Twitter Thread by Billy Bostickson ■■&■ ■

Billy Bostickson ■■&■ ■
@BillyBostickson

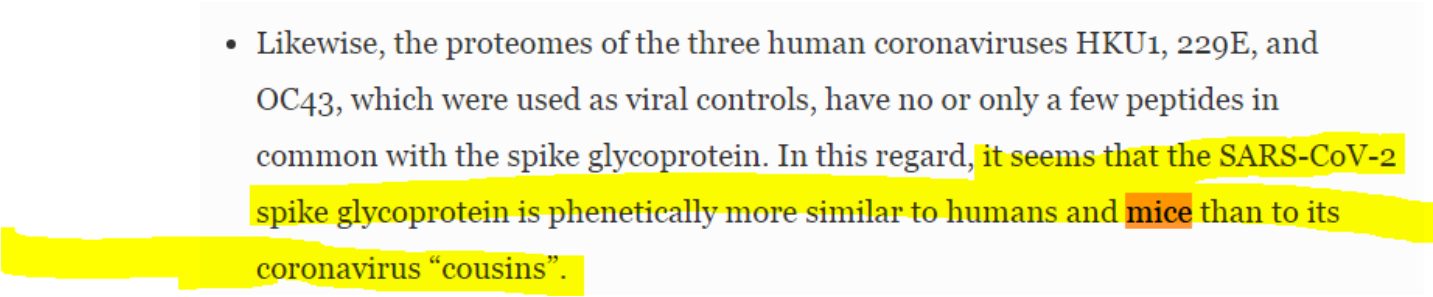
1. High Probability of serial passaging in Transgenic Mice expressing hACE2 in genesis of SARS-COV-2!
2 papers:
Human–viral molecular mimicry
https://t.co/irfH0Zgrve
Molecular Mimicry
https://t.co/yLQoUtfS6s

2. Must Read! Confirmation with supporting evidence via @flavinkins
https://t.co/NEf9HK6ReB
"ONLY place where this thing could emerge, naturally or Artificially, is by passage in HUMANIZED MICE"

3. Springer Article https://t.co/iGYJQ2s3T5

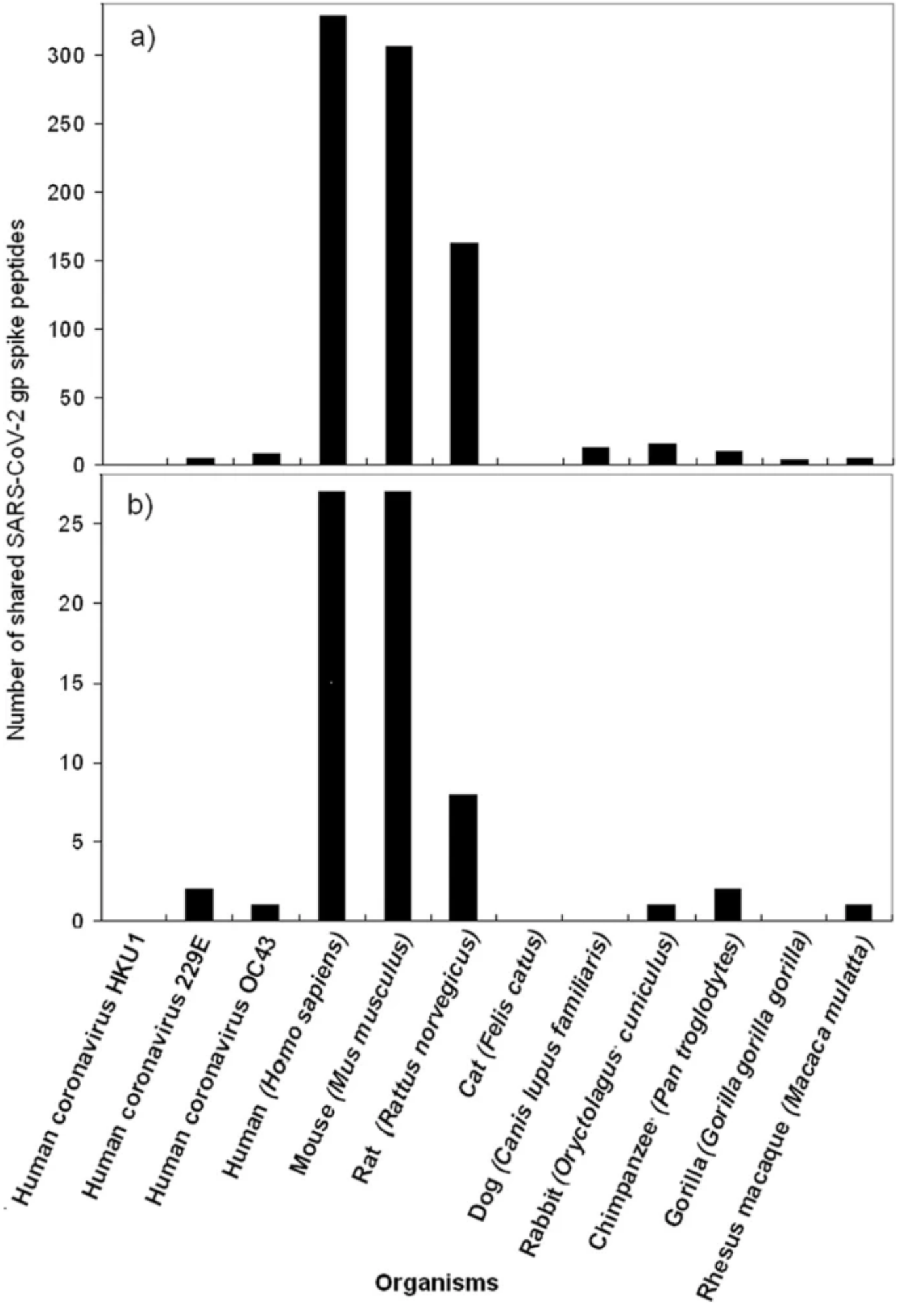
> The PEPTIDES again!
> "Such a peptide commonality is unexpected and highly improbable from a mathematical point of view"
> Molecular mimicry between SARS-CoV-2 spike glycoprotein and mammalian proteomes: implications for the vaccinehttps://t.co/yLQoUtxtv2
> via @gerdosi https://t.co/lsCv2j4gf9 pic.twitter.com/hdgM5KZd39
>
> — Billy Bostickson \U0001f3f4\U0001f441&\U0001f441 \U0001f193 (@BillyBostickson) October 21, 2020

4. Takeaway most significant quotes from Springer Article, burn this into your brain:
"Such a peptide commonality is unexpected and highly improbable from a mathematical point of view"



- Likewise, the proteomes of the three human coronaviruses HKU1, 229E, and OC43, which were used as viral controls, have no or only a few peptides in common with the spike glycoprotein. In this regard, it seems that the SARS-CoV-2 spike glycoprotein is phenetically more similar to humans and mice than to its coronavirus "cousins".

5. One image to explain it all!


a)
b)
Number of shared SARS-CoV-2 gp spike peptides
300
250
200
150
100
50
0
25
20
15
10
5
0
Human coronavirus HKU1
Human coronavirus 229E
Human coronavirus OC43
Human (Homo sapiens)
Mouse (Mus musculus)
Rat (Rattus norvegicus)
Cat (Felis catus)
Dog (Canis lupus familiaris)
Rabbit (Oryctolagus cuniculus)
Chimpanzee (Pan troglodytes)
Gorilla (Gorilla gorilla gorilla)
Rhesus macaque (Macaca mulatta)
Organisms

6. If there is one thread you read today, it should be this!
https://t.co/NEf9HK6ReB
@flavinkins
Check every link, take your time.

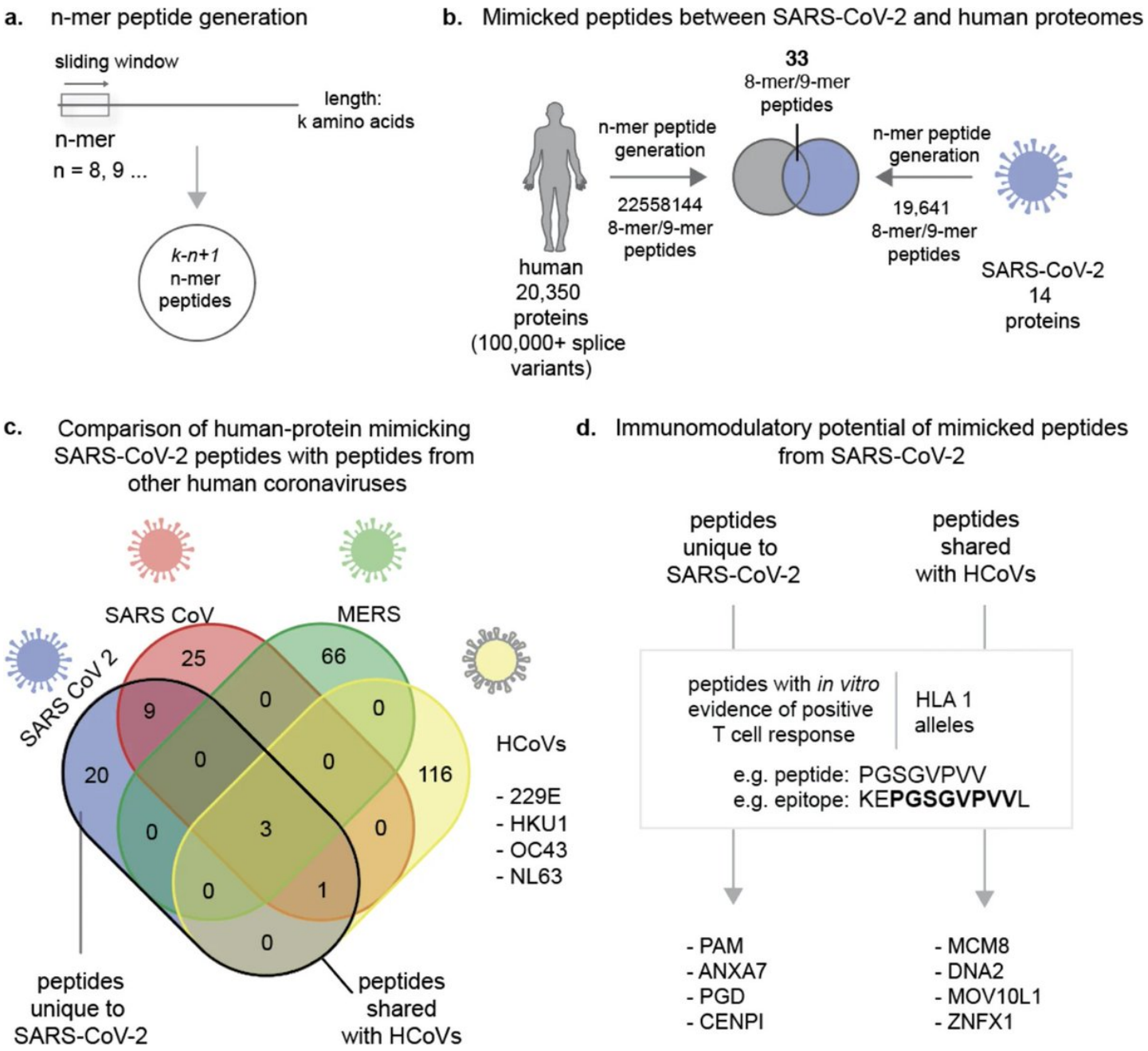
7. A timely vindication for Sørensen, Susrud & Dalgleish
Biovacc-19: A Candidate Vaccine for SARS-CoV-2 Developed from Analysis of its General Method of Action for Infectivity
https://t.co/lwnZSnmyVA
Image: Nonhuman-like (NHL) sequences found in SARS-CoV-2 spike protein S1.

Seq no.	Sequence	Seq no.	Sequence	Seq no.	Sequence	Seq no.	Sequence
1	PLVSSQ	41	SKHTPI	81	GKIADY	121	GVLTES
2	SSQCVN	42	LVRDLP	82	KIADYN	122	TESNKK
3	VNLTTR	43	RDLPQG	83	DDFTGC	123	PFQQFG
4	LTTRTQ	44	PQGFSA	84	FTGCVI	124	QQFGRD
5	TRTQLP	45	GFSALE	85	GCVIAW	125	ADTTDA
6	PAYTNS	46	VDLPIG	86	LDSKVG	126	DTTDAV
7	VFRSSV	47	PIGINI	87	DSKVGG	127	TTDAVR
8	VLHSTQ	48	GINITR	88	KVGGNY	128	DAVRDP
9	LFLPFF	49	LTPGDS	89	GGNYNY	129	AVRDPQ
10	SNVTWF	50	TPGDSS	90	KSNLKP	130	DITPCS
11	VSGTNG	51	AAYYVG	91	PFERDI	131	ITPCSF
12	SGTNGT	52	GYLQPR	92	ISTEIY	132	TPCSFG
13	TNGTKR	53	ALDPLS	93	STEIYQ	133	FGGVSV
14	NGTKRF	54	LDPLSE	94	EIYQAG	134	GGVSVI
15	RFDNPV	55	PLSETK	95	STPCNG	135	SVITPG
16	VYFAST	56	SETKCT	96	TPCNGV	136	ITPGTN
17	ASTEKS	57	KCTLKS	97	PCNGVE	137	TPGTNT
18	STEKSN	58	TVEKGI	98	GVEGFN	138	PGTNTS
19	IRGWIF	59	TSNFRV	99	PLQSYG	139	TSNQVA
20	WIFGTT	60	FRVQPT	100	FQPTNG	140	VAVLYQ
21	FGTTLD	61	TESIVR	101	TNGVGY	141	QLTPTW
22	TTLDSK	62	SIVRFP	102	GVGYQP	142	STGSNV
23	LDSKTQ	63	PNITNL	103	LLHAPA	143	GSNVFQ
24	DSKTQS	64	ITNLCP	104	LHAPAT	144	FQTRAG
25	SKTQSL	65	NLCPFG	105	HAPATV	145	QTRAGC
26	KTQSLL	66	LCPFGE	106	APATVC	146	RAGCLI
27	VNNATN	67	ATRFAS	107	PATVCG	147	AGCLIG
28	ATNVVI	68	TRFASV	108	ATVCGP	148	AEHVNN
29	CEFQFC	69	SNCVAD	109	TVCGPK	149	IPIGAG
30	FCNDPF	70	VLYNSA	110	VCGPKK	150	AGICAS
31	CNDPFL	71	FKCYGV	111	GPKKST	151	SYQTQT
32	LGVYYH	72	KCYGVS	112	PKKSTN	152	QTQTNS
33	GVYYHK	73	CYGVSP	113	KKSTNL	153	TQTNSP
34	VYSSAN	74	YGVSPT	114	KSTNLV	154	TNSPRR
35	SANNCT	75	GVSPTK	115	VKNKCV		
36	YVSQPF	76	VSPTKL	116	FNFNGL		
37	VSQPFL	77	ADSFVI	117	FNGLTG		
38	LEGKQG	78	QIAPGQ	118	NGLTGT		
39	EGKQGN	79	APGQTG	119	TGTGVL		
40	GKQGNF	80	TGKIAD	120	GTGVLT		

8. Visual Reference

Benchmarking evolutionary tinkering underlying human–viral molecular mimicry shows multiple host pulmonary–arterial peptides mimicked by SARS-CoV-2

https://t.co/irfH0Zgrve



9. What kind of Mice?

Human Immune System Mice for Study of HIV-1 Infection of CNS

https://t.co/QwrCbNtUBc

"Immunodeficient mice transplanted with human cell populations or tissues, also known as human immune system mice, have become important & versatile tools for in vivo study"

HIS mouse model (reference)	Method of generation	Salient CNS findings in response to HIV-1 infection
Severe combined immunodeficiency (SCID)–HIV encephalitis (HIVE) (79–84)	Direct injection of HIV-1-infected human microglia or macrophages into the brain of SCID mice	Measurable HIV-1 brain viral load and neuropathological features of HIVE including astrogliosis and microgliosis. Reduction in CNS pathology in response to combination antiretroviral therapy (cART).
NSG-huPBL (93)	Intraperitoneal injection of human donor PBMCs into non-irradiated NSG mice	HIV-1-infected human CD4+ T cells present in meninges and cortex of infected animals. Appearance of neurodegeneration, microgliosis, and astrogliosis dependent on infecting viral strain.
CD34+-NSG (85, 86, 89–91, 105)	NSG mice transplanted with human CD34+ hematopoietic stem cells (hCD34+)	Low CNS viral burdens, transmigration of HIV-infected human monocytes and macrophages into the mouse CNS, regional activation of resident murine microglia and astrocytes, neuroinflammation, and neurodegeneration. Reduction in CNS pathology with long-acting nanoparticle-based cART. Increased blood–brain barrier integrity in acutely infected CD34+-NSG mice and decreased leukocyte extravasation into CNS following treatment with a novel sonic hedgehog mimetic.
CD34+-NSG (+hNPC) (133)	NSG mice transplanted with hCD34+ combined with intraventricular injection of neural progenitor cells	Detection of human glia in diverse brain regions of HIS mice including periventricular areas, white matter tracts and brain stem. Mice infected with HIV-1 display glial transcriptional signatures and viral defense signaling pathways that mirror human disease.
Myeloid-only mice (60)	NOD/SCID mice transplanted with hCD34+	HIV-1 DNA and RNA as well as macrophages expressing HIV-1 p24 detected in the brains of infected animals.
DRAG (121)	NRG mice expressing human leukocyte antigen (HLA) class II (DR4) transplanted with HLA-matched hHSC	HIV-1 replication in brain following mucosal infection.

10. SARS-CoV-2, the autoimmune virus
https://t.co/MjVKVb7MTx
confirmation of peptide findings + autoimmune factors

4. Sharing peptides between SARS-CoV-2 virus and Human antigens: implication for the upcoming vaccine against COVID-19

Go to:

Molecular mimicry phenomena between pathogenic viruses and human proteins - have been already analyzed and suggested to play a major role in the etiologies of various inflammatory and autoimmune diseases [23,24]. We recently have been thoroughly quantifying hexa- and heptapeptide sharing of SARS-CoV-2 spike glycoprotein with mammalian proteomes and found that a massive heptapeptide sharing exist between SARS-CoV-2 spike glycoprotein and human proteins [25]. This study highlights the possibility of molecular mimicry–induced adverse autoimmune-related manifestations, already reported in SARS-CoV-2-infected patients, and raise concern regarding the upcoming desired vaccine, indicating the need for vaccines based on minimal immune determinants unique to pathogens and absent in the human proteome [26]. With regard to the concern of future post COVID-19 vaccine-related autoimmune manifestations, it is worth to mention the recent reports regarding participants who developed symptoms of transverse myelitis, an inflammation of the spinal cord (already reported secondary to COVID-19 infection [27]) – in the trial assessing the safety and efficacy of COVID-19 vaccine by AstraZeneca company.

11. Useful Mouse Graphic from @RandFanshier https://t.co/lEtVvmuwF9)
showing different kinds of transgenic mouse experiments
@RandFanshier asks:
"was it given human umbilical cord stem cells as an embryo, or did it get human epithelial tissue implanted as a SCID mouse?

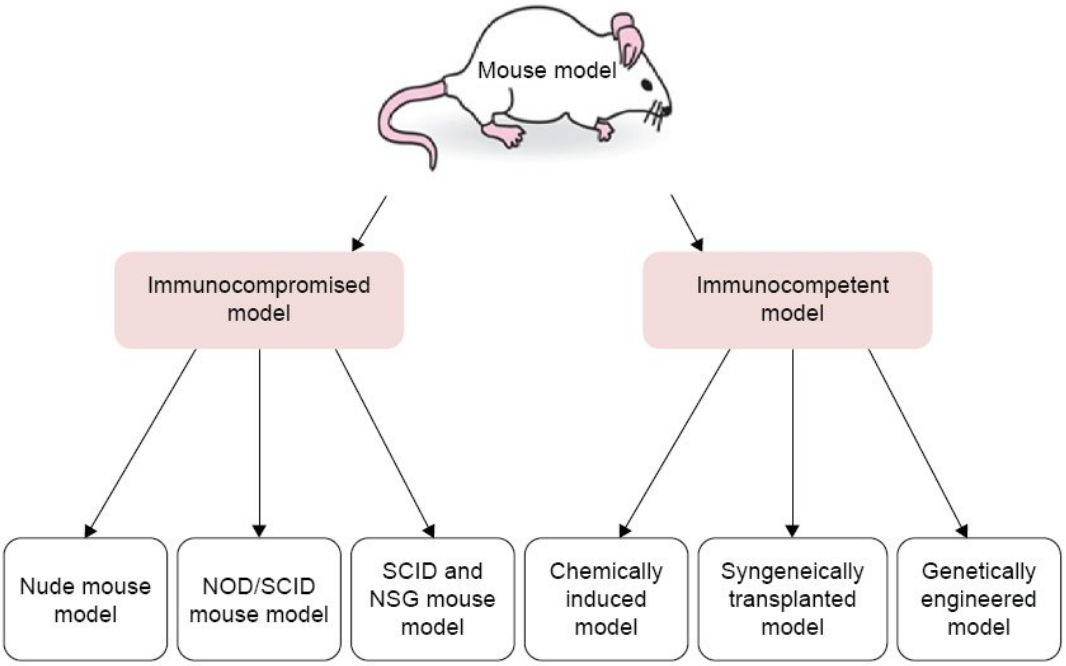


Figure 1 Mouse models of oral cancer.
Abbreviations: NOD, nonobese diabetic; SCID, severe combined immunodeficiency; NSG, NOD/SCID gamma.

12. Did Experimental vaccine immuno-suppressed transgenic hAce2 Mice from WIV Lab ended up on the dinner plate for the "three squeaks" delicacy?
once when it is picked up!
once when it is dipped in sauce.!
once when it is eaten..!
https://t.co/6hQREvU6RG

> @BBCWorld @CNN @shujamtaro @SolomonYue @HawleyMO @BorisJohnson @lukedepulford @DanGarrett97 @SenRickScott @swsjoerdsma @aaronMCN @tommycheungsy I can't believe these pictures. In this civilized society, we eat newborn mouse Scared me intolerable. #chinazi #WuhanCoronavirus \U0001f92e\U0001f92e pic.twitter.com/89Gc3fJafP
>
> — Aura\u4e9e\u6a02 (@sauwingso) January 22, 2020

13. Three Blind Mice

newly born mice (still hairless and barely able to open their eyes). It is typically served with some type of cold soy based sauce. The first squeak is when the mouse/rat is picked up with the chopsticks.

14. The second is when the mouse/rat is dipped into the sauce (temperature change causing the squeak). The third is when the mouse/rat is placed into your mouth (another temperature change).

Typically, they are very newborn and thus the bone structure is still fairly loose. I've heard that these have been served wrapped in seaweed before, but that may be more rumored than anything else.
https://t.co/jPE10AK32N

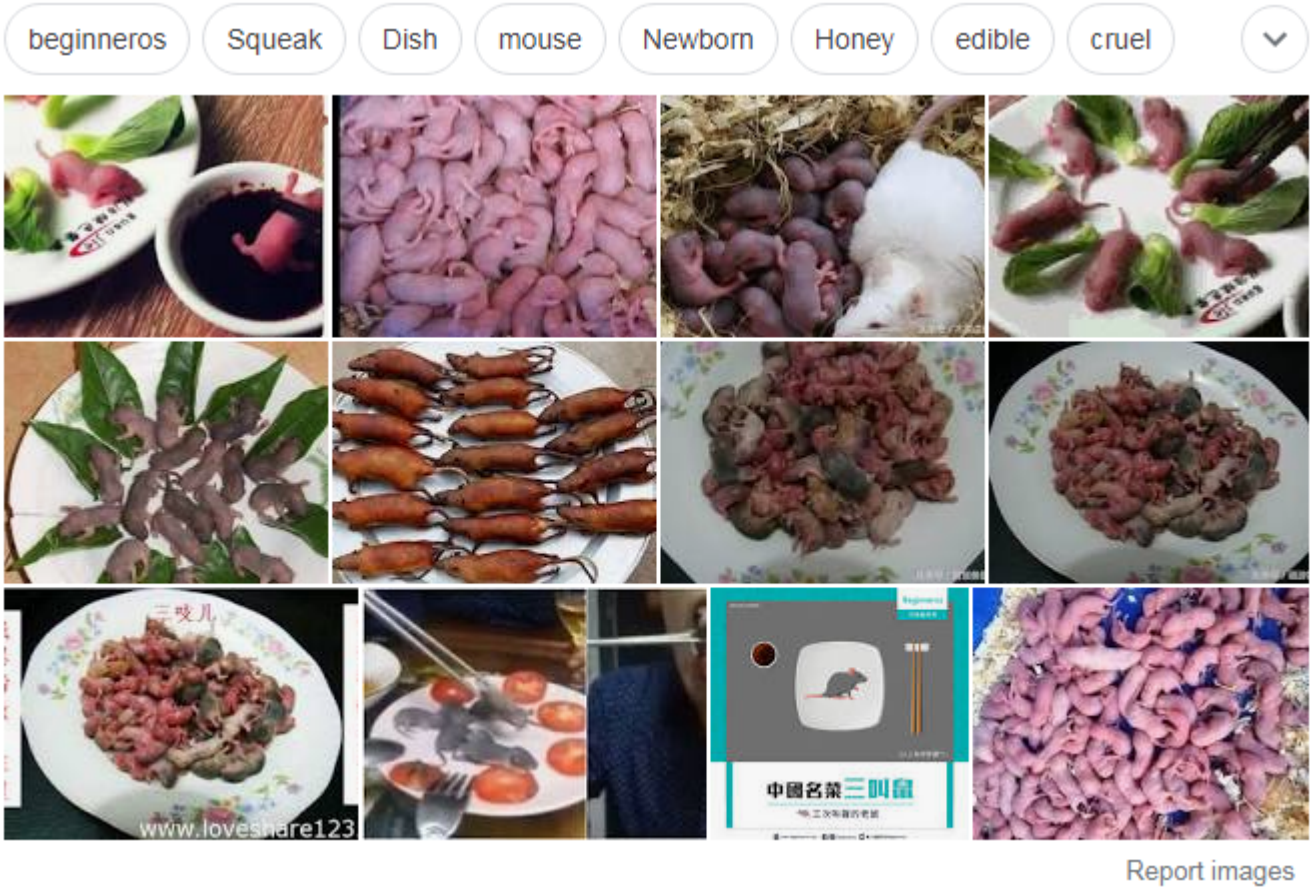
16. Baby Mice ■■■
Newborn mice (San Zhi Er) are eaten alive with chopsticks & served in a spicy sauce.
They are called "3 squeaks babies" because they scream 3 times.
Chinese Baike Baidu scrubbed the page
https://t.co/3IiIHOqtBp
Google Search shows it "item/■■■/3857789"

17. Not Bats. Mice! ■■■

1. https://t.co/0XPEMIN5Oo (https://t.co/xs9pDkG2kE)

2. https://t.co/I2DbfJUChq (https://t.co/X7tR3Md491)

3. so-called dark dish "San Zhier". Is this dish really available? Or is it just a rumor?
https://t.co/OtXZOujPnd (https://t.co/0XPMxdLfmU)



18. Whether Experimental lab mice were sold by WIV or other lab employees OR a lab researcher got bitten by one, we cannot know for sure as yet
https://t.co/7qbmZ02Ojc
and
https://t.co/oL8oUqQPqv
and
https://t.co/lfnCiDl5V5
and
https://t.co/68vEE8GYw8

> Global Times, a popular state-run newspaper, then published an article on "chronic inadequate management issues" at laboratories, including problems with biological disposal.

Oh. From that article:

> The release of the guideline deals with chronic loopholes at laboratories, Yang Zhanqiu, a deputy director of the pathogen biology department at Wuhan University in Hubei Province, told the Global Times on Sunday.
>
> "The mention of biosafety at labs by the ministry has nothing to do with some saying that the coronavirus leaked from the Wuhan Institute of Virology of the Chinese Academy of Sciences," Yang said.
>
> Laboratories in China have paid insufficient attention to biological disposal, Yang said.
>
> Lab trash can contain man-made viruses, bacteria or microbes with a potentially deadly impact on human beings, animals or plants.
>
> Some researchers discharge laboratory materials into the sewer after experiments without a specific biological disposal mechanism, Yang explained.

Oh, wait... the same sewer system that wet-market cooks use to collect "gutter oil" for use in cooking?

`19. Back to the Labs..and Mice (1)

Dr. Anony Mouse kindly provides some useful insights:

"Perhaps a glance at the ACE2 transgenic mouse paper would be nice:

https://t.co/VSSciCGeAl

Pathogenesis of SARS-CoV-2 in Transgenic Mice Expressing Human Angiotensin-Converting Enzyme 2

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20. Dr. Anony Mouse explains

Paper submitted for publication on March 12th

At the time of these experiments, a viral pandemic was raging in Wuhan during the 2 months from “discovery” of virus to this publication & all interactions with the outside world were completely closed off

21. Dr. Anony Mouse (3)
The HfH-ACE2 transgenic mouse was developed in this paper in 2016 from the Baric lab, which people have pointed to back in May, when questions started to arise about what was going on. https://t.co/YuhcLfTBLZ. SARS-like WIV1-CoV poised for human emergence

22. Dr. Anony Mouse (4)
Remember, no reference to the Mojang miners was made in this 2016 paper.
Looking at the Methods section of the 2020 transgenic ACE2 mouse paper, it states that this mouse was from “Ralph S Baric lab.”

23. Dr. Anony Mouse (5)
This mouse had to have been at the WIV prior to the pandemic, since everything in Wuhan was closed from January to March. Also, how did any research get done at the WIV at that time, during total lockdown?

24. Dr. Anony Mouse (6)
From the Methods section of the paper:

HFH4-hACE2 mice

The transgenic mice (HFH4-hACE2 mice) expressing the human ACE2 protein (hACE2) under mixed genetic backgrounds (C3H, C57BL/6) were obtained from Ralph S. Baric's lab (Menachery et al., 2016).

The HFH4-hACE2 mice were bred and maintained in specific pathogen free (SPF) environment at the Laboratory Animal Center of Wuhan Institute of Virology, CAS.

Twenty-two male and twelve female mice at eight to ten weeks-old were used in this study. Littermates of the same sex were randomly assigned to mock, 1, 3, 5, 7 DPI and survival groups.

Viral infections were performed in a biosafety level 3 (BSL3) facility in accordance with recommendations for the care and use of laboratory animals and the Institutional Review Board of the Wuhan Institute of Virology, CAS (ethics number WIVA05202003).

25. Dr. Anony Mouse (7)
Those of us who do science for a living understand the sheer implausibility of performing these experiments, writing them up, and submitting for publication in a 7-8 week period from viral isolation to publication.

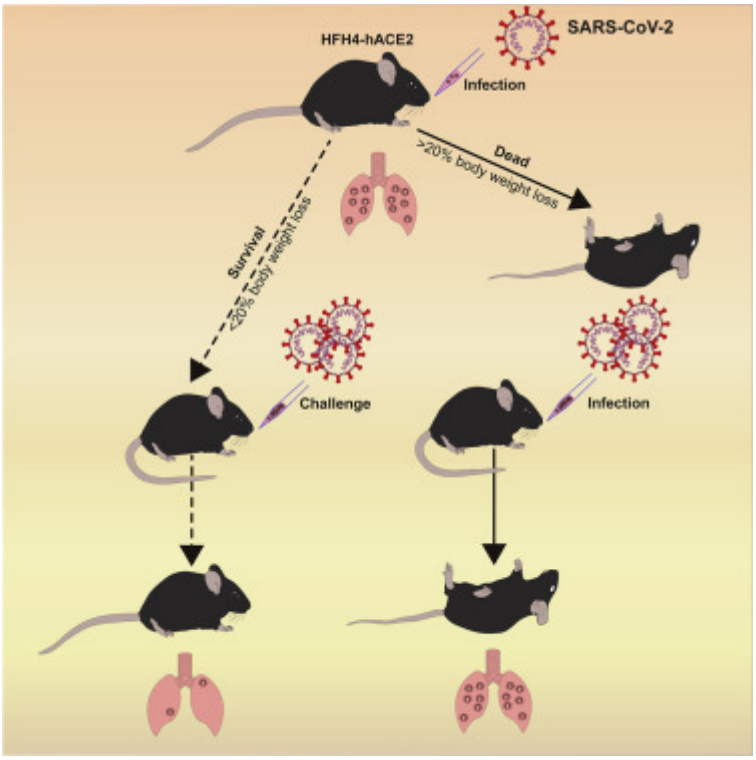
26. Dr. Anony Mouse (8)

Especially during a viral pandemic where the entire city was completely shut down and movement restricted.

Possible? Yes. Probable?

I'll leave that determination to the scientific community...

So what was really going on?



27. Dr. Anony Mouse (9)

What likely happened is that they took the ACE2 transgenic mouse from the Baric lab and gave it a human immune system.

This could be done by crossing the ACE2 transgenic mice with a mouse model (rag-/rag-) without a functioning immune system.

28. Dr. Anony Mouse (10)

These animal crosses are all the rage in immunology.

By crossing various "knock out" and "knock in" mice, you get all sorts of interesting immune things to study.

It's big in cancer immunology right now.

29. WTF did they do to me?

30. A "mice little experiment" that our dear Dr. Anony Mouse would have done...

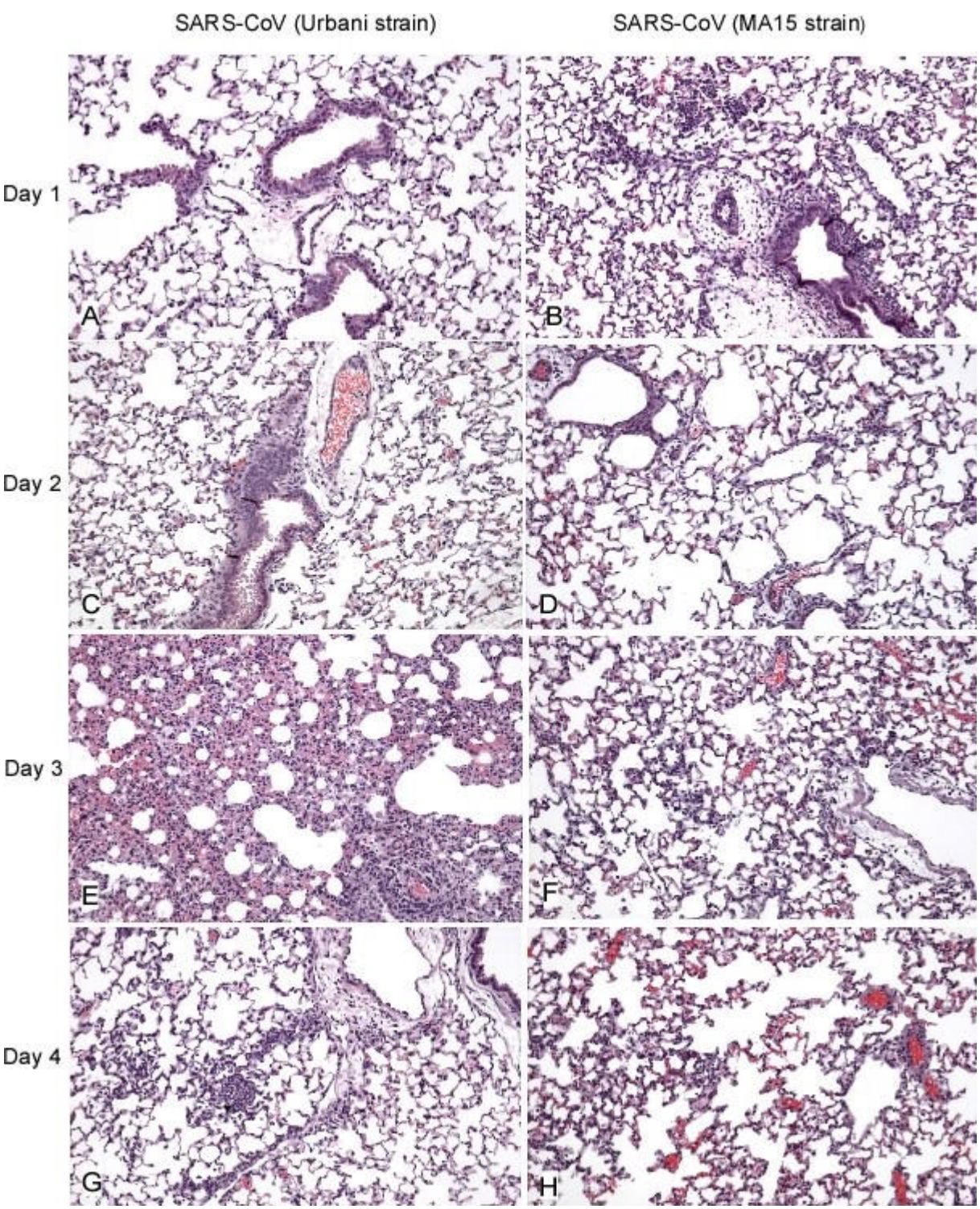
This animal then would be given human bone marrow to repopulate its immune system with human immune cells, which in the original ACE2 transgenic mouse were not infected by SARS CoV.

It's a natural progression to do this experiment, and the Baric lab was well aware by 2007 that SARS infected human innate immune cells like dendritic cells and macrophages, and this changed the cytokine profile to make a dysfunctional immune response.

MERS CoV uses DPP4 (CD26) for entry, and this receptor is highly expressed on dendritic cells. Mouse innate immunity is different enough from human innate immunity than the best viral infection models needed to incorporate human immunity.

31. Dr. Anony Mouse explains (11)

What the researchers at WIV didn't plan for, I guess, is that SARS-CoV Urbani MA15 mouse adapted viral strain they were using continued to mutate in the animal model during passage.....



32. Dr. Anony Mouse explains (12)

Even in the ACE2 transgenic experiments in the 2020 Cell paper, two mutations were found in S and nsp13 that led to brain tropism and death in a few of the mice, even with only one passage.

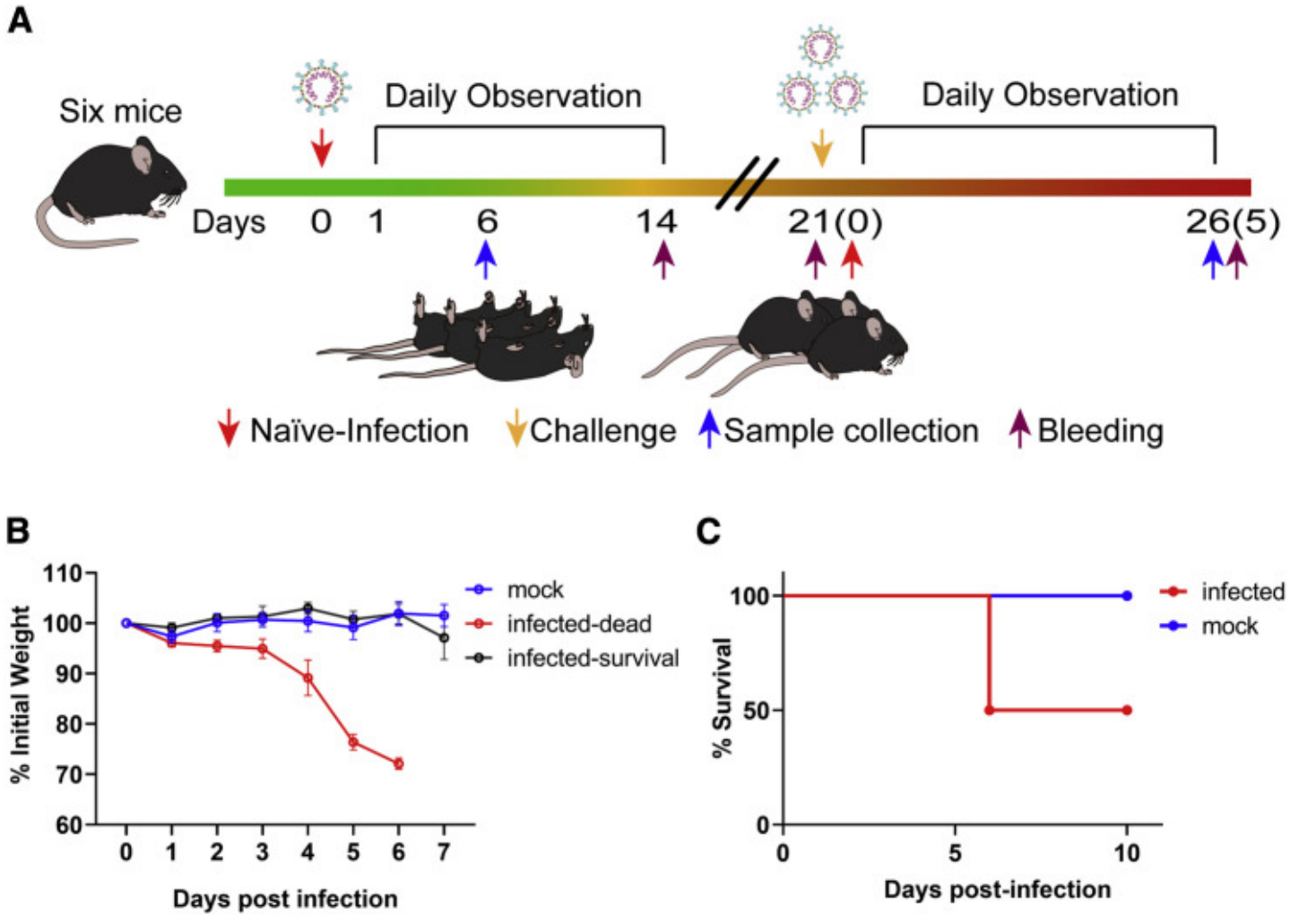
https://t.co/w4hhjzqW6K

Notably, four of the animals demonstrated SARS-CoV-2 neuroinvasion of the brain but only in the deceased mice (Figure 3D). However, the exact details and mechanisms regulating SARS-CoV-2 neuroinvasion remain unclear, as this phenomenon has been previously described with this mouse model (Menachery et al., 2016). We then tried to re-isolate SARS-CoV-2 from infected animals. We inoculated Vero E6 cells with infected mouse (G-D7-M1) lung and brain homogenate supernatant and observed a noticeable cytopathic effect (CPE) in the infected cells (Figures S4B and S4C) compared with the control (Figure S4A). The re-isolated virus from lung and brain of G-D7-M1 was confirmed by indirect imunofluorescence assays (IFAs) and genome sequencing (Figures S4D–S4F; Table S3). The lung isolates indicated two mutations, C14554T (nsp13, L372F) and C23525T (spike, H644Y), compared with the genome of SARS-CoV-2-WIV04 (GISAID: EPI_ISL_402124). The mutation at nsp13 was unique compared with published viral sequences

33. Dr. Mouse explains (13)

Serial passaging in the chimeric mice selected for an even better human adapted strain.

This became more & more important to the scientists, since the better human adapted the strain became, the more like a real human infection it became in the mice.



34. Dr. Mouse explains (14)

I am sure the “dual use” potential of this sort of experiment did not escape the notice of the CCP, though it would have been true insanity to develop it in that direction.

35. Billy Talking Now

But then again, they did very similar experiments in a Peking military laboratory back in September, where they developed the infamous N501 mutation (6 passages in mice)

Similar to one currently plaguing GB

https://t.co/su4MYQpM9I

&

https://t.co/I90OOCJg7o

> In fact interestingly the mutation was created in lab for mouse models between June and September by Chinese researchers from the State Key Laboratory of Pathogen and Biosecurity, Beijing Institute of Microbiology and Epidemiology, Academy of Military Medical Sciences- China, to make it more infectious and to use these models for research with vaccine candidates and other therapeutics. https://science.sciencemag.org/content/369/6511/1603
>
> Thailand medical news sticking the boot in again & raising suspicions about Chinese military research in above tweet which mutated Asn501 to Tyr (N501Y), within the RBD of the spike protein. https://t.co/I90OOCJg7o
> to make it deadlier for mice..and Brits?https://t.co/Or6aCkzKlP pic.twitter.com/XkurR21l4c
>
> — Billy Bostickson \U0001f3f4\U0001f441&\U0001f441 \U0001f193 (@BillyBostickson) December 16, 2020

36. Back to Dr. Mouse

"Like Icarus flying too close to the sun, they could not stop themselves"

The researchers and the mice ;)

37. Dr. Mouse concludes (1)
It was only lethal in this very inbred, manipulated mouse strain. At least theoretically. Though a virus with human potential for transmission was being used (mouse adapted SARS Urbani) the possibilities were endless.

38. Dr. Mouse concludes (2)
The best laid plans of transgenic mice and men...
They could develop drugs to blunt the immune response. They could develop anti-virals.
They could design recombinant live attenuated coronavirus vaccines and rapidly test them in these mice.

39. Dr. Mouse concludes (3)

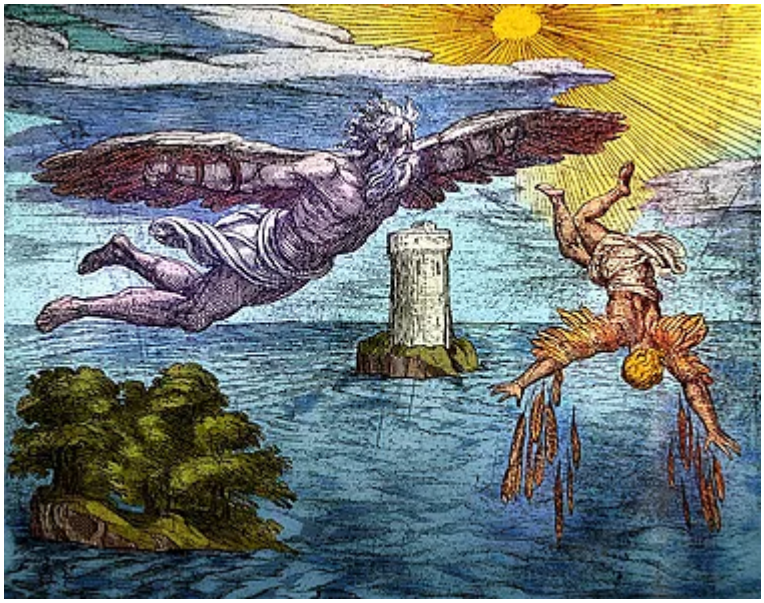
The end of coronavirus as a threat to humans was at hand, if the experiments could just be performed correctly.

40. Dr. Mouse concludes (4)
It’s exactly what some of us would have done
They likely said screw the GOF ethics
The experiments were just too cool, the potential benefit to humanity too great, and the ego boost from the possible accolades too strong.
We scientists totally get it.

41. Billy Talking Now

But we all know what happened to Icarus, don't we?

There is old Baric looking on in horror as his dear Chinese Icarus plunges..... to our death!



42. Dr. Mouse concludes (5)
These are the experiments I think they were doing in Wuhan during the past 18-24 months when the darn thing escaped.
Who knows what happened?
I suspect a lab tech handling an infected mouse was infected despite all the precautions.

43. Dr. Mouse concludes (5)
Maybe animal waste wasn't handled properly.
(Billy suspects they sold the lab mice)

A human adapted SARS strain, with wider tissue tropism, better ACE2 binding & better ability to shut off interferon production than SARS was produced, and it LEAKED..

44. A mice story, thanks to Dr. Anony Mouse.

45. Connections, connections - of mice and vaccines.
Of course this tragic mice story ties in well with DRASTIC research into "vaccines gone wrong" posted a while back on Twitter by @Rossana38510044
https://t.co/sY7A17nASd

1/ Was the pandemic caused by SARS2 the result of vaccine research gone wrong? The following thread is the product of a DRASTIC* investigation: the possibility that SARS2 and RaTG13 might be two different vaccine strategies and that SARS2 leaked from a lab during its development.

— Rossana Segreto (@Rossana38510044) October 3, 2020

46. Unroll the Knocked Out Mice Hypothesis @threadreaderapp