eddie Holm~ 14:S8

,-..; Ye-s. I'd be interested to see that rc-sponsc on Virological. When we were releasing the first genome I remember th.at Andrew & I had a dis.cussion about what date info to give. We decided to only

use the month {12/2019) rather than the ex3a: day because of potential ident:ifaability issues. I got a number of emails moaning that it didn't h."lve the exact day. The date wns later provided in the

paper. I think Oli has. argued for mor~th ooly.

REV0002990

~ Krirtlan Andersen 11-21

March 6th. 2020

v

mt! Fucklng Snow Mexicans -I knew it!

This is gre,1t -thanks Andrew. I'm meeting with our OOH on Monday and we'll t.alk a lot about scqucncfng and prcpc1rcdncss. so it's important to Mve a sense of wh.-.rs going on. I'm glad to sec

that some of these things arc connected • don't want to sec an Italy sccoarlo with a bunch of different chains going on.

• Andrew Rambaut l7-25

•• Oli and I told Charles th.it we we,eo't goiog to wo,k with him unless he (eleased all his data immediat~ty and prepdnted his pape<. He agte-ed.

~ KristianAndersen 1n.6

March 7th.. 2020 "

F,I Eddie Holmes 00:33

...... I.ansent me-this. 1an. https://protttt-au.mimecast.com/s/X81iCSQZ29FZORVANfzl2GG?dOf'l"lain•lr'adiatfme-s.com

;t lndlatimes.com

World's Best Vitologist Blames Coronavirus On Cfimate Change, Wants Ban On Wild

Animal Markets

P-rofes.sorW. l;;m Lipkin, direttor of the Center for tnfec:tion and Immunity at

Columbicl University's Mailman School of Public Health was in China, studying the

effects of the novel coronavirus. He was in Chin.a also dudng the SARS epidemic in

2002. In a receflt interview, he spoke about COVID· 19 and how its human's who

I

aren't property differentiating between wild and domestie,ated animals.

Mar6th,2(120

@ii.\MJl::141=@

REV0002991

REV0002992

REV0002993

REV0002994

Robert Garry 12-<>'1

■ The low substitutior\ rate is the obvious challenge• is there any w:iy to compare-this to vi,uses like OC43 o, HKUt tl\at have been in human:s for a long time?

I

• And ...ew Ramb.aut 1s,oe

•• https:l/wv1W.sc-iencedirect.com/scienc:e/art1c-le/pii/S0166354220300528?vla%3Dihub

[ sdencedlrect.com

The 1pike glycoprotein of the new coronavirus 2019-nCoV contains a furin-like

de..wa.ge 5ite oilb5ent in CoV of the 5,ame clade

In 2019. a new c:orol\avirus (2019•nCoV) infecting HumaM has eme-rged in Wuhan.

China. Its genome has been sequenced and the genomic: informatioo promptL.

• Andl"eW Rambaut 1SA2

• ■ Fiona Leth bridge (a formC< Edinburgh PhD who now wotks for lhc Sc~ncc Media Centre in London) sent me this:

March 10th. 2020 "

-A. p.,p+r into 01• &•noaiC .a.kit up of th• CONH'lilvirus hH btit.n pUblhtuld in th;i journ.-~ ••m~vu·u "~••l'Ch:httpi://-.1ci..ncltdir-KLCOII/ICitnU/i1rtlcl•/pi1/S0Ui63S42:28).e'52i~viil%Y>ih.ib,tl

In one j)HUI♦, th• ~Pf'!" U)'S:

5trU::l1'1Jly, tt\t 2'tl9-nCoV S-protein Stq\lt"1(t <onuin, 11 ldditi.ONl nu<lt-0ticlu 1,1p1tl't!• of tht-sln1l• ~,.,, de~•,· sit, 1 {fig. 1, Fi,. 2) lHdin1 to I pr-edictiv,ly JOlV"1t·tXPOHd PRAAlUW

HQIJl!n<,it, '-'ilc:h c:orritSponds to• unQniuJ f\lrin-Uh c:lHv♦gt sit• (e,.11.1n♦nd S,r,IIT;•r-, 2el9; lug1,1irr•, 201,; ~td♦h ~ Pr♦t, ~11). T11h furin-lil(it c:lo"•C• ,it,, h $Up.po$~ to bit cluvtd

-chldna vir1a "i"•H (~11• ;a,nd 1-.ti!tt;iik•r-., 2814) for $•p,rott1n •pri■in1• ,11,-.d11,1y pl'(IYidt ;a 111in•of•func:ti0fl to tht 2iru,.ricov for effidtr1t 5prt11din1 in tht hun;an popuhtion c:oap;a~ to other

line-age b Ntacoronaviruses. This pauibly illustrates a convergent evolution p.athw-ey between Uflr'e\,1ted (O\'s.

~ Daily f)lpN!n ntwsp,1per-ri.n -writtffl up• s-.ry of tlw N!U-&rc~, rtpoM:l"'I u,n 1t clilii:.s: ifirtH ·cene-t1c.11lly enc1i--r+c1 f<x" ef+'1dent spre.adin& 1n ~n.s·

11-ttpt://-.tl(pt"♦U.(0.1111:/nwt/w.ir-cl/l2>lU5/(0r"Ofl.llVirvs-,en•tic•lly-•r,ginHr-tcl-biOIMIPOfl•'lilUtl-t11-hb•lHlc-<ovidl')-$Pt

ffl• ,1rtlcl, says:

~urilt is • •Matily Hf>rUH'(r protein foood in the lUfl&S of hun,.ns th.at could hv• bffn us..d 'tO .tctivat• • virus tl'Mlt JN'•vlously could h.ave only be•n pa.u...t bfhffl"t ,..,111.is.

Th<i!!4!Jlp@l'tsbel!.♦vll! thh ·pH"ul1.111' furil'I" h •n •no.,a,ly a1'd tould be used to ·suausfully 4!.Kplait"' en?yatl th.Ill l:N'!.llte lniu1'1ty in hYNnl.

Tl\t paper sees en to expb1" !'low sciel\tisu h,.ie not uen •nytMnc 1th this 111 pr,v1ous strdAS.

lk.lt, it 111u not ju•t • dl'lgl• ~ly.

It ~ds.: ·a.fof"11 tti, -r-el'n-tl' of th• 2e1<1°nCoY, thh iirport..nt ft11<JturirWH not obnrvird in oth-lr <oroei.11vill"USH,

·strikingly, th• 2e1'l 0 ntov sc:ql.l(lnCt" corihins 12 .:idditi,on,al n1.K)t<0ti..:lu upuuaa of the single <luv.aa:e sit•.

N

cor-ot1.11Yirusu.·

It adds: ·rh11 possibl)' 1llustr•tes I conver1ent •volutiol\ p.atnway Htwe•~ unrdattd cov,.·

I

00 you hh·· •ny (otlUt'nl •~t th• Idly thh h.U be~ Np(ll"'td? Parti(Uhf'ly tM hprwss" UHrtion tint th• rHHrch pjptl" suuesu thit ONA hu been ·ta11p,recl ldth· to sprHd to oth•I"

lu1nnsr

REV0002995

Daitv Exp,ess is one of our worst tabloids. 8ut the Science Media Ce-ntre is agood institution• they try to get apixopriate scientists in 1ovchwith iouma.lists for s11eciflc queries. Probably worth

ttc;lpin.; thc;m f.:,Q:·<::h~k thi5. I forwMdcd our preprint but pcrh:ip::; ~ion.a cQUld g:d in touc;:h with )-01.f @Kri~t..:,n ?

Also it would bea:oodtoseewe.re Nat Med are at if ttvs is in a P<l()ularUK tabloid based onan actual paper.

Ican't sec.:tiythi'lg in the paper that suggests engineering • even the •gain·of •function comment seems to meanit litctally • i.e .• it gained a function.

~ Kristfan Andersen l6◄0

!G Hey Mdrcw • happy to a.nswc, the questioo of whcth~r this is an accurate representation of th-c paper, since it's not. I'm toblty swamped at the momc,ntthough. so I wouldn't be able to provide

much more than th..at.

e Andrew Rambaut tU4

•• 0oo·t worry ifyou can't doc. No one tXJ>ects the E>cpress to be sensible. I think it was them sayiflt it w.as the asteroid. So at least You can sat they can't Ill.Ike up thcir mind.

It is good for us ifthis blows up again ;,st befor~ the paper is publiShed.

tr.!111 Andcnen 16.51

Kristian

~ Sil~rlining ..

... EddieHofmes 20:08

~ DoYoUkOOY'1w'hcnthe Nature Med papc, is coning out?

11&.1-Kristian Andersen 14.19

!l9 @,ch.inn cl • j1,1$t got die proof$, 50 if yov <:.:in plq.:it;e take;, a qvick look. @Andrew R.;amb,11,1t• ;) couple;, o! qm,:stion$ I loft open for you"' p'cM:c t:00 them di1,pl~d in red:

https:Uel)(cofing,pr;ng«.com/jouri,,1,\_v2nndcxphp?tokco•ZT3J6,TOvyPDA8"7Wvy8aV!AkXamH,S5WfpJ60cll<a4

(if you mak.t any changes. please make sure you hit 's.ave' • not 'submit;

Robert Garry 1608

■ lc>1t look~ line to me ...

I

REV0002996

Man:h 11th, 2020 ..,

r,I; Eddie Holme.$10:28

,--.; Yeh. look line tome as wen.

111!111 Ktlttl-tn AndctSM 16.Z'I

£ft Okay. great• just need @Andrev, Rarrbaut to chime in on tbe last few comments then

• Andrew Rambaut 16~1

• ■ On it. t hour Oigh1.

8~

• Andrew lbml»ut t'-·2:6

411111A.re all the remainingones for mt?

■

lltlllKristun Andersen 1634

rl!I Yup

1f!i1Kristian Andersen 11~1

r.cl ~AndrewJbmbaut •didvou get a chance to check out the questions?

W.. EddieHofme.s 23:08

,..... Iassume d·19·casc-tr.xtd·bacl<

yco saw this: https://v1WW.scmp.com/ntws/china/socicty/article/3)74991/coronalirus·chinas·first·conflrmed·cov

• South China Morning Post

Chi.11a'sfirst conftrrred Covid·19 case traced back to No,.-ember 17

GO\'emmmt records suggest fot person infected with n~ disease may have been a

Hube4 re~ldent aged 55, but 'patient zero' has yet to be cooflnried.

M.vl2th.2020(117kEQ•

6MMl111MtJ&A

I

REV0002997

ll'!iil Kristian Andersen 00.20 M¥<:h 13tl'i. 2020 "

r:£11Hadn't 'Secf'I this • that''S pretty interesting.. Still compatible with the TM RCA but it's getting a little towards the tail end .. It's interested that they couldn't confirm whether these cases were from

Robert Garry 10:33

• Kristian -arc we good on the proof? Any idea on pubUcation date • embargo?

....aKristian Andersen J0:37

~ We're good on proof. Aiming for early nex:t wccl< but we don't have a fixed date yet

March 16th. 2020 ,.,

March 17th, 2020 ,.,

~ Kristian Andersen 1s·◄◄

~ Ehm. so it's on1inc ... https:Uwww.naturc.com/articlcs/s41591-020-0820-9

Nature Medicine

The proximal origin of SARS-CoV-2

The proximal origin of SARS-CoV· 2

r,i Eddie Holmes 1?:42

,.....\_ Excellent!

• Andrew Ramb.aut 17 42

•• Aod voogot your ITI.lte Eric Topol to tweet it

tl!II Kristian Andersen 17'43

rD I can see my Twitter has exploded. but I haven't had a moment to take a look why ...

I can s~ the Altme-tric sc0re-is vety high tho~h. so I hope that's a good sign ..\_

Does .1nybody h;:ive time to talk to reporters ;:ibout this stuclv?Bec.1useI unfortunatelv clo not. ..

• Andrew Ramb.aut 17,44

•• We did miss an origin hypothesisthough, Ian Goodfellow got this mess.Jge:

~<Qr'IB.,

REV0002998

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""°"·

----=~...,\_ .........-

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~~-==

-·---•-...-·

~~=:!...~

.......... ,\_\_\_ .,.\_

·----------~

Here is theevideoce ...

The before picture ...

And the defmitivc an~vsis.~

I

M.wd,17th,2020 •

11!!1!: An lN8

Gif Keyboard

~

@Krir.ti~n: /aifs, l:iuahina (86 k8) •

4114il::i42

iii♦ I

.. KrfsttanAndersen 17'48

ra Sefiously?

r'9 EddieHolmes t7:S2

~ Amazing. I've got model fa~ue. My son has ~tatted trial remote ~arning today so thats my day gone.

11!1111 11,J

Krlsttan Andersen

~ I somttime wish I had the kind of imag;nation th~ led to this 'identi6cation· • or tMt I had a conspiratorial mind. Would makt life SO much more exciting!

I

... Eddie Holmes 11:57

~ I had an irna,ge: 01 Roy Anderson $ltbng in his gard'en at homt waiting tor the phone call to come and save us. a bit like Sarne1 Wallis in lhe Oamb1.,sters

March 18th, 2020 ,.,

~ Krlstun Andersen 02·-42

m9okay,

Scree-nShot2020·03-t? .1111 "1.44 PM.org •

eweoo\_. z....,

··-

1"-#ttlflfW,lte ... ~~"""'°' ... W6.\*.,.., ... ol&

..,\_&fflfllll~"'.,\_\_,.~IIWIIMl'l"l.,N13~

....----...~-

e Andrew Rambaut 03.'(13

•• See thJt N.ture!

e Andrew Rambaut 03:09

•• Mainly the SpJnish(boredand on lock·dow11):

I

REV0002999

Geographical breakdown

Country Count ....

Spa:in 1784 12'

United States 1062

,..

8razil S59 ...

M,e)U(O 42S

united Kingdom 306 "' 2'

Chit• 283 2'

V4'ntt'Utlj, SOIIYI~ RtpubliC 202

of

"'

Et<YP' 197 "'

Turkey 195 1 ..

F"I Eddie Holmes 05:46

I

~ Is it banned in China? Glacl to see Venezueb, Solivarian Rept1blic of in the mix.

P"I Eddie Holmes 06:05

,...... https://www.leonarddobsonart.e:o.uk/

leonarddobso~rt

Commlssk>ncdArtwork ILeonard Dobson Art I Fleet

Leonarddobsonart.co.uk offers Art and commis.ioned art. Covering Northern .-rt. be3Ch

scences.local scence-s, retroromantic.ism.absttac"t,landscapes, portrait. citv skyiines

and illustrations.

e Andrew R.ambaut 06:36

•• I can see aliens in that picture.

P'I Eddie Holmes 16:19

,-...; Priceless: https:Htwittcr.com/CARRENEAN

.., twitter.com

LEONARD DOBSON (@CARRENEAN) ITw;tte,

The lal~l Tweets from LEONARD DOBSON (@CARRENEAN): ~There's m0<~ to a1r

crash investig,nion than concluding 'Pilot Error' or 'Mechantcal Failure~ .........

I

https,//t.co/lwHj;lSpZU"

.,.J Krisrbn Andersen 16'41

~ I don't know man -he might be on to something,https:l/twitter.com/CARRENEAN/status/1078041436975755264?s•20

~rch 19th, 2020 "

if'MIKristian Andersen oo-os

~ This is nuts • we officially past the highest sco,ing paper of last year ... Given tt,e number of completely ootso emails I have received today, I'm not quite surewe managed to convince nit the

conspiracy theorists oul there ...

So~ Shot 2020 00· 18 at 9.M 11 PM Pf'I& •

o~•~~~nni,Snlr"

I·"·~---·

----~

......... .,

ir

r-111£ddie Holmes 01:2.:

,.....Wow!

Tod,v. I ,.,, • middle-aged woman arrested at woomes I• supem,a,keU ,,ner, I 1;,.. -and taken away ;n handcuff> -fo, ,,,,;ng to hoaro food. I qu;ckly P<'t back the 2nd pack of hol ''°'' buns I h.>d.1

~ &r

6 1,J&H::liki-G

REV0003000

... Eddie Holme5 01:34

,-..; Nature Nature missed a trick with that paper .. .l hope they arewatching this ...

.....m Kristian Andersen 02 33

f!a No kidding.. This is by far the highest scori"S Nature Medicine paper ever -I sospcd hig~r than any olher Nature paper aswell. I hope that one re,,,oieweris proud of his hard work..

• Andrew Rambaut 03: 13

•• ifflalepn1 ...

11WKristbn Andersen 031t

~ Wait. it's the highest?

• Andrew R.ambaut 03 24

•• That is what thrs is s.wing no?

Ill.MlKtistian Andersen, 00.24

1£1 I believe so, yes.

I

• Andrew Rambaut 0326

•• Perhapsthis month or this year so far.

lll!lill Krlstbn Andersen, 00.26

It! The highest Altmctric score ever. Fuck me. surely that's gotta be some sort of academic achievement. It's like winning a prize for having the biggest pumpkin at the county fare.

• Andrew R.ambaut03:26

•• What was the snake Ou paper?

.W Kristian Andersen 03:28

f!l! I thought that was higher ... But maybe they refuse to track it \:

Hmmm, much lo-M?r: https://w1fey.altmetric.com/dct.aiils/743S4946

LIiwiley.altmetrlc.com

Report for: Cross-species tr.ainsmission of the newly identified coronavirus 2019·

r.eov

lo the top 5% of .ill research ovtpt.1ts.scored by Altmetric

• Andrew Rambaut 03·29

•• https://www..attmetric.com/top100/2019/

I

0 Altmclric

ThcAltmetrlCTop 100-2019

What research CJught the pu-bUcimagination in 2019? Checkout our aoflUJI list of

~per$ with the most attention. (33 kB)... &£SJ..f..Q££L

TOI) l<11st year w<'IS 13557

ilflllil Kristian Andersen 03:30

f!n Ye.aih,we're wcll .lbove that

I

e Andrew fQmb.Jut 03 30

•• lnafcwdays.

a..J Kristian Andersen 03:31

!n Ehm, well above already .. http:;://~w.altmetric.com/details/77676422#~re

~ altmetric.com

Report for: The proximal origin of SARS•CoV-2

In the top 5% or all f~arch outputs scored by Alhnetric

• Andrew Ramb.aut OJ·32

•• Aod previous ,,.cars arc all much lowe:r. So yes! Top! Fuck me.

w.!lil Kristian Andersen 03·32

Ea WE RUUUUUUULE. Thal's tenure secured, right lhere.

~ Kristian Andersen oo,38

~ Importantly. https://bloo:iv.altmctric:.com/dctalts/74957328

8 biorxiv.altmetric.com

Report for: Uncanny $imilarity of unique inserts in the 2019•nCoV spike protein to

HIV•1 gp120and Gag

In the top 5% of all research outputs scored by Altmetric

REV0003001

e Andrew Rambaut 03,<0

M.1teh19th,2020,.,

• ■ Ar\d th:it It r<itr:.cted!

llflilKrlstianAndersen 0341

~ Yay! We beat a papc, that was ,cm>cted!!! look at us. Wow,

r'WEddieHolmes 04:40

~ .JMu~. tl\:u•~ ::im:i.dng!

Ask fcr a pay rise.

... EddleHolmH 0S:31

,....\_ .h.lst got this from Ek1tt Lesion:

J, conta&iOll cast aoefcrew a,e dOif.g public serviee vigoettcs based on tl)Ci1 chcu.Ktc,s.

2.Bulletin of Atomic Scieotiits and Ebright are goingafter the paper for the part that cfscounts the Jl0$$ibility of l.1b release.

1111111111

KrlSNn Andersen 1CM1

fta Of course.

• Andrew Rambavt ut,a

•• I had to block Ebright on T111it:ter. What an eejit.

Robert Garry 121,

■ 1..vrote a review of Cont;:igion • f might h;:ive had a littte to drink thJt nice

I

htp.//www.sc:icnceandfilm.org/artidcs/3294/cont.lgion th~ movk! ,ec:onsidcred in·thc·timc·of covid·19

"' sci11nceanclfilm.org

Sl~n Science & Film

Sloan Science and Film is a website devoted to cxploril'\6 the intcr$Ccrion of science

and film.and cnh,mcing the pt,.blic \l"lden.tand·ng of sCie('(;e a~ technology.

~0

... EddieHolmes U:09

~ Good !Ob Bob! I blOCktd Ebright as well.

• Andrew RAmb.avt 11.se

•• a'\itgt",Plllit •

Not th::.t I :,m following it or ::.nythll\g .

..,. Krbti•n Andcrnn 16

◄

t

ra Men8ther

Scteef'IShot2020-03-19Jt 3.48.S2 PM.png "'

e Andrew Rambaut 19·20

•• I thi(1k you ,nade th<: HIV One go up:

I

e11m1,,;;,111a

REV0003002

Uncanny similarit

Gag

{M>tv,twd ~ffllOn f« at'tidt~

....aKristbn Andersen 1925

~ Fuck! Let me delete tNt tweet.

... Eddie Holmes 20:27

~ I.Ot's J:l'•Sh for 20K. ~n y<>1.1Tho Oo~ld to h.ivo:; T~t?

.... Kristian Andenen 20.29

r.1:1"Hcy@rcaldonaltftrurnp, here's the <!videnct you have been lookhg for• it's totally the Chinese Virus! IIMACA". Yeah?

M:itch20th, 2020 "'

... Eddie Holmes Oo:43

,-.... • 92.2k Accesses

• 16822 Altmetric

Matt-h2Ut.2020 ...

W-. Eddie Holmes 03:24

~ 1.32m At;ec:,~,,; 17904 Altmc;-tric

... £ddieHolmes 0~'1)4

,--; .h.1stri;vieweda ':>aper' suggestif'Yi tha1 squirret~ ;re the source of SARS•CoV• 19 Qn the b;isi~ that "'We have noticed that a 1-:rge number ot squirrelshave been released in Wuhan since 2013. and a

park of wild squirrels lta~ b~n built In WuhanM. Thar~ It.

• Andrew Rambaut OS 13

411111

■ Why 2013? Justhappe-M to be the date that RaTG13 was collecte-d?

... Eddie Holmes OS:S4

~ Yes. perhaps, they relc~ed I.he ~trrcls as a:decoy for the ON passaging cxpcrlmcnts they were ).tst siarting at the WIV?

Rob@rt C.arry 01.112

I

■ They might be on to something.

J!ttps:YwwwspJiCe.wRl/33623·chetv.l>insk·meteor-w3ke·w·call·for-t.arthJ'ltml

~ space.com

Chelyabinsk Meteor: A V/akc-Up Call for Earth

The smaU asteroid that broke 1,1poverthe city of Chelyabilsk. Russia,on Feb. 15. 2013.

wa, .aremindo-about the importance of motiltoril'lg sm~II bod,C1 in )1)6CC th,it could

pose a threat to Earth.

Squirrels are released, RaTG13 found, ANO the 20mast·eroidhits Earth• all in 2013? (edited)

~ Kristian Andersen 14:48

P.ellma11 1-om )l.ltlt fot <,mai ..

Are you aware you're ~rtkipatfng in a wartrime? Mar 21st. 2020

From H,'r.,ntd?Th(> 8igH()IKC (No contcrd

Ithought thiswasooeof the more amusingemt1ils I have received •ard there are many to choosefrorT' ... (rdittd)

• Andrew Rambavt 111,)'I

.a

■ I bet Dan is a nice guy to hang out and have a beer with.

I

In the basement of his mum's house.

REV0003003

~ Kristian Andersen 14:59

~ Yeah,I thought about inviting him over. As tong as he keeps a distance of 6ft.

• Andrew Rambaut 19~1

•• https:llwww.altme-trk.com/detaits.php?domaln .. aUmetric.com&dtation\_id•77676422

~-Pfli

T

lifl'lilKristianAndersen 1~·20

ri! More th;:in J million vte\'IS on the art'Kle itself too. It's pretty fucking crazy.

I have also gotten about a million emails from total nutjobs..so I think we need to include that in the metrics too.

• Andrew Rambaut 19:34

•• That is because you put your emafl address on iL

~es;

r,i E"ddie Holmes 21:11

......-; Nutmctric;. Add it up.

~ Kristian Andersen 19:44

~ Come.on lads -just a few more tw"ec-ts needed.

Screen Shot 2020·03·23 at

◄

.44.16 PM png ...

I

REV0003004

I

• Ano..-ew Rambaut. zo-<Mt

•• re.lax.will gd there soon. 2SOOO is a nker number though. I think

Still weird tnat it is ~in (and some Spanish spea<ing countries) that is doing most of tile tweeting about lhis.

ffl.13('{11'1,t ..

C..,,t,y Count ....

......

.... -

tkli.1tdSWi~s

-...

...

"'""

'"'

11S9 3"

""'

V~nt1utla. BQlivarian RcpubllCol 1!5l

Mox<o 1!4S

"'

"'

c..,,, ... 1137

"'

...... m ,..

Un~tdl(I~ 930

"'

~ KritftwnAndeJ$en 20.11

~ Let's .aim f0<50.000! And ytJh • superwcir4 it's Spain • not sure wh,;1t'$ up with that. Nothing from China, which is peculi;u • bot I guffl they don't re<1lly use Twitter (and maybe c;an't access the

I

t•Por eithef)

Screen Shot !020-03-24 at 10.31.42..png •

REV0003005

&;

March 24th, 2020 "'

P.Eddie Holmes 18:31

... 't,

r"li Eddie HolmH 2t,S9

~ W.1s that you getting the Bedfo«I Jpprov.il on Twitter Andrew? You might be honoured .

.,..a Kristian AndersM 22, 10

~ It's .actually this; https:Utwitte-r.com/nickpicldes/status./124115650230S427459 I

https:Udocs.googte.com/forrTI$/d/eJlFAlpQLScCxMT877v16ya7RnDQSLb9pdUObP8VPdWgOS\_ptlgXCwM72g/vicwform

Somebody had put me on a list too so it came through via email.

REV0003006

r,i Eddie Holmes 01:57

,,.....\_ Well, that's made my day: https:llwww.usatoday.com/story/entertalnment/movies/2020/03/24/contagion·medical·adviser·dr·i.an-lipkin-has-<.oronavirus/5076231002/

0 USA TODAY

'Contagion' medial adviser Or. Ian Lipkin has coronavirus: 'If it can hit me. it can hit

anyone·

Dr. Ian Li~in., the medical adviser oo 201 l's "'Contagion." revealed on Tuesday thJt he

has (:C)ronavirus, c~lint the diseas<! •miS(!rablc.• (627 k8) •

Mafch 29th. 2020 ,.

...... Just got this from my guy Mang:

Here is the link (although you might nee-d ttanslation. ot m.aybe google ttaoslate the title):

https:Nb.,iji;ihao.bi1idu.com/s?id:11:16624?6SS9990302127&wfr•'jpidCf'&for"'pc

Their trick is. although the paper focused on lab escape, the sneak in another layer of information saying "the paper say Wuhan is not the origin~ etc. .. Cell paper is also involved

The news is on top Len list of the most se,en news.

The translation of the tide is: "Americ-,n scientists: The soorce of the ne-,y crown virus is not Wuhan. nor is it a laboratory construction, whtch may originate from nature'"

... Eddie Holmes OS:08

,..... There is so much repression !ind deceit it i-sriditt,JIOVS.The tnie number of cases probably a log more than r~portin.g (I was constStentty hearing 596 prevalence in Wuhan). I've also heard that some

of the hOSS)itals in Wuhan afe dedining to test because they want to r'eJ'.IOl'tlow/no numbefs.

Kristian • don't be fooled by George Gao. The CDC had a genome sequence on Dec. 26th. They told peopleit would not pass betweeo hum.ins. Endless cover•ups.

1111111

r-.11Eddie Holmes os:02

Kristian Andersen 12:09

II! Ye.1h. I got a bunch of emails overnight pointing to similar sources. No Question this PJper has tic:kSed the underbelly of the inlerwebs ...

""1 G1"

REV0003007

Robert Garry 1136 M~rth29lh,2020..,

■ Oh Ye.'th irs tickled.From: Yuchen Liang

Date: Saturday, March 28. 2020 •• 11:35 PM

To: RcbC<t Garry

$ubj~t: Prc;>fc»or, yq1,1r mum: i:i, tn::ndf1g Qt\ Chine:,c: lwith:r

CxtcrAAI Santkir. & :iw:iim of lin~ 3l1~hm(!nts Md rcquf'..$t<.

0e.1r Professor G.:irry.

Please excuse me for not including my name here fot tt.cpl.ll'post of confidcntiali:y. 011c lntttvicw you gave to ABC was que-tc byChin11's state tdcvis.ion as J)(oof that Covld-19 did not stan: In

\Vuh.in o1ndit ii now tref'ldins $C<.On<fin Wcibo. Chin,.,•~vcr~on of Twitter,

I looked at the ofiginal interv;cv,, 1 bel~e you said ori&inally: "our anal•,scs ,100 others too, s,oint to an ear1ier orign tha-1 that (that the virus originated .it a 6$h market in Wl.han), there were

definitely cases there. but that wasn't the 01igin of the virus:

lhis vr.is tr,mslated .ind quoted bv the Chinese med~ JS s:1'>•ing th:.t t~e is an eartier orig.in than Wuhan. Is this what \'00 rrollv meant or did you meanthat the virus dd not originate from !he hsh

market but still has its 11kelyorigin in Wuhan? If itis the secolid case, your words !lave been m.anipubted and used by Olin.esc state media to push for the theory that the virus has anon•Ch~e.

likely AmCfbln Ol'igin. In rau. most Chinese ncn2COS. tt a.nd ornc.1a1s

l<!Mr mosc whO arc not censored, already bOujht mu theory pushed by state 1ne<1Ja such as Foreign mit)tsrry spokepc<son

Zhao lijian. who claimed th3t the virus wert brought to ChiM by American soldie-s.

I am just writing to let you know what is happening with your interview in China. I undttSland that one purposed the researchpaper ',Ou did on Covid-19 was to dt$()cl compiracy the::iries. I just

don't want yo.Jf word!>to be used aga9'lst your lntcnOOo. Have a pleasant dby.

Best wishes.

(Sony that I cannot f(l'ave ,ny na.me here. yo1.1 canjust ask anvone who knom Chinese to check Vi/eibo,they can vtrify what I saidJ

"the S.'leak il 3nother byer of information s.1ying ·the paper say Wuhan is not the origi11"'

I

He-rein lays the issue.

♦IHfil::Jfi@♦

M:lrch 29th, 2020 ,.,

• Andrew Rambaut 1, 11

•• Appa,rcf"ltlyW<; said it <ould have b<:cncircularingin humans for decades •..

trttps:/IWW1v.SOJ1).com/news/china/science/artide/3077442/coron.avirus•pat.hogen•coutd•have-been•spreading•hum•ns•d~Jdt;S

• South China M()n'ling Post

Corunaviru;) ma,y hi:rvc been >preoding in hunun> for deciKle.s, >tudy >tty>

Vi,11s may haw jumpe-d f ,om animal to humans long befo;e the firsl detection in

Wuhan. according to rC'Scarch by an international team of sci<!ntists.

M2"'10th X,,00241<9)•

....aKristian Anderstn 1•J1

fl!I Appan:nllv $0 ...

I

• Andrew Rambaut 1~ 32

•• Actuaty ~ decades bit may have beo, extrapolated from Collins

-rhen, as a re:9.Jlt of gradual e'IIOlutionarych;mge$ over years o, ped~ps decades. the virus eventu3lly gained the ability tospre¥;1 fr(m human to human (11)(1ca11seserioos. often life•threatening

disease,· he said in anarticle p.Jbllshed on the hstitute·s webstte on Thursday.

1f11i1 14:J&KrlstianAnderseo

f'.B Ahhh. inte-rtsling • a fai, number of in~cur;icies ifl Colin's de-sctiption of tht paper. Wheo the guy whow,ote it contacted me U1e-e were soman)' mishkes I told him to read the luckif'lg pap(!r

first ... luckily Bob toot care of the mon egregious mislakes • I just c.oUdn't find the tirne.

RObert Garry 14A9

■ Yeah• just tried to fix the ooe that were• well 180 deirees off.

Robtrt Garry 14:58

■ Could have been.a million yea,s. really• wt,() knows.

yeall • kinda what I said

Robert Garry t.$~?

■ doi: hltp<://doi.org/10.110!12020.03.22.002204

I

bR bioR,:iv

Characterisation of the transaiptorne and proteome of SARS-CoV•2 usingdirect

RNA sequencing and tandem ,nassspe,ctromet:rvr-tvealsevidtnce for a ceU pass~e

induced in·frarne deletion in the spJce glyeoproteinthat removes the furin·like

clc:.avagc:aitc

Dirttt RNA sequeocing using an Oxfurd Nanopore MinlCN charac-teristdtht

transcrip1omeof SAAS·CoV·2 grown in Vero E6 cells. This cell line is being wide-ly

vs8d to prop;ig:eite the novel <"oron.wirvs The vir.:11lt;an~riptonw:t w;,is ~n;ilysed l•~ing

a r«ently developed ORF-centric pipe-line. Thi~ ,~~led the l).ltternof viral

transcripts. (j.e. subgcnomic mRNAs}. generally fitted the predicted replkatfon ind

trans<;riptionmodel for coroo,"f.riruses.A 24 nt in•fr;:me deletion w,1s detected n

subgenomic mRNAs encoding the spike (S) glycoprcxein. This ftaturt wasidentified

in over h.a,lf of the mapped transcripts and was predicted to remove a proposed ftirin

cleqV,1gesite from the S &IVOOC!<0tein.

This motif d ... Show more

M.124th.:1020

I

This kind of thing much more inte<estirtg..\_

REV0003008

~ Kristbn Andersen 1:5:31

P:B Ye,~h. that's pretty cool• kinda even further rules out tissue culture pasS,,;1ge

Robert Garry l S:3S

■ Climbing toward 3M accesses and 25K 011Altmetric

iin'la!,.'(>png•

The proximal origin of SARS-CoV-2

~o,.,,\_...,.-\,,....\_~.,,....,~c .... e....,.,

-·

,..,. ..... (2020)C..1Hs.n.dl

2-1K1111.-a-1~ 244,15All-1e ~

I think Al'ld,ew should go on CNN London since-h~ is dosest geographically.

REV0003009

March 30th, 2020 v

Robert Garry t?.-11

■ CNN Interview completedHello again Robert,

Just wanted to s:ry thank you fO( speaking to us, you were g,cat.

As Nic:k ~ntioned, please do stay in touch if there is something noteworthy in the s.cientift<: ftcld about the virus that you think should d~rvc more attention.

Keith, that BROLL would be great to have for our TV piec.e. let me knowwhenvou are in a position to send it.

Thanks.

Vasco

®~

Probably be trending on Chinese twitter again.M

• Andrew Rambaut 12,48

•• Did you say that il ptobabJy started in the US?

Robert Wrry 12-53

■ I may have used the-"may have origir\ated sometime in the past" c.atchphrase. But. yes lhe probable US origin was the f,rst mes.sage· I'm really thinking a lab somewhere hidden· n,aybe near

swamps or backwaters. Tile fiend prob.lbly unleashed the virus a~in during Mardi Gras..

• Andrew Rambaut 15:50

•• https://www.thedailymash.eo.uk/ncws/arts•cntertainmcf'lt/disncy•shelvcs-hcartwarming-movic-about-sick-pangolin-being-cared-for·by-his-bat-friend-20200330195036

I

,. The Daily Ma.sh

Disney shelves heartwarming movfc about sick pangolin being cared for by hls bat

friend

DISNEY have annOllnced that they ar'C delaying a film about a loveabh~ ill pangolin who

Is saved by his trusty friend, a market-dwelling bat,

Mar 30th, 2020 (507 kB)•

..,;

I

~ Kristian Andersen 27 57

&I! @Robert Garry • have you been looking into k>nge'lity of humoral immunity in SARS and/or MERS patients? And how long AAbs last? I have been going through a few papers and what I'm finding

isn't re.-ssuring at all· from wh.:)t I can frnd, it appe.-rs that nAbs decrease dramJtie.1lly after -1.Syears and anti-SARS lgGs start rapidty declining after 2·3 years. MERS appears to be simit.Jr 0<

worse.

If wh.Jt l"m finding is true. then that bodes very bJdly for tryiog to build up <mypopulation immunity against HCoV-19 -immunity might just not reJlly be a thing for these ... I'm wondering wh.Jt

those O•linked glyains might do as well.

Not sure if there's a cellular component -just ~n looking at B cells for now. but I 'effmg hope there's immunity against this thing clfld we're nol going to end up with another betac.oronavirus

where we can't seem to devefop immunity. Only, this time, it ain't no common cold virus ...

March 3bt. 2020 ..

Robert Garry t4:43

■ Don't know -should have finished the SARS vaccine studies bclCk in 2005. Agree· the gtycan shield is formidable. JuSl looking at HCoV-19 si>ike °'otherCoVs it's loaded with N-glvcans • the Ogtycans

art just falling in some gaps • maybe an important one or two. There might not be any good accessible epitope-s to target. Just part of the story though the spike protein itself is a swi» army

knife of seriously dar-.gerous motifs.

I tan·t bear to 5ookat twitter ...

r'li Eddie Holmes 11:32

,....\_ • 3.09m Acce$Ses

• 2 Citations

• 25005 Altmetric

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e Andrew R.Jmbaut 17:54

II •....:•• •"-' O I I I, I I, t U • •• • I • • O <9' IO•• 1 • ,h I • •~• • • , •••I I • O II "I. • • O O

~ Kristian Andtt1en 17:56

P.I! Luckily we have ThcBaseballNCfd to explain the majn .arguments (o the plebeians,

REV0003010

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--·--·----""-"--'-

~ Kri$tlan Ander$en 20.57

r.t!I @Andrew Rambaut -where you p,cv;ousty asked aboot the deletion, is th.is the study you WC<e referring to? Pretty ,mcrcstmg: hrrp:hv1tologicaLorg/tlldcntiflc.arion-of-a-common-~ctioo-in-thcspikc

·protein•of-sars C<1'J2/451

O Virologic.il

klentification of a common deletion in the $pikt? J)(Olt'!in of SARS·CoV-2

ldentifK.ation of a common deletion in the spike p,otein of SARS-CoV-2 Zhe Liut.2.

Huanying Zhcng2, RunyuYuanl.2, Mlngyue Li3. Huifa~ Linl,2, Jin.giu Pcngl.2,

Qianlln Xlong1.2. Jiufcng Sun1 .2. Baisheng U2. JicWu 2, Ruben J.G. Huls.wlt4.

ThomasA. Bowden4. Andrew RJmb.JulS, Nick Loman6, Oliver G Pyb1JS4. Ch.Jngwen

Kc2. Jing Lul.2 Affiliations.: 1 Guangdong Provincial Institution of Public Ht'!alth,

Guangzhou. China: 2 Guangdong Provincial Ccnrct for Disease Conlro1 and

Prevention. Guang;ztiou. Chin.:i ...

Reading time

4mins2)

M.11'3ht.2020

REV0003011

Aprill st, 2020 ...

• Andrew Rombout 02\S

•• It was.Also this.,. https:Hwww.blorxivorg/content/10.t 10l/202(l03.22.002204v1

bl bloR:x:lv

Char:actetisationof the ttansaiptomc and proe:comc of SA.RS-COV-2

usirc direct

RNA sequencingand tanclem inass spectrome«y reveals evidence for acell l)ilSsage

ind11Ced in-frame deletion in the splce glycoprotein that removes the furin·like

cleavagesite

Oir«t RNA s,cquc:nc;ing u,ing ,n ~Ofd Nanopore MinlCN c:hnach:rbed the

tra~ptome of SAAS•CoV-2

grown in Vero E6 cells. Thi.s cell line isbeing widely

used to i:,ropagat~the novel coronavirus.The viral transe:l'iptorMwas analvsed using

3 r«ent~y dcv~loped ORS:-centric pipcliM. Thii revealed the p~ttem of viral

lr.:mscripts.(i.e subgenomic mRNAsJ, geoorally fitted the predicted replte.:ltion ;met

transcription model tor coronaviruses. A 24 nt in·fr3me deletion was detected n

subic-1\00'lic mRNAs c-ncodina: the spike (S) a:lvcoproc.cin. This fc:aturt was identified

in (lier h;,lf of the fTl3pped transcripts Jnd was P<edicted lo remove i proposeo furin

cleavage s1te from the Sglycoproteln. This motif d ... Show more

Mar 24th. 2020

lli,III Krittian Andersen 10.24

mt! Very interesting.Honestly don't know what to make of it.

Robert Garry 15.15

• l!ttl)$;,Vwww.snopos.c:om/n♦ws/2020I04/01/<ovid 19+bi<>W<l~por\l

>< ~ Snopes.com

Why You Shouldn't Fall for theCOVI0· 1t "8ioweapon' Conspiracy Th~ry

The 00<0navirus rcspon:si>lc f« COVID-19 has dc<3dly ndlptations that r'r'll)kcit perfect

10< Wlfecting hum~ms. But this is a test.1ment to natur.11 sele<:tion. not bioena,ineering.

(19S kB)•

I

I

~ Krlstun Andersen 1S:SO AP'i1h'-20:zo ...

rD Th.inks Bob for ans"Ving his emiils ~ I got severalbut had to b~k them (together with a millk>nothe1s. I'll loop vou in if anvbQc:1•1

. .). Request frcm 88C coming through too• has time

Robert Garry 19:37

■ Snope<;-actu;illypretty legit .. ,

:. 1reply J yeai~ .JtO

WIii Kristi.lo Andersen 20.58

rB Our comparative genomics iuju is uninralleled. Afflosta-s ifwe created the virus ourselves ... ·:

2hlo>.

e six residues differ between SA ::-·-:-------·

and SARS-CoV (Fig. la). On ti"=----:.-f

structural studies'-•and bioch, -\_\_\_\_\_\_\_

,\_,,...\_,..

9 10

nenti,1• .\_\_S.ARS-C9~2s\_eem$ t• ===""::::-=E::::.:::··

•

1 RBD that binds with high affu ==:;:;:':.~.:::~::.

from humans, ferrets.cats and c ~:::-.:::::.:::.;...--:::=.::....-::

with high receptor homology7• \_ ::..--:::..-:.:.·=:=-=--=

Aprll?nd. 2020 •

lilllll Kristian Andersen 1cuo

etl I gues~ we didn't cons.kier this PoS,Sibil1ly

I

...

Re: The proximal o,-"in ot SARS·CoV-2 A:.>r 2nd, Z020

FtomThomas Busse (No contoot)

REV0003012

e Andrew Rambaut 10'.l?

•• Is thiscomillg from tht whde HIV•denial tl'ing?

lf!il Kristian Andersen 1018

!£1 Oh int~resting. I'm not muct. of a HlV deni31'ologisl. but lha1 woukl make sense• he does mtotiOf'Iretroviruses . Shameon them exosome,s!

e Andrew Rambaut 10 '7

• ■ 'wide~re:id h·u\unier:icy in the Mcdte:JI ncld'

lilal KristianAndersen 1100

~ lhavetogivehjmc>ro,sforth.atpar't

11WKri5tianAndersen 13:18

fa BBC •"Just to b~e:I~~,, I re.xi t~res~)rt:h :ind otherpicc~s :.bout ir• -proc:~dt. to !1t.k,ngqu~sti«1s th.lt :irc~II ~nsw~ in the p)per .. I don't h~v<!, tim~ for this ltind of joum;111ism!

~niA.is~ie& U,trtfltv3ve~..,\_,,

wlil Kristun Andersen 13'49 ra This one is actually pcetty interesting!

(IT\3il f'Offl Sl)Ck fOf G~ •

I

(No Subject) A?r2nd. 2020

F'mm Wharton Kristi (No content)

Here's the paper she mentions A,pri12nd, 2020 •

POr •

II

II

Allderson JOC 2017 cornplete.,pdf

POf

\_\_\_\_ ......

\_\_\_\_ .., \_\_\_\_\_\_\_ ,.\_......"'",...\_----··•~"--"-"

...,\_\_ .....,\_..,\_,..,..,.\_.. .. ...,., ..\_\_ o~

\_\_....,.. \_ \_....,.,... \_\_\_ ,Q,,,,\_....,. \_\_

r"I Eddl~Holme-s18'.47

~ DearProf Hotmes. I h.ave been reading a bit. in the context of thecurrtnt crisis. on the subject of viroloe:y. I came upon a text written by some of -,oor UK co~eaguc-s entitled: The antigenic

evotutlon of Influenza· Orlft oc l?tctft?

Init, they rtfor to the ex,pression: Antigenic Thrift as an expression coil'l@d by EddfHolmes: "Thismodtl-which wt

willhenceforwordreferto thrift' model

os rhe 'anh$e11k:

(11$swuestcd by Cddic 1-10,mcs)-ckpqrh /rorn the wnverti'onol

Ontisenicdrift' hypothes,j's i'n o nurnbtr of importantways:" The probitm. it ls dont in such a familiar way . ..l could not fu\d the docurMnt in which you fi~t used it.

It would be inte<tsting in the current context of political insteurity if Y'()\l culd somewhat find a way to put vouc C>P(eS5ion al the 'orefront. which may help C><plain the variabilityin fatalities .amol'lg

some Cauusian domil\3nt countries vs Chin:1. We know th:it sbndardited hveiene of tl\e food c.hairt.while increasina safety in an indivOual PE!fSpedive as a consumer. lowe-the eeneral immunity

ofa population,is cpit~ cross inmUl'lity p-oh~ction stands as a model or theory.

ThOmpsontt al. also covers the cxprcssk>n In a recent 2016 .arttdc: A naruriny prorccrrvc cpltopc or hnitedvaria!>lllty as an intrucnza v.a«inc-rargct

Red.>irnYOIIfexrxession .>nd help diH\6epc:fiticafp.,ranoia. in a setting where politics rxealready quite noisy,

Thank you fot yOJrwQr1t

OcnysPlcard

US and can.idian citizen

.ind dilettante of course ...

I

At>nl 2nd. 2020 •

•>PubMe<I central (PMC)

The antigenic: evolution of influenz.1: drift or tllrift?

It is commonly assumedthat antibody re5POOses againstthe irwlueruavirus are

pol.11ri~cdin the following m~~f': stron.s :inrlbody ~spon~s ~ directed :,t highly

variabJe .'lfltigelic epitopcs. which conseciuently undergo 'Mtige:nk drift' .....

Nature Communlcadons

A nitu,ally protective epitop,c or limited variability •s aninnu

Current influenza v.iccine JPPfOJ<::hes

larietv focuson highlyv;iriJble epitopes with

high immunogenidty or epitopes of low variability that oftC!n have lo.•,

immunog,cntCity. H«e-. Thompson c1:ii. identify o hig.hly immunogcn· c cpitopc of

limited viriabi1ity in the head OOm..1iriof the Hl haein.lgglltinin andshow protection

from div«se HlNl strains in mic~.

l'veliterallyno clue what the tvc;k thatwtls about

~ Krl5tlin Andersen 18:52

!B Hah.l,this i$ completelynonsens:Cal • but thank ')00 forycurworl:.

Arc these types of emails SC!nt byactl.1,)Ipcciplc? lgct lots tt-at dM't imkeany scnsc.atall • t.g ..

StrN'nShot 2020-04·02 at 1>-50.53.p,ng•

I

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-·-••· ------·•

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!do read the one from Kristi above thOJgh • that one is re.alt)' cool and could hclpexpla1n tha mysterious 'P' inscrtioll. which is just such a cool evolutionary trick given that those O·link:cd residues

direact, existed, but weren't O·lirked until the insertion of Pl.

F'W EddieHolme:s n:21

,-..: There .are.a lot of .actual v«'! m.ad people. !cxlitd

REV0003013

~ Kristian Andersen 13;35 Aprll3c-d2020,.,

!a This wholo fvrin sitq l»ine mo(.s«t wilt\ in TIC h::$ mo i:cc::ond•S\•~ssing m~lf. When , ...... ~-.. ·~·-......0 .. this. 'Nholo p,oceu, ron"loml>orwo t~lk,od ~l)o\1t "~~ggc l"l'light ,n;.ko vin.sso-s xq:~1irl) thcs,o

sites·? We couldl'l't flnd a rcfe<encc, but somebody just posted on Virological. whch led meto this: https:Hjoomak.pk>s.org/plosonc/articlc?.d.s10.1371/joumal.pon('.0052752#por.c·OOS2752·

t002

-Joum:ilc.pbc.ora

The Role of Viral Population Diversityin Adaptation of Bovine Corona virus to New

Host El'lvir<>nments

The high mutation rate of RNA viruses cnabtc-s a diverse tel\Ctic oopul.ation of viral

gerotypesto exist within J singleinfected host. ln·host genetic: diversity c:ouldbetter

posldon !he virus popula!lon to re5pond and adapt to a diverse array of 5electfv,e

pressures such as host-switching cvcots. Mul1".)lc 00·1 comnavi,uscs. including

SARS,h1we been identified in hum.JI\safll.)k?s just within the l.'ISt ten yeJrs,

dcrnon~tr:.ting the potenl'bl of ~oron~viru~c,~ emergent human p~thOQcns.-. Occp

scqucncil'lgwas used to characterize genomic changes in coronavirus quasispccics

du(ng simulated host•sv,itchin&, Three bovine 0c1sals.1mplesinfectedwit It bowie

coronavir~ were used to infect humanand bovine ... Sho,,1mom

SoeciflCJlly"Theconsensusseauenc::eof many of the PilS.SJgedsamples h..Kf a 12 m,c:leotide insert in tre consenStJs se<1uenc:e

of tl'le soike ge,e, and multiple ooint mutations we,e assoc~ted with

the presence of the imcrt" • those insertio~ beingArg dch. which ls exactly what HC.CW has.

Robert Garry 13A8

■ Wo',-ep;ass:isinsMCo..,.19onfling celllines;md\~os,8vt yes• totilllymis~c:i dut 2013 p3P43r! lslK!'!-sif~ got 1:hiedclotions ~dicxlld rxus thoo.e b:)Clc onhmgce!k Thq 12 b;,:i~einsertionis

I

ffeaky though.

w.J Krlstun Andersen 13;50

f'9 Yeah, I'd be very iOlefESliOf;iO krowifll whe(llel ,ln HCOV·19 witl.l()Ul the lurin Site COvXI ,1'Cquire I h:weo•1 fully ff:Jd lhal Pl0Sf.t.:1J)t:f yet, but the :.i111U;ui1y

l( ~ID. i:-,vety i1ltert:$ti1)8,

I :.'11$-0 bfk. oboot: bb too: https:UwWN.sci-enriftc:.1mcri~<omhrtickl/how-chinl$•b:.'lt·WOffl.,n•hutlt~d-down•vir'Uscs-frotn-s3rs•10-th~-naw-coron#Yil\tSt/

thought thi!:: oncw.:.s interC$tins • ~Of'l'IQ

M Scientiflc American

How Chi1'a&rsquo;.s &ldquo;Bat Woman&rdquo; Hunted OoY.n Viruses from SARS to

the New Coron:wiru~

Wuhan-based virologist Shi Zhengli has identified dozensof deadty SARS·like -.A.rusesin

bat caves. and she warns there are more out there (376 k8) •

Tl'W?2013 pape<issummarized nttly here: http:f.virologkalorg/t/identifiGtio1,-of·c1·co.nmon·deletion·in·thc·spke·p10tetn,.of.sars·cov·2/451/6

Q Vlrologlcal

,dentihcation of a common defetiOfl in the spike protein of SARS•CoV•2

Thepresence of inserts or deletions in c~scnsus sequencesoras vc:riants of SARS·

like COfOnovi,uses i:s :,Jso observed i1' bo,,,ine eot01,~irU'!h ~lso a rnel'rlbet>of

bcucoronavinJs (https.:Hjourn;ls.olos.org/plosone/artic.le?

;d•I0.1371/jcurnalpone.0052752'pone•OOS2752-1002). For example. ,fter

oassina 3 diffeu~nt nalul';)lly infectedbov ne ,,.,.S-.)1 in dfferent ceh line-s we

Sdm.ples

observed the consensus scqumces of maw virai sa11ples acqu'..red a 12-nucleotidc

Insert encoding. 4 amino aclcts!Ser, Arg, At ...

At,tJ«12020

Espec.i.111',': bovine nasal sampks in different cell line:s of manv viral samples acquired a 12~

"For example, after f)a>sin,g3 different natu1allyi11fected we observedthe ccnsensus sequences

liudeotide .nsett ericoding 4 amioo acids (Set.Art. A,g. Arg)k>cattd at nt 2737 of the sc:,ike iene 1S2 S1JbuniO. where.as none of the unpassagedsamplescontaii,edthis inS(!rt at the consensuslever

It's noc just a Single experirrent • three different strain$ all e;cac;ttyacqUred ii 12bp t-urin cleavage site. That's dehnitely peculiar.

This too very int~n:.sting as a potc-ntial mechanism -ocep sequencing revealed th•t the insert gcrotype was present but very rare in the unpnsaged sarnpk:$ but quickly bc<.aimc conscn-susaftcr

I

pass.1gein cell c1.1lture," • so it's ttrere in their input (presumably directly from cow~

Robert Garry 1<109

■ MutabOns.

including ooint mutations. inse<oons ¥Kl deletions. CJn occur ne.ir the S1/S2 junction of

coronaviru$CS 34.40-43 suggesting th.:it tM pol,,t,asksite could arise by a natural evolutionary pocess.

I think this covers us prettywell -yes• there is natural variation ~ding and wbtnctinsthe furin 5ite inseveralC<Ns • .ilso note thilt BovineC<N is reallya Vf5Ybroad host r.n.gev·f\Js

ttnps:.i/www.nc01.n1m.nin.gov/prrc1arnc.1cs/PMCZ395l24/

•>PubMed Central (PMC)

Cleavage of Group 1 Coronavirus Spike Proteills: How Furin Cleava,e Is Traded Off

against Heparin Sulfate Bindingupon Cell Culture Adaptation

A lengstanding eni)1fnatic foatl re of tM grouo 1 coronaviruses is tht undtaved

phenotype of their spike protein. an exceptionalpropertv amol\g class I fusion

pro:ei~. Here, hQW"Cver, we )how thot :,ome group 1 CQfomwirv> :,p:ke p,oteirl) ¢.,ny

a ft.trin enzyme ..

~ Kristian Andersen 14:13

!a Yeah.ck?arty this p.3rt of the g.enome is very'acfr.e' • v-.4lich cs super freaky.because are we ;ustwaitiog '°'othof SARS·likeCoVspoppiriguJ)thal haw pandemic poten1i31too.

1 don't think any of this new knowledge goes, aga nst lAflat we said in the paper, bllt h cloes make our-oefmltely not passage· argument weaker.

1 .. voukl bo very intcrcs.tcd in seeing some vtry in depth stvdi-es of high coverage bngitvdin.al ,..;,al scqvcncinc: of mild vssevere cases.I wouldn't be surprised if WfJ mightobserve loss c#the furin

site in more sevue caws. \_\_\_\_\_\_

I

REV0003014

Robert Garry 1◄

21

■ Y<.•ah·dcflnitelv foOd for sott tOOu~,1 • aod wv c.M do rnild vs stv(!r<.•. • worm k>oki,.gat high ir~tt.-oSity hun\'lll p.bsag<> as \"4('fl. Vic have a bunch or s.arns,lcs from a nearby psyd1iatrie hOSJ:,italwi:are

testing today th.at is having aserious (hei.lrtbreJkin;) COVID prob'em (inm.ates and st3ff) • not sure ;:,00\t the irb issues for sequencing. but pote,,tial to get a waiver i suwose (we .Jlre.JdY have

a waivtr fo, clink.al t.xctss deidenti6ed).

Wlil KristianAndersen tA2S

~ Ye-ah. I think th~ studies will bevctYinforinativ~. ThetRBis ~&d up on vour end f0< now. not Otl'.f'S.corroo?

Robert Garry 14-31

■ not held upw~ arc planning on shooting you a bunch of Mardi Gras samples ptus veropassed nCoV• 19 mid week.

~0

Robert Garry P-44

■ i am thinking for te<tiving monkey sample-s'(Ou needa sr iaruc approval • nor sure~ sortl!d that out ytt

~ Kristian Andersen 17:S8 ta Ye-ah • almost there with that.

~ Kri:ttt•n Anden-en 1896

r.£1 Goodone

Email f'Offl Sl.ldc fo• Cm:i •

covid-19fromlaboratorvnot natural Aor3m, 2020

From ko8.7t+-2zxcJ<\ljai3v (No contet1t)

r"I EddieHolmes 23:32

,...\_ What arc tl!c bags?

April4th. 2020 .,

9'il Kristian Andersen 0006

fa Bcc-n wondering about that...

r"'I EddleHolmes 00'.48

I

,...... Perhapsthty give out goodie bags at thi: G7? The quality of the co1uent reflects your GDP?

Robert Garry 19.SO

■ Garrett said something to the effect that Eddie found the animalhost for HCoV· 19· pangolils! She and her buddy Josc,)h "tl)e idiot" F.w-c are doire as much damage to virology as they canon

N8C/MSN0C. Yes• ~s for the Whitohouse • its possit'e • ifTn.1"1) h;:i(I tho :ibility to fue las('rs ovt of his OY'(!S TQ<¥ r:allci w01.1ld be fried tcxby .

... Eddie Holmes 20:02

,....... I shut thill down pretty qvic;kly and she deleted the t-Neet. Clearly a lot of people have had enoogll of her.

REV0003015

Apn15th, J)2(I ..

e Andrew Ram.baut 14:02

•• @channel Seen hefplng out a colteag\le of Ofi's with 3 littJe p.iper about <leletions that take out the funn cleJ'Y.ige site.

httpS://www.biooc.iv.org/contcntJ10.1101/2020.03.3l.01S941vl.full.pdfi-html

bit bloRxlv

ldcntfheatioo of a common dd:ction in the spike pr'otcln of SARS·CoV-2

AbstroctTwo not.ible fe~ureshavebeenidentifled in the SARS-CoV-2 genome: (1)

the receptor binding domain of SARS•CoV•2; (2} a unique insertion of tw~vc

nucleotide or fouraninoacids(PRRA) at the 51 andS2 boundary. For thcflrst

feature. the similar RBD identifted in SARs·likevirus from pangolin suggests the RBO

in SAR$-CoV•2 m;;ryalreidy exist in anirml host{s} bef0<e it tr,:il'i$mitted into hvm;in.

The loft punk: tsstOO hi$:tory :ind funetlot1 ol ll,e ins.ertior\ :,t S1/S2bound::uy. which

is uniquely identified in SARS·CoV42. In this stu-dy. we identified two variants from

the hrst Guangrlong SARS•CoV•2 cell stf(in, with ddetion mut.ltions on rx:,lyb;isic

cle;wa2e site (PRRAR) and its flank sites ... Show mo1~

f'll'llnd.2020

ljus.t wanted to run by an id(!-a by you an ... What do thi'tk abc>ut the hypoUltsis that kooc:ki~ out the fufin site is being selected in cells and n SOt"leP3tients but b3sidlv it needs it to successfully

Yled in the lungs and/or infect the next lun,g~?

ThuswithoJt it it is more S.ARS lik.t in iH lr~smiu:fl)ility.

Aprll5th. 2020 ,.

Robert Garry 1:i'24

■ This is massiv<.-ty imJ)Ortant.I ver')' much ag,ee with the hypothesis • needs to be tested in animal modes ASAP.

~ Kristian Andersen 17:32

&\9 @Andrew Rambaut -ye.ah. reasct'lable hvi>othe:ses and vou can see a DOSedsomtthinl? similar' above. h's oossible that a lack of Ult fur'n e:leavaa:e site mi~ht 'drive' the virus deeotr into t~ lullj!S

ttence leading to more severe disease • the opposite v-'Oold then also betrue, bvt could then lead to more spre(ld.

I'm not corwirw:,ed pas~gc pc, sein tiswo cultutewill lcad to the dcletk>n of the site. I think this is likely going to be highly dependent en wh:it cell line it's bdng passaged in • e.g.. Vero celts arc

(inonkoy)kidn9yqpith@l~I ~11,. so likdy JXGtty difforiottt thon tho ~inoou, HCoVwouldtypic..>llyinf~a • vn!ik9, q,s .. l»".'.18QOf'I lms oolls. Somo of tl\.Qoxpc:rimont5 8qb ond I diS<:us.,W.abQV9

CO\lldbe veryilluminating here and it'd definitely be inttrC'Sting to do a clinical outcome association study with abscnce/p~enceof furin site.

Kristian Andel'len 2<>.25

~Andrew ftambaut one question that Just occurred to me• did they grow the viruses In the prestnce or absence of tl)psln?{SARS needs u•,-psln, HCoY docs not, but If this was done ~Im liar to

SARS then they might have added tf"YJ)sin to the culture 4 which could drive the deletion of the furin site).

e Andrew Rambaut 20;56

•• Yes -I think we dswssed this earlier~ the thread some ..-mere. I bem~ve they did use trypsin in the eel medium (this is oormal I think to stop the cells buncting?).

~ Krist.tan Andersen 210.t

E£! Interesting• I think this might dfile it. Yes. oypsin is often used to disJodgc dle cetl-s when you split them• but th.en it's typically ...vashed off pretty thoroughly. so 5hooldn't really be p~nt at a

fligh k-vel in tho coltvre itsdf -bt1tit might be sufficient here. Vel'O$ c;in be split withotA add'.ng trypsin though • just by scraping the eels off. If possible. it'd be very intetested in seeing an

exp~riment with or without trypiin to g~t :, ,en~e of ....tl~t~r th,:,t might dl'h-C th~ pheootyp~ .

... Eddie Holmes 22:11

,....\_ And on it goes: https:lwww.nationalrtvtCw.com/2020/04/cororovirus--chira·traJ-le.ading back•to•wuhan•l;abs/

Nt National Review

The T,-,:,rJ Le:,din:g O~k to the Wuh:,n L:a~ I N~tion:,I Review

There's no proof the corcoaviNs ~inated in ;alaba-atory. but wecan't t.'lke the

Chinese govemmenrs cSeni;ils at face value.

Acr J,d. 2020(1« kB)•

Robert G:srry '22'.Y.!

■ yes• good idea K -pa~aging with and without trypsin

I

wlliilKrlstun Andersen 23·32

f'n @Eckle Holme:; we ;:)fflO:;t hove;, 30k Alt metric. ~ore :;o I wclc.omc ~l'IY "ill'Y theory :I

r'W [ddlci Holmes 23.47

r,-,; Good point. let's keep pusfi•\8 for 30k.

April6th. 2020 ..,

REV0003016

... EddieHolmes U:01 ... EddieHolmes U:01

,....\_ Cid you see this bollocks?https:.8www.grain.org/en/artide/643'7•new•res,e1rch•sugg~s-industri;:i,Mivestod<•not•wet-ma.r1<eu~mig:ht•be--<>rigin•of~covid·19

gl'#lln,org

New research suggests industrial livest0<:k.not wet markets. might be origin of

co,,;d-19

Let') be deilln there i$ no $Olid evidence that the ori,&in of the SARS·CoV·2 virus..

which is 1hc uusc of thecvrrent Covid•19 disease pandemic, isan open seafood

mark(:l in Wuh3n that al:!» ttades ir, domtStic and wikt anim;-,ls. All lhal we kno.v is

that sever.al early c~es o( people dUgnoscd with Covid-19 either wotked .at this

rl\i'tket or shopped there tn the days preceding their diagnosis.

~ Kristun Andersen 1M1

fa ean·t s;:iy rm a frequent reooef of graln.org. but what a 1000 of bolocks indeed. A!ot of that going around.

r"I EddieHolmos ~3,1

,.....\_ NO<me. It was ~ssed to me in 0lle of those 'did '(Ou re..-llySJYth,t' emails. Fuck no.

Al)ril8th, 2020 .,

11,\11Kris-tun Andersen 16;2'4

~ WTFm?!!!!!!!!!

xr-nShot Z020•(),••00 ;)1 13.2:).50.png ..

8«,);)tby <:hloroquine m.-aybf.11

~ Eddie Holmes to:S3

~ loppled! 1tlK>ughtit might be the face mosk study froin HKU bot tl\Jt is at 14.477 (bvl it orly e.1me out last week). WOJld be badii it was trot dire chlorOQuine study from Raoult

...aKristian Andersen t6:S6

t.t!I We need to trxk these h.icters down • crossed the wron,g people they didl

e AndrewRambaut 16S9

•• Not R,oulc https:Uwww.altmetrk..com/deuils/77952531

l!I altmetric.com

Rel)Ort for: Hydroxychloroquine and azithromycin as a treatment of COV1D•19:

results of an cp,en·bbel non•r'andomiz:ed clinical trial

lo the: top 5'Xiof all r~ardtootpob ~cored byAltmetric

Lets publish somelhing evell mote outrageous.

I

Ro~rt Garry t7.s.J

April8th. 2020 ..

■ •Lets publish something evtn more ootrageous:

Allforit!

P.Eddie Holmes U:li

Th•.--. ,... th♦t. 11,,H .-. ♦t.xrt. tlio• ,.,.,..,lv•l ol t..\_ vJ.~.,, on ,,..,..fH·••· ,.

"Aetosol and Sud~~ Stability ol SARS•C0V•2 as Compared with SARS<:oV•l ". Can't hnd lht Altl'netric. Acccrdlllg to NE.JM it is thefr #1 p.1perbut it ranks 3rd of Mieles: in atl joumals ...

li!II Kri:stianAndcncn 1&4i

la Oh, aftn0s-t • that ooe is close (113) ... https:Hwww.altmttr'tc.com/detailsl'7'769'939◄

?src=boobnal'ldet#stom

R altmetric.com

Report fc;i,r:Aero1ol and Surf~e SU!bility of SARS·CoV·2 H Com~red with SARSCoV•

1

In the top 5% of all re-search outputs scored by Alt metric

I wa-s thinking mivbe C.hrisloptie·s paper• which would maJGe me kinda happy., Need to c.he<k

waaaaaay oft. hUps://www.attmttric.com/detailS/78618646

(II altmetric.com

I

Report for: Quantifying SARS·CoV-2 transmission suggests ePdemc. coritrol with

digital contact tracing

In the top 5% of all research outputs scored byAllmettic

REV0003017

... EddieHofmes 19:08

~ Let's hope it's SOMe bat shit c,,:12:y waokJesl so wt cao still dlim the mo..-al h(;h grou,'td. I'm ke(:,, to fu)d oul. ..without a~kin.g Twitt~, thereby admiWo.g that I am ktt<• to tiod -0-uL

Apnl9th,3'.>20 ..

• Andrew Rambaut 12'.SS

• ■ This Question ...

•~11115.

\_\_..............,\_...\_. \_\_\_ .,........

......~...... ~

& .,..\_..,.f'Cf:•~t>tCO\IIOo.;.,..

ir~N--•uts#'4t1-~1illl--l,\_

... -...---...---~-..... ~.....

~ .... ~'-•"-"' .....°"''""

make!seosa now ...

I

iinaaePllC•

~ Kristbn Anders.en 1300

la Haha.I think he might havedone more." than just sequen-ce the genome of that 2011 project.

• Andrew Rambaut: 13,37

•• Yup.

'seQumced it' if vou know what I mean. man.

I

0&

Ap..CI 10.h, 2020 .,

Robert Garry 07.47

■ ~u,ence evidence for SARS-Cov-2 existed five -,ears.)80.

SECRET•mail •

l inkf-,http~ : / / ~n. b.aidu. co,,/ ~/lQnlJdV)S-ty! •••n•7Pl4l

p.tSSIClfitllot.

oca,ALL prorcssors.

I h.we found ol.i: th;at the SARS·Cov·2 is existed in "A\.th3n in the ye~r 2015, 2017. 2018.

The stquc-nce ~dcncc detected for P<)tients with infectious dis~asc is in t~ att~hcd fokfc!rs. I think you can do more similar work to the Stqucncc data submitted by guys in Hubci p,ovil'Kc.

China.

I think You ,1re right. SARS·Cov• 2 is existed in H\bei fer along time, imybe lhe common coronJ virus rove some ,ommuniCJtion with other viruses such as novel8\lnyi virus on aenetic maleri.als.

Maybt the environment in Hubei td~r so~ switch to speed up the evolution of SARS•Cc,.,• 2, since high temperaturt envi'onment in Wutt-an, make the ecosvsttm there chaos. some food chains

was d<?o;tro'j(!dby ~t~rc and JYUk~ t~vin& jump into hul'l'l:lnheing ;ind bqi;in tti~longjou,ncyto fini,thrtl\Olurion to kill morc'!o~ poopl~ to b:al;:inc~ the tM:l)$.'f$,te,rnt~ro. !:O th:acthe food

chain can be restored.

Please keep the data secret tor me, sincetht data is from 04.lr company, and the data a,c actually :rom CDC in the country. And I tiavc Emailed to Kristian G. Aoct-erscn.

Yours.

ShaofeiLiu

RobM Garry07.><

• phid\?

• Andrew Rambaut 07 SS

I

•• Strange link ill an ema1 from China'? Sure tobe legit.

REV0003018

• Andrew Rambaut 08<01

•• Mu')d '(Ou. I so wa,~t tose-e this. Perhaps I wll b(eak into anothe( off1ceand use a studenrs compute, ...

Robert Garry Qr&.43

■ Let us know what y00 find down the tabbit hole ...

~ Kristian Andersen 11).33

I.a Tile link is ltgit enough and there ar'e tastq flies in the~ ...

tittp$:/lpi)n.b.Jidu.com/$/1QnVdVJ3mmByo,MWm7P84A

Pass:tlwm

I find it kincla interesting th.t he emailed y'all sep,Jratety • could be a Chinese whinleblovlef .., I'll OOwnload some of these and run a Kroken screen. beciuse why the he(.k not. (Mi~

e Andrew Rambaut 10.ss

.a

■ Cbdyouwtro-willing to takothebiJllct fOf' "'•

took fotward to heafint about what y()U find .

....aKristian Andersen tl)SO

~ Alw~ count on me to do the dt.mbest thirgs. ~

Kristian Andersen 12.27

Iswear-there are f astq tiles in th~rt! • and all named k>gically. Issue is. I can't bloody figur¢ out how to <bwnload stuff since its all n Ma1darin.

I

• Andrew R.ambaut 11' ~s

•• Get tl-c goog1e transl.ate app on your s:f,one -it can do live transl.iring through the camera.

if'lil KrlstunAndersen 12;-46

li9 Oriltiont!

e Andrew Rambaut 12 46

4111

■ No. It off ell you a software download• pre$umabtywhat YoUneed to install so the Chinese govcmmert v1n take control of your oomputer

llf'6IKrlstun Andersen 12'47

!J!I £x<'lctt,, -need to downlQ..,d the 8;,idu app. I b-u$t my M;,c;: won't be t;:,kcn over ... (I crq.,1<:Xf., protoch::d .1c:c:ountjvst for ihi~)

I'm suf'ficieftttv intrigued here be<ausc these arc clcarty seaucncint tiles and this wvcould be from BGI

Wl6IKristian Andersen 13.37

lil:I Still trying to work through this ... Here's the readinc

-.....\_...--

---·----

& il£5 .. IJ213§L I

U:37 1 tnlflk we dOF\a\lCa Y81iStJcl)low~r ncrc • Jus:t not SllrC\Yt\3t the oata lsactu.,lly going to shON ...

~ Kr;,-tbnAndersen 1540

~ V«y $<YWgoing. but at least now we know that ,1's &cgtt (but could vc,y well be misdaS'S1tication)

Scr~nShot2020·04·10il112«>.00.pn11:..

\_, ..\_\_\_\_\_\_ \_

---·-.,\_ ..\_\_-.:.=:..-..-......

\_\_ ,\_,.\_,. \_\_·-----

--·--\_--:.=--=-=.. -=-=-•-..

Robert Carry 1S47

■ Wow· kcq, c1fter this and k~cp u.s po,-ted ·BTW· I think that thi$ individual pl'O'lided a fermk name .. did they R"nd U1c ITIC'l~c lhru ttn c-nc-rypted $ite?

.Ml Krldhn Andorun 11,, c;,

ea Yeah. this was a w::rystrange emdil so while the message itself wasn't <1lcrypted. I think this persoo went to some length to hide their nae ks. The data download is very slow so it'll take me a while

to t.ake a look at the ~tual d;1ta • I S\lspect these are just mi5Classihtah0ns.b\lt l'I defmitely take a look.

~ EddlcHolmc$ 11:20

,..\_ lean e.asilyget a Mandarin speakef to look at these Kristian.Justtet me know.

60f4iu\·t£1)$

Do you want to try to hnd out who this pcr~on is! I catt ask aroord.

... Eddie Holmes 17:27

~ The Chinese govt havt conuol 01my computer anyway so no wotries there. Whistlcblowe<, hoax.O( set·up? Remember.we looked at 8XJ mctatranscriptom.csamplesr,om Wuhan In 2018 and

saw no knowSARS•CoV-2 .

.Iii KristbnAndcrstn 17-41

In We h.ive two guvs from Ch 'nll here .1t e>ur institute and they managed to start the downlo,;1ds. The;'re downlwding .aswespeJk, ,1lbeit stow~,.

.!lllgni.1g. bot

It IOOkS to methat tl'ICSCarc :,Ingle rca(h so 1'n0St likdy mlsc1as:s1ncat1on let's5«: or·.::e I rave tile fa:itqs

r"I [ddi~Mofmecs 19:01

,-...\_ Make$ sense. Cock·upis always lhc mc>stlikcly c.plan1tfon.

April 11th. 2020 ...

wit.IKristianAndersen 00:08

fa PREDICT rcsurroctcd .. https:HWNw.cnn.co-n/2020/04/10/pol1n:::s/trump·t.sa,d-prCVt't'lt·pmgram-coronav11us/1iidt'X.html

Cl CNN

REV0003019

Trump administration shuttered pandem~ monitorng program, then scrambled to

extend it

As earty indicationsof Clina•s coronavirus outbreak emerged in lat~ Dec~bef'. t~

I

Trum.padmlnlstrat1cnnotified congress It would st111 toJlcv1 through w1th Its pl.In to

shutter a US~ency for lntecmtionaJ Qe\•ek)pment wrveillance program tasked with

detteling new. potentially dangerous infectiolS diseases and retping foreign labs

stop emcrgingpaOOCmk thrcau arwnd the world.

li'1IIII

Kristi11n Andersen 1\*◄

1

1'.13Alrighty,t <ftclend up going down that rabbit hole with the Chi~ data. The emal was legitand the data too • but as expected. niscfassific.r.ioc, caused faJse SARS•CoY•2 uUs.

~ EddieHotmes 18:19

~ Y~. I had a look as well. Couldn't !>ee cmyread!:. ltlat mapped lo SARS•CoV•2.

fi'iiii,:l&i-Q

RobertGarry ,an

■ So• not .i tot3llyworthl-ess effort• sorn,ewhere in Chin:, • orm3ybe elsewhere there 3,e tissve spe,cimens from people with \lnd~g.nosed respir3toiy illness-es. I h3ve to s.;ay th;at the nurrb,ersof

people contacti"-t me with stories of multiple peopte coming down in a dep.1rtm-cntorbusi~ss v,ith COVID like symptoms make$ me wonder. Tht h~ad of p.ilmooology is (onvinced that student

in the SMSprogra,m v-.ho workS 1n a path lab had ,t and passed it to him and several fctows.. She tndcd up on a oJCnt beforeJ <hfncutt rteovo-y • tested neganvc on ,esp1ratory virus Film Attay

panel. He c'.hest )(r.lv is identiC.JI to COV10 4 am bleeding her next week. for ser~y.

REV0003020

R.obertGarry 1139

■ @ch'1nnel @§Hf::iflfj§j

tttps:lwww.bing.com/search!q•Bcijing%20tiglllens%20grip%2Qo...,rl<,20coronavirus%20rescat<h%2C%20am""'20US·

China~20row%20oo~20vims.9'20orii:in&rx:•crnp&ptag•G6C9~N104800022419AA/JB84BB086&fnml•CONBOf&conlogo•CT32t0127

"China has inposed restrictions M the publcation of acade'nic researchon the origins of the oovel coronavirus. ace-Ordingto a central govcmment directive and ooline notices l)\J)lished by two

ChineseunVCrsiiies,that have Sir1r;e been removed frc:m the wen·

=CNN

April 12 eoo>navirusn<:ws• CNN

The novd coronavirus has killed more than 102,000 people worldwi.1e. f,o,Howhere for

livcupcbtc5

Af)f'.1tf\m0(100k8l•

....,,.,~.. u,,,..,..\_.,

ilW Kristian Andersen t4'45

113 Yeah... This ctrtcinly doesn't help: https://(!;ditionc:nn.com/2020/04/12/asia/china•cOf'Onavrus-rtsear<h•resttktions•intf-hnk/inde:x.ht11I

=CNN

ChiAa imposes te:strictions on research into origins of cor0navirus

China has imposed restrictions on the publication of academic research OJ\ the origins

of tile nCW'elcomna·,irus. accOfdine to a central eovernment directive and onlin?

noti:es published by two Chines~ univel'SiUes. that bave si.-.ce been ,emo-red from the

web. (68 kB) •

REV0003021

Apr11 lJtn, 2020e Andrew Rambaut 16'.)4

y

•• On the other hand thh i:,. an intcr~tin& re~: http:,.://wNW.thegunrdinnwm/wc,rld/20:20/tipr/10/birlh-of•.it•1)0ndc1ni(;•ifl'lide•thc·(1r:,.t·-=ek~·"Of•lhc·corun~vin,1:,.·c;ulbrc,ok•in•wuh,,n?

CMP•Share\_iOSApp\_Oll1e,

(ft the Guardian

Birth of a pandemic Inside th4! r,rst weeks of the coronaYlrl.15outbrt-ak In Wutlan

lntcrvievis witll patients.. medical workers alld residents rtYeal delays with far-reaching

consequences for tt.e city, the world ;ind China's leadefstup

~:°"", Z>20(6Sk8}•

... EddieHolme, 21:41

~ 01l(;e 1hls Is over me $lit w!II hil the tan. 1..Q•sof .storle$wlll ne,ed to betolt'J.

April 14th, 2020 "'

Robert Carry 1501

■ Hi Dr. Garty.

Our episode on virus tivnting and bat virology for Short W-;ive, NPR''s daily scieoncepodcast. will publish tomouow at 4 i.m. EST.

You'llfind it at the top of this web page hert: htt~//www.npr.o,i/podcasts.'510351/short-wavcorwherevtryoo get your J)odcasts. It includes quotes from yourself. Or. Unfa W,mg in Singapore-.

:ind Or. Peter D,nwk (It EcoHe~Uh Allimce. Thank vouso rruch for ta!Cn\_gthe time to weak with me. and I hor>e ,101.J'retaking c.Jre in Nev, 0-leam.

·Emily

-NPR.org

Short Wave

New discovCties. C\ICr'Vdav mysteries. and the .science bctlind the headlines -all in

about 10 min\A.es, every weekday. It's science ior eYeryone, usfl& .t k>tof creativity

and a little humor. Join host Maddle Sof1afor s,c:lence-on a different ,vavcteogth.

Kr'i:,.tion • I hope you (Ire provd of whtit yo1,.1got rne into tltf't • LOL

~ Kristian AndeHen 1S06

!rn I hope so too Bol:>. I hope so too\_,

r"I Eddie Holmes 18:16

~ Did you lot set lhi~?

5oe-t-n$hot 2020-04·15at 8.lo01 .:.n,png ...

·-·----°""----~--1,a

=.-a-:a.=.-===.=====~....:::::-=··

to..\_, \_\_\_\_\_\_ \_,. \_\_\_\_\_\_ .. \_\_

=-~~-===-===:.-:r;:....-:::..

c.., \_\_\_ ,.. \_\_ .,. \_\_\_\_ \_

--4 .. \_,.\_,, \_\_\_\_\_\_\_\_\_\_ ,\_

,\_\_\_\_\_\_\_\_\_\_\_\_\_\_ .,...

\_\_\_\_\_ ,.\_\_\_\_\_\_ ....,,\_\_\_ \_ \_

◄'li-11::IH♦

REV0003022

Ap,il 14th. 2020 ¥

rm not sure what The EPo(.h Times is

W!IJKris&n Andersen 18:19

1£11didn't ge,t this particular one-. but I have had several othe,rs mentioning Epoch Times. It's complete ttash • I don't understand why news outl~ts have to follow up on all these complete BS papers

(e.g.. PNAS paper,.,) and 'nCINs' stories, Not that the Daily Mail is the bcn of papers. mind you .:

r--1 EddieHolmes 20:-0S

,-....; Because the currency for Journ.:-ilists arc stories, not ncccssan1y the-truth. They look for every crack and thc-o try to wedge-It open.

ll!WIKrfstbn Andersen 20:57

ra Or. K has a point "Whenone conskkrs rh~decodes lf not loflser. 1ho1the Chinesepopufotion hove been consuming variousmeots. I fu,d ,t moretMn surprising rhot o,,.swus suddenlytook ott: Silty us not

COflsi<:lerinJ; -so mysterious.

that ~rt

I

Ap-ll 15th. 2020 '"'

Ap~ 16th. 2020 ..

....aKristbn Andersen 00.55

~ Front page ... https:dwww.cnn.com/2020/04/15/pofitics/us-intellig:ence-virus-started·chinese•lab/index.html

l!:ICNN

US explores possibility that coronavirus started in Chinese bb, not a market

US intelligence and national security offu;ials say the United States government is

looking into the possibility that the novtl coronavitus originated in a Chinese

laboratory rather than a market according to multiple sources familiar with the

matter who c;iution it is premJture to dr~ .Jnvconclu$iolls.

I

r-11 EddieHolmes 02:53

~ Isit kicking off agai,1? Could we get #1 spot back??

.£. 2~les U,t,oeplv3y,e-.at'i-a80

... Eddie Holmes 03:44

,.....\_ https:Qwww.9news.eom.au/world/united•state~•trump~investigatin.g•o;;ource•of•coronavirus•in-<:hina/db10f008·9ea0•4434•bf69-748d63f9480e

https://www.theguardian.com/world/2020/apd15/trump•us-coronavirus-theory•china

https;//www.ncws.com.au/lifestylc/hcallh/hcahh·probtem-s/us-urgcs·china·come-dcan-on·m.)nmaclc·virus·rumoor/ncws·story/adlc75545fb8484d08bded54e06027d5

https://\W1W.ktvv.com/new"$/sourtes·believe-covid-l9·origin;:ited·in·wuh;m-1Jb·.1S·?,,lrt·of-ch~s-efforts-to-compete-with-1JS

.. Breaking Australian and World News Headlines• 9News

United States investigating '°urce of coron.avirus .as Pence calls on 'Chinese

government to come clean'

US Preskler1t Donald Tr\HYlp sayS his government is trying to determirle whether the

coron.avirus emanated from ... (49 kB} •

I

I

(B the Guardian

Trump fans flames of Chinese bb coronavlrus theory during da.lty briefmg

The ~sident attacked those who favored China. including the WHO. for which he

previously announced a hold on funding

Ao, 15UI. 2020 (80 kB) ...

REV0003023

NX !5th. mo(8:)k8l• April 16tti. 2020 ..

• NewsComAu

US urges China: 'Come dean' on virus

The US i1 vrsins Ctin.t to •c~ c;le~n• ..-bovt ttie origin ot COVI0-1 ~ ~., <I.aim,; cin:-td::1te

that it was manufacturedin aWuhan labofatory.

~ ,..,\_ moc22 kBJ •

April 16th. 2020 ..

f!l KTVUFOX2

SoUl'CeSbelieve COVJ0· 19 originated in Wuhan lab a:spart of China's effo.rts to

compete with US

Thi1 m.,.-y bet~ "c:odl'(Kt ao~rnm('nt eo-.,-en.1pof ..-11time," otWJ of the so~ ~icl

(30k8) •

I

April 16th, 2020 ·~

Robert Garry 08 S7

■ Tf\lmp/,:oox rC3lly need to ~tUc oo one c.ospir'.)C)'theoc'y°'another father I.Mn somc-hOwconflating tile two h\lOone gfand consptfatorial mash·-i.p.

EitherNCoV-19 t}c:~m~ frQm the morket Of 2) it woscrentetl<w ei,eaped from WIVQf' 3) it «;:41nfrQrn 011turolprQCo:,,es.

Fine • push 1 or 2 I suppose. but \N'h,at Trump/F"IO)( is pushingis a m,ash•uP coospir..cy thcoty where sol'l"M?OOefrom WIV re,le•sed NCoV-19 ir,to the fts.h m,arket.

• Andrew Rambaut 09-09

•• Project restore #1 Altmctric is underway•

<f:v~

I

...aKrist1in Andersen 1004

la It's disgusting what's going on here. Once JJ:Jin he will manage to blame otters .i,d come out st,ongerwith his bJse. Put it ~I on Chinaood WHO• he obvi<:vsly did his job perfectly .iloog tile w;,y.

• Andrew ~mb.lut 10"23

•• And thew;Jf it is made to look like his own rnmblng th:lugtts. This is done by design bvthe people who ,unhim.

tl.J Kristun Andersen t0.25 ea It'&. not oi<;>c;tty ok1$;int. bvt it'&. (vnfortt.1n3tely) efmti,.,., I w~nt O\lt, Anybody h\_,.s tontxt&. in Norw3y?

e Andrew Rambaut 10.31

•• A colleague is fran Norway. But he is, bit concerned ibout the rise of the ,ight •wing there too.

Robert Garry 1033

■ ABC • national n,ews • so 3 st.lrt. • Hi Or. GJrry!

I hol)e y0u'1e doing w,U!

Asconspiracy theories continue 10 posit that SARS.Cd/·2 is anthr(){)Qgenic. I thought it could bean apt time to r~visit your te;im's fmdhgs ;ind he.ir h0tv y0t1r thc;x,1ghts ~yhave evolved o,oer the

p.astftwwms.

wnat are you aM Y01.I'colleagues thinking an<1hearing? Has new evidence surttKC<I to turttter sl.C)portY'O\lf rese.irch!

Please k:t me know wh-cn you might be tw.'litablc to speak aiainl I would lov-e to do so~ kind of fo•llow--up.

Thankvou!

Kate

I

• Andrew SbmMut 1n2

•• Up another 120. Keep it up

REV0003024

I

P'lil Eddie Holmes 17:43

~ 28,951 now. Also 102 citation$ according to my googlc scholar page. Together we can do this.

Robert Garry 18.-07

■ I pointed Kate to the studles on the cleavage s.itc deletions. which ls supportive of important bits of the paper. Definitely seeing a bending of the curve in a good way on the Altmct,ics. I'm pretty

sure we'll be getting addition media inQuiries Riven Trump's bloviJtin,g. Mostly I'm getting c.llls on the serol~y le$ting.

Robert Carry 09:14

■ This is dis.appoii1ting • whats up with the F,eoch "scM!nt~ts? M Hello Dr. G.arfy,

•

I am Nicolas Gutierrez. science journalist for the French $Cience magi:izine Sciences el Avenir. I am writing an a.rtide about the origin of SARS·CoV•2. speciftcalty about the declarations of French

Nobel prire Luc "'1ontagnier, who said yesterday that U1e virus was probably mao-made because it had piec~ of the genome of the virus responsible for AJDS. I would like to ask you some

questions about your study "Theproximal origin of SARS-CoV-2" and why such a hypothes.is is unlikely. Arc you available for a short interview today{Skype. WhatsApp or phone)?

Best regatd!i-.

I

Nkofas Gutierrez C. PhD

Hey guys -just a heads-uphe<e(ptimarily for Bob ... ).

Y~ • I know that 1 have a ~special .. talelll for bti1)ging out the crazier in the crazy. It's kinda like a wperpow~r. just not as useful.

• Andrew R.ambaut 09 23

•• Nobel Prize Disease is a known thing.

We are going to do a proper paper on the origins and spread of the virus. Will keepyou all in the loop and fl5kYQU -illl to be on it. Quite frankly everyone iswelcome to be on it.

I just can't copewith the bullshit anymore -the Cambridgeanthropologists are now s.aying they are daring it to Septemberaod saying it originated in SouthernChina (presumabfy their RaTG13

outgroup).

Robert G.arry 10-Sol

■ Bravo Andrew! All in • Let me know what would be usefulin term of somespikestructural pictures. cleavage site • rbd interactions etc.

By the way just did the Freoch interview-it's possible I was not exceptionally kind to Montagnier.

REV0003025

httpS://www.resear-c:hgale.net/publtcalion/340100582\_WUHAN\_ COVI0-19 \_SYNTHETIC\_ ORIG1NS\_ANO \_EVOLUTION

Here's the link to the OC\Vpaper that Monbgnier thinks is wonderful • my head started to explode about a page or so in (but go figure I had the same ,espoose when I started to rea,cl Harry Potter).

• Andrew Rambaut u..33

•• I think this may be Ff'eflch post•modemism. RCl.lriously. characterizing the 9 SARS genomes stt.JclieQ whole numbers: the -Fibonacci numbers-.R

these digital W.'Jves here are c;:h<1r(lc:t'eristic:

Robert Garry ll'.S2

■ https.:Un.Jm03.safelinks.protoction.outlook.c;:om/?ur1•htti>s%3A"2F9'2Fwww.foxnews.com'62Fpolitics"2Fcoron.avirus·wuhan·l.lb·c.hina·compete•l.ls·

sou«es&amp:data•02%7C01%7Crtga,ry%40tulant.edu%7C8e15fc5745344661dk808<17e2e31306%7C9de9818325d94b139fc34de5489clf3b%7C0%7C0%7C637227337228352836&amp:s

data•TJUNUjpxiZygqeolaFMxS6KzNkT5HfDF95iul93941E%30&amp;res.ct'\l(!d-"'O

~ Fox News

Source$ be4ieve coronavirus outbreak originated in Wuhiln lab as part of China·s

~fforts to compete with US

The-re is increasing confidence that COVID-19 likely originated in a Wuhan laboratory

not as a bioweapon, but as part of ChiM's effort to demonstrate that its efforts lo

identify and combat viruses are equal to or greater than the capabilities of the United

States. multiple-sources who !lave been briefed on the details of early actions by

China·s govemment ;ind seenreh?vant materials tell F'ox News.

Coronavirus: Is there any evidence for lab release theory?

B8C News examines alleg,11tions th.It the coronavirus was accidentally released lrom a Lab.

• SBCNews

Is there any evidence for coronaviru.'i lab release idea?

BBC N~ws examines alk!gations that the co(onavir'us wasaccidentatty released from a

l•b. (67 kB)•

I

Fox· BBC it"s realty hard to tell the-diff

.-...I Kristian Andenen 1~57

r.l! We aregoing to do a proper pa~r On the origins and spread of the virus

@Andrew Rambaut -ple.ase keep U'i po<\_;ted -I'd love to be part or thi'i if I c.anbe hctpful {or even if I can't... -~ ,

Okay, so about the cur1ent news. Is there any reason to believe tllat they might be onto something. or is it all smoke and mirrors? @Eddie Holmes • any insights on the ChiM side? The main things

from my perspective-:

1. 8ioweapon and engineered totally off the table

2. If there is no engineering and no cu11uring, then it means that somebody magically foond a pre-formed pandemic virus. put it in the lab. and then infected themscl~s. The prior on that V'$

somebody coming into contact with an animal sourcc infc-clcd with the virus is as dose 10 zero as you can get. Humans come into contact afJthe time with SARS-like CoVs. but the-likelihood of

somebody finding exactty that pandemic virus and infecting themselves is very very low !make no mistake -if they did fmd that pandemic virus. then they wourdget infected if they grew it in

the lab• but the likelihood of thtm finding it in the first place is excttdingty small (or so one woold hope •otherwise.good tuck World avoiding futur't parw:tetnic).

3. But hctc-'sthe issue-· I'm still not fully convinced that no culture was involved. If culture W(lS invol,,.cd. then the prior completely changes -because this could Mlle happened with any random

SARS-l1keCoV. of which there ;,re very mJny So are we absolutely cert:J1n th.it no culture coufd have beeo involved? What concerns me he1eare some of the comrnents by Shi tn the S<.,Am

I

article (~I had to check the l<1b" etc.) and the fact that the furin site rs being messed with in vitro Yes rt fosesit but that could be context dc:pcndent Finally. the paper that wasshal'edwith us

show,ng a very s,mrlar phenomenon (exactly 12bp mscmon) 1n other CoVs has me-concerned https;//joumals pk>s.o,g/pl0'-'onc/art1ctc'1ds 10 1371/journal pone 0052752 -best sommanzed

here: http'#\flrolog1cal.0'1,/t/1dentificatioo-of-a·common--clefenon-m·the•sp1ke•prote1n·of·s.ars-cov·2/451/6

I really really want to go out there guns swinging saying "don't be such an idiot bchcv1ng these dumb theories -the president is deflecting from the real problems" but I'm worried that we can't fully

disprove culture (our Jrgument was mostly b.lsed on the presence of the 0-linked glyc.lns-but they could likely ~ily a diffe,ent role: https:l/www.nc.bi.ntm.nih.gov/pubmed/28924042). We 3150

can't fully rule out engineering (for basic rcsca,ch) • yes. no obvious signs of engineering anvwhcre. but that fur in site coo Id still have been inserted via gibson assembly (and dca,ty creating the

,cverse genetic system Isn't hard -the Ge:rmans managed to do exactly that for SARS·CoV-2 in less than a month).

• Jouma.l.s.plos..org; April171"-2020 .,.

The Roleof Vlral Population Diversity in Acbptation of Bovine Coronaviru.'i to N~w

Host Environments

The high mutation rate of RNA viruses enables a diverse genetic population of vir.11

genotypes to exist within asingle infected host. In-host genetic diversity CO\Jld better

position the virus population to respond and adapt to a divcrsc-array of selective

pressures such as host-switching events. Multiple Ile\"/ eo«>naviruses.including

SARS. h.ave been idcnrifie?'d in hum.an samples just within the last ten years,

demonstrating the potential of coronaviru.'ic-s as cmergc-:nt human pathogcn.'i. Oc-cp

seQueocingwas used to characterize genomic changes in coronavirus Quasispeete-s

during simulated host•switc;:hing. Three bovine nasal pmplcs infected wlth bovine

corona...iruswere used to infect human and bovine ... Show m01e:

O Vtrological

Identification of a common deletion in the spike pro(ein of SARS-CoV-2

The J)l'esence of inserts or deletions in consensus sequenc;:es of SARS·

or .-s 11rari<1nts

like coronaviruses is also observed in bovine coronavirus. also a memb~ of

bct.lcoronaviru-s (https:Ujournals plos.org/plosonc/articlc?

id•10.1371/jourrol.pone.0052752#pone-0052752-t002). For exi;lmple, ,1fter

passing 3 different naturally infected bovine nasal sample$ in different cell linc-s we

obscNCd the consensus scq1.Jcncc-s

of many ,,.iral samples acquired a 12-nuclcotidcinsert

encoding 4 amino Jcids (Sef, Arg. Ar ...

REV0003026

Atw.i<d.2020

April 17th, 2020 ...

•>ncbi.nlm.nih.go,

Att:unatwe cleavage of the bone morphogenetic protein(BMP), Cbb, produces lig<l'lds

with distinct develcipmentat functions and receptorpreftrencts. • PubMed • NCSJ

J Bio-I Chem. 2017 Nov24:292{47):1.9160-19178. cbi~ 10.1074/jbc.M117.793513.

Epub 2017 Sep 18.Reseorch SVpport, N.LH .. Extramurol (13 ~B)•

~ Eddie Holmes 18:23

,.....\_ Yc-s.Andrew. I'm in. Vtry happy to help. Haw the Cambridge anthropologists publ$hcd anything tlsc?

r"W Eddie Holmes 18:38

..... This is what I know. 1.China arc dchnitcty trying to tCWritc what happened.but Im pretty certain that's because they don't what a.nyonc to think about the 0tigin in any context rather than trying

to s:uppros.s the I.ab cs,apci theory. They've bcon nying to suppress this from day l in Ocx:ombcr l:oGausc th'1 word 'SARS' is.just s.otox:it to tho r,-;gimc. 2. Th"re are lots mor'1 Chinc&c senomc

sequences available but the ones that I haveSeefl don't provide any n~v insights. I am meant to be on~ paper ~bout the genetic diversity of theviru5 in Wuhan that they keep changing to say the

\'irus might have emetged somewhere e1se and I keep than,ing OOCk.3. I've not he.ird of at\)' cover•ups etc. Goo<ge Gao has led rnost of U1e sam~ing and gooomic work and he's too dumb to set

1.10.:isophisti<~ted theory. 4 Was Or. Shi from the WIV cveri doine GOF work in that I~"' I tfl<M.1ght

JII the reev~rc (')(periments were done in 8arit's tab? I thought Shi ju-st did

sequencing/ecotogic-i!lwork 5. I think the simplest expl(lnation is very likely the correct one: th<1t tile virus originated in b.:lts, jumped to <1n as yet unknown intermed'3te host (I dm't think it c~me

~raighl froltt bab). and thet1 jum~ to humans in th3t mar•:~l !>torlly before we detectt..>d iL The rnark,l ts jtr.,t too coinc.kkmtal to ignore. All lite compoutmt bils of this vim\ arc k>u1'l(Jin nature

and I sec no reason toinvoke lab escape whatsoever.

I'mv-ervconcerned that Ebnght/Upsitch/Bcrgstrom are going to try to use this to end GOF resea-ch wh¢n I think this is goirg to be tim~wt need it most.

~ KristianAndersen 1ss1

!IS Shi didn't do anyGOF\vortcthat I'm av,arc of 4 but GOF WOfk Isn't theconctrn htre. $1)e did A LOT orwork 1hat Involved Isolating and c-ultu1lng SARS•llkc viruses from bats tin 8SL·2) and that"s my

main concemirtg.scct'lario (we cite several of those in the paper • if y0u haw a look at those origi"11 puMcations. it's deflnitEiy coocetning work. no question about it • and is the main reason I have

been so concerned about the 'culture' scenario).

~ Eddie Hof mes 1':00

,...... Culturine inwh:1;? Why wookf culturire m;1teit more human adapted?The WIV eroupSeQ\lence so m.,ny of their viruses I just be anuM!d if they were doina experimeflts on one for which tllev h:td

no publish«! thesequet'lce. and ill their virus~ art from Yunnan. TM closest bat virus to SARS•CoV•2 from that lab is RaTGl3 wt:ich ain't th.lt clost. RmYN02 • vA'lkh isnot from WIV or anv lab h

Wuhan • is a bit closer to SARS·COV·2in most of the gcnorne. we h.avea mini sci.Ce sample<1fbat virus in nature and al/OOSt none rrom Hu~t we know cnacpeoi:i1c do get r..atorally spill-over

intected by bat coroo;wiruses. Surely this ro.,te istar. far mere likely th;m the IJb esQpe scen,nio?

llfllilKristian Andersen 19:02

rl! Scre<-nShol2020 •

04 17 at 16.02.10.png

I

... EddieHolme:s 1,:03

~ And RmYN02. a bat from nature.also includes insc-rtions at that site.

ti!alKristian Andersen 19<>.3

PD Here are iust fot.r e)(,:1motes of some of the culturing work that's concerning

ttt,ps:flwv,w.ncbi.nlm.nih.gov/pubmed/24112901

ttt~:Kwww.1,cb.nlm.nih.gov/vut>mcd.120567988

hltps;V,w,w.ncbl.nlmJ\ih.gov/plbmed/29500692

tittps:,Vwww.ncb.nlm.nih.gov/plbmed/26719272

•>ncbl,nlm,n!h..go,

Isolation and characterization of a bat SARS•like coronaNirus that uses the ACE2

rcctpto,, • PlbMcd• NCBI

N.1tvre, 2013 Nov 28.503(7477).535·8, doi: 10,1038/nature12711. Epub 2013 O<t

30. Research Support, N.I.H., Extramural; Research Suppcrt, Non•U.S. Gov't; Rtscarth

I

SVpport, U.S. Gov't. Non·P.H.S. (13 tB) •

69&1::i&i-S

REV0003027

I) ncbl.nlm.nlh.gov

Angiotensin--convetting enzyme 2 IACE2) proteins of different bat species confer

variable susc.epHbmty to SARS·C.OVentry. • PubMed • NCBI

Arch v;,01. 2010 Oct.155(10),1563•9. doi, 10.1007/,00705·010-0729•6. £pub 2010

Jun 22. Resea,ch Suppo,t, Non-U.S. Gov't (13 kB) ..

I

I} ncbi.ntm.nlh.g:ov

longitudinal Surveillance of 8etacoronaviruscs in Fruit Bats in Yunnan Province, China

During 2009,2016. • PubMed • NC8t

Virol Sin. 2018 Feb,33(I),87-95. doi, I0.I007/sl2250-0I8-00I7-2. £pub 2018 Mar 2.

(13 kB)•

I

I} ncbi.n1m.nih.gov

Isolation and Characterization of a Novcl Bat Coronavirus Closely Related to the

Direct Progenitor of Severe Acute Respiratory Syndrome Coronavirus. • PubMed •

NCBI

JVirol. 2015 Dec 30:90(6):3253-6. doi: 10.1128/JVl.02582·15. Research Support,

N.LH .. ExtrJmural; Research Support, Non•U.S. Gov't (13 kB)•

I

RmYN02 has a rearrangement around that site, but it's not this type of insertion. I ag:re~ with you th.at it's evidence for 'this alJ occurs naturally', but it still docsn'I put a nail in the coffin of that

theory

r"I! Eddie Holmes 19:0S

~ Let's face it. unless there is awhistteblower from the WIVwho is doing to defect and Uve in the west under a new identitvweare NEVER going to know hai>pened in that lab, Never.

tlr'MIKristian Andersen 19 06

&I'!! That's my lhinking too. But tt\al's why I'm a little wonic<I about t~e 'cables'· because is it possible that they might have something? I'm putting all of this to typical Trump BS smoke and mirrors

(and just plain idiocy}. but I'm not quite willing to d~ on this hill.

F-. Eddie Holmes 1/J:48

,....\_ Yes, rm not dying ori a hill either.

Robert Garry :21.48

■ I pretty sure that •a proper paper on the origins and spread of the virus• can be crafted that will not result in any caSU.1lties. And I agree with Andrew that the load of BS is getting pretty hard to

take. To Kristian's point 3 -could this • have happened with ;iny random SARS•like Co\/" from passage in culture -seems pretty unlikely-that random bat CoVwould have had to be Yery dose

[>99%] and H-.en by so,ne astrooomical chance gtmerate<I a precise pangolin CoV•lfke ROB across a pretty broad st,etch • that's not 10 mention the 12 b.tse pair out•of•frame in~rtion that adds

PRRA. Point taken that there rrufycould be inte«:epted "cables," but of what? We already koow that the Chinese went into deep cover-up mode for example by shutting down the market and

destroying the •evidence; It's possible WIV char,3cterized a NCoV· 19 isolate e.arlier than the lirn noted cases in Dec I svPf)()Se. but that doesn't make WIV the proximal origin of the virus. It's ;1lso

PoSSibfe that the Chinese knew about a new respiratory virus s~ading before tile lish maricet case-s • this would be bad public health but consistent with out cryptic human spread model (giving a

somc,.-.ihatm0<c nefarious spin on cryptic). As Kristian noted they did a lot of science remarkably fast.

I

REV0003028

April l8th. 2020 ,,

.,. Eddie HolmM 03:0S

~ I don't think China co,,:~d·up at the f'i~h m;,rket. R.athet, I bclic'Vt lkat the publk:health ofhdah just did what )hou)d h.tve alld nuked everything without thinking about animal ~mpli~. Thty ju)t

wanted to stamp out the ovtbre;:lt. To me tticre~ too bng ,aseries of irnplausible events to $ug&est inadvertent escape via l~b passage: (i)TheShi grovp sequence and pubfi~ their bat viruses all

the time. but r,Ofle of these are theobvious J><O&tnitOf of SARS·CoV· 2. It seems impfobable to mt that the one that escapedwas not one that they had seq~oced alfeady. Andv.hvdo lab P1Ssa~

on 3 virus that to you h-3Venot sequenced? (ii.) If there had been a lab csope then we would c.xp«t an initi.aloutbrezik ,lt the WIV. Where's the cvidenro of that outbrNk? Hew., coo Id this be

hidden. That group were ;ilsowell enough to sequence an e;1rly genome of SARS-CoV-2and RaTG13: (ii) What are the odds that 1he virus the,1 first appears in the very place• a v,ildlife market •

whee-ewe exactly expect a natur"al species jurnp to OCOJf? Why not in a fa( mo,e crowded pla.ce in Wuhan of which there are many: (Mwhy would the Shi group then publish RaTG13 th3t would

ooly heto ooint the finger a1 them?Makes no seme. (tdittd)

Robert Garry CX137

■ Good ooint Eddieabout the public he~lth official~ doing theif job • was k>okingfrom my own self interest.

• Andrew Ram.baut OJ,•2

41111■ I ag(ct with Eddie here • oocc vou ha~ ruk.-d ou1 the ,..in,s being anything odlcr than a virus di(CGt from a wild bat. the whole lab escape thing bc<omcs a much more complOtcd a.nd implaJslble

sequence of eve11ts th3n the direct jump.

(when I say direct~ I aiil more than happy to have ao irlte,n,edia.t~ hos1 fadlitatiog tl\.iltjufl'IP it b jt.JStl'tOt required as ,n evolutio11c1ryinter,"nCdia1e).ted1e'd>

IshoUd s.avth.it the p.1pe< I was $ug,gesting woutl not bckle these hypotheses (cdW!fthan to te•ite<3te the date estim3te fa the root of the tree • th.at has ~ready been estimated}. It ic.more to

tackle the shit from Forster and other-s.itdit~

•

r-'I Eddie Holmes CM:12

~ VERYhaw, to be on a paper that nuke!> Forster. I watcht"d h.ls YouTulx Interview alld it's llkie-SOfl'e sort of Monty Python parody. He's probably been locked In his room at Peterhouse k>r the last

25 ye.a rs and only coo.es out for tiffin once i day.

Robert Garry 09:32

■ -What arethe odds that the virus thenfirstappe.irs in the very p~ce • awiklllfc market-wherev,e exactty expect a natural specits ;ump to occur?Whynotin a f,u more crowded place in Wuhan

o-fwhith there aremany:" This is the one I stillCiln'tget mvheadaround.

f(om ;he WU<J: The e~rliest known persoo with symptoms was lacer diKOVered to have fallen ill en 1 December 2019, and th.atptfSon dtd not have visible C'Onnections with the l~tcf wet

mairket cluster.f3S8)l359) Of theearly(.luster of c.asesreported in December 2019, two-thirds were fo1mdto h;ive a link witB the market..l360ll3611(362) On 13 March 2020, an unverified report

from Uu> South Chirta Mornir,g Pou t.usgiQ<tod:i, ~~~ t~I b:iockle) 17 NOW:mb~r2019,i,, :eSS·~~r-old frmn Mubf.tiprovinct, m:ioy h:wv b"9'1 lh(!ohrs:1.()631(3641,

So I interp<et this on fKe v.lue thJt tl"e wild m;Jt1cetms not the origirol source d the virus. But whJt? A super-spreaderevent? M independent introduction? Observalion..11 biJs -this was a logK.'11

place to bok for cases? An tlaboratety schemed rM ht(ting? AllO( none of the above?

Robert Garry tt :3A

■ Looked at tM"voutube •vc-swrvbad • not savingl could do better. whxh is why Kristian forbids mefrom puttinephvkleenic t~ in anypai,er. It's sound a6'1icc .

...aKristianAndersen 1158

Ira totally agree with Edd,C on all the points• as we discus.sed on Zoom ~ ... I wspea: it's all smoke.a,d mffors, but the concerns I highlight alxm, rebtc to ex,actty Andre-w's comment• "onceyt>tJ

have ruled out the vlro.sbcil\g anything othtr than a .,,;rus d.-Cct from awl Id b.>t•.I tota'ly agtee. b.it the Issue is thlt wN!c our c,.,.l~fonceagalnst ci-elne«il"\g kvcry(vcl")'!} strong, our cvidc,ncc

,1g;1instculturing isn't llhe p-esence of 0-li™ed glyc.1ni probably controls activity of the pol)-t>o1sic site ,mdisn't a mucinlike dom.1n as we describe)• this is especi.:1lly true gi'.•en the paper showing,

12bpinsertion and the newpap(fs showing that the furin site is being messed with in tissue culture. 811t I agree with atl the pcints that Eddie is rraking • if this had accidentally infected somebody

~t w,v. whv u~ neck would the OUlbteak only sun (Of be detecte(f) al a wet .,,...,v,..,

mask.et':"''''""' "'~into <O0t.Ktwill) a t01, 01 a,,1ma1scanyiog SARS·likt viruses).

~ EddieHotmes 17:03

,...... lntereiting about O/G. Keepw;,tchin:g I guess. Just to k>Uow•up and e.irltef point ~The earfieit known per$0n with symptoms wasl;iter diseo'leced to h;Ne falen i1ton l December 2019. and that

~''°n dkl no! h:ivo vklhl• ~nn..etiot$". W11rolhMt.i symptom< on D« 1 rfr.'.lilly COV10~19? Do""°' know tlul lhfydidl'l'l tu~ eor.t.:aclwilh tc>i'nOOnehow wodced :Ill tho, m.:trkot? U't. ~n i.mJ)(lf"t~l'll

data point. but I would also arguta vatueone.

... Eddie Holmes 17:16

~ I am enjoying ou, 2nd•wavc on AJtmctric.

~@

.£.1 res,fy 3 ~ars ago

REV0003029

Robert Garry t 7-18

■ True enough· as is the-possible case-hom mid Nov. If I had a nickel for e~rv pe-t!.Onthat :said they thing they had COVID•19 in Janucn-y or eatlier ... well I would ha.v@' a c.oupll!!' of dollars.. But srill

it will be interesting to test 'Some of these for antil>odies.. Yes -'l"tcll over 30K now-can't s.cchow #1 could be all that far ahead at this.juoction. (edited)

R.obi!rt Garry 1s.1a

■ l"m a little dis.appointed my smackdown of Montagnier, who was pushing the HIV rccombi.nant engineering memc. got s.o warercd down. Maybe it was just the trat1'Slarioo to eheue e11?i,,t

so e. de , o I c, 104goose Frerich.

r, Eddie Holmes ta:S9

,...\_ It is s.o like HIV U,ough, A buoch of conspif'.KV theories over its origin that were resolved throogh more SJmi:,ling of widlife,

AQril lli'th. 2Q20 ..

• Andrew Rambaut 04:1CI

I

•• Also UkeHIV there will be those that just continue to spout nonsense but they ~viii be i~reasingly irrelevant.

R.obcrt Carty 09:.02

■ https:Nwww.ncbi.nlm.nih.gov/pmc /articles/PMC4:26S93 l/ (Nim!]

Very insightful • HIV corl'Spiracies used politic.-.lly to majot effect a:r\d wry damaging.

https://mbio..asm.org/content/6/4/e0t013·1S This p::1per mvking the rounds on the conservative underbelly of the Internet• cited as proof ot intentional/accident;il release of NCoV•19 .

.. mBio

The Reemergent 197? H 1 N1 Strain and the Ga in.-of•Function Debate

The 1977• 19 78 influenza epidemk was probably not a natural event,. as the genetic

scQuence of the virus was nearly identical to the seQuences of dcc.adcs-otd straiM.

While there .are several hypolheses that covld explain its origin. the possibility that

lhe 1977 epidC!mic resulted from a laboratory accident has recently gained popularity

In dtscusslons aboul the blosafcty risks of galn-oMunctfoo (GOF) Influenza -Ylrus

reseJrch. .as ;,n argument lorwhy this rese;>rch should not be performed. There is

now a moratorium in the Unitt?d States on fonding GOF research while the bencfrts

and dsks, including the potenti.rl for accidont. are analyzed. Given the importance or

this historical epidemic to on .. , Show more

5f,ph1 20!S

• Andrew Rambaut u.3e

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41111

■ Founc1number 3: https://dimcnsions.altmetrk.com/dctails/77699394#'scorc

~ dlmtns.lonu1tmct.ric.com

Report for: Aerosol and Surface Stability of SARS-Cov ..2 as Compared with SARS·

CoV•t

In the top 5% of all research outputs scored by Altmetric

April 19th, 2020 .,

https://app.dimensions.ai/dis:cover/pubtica.tion?orde,

.. altmet,k

• app.dlmensions.al

Dimensions

Re..imogining discovery and access to research: gmnts, d;ita-sets. JXJblications. citations.

clinic.al trials. patents and policy documents in one place. With mor"e than 100 million

publications. and l billion citations freely available for personal us.e. Dimensions

provides studerits .lnd reseiJrchers uc.c.e5s lo the dab and information they lleed • with

Robert G.any 1 HA

■ I find myself rooting for POTUS to say more dumb stuff abollt the origir.s of the-China virus. po,ss.ibly poisoning Sino-American tela.tionships f0tdec..ad~. Does this make me a bad pe-~on?

r-11 Eddie Holme5, 17:2:3

,.....\_ Keep rooting Bob because il is. working: nQ'l,·1 at 31.175. What is #1 though? lt'S c:~arly somethrn,g over which Twitter has gone mad.

I

April 20th. 2(120 "

KristianAndersen 13.lS

l reallvwant to know who's #1 too ... Gotta be quite a wack'I l).lpet!!

Separately -this is from Ed Yong -any idea? •0o vou rec a If a l)(lp,er or (lsure recently show ins toot bats don't octualrv harbor mOfe viruse5 than exu,ected for a sroup oftheir sve,ros;ty?"

Rc~rt Garry 13:53

April 20lh, 2"Cl20 ..

• Not s.urc that's the rlgh( word -maybe somcrimc about the number5 of bat species?

~pnii: ..

~~--

it:'11'~4

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'OTl -===-..-..=.::::.:::--..::--...----~

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.,.\_,..\_., \_\_\_\_ ..,\_ ..,--~-...

hrtps://www.sc.icna::mag.org/ncws/2017/06/b.3c:s•1callrdo·h.1rbor·motc--dangcrous-vi,uscs·othcr-spccics

REV0003030

, Science IAAAS

B:ih; t"eally do h,ubcr more dangerous ,.,iru$,e:;: than other !ipecies

A n@w s.tudy is se-t to end a long-running deb.ate amon& vfrus. ecologi.sts

Jt.m2bL2017{192k.B] •

htlps;/l-.w,w.oature.c.om/;,rtit.les/n;:iture2297:5

I

Nature

Host and viral traits predict :zoonotic spillover from mammals

Zoonotic viruses, manv originatins in wild mammals. pose .J serious threat to global

public health. Peter Dasuk and colleag\Jcs c:reatc a comprehensive database of

mammalian host&.#8211:virus rdatfonships. which they ;;,nalysc to dctc-rminc

patterns of virus and zoonotic virus distribt.Ation in mammals, They identify varioo,s

factors 1hat influence the number and diversity ofvirmes that inkct a given S?('c:ics

as wall as facto~ that predict chc proportion of zoonoric viruses pct s,,cdcs. In doing

so. they identify miJmmalian species and geographic locations where novel zoonoses

arc likely ro be found.

Kristian Andersen 13-Sb

Yeah • thos.e arll!: tht PREDICT HudiM and they baskally show the oppo!dte of what Ed's asking.

Robert Garry 1.11-00

■ I'm thinking the bats are not special bit came from Da'SZak. From the KK article-: ''Wang has spent many yf'ars arguing whether bats are special wlth Daszak, and 5.lyS h's e.xciting that the new papet

I

comes from his groop. Daszak. meanwhile, is gracious in defeat: -unfa was right 311along." hes.av-;:,"

Robert Garry 1-11;11

■ https:l/wwwnc.cdc.govlcid/article/11112/05·0997 \_article

Emerging Infectious Diseases journal

Host Range and Emersing and Reemerging Pathogens

An updated literature survey identified 1.407 recogni~ed species of hum~n pathogen,

58% of whid1 are 2oonot-ic:. Of the-total, 177 are regarded as ieme-rg ... (132 kBI •

EMERGING

INFECTIOUS

DISEASES

,r...1.....iJoom11 .. m,mcw,,;.,o;,,,,,1no1,

Mig.ht be ~per by t.hi'Sgroup Woolhouse. (cd4ted)

Robert Garry 111:st

■ https:/lwww.sc~enceopen,com/:search#('o,der'-O\_'contex.t•-fcoUection'-rid'-'d6ba10ea-809d-4f28-96b9·d2ed47Sec319'\_'kind.--OL0kind'-t 1L 'v'-3\_ 'kind'-77)

So 111 may nol be a COVI D p:.per

Kristian Andersen 1 S: 10

lnte-resting... If I sort all papets on that tesource-, our papil!f is :11!1: htttis://'www.sciel'lceol'@"n.com/se,arch#c:ontent

So # 1 may not be a COVI D p.1per ~ril 20th, 20:20 ..,

Kristian Andersen 15:to

lntcrcs.ting ... If I s.orta.IIpapc<s on that rc-;ourcc-. our paper is. :ill: https:Uwww.sciCl'lccopcn.com/scarch#conten(

R.o~rt Garry l 5:"46

■ Ag,cc -and that is ,.60 million papers compared to a measly 14M. I think Altmc-tric might be-screwing up. \'Vh.,t scfcntiflc paper came out c1ftcrours in midMarch that got more •attention?" I can't

think ol one.

• Andrew Rambaut 1.S'-49

•• SiJme on this website: htti:,s://app..dimensions.ai/discover/pu,bl.c.Jtion?cJder•arunetri,

.. app.dlm@nslons.al

Dimensions

Re-imagining dis.covery .1nd .Kccss. ro research: grant'i, datasets.. publications. citations,

i:;:linic:al trials, patents t1ndpolicy doc:ume-nts in one place. With more th,:1n 100 million

publications and 1 billion citations r~v available for i:itfsonal use. Dimensions

provides students and researchers access to the data and information they r'W!C<I

• with

I he lowest l>arricrs possible.

Kristi.an Andersen 15:"19

Wewin!l

I

REV0003031

April 20th,2020

v

Robert ~rry lS'.Sl

■ OMG THAT IS 109M PUBLICATIONS.

r'li Eddie HolmH 18:30

~ Catching up. The bats arc not special is a new paper by Daniel Streidr:cr in PNAS.

r'li Eddie HolmH 18:.36

,-...; I've sprot most of my waking hours over the last w•cck trying to work out who might be #1 and I can't ftgure it out. So. those websites make sense. Perhaps we can contact Altmctri<:?

Robert ~rry 2~"41

■ "The bats arc not sp~lal is a new paper by Daniel Strcickcr in PNAS."

Does this mean I can start taring bat soup .again?

ii!lil Kris.tbn Anders.en 22 55

~ 11vou want to go down a rabbit hole: https:Qprojcct•tvldenc,e.github.io/

{Disclaimer • all concerns they bring up we have already discussed and considered, They also make a number of logic.al mistakes, but hey},

r"I Eddie Holmes 23:38

,-,; I assumethat is Ebright et al.? Pathetic that they want to remain anonvmous.

llil'lalKristian Ande,sen 23:56

~ Ah.yeah. didn't think of tllat • coufd be him

I

Aptll2 ht. 2020 v

e Andrew Rambaut 00<12

Al■ Someone uploaded this document and then deleted it again (Github tracking everythin.g of c.ourse).

Worrl Oou1mN'lt •

II

II

Response to Proximal Origins paper edits April 8 ..

WordOooJITlffll

Tl<a-0.•-• ...... --°'1'1'" .. Ul:J.GV.,1•..--1:.»•11o

·---~ .... -""".-.-... \_,, .. ~..,--#;1.-

.........\_...,.. \_\_\_\_ ~•--..---.~-lo ......

--••<.t,,\_.,.,.,\_ \_\_ d...W--•-.,.n,A,n,t-iloo

U~\''1'\ \_\_ ..,..\_.,...,..,...... -~--••

.\_....,-~\_,.\_,..,....,...\_liCfCll..\_,.... \_\_\_ \_\_..........

\_\_\_\_ ..,.......,,.w.,.

\_\_\_,,\_

....--CJ:1'0.1..i....,.\_~ ....... --... .-• .--.

-~\_,CWl\_\_ \_, \_\_\_ ,.,. .. 1o,..,.o1•--..,--.... -,..

'DrKarlSirotki

a.,-1 Kristian Andersen lf):26

r.B People have too much tm\C on their hands ...

I

Also, we gol oor llrst PubPeer Wm surp,-ised he didn't say HIV): https://pubpeer.com/public;1tions./8319A\3E717F8C86789S8SSCE67O63

■ pubpeer.com

PubPeer • The proximal origin of SARS•CoV• 2

There arc commems on Pub~er for publication: The proximal origin of SARS-CoV-2

(2020)

Robert Garry 10-sa

■ I savlet~ {myc;oplc1.sma hopefully Sirotkin (at NIH at one time) g()ts his letter

critiC$ pile on. Probablynot worth responding on P1,11:>Pcer cont~minated cell lines• why didn't we think of that?). l:M.it

in a joumal somewhere. How else [except for having Trump dirtttly tweet about the papet) ace wegoing to drive this Altrnetrk score past 40.000?

~ KristianAnders.en,11·37

&I! IsPubPccr indC.l(cdbv Altmetric? It should be '-4.How in the name of the lord a myc:oplasma co·infcction would lead to insertion of a furin site into .a vil\ls I do not know -thal's not cxaetty how

recombination works· but at least he didn't suggest HIV, so it's a novel idea. Points for that.

Robert Garry 11-5.9

• NIH might consider sorne 2-fac.tor autheoticatfon for Blast as well • keep that tool out of the wrong haods.

r, Eddie Holmes 1843 H ii I+ifI

,..... 2·factor authentication for Blast is a g,e.at ide.l. I also propose that all human geneticists go through an intensive period of de•netwcrldfcation befo~ they are.allowed to we-•.:-;..\_---~ \_, .

~ Kristian Andersen, 1a.s1

~ I think 3·fac:tor authentication might bC'better· 1, Password, 2. Temporary code. 3. Ptof. AAdC'rsen's approval. That should work wC'IL

Mal Kristian Andersen 22'.44

ID It's an eel!! Eel!!!

Doh.

Em.ail fromSl.1CtforGmsi •

SARS•CoV•2 • Horizontil tr~nsfer from As.ian eel /\pr21>t. 2020

From Bradley Porter (No content}

r-11 Eddie Holmes 23:42

~ I was just about to send that to you!!

He's got apoint though ... the Loch Ness monster t\Jrned out to be eels.

(iv 0

r'lil Eddie Holmes 23:S9

~ I was diSJwointed by Loch Ness. I was sure it was scuOO camels,

I

REV0003032

~ Kristian Andersen 0005

tB I believe that theory tS5till beingexplored.

Robert Garry 01-.11,1

■ Seu~ camet.s is defmitely tt thing. It's in E.gypt. where they have fn.iit bats. IIRC camels do have a little bet;icoron;:ivirus. Like Fox news said about WIV the dots are fallingin place. l'r<fittd)

~.ong •

corddNeck.l:>&""""

A

r-111Eddie Holmes 18:29 April 27th. 2020

w

,.......\_ Charming.

Screen Shot 2020-04-28,n 8.28.47 am.png •

-·---IM'

.

~ Kristian Andersen 18:33

mt! Okay, traitor. so how much orethey actually paying you? I think they got me kinda cheap. so maybe I could have made a better deal.

r"I EddieHolmes 18:41

,-.... Hc'.tl/c-a cent. although I did ge:t that preslde:ntial plate and a woodc-n elephant from Yunnan. In many waysI found the: following cm.iii cvc-n morn disturbing:

never paid~

Scre4:-nShot2020-04·28 .it 8.38.30 am.Pfli: •

\_\_\_\_\_ ..,\_

.

\_,\_\_\_\_ .,\_\_\_\_\_\_\_\_ \_,.....,..

------~.. \_\_\_\_\_\_\_.,

---·-.,. \_\_

il!tiil Kristian Andersen 18A8

I

el! Well, t can't really blame-these pec,ple • I mean, I live in a country where the p~ident suggested we treat thrs by drinking bleach. And blasting it with UV -inside the-body, or maybe outside with

very strong light''.So compared lo thal John'-sa fucking genius• I mean. BLAST "'adv<inced stuff.

P"'I £ddie Holmes 18:SO Ap'1127th.2020 ,,

,-. Hoocs1ly. about 80% of daily inbox is composed of press (e.g. Vanity Fair today). threats ana accusanons. amazing 1reatmcnts based on things like bathing In the: natural essence of rhubarb and

goat's piss, nutters who think they hJve found something profound, ,lfld corispiracy theory loons.

11f!ti1Kristi.an Andersen 18,SS

rB Sounds remark.ably like my inbox ... The good thing about that is that I can pretty much just ignore everything coming in and go dririk beer inste.ad.

F"II Eddie Holmes t 9:00

,.....\_ I drink to that.

April :2"81h. :2"020 ,,

Robert Garry ~

■ https:Umercol.a.ftleburst.com/PDF/ExpertlnterviewTranscripts/lnterview·FrancisBoyle•SARS-COV·2,pdf

I get shil like this -same old same old -email started oot calling me a traitor.

https://naljagists.com/zairec-bola·vi,us-originated·from-us~bio-warfare ·labs-in•west Jf rica-ameriun·protcssor-frantis boyk!·blows~whi-stlc/

REV0003033

REV0003034

~ EddieHolmes11:31

,....\_ This is better: https:Uwww.smh.rom.au/poliric.s/feder4l/ausu-alian·intelligence·ofli<:iJls·have·no·evidence·of·'NUhcm·lab·link·to·c.orooaviNs·20200429·PS405i.html

The Sydney Morning Herald

Australian intelligence officials havt no evidence of Wuhan lab link to corona'-lirus

Australitta intelligen.:e officials have foond no evidence t~ coron,wi"us st.1rted in a

Wu~I\ l~bor.:itor'y. 1p:irkins Prime Mini!;ter Scott Mo.-riron to pr'iv:itely di1mi~$ the

theOf)'.

A1><29<h. April ?9th, 1020 .,,

2020(115kB!•

I

llflil Kristian Andersen 18:58

fB Thnt's a m good one. I said :is much ina Twitt Of' convcrsarioft ycstcrd.1y • unless specific datt, Is prescmtcd showing thatthCN! is a connccriOf\ to a bb. this discussion is over .

.!Iii Kristian Andersen 19'.13

E£I Anybody heard about this l~cly lis?

£m..1ilf•om Slack fo1Gm:lt •

Fwct question from The Times (London} Apr 28th. 2020

~rom K.ris:tfa.nG. Andcrscl\ (No cootcnt)

I

REV0003035

r'lil Eddie Holmes 20:21

~ I've not heard this. They can't have any more data than we've looked at. I wonder whc<e it will be 'puDlishcd'. A large pri0< on this bcin complete bollocks.

r'lil Eddie Holmes 23:21

~POF•

• ;;;: 28 Ap,;I 2020.pdf

Coronavirus Austral.ia: Chinese scientists

linked to virus probe studied live bats in

Australia

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a, ~jo;.,i,, A,...\_.,..\_.,

..... 1.,-.at"..,...,."'""'""'""'·

Sorry. the cover is the best bit:

April 29th, 2020 ..

I

Such shit. Thi"i guy did ii bit of his PhO in Au5trali<I then went back to WIV.

li'I\II Krtstun Andersen 23,25

In Haha. Former student of yoors? I thought tor a second you'd be the one on the f-rontm1ge • Eddie "Bat Man· Holmes. It's got a nice ring to it.

And this is fucking unbelievable • the stupidity of people and j<kJmalists these days. ..

r,i Eddie Holmes 23:25 April 29th, 2020 ..

,-..; l"d be the "Twat Man'.

® &I

April 30th, 2020 ..,

~ Kristian Andersen 01:29

~ @Robert Garry foryo1..1: htt~Ntwitter.com/nextstrain/status/1255708669091S73760?s"'21

• Andrew Ramb.aut00--49

•• This is just going on and on.

This .lrtide just flips back and forth:

https://www\_newsweek.com/con,!'OVetSial•wuhan•lab•experir"rlents•that•may-havt•started•coronavitus•pandemic:•1500S03

CJNewsweek

The controversial experimenls aOO Wuhan lab suspected of starting the coron.avirus

~ndemic

Atter reporting that Covid-19 occurred naturally. U.S. intelligence modifted its stance to

SJYit might have leaked from a lab,

I

Af',f27th 2020(8l9t!B)•

REV0003036

r'li £ddie Holme$. OS:~t

~ I have to agree with Ebright on PREDICT though. We anooycd that some people have pointed the f'lngcr at the Wuhan CDC and my mate nan. There arc no bat samples the.re .. they all go srrnlght

to Beijing. No passage ,vork is done at all. Plus. Tian was tested and is SARS·CoV-2 negative and has no antibodies to it

Robert Garry 08:ts

■ @Robert Garry for you: https:Qtwitter.com/nextstrain/statuS/12S5708669091573760?s•21 i assume you .arc holding back on submitting all of the weird ltalian·Chinese•Gcm1an recombinants

with the eelcrawf,sh inserts. (cditC!dl

I

~ Kristian Andersen 14.32

~ So mvch 001I.shitagain.I Mv~ decided that I om going to die on this hill, so 1'11 talk to a few reporters and try to beat some sense into them. NYT had an artide e<1rtiertoday (I talked to them a

couple of weeks back): https://www.nytime-s.com/2020/04/30/us/politics/trump•admir\lslrclt'io1lninle11igence•cor01,avirus-<:hirkl.html

i!; The New York Times By Mart,; Mazzetti, Julian E. 8.:imes. Edward Wong omd Adam

Goldman

Trump Officials Are Said to Press SpiE!s to Link Virus and Wuhan Labs

Some analysts a,e worried that the pressure from senior offlcfals could distort

assessments about the coronavirus and be used as a weaPQfl in an esulating battle

with China.

Robert ~,ry 15 37

■ Keep at it Kristian• I will take the rebound as needed • looks like the WashPost is also following up with a story.

~ Kristian Andersen 1{>.01

~ Yeah. Paul Sonne? Just talked to him.

I pinged Ed Yong about potencialtvwriting something· I really would love to see him write an article about this as I know he'll do it right

Robert Garry 1&19 April30th. 2020 ,.

■ Yes• Paul Sonne. Tricky to stay in the science lane and not venture to much into the political brea<h. Think it's fme to comment that science should transcend paitics. but I always been rather

naive or call it aspirational about such things. Yes • Ed would do it right.

~ Kristian Andersen 16.25 ra Indeed. In fact, I ble\•1up the c;;IIIwith the White House p,anet I'm on earlier this morning by suggesting fh.."lt maybe we .~sa country should stop bl."lmingothers for our own failures ;md instead

focus on making sde.'ICe•based decisions to get in front of this disaster • and that maybe we could wfite a letter to the president about that. I doubt I'll be invited back.

Robert Carry 1643

■ Kinda $hocking. to sec the "WIVo, China COC released this thing on the world~ coming from both the left and the rig.ht. Trump has a few adlli$0r$ that kr\OW exactly how to create a

distraction. led tt'd)

• Andrew R.ambaut 18,12

.a■ It really doesn't help that the Chinese are tryir.g to suggest thal it didn't start in Wuhan {or Hubei. o, even China}.

~ Kristian Andersen 18:23

~ No. The Chioc:.se bl.ami,,g U'le Amedcans is about as ur1helpful as the Americans blaming the Chi1,ese.

r"li Eddie Holmes 19:08

~ Ye-s.both a~e in the wrong. For China. I think it's a large part about s.wingface and the perceived shame of being tht place where the outbreak started. It has seriously weakened their global

standing so they arc rrying to change the nar,ativc to sow uncertainty around this.. Plus the CCP arc dearly c.ontrol freaks: they have to concrol every message. The word 'SARS' is just toxic to them.

The China CDC are gui1lyof bungling the e..'lrly response to this ... but that's cock•up, not co~piracy,

I

Really interested to sec this Norwegian/St. Gco!'ges thing.

... Eddie Holmes 19:23

,-. Coronavirus US live: intetligence report concludes Covid• 19 was not ·manmade or genetic.ally modi6e<r https://www.theguardian.com/world/live/2020/apr/30/corooavirus•us•live·lederal

guidclines·social•dist.lncing cxpirc·trump•cuomo·latcst·ncws•updatcs?CMP20$harc\_btn\_tw&,page•with:block·Sc1b41b68f08f76ffc19f175#block·Sc~b41b68f08f76fk:19fl7S

(8 the Guardian

CoronavituS US live: intelligenc:e rep0rt conc:lude:s Covid•19 was not 'manmade or

genetically modified'

Offtce of director of US intelligence releases st~temeot Jfter Trump reportedly asked

officials to inV1?srigatewhether virus wa$ made in Chin¢$(! lab

Atw301h.2020 (85 kB)•

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r'I Eddie Holmes 19:36

,-... https:I/M-1W.btx:..com/ncws/WO<ld-us-canada·52496098

• BBC News

US intelligence debunks manmade coronavirus theory

US spies say they are still inve!.ligati,-.g the vitus otigirlS,as Mt Trump suggests it came

from a lal>. 174 kB)•

~ Kristian Andersen 19:43

~ Ye-syes, but our Great Leader sets the record straight with some clear language.

Screen Shot 2020·04-30 ,!JC4.41.45 PM png •

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What did PresidentTrumpsay?

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""""'-~IDr°""'-"

Ha..., ~.....,.t<>nJ-•-................ .

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