

# Vision Medicals: SARS-CoV-2 sequencing and analysis in late Dec 19

## Post 1: Weixin post by 小山狗 (Little Mountain Dog), on the 28<sup>th</sup> Jan 2020

Using screenshots (some with blurred sections)  
of her WeChat conversation with colleagues from end Dec 19

小山狗 = Xiǎoshān Gǒu, a nickname for an employee of Vision Medicals (微远基因)

links for the post:

[original](#) page deleted by author  
[archived](#) post, [pdf version](#), [weibo](#) copy,  
[archived Weixin search](#) showing multiple copies (29 Mar 22)  
compare with censored [latest Weixin search](#)

记录一下首次发现新型冠状病毒的经历  
Winjor 小山狗 2020-01-30

2019年12月26日刚上班，还是如往常一样先大概浏览一下这一天的mNGS病原微生物自动解读结果，没问题的话就开始一天的研发工作了。

意外的是，发现有一个样本报出了敏感病原体——SARS冠状病毒，有几十条的序列，且这个样本只有这么一个有意义的病原体，如果是普通病毒，这已经是一个相当可靠的结果了。心头一紧，赶紧后台查看详细的数据，发现相似度并不算很高，只有大约94.5%（这跟卡相似度的阈值有关，相当于只筛选下了相似度比较高的序列）。

想到有几种可能：1、SARS不同毒株基因组有一定差异；2、RNA病毒容易突变，距离SRAS事件17年了，变异比较大；3、近缘物种的错误比对等等。为了确认结果的可靠性，开始了详细分析。

好在之前已经遇到过几次这种类似的敏感的病原体确认分析工作，而且领导也曾跟我讨论过几次能不能做一个新发病原自动挖掘的分析流程，心里一直记着这个事情，在做其他权重更高优先级更高的项目时也随手做了一个初步的版本出来，这个样本刚好可以派上用场。我给它起了个名字，相比于日常生产用的分析流程，它多了个后缀：“探索版”，包含了几乎所有已测序的病毒基因组。

探索版的分析结果提示这个病原体跟Bat SARS like coronavirus最相似，整体相似度在87%左右，而跟SARS的相似度是约81%。比对上的序列数由几十条上升到了500多条，此外也组装出了5条contig，加起来有1200多bp，此时基本上可以确认是一种冠状病毒，可以针对冠状病毒进行详细分析。分析期间也开始跟解读负责人和领导小范围内部分保密讨论。

**Recording the experience of being the first to discover the novel coronavirus**

Winjor Small Mountain Dog 2020-01-30

I just started work on December 26, 2019, and as usual, I first roughly browsed through the mNGS pathogenic microorganism auto-read results for the day. If there is no problem, I will start the R&D work for the day.

Unexpectedly, I found that one sample reported a sensitive pathogen - SARS coronavirus, with dozens of sequences, and this sample only has such a meaningful pathogen. If it is a common virus, this is already a fairly reliable result. Feeling nervous, I quickly checked the detailed analysis data in the background, and found that the similarity is not very high, only about 94.5% (this is related to the similarity threshold, which is equivalent to only screening out sequences with relatively high similarity).

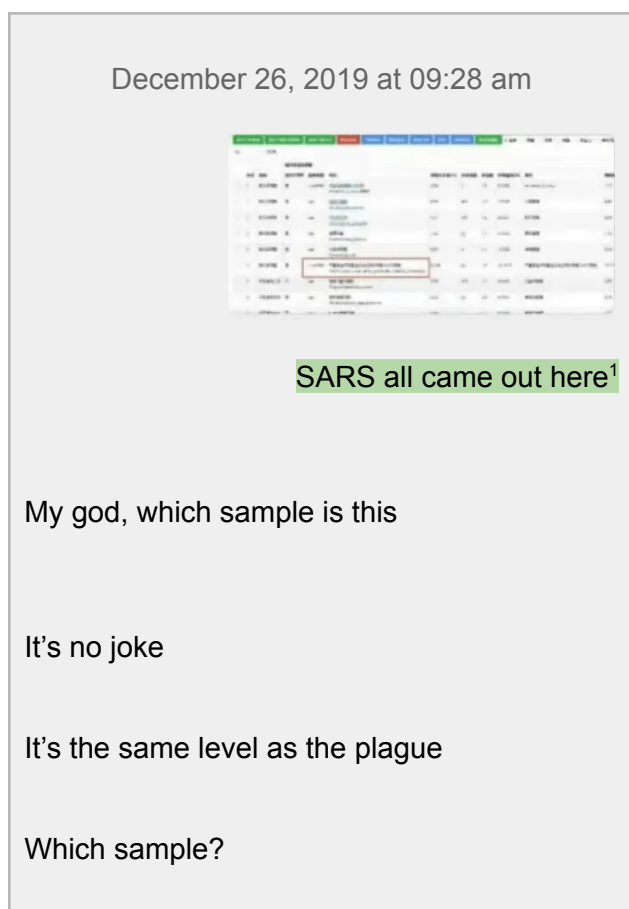
Several possibilities come to mind: 1. There are certain differences in the genomes of different strains of SARS; 2. RNA viruses are easy to mutate, and it has been 17 years since the SARS event, and the mutation is relatively large; 3. The wrong alignment of closely related species, etc.

To confirm the reliability of the results, a detailed analysis was started.

Fortunately, I have encountered this kind of similar sensitive pathogen confirmation analysis several times before, and the leader has discussed with me several times whether it is possible to do an analysis process for automatic discovery of new pathogens in the samples, and I have always kept this in mind. While working on other projects with higher weight and higher priority, I made a preliminary version of [the analysis process], and this sample can just come in handy.

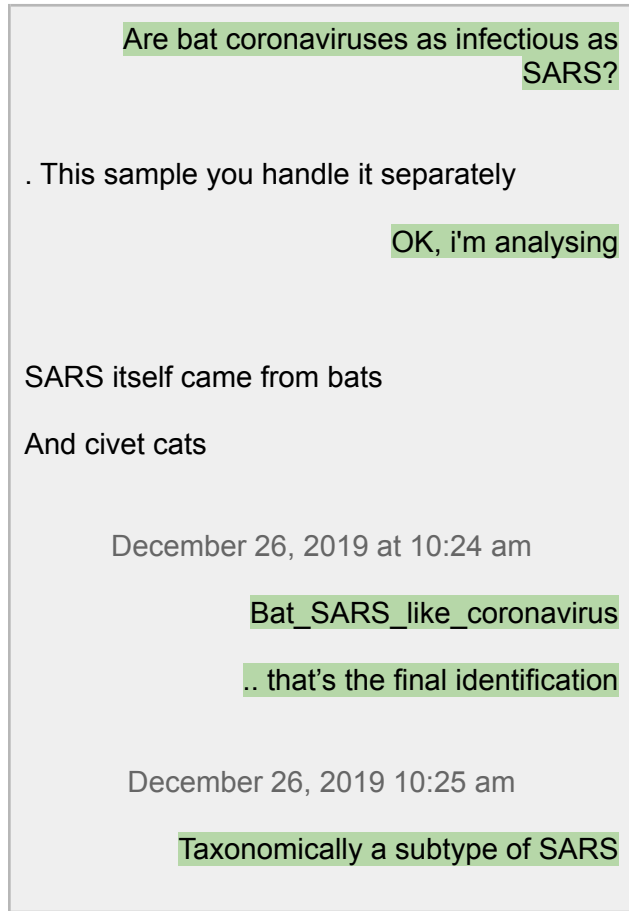
I gave a name [to that process]. Compared with the analysis process used in daily production, that process has an additional suffix: "Exploration Edition", which contains almost all sequenced viral genomes.

The analysis results of that Exploratory Edition suggest that this pathogen is most similar to Bat SARS like coronavirus, with an overall similarity of about 87%, and a similarity to SARS of about 81%. The number of sequences in the alignment has increased from dozens to more than 500 [in that exploratory process]. In addition, 5 contigs have been assembled, which add up to more than 1200 bp. At this time, it can basically be confirmed that it is a coronavirus, and the detailed analysis of the coronavirus can be carried out. During the analysis, we also started a small internal confidential discussion with the head and leader of the interpretation team.



进一步分析，无论是拿原始序列去NCBI nt库blastn，还是拿组装后的序列去blastn，结果都是跟Bat SARS like coronavirus最相似，但整体的相似度也是只有87%左右，进行nr库蛋白blastx对比的相似度也差不多，因此对结果保留怀疑。

Further analysis, whether the original sequence is used as a query sequence for blastn to NCBI nt library, or the assembled sequence is used for blastn, the results are the most similar to Bat SARS like coronavirus, but the overall similarity is only about 87%. When blastx against the nr library protein is performed, the comparison returns about the same similarity, so the results remain fuzzy.



病毒的分类信息一直都很混乱，分类规则不统一，有些基于分型基因（比如甲流）、有些则没有明确的分型基因，通过其他方法去分类。此前并没有去调研过Bat SARS like 跟SARS的分类方法，在NCBI Taxonomy上，Bat SARS like 是划分到SARS下面的

The classification information of viruses has always been confusing, and the classification rules are not uniform. Some are based on typing genes (such as influenza A), and some have no clear typing genes, and are classified by other methods. I have not investigated the classification method of Bat SARS like and SARS before. On NCBI Taxonomy, Bat SARS like is classified under SARS.

如此紧急的情况下，没有时间去调研文献，手上的数据也不多，基于基因组的相似度，潜意识里认为既然Bat SARS like是SARS的下属分类，那么这个检测到的未知病毒至少也是一个跟Bat SARS like平行的物种，即一个新型的Bat SARS like(后来看文献SARS和Bat SARS like是通过几个非结构蛋白进行分类)。

In such an urgent situation, there is no time to research the literature, and there is not much data in hand. Based on the similarity of the genome, I subconsciously think that since Bat SARS like is a subordinate classification of SARS, then this detected unknown virus is at least a related virus. Bat SARS-like parallel species, that is, a new type of Bat SARS like (later I saw in the literature that SARS and Bat SARS-like are classified by several non-structural proteins).

<sup>1</sup> Little Mountain dog WeChat messages are in green on the right. The messages of the person she is talking to at the time are against a white background on the left.

Lineage (full): [Viruses](#); [Riboviria](#); [Nidovirales](#); [Coronavirineae](#); [Coronaviridae](#); [Orthocoronavirinae](#); [Betacoronavirus](#); [Sarbecovirus](#)

- [Severe acute respiratory syndrome-related coronavirus](#) *Click on organism name to get more information.*
  - [Bat coronavirus Cp/Yunnan2011](#)
  - [Bat coronavirus Rp/Shaanxi2011](#)
  - [Bat SARS coronavirus HKU3](#)
  - [Bat SARS coronavirus Rp1](#)
  - [Bat SARS coronavirus Rp2](#)
  - [Bat SARS CoV Rf1/2004](#)
  - [Bat SARS CoV Rm1/2004](#)
  - [Bat SARS CoV Rp3/2004](#)
  - [Bat SARS-like coronavirus](#)
  - [Bat SARS-like coronavirus Rs3367](#)
  - [Bat SARS-like coronavirus RsSHC014](#)
  - [Bat SARS-like coronavirus WIV1](#)
  - [Bat SARS-like coronavirus YNLF\\_31C](#)
  - [Bat SARS-like coronavirus YNLF\\_34C](#)
  - [BtRf-BetaCoV/HeB2013](#)
  - [BtRf-BetaCoV/JL2012](#)



进一步地毯式地分析了几千个冠状病毒基因组，从相似度、覆盖率、基因组分布均匀等几方面进行评估，最终找出两株最相似的基因组，bat-SL-CoVZC45和bat-SL-CoVZXC21(1月9号公布基因组序列后，很多文章分析的也是这两个)。

We further did a very very broad comparison of the virus to thousands of coronavirus genomes, which we evaluated in terms of similarity, coverage, and even genome distribution, and finally found the two most similar genomes, bat-SL-CoVZC45 and bat-SL-CoVZXC21 (After the genome sequence was released on January 9, many articles analysed these two).

(下午才发到群里的图)

(The picture was sent to the group in the afternoon)

2019年12月26日 下午14:42

现在信息分析上可以确认是 SARS 病毒，只不过不确定是否是什么新发的亚型而已

2019年12月26日 下午15:01

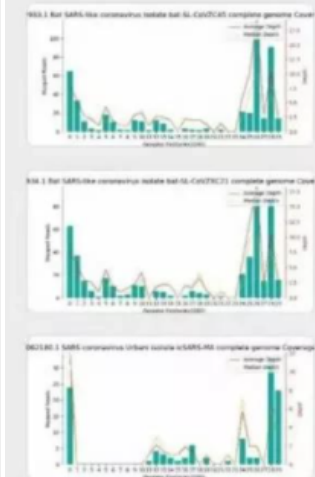


从序列数和覆盖图上看，都是 Bat\_SARS\_like\_coronavirus 最吻合的

December 26, 2019 14:42 pm

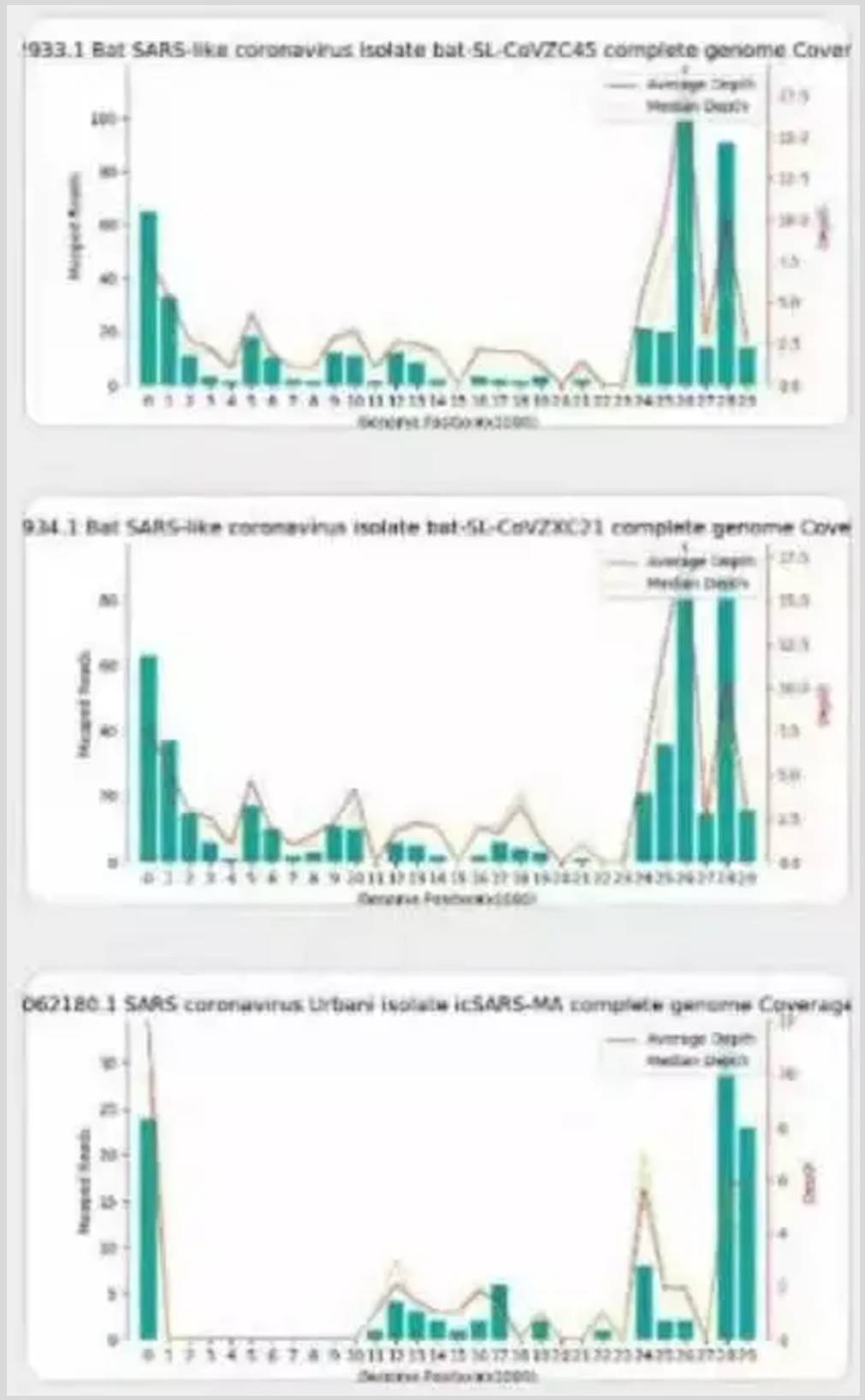
Now the information analysis can confirm that it is SARS virus, but it is not clear whether it is a new subtype.

December 26, 2019 15:01 pm



From the sequence number and coverage map, it is the best fit for Bat\_SARS\_like\_coronavirus





[image repeated]

仅仅这些信息还是不够的，至少还要看看进化上的信息，于是开始着手做进化树分析。

This information alone is not enough, at least we have to look at the evolutionary information, so I started to do a phylogenetic tree analysis.

2019年12月26日 早上10:25

分类上是 SARS 的一个亚型

能不能做个 phylogeny tree, 加上人、蝙蝠、果子狸和几种其他哺乳动物的冠状病毒、SARS、MERS

我在找基因组做这个

嗯呢

分类太多了不好找 😊

December 26, 2019 10:25 am

Taxonomically a subtype of SARS

Can you make a phylogeny tree, plus coronavirus, SARS, MERS from humans, fruit bats and several other mammals

I'm looking for genomes to do this

Sure

Too many categories, hard to find 😊

下载了所有冠状病毒的基因组，最后经过质量过滤、聚类分析，筛选出了160株的冠状病毒基因(基本包含了所有已知的各种动物的冠状病毒)。将组装的序列与160株冠状病毒基因组基于全基因组平均相似度做了进化分析

Downloaded the genomes of all coronaviruses, and finally 160 coronavirus genes (basically including all known coronaviruses of various animals) were kept after quality filtering, clustering and other analysis. The assembled sequence and 160 coronavirus genomes were analysed based on the average similarity of the whole genome.

(题外话，个人认为在物种进化分析上，基于全基因平均相似度构建进化树，比基于某个基因构建的进化树要更准确、合理一些，毕竟是从全局来考量，当然，研究结构、功能等另说，此时组装的序列也很短，没有完整的基因序列)，

(As an aside, I personally think that in the analysis of species evolution, it is more accurate and reasonable to construct an evolutionary tree based on the average similarity of the whole genome than one based on a certain gene. After all, it is considered from a global perspective.



结果不出意外, 还是跟Bat SARS like coronavirus聚得最近, 而且也是在SARS的大支上。

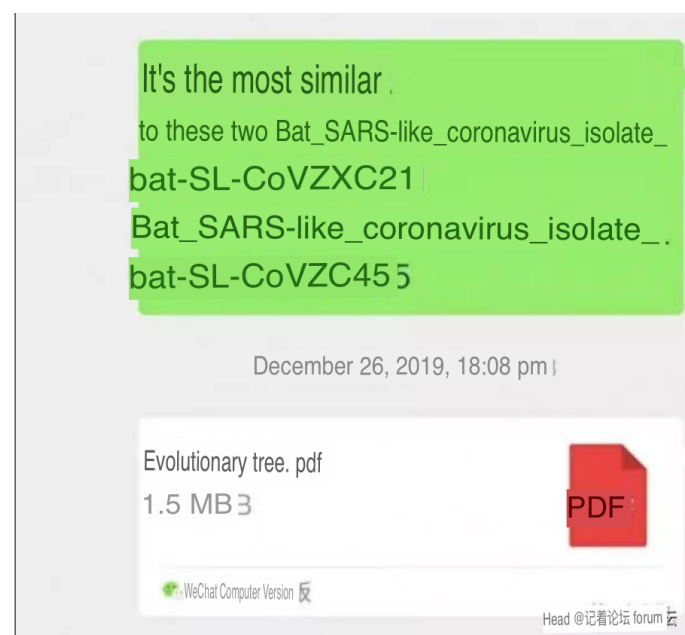
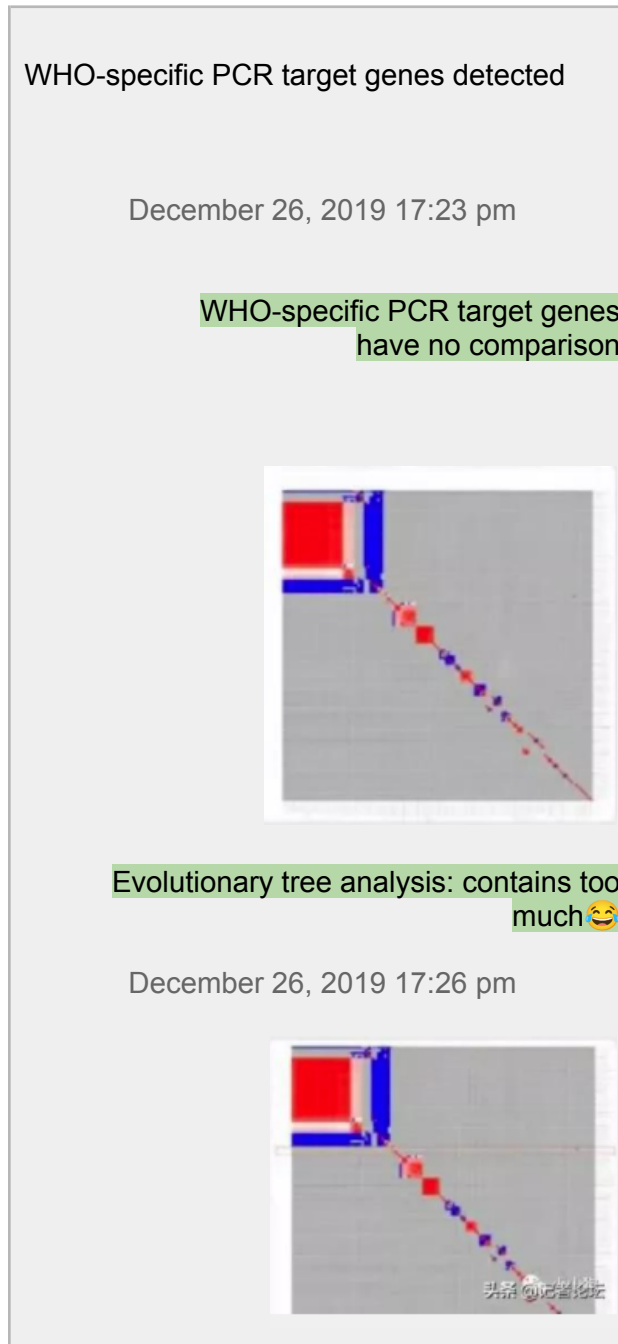
(跑到了傍晚才出图)

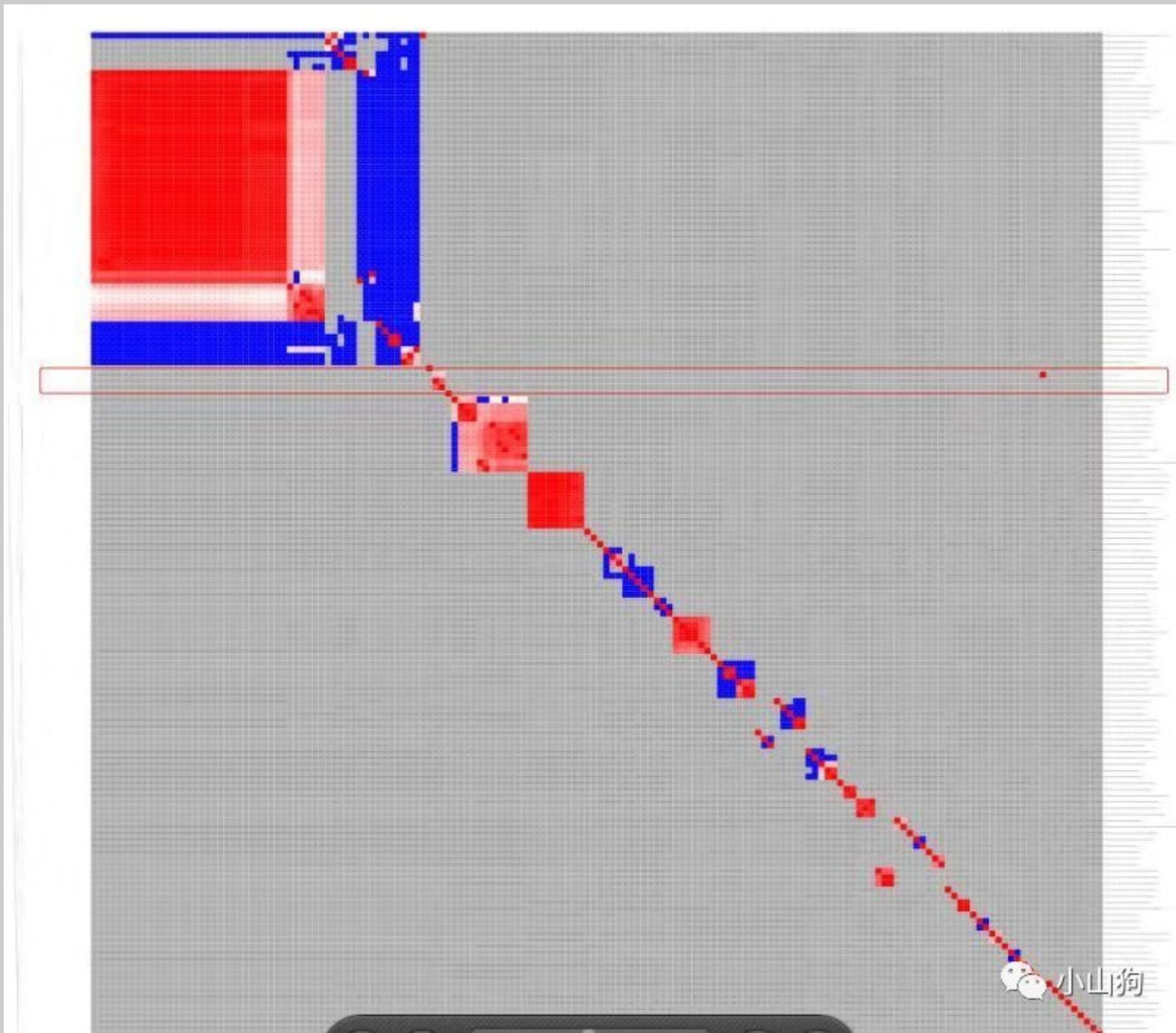


In addition, the assembled sequence was also very short at that time [26<sup>th</sup> Dec], and there was no complete gene sequence.)

The result is not unexpected, it is still close to Bat SARS like coronavirus, and it is also on the big branch of SARS.

(Picture in the evening)





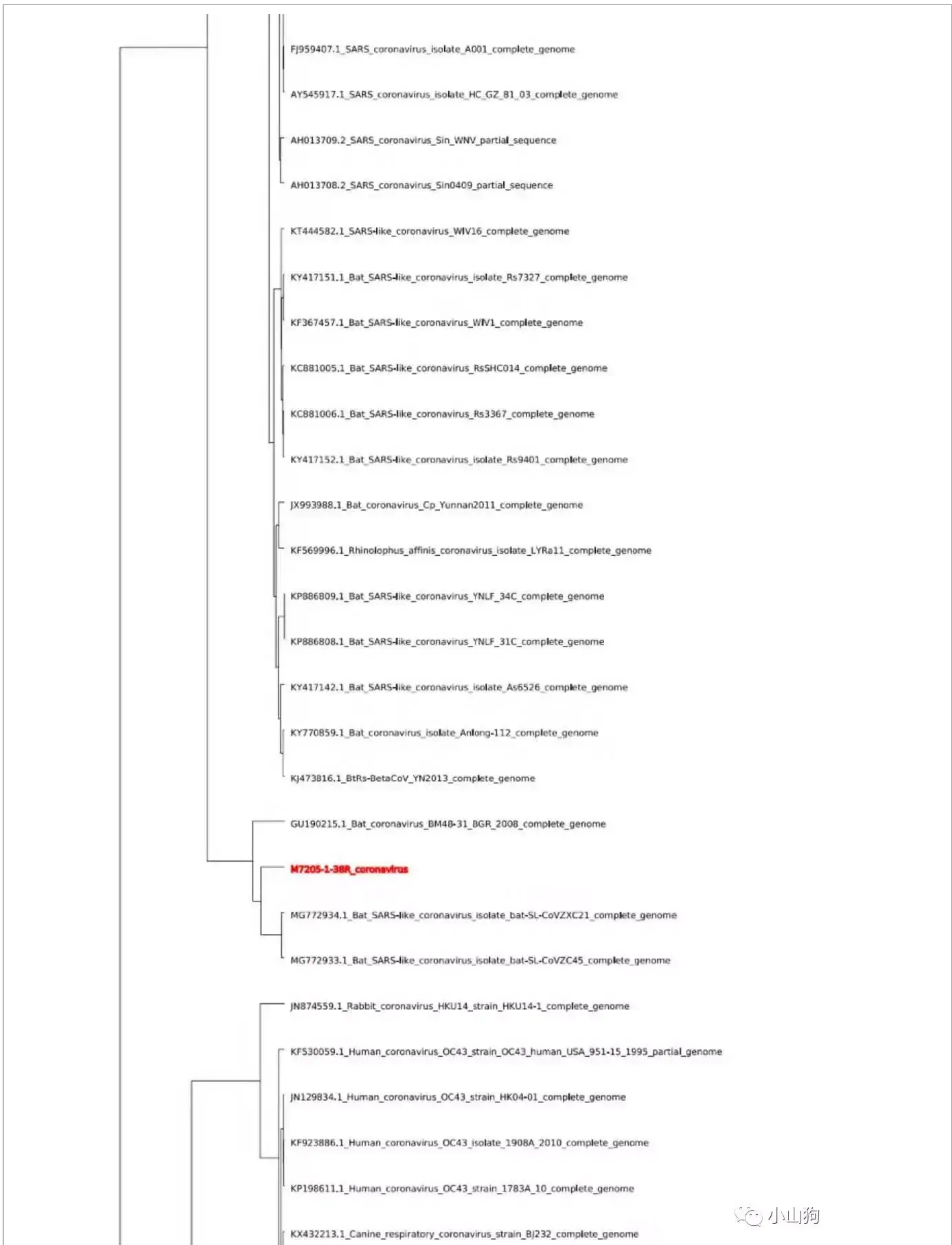
[image repeated]

图注:左上角一大块红色是SARS,边缘颜色没那么红的是Bat SARS like,再往外的大蓝边是另一群Bat SARS like,未知的病毒跟45、21聚在比较独立的一支上了,红框圈起来的。

比较奇怪的是,这个未知的病毒跟bat-SL-CoVZC45和 bat-SL-CoVZXC21聚到了一个相对独立的分枝上,而其它Bat SARS like则很集中地聚在SRAS那一群里面,想着也许是这两个的分类有点问题,但去看了出处的文献,方法上跟其它的也没啥区别,尊重文献的分类吧,暂且认为是对的。(这也是后面某些专家们把这个未知病毒判定为新型冠状病毒的依据之一)

**Legend:** A large red block in the upper left corner is SARS, the edge colour that is not so red is for Bat SARS like, and the big blue border outside is another group of Bat SARS like, the unknown virus is clustered with 45 and 21 in a relatively independent branch up there, the red frame is circled.

It is strange that this unknown virus clustered with bat-SL-CoVZC45 and bat-SL-CoVZXC21 in a relatively independent branch, while other Bat SARS-like viruses were clustered in the SARS group. I thought that maybe there is a problem with the classification of these two. However, after reading the literature, there is no difference between the method and the others, so I respect the classification of the literature and I think that it is correct for the time being. (This is also one of the bases for some experts to later consider this unknown virus as a novel coronavirus)



(部分进化树截图)

前端反馈这个患者病重，着急要检测结果，但是这么一个重大的病原体确实不可轻易报出，中午跟几个领导紧急开了个会，决定继续深入分析，延迟发放报告，同时分享数据给中国医科学院病原所一块分析。

后面从基因层面 ( orf1ab、S、N等基因 ) 进行了深入分析，并没有什么

(Partial evolution tree screenshot)

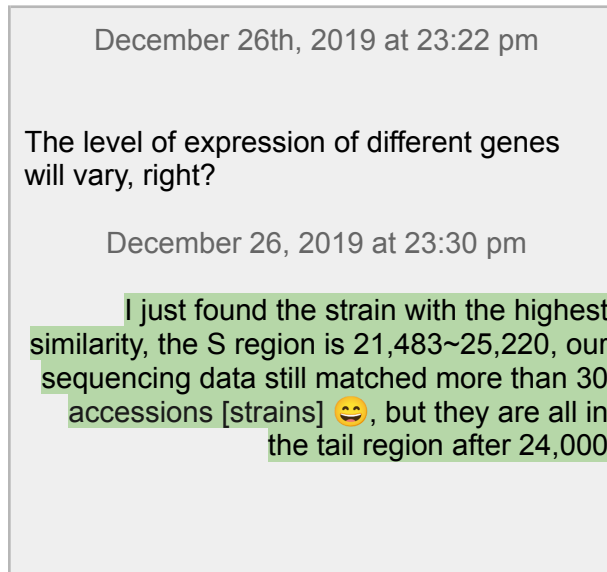
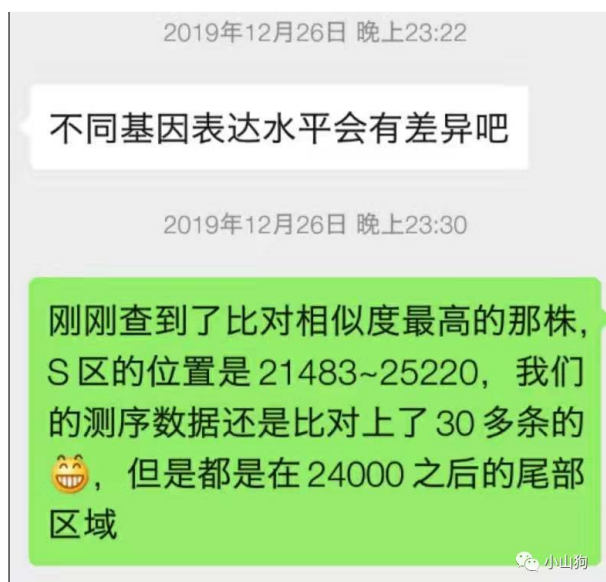
The front-end feedback was that the patient is seriously ill and is anxious to get the test results, but such a major pathogen cannot be easily reported. I had an emergency meeting with several leaders at noon and decided to continue the in-depth analysis, delay the release of the report, while sharing the data to the Institute of Pathogenesis of the Chinese Academy of Medical Sciences so that they can get a piece of the analysis.

Later in-depth analysis was carried out at the gene level (orf1ab, S, N



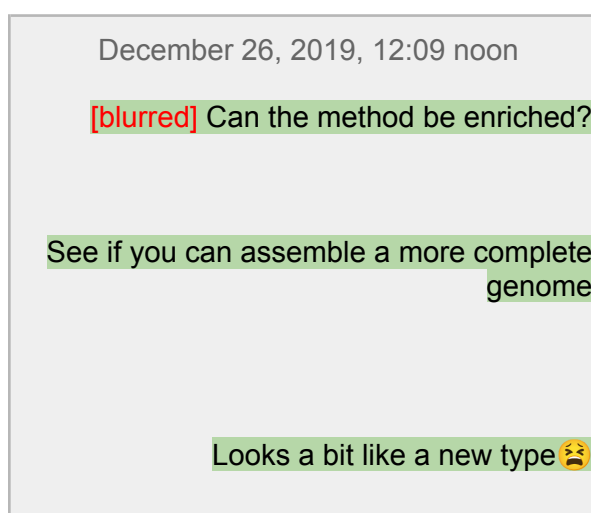
义比较大的发现了，主要还是检测到的序列数少，覆盖率太低，都是不完整的基因，做不了什么。

and other genes), and there was no significant discovery, mainly because the number of detected sequences was small, the coverage rate was too low, and they were all incomplete genes to do anything.



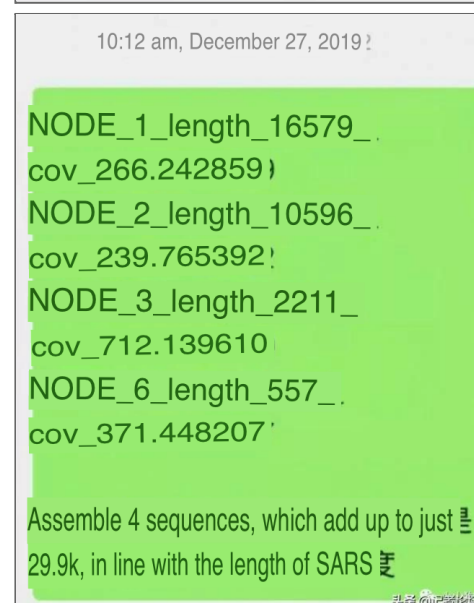
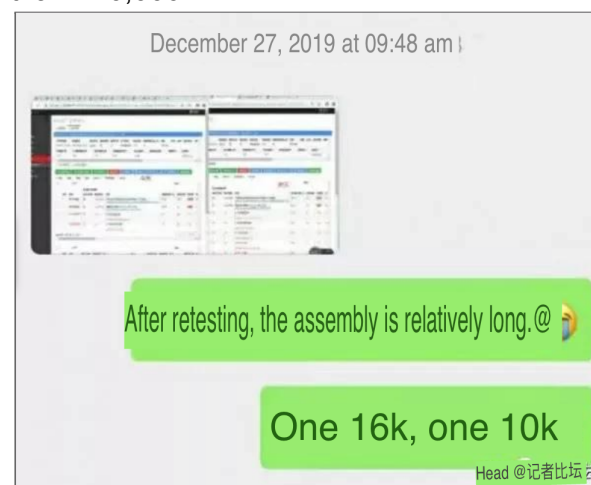
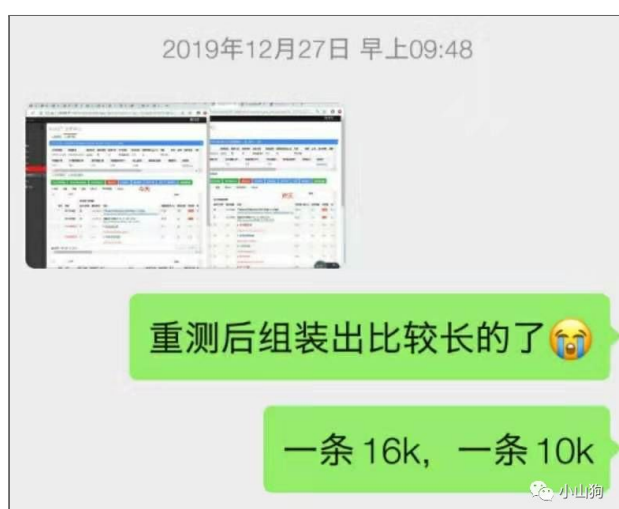
中午时已经提出了重测补数据进行分析。重测可以进行技术重复性验证，避免一些未知因素的污染导致的假阳，确保样本确实有该病原体，另外可以有更多的数据进行分析，如能组装出完整的基因组，分析结果更可靠，能做的深入分析也更多。

Retesting of complementary data for analysis was proposed at noon. Retesting can be used to verify technical reproducibility, avoid false positives due to contamination by some unknown factors, and ensure that the sample does contain the pathogen. In addition, more data can be analysed. For example, if a complete genome can be assembled, the analysis results are more reliable, and more in-depth analysis can be done.



第二天(2019.12.27)一早数据出来后，赶紧进行了组装分析，终于组装出了接近完整的基因组序列。数据同时也共享给了中国医学科学院病原所做其他深入分析。这次的序列数由之前的500多条升到了47万多条！

The next day (2019.12.27), after the data came out early in the morning, the assembly analysis was carried out quickly, and a nearly complete genome sequence was finally assembled. The data was also shared, with the Institute of Pathogenesis, Chinese Academy of Medical Sciences, for other in-depth analyses. This time, the number of sequences has increased from more than 500 to more than 470,000!



因为时间有限，还有其他研发项目需要做，就没有详细去对组装结果进

行补gap获取完整基因组了。另外也已经分享数据给病原所了，他们也会做这个，所以就没有去组装出一条完整的基因组了，已有的组装结果能满足大部分分析需求了。

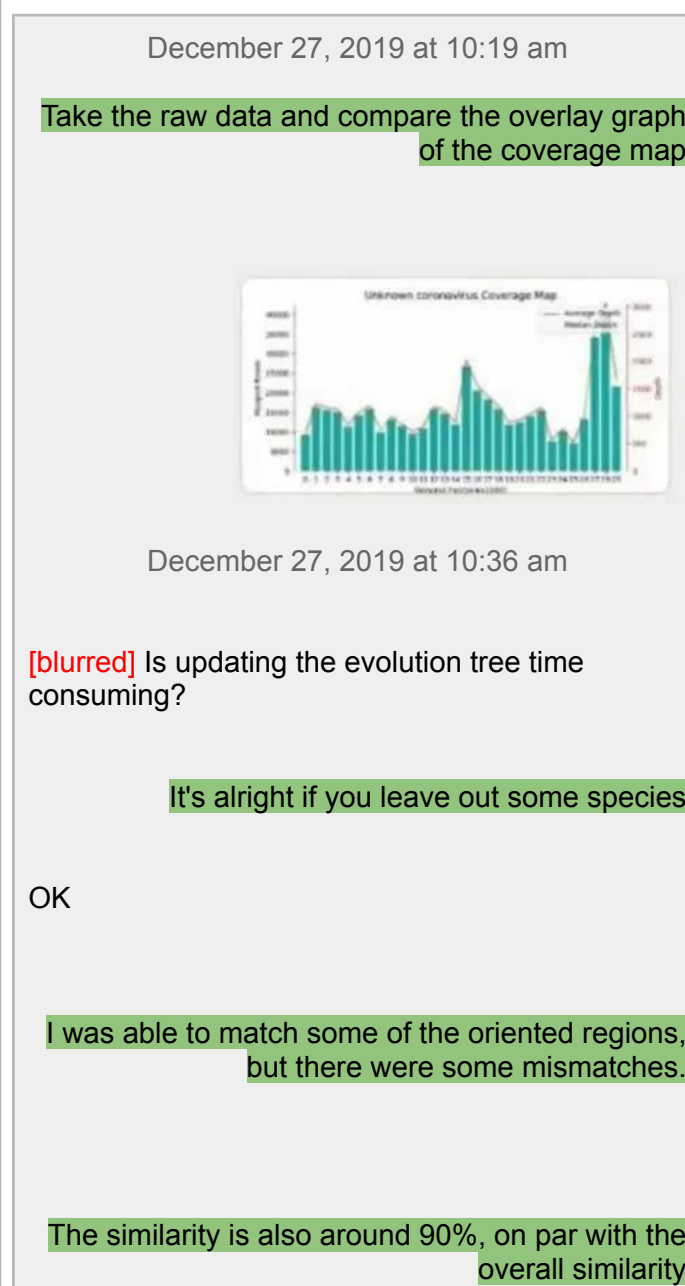
后面也继续做了一些深入的分析。

回帖序列分布均匀，没有明显的偏好，平均深度和中位深度基本一致，深度达到了1000x，说明组装没啥问题，测序也挺好，未知病原体也是完整的基因组存在。

Because of time constraints and other R&D projects, we did not go into detail to fill in the gaps in the assembly results to obtain the complete genome. In addition, we have already shared the data with the Pathogenic Institute [of the Chinese Academy of Medical Sciences], and they will also do that, so we did not assemble a complete genome sequence, and the existing assembly results can meet most of the analysis needs.

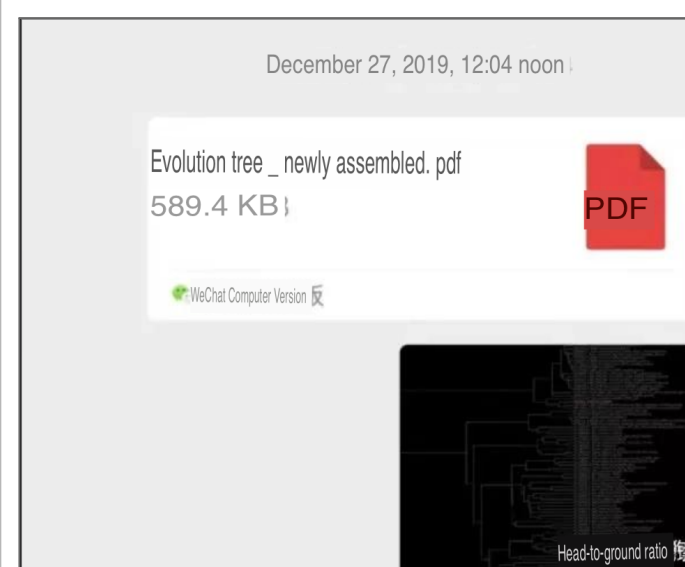
Some in-depth analysis is also continued later.

The sequence distribution of the repeats is even, there is no obvious preference, the average depth and median depth are basically the same, and the depth reaches 1000x, indicating that there is no problem with the assembly and that the sequencing is also rather good, and that the unknown pathogen also has a complete genome.



重新构建了进化树，这次选择了NCBI所有冠状病毒的参考株（以登录号以NC开头，官方认为最可信的），外加几株前一天分析最近源的株。

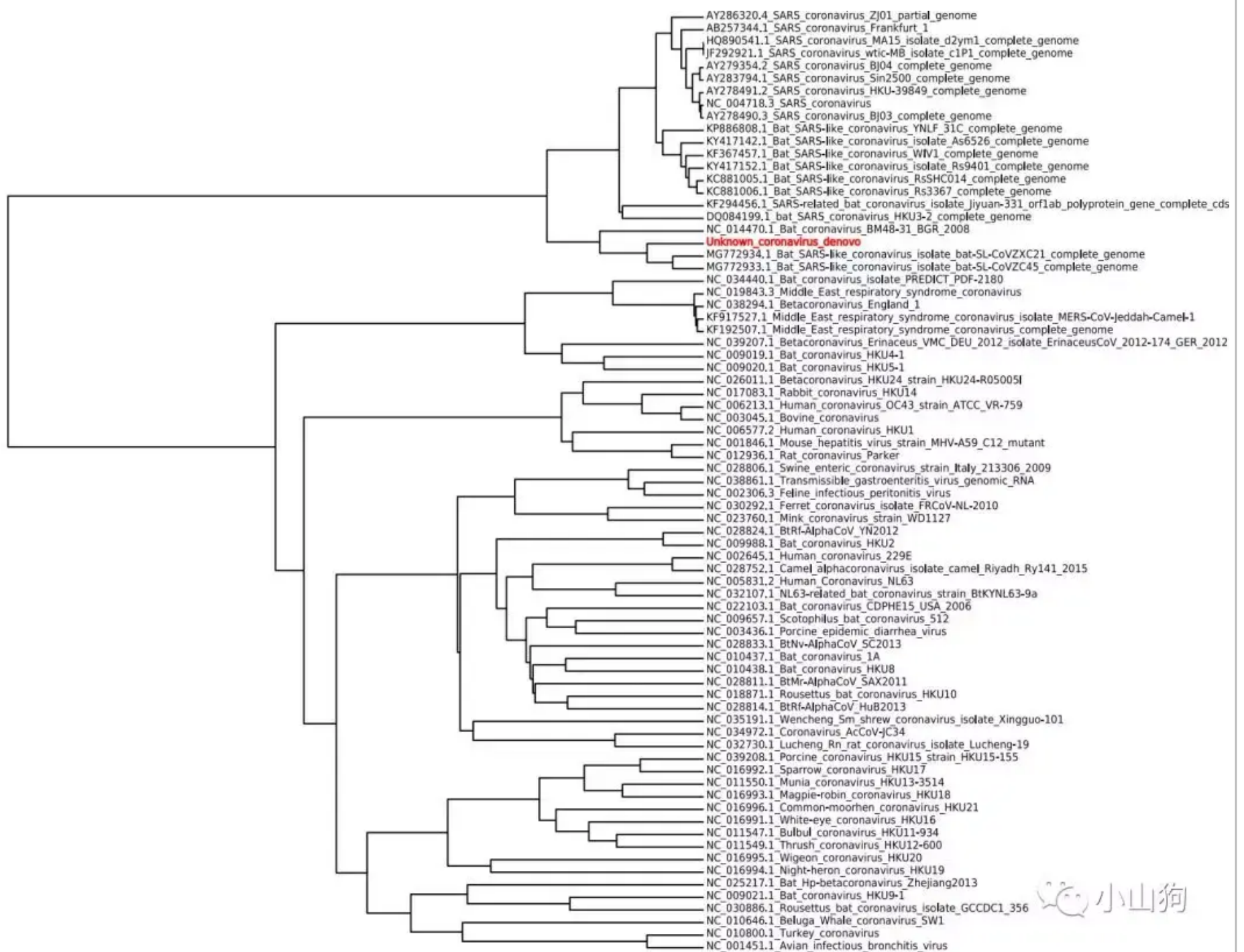
The evolutionary tree was constructed again. This time, the reference strains of all coronaviruses in NCBI were selected (the accession number starts with NC, which is officially considered the most credible), plus a few strains from the most recent source analysed the day before. [image in black is the detailed tree]



进化树结果跟前一天的基本一致。

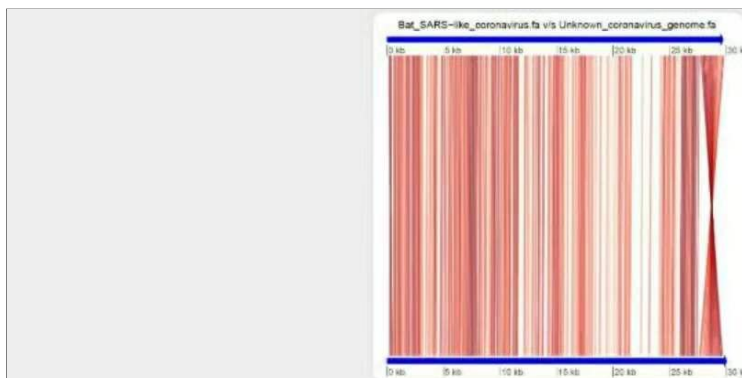
The evolutionary tree results are basically the same as the previous day one.



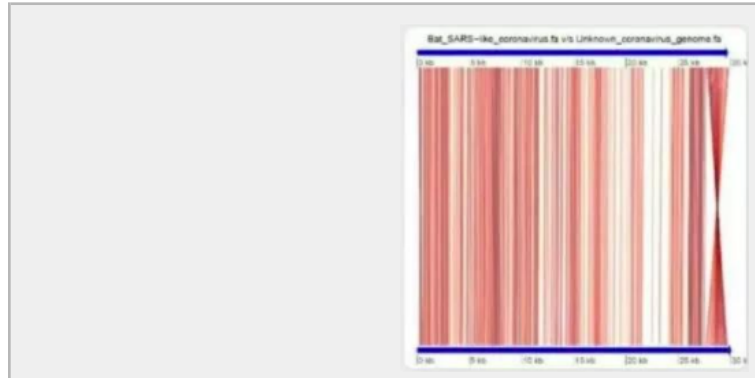


基因组共线性分析、ORF注释等表明这个未知冠状病毒是典型的BetaCoV(orf1ab、S、M、N、E等基因)。共线性图里颜色较浅的是S蛋白区域，是差异最大的基因。

Genome collinearity analysis, ORF annotation, etc. indicate that this unknown coronavirus is a typical BetaCoV (orf1ab, S, M, N, E, etc. genes). The lighter colour in the collinearity map is the S protein region, which is the gene with the greatest difference.



调整了我们组装结果的顺序后，跟Bat\_SARS-like\_coronavirus基因组结构基本一致



After adjusting the order of our assembly results, it is basically consistent with the genome structure of Bat\_SARS-like coronavirus

经过与WHO官网推荐的SARS 7条PCR验证靶标序列比对，发现平均相似度也只有90%左右，关键是引物序列也有几个变异，推测SARS的检测试剂盒无法检测这个未知病原体（后面的很多地方的实验验证也是如此）。

After comparing with the 7 PCR-verified target sequences of SARS recommended by the WHO official website, it was found that the average similarity was only about 90%. The key is that the primer sequences also have several variations. It is speculated that the SARS detection kit cannot detect this unknown pathogen (This was also true for many of the later local experimental validations).

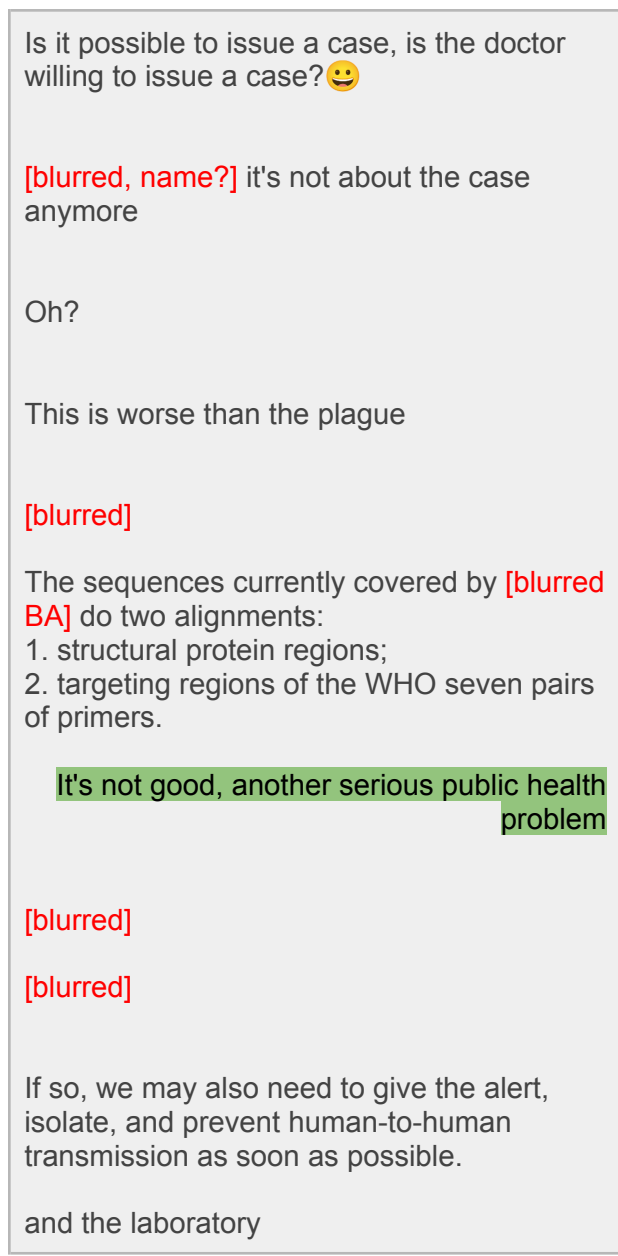
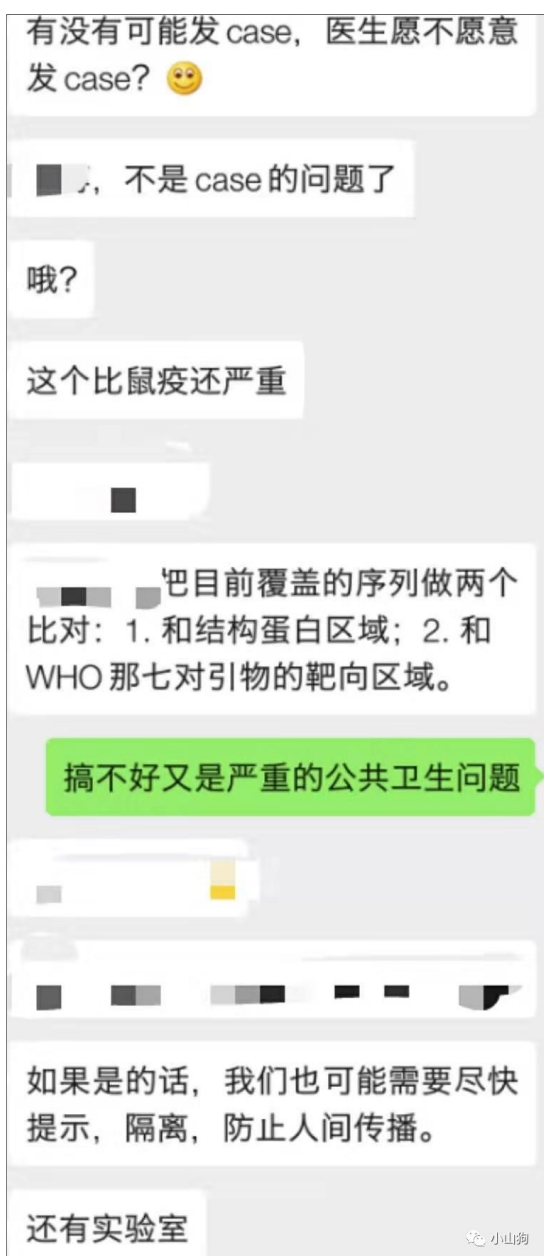
此外还做了很多其他针对基因、蛋白等详细的深入分析，不再赘述了。

In addition, many other detailed in-depth analyses of genes and proteins were carried out, which will not be repeated here.

分析至此已经基本可以确认这个患者的样本里面确实有一个病毒，但这个病毒与所有已知基因组信息的病毒都不太像，可能是一种跟Bat SARS like coronavirus类似的新型病毒。

At this point in the analysis, it was basically confirmed that there was indeed a virus in this patient's sample, but this virus was not very similar to all viruses with known genomic information, and may be a new virus similar to Bat SARS like coronavirus





(现在看回我当时的那句话, 真是一语成谶, 对不起全国人民了, 都怪我这个乌鸦嘴)

(Looking back at what I said at the time, it was a prophecy. I'm sorry for the people of the whole country. Blame me for jinxing it<sup>2</sup>.)

这不一定是SARS, 传染性、致病性都未知, 同时也意识到了问题潜在的严重性, 对实验室做了全面清理消毒, 样本无害化销毁, 实验操作相关人员进行相关监测。

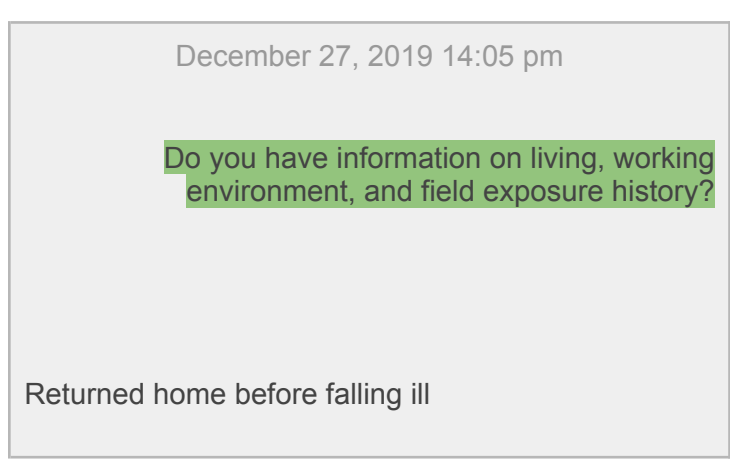
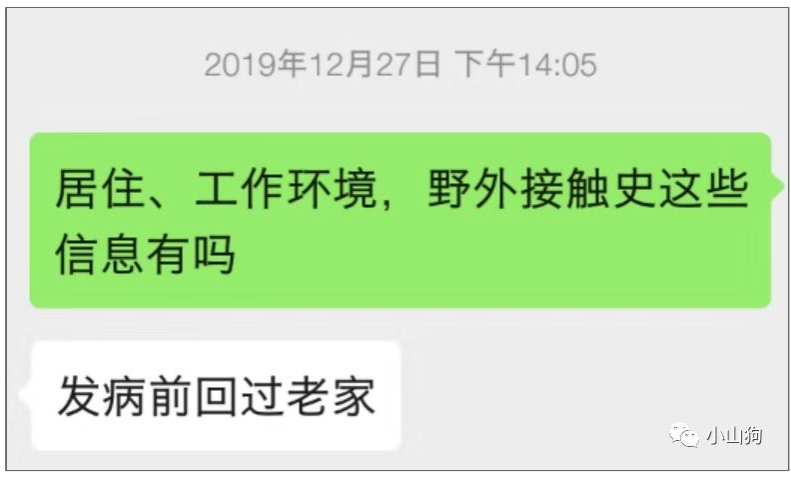
This is not necessarily SARS, the infectivity and pathogenicity are unknown, and at the same time, aware of the potential seriousness of the problem, the laboratory<sup>3</sup> has been thoroughly cleaned and disinfected, the samples were harmlessly destroyed, and the relevant personnel involved in the experimental operation went through the relevant monitoring.

接下来就是怎么去报告的问题了, 直接报可能会吓着医生, 何况这可能是一个新发病毒, 报错了就是重大的事故。有一些必要的信息还是需要先进行排查的。

The next step is how to report the problem. Reporting directly may scare the doctor, not to mention that this may be a new virus, and a wrong report will be a major accident. Some necessary information still needs to be checked first.

最先想到的当然是野生动物接触史, 当时得到的信息是这个病人回过老家, 不排除接触过蝙蝠, 或者被蝙蝠咬了都可能。

The first thing that comes to mind is, of course, the history of contact with wild animals. At that time, the information was that the patient had returned to his hometown, and it was not ruled out that he had come into contact with bats or was bitten by bats.



也曾怀疑是不是哪里的人工病毒相关工作人员操作不慎误感染, 毕竟前一段时间的布鲁菌集体感染就是因为某个工厂灭菌不彻底引发的。

It was also suspected that some staff working somewhere<sup>4</sup> with man-made viruses may have been infected by accident because of careless handling. After all, the outbreak of Brucellosis some time ago was caused by incomplete sterilisation of the bacteria at a certain

<sup>2</sup> The Chinese idiom is 'blame me for my crow's mouth' (都怪我这个乌鸦嘴).

<sup>3</sup> Meaning the Vision Medicals laboratory where that SARS-CoV-2 sample was handled.

<sup>4</sup> In the post following one of Little Mountain Dog's colleagues specifically mentions the WIV which is not far in the city. Hence in the present sentence, somewhere is likely to be quite specific, by it may also more generally mean any lab in the city doing such work..

2019年12月27日 早上09:54

昨天我看老师说武汉病毒所在附近

然后那个布鲁是上游的疫苗厂商没有消毒完全气溶胶出来的

小山的

没有更多信息了，还是要赶紧跟医生沟通这个事情，毕竟我们能保证送检的样本里面就是有这个未知病毒，其他事情就交给医生去调查处理了。

中午前已经跟医生沟通了，患者也隔离了。

现在什么决定？跟医生沟通了吗？

沟通了冠状病毒，患者很重，采取了隔离措施

2019年12月27日 下午13:47

小山的

因为没有掌握其他更多信息，患者也隔离了，这个病毒又不是真正的SARS，想着或者仅仅只是个野生的Bat SARS like，传染性未知，所以紧张的心情也有些放松了。但因为患者病重，也不容小觑，仍然密切跟医院沟通中。期间也在继续做一些深入分析。

27号、28号公司领导也在跟医院和疾控的人电话沟通这个事，29号、30号还亲自去武汉跟医院、疾控中心的领导当面汇报交流这个事情，包括所有我们的分析结果以及医学科学院病原所的分析结果。

一切都在紧张、保密、严格的调查中（此时医院和疾控的人早已经知道有多名类似患者，我们沟通了检测结果之后已经开始了应急处理，但我不知道而已）。

本以为这个事情会很快过去，毕竟除了这个患者，好像也没有听到其他患者感染的消息，但到12月30号的时候，听到消息说类似症状的患者还有挺多个，神经又一下子绷紧了。

特别是，大概是30号下午吧，一个“友商”在另一个患者的样本里面可能也检测到了同一种病毒，但他们直接发了检测到SARS冠状病毒的报告，瞬间把消息给引爆了。

晚间相关部门也发了“不明原因肺炎”的公告，31号凌晨时相关流言也开始在微博上大肆传播。

真正让我再度紧张的是，友商共享了序列给我们分析，我分析一看，确实就是同一种病毒！潜意识里的第一个想法就是“这病毒具有传染性”！可能还真是一种新型的SARS！

30号深夜拿到友商的序列进行分析。

production plant.<sup>5</sup>

December 27, 2019 at 09:54 am

Yesterday I saw that the teacher [name? blurred] said that the Wuhan Institute of Virology is located nearby.<sup>6</sup>

Then Brucella was produced by the upstream vaccine manufacturer without sterilising the aerosol completely.

If there is no more information, it is still necessary to communicate this matter with the doctor quickly. After all, we can guarantee that the sample sent for inspection contains this unknown virus, and other matters will be handed over to the doctor to investigate and deal with.

Information has been shared with the doctor before noon, and the patient has also been isolated.

What is the decision now? Have you communicated with the doctor?

Coronavirus is communicated, the patient is in very serious condition, quarantine measures are taken

December 27, 2019 at 13:47 am  
[following message]

Because there is no other information, the patient is also isolated, and this virus is not a real SARS. I think that it is just a wild Bat SARS like, and the infectivity is unknown, so my nervousness is somewhat relaxed. However, because the patient is seriously ill, it should not be underestimated, and we are still in close communication with the hospital. During that period, we continue to do some in-depth analysis.

**On the 27<sup>th</sup> and 28<sup>th</sup>, the leaders of the company also communicated with the hospital and the CDC people by telephone on that matter. On the 29<sup>th</sup> and 30<sup>th</sup>, they also went to Wuhan in person to report and exchange this matter with the leaders of the hospital and the CDC, including all our analysis results and the analysis results of the Institute of Pathogens of the Academy of Medical Sciences.**

**Everything was under intense, confidential, and rigorous investigation** (at this time, the hospital and CDC people already knew that there were many similar patients, and after we communicated the test results, emergency treatment was started, but I didn't know it).

I thought that this matter would pass soon. After all, apart from this patient, it seems that no other patients have been infected. However, by December 30, I heard that there are quite a few patients with similar symptoms.

Suddenly I was again tense. In particular, about the afternoon of the 30<sup>th</sup>, **a "friend business" may have detected the same virus in another patient's sample**, but they directly sent a report on the detection of SARS coronavirus, which instantly went viral in the news.

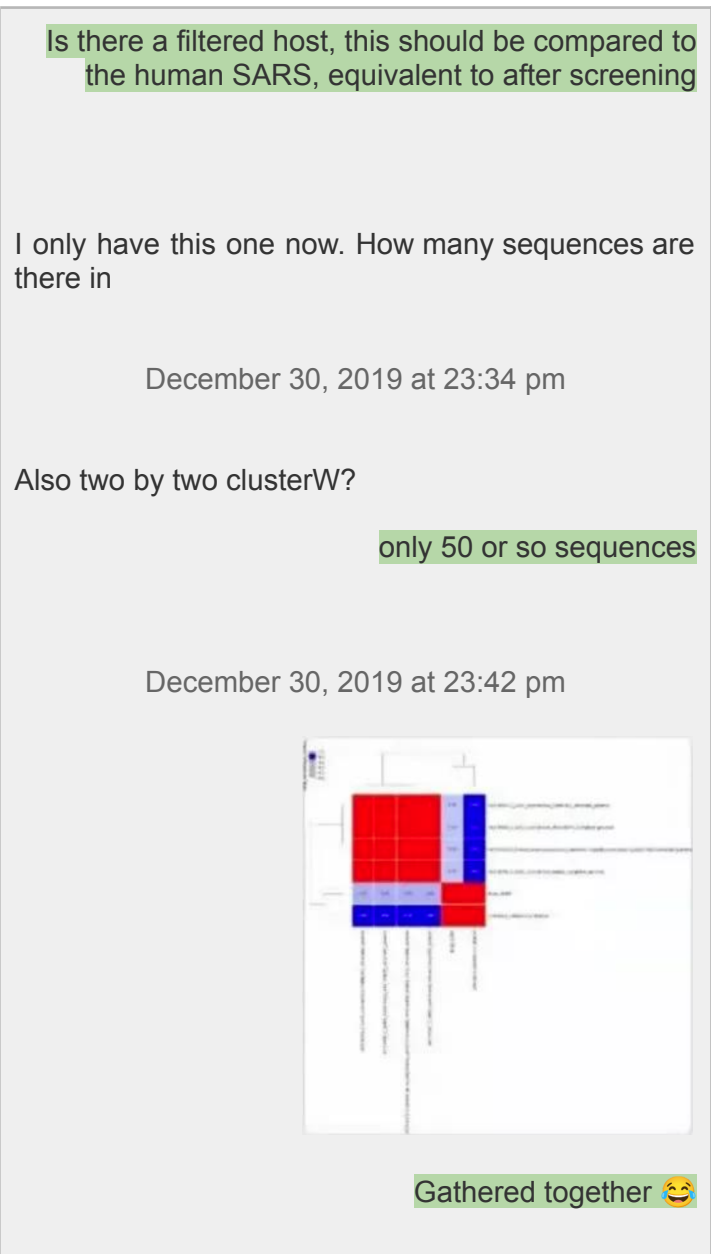
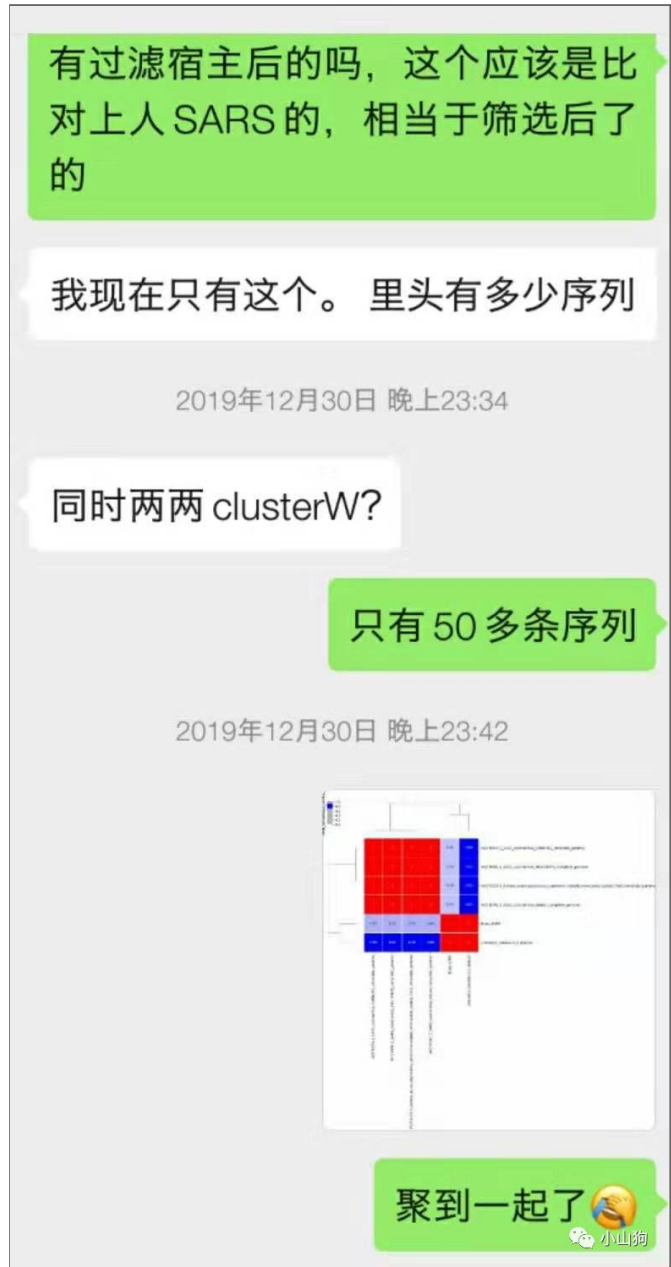
In the evening, relevant departments also issued an announcement of "pneumonia of unknown cause", and in the early hours of the 31<sup>st</sup>, related rumours also began to spread on Weibo.

**What really made me nervous again was that a friend's business shared the sequence for us to analyse.** I analysed it and found that it was indeed the same virus! The first thought in the subconscious is "this virus is contagious"! It may really be a new type of SARS!

In the middle of the night on the 30<sup>th</sup>, I got the sequence from a friend's business for analysis.

<sup>5</sup> This is a reference to the Lanzhou brucellosis outbreak that started in July 2019. **On precisely the 26<sup>th</sup> Dec 2019 a joint investigation had just disclosed** that the outbreak was due to escaped aerosols carried downwind from a vaccine factory, resulting in 200 cases, following [detection in November](#), especially after students at a nearby downwind institute started falling ill. In the following months, the [official tally would climb to 10,528 people](#) infected over 2019, once so many of the previously undisclosed cases were eventually revealed.

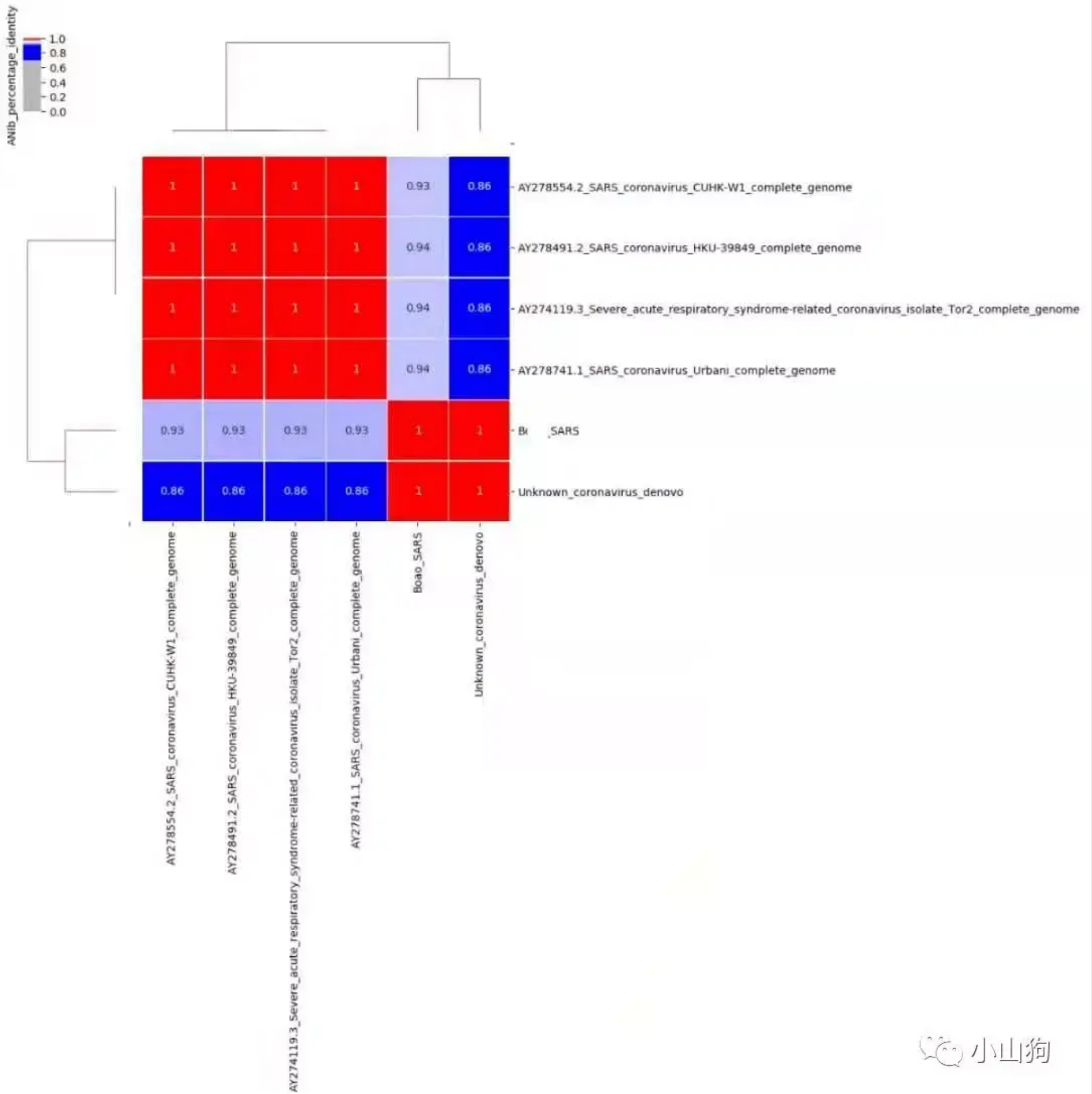
<sup>6</sup> Little Mountain Dog's posts are in green on the right of the screenshots. In white on the left is whomever she is chatting with on WeChat at the time. Here that person (most likely another employee of Vision medicals) mentioned on the 26<sup>th</sup> Dec that someone had pointed out that the WIV is nearby (most likely simply meaning that it is also in Wuhan city centre - no market is ever mentioned at that stage). Given the timing that 'someone' is very likely one of the Vision Medicals senior people who may also be a mentor or professor. For instance [Dr. Xu Teng](#), Vision Medicals CTO, is also a visiting professor of Yunnan Provincial Key Laboratory of Gene Editing.



两个未知病毒聚在了一起, 相似度超过99%

Two unknown viruses are clustered together, and the similarity is more than 99%





小山狗

(由于友商的序列是经过与SARS比对筛选的，所以跟SARS相似度达到93%，而我们的完整的序列则约86%，但两者的同源性还是接近100%)

(Because the sequence of the friend business was compared with SARS, the similarity with SARS reached 93%, while our complete sequence was about 86%, but the homology between the two was still close to 100%)

2019年12月30日 晚上23:50

直接拿我们的做参考，拿他们的fq直接比对，错配率很低

嗯 发个数据

2019年12月31日 凌晨00:02

|   |          |    |
|---|----------|----|
| 9 | Map_read | 59 |
|---|----------|----|

所以抛开序列被过滤，基本上是一个东西了

是的

December 30, 2019 23:50 pm

Take ours directly as a reference and compare their fq directly, the mismatch rate is very low

OK send data

December 31, 2019 00:02 am

|   |          |    |
|---|----------|----|
| 9 | Map_read | 59 |
|---|----------|----|

So putting aside the sequence being filtered, it's basically the same thing

Yes

两两直接比对，所有序列均能比对上，相似度达99.6%，再保守的区域，不同物种间的相似度几乎不可能这样高，而且全基因组覆盖率超过了20%，确认是同一种病毒无疑！

| #Sample | Total_read | Map_read | Map_rate | Identity    |
|---------|------------|----------|----------|-------------|
| 1 SARS  | 59         | 59       | 1        | 0.995676364 |

此时的心情既很紧张，也很激动。紧张在于，这个未知的病毒可能会像SARS那样恐怖；激动在于，我们通过mNGS技术及早发现并确认了这个病原体，并且对患者进行了隔离，在病毒大范围传播之前有可能通过防控措施把它扼杀在摇篮中！

心情复杂，感慨万分，随即发了条没几人能懂的朋友圈。

无数个独自加班的深夜，只为打磨更好的技术，当这一刻来临时不会束手无策，以前理论上应用，今夜再次被证实，mNGS技术将被推向神坛...

我们深深明了，每一份珍贵标本的背后，都有一位亟待救治的患者。

2019年12月31日 00:33 删除

小山狗

12月31号早间，微博上关于SARS的流言开始大肆传播。我一直在等着看官方如何回应。下午官方发布通告，只说了是“不明原因肺炎”，并未提是什么病原体，有27例类似的病例，其中7例重症。看到这个消息后，我感觉事情不妙了，猜测这个病毒传染能力并不低。

然而官方的通报却是“未发现明显人传人现象”，早期掌握的数据并不多，局势不好判断，何况是新发病毒，为了稳住社会情绪，避免民众过度恐慌，这样的通告其实也可以理解。

此时专家组已经开始介入，武汉病毒所等“国家队”也开始分析鉴定，他们知道更多信息，有更多样本和数据，也更有条件更专业，所以后续我就没有做太多深入分析的工作了，等待官方的结果。

刚开始我对国家在处理这些突发的重大公共卫生事件的能力还是挺有信心的，毕竟经过了SARS、甲流等事件的洗礼。此外，就在两个多月前的北京鼠疫事件，也是由我们通过mNGS检测出来上报的，当天上报后他们就启动了应急处理程序，马上用了其他方法再次验证，第二天一早就看到新闻了，后续也没有发现新传染的病例，防控做得很好。mNGS在鼠疫事件中立了大功，想着在这个未知病毒的防控中也能起很大作用吧。

媒体开始辟谣，最早见新京报发出“SARS系谣言”，人民日报等则用词稍微委婉些“不能断定是SARS”，后面8位“造谣”的人被抓了。

看到这些新闻后，不知怎么的，心里突然有点失望了。科学上尚未有定论或者有争议的东西，直接就是谣言了？

Pairwise direct comparison, all sequences can be compared, the similarity is 99.6%, and the similarity between different species is almost impossible in the conserved region, and the whole genome coverage rate exceeds 20%, confirming that it is the same virus without a doubt!

| #Sample | Total_read | Map_read | Map_rate | Identity    |
|---------|------------|----------|----------|-------------|
| 1 SARS  | 59         | 59       | 1        | 0.995676364 |

The mood at this time was both nervous and excited. The nervousness was due to the fact that this unknown virus may be as terrifying as SARS; the excitement was that we detected and confirmed this pathogen early through mNGS technology, and quarantined the patient, so it may be possible to prevent and control the virus before it spreads widely. Strangled in the cradle!

With mixed feelings and emotions, I immediately posted a circle of friends that few people can understand.

Countless late nights of working overtime alone, just to polish better technology, will not be helpless when this moment comes. The theoretical application in the past has been confirmed again tonight, and the mNGS technology will be pushed to the altar...

We are well aware, behind every precious sample there is a patient waiting treatment?

December 31, 2019 00:33 Deleted

On the morning of December 31, rumours about SARS on Weibo began to spread wildly. I've been waiting to see how the officials would respond. In the afternoon, the official announcement was issued, only stating that it was "**pneumonia of unknown cause**" **without mentioning the pathogen**, and that there were 27 similar cases, 7 of which were severe.

After seeing the news, I felt that things were not good, and I guessed that the infectious ability of this virus was not low. However, the official notification is that "no obvious human-to-human transmission has been found". There is not much data in the early stage, and the situation is not easy to judge, not to mention [that this is] a new virus. **In order to stabilise social sentiment and avoid excessive panic among the people, such a notification is actually understandable.**

At this time, the expert group has begun to intervene, and the "national team" **such as the Wuhan Institute of Virology has also begun to analyse and identify. They know more information, have more samples and data, and are more qualified and professional, so I will not do much in-depth follow-up.** The analysis is done, waiting for the official results.

At the beginning, I was quite confident in the country's ability to deal with these sudden and major public health events. After all, it has been battle-hardened by events such as SARS and influenza A. In addition, the [Beijing plague incident](#) just over two months ago was also detected and reported by us through mNGS. After the report was communicated that day, they started the emergency response procedure and immediately used other methods to verify it again. The next morning I saw it. The news was out, and no new cases of infection had been found in the follow-up, and the prevention and control had been done very well. mNGS has made great contributions to the plague incident, and I think it can also play a great role in the prevention and control of this unknown virus.

The media began to refute the rumours. The first time the Beijing News mentioned "the SARS-related rumours", the People's Daily and others used a slightly more euphemistic wording, "It cannot be concluded that it is SARS." The latter eight people who "spread rumours" were arrested.

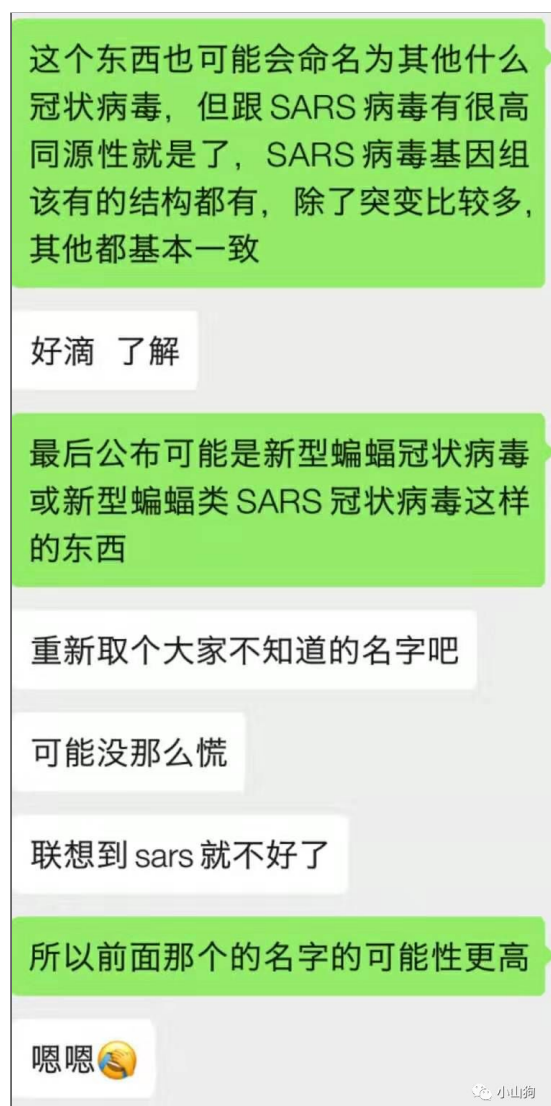
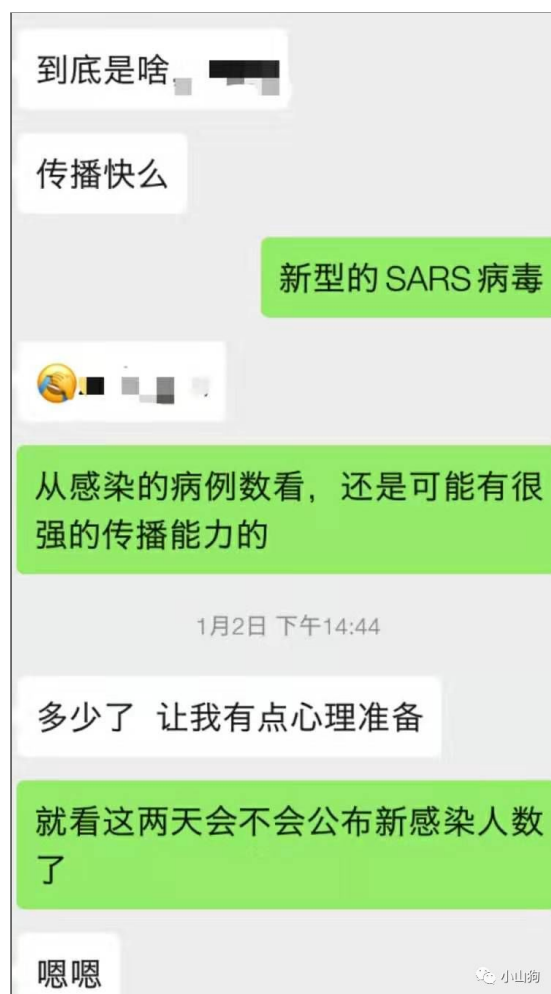
After seeing the news, for some reason, I was suddenly a little disappointed. Are things that have not yet been conclusive or are controversial in science, just rumours?

<sup>7</sup> This is the motto of IDSeq™, a key technology platform developed by Vision Medicals, which was used in the analysis of the samples on the 26<sup>th</sup>/27<sup>th</sup> Dec 19. See <https://archive.ph/VX0Kb>. IDSeq trademark was applied for in [July 2019](#).



开始有一种感觉：这种辟谣的论调，以及那些过度乐观的宣传都会把这个事情推向难以挽回的局面。媒体的高调辟谣会干预这个病毒科学的定性，过度乐观的宣传会让大众缺乏敬畏之心，不会采取防卫措施。后续事态的发展又一次验证了我的担忧。

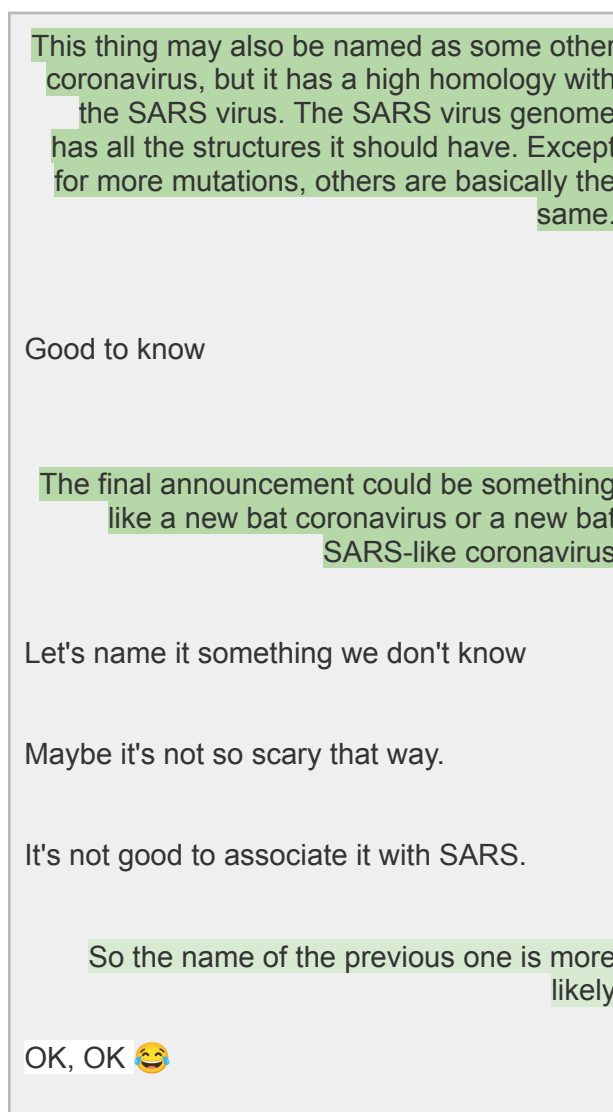
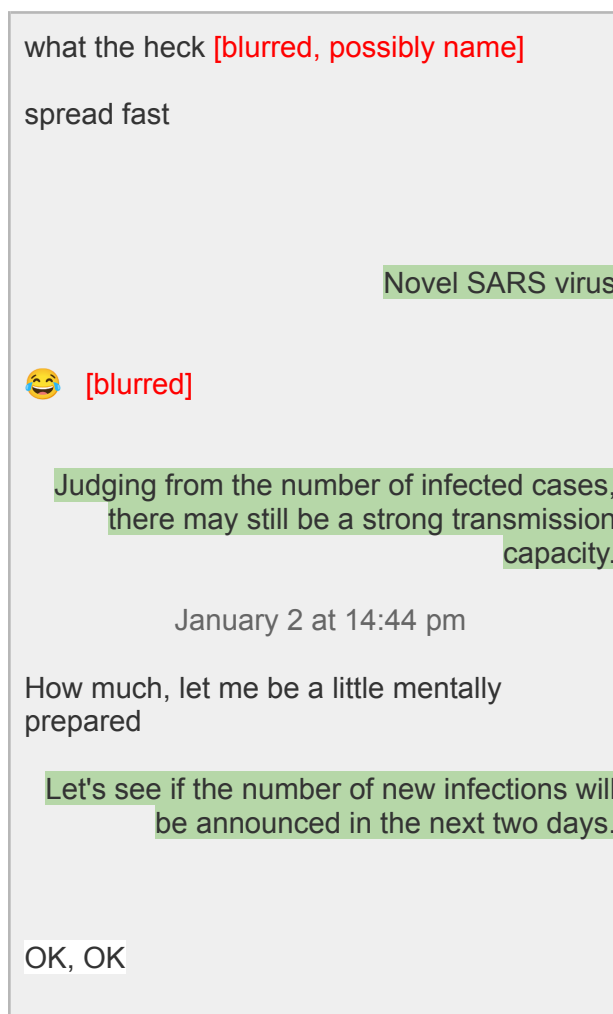
事件引爆了以后，也有些朋友来问我是否知情，特别是武汉的朋友。在告知一定要先严格保密后（毕竟有人被抓了），我还是透露了一点消息给他们，让他们一定要注意防护。



这个对话或许也能理解为什么要辟谣SARS，以及命名为新型冠状病毒，毕竟基因组相似度只有80%左右（题外话，肠道病毒同一个型别的不同毒株，很多的相似度也才80%左右），SARS给我们带来了太多创伤，大众对其极为恐慌。

There was a feeling that this dispelling rhetoric, as well as that overly optimistic propaganda, would push the matter into an irreversible situation. The high-profile refutation of rumours by the media will interfere with the characterization of this virus science, and the overly optimistic propaganda would leave the public lacking in respect and not taking defensive measures. Subsequent developments have once again confirmed my concerns.

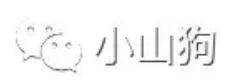
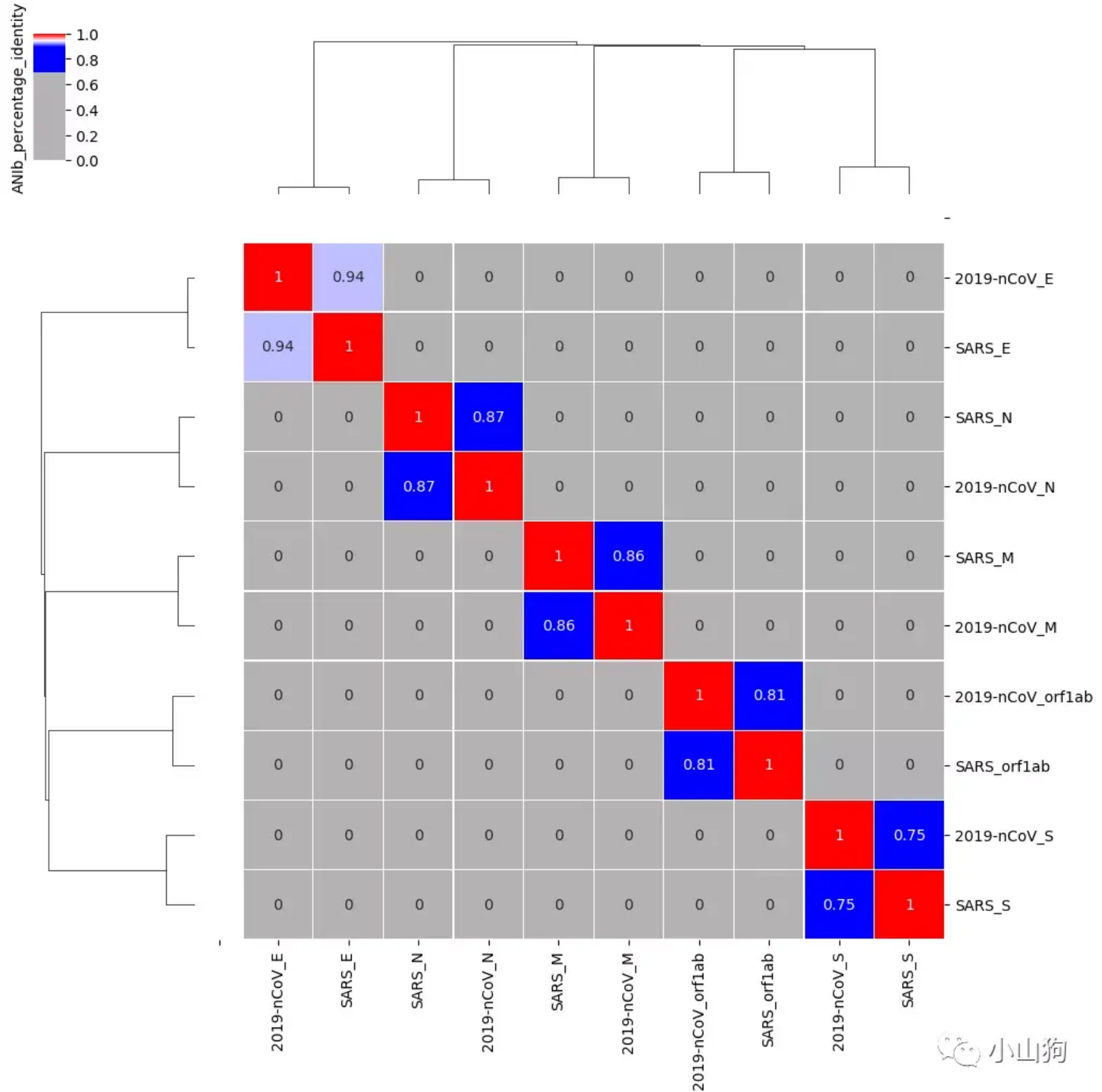
After the incident went viral, some friends also came to ask me if I knew anything, especially friends from Wuhan. After telling them that this must be kept strictly confidential (after all, someone was arrested), I still revealed a little bit of information to them, so that they may pay attention to protection.



This dialogue may also clarify why it is necessary to refute the rumours about SARS, and the naming of a novel coronavirus. After all, the genome similarity is only about 80% (off topic, many different strains of the same type of enterovirus are only 80% similar). SARS has caused



so much trauma to us that the public is extremely panicked by it.



新型冠状病毒和SARS不同的基因的相似度不同，从75%到94%不等，特别是S基因，与人细胞受体 (ACE2) 相关，相似度才75%。所以说不属于SARS，那也算是有依据吧。

不过后来石正丽的文章中，通过他们的方法分析，新型冠状病毒也是属于SARSr-CoV(SARS相关冠状病毒)。

事件后续的发展大家都知道了。这里再说说几个问题。

为什么我们两天就已经分析出了这个未知的病毒是一个跟SARS很像的冠状病毒，并且上报了所有分析结果，官方要到1月7号才发布消息明确肺炎是由新型冠状病毒引起的？

其实我们做的工作只是分析鉴定了送检样本里面有这么个病毒，但肺炎是否是这个病毒导致的，我们并没有去分析，也无法去分析，检测到病毒不等于肺炎由该病毒引起。

如此重大的卫生事件，官方自然要严谨论证，而且也有一套国际参考验证流程 (科赫法则)。官方要做的不仅是检测到多个样本都有这么个病毒，还要验证肺炎是因为这个病毒导致的等等。

The similarity of different genes of the new coronavirus compared to SARS is different, ranging from 75% to 94%. In particular the S gene, which is related to the human cell receptor (ACE2), is only 75% similar. Therefore, it is not SARS, and that is a good basis for it.

However, in [Shi Zhengli's article later](#), according to their methodological analysis, the new coronavirus also belongs to SARSr-CoV (SARS-related coronavirus).

We all know what happened next. Here are a few more questions.

Q: Why did we conclude that this unknown virus was a coronavirus very similar to SARS within two days, and reported all the analysis results, while it took until January 7 for the official announcement to clarify that the pneumonia was caused by the novel coronavirus?

In fact, what we did was to analyse and identify such a virus in the samples submitted for inspection, but whether the pneumonia was caused by this virus, we did not analyse it, nor could we analyse it. And the detection of the virus does not mean that the pneumonia was caused by the virus.

For such a major health event, the officials naturally have to be rigorous in their arguments, and there is also a set of international reference verification procedures (Koch's postulates). What the official has to do is not only to detect that multiple samples have such a virus, but also to verify that the pneumonia is caused by this virus, etc.

柯霍氏法则主要分为四个步骤: [1]

1. 病体罹病部位经常可以找到大量的病原体, 而在健康活体中找不到这些病原体。
2. 病原菌可被分离并在培养基中进行培养, 并记录各项特征。
3. 纯粹培养的病原菌应该接种至与病株相同品种的健康植株, 并产生与病株相同的病症。
4. 从接种的病株上以相同的分离方法应能再分离出病原, 且其特征与由原病株分离者应完全相同。

分离、培养、验证等等这些都是很花时间的, 还要经过专家讨论, 达成共识。从近段时间发表的很多关于新型冠状病毒的论文上也可以看到, 很多测序数据都是在1月份的头两三天就完成了的。

这个事情还有一个很感概的事情就是, 知道真相的人噤如寒蝉, 不知道真相的人各种“大力科普”、“深度分析”; 亲身经历的公司只字不敢言, 其他公司各种借势营销。从鼠疫到新型冠状病毒皆是如此, 呵呵, 好有意思。

要谈对整个事件的想法, 最大的感觉就是失望, 痛心, 还有愤怒。我们都已经发现那么及时了, 为啥现在还是没能控制住? 让全国进入的疫情大战? 更多的不是科学因素, 也不是技术因素, 而是决策和媒体。

我曾经是个很愤青的人, 事已至此, 无力回天, 传递信心才是最重要的吧。马后炮, 人人都是精英, 谁都不曾想到事情发展成这个样子, 所以也懒得去批判很多事情了。但有些话还是想说几句。

辟谣SARS、媒体宣扬的乐观情绪, 这些在最早期的时候都没有太大问题, 毕竟对这个病毒的认知非常有限。在应对这些重大公共卫生事件时, 疾控系统可能采用“内严外松”的规则, 内部谨慎小心、严格验证、仔细评估, 对外通告却可能偏向乐观, 避免引起过度恐慌。何况在这次事件上, 怎么去给公众交代, 显然已经不是疾控系统能单独决策的事了。

武汉交通枢纽的地位不必多言, 当时也临近春节, 正是餐饮、旅游、电影等服务业的旺季。悲观的宣传无疑会重创这些服务业, 还会引起大众过度恐慌, 导致物资哄抢, 社会混乱等严重后果。

若这病毒真无什么传播能力, 或者因为采取了这些措施扼杀了病毒的传播, 社会没看到这个病毒能带来什么危害, 决策者必然会被骂反应过度、小题大做, 到时自然要背锅。

相反, 过于乐观的宣传, 病毒不强则皆大欢喜, 开心过大年, 病毒强则会致大众缺乏防范意识, 防控工作难以展开, 最终导致病毒的快速传播, 产生更加严重的后果。

所以, 当你作为一个决策者的时候, 你不得不综合考虑方方面面的因素, 社会、经济乃至政治各方面都需要做一个平衡, 非常考验决策者和专家们的能力和远见。

走对了, 平淡无奇, 走错了, 千古罪人。

这个世界没有平行宇宙, 我们无法知道哪种决策才是更正确的, 或更错误的。在国内这种什么事情都喜欢往乐观上面宣传的大氛围下, 以及侥幸心理的存在, 决策者做什么决策, 可想而知。

Koch's postulates are mainly divided into four steps: [1]

1. A large number of pathogens can often be found in the diseased parts of the diseased body, but these pathogens cannot be found in healthy living bodies.
2. The pathogenic bacteria can be isolated and cultured in the medium and the characteristics recorded.
3. The pathogenic bacteria cultivated in pure catalpa should be inoculated into healthy plants of the same variety as the diseased plants, and produce the same fatigue symptoms as the diseased plants.
4. The pathogen should be able to be re-isolated from the inoculated diseased strain by the same separation method, and its characteristics are the same as those of the original diseased strain.

Virus isolation, cultivation, verification, etc. are all time-consuming, and need to be discussed and agreed upon by experts. It can also be seen from many papers on the new coronavirus published recently that many sequencing data were completed in the first two or three days of January.

There is also a very comprehensible thing about this matter, namely that those people who know the truth are silent, while those who don't know the truth are doing all kinds of "strong science" and "in-depth analysis"; The company I experienced personally did not dare to say a word, and other companies took advantage of all kinds of marketing. This is true from the plague to the new coronavirus, hehe, so interesting.

To talk about my views on the whole incident, the biggest feelings are disappointment, sadness, and anger. We have found it so promptly, why is it still not under control now? Let the whole country enter the epidemic war? It's not so much up to the science, or the technology, but to the decision making process and the media.

I used to be a very cynical person. The matter has come to this point and we can't turn back the clock. Passing on confidence is the most important thing. After the events everyone is an expert, and no one would have thought that things would develop like this, so it's rather lazy to criticise many things. But there are still some things I want to say.

Dispelling rumours of SARS and the optimism promoted by the media were not a big problem in the earliest days, when after all, the understanding of this virus was very limited. In response to these major public health events, the CDC may adopt the rules of "internal strictness and external looseness", with internal caution, strict verification, and careful evaluation, but external announcements may be optimistic to avoid causing excessive panic. What's more, in this incident, how to go public is obviously not something that the CDC can decide alone.

The status of Wuhan as a transportation hub doesn't need any introduction. At that time, the Spring Festival was approaching, which was the peak season for catering, tourism, movies and other service industries. Pessimistic propaganda would undoubtedly hit these service industries hard, and it would also cause excessive panic among the public, leading to serious consequences such as material looting and social chaos.

If the virus really has no ability to spread, or because measures are taken to stifle the spread of the virus, the society does not see what harm the virus can bring, and policymakers will inevitably be called out for overreacting and making a big fuss, and then they will naturally take the blame.

On the contrary, in the case where the propaganda is too optimistic, if the virus is not strong, everyone will be happy, and if the virus is strong, it will cause the public to lack awareness of prevention, and it will be difficult to carry out prevention and control work, which will eventually lead to the rapid spread of the virus and more serious consequences.

Therefore, when you are a decision maker, you have to take all factors into consideration. Social, economic and political aspects need to be balanced, which will test the ability and foresight of decision makers and experts.

Go right, it's bland. Go wrong, you are a sinner forever.

There are no parallel universes in this world, and we have no way of knowing which decision is more right or wrong. In the domestic atmosphere where everyone likes to be optimistic about everything, and the existence of luck, it is understandable what decision decision-makers will make.

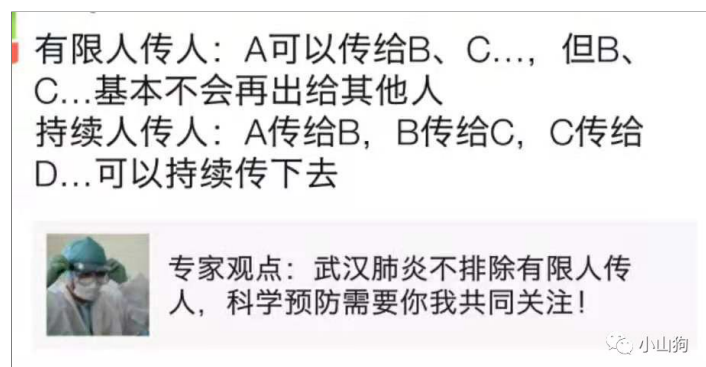


在事件的后期发展中，特别是1月12号左右开始，我相信专家们已经看到事情正在往不好的方向发展了（首批确诊的41例患者，约30%并无海鲜市场接触史，此时多地开始出现疑似病例了，有些已经初步核酸阳性）。

但是在后续的宣传上还是太过于乐观和艺术化了，同时还在不断辟谣，还没任何发布预警的迹象。

“不排除有限人传人，持续人传人风险低，可防可控”，用词颇为谨慎讲究，且不说是否过于乐观，就问有多少普通民众知道什么是“有限人传人”？什么是“持续人传人”？

他们的理解可能就是基本不会人传人，自然毫无戒备之心。我还在朋友圈科普了一下。



有限人传人：A可以传给B、C...，但B、C...基本不会再出给其他人  
持续人传人：A传给B，B传给C，C传给D...可以持续传下去

专家观点：武汉肺炎不排除有限人传人，科学预防需要你我共同关注！  
小山狗

从现在发表的很多论文上也可以看出，很多专家很早就对这个病毒的传播能力有较深的认识了，越往后，掌握的数据越多，对局势的预判越清晰。

我相信专家们早已给出不怎么乐观的预判，但如果某些人，为了顾及某些人或某些媒体的面子（毕竟之前宣传得太乐观，现在打脸太疼），罔顾专家意见，不顾民众健康，不得不往乐观上面去通告，坚持不发布预警，这就不可原谅了。无论是谁，该罚的罚，该撤职的撤职。

别的不多说了，谈点希望吧。

mNGS确实是一个好技术，在疑难、危重病例诊断以及这种突发的重大公共卫生事件的早期监测和爆发监测中起到很大的作用。现在提供mNGS病原体检测服务厂商有很多，建议疾控系统可以跟一些技术好的企业建立直接沟通的渠道，能够更快速地应对像这样的突发事件。另外，mNGS企业们也可以建立一个信息共享平台，在遇到这些事件时及时共享信息，看看是否有爆发（我知道这个很难，一方面本来就是商业机密，另一方面敏感病原体谁都不敢轻易报吧，但我还是觉得这个事情很有意义，希望有朝一日可以成为现实吧）。

也希望我们经历了这次新型冠状病毒事件后，国家的重大公共卫生事件的处理能力有长足进步吧。个人认为，在通告宣传上可以借鉴天气预报的规则——“总是会往危害大些方面去预报”，以提醒民众做更多预防，降低心理预期。俗话说：没有期望就不会失望。

这件事情对我而言，仿佛就是一场年终大考，用尽所学，交了一份还算合格的答卷吧，只是这份答卷是否发挥出最大的作用了呢？第一次亲身参与到了如此重大的公共卫生事件，做出了一点贡献，也锻炼成长了许多。

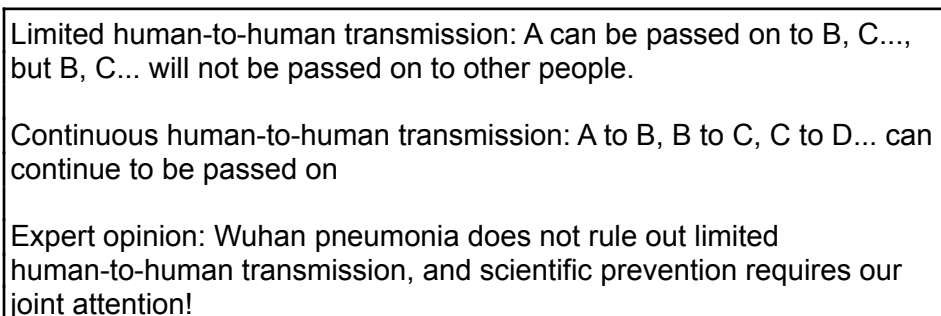
据我目前所知，最早发现这个病毒的应该就是我们就了，因为也是我们上报结果以后，疾控系统开始介入。从GISAID数据库网站上提交的数据看，样本收集的时间也是我们最早的。也许其他机构也测到了这个病毒，但这是未知的病毒，核酸数据库中并没有参考基因组，他们不一定有这个生信能力去分析鉴定。

In the later development of the incident, especially starting around January 12, I believe the experts saw that things were going in a bad direction (about 30% of the first 41 confirmed patients had no history of exposure to the seafood market. At this time, suspected cases began to appear in many places, and some of them were initially positive for nucleic acid).

However, in the follow-up, the public messaging is still too optimistic and artistic, and at the same time, it is still constantly refuting rumours, and there is no sign of issuing an early warning.

"Limited human-to-human transmission is not ruled out, the risk of sustained human-to-human transmission is low, and it is preventable and controllable." The wording is quite cautious, not to mention whether it is too optimistic, just ask how many ordinary people know what "limited human-to-human transmission" is? What is "sustained human-to-human transmission"?

Their understanding may be that there is basically no human-to-human transmission, and they are naturally unsuspecting. I also popularised it in my circle of friends.



Limited human-to-human transmission: A can be passed on to B, C..., but B, C... will not be passed on to other people.

Continuous human-to-human transmission: A to B, B to C, C to D... can continue to be passed on

Expert opinion: Wuhan pneumonia does not rule out limited human-to-human transmission, and scientific prevention requires our joint attention!

It can also be seen from many papers published now that many experts had a deep understanding of the spread of this virus very early, and the more data they had, the clearer the prediction of the situation.

I believe that experts have already given not very optimistic predictions, but if some people, in order to take into account the public standing of certain people or certain media (after all, the propaganda was too optimistic before, and now it is too painful to face), ignoring the opinions of experts and disregarding the public health, it is unforgivable to have to make announcements so optimistic in character and to insist not to issue early warnings. No matter who it is, the penalty gets punished, the dismissal gets dismissed.

Without further ado, let's talk about hope.

mNGS is indeed a good technology, which plays a great role in the diagnosis of difficult and critical cases, as well as in the early surveillance and outbreak surveillance of such sudden and major public health events. There are many manufacturers providing mNGS pathogen detection services. It is suggested that the CDC can establish direct communication channels with some companies with good technology, so that it may respond to emergencies like this more quickly. In addition, mNGS companies can also establish an information sharing platform to share information in time when encountering these incidents to see if there is an outbreak (I know this is difficult. On the one hand, it is a commercial secret. On the other hand, sensitive pathogens are not reported easily by anyone, but I still think this matter is very meaningful, and I hope it will become a reality one day).

I also hope that after we have experienced this new coronavirus incident, the country's ability to handle major public health events has made great progress. Personally, I believe that the rules of weather forecasting can be used for reference in announcements and publicity - "there will always be more harmful aspects to forecast" to remind the public to take more precautions and reduce psychological expectations. As the saying goes: without expectations, you will not be disappointed.

To me, this matter seems to be a year-end exam. I have exhausted what I have learned and handed in a fairly qualified answer sheet, but has this answer sheet played the biggest role? For the first time, I personally participated in such a major public health event, made a little contribution, and practised and grew a lot.

As far as I know, we should have been the first to discover this virus, because **it was after we reported the results that the CDC began to intervene**. From the data submitted on the GISAID database website, the time of sample collection is also our earliest. Maybe other institutions have also detected this virus, but this is an unknown virus, there is no reference genome in the nucleic acid database, and they may not have the ability to analyse and identify it.



| Registered Users                 |              | EpiFlu™                                 |                 | BetaCoV 2019-2020 |       | My profile            |                      |
|----------------------------------|--------------|---|-----------------|-------------------|-------|-----------------------|----------------------|
| BetaCoV 2019-2020                |              | Browse                                  |                 | My Unreleased     |       | Upload                |                      |
| Virus name                       | Passage de   | Accession ID                            | Collection date | Submission Da     | Host  | Originating lab       | Submitting lab       |
| BetaCoV/Wuhan/WIV06/2019         | Original     | EPI_ISL_402129                          | 2019-12-30      | 2020-01-18        | Human | Wuhan Jinyintan H     | Wuhan Institute of   |
| BetaCoV/Wuhan/WIV05/2019         | Original     | EPI_ISL_402128                          | 2019-12-30      | 2020-01-18        | Human | Wuhan Jinyintan H     | Wuhan Institute of   |
| BetaCoV/Wuhan/WIV02/2019         | Original     | EPI_ISL_402127                          | 2019-12-30      | 2020-01-18        | Human | Wuhan Jinyintan H     | Wuhan Institute of   |
| BetaCoV/Nonthaburi/74/2020       | Original     | EPI_ISL_403963                          | 2020-01-13      | 2020-01-17        | Human | Bamrasnaradura H      | 1. Department of I   |
| BetaCoV/Nonthaburi/61/2020       | Original     | EPI_ISL_403962                          | 2020-01-08      | 2020-01-17        | Human | Bamrasnaradura H      | 1. Department of I   |
| BetaCoV/Kanagawa/1/2020          | Original     | EPI_ISL_402126                          | 2020-01-14      | 2020-01-16        | Human | Dept. of Virology III | Dept. of Virology I  |
| BetaCoV/Wuhan-Hu-1/2019          | unknown      | EPI_ISL_402125                          | 2019-12         | 2020-01-12        | Human | unknown               | National Institute f |
| BetaCoV/Wuhan/WIV04/2019         | Original     | EPI_ISL_402124                          | 2019-12-30      | 2020-01-11        | Human | Wuhan Jinyintan H     | Wuhan Institute of   |
| BetaCoV/Wuhan/IPBCAMS-WH-01/2019 | Original     | EPI_ISL_402123                          | 2019-12-24      | 2020-01-11        | Human | Institute of Pathoge  | Institute of Pathog  |
| BetaCoV/Wuhan/IVDC-HB-04/2020    | Original     | EPI_ISL_402120                          | 2020-01-01      | 2020-01-11        | Human | National Institute fo | National Institute f |
| BetaCoV/Wuhan/IVDC-HB-05/2019    | Original     | EPI_ISL_402121                          | 2019-12-30      | 2020-01-10        | Human | National Institute fo | National Institute f |
| BetaCoV/Wuhan/IVDC-HB-01/2019    | Virus Isolat | EPI_ISL_402119                          | 2019-12-30      | 2020-01-10        | Human | National Inst' fo     | National Institute f |
| Total: 29 submissions            |              | << first < prev <b>1</b> next > last >> |                 |                   |       |                       |                      |

所以，应该就是我们首次发现了这个新型冠状病毒吧，记录一下。

希望早点战胜疫情吧。

中国加油！武汉加油！

2020.01.28

So, it should be that we were the first to discover this new coronavirus. Let's record it.

Hope to overcome the epidemic soon.

Go China! Come on, Wuhan!

2020.01.28

**Post 2: Weixin post by Little Mountain Dog, on the 30<sup>th</sup> Jan 2020**  
**Statement on "Recording the experience of first discovering the novel coronavirus"**  
[Original](#) ([web archive](#))

关于《记录一下首次发现新型冠状病毒的经历》的声明  
**Original** 小山狗 小山狗 2020-01-30 23:39

- 1、《记录一下首次发现新型冠状病毒的经历》一文本来是写给我自己日后看的，不料传播出去了，不想牵扯任何事情，所以删了。
- 2、未授权给任何个人或媒体，所有转载均是未授权转载；也未曾给任何人提供任何资料。
- 3、帝国主义亡我之心不死，任何信息都可被外部反华势力捕风作影、添油加醋，欲加之罪何患无辞。公开发表的论文里更多细节也更权威，若本文信息不幸被利用，权当笑料罢了。
- 4、本人单位并非任何公职机构，仅仅只是位于广州黄埔的小小民营企业。
- 5、不想给任何人带来麻烦，不想给社会舆论带去任何搅动。公司待我很好，也不想给公司带来任何麻烦，公司对我发文并不知情，事后领导也理解宽容，我随公司一同成长，不能辜负了公司对我的厚爱与期望。
- 6、我还是太年轻了，这件事情背后太复杂了，我只是发表了下自己的感想。我没有条件也没有能力去判断早期疫情的发展方向，这些都是事后诸葛亮。不是我不去给上面提建议，也不是我知道疫情那么严重却没有勇气在早期向社会公布信息，而是我真的没这个能力，对整个疫情的发展一无所知。
- 7、我只想潜心钻研技术，好好搞研究，能不能造福一方百姓，看运气吧。不想被任何关注和打扰，大伙都散去吧。

**Statement on "Recording the experience of first discovering the novel coronavirus"**  
**Original** Small Mountain Dog Small Mountain Dog 2020-01-30 23:39

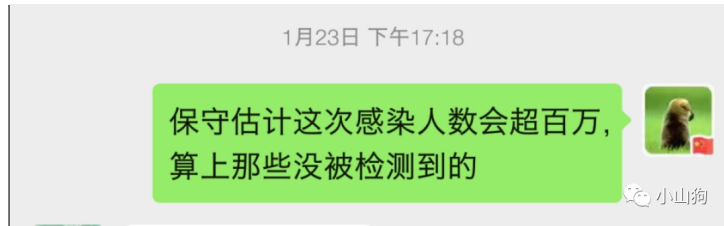
1. The text "Recording the experience of first discovering the new coronavirus" was written for myself to read in the future, but it spread online and I didn't want to get involved in anything, so I deleted it.
2. Not authorised to any individual or media, all reprints are unauthorised reprints; and no information has been provided to anyone.
3. The heart of imperialism will never die, and any information can be swayed by external anti-China forces to add fuel to the scandal. More details in published papers are also more authoritative. If the information in this article is unfortunately used, it will be a joke.
4. My unit is not any public institution, but only a small private enterprise located in Huangpu, Guangzhou.
5. I don't want to cause trouble to anyone, and I don't want to stir up public opinion. The company treated me very well and did not want to cause any trouble to the company. The company did not know about my post, and the leaders were understanding and forgiving afterwards. I grew up with the company and could not live up to the company's love and expectations for me.
6. I'm still too young, and this matter is too complicated. I just expressed my own thoughts. I have neither the conditions nor the ability to judge the development directions of the early epidemic - these are all hindsights. It's not that I didn't go to the top to make suggestions, or that I knew the epidemic was so serious but didn't have the courage to release information to the community at an early stage, but I really didn't have the ability to know anything about the development of the whole epidemic.
7. I just want to devote myself to researching technology and do research well. Whether it can benefit the people on one side depends on luck. I do not want to be disturbed by any attention, so everyone, please just leave.

**Post 3: Weixin (poetic) post by Little Mountain Dog, on the 4<sup>th</sup> Apr 2020**  
“When the ‘prophecies’ of the epidemic came true one by one, I dared not speak”

[Original](#)  
[Copy \(web archive\)](#)

当疫情“预言”一个个成真后，我不敢说话了  
Original 小山狗, 小山狗 2020-04-04 06:49

2020年4月3日  
全世界新冠感染确诊病例超过100万了  
说来也挺戏剧的  
早在1月23日  
武汉刚封城时  
在朋友闲聊群了说了这么一句

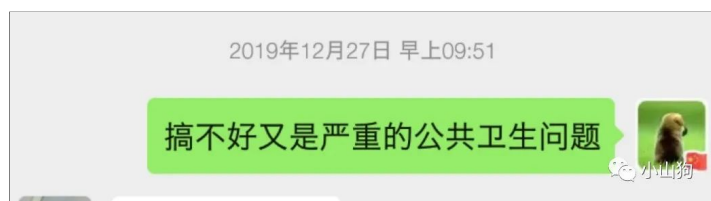


如今确诊的人数都已经不止这个数了  
算上没有被检测的远不止这个数

说预言  
好像也算不上  
大多是有意无意随口一说吧  
或者只是一种直觉  
当时确诊的也就那么几百例  
说会感染超过百万  
几乎没有人相信的  
然而现实真是出乎人意料

就这么一个预言成真了倒是不可怕  
可怕的是几乎我随口一说的预言都成真了  
剧情真是按照我的直觉去走的  
我自己都害怕了

最最最开始莫过于这个  
当时刚分析出是一种新型冠状病毒

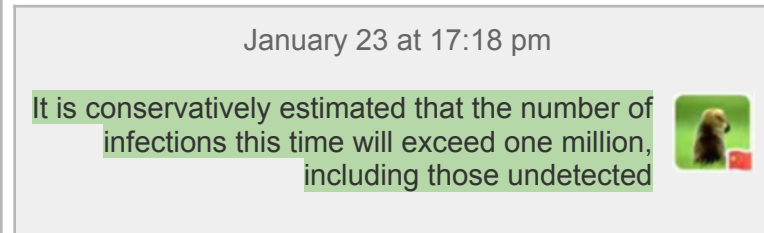


一语成谶  
后来真的爆发疫情了  
那时候真的一无所知啊  
我们只知道这么一个病人  
以为是一个孤例  
以前发现的  
蝙蝠SARS-like病毒  
都基本不会感染人啊  
这个也许就是偶然感染  
不会传播吧？  
然而总有一种不好的直觉  
忐忑了两天  
感觉太奇怪了  
然后发了个疑问

**Statement on "Recording the experience of first discovering the novel coronavirus"**

Original Small Mountain, Dog Small Mountain Dog 2020-01-30 23:39

April 3, 2020  
Confirmed cases of new coronavirus infection worldwide exceed 1 million  
To put it mildly it's dramatic  
As early as January 23  
When Wuhan first closed the city  
I said this in a friends chat group:

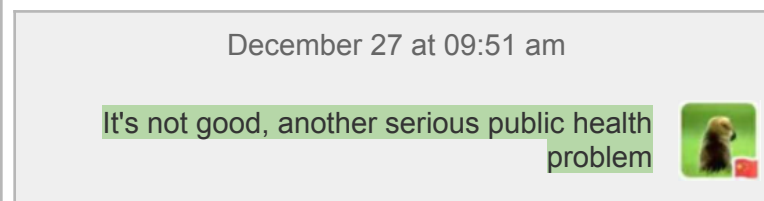


Now the number of people diagnosed is more than that  
When including those who have not been detected it is much more than that.

A prophecy  
I don't think it really is one.  
Most of this was said casually, intentionally or unintentionally.  
Or just a gut feeling  
There were only a few hundred cases diagnosed at the time.<sup>8</sup>  
I said it was to infect more than a million people  
Almost no one believed it  
But the reality is unexpected

It's not scary that such a prophecy came true.  
The scary thing is that almost all my casual predictions have come true  
The plot really went according to my intuition.  
I'm scared myself

At the very beginning there is nothing more than this  
Back then was just diagnosed as a new type of coronavirus:



One prophecy  
Then the epidemic really broke out  
I really didn't know anything back then.  
We only knew about this one such patient,  
We thought it was an isolated case,  
A previously discovered  
Bat SARS-like virus,  
Basically they don't infect people.  
This may be an **accidental** infection.  
It won't spread, right?  
However, I always had a bad feeling.  
I was worried for two days  
- It felt so weird -  
Before I asked a question:<sup>9</sup>

<sup>8</sup> On the 23<sup>rd</sup> Jan 2020 (when Little Mountain Dog made her prediction) there were 639 cases worldwide according to [this site](#). On the 4<sup>th</sup> April 2020 (when she wrote that blog entry), there were 1.19 mln cases.

<sup>9</sup> She asked the question that follows on the 29<sup>th</sup> Dec, two days after the previous post dated 27<sup>th</sup> Dec.

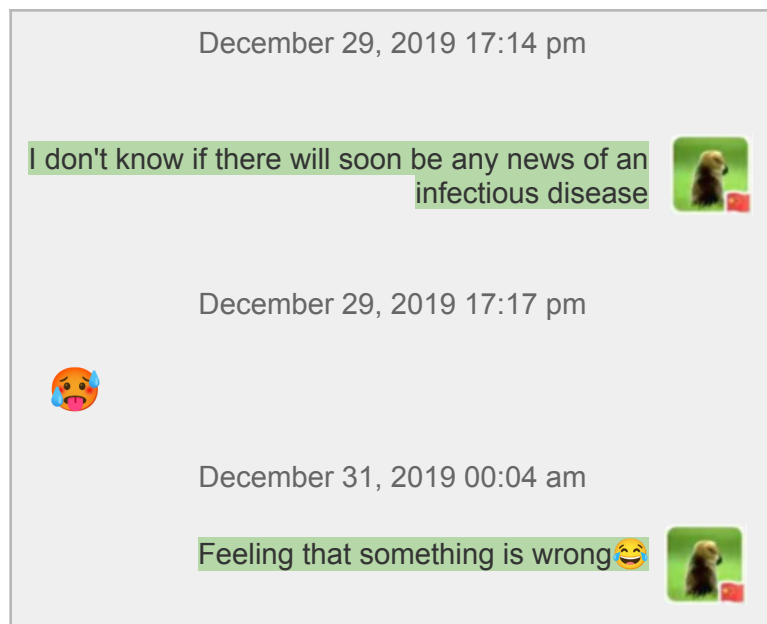




果然12月30号晚有消息  
武汉卫健委不明肺炎公告  
微博流传SARS

开始惊慌  
那不是孤例

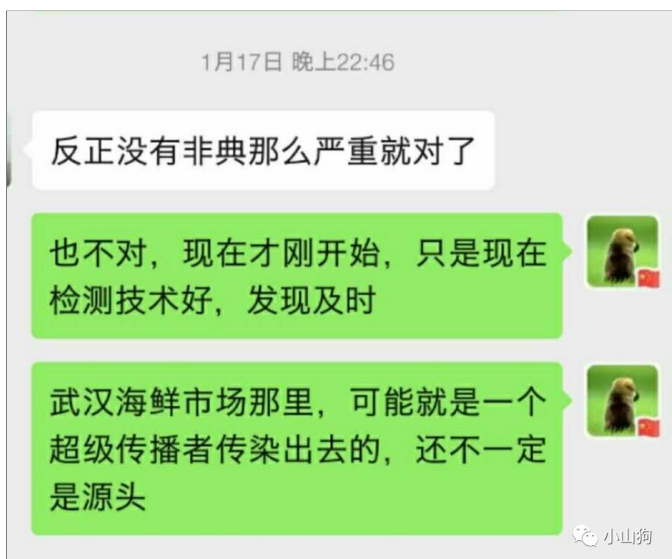
疫情还没有大范围爆发时  
劝说别人注意防护  
说了严重程度不比SARS低  
华南海鲜市场不一定是源头



Sure enough, there was some news on the evening of December 30, Announcement of Unknown Pneumonia by the Wuhan Health Commission.  
SARS spread on Weibo

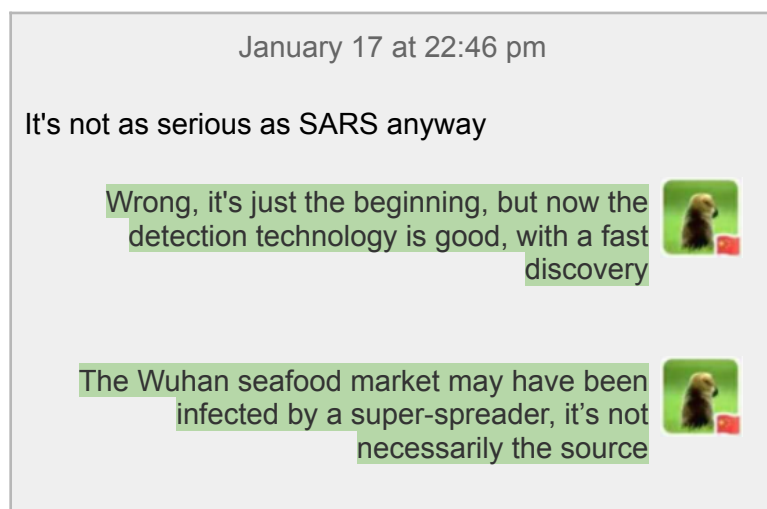
Started panicking,  
That's not an isolated case!

Before the epidemic broke out on a large scale,  
Persuaded others to take precautions.  
I said that the severity is not lower than SARS,  
That Huanan seafood market is not necessarily the source:<sup>10, 11</sup>



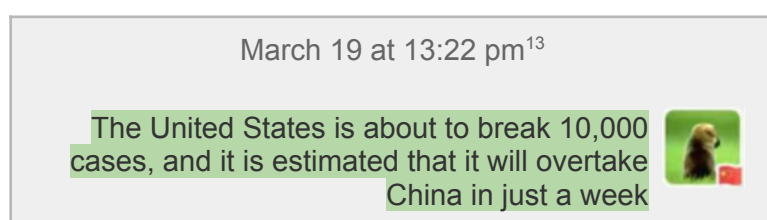
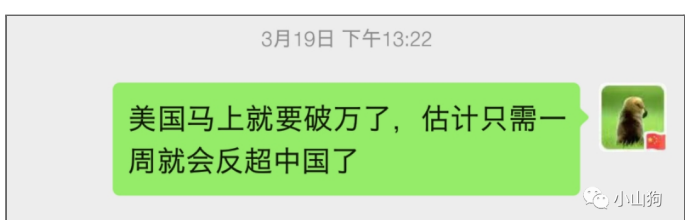
现在来看  
新冠疫情当然是比SARS严重了  
流行病学调查  
分子进化分析  
基本已经排除了华南海鲜市场是源头  
可能就是一个超级传播者

近一点的  
可能是根据一些趋势去推测  
对了也正常



Look now,  
The new crown epidemic is of course more serious than SARS.  
Epidemiological Investigation,<sup>12</sup>  
Molecular Evolutionary Analysis,  
Has basically been ruled out that the South China Seafood Market is the source,  
Possibly a superspreader.

The closest way  
May be to speculate based on some trends  
That's right, it's normal:



<sup>10</sup> The main implication being that human to human transmission is then a likely reality. As long as cases can be confined to the market, one can still hope (or pretend) that there is no human infection - at least for a while. This is exactly what the Chinese authorities were saying until the 20<sup>th</sup> Jan 2020, 20 days after the market was closed and so at a time when insisting on market related infections (from some host animal) just couldn't make any sense any more. See [this timeline](#).

<sup>11</sup> The timing (17<sup>th</sup> Jan post) of that statement is surprising, as it was made very early. Only on the 17<sup>th</sup> Feb 2020 would a team of scientists from Guangzhou (where Vision Medicals is located) [sent an article for publication](#) that concluded that the virus appeared around November 2019, hence before the market outbreak, based on genome evolution. Then on the 19<sup>th</sup> Feb 2020 a very unlikely team led by conservation biologists from Yunnan published [a remarkable paper](#), on a Chinese preprint site, that systematically rejects the wet-market hypothesis based on a careful analysis of available sequences to that date. The 19<sup>th</sup> Feb is also two days before the first WHO team arrived in China (17-22 Feb 2020)

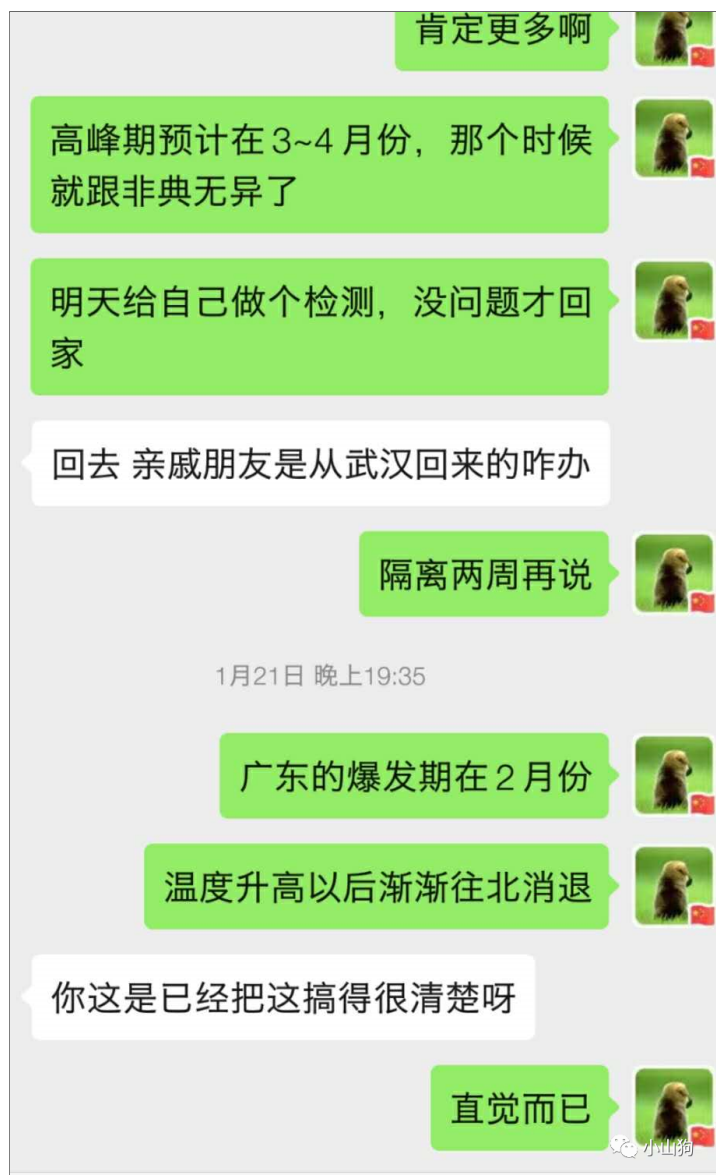
<sup>12</sup> Here she is introducing the next post dated March 19<sup>th</sup>. The 'Epidemiological Investigation' and 'Molecular Evolutionary analysis' refers to points published after the date of her previous post (17<sup>th</sup> Jan) where she made that statement about the market not necessarily being the source. The articles mentioned above are good examples of such research that was published between Jan 17<sup>th</sup> and Mar 19<sup>th</sup>.

<sup>13</sup> The US had 9,169 cases on March 18<sup>th</sup>, then 13,663 one day later. The US overtook China on March 25<sup>th</sup>. See [this site](#).

果然就是大概一周后就反超中国了

如果把所有的可能性都预测了  
肯定是会有撞对的  
不足为奇  
但我关于疫情预测  
或者对疫情的看法  
其实就只大概说过这么多  
基本都成真了  
这才是连我自己都怕的地方  
怎么剧情都按照我想的方向去发展呢？

也不全都是很黑暗吧



很早也说过高峰期在3~4月份  
希望如此吧  
再熬一个月就过去了  
全世界的曙光即将到来

还是觉得很奇怪  
怎么大部分都成真了呢  
感觉就像《楚门世界》  
一切都是导演的安排  
你们是不是都是演员啊？  
我就是那个楚门？

无论在哪个城市  
身边的人总有一种似曾相识的感觉  
长得像  
体型像  
着装像  
……

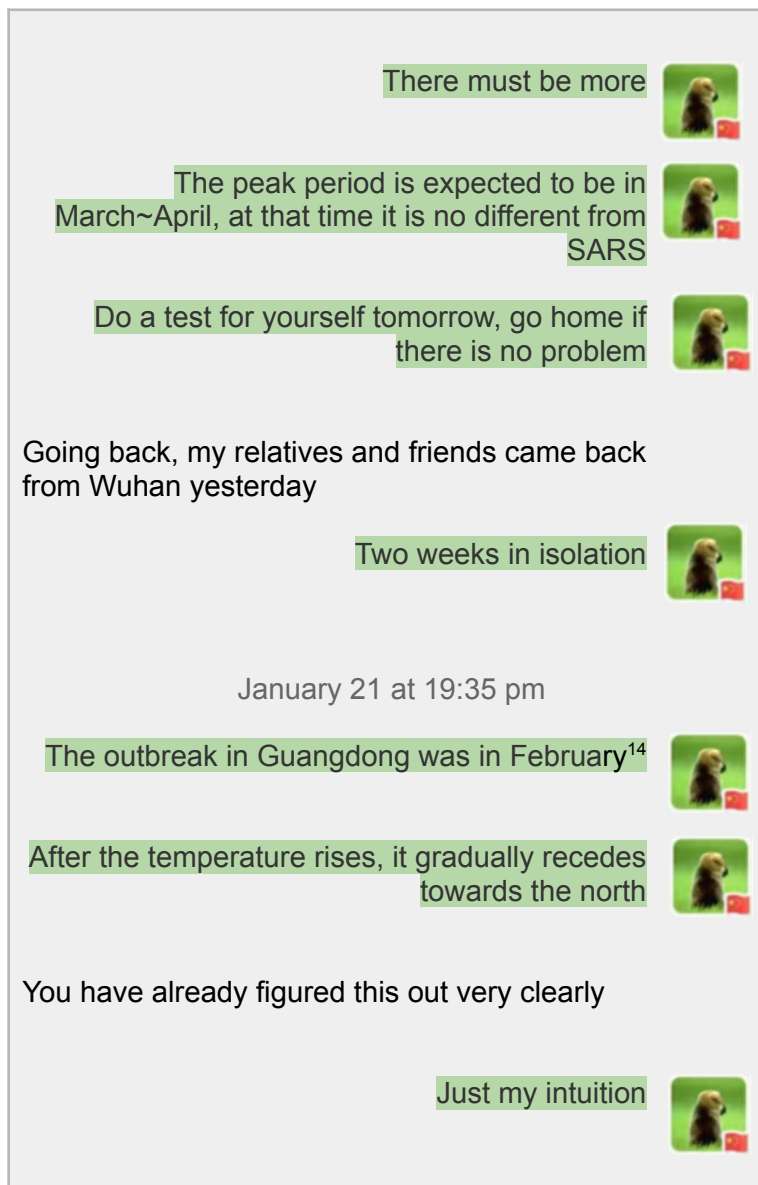
难道是一群演员  
化了不同的装？

当然还有未成真的话  
全世界确诊病例

Sure enough, it would overtake China in about a week.

If all the possibilities are predicted,  
There's bound to be a collision.  
It's not surprising.  
But my prediction about the epidemic,  
Or my views on the epidemic,  
That's all I've said,  
They've all come true  
This is what scares me  
Why does the plot keep going in the direction I want it to go?

It's not all very dark, right?:



It was said earlier that the peak period is in March-April.  
I hope so  
One more month and it will be over  
The dawn of the world is coming

I still feel weird  
How come most of them came true?  
It feels like the "Truman Show"<sup>15</sup>  
Everything is arranged by the director  
Are you all actors?  
Am I Truman?

No matter which city you are in  
There is always a sense of déjà vu with the people around you  
They looks the same  
Similar body type  
Dressing the same  
…

Could it be that the same group of actors  
Wearing different costumes?

Of course there are unreal words  
Confirmed cases worldwide:

<sup>14</sup> She is referring to the SARS outbreak in Guangdong in Q1 2003. See [this link](#).

<sup>15</sup> Little Mountain Dog is a film lover.

3月10日 下午16:36

美国至少会贡献一半



这不是幸灾乐祸  
而是基于美国的防疫措施  
美国的人口数量  
大城市人口密度  
社交仍较频繁  
过于倔强不戴口罩

.....  
基于认知的预测  
无数学模型  
就当瞎说吧

一点一点都成真了  
也许是大乌鸦嘴  
以后还是不说了  
不敢说了

最后

1月14日 上午11:48

这是一场硬仗，春运不好过



我就看看这次有多少官员引咎辞职



1月14日 上午11:49

维稳也不是这样维的，该发布的预警还是要发布



死亡率不高，搞个重症肺炎也不好过



小山狗

March 10 at 16:36 pm

The United States will contribute at least half



It's not schadenfreude  
It is based on the epidemic prevention measures of the US  
The size of the population of the US  
Their big city population density  
Socialising is still more frequent  
Too stubborn to wear a mask

...  
Cognitive-Based Prediction  
No mathematical model  
Just consider it nonsense

Little by little it came true  
Maybe I am such a jinx  
I won't talk about it anymore  
Dare not say it

Finally:

January 14 at 11:48 am

This is a tough battle, the Spring Festival is not making it easy



I'll just see how many officials have resigned this time



January 14 at 11:49 am

This is not the way to maintain stability. The warning that should be issued should still be issued



The mortality rate is not high, but it is not nice to have severe pneumonia





## Doc 4: Weixin post by Little Mountain Dog, on the 24<sup>th</sup> Feb 2020

Question | Are pangolins the intermediate host of the new coronavirus? Rodents may also be possible

[Original](#) ([web archive](#))

质疑 | 穿山甲是新冠病毒的中间宿主么？啮齿类或许也有可能

Original 小山狗 小山狗 2020-02-24 00:11

本来不想再写些什么东西了的，但脑子里总是有一些想法，心里老是惦记着，干扰了工作和生活的其他一些想法，时间精力总是有限的，想这个想那个的会很累，也不专注。所以还是写下来，以前都是这样，写下来就不用惦记着了，可以很快忘记。

另外看了下这几次推送的后台数据，打开率在2~3%左右，如果不发生二次传播，那么估计阅读量会在一两百左右，还是挺安全的，所以以后写点什么都会比较随意。

我写的东西，都是在记录我的想法或经历，而不是在做科普。以上都是废话，正文开始。

国际病毒分类委员会提议将新冠病毒命名为SARS-CoV-2后，不管是媒体文章还是科学论文都采用了这个名称，但这不是最终的命名，有争议，还可能会变，虽然可能性很小。为了响应国内专家的号召，在还没最终正式命名前，以后写东西，我就按照人类冠状病毒2019来称呼新冠病毒吧，拉丁学名为Human coronavirus 2019，缩写HCoV-2019，中文简称人冠病毒19。

自华南农业大学公布穿山甲是人冠病毒19的潜在宿主后，穿山甲成了热点话题，这几天好几篇关于穿山甲冠状病毒的研究论文也预印公开了。

说真的，当时看到华农的新闻发布会后，虽然保留质疑，但心里还是蛮期待的。毕竟当时新闻发布会上说已经分离到了病毒，对基因组分析，序列相似性达99%。当时就想着，如果是全基因组相似度有99%，那穿山甲是中间宿主的可能性就非常大了，对病毒的溯源工作有很大意义。

打开南方+看直播，享受三倍流畅度

直播

聊天

分享海报

11:06

南方+

刘雅红：攻关团队通过分析1000多份宏基因组样品，锁定穿山甲为新型冠状病毒的潜在中间宿主；继而通过分子生物学检测，揭示穿山甲中β冠状病毒的阳性率为70%；进一步对病毒进行分离鉴定，电镜下观察到典型的冠状病毒颗粒结构；最后通过对病毒的基因组分析，发现分离的病毒株与目前感染人的毒株序列相似度高达99%。

11:07

南方+

刘雅红：鉴于当前疫情防控的严峻性，我们第一时间向社会公布，希望有助于大家的科学防控，并为更多科学家开展进一步工作提供

Question | Are pangolins the intermediate host of the new coronavirus? Rodents may also be

Original Small Mountain Dog Small Mountain Dog 2020-02-24 00:11

I didn't want to write anything anymore, but there are always some ideas in my mind, and I always think about other ideas that interfere with work and life. Time and energy are always limited, I should be very tired and unfocused thinking about this and that. So I still write it down. It's always been like this before. I don't have to worry about it anymore when I write it down. It can be quickly forgotten.

In addition, I looked at the background data of these several posts. The open rate on my post is about 2~3%. If there is no forwarding, then it is estimated that the volume of readers will be around one or two hundred, which is quite safe, so it will be more casual to write anything going forward.

Everything I write is to record my thoughts or experiences, not to do popular science. The above is all nonsense, let the text begin.

After the International Committee on Taxonomy of Viruses proposed to name the new coronavirus SARS-CoV-2, this name was adopted in both media articles and scientific papers, but this is not the final name, it is controversial and may change, although the possibility is very small. In response to the call of domestic experts, before the final official name, I will write something later, I will call the new coronavirus according to the human coronavirus 2019, the Latin name is Human coronavirus 2019, abbreviation HCoV-2019, Chinese abbreviation human coronavirus 19.

Since the South China Agricultural University (SCAU) announced that pangolins are potential hosts of human coronavirus 19, pangolins have become a hot topic. In the past few days, several research preprints on pangolin coronaviruses have also been produced.

To be honest, after seeing the SCAU press conference<sup>16</sup> at that time, although I kept my doubts, I was still looking forward to it. After all, it was said at the press conference that the virus had been isolated, and the genome analysis showed that the sequence similarity was 99%. At that time, I thought that if the similarity of the whole genome is 99%, then the possibility of pangolins being the intermediate host is very high, which is of great significance to the traceability of the virus.

Open Southern + Watch live broadcast and enjoy three times the fluency

Live broadcast

chat

(Share poster)

11:06 South+

Liu Yahong: The research team identified pangolins as a potential intermediate host for the new coronavirus by analyzing more than 1,000 metagenomic samples; then, through molecular biology testing, it was revealed that the positive rate of 3 coronaviruses in pangolins was 70%; the virus was further isolated and identified,

The typical coronavirus particle structure was observed under the electron microscope; finally, through the genome analysis of the virus, it was found that the sequence similarity between the isolated virus strain and the currently infected human strain was as high as 99%

11:07 South+

Liu Yahong: In view of the severity of the current epidemic prevention and control, we will announce the results of the research to the society as soon as possible. I hope that the Lord will help

的科学防控，并为更多科学家开展进一步工作提供

<sup>16</sup> The South China Agricultural University (SCAU) press conference was held on the 7<sup>th</sup> Feb 2020. See [here](#) for the official Weixin post from SCAU, and see [video extract](#). That conference was controversial for its announcement of a pangolin virus with 99% similarity to SARS-CoV-2. This was a misrepresentation; the similarity is much lower on the whole genome, the 99% only refers to the RBD (Receptor-Binding Domain).

然而论文和数据公开以后，挺失望的，只能感叹语文的博大精深了。是“序列相似度”，我可没说是全基因组相似度是吧，毕竟有些基因片段是能达到99%呀！（我真不敢说丢脸丢出国了，不然一会又被删文。多少国内外同行或非同行都在盯着，要开新闻发布会用词也严谨些吧？）

华农的论文说了啥？大概就是一顿操作猛如虎，直接从公共数据库中分析了一大批宏基因组测序数据，发现穿山甲测序数据里竟然有一些跟人冠状病毒19很相似的序列（思路值得借鉴，好好利用公共资源），于是赶紧拿穿山甲的样本来分析，发现大概70%（17/25）的马来穿山甲携带有冠状病毒（不一定是同一种），还成功分离出一株跟人冠状病毒19挺像的病毒（全基因组相似度只有90.3%，而不是当时新闻说的99%），命名为Pangolin-CoV。其中E、M、N和S基因的氨基酸同源性分别为100%、98.2%、96.7%和90.4%；S蛋白的受体结合结构域（RBD）只差1个氨基酸。这个RBD是跟AEC2结合的关键，也是华农这篇文章结论的重要依据。

However, after the paper<sup>17</sup> and data were made public, I was very disappointed, and I could only sigh at the breadth and depth of the language. It's "sequence similarity". I didn't say it was whole genome similarity, right? After all, some gene fragments can reach 99%! **(I really don't dare to say that I lost my face and left the country, otherwise my article will be deleted shortly.** How many domestic and foreign colleagues or non-peers are watching? Should we use more rigorous words in the press conference?)

What did SCAU paper say? It was probably just an aggressive operation, and directly analysed a large number of metagenomic sequencing data from the public database, and found that there are some sequences very similar to human coronavirus 19 in the pangolin sequencing data (the idea is worth learning from, make good use of public resources), so I quickly took samples of pangolins for analysis, and found that about 70% (17/25) of Malay pangolins carried coronavirus (not necessarily all of the same), and successfully isolated a virus similar to human coronavirus 19. (The whole genome similarity is only 90.3%, not 99% as the news said at the time), named Pangolin-CoV. The amino acid homology of E, M, N and S genes was 100%, 98.2%, 96.7% and 90.4%, respectively; the receptor binding domain (RBD) of S protein differed by only one amino acid. This RBD is the key to combining with AEC2, and it is also an important basis for the conclusion of the SCAU article.

Table 1: Genomic comparison of Pangolin-CoV with 2019-nCoV, SARS-CoVs and Bat SARSr-CoVs (nt/aa %)

|                      | S         | E         | M         | N         | Full-length genome |
|----------------------|-----------|-----------|-----------|-----------|--------------------|
| 2019-nCoV WHCV       | 89.1/90.4 | 99.1/100  | 93.8/98.2 | 93.7/96.7 | 90.3               |
| SARS-CoV GD01        | 72.2/77.2 | 93.5/93.5 | 85.8/90.0 | 87.5/90.0 | 81.6               |
| Bat SARSr-CoV RaTG13 | 88.5/89.8 | 99.6/100  | 93.6/99.1 | 94.0/96.7 | 88.9               |
| Bat SARSr-CoV ZC45   | 83.1/86.1 | 98.7/100  | 94.2/99.6 | 88.9/93.3 | 88.0               |
| Bat SARSr-CoV ZXC21  | 81.1/85.4 | 98.7/100  | 94.2/99.6 | 88.9/93.3 | 88.4               |

(华农论文截图，Pangolin-CoV和各种冠状病毒不同基因的相似度)

血清学分析表明，穿山甲体内竟然有能跟人冠状病毒19反应的抗体，说明可能曾经被相关病毒感染过！病理学分析表明穿山甲确实有感染迹象，说明这病毒是可以感染穿山甲的。

Pangolin-CoV和HCoV-2019的整体相似度还是没有RaTG13的96%高，只有RBD区域是Pangolin-CoV最高的，通过基因组进化和重组分析，作者认为人冠状病毒19可能起源于Pangolin-CoV-like病毒和RaTG13-like病毒发生的重组。

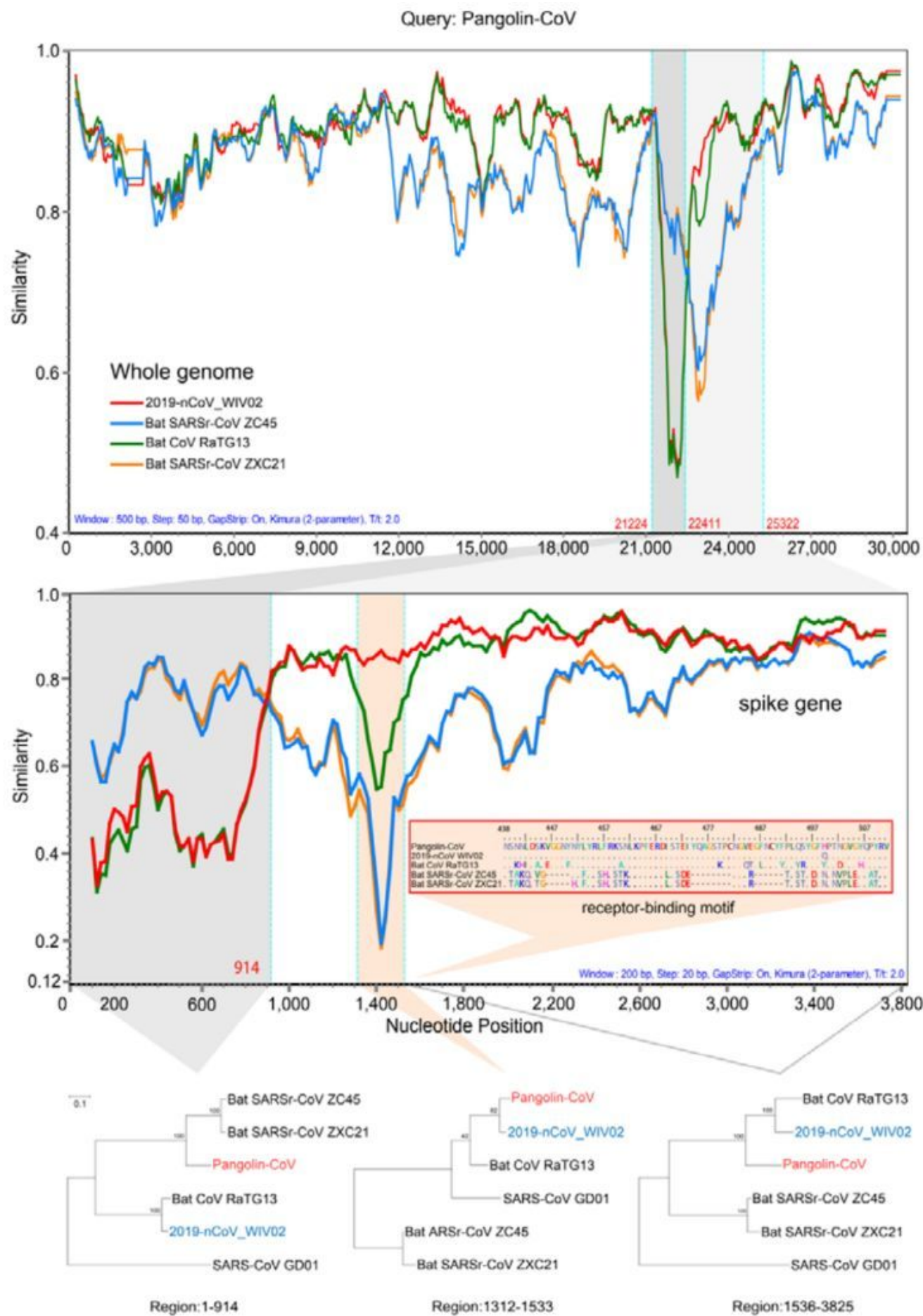
(Screenshot of SCAU paper, similarity of different genes between Pangolin-CoV and various coronaviruses)

Serological analysis shows that pangolins have antibodies that can react with human coronavirus 19, indicating that they may have been infected by related viruses! Pathological analysis showed that pangolins did show signs of infection, indicating that the virus could infect pangolins.

The overall similarity between Pangolin-CoV and HCoV-2019 is still not as high as 96% of RaTG13, and only the RBD region is the highest in Pangolin-CoV. Through genome evolution and recombination analysis, the authors believe that human coronavirus 19 may originate from Pangolin-CoV-like Recombination of virus and RaTG13-like virus.

<sup>17</sup> SCAU sent its [preprint](#) to BioRxiv on the 17<sup>th</sup> Feb where it was published on the 20<sup>th</sup> Feb 2020. All the extracts in Little Mountain Dog's posty (dated 24<sup>th</sup> Feb) are from that preprint. The manuscript was also sent to Nature on the 16<sup>th</sup> Feb, accepted on the 28<sup>th</sup> April and [published](#) on the 7<sup>th</sup> May 2020.





(华农论文图，Pangolin-CoV和各种冠状病毒基因组相似度，其中RBD区域Pangolin-CoV和HCoV-2019相似度最高)

(SCAU paper, Pangolin-CoV and various coronavirus genomes are similar, among which Pangolin-CoV and HCoV-2019 in the RBD region have the highest similarity)

其他一些分析就不介绍了。反正最后作者的结论大意就是穿山甲是合理的中间宿主，大家要好好保护穿山甲这些野生动物。

Some other analyses will not be introduced. Anyway, the author's conclusion in the end is that pangolins are reasonable intermediate hosts, and everyone must protect the wild animals such as pangolins.

客观地说，论文本身没啥问题，而且还很不错，至于能否得出文中的那些结论，感觉有点牵强，说服力不是很强，但这个东西本来就是仁者见仁智者见智。败就败在前期新闻发布会给人太大希望了，唉.....

Objectively speaking, there is nothing wrong with the paper itself, and it is very good. As for whether the conclusions in the paper can be drawn, it feels a bit far-fetched and not very persuasive, but this thing is that the benevolent sees the benevolent and the wise sees the wisdom. Losing in the early press conference gives people too much hope, alas...

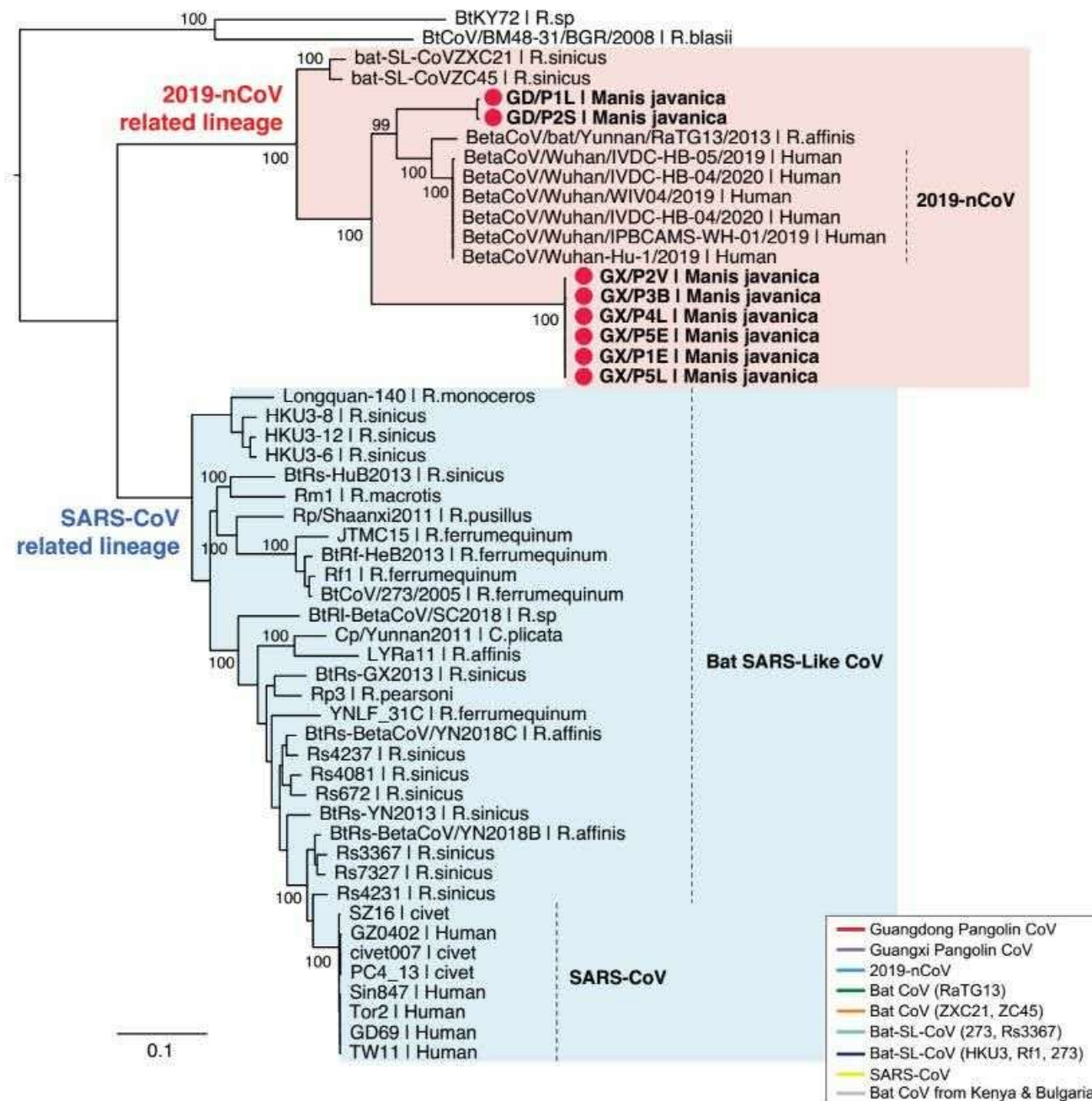
管轶团队也发表了类似的预印文章，同样发现了2种（8株聚成了很近的2类，每类应该就是同一种）跟人冠状病毒19很像的病毒，支持穿山甲确实是携带着这类冠状病毒，而且也认为穿山甲可能是人冠状病毒19的中间宿主。但作者认为人冠状病毒19和穿山甲冠状病毒更可能是趋同进化，而不是重组引起的。

Guan Yi's team also published a similar preprint<sup>18</sup>, and also found 2 types (8 strains clustered into 2 close categories, each type should be the same type) viruses that are very similar to human coronavirus 19, supporting the idea that pangolins do indeed carry this type of coronavirus, and also suggesting that pangolins may be intermediate hosts for human coronavirus 19. However, the authors believe that

<sup>18</sup> Preprint released on the 18<sup>th</sup> Feb 2020, see <https://www.biorxiv.org/content/10.1101/2020.02.13.945485v1.article-info>. The [Nature version](#) has a 'received' date of the 7<sup>th</sup> Feb 2020. Eddie Holmes joined that team after the Farrar/Fauci conference call on the 1<sup>st</sup> Feb 2020 to help with the writing.



human coronavirus 19 and pangolin coronavirus are more likely to be caused by convergent evolution rather than recombination.



(管轶团队论文图，穿山甲冠状病毒跟人冠病毒19聚在一个大支上)

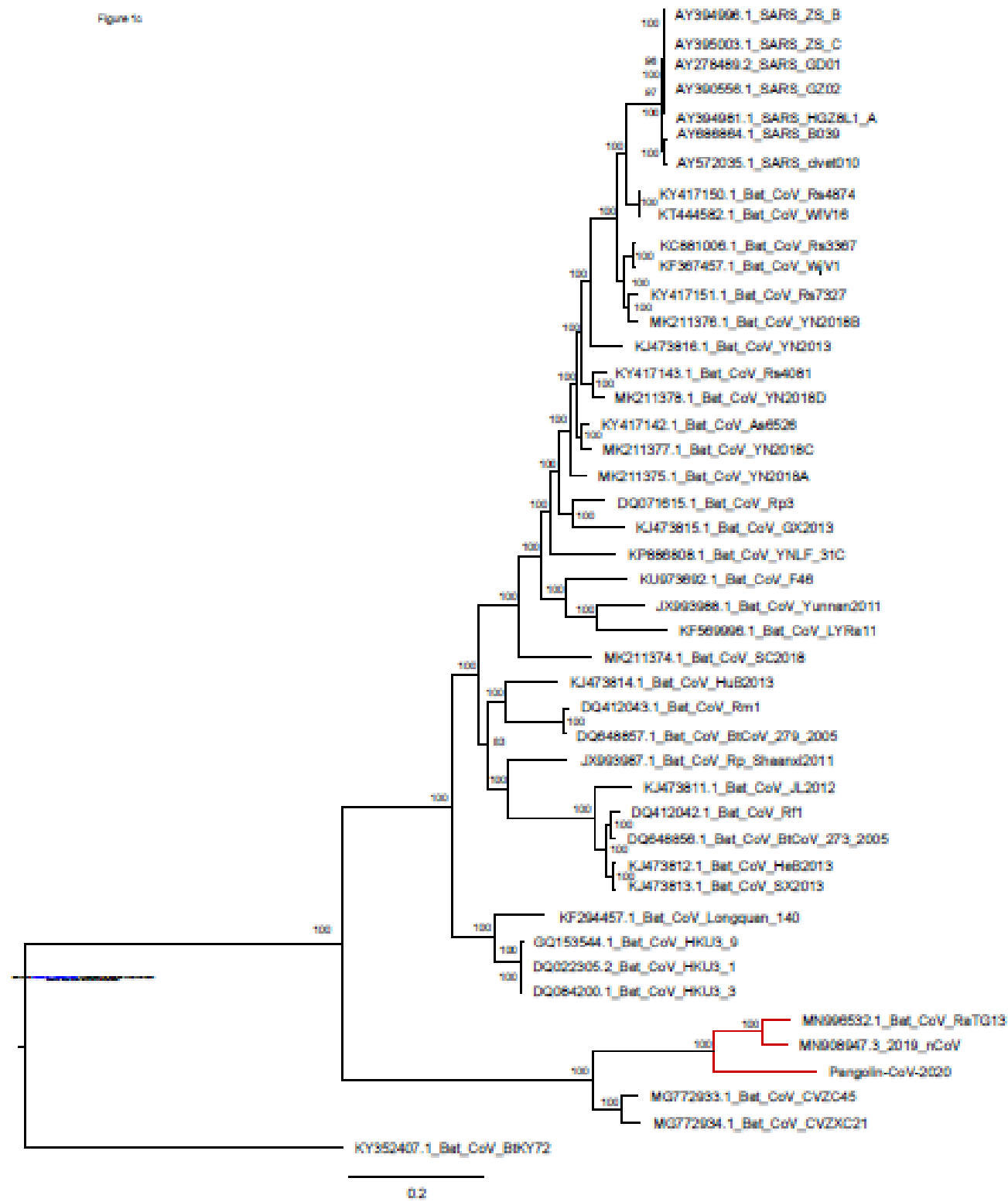
此外陈金平团队则直接发布了题目为《Are pangolins the intermediate host of the 2019 novel coronavirus (2019-nCoV)?》的预印文章，也是发现了穿山甲携带了人冠病毒19类似的病毒。但作者认为他们的研究提示穿山甲是Beta冠状病毒的自然宿主，而且可能还会感染人，但不支持穿山甲是人冠病毒19的中间宿主。

(Photo of Guan Yi's team's paper, pangolin coronavirus and human coronavirus 19 gather on a large branch)

In addition, Jinping Chen's team directly published a preprint<sup>19</sup> entitled "Are pangolins the intermediate host of the 2019 novel coronavirus (2019-nCoV)?", which also found that pangolins carry viruses similar to human coronavirus 19. However, the authors believe that their research suggests that pangolins are the natural host of Beta coronavirus and may infect humans, but do not support pangolins as an intermediate host for human coronavirus 19.

<sup>19</sup> Preprint released on the 20<sup>th</sup> Feb 2020. See <https://www.biorxiv.org/content/10.1101/2020.02.18.954628v1.article-info>.

Figure 10



(陈金平团队论文图，穿山甲冠状病毒也是跟人冠病毒19聚得很近的)

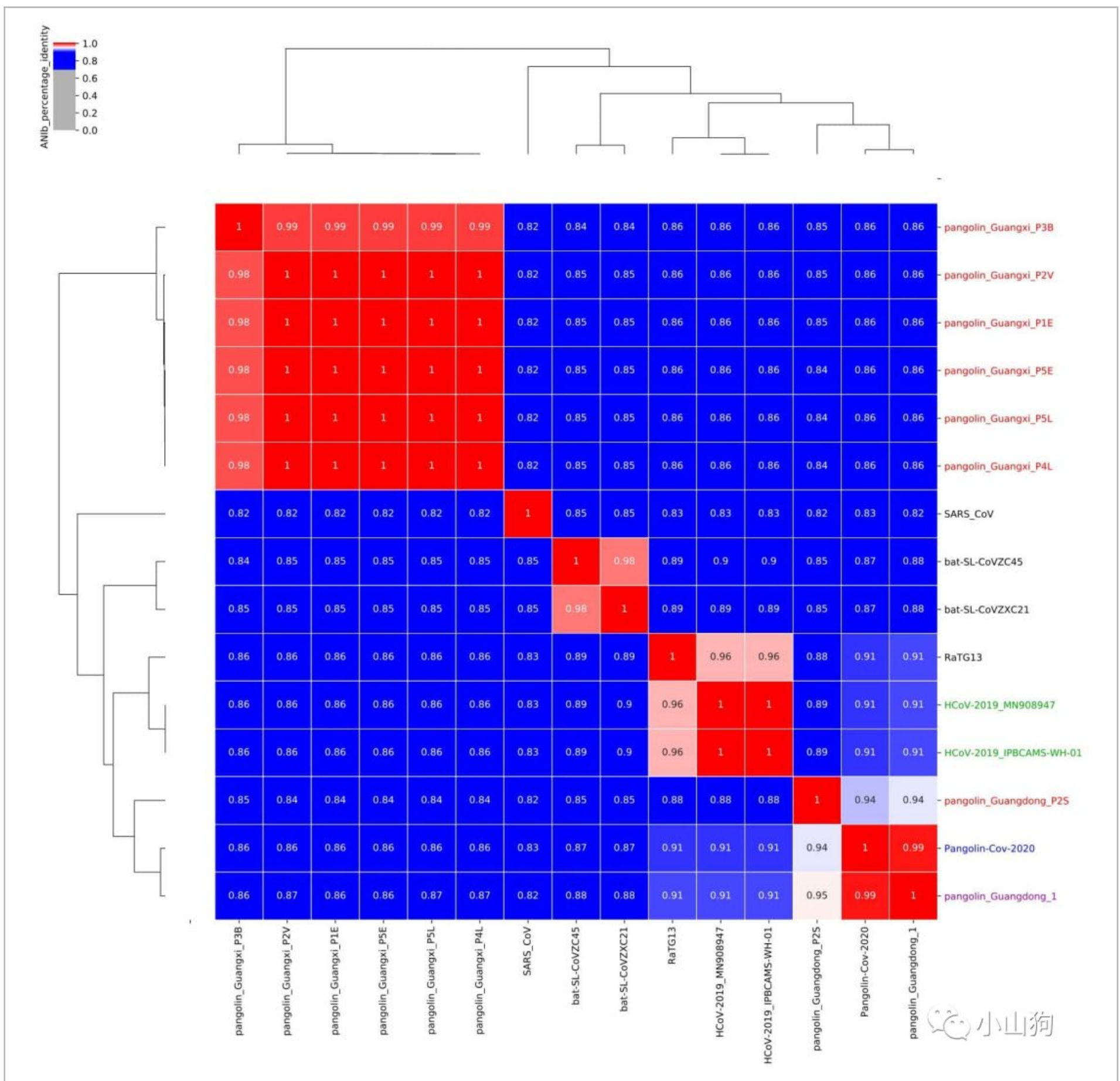
其实这几个研究的分析方法和数据都差不多，但得出的结论都不太相同，这大概就是仁者见仁智者见智吧。

这三篇研究的穿山甲冠状病毒基因组数据都已经公开了，那我可以拿这些数据做下分析，简单做个相似度比较就可以看看这些冠状病毒的差异了。

(Chen Jinping's team's paper map, pangolin coronavirus is also very close to human coronavirus 19)

In fact, the analysis methods and data of these studies are similar, but the conclusions drawn are not the same.

The pangolin coronavirus genome data of these three studies have been made public, so I can use these data for analysis, and simply compare the similarity to see the differences between these coronaviruses.



(穿山甲冠状病毒与其他病毒的全基因组平均相似度图，红色字体出自管轶团队论文，紫色华农团队，蓝色陈金平团队，绿色是人冠病毒19，SARS和bat-SARS-like黑色)

上图可以看出，管轶团队和华农团队、陈金平团队的穿山甲冠状病毒均可能是不同种，但华农团队和陈金平团队的穿山甲冠状病毒可能是同一种！因为两株的相似度达到了99%，陈金平团队穿山甲冠状病毒没有测序完整，质量可能不高，所以排除质量问题，两株病毒相似度可能大于99%，是同一种冠状病毒的可能性极大！有趣的是，他们文章的结论是相反的！

综合以上研究，根据目前仅有的穿山甲冠状病毒数据，我的观点是，穿山甲是人冠病毒19中间宿主的可能性极小，或者说根本就不是。只有90%左右的相似度，差太远了，至少还得经过另一个中间宿主。即便S蛋白RBD区域相似度比较高，但其他区域的差异也有整体的10%，那得是少年才能完成的变异，RaTG13变过来也才4%的突变，所需进化用时更短，还不如说是蝙蝠直接感染的。毕竟RaTG13是7年前采的，在野外的蝙蝠身上变异个7年，完全是有可能变异成今天的人冠病毒19的。

The average similarity map of the whole genome of pangolin coronavirus and other viruses, the red font is from the paper of Guan Yi's team, the purple SCAU team, the blue Chen Jinping team, the green is human coronavirus 19, SARS and bat-SARS-like black)

As can be seen from the above picture, the pangolin coronaviruses of Guan Yi's team, SCAU team, and Chen Jinping's team may be different species, but the pangolin coronavirus of SCAU team and Chen's team may be the same! Because the similarity between the two strains reaches 99%, the pangolin coronavirus in Chen Jinping's team has not been sequenced completely, and the quality may not be high. Therefore, excluding quality problems, the similarity between the two strains may be greater than 99%, which is extremely likely to be the same coronavirus. Big! Interestingly, their article came to the opposite conclusion!

Based on the above studies, according to the only data on pangolin coronaviruses available at present, my opinion is that it is extremely unlikely that pangolins are the intermediate host of human coronavirus 19, or not at all. There is only about 90% similarity, the difference is too big, at least it has to go through another intermediate host. Even though the similarity of the RBD region of the S protein is relatively high, the other regions have an overall 10% difference, that's many years it would take to complete the mutation. RaTG13 overall difference is only 4%, and the evolution time required is shorter. It might as well be a direct infection from the bat. After all, RaTG13 was



那这么说穿山甲就安全了吗？完全不是，穿山甲冠状病毒也是极有可能感染人的，还是RBD区域的问题，跟人冠病毒19的太像了。

不止可能感染人，而且还可能跟人冠病毒19、SARS病毒和MERS病毒一样恐怖，因为目前新发的能感染人的BetaCoV就是这三位了，每个都是猛将。感觉以后再遇到能感染人的BetaCoV就可以拉警报了。从华农的文章可以看出，BetaCoV阳性的穿山甲比例还很高，还是保持敬畏吧！

到这里，寻找人冠病毒19的中间宿主似乎又看不到希望了，没找出中间宿主，要是中间宿主就在我们身边，那么它就是一个定时炸弹，可以让疫情反复出现。

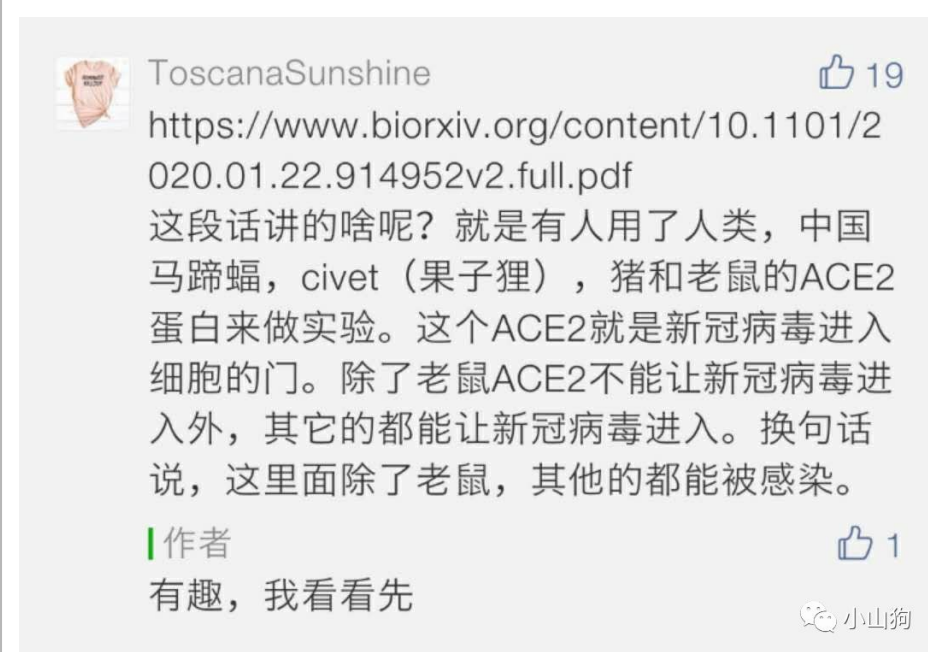
之前还猜测老鼠的嫌疑很大，有位读者提醒了一下有篇论文已经做了人冠病毒19 S蛋白和鼠的ACE2蛋白的结合实验了，似乎不会发生作用。

collected 7 years ago, and mutated in wild bats for 7 years, it is entirely possible to mutate into today's human coronavirus 19.

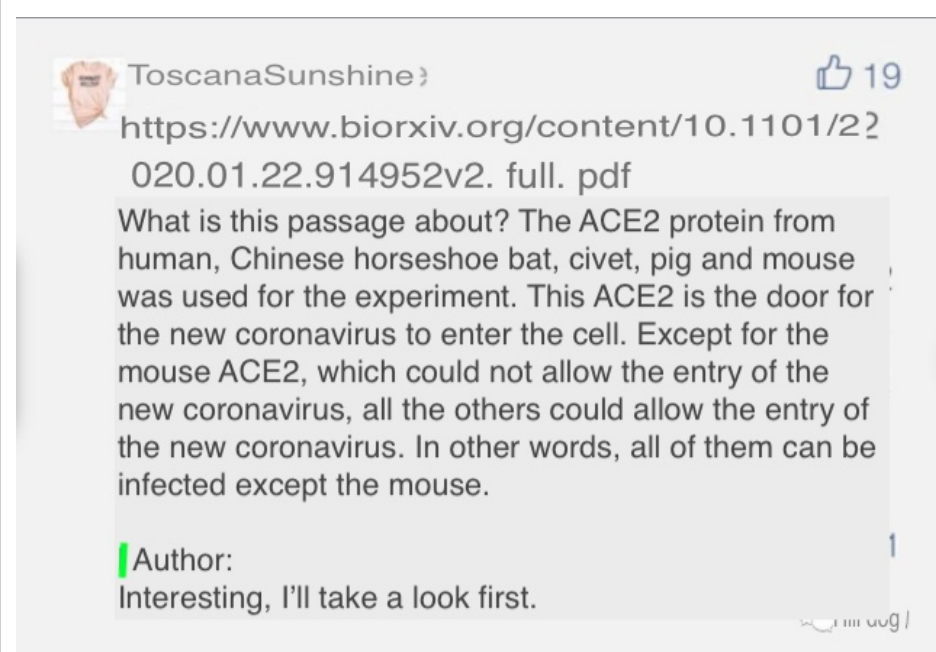
So is pangolin safe? Not at all, the pangolin coronavirus is also very likely to infect humans, and it is still a problem in the RBD area, which is too similar to the human coronavirus 19. Not only is it possible to infect people, but it may also be as terrifying as the human coronavirus 19, SARS virus and MERS virus, because at present, the new BetaCoV that can infect people is these three, and each of them is a strong general. I feel that I can raise the alarm when I encounter BetaCoV that can infect people in the future. It can be seen from Huanong's article that the proportion of BetaCoV-positive pangolins is still very high, so stay in awe!

At this point, it seems that there is no hope in finding the intermediate host of human coronavirus 19. If the intermediate host is not found, if the intermediate host is by our side, then it will be a ticking time bomb that can cause the epidemic to recur.

I had previously guessed that rodents were very suspicious. A reader reminded that a paper had done a binding experiment between the human coronavirus 19 S protein and the mouse ACE2 protein, and it seemed that it would not work.



ToscanaSunshine 19 likes  
<https://www.biorxiv.org/content/10.1101/2020.01.22.914952v2.full.pdf>  
这段话讲的啥呢？就是有人用了人类，中国马蹄蝠，civet（果子狸），猪和老鼠的ACE2蛋白来做实验。这个ACE2就是新冠病毒进入细胞的门。除了老鼠ACE2不能让新冠病毒进入外，其它的都能让新冠病毒进入。换句话说，这里面除了老鼠，其他的都能被感染。  
作者 1 like  
有趣，我看看先



ToscanaSunshine 19 likes  
<https://www.biorxiv.org/content/10.1101/2020.01.22.914952v2.full.pdf>  
What is this passage about? The ACE2 protein from human, Chinese horseshoe bat, civet, pig and mouse was used for the experiment. This ACE2 is the door for the new coronavirus to enter the cell. Except for the mouse ACE2, which could not allow the entry of the new coronavirus, all the others could allow the entry of the new coronavirus. In other words, all of them can be infected except the mouse.  
Author: 1 like  
Interesting, I'll take a look first.

去看了之后才发现原来就是石正丽那篇文章，当时没有留意到里面做实验的动物。

After reading it, I found out that it was Shi Zhengli's article<sup>20</sup>. At that time, I didn't notice the animal experiments in it.

<sup>20</sup> The link that she was pointed to in that exchange is <https://www.biorxiv.org/content/10.1101/2020.01.22.914952v2.full.pdf>. <https://www.biorxiv.org/content/10.1101/2020.01.22.914952v2> is a preprint by Shi Sheng-Li published on the 23<sup>rd</sup> Jan 2020. The paper was eventually published in Nature on the 3<sup>rd</sup> Feb 2020 (<https://www.nature.com/articles/s41586-020-2012-7>).

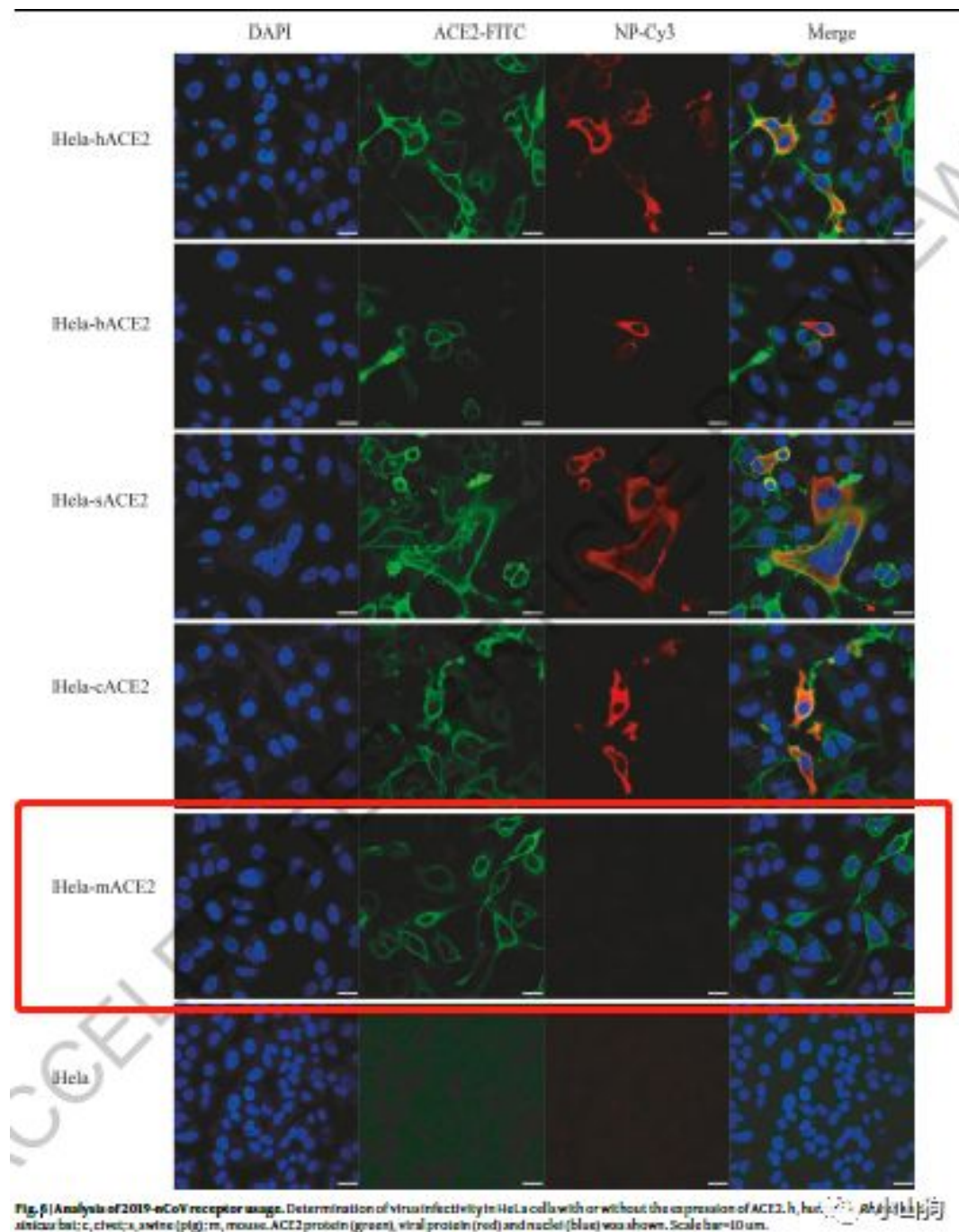


Fig. 8 | Analysis of 2019-nCoV receptor usage. Determination of virus infectivity in HeLa cells with or without the expression of ACE2. h, human; hACE2, human ACE2; s, chicken; c, chicken; m, mouse. ACE2 protein (green), viral protein (red) and nuclei (blue) was shown. Scale bar=10 μm.

虽然不同种类的老鼠可能有点不一样（大鼠、小鼠、田鼠等等），但应该没太大区别，如果实验模型没问题的话，那么老鼠的嫌疑就小了。要不然也许医科学院就不用那么大劲去构建转人ACE2基因小鼠模型了（不过即使能结合，可能也跟人的差异比较大，转基因模型可能是必要的）。

Although different kinds of rodents may be a little different (rats, mice, voles, etc.), there should be no big difference. If the experimental model is OK, then the suspicion of rodent is less. Otherwise, the Academy of Medical Sciences may not have to work so hard to construct a mouse model of human ACE2 gene (but even if it can be combined, it may be quite different from that of humans, and a transgenic model may be necessary).

1月22日，科技部启动新型冠状病毒科技攻关第一批应急项目，确定由医科院医学实验动物研究所主持构建动物模型。随后，该所与中国疾控中心病毒病预防控制所等单位密切合作，分别于1月29日和2月14日成功建立了转基因小鼠模型和恒河猴模型。目前，上述模型已应用于致病机制和传播途径研究、应急药物筛选和疫苗评价，完成了5种成药的评价，正在进行6种疫苗和4种成药的动物实验评价。（首席记者 刘志勇）

On January 22, the Ministry of Science and Technology launched the first batch of emergency projects for new coronavirus scientific and technological research, and determined that the Institute of Medical Laboratory Animals of the Academy of Medical Sciences presided over the construction of animal models. Subsequently, the institute worked closely with the Chinese Center for Viral Disease Control and Prevention and other units, and successfully established a transgenic mouse model and a rhesus monkey model on January 29 and February 14, respectively. At present, the above models have been applied to the research of pathogenic mechanism and transmission route, emergency drug screening and vaccine evaluation. (Chief reporter Liu Zhiyong)

家禽家畜从目前的调查和研究来看，中间宿主的潜在可能应该也基本排除了。

From the current investigation and research, the potential possibility of intermediate hosts should be basically ruled out.

中国动物卫生与流行病学中心的科研团队检测了4800余份家禽家畜（含鸡、鸭、鹅、猪、犬、猫等）样品，新型冠状病毒核酸检测均呈阴性，排除了导致本次疫情的新型冠状病毒来源于家禽家畜的传播路径。

The scientific research team of the China Center for Animal Health and Epidemiology has tested more than 4,800 samples of poultry and livestock (including chickens, ducks, scallops, pigs, dogs, cats, etc.) The nucleic acid test of the new coronavirus in the samples was negative, which ruled out the transmission route of the new coronavirus that caused the outbreak from poultry and livestock..



以上这些方法都是通过病毒本身去找，比较病毒的相似性，当然也是最直接的。那我们可不可以换个角度去寻找？直接查找病毒如同大海捞针，看不到什么希望，那么是否可以从最可能的宿主去筛呢？那怎么找最可能的宿主？也许ACE2这个蛋白能帮上忙呢。我们可以尝试从宿主上面去分析，看有哪些动物的ACE2蛋白跟人的最像的，甚至找RBD结合的区域相似度最高的，锁定某几种动物后再去筛。

The above methods are all found through the virus itself, and comparing the similarity of the virus is of course the most direct. So can we look at it from a different angle? Looking for a virus directly is like looking for a needle in a haystack, and there is no hope in sight, so is it possible to screen from the most likely host? How to find the most likely host? Maybe the protein ACE2 can help. We can try to analyse from the host to see which animals have the most similar ACE2 proteins to humans, and even find the regions bound by RBD with the highest similarity, and then screen after certain animals.

说干就干，从公共数据库入手，直接将人ACE2拿去跟NCBI蛋白数据库(nr)比对一下。

Just do it, start with the public database, and directly compare the human ACE2 with the NCBI protein database (nr).

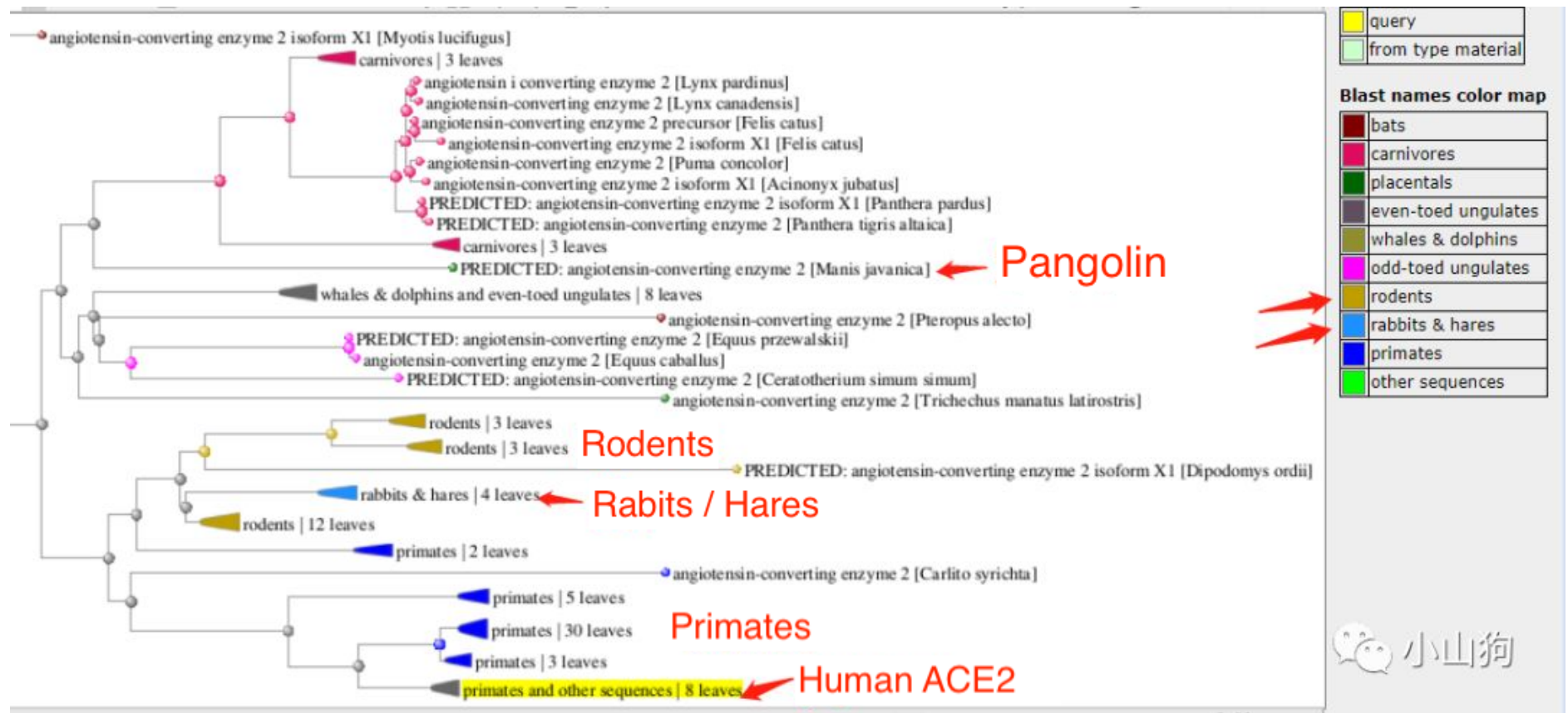
| Description  | Max Score | Total Score | Query Cover | E value | Per. Ident | Accession      |
|--|-----------|-------------|-------------|---------|------------|----------------|
| angiotensin I converting enzyme (peptidyl-dipeptidase A) 2 [synthetic construct] | 1684      | 1684        | 100%        | 0.0     | 99.88%     | BAJ21180.1     |
| angiotensin-converting enzyme 2 [Gorilla gorilla gorilla]                        | 1671      | 1671        | 100%        | 0.0     | 99.01%     | XP_018874749.1 |
| angiotensin-converting enzyme 2 isoform X1 [Pan troglodytes]                     | 1670      | 1670        | 100%        | 0.0     | 99.01%     | XP_016798468.1 |
| angiotensin-converting enzyme 2 isoform X1 [Pan paniscus]                        | 1669      | 1669        | 100%        | 0.0     | 99.01%     | XP_008972428.1 |
| angiotensin-converting enzyme 2 isoform X1 [Pongo abelii]                        | 1660      | 1660        | 100%        | 0.0     | 98.39%     | XP_024096013.1 |
| angiotensin-converting enzyme 2 precursor [Pongo abelii]                         | 1657      | 1657        | 100%        | 0.0     | 98.14%     | NP_001124604.1 |
| angiotensin-converting enzyme 2 [Nomascus leucogenys]                            | 1654      | 1654        | 100%        | 0.0     | 97.76%     | XP_003261132.2 |
| angiotensin-converting enzyme 2 [Ptilinopus tephrosceles]                        | 1615      | 1615        | 100%        | 0.0     | 95.03%     | XP_023054821.1 |
| angiotensin-converting enzyme 2 [Rhinopithecus roxellana]                        | 1602      | 1602        | 98%         | 0.0     | 95.34%     | XP_010364367.2 |
| angiotensin-converting enzyme 2 [Theropithecus gelada]                           | 1597      | 1597        | 98%         | 0.0     | 95.34%     | XP_025227847.1 |
| angiotensin-converting enzyme 2 [Papio anubis]                                   | 1597      | 1597        | 98%         | 0.0     | 95.34%     | XP_021788732.1 |
| angiotensin-converting enzyme 2 [Macaca nemestrina]                              | 1596      | 1596        | 98%         | 0.0     | 95.34%     | XP_011733505.1 |
| angiotensin converting enzyme 2 [Macaca mulatta]                                 | 1595      | 1595        | 98%         | 0.0     | 95.21%     | ACI04554.1     |
| angiotensin converting enzyme 2 [Macaca mulatta]                                 | 1595      | 1595        | 98%         | 0.0     | 95.21%     | ACI04554.1     |

果然，排位靠前的除了一条人工合成的外，剩下的都是非人灵长类了，从这个角度说非人灵长类是最大的嫌疑，但即使是中间宿主也不是最大的隐患，还是得关注其他动物。

Sure enough, except for one synthetic, the rest are non-human primates. From this perspective, non-human primates are the biggest suspects, but even the intermediate host is not the biggest hidden danger. Still have to pay attention to other animals.

取前100位的看看进化树。

Take the top 100 and look at the evolutionary tree.



从全长的ACE2的进化树可以看出，穿山甲跟人的进化关系还是比较远的，除了灵长类，进化关系最近的就是啮齿类了。兔子似乎也是比较可能的嫌疑。

It can be seen from the evolutionary tree of the full-length ACE2 that the evolutionary relationship between pangolins and humans is relatively far away. Except for primates, the closest evolutionary relationship is rodents. Rabbits also seem a more likely suspect.

排除灵长类后再次比对，最像的竟然是松鼠类？可能要抓几只松鼠来检测一下咯。

After excluding primates, we compared them again, and the most similar ones turned out to be squirrels? Might have to catch a few squirrels to test it out.



| Description  | Max Score | Total Score | Query Cover | E value | Per. Ident | Accession      |
|--|-----------|-------------|-------------|---------|------------|----------------|
| angiotensin I converting enzyme (peptidyl-dipeptidase A) 2 [synthetic construct] | 1684      | 1684        | 100%        | 0.0     | 99.88%     | BAJ21180.1     |
| angiotensin-converting enzyme 2 [Ictidomys tridecemlineatus]                     | 1456      | 1456        | 100%        | 0.0     | 85.38%     | XP_005316051.3 |
| PREDICTED: angiotensin-converting enzyme 2 isoform X1 [Chinchilla lanigera]      | 1451      | 1451        | 100%        | 0.0     | 84.72%     | XP_013362428.1 |
| PREDICTED: angiotensin-converting enzyme 2 [Oryctolagus cuniculus]               | 1449      | 1449        | 98%         | 0.0     | 85.14%     | XP_002719891.1 |
| angiotensin-converting enzyme 2 isoform X1 [Urocyon v. parryi]                   | 1448      | 1448        | 100%        | 0.0     | 84.76%     | XP_026252505.1 |
| PREDICTED: angiotensin-converting enzyme 2 [Marmota marmota marmota]             | 1447      | 1447        | 100%        | 0.0     | 84.88%     | XP_015343540.1 |
| PREDICTED: angiotensin-converting enzyme 2 [Fukomys damarensis]                  | 1446      | 1446        | 100%        | 0.0     | 84.72%     | XP_010643477.1 |
| angiotensin-converting enzyme 2 [Marmota flaviventris]                           | 1445      | 1445        | 100%        | 0.0     | 84.76%     | XP_027802308.1 |
| angiotensin-converting enzyme 2 [Heterocephalus glaber]                          | 1441      | 1441        | 100%        | 0.0     | 84.76%     | XP_004865157.1 |
| angiotensin I converting enzyme 2 [Oryctolagus cuniculus]                        | 1440      | 1440        | 98%         | 0.0     | 84.76%     | CHX359726.1    |
| Angiotensin-converting enzyme 2 [Heterocephalus glaber]                          | 1439      | 1439        | 100%        | 0.0     | 84.47%     | EHB15595.1     |

但ACE2关键的应该还是跟人冠状病毒19的S蛋白RBD区域结合的区域，也即是ACE2-PD区域，就拿ACE2-PD重复上面的分析看看。

But the key to ACE2 should be the region that binds to the RBD region of the S protein of human coronavirus 19, that is, the ACE2-PD region. Just repeat the above analysis with ACE2-PD.

| Description  | Max Score | Total Score | Query Cover | E value | Per. Ident | Accession      |
|--|-----------|-------------|-------------|---------|------------|----------------|
| angiotensin I converting enzyme_(peptidyl-dipeptidase A) 2 [synthetic construct] | 1242      | 1242        | 100 %       | 0.0     | 100.00%    | BAJ21180.1     |
| Chain A. Angiotensin-converting enzyme 2 [Paguma larvata]                        | 1216      | 1216        | 100 %       | 0.0     | 98.47%     | 3D0G_A         |
| Chain A Angiotensin-converting enzyme 2 chimera [Paguma larvata]                 | 1214      | 1214        | 100 %       | 0.0     | 98.30%     | 3SCK_A         |
| angiotensin-converting enzyme 2 [Octodon degus]                                  | 1105      | 1105        | 99 %        | 0.0     | 88.07%     | XP_023575315.1 |
| Angiotensin-converting enzyme 2 [Heterocephalus glaber]                          | 1105      | 1105        | 99 %        | 0.0     | 88.76%     | EHB15595.1     |
| angiotensin-converting enzyme 2 [Heterocephalus glaber]                          | 1104      | 1104        | 99 %        | 0.0     | 88.76%     | XP_004866157.1 |
| angiotensin-converting enzyme 2 [Mesocricetus auratus]                           | 1100      | 1100        | 100 %       | 0.0     | 87.59%     | XP_005074266.1 |
| PREDICTED: angiotensin-converting enzyme 2 [Equus przewalski]                    | 1099      | 1099        | 100 %       | 0.0     | 87.41%     | XP_008542995.1 |
| angiotensin I converting enzyme 2 [Mesocricetus auratus]                         | 1099      | 1099        | 100 %       | 0.0     | 87.59%     | ACT66278.1     |
| angiotensin-converting enzyme 2 [Equus caballus]                                 | 1098      | 1098        | 100 %       | 0.0     | 87.41%     | XP_001490241.1 |
| PREDICTED: angiotensin-converting enzyme 2 [Oryctolagus cuniculus]               | 1098      | 1098        | 100%        | 0.0     | 87.24%     | XP_002719891.1 |
| PREDICTED: angiotensin-converting enzyme 2 isoform X1 [Chinchilla lanigera]      | 1097      | 1097        | 100%        | 0.0     | 87.24%     | XP_013362428.1 |
| angiotensin I converting enzyme 2 [Oryctolagus cuniculus]                        | 1097      | 1097        | 100 %       | 0.0     | 87.24%     | ACT66271.1     |

排除灵长类，最像的是果子狸，而且达到了98%的相似度！比很多灵长类的相似度都要高，怪不得SARS的中间宿主是果子狸！不会这次的人冠状病毒19的中间宿主也是果子狸吧？这么说的话，通过这个ACE2-PD的同源分析找中间宿主的方法也是很有帮助的？只可惜除了果子狸，找不到其他物种还有这么高的相似度了。

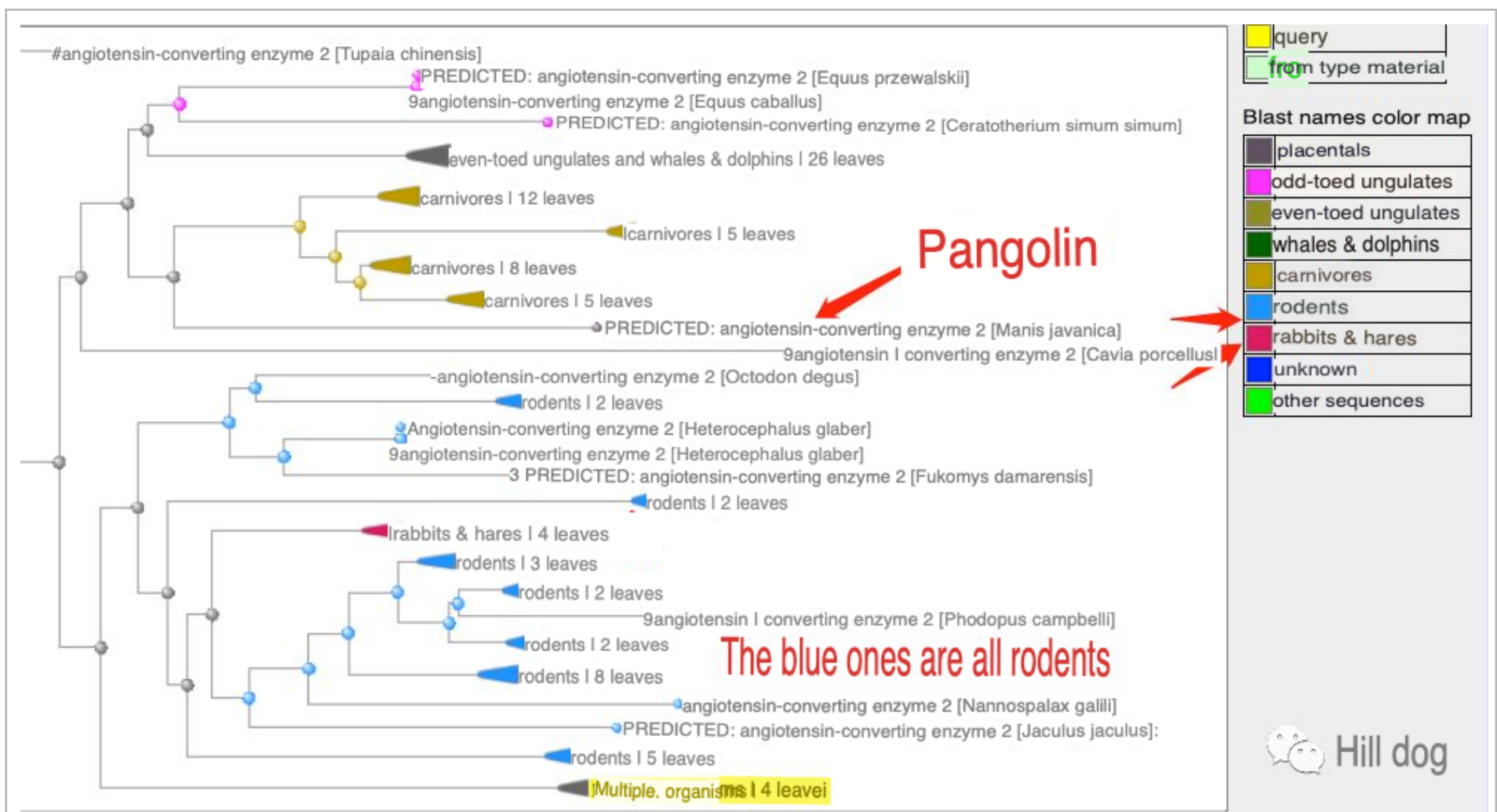
Excluding primates, the most similar is the civet cat, and it has a similarity of 98%! The similarity is higher than that of many primates. No wonder the intermediate host of SARS is the civet cat! Wouldn't the intermediate host of the human coronavirus 19 this time also be a civet cat? In this case, would it be also helpful to find the intermediate host through the homology analysis of ACE2-PD? It's a pity that other than civet cats, there are no other species with such a high degree of similarity.

ACE2-PD的同源分析除了灵长类和果子狸外，最像的就是一些不知道叫什么鼠(不是老鼠，是八齿鼠、裸鼯鼠、仓鼠这些)的啮齿类了，但也只有90%不到的相似度。

In addition to primates and civet cats, the homology analysis of ACE2-PD is most similar to some rodents that do not know what they are called (not mice, but degus, naked mole rats, hamsters, etc.), but only Less than 90% similarity.

进化树长这样：

The evolutionary tree looks like this:



穿山甲还是没有啮齿类同源性高，感觉啮齿类的可能性比穿山甲更大。

综上，从ACE2同源性的角度来分析宿主，同源性最高的是非人灵长类，但如果非人灵长类是中间宿主，那么这些病毒也极可能可以直接感染人，而不需要经过非人灵长类这个中间宿主。果子狸依然是有嫌疑，但估计已经被检测很多了，所以剩下最可能的就是啮齿类了，同源性上面比穿山甲还高。八齿鼠、裸鼯鼠、仓鼠等，以及兔子、野兔等等都是值得去研究的。

这个方法当然也是有缺陷的，毕竟只是从公共数据库上面来分析，要是真正的中间宿主根本没有被测序过基因，那就没有ACE2这个蛋白的序列了，所以也就无法分析了。何况这也是纸上谈兵，还是要通过实验的手段检测到了高度同源的病毒才能说明问题。

另外，武汉也许不是0号病人的诞生地呢？或许是从其他地方感染了带去武汉后爆发的？所以寻找中间宿主目光也不能局限于武汉了。也许可以再采采蝙蝠的样本，看看那个RaTG13相关病毒现在演变成什么样了，是不是跟人冠状病毒19很像了？说不定就是蝙蝠直接传过来的呢？

最后，华农团队等关于穿山甲冠状病毒的研究还是有很大价值和启发意义的，起码让我们认识了穿山甲携带了不少和人冠状病毒19相似的病毒，S蛋白RBD区域还高度相似，提示也很可能会感染人，从预防的角度讲价值重大。但我认为这些研究都无法支持穿山甲是人冠状病毒19的中间宿主。根据ACE2的同源性分析，啮齿类值得研究

Pangolins are still not as homologous as rodents, and they are more likely to feel rodents than pangolins.

To sum up, analysing the host from the perspective of ACE2 homology, non-human primates have the highest homology, but if non-human primates are intermediate hosts, then these viruses are very likely to directly infect humans without the need for through the intermediate host of non-human primates. The civet cat is still suspected, but it is estimated that it has been tested a lot, so the most likely thing left is the rodent, and the homology is higher than that of the pangolin. Degus, naked mole rat, hamster, etc., as well as rabbits, hares, etc. are all worth studying.

Of course, this method is also flawed. After all, it is only analysed from the public database. If the real intermediate host has not been sequenced at all, then there is no sequence of the ACE2 protein, so it cannot be analysed. What's more, this is only on paper, and the problem can only be explained by the detection of highly homologous viruses by experimental means.

In addition, Wuhan may not be the birthplace of patient 0? Maybe the outbreak occurred after being infected from other places and brought to Wuhan? Therefore, the search for an intermediate host cannot be limited to Wuhan. Maybe we can take another bat sample to see what the RaTG13-related virus has evolved into now. Is it similar to the human coronavirus 19? Maybe it was passed directly from the bat?

Finally, the research on pangolin coronaviruses by the SCAU team is still of great value and inspiration. At least it allows us to know that pangolins carry many viruses similar to human coronavirus 19, and the RBD region of the S protein is also highly similar. It is likely to infect people, and it is of great value from a preventive point of view. But I don't think any of these studies support pangolins as an intermediate host for 2019-nCoV. Rodents Worth Studying Based on Homology Analysis of ACE2



### On the article:

There are **3 versions** of the article.

1. The Full Caixin article (in Chinese) which is most detailed and was quickly deleted (<https://archive.li/YyIMt#selection-499.3-499.22>)
2. A Caixin blog entry (in Chinese) (<https://zhuanlan.zhihu.com/p/109427040>) which is still available and is the same as (1) without the last 2 of the 4 sections (so half size). It included at the end a link to the full version (1) above.
3. A short Caixin article in English which is much more limited and still available online via [asia.nikkei.com](http://asia.nikkei.com).

This article (in form 1) is explicitly mentioned by Little Mountain Dog [on Weixin](#):

First of all, I have to admire the reporters from Caixin.com, who dug up so much accurate information from the messy information in the early days, and wrote an article titled "New Coronavirus Gene Sequencing Traceability: when did the alarm sound."

Since writing about that experience, many reporters wanted to interview, including Caixin.com. They made more than one phone call (too many reporters, I can't remember how many repeats), but refused. Later, they basically restored the whole incident from clues. Later, many other organisations also sorted out the timeline based on this report.

The Caixin article seems to have been accompanied by a detailed [Timeline chart](#), now deleted but preserved in her blog entry (very much worth checking).

### #1. Full article (Chinese) of the 26th Feb 2020 @22:10:

This Caixin article seems to have been [deleted within one day](#)

- Here is the 404'd original link: <http://china.caixin.com/2020-02-26/101520972.html>
- Web Archive of the original link: <https://archive.li/YyIMt#selection-499.3-499.22>

A full translation is provided [here](#), with size by side Chinese and English.

### Exclusive | New coronavirus gene sequencing traceability: when the alarm was sounded February 26, 2020 22:10 Source: Caixin.com

The isolation, detection and gene sequencing of the new coronavirus are the basis for understanding and determining the infectiousness and harmfulness of the new coronavirus epidemic. On January 11, the Wuhan Health Commission, which had stopped giving updates for several days, changed the name of "viral pneumonia of unknown origin" to "pneumonia of novel coronavirus infection" for the first time, saying that as of January 10, 2020 24:00, there were 41 cases of preliminary diagnosis of new coronavirus pneumonia.



*On December 30, the Institute of Virology of the Chinese Academy of Sciences got the virus samples, January 1, 2020, virus isolation, January 2, completed the gene sequencing of the virus, January 5, isolated the virus strain, January 9, completed the national virus repository into the library and standardised storage.*

**[Caixin.com]** (Reporter Gao Yu, Peng Yanfeng, Yang Rui, Feng Yuding, Ma Danmeng)

Tracing back the roots of the new coronavirus, which has killed more than 2,660 people and caused more than 77,000 confirmed infections as of Feb. 24, when was this new coronavirus, similar to SARS, discovered? The Caixin reporters went through multiple interviews, and combed through the relevant papers, database information corroboration, so that the information puzzle gradually fully emerges.

All kinds of evidence show that before the end of December last year, samples of no less than nine unidentified pneumonia cases were collected from various hospitals in Wuhan, and genetic sequencing showed that the pathogen was a type of SARS coronavirus, and these test results were successively returned to the hospitals and reported to the Health and Welfare Commission and the CDC. On January 9, CCTV reported that the "Wuhan Viral Pneumonia Pathogenic Test Results Preliminary Evaluation Expert Group" officially declared the pathogen as a "novel coronavirus".



## The first case was released on December 27

On December 15, 2019, a 65-year-old male delivery man from the South China Seafood Market began to develop a fever. On December 18, he came to the emergency department of Wuhan Central Hospital Main Hospital (Nanjing Road Campus) to see a doctor, who suspected that it might be community-acquired pneumonia and admitted him to the emergency department ward of the hospital. Community-acquired pneumonia is a general term for pneumonia caused by a variety of microorganisms, including bacteria, viruses, chlamydia and mycoplasma, with the main clinical symptoms being cough, with or without sputum and chest pain.

On December 22, this patient's condition worsened and he was admitted to the ICU, where doctors used various antibiotics to treat him without results. Professor Zhao Su, chief physician of the Department of Respiratory Medicine at Wuhan Central Hospital, told Caixin that on December 24, a deputy chief physician of the Department of Respiratory Medicine performed a tracheoscopic sampling of this patient, and then sent the patient's alveolar lavage fluid sample to a third-party testing organisation, Guangzhou Weiyuan Gene Technology Co. for NGS testing, hoping to use its second-generation high-throughput gene sequencing technology (mNGS) based on macrogenomics, to identify the pathogen. Alveolar lavage is a therapeutic method to remove inflammatory secretions, etc. from the alveoli and improve respiratory function. For lower respiratory tract and lung diseases, the pathogen content in alveolar lavage fluid is higher than that in pharyngeal swabs.

Vision Medicals, whose full [Chinese] name is Guangzhou Weiyuan Gene Technology Co., was established in June 2018. Its communication says it focuses on precision medicine in oncology and infection pathogenesis and has a sequencing platform (NGS) based on second-generation high-throughput sequencing technology.

"Since BGI started using sequencing technology, there have been many gene sequencing companies in China, large and small. Over the years, in our various medical seminars, the second-generation high-throughput gene sequencing technology has been continuously introduced, and these companies have also sent pharmaceutical companies. Representatives go to major hospitals to preach." Zhao Su told Caixin reporters.

The full name of BGI (300676.SZ) is Shenzhen BGI Co., Ltd., formerly known as Beijing BGI Research Center, Founded in 1999, it has successively completed a number of genome research projects at the international advanced level, including the Chinese part of the International Human Genome Project, the Rice and Giant Panda Genome Projects, etc. In July 2017, it was listed on the Growth Enterprise Market with the "First Gene Sequencing Unit", and it is the world's largest genomics R&D institution. Another doctor at the Wuhan Union Hospital also introduced, "Test once, 6 million base sequences, 3,000 yuan, the 3,000 yuan can find out what the pathogen is a virus or bacteria, it may save lives."

Generally speaking, the gene sequencing company should give feedback on the test results three days later, on Dec. 27, but Weiyuan Gene did not give a written report. "They just notified us by phone that it was a new coronavirus." Zhao Su said. By this time the patient had been transferred to Wuhan Tongji Hospital on Dec. 25.

On Feb. 21, 2020, the genetic test information of this case was disclosed in an article by the WeChat public website "Weiyuan Gene". According to the article, the [Chinese Medical Journal](#) (English version) published a paper on January 27 about the discovery of the new coronavirus and the involvement of Weiyuan Gene in the early detection of the new coronavirus.

The aforementioned paper published in the Chinese Medical Journal refers to the article "Identification of a novel coronavirus that causes severe pneumonia in humans: a descriptive study" published on January 29. The authors of the paper are from the Institute of Pathogen Biology, Chinese Academy of Medical Sciences/Beijing Union Medical College (hereafter referred to as the Institute of Pathogen Biology, Chinese Academy of Medical Sciences), China-Japan Friendship Hospital, Hubei Provincial CDC, Wuhan Jinyintan Hospital, Wuhan Central Hospital, and Guangzhou Microgene Technology Co. Xu Teng, chief technology officer of Microgene, is the co-first author of the paper, and Li Yongjun, CEO, and Wang Xiaorui, chief operating officer, are the byline authors. Li Yongjun was a bioinformatics analyst at the Institute of Pathogenesis, Chinese Academy of Medical Sciences.

According to the paper, the researchers collected clinical data and bronchoalveolar lavage samples from five patients with severe pneumonia at Jinyintan Hospital in Wuhan, Hubei, and performed pathogenic macrogenomics (mNGS) analysis. As a result, a coronavirus with 79% nucleotide sequence similarity to SARS virus, which has never been reported before, was found in all these samples. The paper shows that the first clinical sample from these five patients to be genetically sequenced was a sample from a 65-year-old patient collected on December 24. He developed a high fever and cough with little sputum on December 15. He was admitted to the hospital on the 18th and to the ICU on December 22. 16 days later he still had a persistent high fever that developed into severe shortness of breath.

Also highly consistent with the above information is an article titled "Record the experience of discovering the new coronavirus for the first time" published by the WeChat public account "Small Mountain Dog" (Xiaoshan Gou) on January 28. The author claimed to be working in a private enterprise in Huangpu, Guangzhou, and recorded in the article: "I just went to work on December 26, 2019, and as usual, I first browsed through the mNGS pathogenic microorganism automatic interpretation results for the day. Unexpectedly, I found that one sample reported a sensitive pathogen - SARS coronavirus, with dozens of sequences, and only this sample had such a meaningful pathogen. With a tight heart, I hurriedly checked the detailed analysis data in the background and found that the similarity was not very high, only about 94.5%. In order to confirm the reliability of the results, a detailed analysis was started. The results of the exploratory version of the analysis suggested that this pathogen was most similar to Bat SARS like coronavirus (bat-like SARS coronavirus), with an overall similarity of about 87%, while the similarity to SARS was about 81%."

According to the author, the patient's sample was also collected on December 24. The article mentions that "the front-end feedback is that this patient is seriously ill and is anxious to have the test results, but such a significant pathogen really cannot be reported easily, so I had an urgent meeting with several company bosses at noon and decided to continue the in-depth analysis and delay the release of the report, while sharing the data to the Pathogen Institute of the Chinese Academy of Medical Sciences so that they can get a piece of the analysis". The Institute of Pathogenesis of the Chinese Academy of Medical Sciences is one of the authors institutions for the above-mentioned paper in the Chinese Medical Journal (English version), and the CEO of Weiyuan Gene, Li Yongjun, worked for the Institute of Pathogenesis of the Chinese Academy of Medical Sciences, whose immediate superior, the president of the Chinese Academy of Medical Sciences, is academician Wang Chen, vice president of the Chinese Academy of Engineering.

On Dec. 27, the lab assembled a near-complete sequence of the viral genome, and the data was also shared with the Institute of Pathogenesis of the Chinese Academy of Medical Sciences. "It was basically confirmed that this patient's sample did have a novel virus similar to Bat SARS like coronavirus inside." The article writes, "The information received at the time was that this patient had been back to his hometown and exposure to bats could not be ruled out. Aware of the potential seriousness of the problem, the laboratory was fully cleaned and disinfected, samples were harmlessly destroyed, and the personnel involved in the experimental operation were monitored for this. We have communicated with the doctor before noon, the patient was also isolated."

"It should be that we first discovered this new coronavirus." The article by "Little Mountain Dog" also gives a screenshot of the GISAID database, "From the data submitted on the GISAID database website, the earliest sample collection time is also us."

GISAID is a global platform for sharing data on influenza viruses, and researchers can upload their extracted viral genetic sequences after registering. Each strain is given a unique number, and information such as the time of collection, date of submission, and laboratory of submission is also recorded. The Caixin reporter checked and found that, according to the sample collection time, the earliest gene sequence of a new coronavirus on GISAIDS was collected on December 24, 2019 and uploaded by the Institute of Pathogenesis of the Chinese Academy of Medical

Sciences on January 11. This is the sample sequence marked in the screenshot of the article "Little Mountain Dog" that their company participated in testing.

The article also mentioned that the company's leaders communicated with the hospital and the CDC (department) by phone on December 27 and 28, and even personally went to Wuhan on the 29th and 30th to report and exchange all the analysis results with the hospital and CDC leaders in person, "including all our analysis results and the analysis results of the Institute of Pathogenesis of the Academy of Medical Sciences. Everything is under intense, confidential and strict investigation (at this time, people at the hospital and CDC already knew that there were several similar patients, and had already started emergency treatment after we communicated the test results)".

The owner of the earliest known sample to complete the genetic sequencing mentioned above, later died in Jinyintan Hospital. The results of this research, which had detected the new outbreak virus on December 27, also did not play any role at that time.

### **"SARS coronavirus" exploded on social media**

In fact, in addition to the earliest known case, at the end of December 2019, there were two other cases of "unexplained pneumonia" in Wuhan Central Hospital where samples from patients were sent to different institutions for genetic sequencing. The test results of these two cases had a significant impact on the disclosure of the outbreak by different pathways.

On December 27, a 41-year-old man surnamed Chen visited Wuhan Central Hospital Nanjing Road Campus. "He is an accountant, his family lives in Wuchang, has not been to the South China Seafood Market in Hankow at all, probably on December 16 without obvious cause began to fever, the highest temperature of 39.5 ° C, accompanied by palpitations, chest tightness, breathing difficulties after activity, physical strength decreased significantly, first on December 22 in the Jiangxia District First People's Hospital to see a doctor, no improvement." Zhao Su revealed to the Caixin reporter, "he is an acquaintance of a doctor in our hospital, was transferred to our hospital on the 27th, also admitted to the emergency department." In the evening of December 27, the patient had a bronchoscopy sample done in the hospital's respiratory ICU, and this time the sample was sent to another company engaged in NGS testing, Beijing Boao Medical Laboratory Co.

On December 30, the Beijing Boao Medical Laboratory sent the patient's test report back to the doctor, and the test result was directly "SARS coronavirus" (SARS coronavirus).

The test report of the Beijing Boao Medical Laboratory obtained by the Caixin reporter showed that high confidence positive indicators for SARS coronavirus and *Pseudomonas aeruginosa* were detected in the patient's sample. The SARS coronavirus is explained therein as a single-stranded positive-stranded RNA virus that is transmitted by proximal droplet transmission or contact with the patient's respiratory secretions and can cause a specific type of pneumonia, also known as atypical pneumonia, that is significantly infectious and can involve multiple organ systems.

"Their gene pool is not complete enough, or maybe they didn't do a review, so they made a small mistake, which is the fact that the virus is actually not the same thing as SARS, but a new coronavirus." A gene sequencing expert revealed to Caixin reporters.

However, it was the test report that contained a small mistake that directly caught the attention of Wuhan doctors who blew the alarm whistle to the public through social media, saving the lives of a considerable number of people to some extent.

On December 30, the test report of Beijing Boao Medical Laboratory appeared on the WeChat of a doctor at Wuhan Central Hospital. At 17:48 that evening, Li Wenliang, an ophthalmologist at Wuhan Central Hospital, posted a message among his classmates: "7 cases of SARS were diagnosed in the South China Fruit and Seafood Market, and they are quarantined in the emergency department of our hospital"; at 19:39, the Wuhan Red Cross Society Liu Wen, a neurologist at the hospital, posted a message in the work WeChat group "Concordia Red Cross Society", saying: "A case of coronavirus pneumonia has just been confirmed in the Houhu District of the Second Hospital (i.e. Wuhan Central Hospital). Maybe the surrounding areas in South China will be quarantined." "SARS has basically been determined, nurses and sisters, don't go out to shake it"; at 20:48, Xie Linka, a doctor at the Cancer Centre of Wuhan Union Medical College Hospital, posted a message in the WeChat group of the cancer centre, "Don't go to the Huanan Seafood Market in the near future, it is happening there now. Many people have suffered from pneumonia of unknown cause (similar to SARS). Today, our hospital has treated many patients with pneumonia in the Huanan Seafood Market. Everyone pays attention to wearing masks and ventilating." These three doctors have since been admonished by the police.

On the same day, the author of the article, "Little Mountain Dog" in Huangpu, Guangzhou, was also informed of the above news, he recounted: "By December 30, I heard the news that there were more than a few patients with similar symptoms, and my nerves were suddenly tense. In particular, about the afternoon of the 30th, a friend of the business may have detected the same virus in another patient's sample, but they directly sent a report of the detection of SARS coronavirus, which instantly set off the news ..... friends shared the sequence for our analysis, and when I analysed it, it was indeed the same virus! The first subconscious thought was 'this virus is contagious!'"

Li Wenliang and others lifted the lid, and the story of the gene company's sequencing of this pathogen intersected with another story of clinician warning. While the doctors in Wuhan Central Hospital were ineffective in their routine treatments for the emerging viral pneumonia patients and hoped to seek answers through gene sequencing companies, Zhang Jixian, director of the Department of Respiratory and Critical Care Medicine of Hubei Xinhua Hospital, which is adjacent to the South China Seafood Market, on December 26 On December 27, Zhang Jixian reported four cases of "unknown viral pneumonia" to the hospital, and the hospital reported it to the Jiangnan District Centre for Disease Control and Prevention (CDC).

On December 28-29, Xinhua Hospital admitted three more patients from the South China Seafood Market, who had similar symptoms of viral pneumonia. According to later reports such as the Wuhan Evening News, at 1 p.m. on December 29, Xinhua Hospital Vice President Xia Wenguang called ten experts to discuss the seven cases, and the experts agreed that the situation was unusual and Xia Wenguang reported the case directly to the Disease Control Division of the provincial and municipal health committees. Also reported to on the same day was the Public Health Department of Wuhan Central Hospital. In the afternoon of the same day, Hubei Province, Wuhan City Health Commission CDC notified the provincial, municipal and district level CDC that Xinhua Hospital and the Downtown Hospital Houhu Hospital had admitted a number of patients with unknown pneumonia with a history of exposure to the seafood market, which triggered the start of an emergency response.

The Hubei Province CDC, the Wuhan CDC in conjunction with Jiangnan District, Qiaokou District, East and the West Lake District CDCs, all began an epidemiological investigation. Wuhan Jinyintan Hospital Vice President of Operations Huang Chaolin and others came to Xinhua Hospital, picking up six patients. Wuhan Tongji Hospital also transferred the aforementioned first patient from the downtown hospital to Jinyintan Hospital to do genetic testing.

On December 30, the tertiary CDC produced the "Report on the investigation and disposition of the situation of multiple cases of pneumonia in the South China seafood market reported by hospitals". On the same day, the Wuhan Municipal Health Commission issued an internal notice, mentioning that at a number of medical institutions in Wuhan multiple cases of unexplained pneumonia, associated with the Wuhan South China Seafood Wholesale Market, appeared one after the other on. And it required medical institutions to report patients with similar characteristics of unexplained pneumonia seen in the past week.

This "Urgent Notice on the Treatment of Pneumonia of Unknown Origin" by the Wuhan Health Care Commission, which was triggered by Zhang Jixian's insistence on reporting, was soon to be found online, along with a WeChat alert from doctors such as Li Wenliang who saw the gene



sequencing report, allowing information about the outbreak that started in Wuhan to reach the outside world for the first time.

## A warning from Shanghai

Another case sample from Wuhan Central Hospital came from the Houhu hospital area, also adjacent to the South China Seafood Market, and was admitted a day earlier. The patient, also surnamed Chen, is a 41-year-old self-employed seafood market operator from Quanzhou, Fujian Province, who developed a high fever of 40°C, general aching and weakness, coughing and pus, chest tightness and shortness of breath after suffering a cold on December 20, and was admitted to Wuhan Central Hospital Houhu Hospital on December 26 with "fever investigation and lung infection", and on December 30 The hospital took a bronchoscopic sample and left an extra copy of the respiratory lavage fluid sample in the refrigerator at -80°C for storage.

"The reason for keeping an extra sample is that we have been cooperating with the Shanghai Public Health Clinical Centre affiliated with Fudan University (hereinafter referred to as Shanghai Public Health Centre) and Wuhan CDC on a major national science and technology project, 'China's major natural epidemic virus resources'. Wuhan CDC is responsible for the collection of clinical samples and environmental specimens in the Central China region, which are regularly sent to the Shanghai Public Health Centre for pathogen testing, and they have a biosafety level 3 (BSL-3) laboratory with high-throughput sequencing and bioinformatics analysis platform, while hospitals like ours are sentinel hospitals of the Wuhan CDC." Professor Zhao Su, Department of Respiratory Medicine, Wuhan Central Hospital, introduced.

On the afternoon of December 30, the samples were taken by a chief physician of the Wuhan Centre for Disease Control and Prevention (CDC)<sup>21</sup>. On Jan. 2, another researcher at the Wuhan CDC wrapped the samples heavily in dry ice, iron boxes and foam boxes and sent them, along with other animal specimens, by rail express to Shanghai. On Jan. 3, Professor Zhang Yongzhen's team at the Shanghai Public Health Clinical Centre received the samples. This centre belongs to Fudan University, Zhang Yongzhen himself is a researcher at the Institute of Infectious Disease Prevention and Control of the Chinese Centre for Disease Control and Prevention (CDC), and adjunct professor at the Institute of Biomedical Research of Fudan University and the Shanghai Public Health Centre. He has been engaged in scientific research work on human-animal infectious diseases and the investigation of major natural epidemic viral foci in China in recent years under the funding of the National Natural Foundation of China, national major special projects and national key research and development programs. Many hospitals, including Wuhan Central Hospital, Wuhan Centre for Disease Control and Prevention (CDC), and the University of Sydney, Australia, etc, are members of the project team.

In the early morning of January 5, Zhang Yongzhen's research team detected a novel SARS-like coronavirus from the sample and obtained the whole genome sequence of the virus through high-throughput sequencing; the evolutionary tree drawn from the sequencing data also confirmed that the novel coronavirus in Wuhan had never been seen before in history. The Shanghai Public Health Centre immediately reported to the Shanghai Municipal Health and Wellness Commission and the National Health and Wellness Commission and other authorities that day, alerting them that the new virus was homologous with SARS and should be transmitted via the respiratory tract, and suggesting appropriate disease control and epidemic prevention measures in public places. On January 6, the CDC initiated a Level 2 emergency response internally.

"We have been working with the Wuhan CDC and Wuhan Central Hospital to collect new viruses of natural epidemic origin, which is part of our major national project, including the use of the P3 laboratory, which is also accredited by the China National Accreditation Service for Conformity Assessment." A researcher at the Shanghai Public Health Centre told Caixin, "We are in routine scientific research, and when we find it by chance, the matter is so important that we immediately report it."

## At least nine samples collected late last year for testing

The Caixin reporter confirmed that several other gene sequencing companies obtained samples of unidentified pneumonia cases from Wuhan Hospital almost around the same time as Guangzhou Weiyuan Gene Technology Co. and Beijing Boao Medical Laboratory. This includes the industry's "leader", BGI, which received a gene sequencing commission from a local hospital in Wuhan on Dec. 26, 2019. On Dec. 29, the gene sequencing results completed by BGI on the case sample showed that the virus had 80% gene sequence similarity to SARS, but was not SARS, but a previously unavailable coronavirus. BGI also tested the case with their SARS test kit and the results were negative, denying that it was SARS.

A BGI source told Caixin that when they sequenced samples from cases of unexplained viral pneumonia in late December, they were unaware that the virus had clinically infected many people and had even caused aggregated infections in the same family.

"We are a technology company that does genetic sequencing, and we receive many sequencing commissions every day, and we are exposed to a large number of viruses, and we find many new viruses. The company is a genetic sequencing technology company that receives many sequencing commissions every day and is exposed to a large number of viruses, and also discovers many new viruses. There are many kinds of coronaviruses, including SARS, and there are only six coronaviruses associated with people, and the only ones that are more infectious to people are SARS and MERS. At that time we did not know whether this virus was 'good' or 'bad'."

BGI has been cooperating with local hospitals in Wuhan for many years. According to a Caixin reporter's investigation, local hospitals in Wuhan sent at least 30 samples of difficult pneumonia cases to BGI for sequencing in December 2019. BGI found a total of three cases of pneumonia caused by new coronavirus infection. Except for the case on December 26, the other two cases were collected on December 29 and 30 respectively. They mixed three SARS-like coronaviruses, that is, combined the three viral gene sequence fragments together to form a mixed viral gene sequence. On January 1, the test reports of the three samples were reported to the Wuhan Municipal Health Commission. On January 3, BGI conducted a high-depth full-gene sequence sequencing of the viruses in the three samples.

Caixin reporters found that as of January 19, 2020, a total of 13 samples of the new coronavirus genome sequence had been uploaded on the GISAID platform. Except for the three articles from Japan and Thailand, the remaining 10 articles were all uploaded by Chinese scientific research institutions. Judging from the time of sample collection, the earliest is the aforementioned case collected on December 24, 2019 and uploaded by the Pathogen Institute of the Chinese Academy of Medical Sciences.

Eight other samples were collected on December 30, from Wuhan Jinyintan Hospital and Hubei Provincial CDC (1 entry), Jinyintan Hospital and Wuhan Institute of Virus Research, Chinese Academy of Sciences (5 entries), and the Institute of Prevention and Control of Viral Diseases, China CDC (2 entries). In addition, the Institute for Prevention and Control of Viral Diseases of the Chinese CDC uploaded a gene sequence for samples completed for collection on January 1, 2020.

Corroborating with this, according to Hubei Daily, on the day of December 30, Jinyintan Hospital President Zhang Dingyu led the collection of bronchoalveolar lavage fluid from the first seven patients admitted to the hospital and sent it to the Wuhan Institute of Virus, Chinese Academy of Sciences for testing.

Based on the industry's average detection cycle of three days, by around January 2, the gene sequencing results of the above-mentioned eight samples collected on December 30 should have been obtained. The Wuhan Institute of Virology of the Chinese Academy of Sciences said in an

<sup>21</sup> DRASTIC note: Disinfection of the market started on the 30<sup>th</sup> December evening (after market hours). Possibly animal samples were then taken that day, if not then the following days. This passage suggests that some animal samples from the market were then sent to Shanghai on the 2<sup>nd</sup> Jan.

open letter "Wuhan Institute of Virology Fully Launches Scientific Research on New Coronary Virus Pneumonia" that the Institute of Virology received an unidentified pneumonia sample from Jinyintan Hospital on the evening of December 30. The complete genome sequence of the new coronavirus was determined on January 2, and uploaded to GISAID on January 11.

The aforementioned paper published in the Chinese Medical Journal (English version) also showed that alveolar lavage fluid samples from five patients were collected and sent for testing and analysis during the nine-day period from December 24, 2019 to January 1, 2020, and that two of these five patients had no history of exposure to the South China Seafood Market.

Of the five patients, in addition to the 65-year-old patient sample mentioned above, three other patients had samples collected on December 30, 2019. Of these, patient #2 was a 49-year-old female working at the South China Seafood Market who began having a high fever and dry cough on December 22, developed respiratory distress and was hospitalised five days later, and was admitted to the ICU on December 29; patient #3 was also a female, 52 years old, who developed a fever on December 22 and was hospitalised on December 29, but she had no history of seafood market exposure; patient #4 was a 41-year-old male who on December 16 He began to have a high fever and dry cough and was hospitalised on the 22nd - this male, who also had no history of seafood market exposure, was apparently the Wuchang accountant seen above at Wuhan Central Hospital; patient #5, whose alveolar lavage fluid sample was collected on January 1, 2020, was a 61-year-old male who worked at the South China Seafood Market and who himself had chronic liver disease and abdominal mucinous tumour, was admitted to a local hospital after seven days of fever, cough, and respiratory distress, and began resuscitation using ECMO on January 2 before succumbing.

According to the paper, a novel coronavirus was thus identified in the laboratory with 79% nucleotide sequence similarity to the SARS virus, which is phylogenetically closest to the SARS-like coronavirus carried by bats, but forms a separate evolutionary branch of the coronavirus beta genus strain sequence. After conducting virus isolation for morphological confirmation and serological testing, the new pathogen was finally confirmed to be a novel coronavirus. The structural domain of this virus that binds to the receptor has an amino acid sequence similar to that of the SARS coronavirus, suggesting that both viruses may bind to the same receptor on human cells.

Looking back at those few days from the end of December 2019 to the beginning of January this year, it should have been a critical moment to decide the fate of countless people. But at that time, the public was still unaware of the consequences that the virus would later trigger.

A gene sequencing company source revealed that on January 1, 2020, he received a phone call from an official of the Hubei Provincial Health Commission, informing him that if there were samples of cases of new crown pneumonia in Wuhan to be sent for testing, they could not be tested again; samples of existing cases had to be destroyed, no information about the samples could be disclosed to the public, no relevant papers or relevant data could be released to the public, and "if you detect it at a later date, you must report it to us."

On January 3, the General Office of the National Health Commission issued a notice titled "Notice on Strengthening the Management of Biological Sample Resources and Related Scientific Research Activities in the Prevention and Control of Major Emerging Infectious Diseases," this National Health Office Science and Education Letter (2020) No. 3 document said that for the recent Wuhan pneumonia case samples, based on the currently available information such as etiological characteristics, transmissibility, pathogenicity, clinical data, etc., until the pathogen information is further clarified, it is temporarily classified as highly pathogenic pathogenic microorganisms. (Class II).

The transport of samples should be in accordance with the former Ministry of Health "infectious human highly pathogenic microorganisms strains (viruses) or samples transport management regulations"; pathogen-related experimental activities should be carried out in biosafety laboratories with the appropriate level of protection.

Document No. 3 further stipulates that (i) all relevant institutions should provide biological samples to designated pathogen detection institutions for pathogenic testing and proper handover procedures in accordance with the requirements of the administrative departments of health at the provincial level or above; (ii) without approval, biological samples and their related information shall not be provided to other institutions and individuals; institutions and individuals who have obtained biological samples of relevant cases from relevant medical and health institutions shall immediately destroy the samples in situ or send them to the state-designated preservation institution for safekeeping, and properly keep records of relevant experimental activities and experiments, (iii) during the period of epidemic prevention and control, the information generated by various institutions undertaking pathogenic testing tasks is a special public resource, and no institution or individual may release information about pathogenic testing or experimental results without permission.

As for which institutions belong to the "designated pathogen detection institutions", the document does not mention it. Virologists revealed that even the Wuhan Institute of Chinese Academy of Sciences were once asked to stop pathogen testing, the destruction of existing samples, "because according to the current "Prevention and Control of Infectious Diseases Law", to carry out laboratory testing of infectious diseases, diagnosis, pathogenic identification is the legal responsibility of disease prevention and control agencies at all levels, only the national and provincial institutions of the CDC are authorised to carry out pathogenic identification of infectious diseases. The Wuhan Institute of Virus of the Chinese Academy of Sciences is clearly not among them, not to mention those unauthorised commercial research institutions".

Perhaps because of this, the Institute of Virology, Chinese Academy of Sciences, which got the virus sample on December 30, carried out virus isolation on January 1, 2020, completed the gene sequencing of the virus on January 2, and isolated the virus strain on January 5, 1 On March 9, the storage and standardised preservation of the National Virus Resource Bank was completed. These research works, which can obviously be completed around the clock, were not announced to the public for a long time. Only in February when they faced rumours and criticism from the outside world, they only gave a few words of disclosure.

On January 9, CCTV reported that the "Wuhan Viral Pneumonia Pathogen Test Results Preliminary Evaluation Expert Group" led by the China CDC determined that the pathogen was a new type of coronavirus. "As of 21:00 on January 7, 2020, the laboratory A new type of coronavirus was detected, and the whole genome sequence of the virus was obtained. A total of 15 positive results of the new type of coronavirus were detected by the nucleic acid detection method. The virus was isolated from the sample of 1 positive patient, and the electron microscope showed a typical coronavirus form."

On January 11, Zhang Yongzhen's research team shared the virus genome sequence information on Virologic.org and GenBank, the first team in the world to publish the virus sequence.

Later that day, the National Health Commission announced that China would share the genetic sequence of the new coronavirus with the WHO. The next day, five other viral genome sequences from different patients were released on GISAID, the Global Shared Influenza Virus Database, by a team led by the National Health and Wellness Commission. Which organisation did this sharing of new coronavirus gene sequence information to WHO come from? Gao Fu, director of the Chinese CDC, responded to the Caixin reporter, saying that the gene sequence came from three institutions, the Chinese CDC, the Chinese Academy of Medical Sciences and the Chinese Academy of Sciences, and this is a joint research. The WHO said it has obtained more detailed information about Wuhan unexplained viral pneumonia from China's National Health Commission, including information on the gene sequence of the novel coronavirus detected from the case, which is important for other countries to develop specific diagnostic tools.

At this point it is not really necessary to go into detail about who was the first to pick the pearl in the scientific crown, as 15 days have passed since the first case of genetic sequencing identified the new coronavirus.

On January 11, the Wuhan Health Commission, which had stopped providing updates for several days, changed the name of "viral pneumonia of unknown origin" to "pneumonia of new coronavirus infection" for the first time, saying that as of 24:00 on January 10, 2020, 41 cases of new



coronary pneumonia were initially diagnosed. On the same day, the "two sessions" of Hubei were held. Until the end of Hubei's "two sessions" on January 17, this number did not increase.

Caixin reporter Zhao Jinzhao and intern reporter Huang Yuxin also contributed to this article.

## #2. Caixin blog entry (Chinese, half-size) published on the 27<sup>th</sup> Feb 2020 @17:04:

<https://zhuanlan.zhihu.com/p/109427040>



独家 | 新冠病毒基因测序溯源：警报是何时拉响的

财新网  
已认证帐号

288 人赞同了该文章

This is basically a half-sized version of the full article (#1). A link at the bottom points to the new deleted full article:

Exclusive | Retrospective source of  
neoconovirus gene sequencing: when...  
[china.caixin.com/2020-02-26/101520972...](https://china.caixin.com/2020-02-26/101520972...)



## #3. Short article (English) of the 3<sup>rd</sup> March 2020:

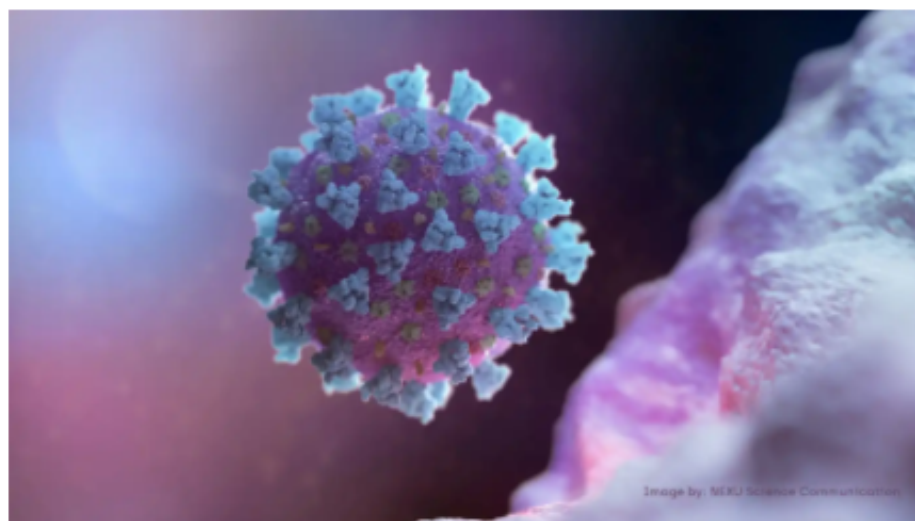
This is a considerably simplified English version of the main article, reworked with Flynn Murphy, Han Wei and Timmy Shen, and with a new title ('In Depth: How early coronavirus signs were spotted and throttled'). This short version in English is still available via [asia.nikkei.com](https://asia.nikkei.com).

<https://asia.nikkei.com/Spotlight/Caixin/In-Depth-How-early-coronavirus-signs-were-spotted-and-throttled>

CAIXIN

### In Depth: How early coronavirus signs were spotted and throttled

Labs identified SARS-like virus weeks before official announcements



China's National Health Commission ordered institutions on Jan. 3 not to publish information related to the disease. © NEXU Science Communication/ Reuters

GAO YU, PENG YANFENG, YANG RUI, FENG YUDING, MA DANMENG, FLYNN MURPHY, HAN WEI, TIMMY SHEN, Caixin  
March 3, 2020 11:09 JST



## Annexe 2 - About Vision Medicals:

Vision Medicals is the English name for [微远基因 科技有限公司 进行](#) (Weiyuan Gene Technology Co., Ltd).

It was set up in Guangzhou (广州) in [June 2018](#) and still very much a start-up in Dec 2019.

Vision Medicals was involved in the sequencing of the [Beijing plague cases](#) in Nov 2019 and in the sequencing of the Guangxi pangolins in Q1 2020 (see [Nature article](#)). Incidentally Little Mountain Dog wrote a [Weixin post about the Pangolins sequences](#) where she correctly noticed that some sequences were identical across the papers.

Vision Medicals Vision appears in the [Chinese Medical Journal paper](#) sent for publication on the 27 Jan 2020 (published May 2020) introducing the discovery of SARS-CoV-2, with CTO Dr. Xu Teng as the co-first author of the article, Li Yongjun and Wang Xiaorui as the signed authors.

### Original Article

#### Identification of a novel coronavirus causing severe pneumonia in human: a descriptive study

Li-Li Ren<sup>1</sup>, Ye-Ming Wang<sup>2,3</sup>, Zhi-Qiang Wu<sup>4</sup>, Zi-Chun Xiang<sup>1</sup>, Li Guo<sup>1</sup>, [Teng Xu<sup>5</sup>](#)  
Yong-Zhong Jiang<sup>6</sup>, Yan Xiong<sup>7</sup>, [Yong-Jun Li<sup>8</sup>](#), Hui Li<sup>8</sup>, Guo-Hui Fan<sup>2,3,9</sup>, Xiao-Ying Gu<sup>2,3,9</sup>, Yan Xiao<sup>1</sup>, Hong Gao<sup>10</sup>, Jiu-Yang Xu<sup>11</sup>, Fan Yang<sup>4</sup>, Xin-Ming Wang<sup>1</sup>, Chao Wu<sup>1</sup>, Lan Chen<sup>1</sup>, Yi-Wei Liu<sup>1</sup>, Bo Liu<sup>4</sup>, Jian Yang<sup>4</sup>, [Xiao-Rui Wang<sup>5</sup>](#), Jie Dong<sup>4</sup>, Li Li<sup>4</sup>, Chao-Lin Huang<sup>12</sup>, Jian-Ping Zhao<sup>13</sup>, Yi Hu<sup>14</sup>, Zhen-Shun Cheng<sup>15</sup>, Lin-Lin Liu<sup>6</sup>, Zhao-Hui Qian<sup>4</sup>, Chuan Qin<sup>10</sup>, Qi Jin<sup>4</sup>, Bin Cao<sup>2,3</sup>, Jian-Wei Wang<sup>1</sup>

Vision Medicals is correctly listed in the contacts for the very first SARS-CoV-2 sequence ([WH-01](#), also [CNBC](#)):

#### Severe acute respiratory syndrome coronavirus 2 / IPBCAMS-WH-01

**Scientific Name :** *Severe acute respiratory syndrome coronavirus 2*  
**Common Names :** -  
**Bioproject :** [PRJCA002165](#)  
**Biosample :** [SAMC133241](#)  
**Accession No. :** GWHABKF00000000  
**Submitter Organization :** NHC Key Laboratory of Systems Biology of Pathogens and Christophe Mérieux Laboratory, Institute of Pathogen Biology, Chinese Academy of Medical Sciences & Peking Union Medical College; [Vision Medicals Co., Ltd](#)  
**Contacts :** Lili Ren, renlili@ipb.com  
Jianwei Wang, wangjw28@163.com  
Qi Jin, jinqi@ipbcams.ac.cn  
Zichun Xiang, xiangzch@163.com  
[Yongjun Li, yjli@visionmedicals.com](#)  
Zhiqiang Wu, wuzq2009@ipbcams.ac.cn  
Chao Wu, feifeifly214@sina.com  
Yiwei Liu, liuyiwei\_1314@163.com

In March 2020, Vision Medicals [received the CE-IVD mark](#) for its SARS-CoV-2 Clinical Sequencing assay, which uses next-generation sequencing.

## Annexe 3 - About 小山狗 (Little Mountain Dog) [true identity withheld]:

小山狗 = **Xiǎoshān Gǒu**, is a nickname for an employee of Vision Medicals (广州 微远基因 科技有限公司, Chinese: Guangzhou Weiyuan Gene Technology Co., Ltd).

She was most likely born in the early 1990s, is very cultured and sensitive and a film lover.

### Short CV:

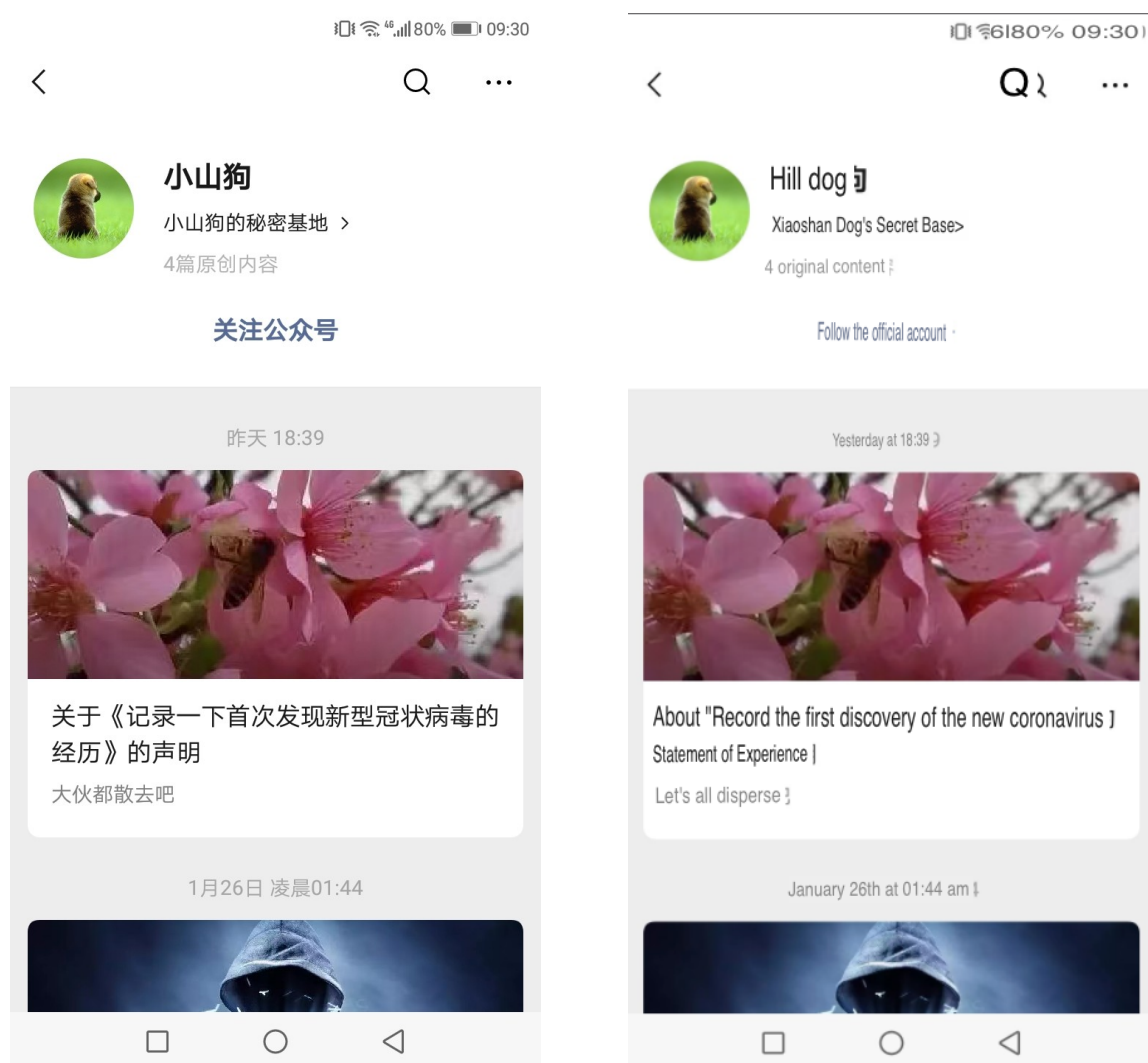
- 2015 or earlier - 2018: Masters in Microbiology at Sun Yat-sen University, Guangzhou
- 2018 or 2019: Joins Vision Medicals, Guangzhou, China, after a possible short stint at a local competitor (maybe for an internship)
- 2022: Still at vision Medicals

### Weixin posts:

For a list of Weixin articles by Little Mountain Dog see:

<https://web.archive.org/web/20220317075910/https://wemp.app/accounts/06c77e26-4bf4-4d22-b4ea-01698f56b4ca>.

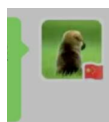
In particular the [Timeline post](#) is interesting.



### Weixin ID:

小山狗 uses a little dog as his Weixin icon (see for instance <https://freewechat.com/profile/MzAxMjMyMDk0Ng==>).

小山狗 cut her handle from all the post pictures in in Document 1. This is what they should look like.



### Details:

小山狗 ((Little Mountain Dog)

Weixin ID: Winjor001

About FeatureL: 小山狗的秘密基地 (Little Mountain Dog's Secret Base)



[https://mp.weixin.qq.com/s?\\_\\_biz=MzAxMjMyMDk0Ng==&mid=2650112061&idx=1&sn=4f32f2392dc194f780e932ca175ed8a6&chksm=83b289e0b4c500f66f12fad8a476f1692024fc627241d7a997116052f876394ab344b341be25](https://mp.weixin.qq.com/s?__biz=MzAxMjMyMDk0Ng==&mid=2650112061&idx=1&sn=4f32f2392dc194f780e932ca175ed8a6&chksm=83b289e0b4c500f66f12fad8a476f1692024fc627241d7a997116052f876394ab344b341be25)



## Annexe 4 - Timeline:

Caixin [original article](#) was supplemented by a great [timeline](#) (now deleted) that Little Mountain Dog reproduced [in a blog](#). That timelines focussed on the early cases, the earliest sequencings and the role of the authorities at that time. She also added a shorter [timeline](#) from Southern Metropolis Daily (the heir of the great investigative Southern Weekly), based in Guangzhou.

Here is a more general timeline:

| Key dates<br>(Beijing time) |  | Timeline by gilles@demaneuf.com (DRASTIC) |
|-----------------------------|--|---|
| end Nov 2019                | According to <a href="#">multiple detailed reports never denied</a> , at the end of Nov 19, the DIA, whose mandate includes defence diplomacy, alerts NATO and the IDF of a concerning disease with new characteristic development in Wuhan. That alert is based on intelligence data points accumulating since the 2 <sup>nd</sup> week of November. A formal assessment for larger consumption across the government and its agencies (an 'intelligence product') will be written in December.   |   |
| 30 Nov 2019                 | According to <a href="#">official Chinese documents</a> leaked to the South China Morning Post, using data compiled before the 13 <sup>th</sup> March 2020, at least <b>9</b> people have already fallen ill with what will be known as Covid-19 (confirmed cases): 4 men and 5 women, aged 39 to 79. First onset date amongst these 9 is 17 <sup>th</sup> Nov.  |   |
| 15 Dec 2019                 | Ian Lipkin, professor of epidemiology at Columbia University, <a href="#">learns of a weird outbreak going on in Wuhan</a> , in a conversation with <a href="#">Lu Jiahai</a> , the Director of One Health Research Center of the School of Public Health at Sun Yat-Sen University (Guangzhou).   |   |
| 15 Dec 2019                 | According to the South China Morning Post leak (see 30 Nov 2019), using data compiled before the 13 <sup>th</sup> March 2020, there were at least <b>27</b> confirmed cases with onset date to the 15 <sup>th</sup> Dec. Please note that not all of them would have sought treatment by that time, and/or been recognized as having atypical pneumonia.   |   |
| 24 Dec 2019                 | Foreign students in one of Wuhan universities <a href="#">start taking precautions</a> when moving around the city as they have heard of a particularly bad pneumonia outbreak developing in Wuhan, in the wake of what first seemed like a fierce but seasonal pneumonia outbreak in November.  |   |
| 25 Dec 2019                 | In <a href="#">an article in Freezing Point</a> <sup>22</sup> published the following month, investigative journalist <a href="#">Wang Jiaxing</a> (himself a native of Wuhan who went back to his city on the 18 <sup>th</sup> Jan to report on the outbreak), quotes Dr Lu Xiaohong (吕小红), Director in the Department of Gastroenterology, Wuhan Fifth Hospital:<br>"On December 25, 2019, I heard that medical staff in two hospitals in Wuhan were suspected of contracting viral pneumonia of unknown cause and were quarantined, including medical staff from the respiratory department. I realised then that the situation might not be easy."<br>This shows that medical staff had already been infected by patients, and consequently isolated by the 25 <sup>th</sup> Dec, which should have provided ample proof of human to human infection. Incidentally exactly 2 health care workers infections in 2 hospitals will be <a href="#">later acknowledged for 2019</a> , with diagnosis supposedly 60 days after late Dec onset dates.   |   |
| 26-30 Dec 2019              | According to a WeChat post of 28 <sup>th</sup> Jan 20 which was <a href="#">deleted</a> within a few days <a href="#">by the author</a> but fortunately saved and still available on <a href="#">sina.cn</a> , <b>Vision Medicals</b> ( <a href="#">Huangpu, Guangzhou</a> ) tested sample from a patent taken on 24 <sup>th</sup> Dec and found that it was a Bat coronavirus on the 26 <sup>th</sup> Dec. After having sequenced most of the virus on the 27 <sup>th</sup> , they immediately called the <b>Central Hospital of Wuhan</b> (which sent them the sample) on the 27 <sup>th</sup> to inform them that it was a new coronavirus.<br>Company executives then paid a visit to Wuhan to discuss their findings with <b>local hospital officials</b> and disease control authorities and informed the <b>CDC</b> and <b>Chinese Academy of Sciences</b> .<br>From the WeChat post: "On the 27 <sup>th</sup> and 28 <sup>th</sup> , the leaders of the company also communicated with the hospital and the CDC on the phone. On the 29 <sup>th</sup> and 30 <sup>th</sup> , they also went to Wuhan to report this matter in person with the leaders of the hospital and the CDC, including all our analysis results, and with the Institute of Pathogens of the Academy of Medical Sciences. Everything is under <b>intense, confidential, and rigorous investigation</b> (at this time, the hospital and disease control people already knew that there were many similar patients, and after we communicated the test results, emergency treatment was started, but I didn't know it)." The story was <a href="#">confirmed by Caixin</a> who also checked with a doctor at the Wuhan Central Hospital.<br>On the 27 <sup>th</sup> Dec 19, the Vision Medicals people who were analysing the new coronavirus were discussing the <b>possibility of a lab accident with an 'artificial' virus</b> :<br>"It was also suspected that some artificial virus-related staff were inadvertently infected by accident. After all, the community infection of Brucella some time ago was caused by the incomplete sterilisation of a certain factory (abbreviated 'Bru' in the original WeChat post)" |   |
| 27 Dec 2019                 | Zhang Jixian, director of the Department of Respiratory and Critical Care Medicine at Hubei Provincial Hospital of Integrated Traditional Chinese and Western Medicine <a href="#">found that the chest CT films of a couple and their son</a> showed completely different changes from other viral pneumonias, thinking: "Generally, three people will not get the same disease at the same time, unless it is an infectious disease. ." She reported the situation to the hospital leadership and relevant departments.  |   |
| 29 Dec 2019                 | Epidemiological investigation begins in Wuhan  |   |

<sup>22</sup> [Freezing Point](#) is well known for its occasional positions - in 2006 it was sanctioned for the publication of a key piece on the Boxer Rebellion by Yuan Weishi of Sun Yat-sen University. It was relaunched within a few months but without his star editor, Li Datong, who later would be known for his [opposition to constitutional derives](#) in China.

|             |   |
|-------------|---|
| 30 Dec 2019 | After noticing at around 5:30pm a message from Ai Fen (the head of the EA department of the hospital where he works as an ophthalmologist) reposted by some colleagues, at around 5.42pm Li Wenliang <a href="#">posts a message</a> on his Weibo medical graduates group of about <a href="#">150 members (2004 Wuhan University Clinical Class)</a> <a href="#">about 7 patients at the hospital with a pulmonary infection</a> which returned positive tests for SARS virus. At 6:42pm Li Wenliang posts a new message where is careful to (1) make it clear that the virus is not necessarily SARS and is being identified, (2) alert his graduates group WeChat group that the previous post has been reported, (3) ask people to take precautions in case of human-to-human transmission. The messages are quickly shared, even worldwide.  |
| 30 Dec 2020 | After cases started appearing in hospitals, the <a href="#">Wuhan Municipal Health and Health Commission</a> organised an expert team to investigate and issued two departmental documents: the " <a href="#">Urgent Notice on Reporting the Treatment of Unexplained Pneumonia</a> " and the " <a href="#">Emergency Notice on Doing a Good job in the Treatment of Unexplained Pneumonia</a> ". The two notices were <a href="#">shared on the Internet at 15:22 and 19:00</a> respectively. These documents required respectively to conduct a comprehensive search and retrospective investigation of pneumonia cases related to the South China Seafood Market (by returning a case declaration form by 4pm the same day) and to organise a strong structured effort to handle the situation.<br>The second notice also prevented the release of treatment information without authorization. See <a href="#">link</a> for instance. |
| 30 Dec 2020 | Light disinfection of <a href="#">some stalls' metal curtains</a> in the evening (when the stalls are closed after market hours). That disinfection may actually be routine - it happened several times a week, after closure (around 6 to 7pm). More (non-routine) disinfection of public space (not the inside of stalls) happened the following day in the early morning (~2am), and then in the morning while the market was open.  |
| 31 Dec 2019 | The outbreak becomes known worldwide as Mr Chen's case file and indication of a SARS-like infection hits social media, largely due to the postings of Ai Fen and Li Wenliang from the Wuhan central hospital the day before (30th Dec).<br>After <a href="#">receiving a call at 1:30am</a> on the 31st, Li Wenliang spent 2 hours at the Wuhan Municipal Health Commission where he was asked about his source before being able to go back home at 4am.   |
| 31 Dec 2019 | At 13:38 the Wuhan Municipal Health and Health Commission issued the "Circular on the Current Pneumonia Epidemic in Our City", stating that <a href="#">27 cases have been found</a> and that "so far, <a href="#">no obvious human-to-human transmission</a> has been found in the investigation, and no medical staff infection has been found." (see also <a href="#">Caixin</a> ).  |
| 31 Dec 2019 | China notifies the World Health Organisation (WHO) about the emergence of an unidentified infectious disease. China CDC experts arrived to launch a three-level joint task force. It was agreed that the identified cases were pneumonia of unknown aetiology. (see China-WHO report Annexe D4).<br>Hubei provincial officials, and experts from the main China CDC in Beijing were all in <a href="#">Wuhan working together on the investigation</a> .  |
| 31 Dec 2019 | According to the South China Morning Post leak (see 30 Nov 2019), using data compiled before the 13 <sup>th</sup> March 2020, there were in total at <b>266</b> confirmed cases with onset date in 2019.  |
| 1 Jan 2020  | The <a href="#">Huanan Seafood market is closed. at 8am</a> . See also <a href="#">Beijing News</a> .<br>First environmental samples are collected.   |
| 1 Jan 2020  | A first team of experts from the National Health and Health Commission <a href="#">arrived in Wuhan in the morning</a> .  |
| 1 Jan 2020  | According to the South China Morning Post leak (see 30 Nov 2019), using data compiled before the 13 <sup>th</sup> March 2020, there were in total at <b>381</b> confirmed cases with onset date up to Jan 1 <sup>st</sup> , a jump of 115 from the previous day.  |
| 1 Jan 2020  | <a href="#">BGI tested samples received</a> on Dec 26 (x1) and Dec 29 (x2) and reports the results to the Wuhan Municipal Health Commission on the 1st Jan 2020.  |
| 1 Jan 2020  | After several batches of genome sequence results had been returned to hospitals and submitted to health authorities, an employee of one genomics company received a phone call from an official at the <b>Hubei Provincial Health Commission</b> , ordering the company to stop testing samples from Wuhan related to the new disease and destroy all existing samples. They were told to immediately cease releasing test results and information about the tests, and report any future results to authorities.<br><a href="#">According to Caixin</a> this happened at all gene sequencing companies in Wuhan (and likely not in other parts of China, like <b>Shanghai</b> ). This <a href="#">also happened at the WIV</a> .   |
| 2 Jan 2020  | <b>Wuhan Central Hospital</b> requires medical staff not to discuss the condition publicly, especially through text and pictures, and the condition can only be mentioned orally during shifts.<br>At the same time, due to administrative intervention, the hospital almost stopped "direct online reporting" <a href="http://iolaw.cssn.cn/zt/gzyq/fydt/202005/t20200507_5124529.shtml">http://iolaw.cssn.cn/zt/gzyq/fydt/202005/t20200507_5124529.shtml</a>  |
| 2 Jan 2020  | The Wuhan Institute of Virology <a href="#">fully sequences SARS-CoV-2</a> after it received a sample from Jinyintan Hospital the 30th Dec 2019 and isolated the virus strain on January 5.   |
| 3 Jan 2020  | <b>The National Health Commission</b> , China's top medical authority, <a href="#">issued its own gagging order</a> . Laboratories were told not to release any information and to hand over or destroy the sample.   |
| 3 Jan 2020  | <b>The Wuhan Municipal Public Security Bureau</b> admonished <a href="#">8 doctors</a> who spread information about the epidemic on the Internet (including Li Wenliang, Xie Linka and Liu Wen), and publicised it through CCTV and other public opinion channels.  |
| 3 Jan 2020  | As a result of the initial observation in a few key hospitals of an epi-link with this seafood market, the initial case definition included an epi-link to the market in the Wuhan issued (Green book)<br>Professor Zhang Xiaochun of the Department of Imaging, Zhongnan Hospital of Wuhan University, publicly questioned the reliability of nucleic acid detection for diagnosing new coronary pneumonia, and suggested that CT  |



|               |   |
|---------------|---|
|               | <p>images should be used as the main basis for diagnosis.<br/>This won't be done before the 5th Feb.</p>  |
| 3 Jan 2020    | China answers an official request for information from the WHO (posted 1st Jan) within the required 2-day window.   |
| 3 Jan 2020    | <p>Professor Zhang Yongzhen of Fudan University in Shanghai received biological samples packed in dry ice in metal boxes and shipped by rail from Wuhan Central Hospital.<br/>By January 5, Zhang's team had also identified the new, SARS-like coronavirus by using high-throughput sequencing. The sequence will be released to the world with pressure from Farrar and Holmes on the 10th Jan 20.</p>  |
| 3-7 Jan 2020  | <p>On the 3rd Jan 2020, the first complete genome of the novel <math>\beta</math> genus coronaviruses (2019- nCoVs) <a href="#">was identified in samples</a> of bronchoalveolar lavage fluid (BALF) from a patient from Wuhan by scientists of the National Institute of Viral Disease Control and Prevention in Beijing (IVDC, part of the CDC) through a combination of Sanger sequencing, Illumina sequencing, and nanopore sequencing.<br/>On the 7th Jan Song Jingdong (宋敬东), associate researcher and a student of Hong Tao (who was implicated in the 2004 SARS leaks at the IVDC, with 4 primary cases including 2 covered-up), takes the <a href="#">first electron microscope picture</a> of SARS-CoV-2.<br/>Sometime in Jan 2020 or Feb 2020 an researcher <a href="#">gets infected with SARS CoV-2</a> during lab work at the IVDC. The case was never officially disclosed.</p>  |
| 4 Jan 2020    | The head of the University of Hong Kong's Centre for Infectious Diseases, Ho Pak-leung, warns that the city should implement the strictest possible monitoring system for the new pneumonia, as it is <a href="#">highly possible that the illness is spreading from human to human</a> .   |
| 5 Jan 2020    | <p>The Wuhan Municipal Health Commission notified that <b>59</b> cases of diagnosed viral pneumonia were in line with unknown causes; and re-emphasized that the preliminary investigation showed that no obvious human transmission was found and no medical personnel were infected. [As Daszak <a href="#">would soon point out</a>, it was actually difficult to imagine how there could be 59 primary cases, all infected directly by animals].<br/>These 59 are likely the (41 + 18) of the Lancet study, with 18 clinically diagnosed but no showing any viral load by RT-PCR (which would have difficulties detecting any case 2 weeks after onset - the blood samples were taken AFTER transfer to the designate hospital on 31st Dec 2019 - typically 2 to 5 days after transfer).<br/>- Serological detection was not done to look for 2019-nCoV antibody rises in 18 patients with undetectable viral RNA. kinetics of viral load and antibody titres were not available.<br/>- 59 suspected cases with fever and dry cough were transferred to a designated hospital (Jin Yin-tan Hospital ) starting from Dec 31, 2019 (59-18=41).</p>  |
| 5 Jan 2020    | <p>The Jiangnan District Center for Disease Control and Prevention required the completion of hospital and district consultations before reporting;<br/>The Health Committee requires that the report can only be reported after the approval of the provincial and municipal health and health committees.<br/><a href="http://iolaw.cssn.cn/zt/gzyq/fydt/202005/t20200507_5124529.shtml">http://iolaw.cssn.cn/zt/gzyq/fydt/202005/t20200507_5124529.shtml</a></p>   |
| 5 Jan 2010    | <p>After the CDC (NIVDC) on the 3rd Jan, the WIV on the 2nd and BGI and Vision Medicals respectively on the 30th and 27th Dec, the Chinese of Medical Sciences (which was in contact with Vision Medicals since the 27th Dec) fully sequenced the virus in the early hours (just after midnight).<br/>The same day the Shanghai Public Clinical Health Center, led by famed virologist Zhang Yongzhen, was the latest to sequence the virus.</p>  |
| 6 Jan 2020    | After Zhang <a href="#">reported his findings of a new coronavirus</a> which he had just sequenced (on the 5th) to the Shanghai Municipal Health Commission as well as <b>China's National Health Commission</b> , warning the new virus was like SARS, and was being transmitted through the respiratory route. This sparked a secondary emergency response within the Chinese Centre for Disease Control and Prevention (CDC) on January 6.   |
| 6-17 Jan 2020 | " <a href="#">Two sessions</a> " (两会) of Wuhan City and Hubei Province were held successively.  |
| 6-17 Jan 2020 | No new cases are published by the Center for Disease Control or the Wuhan Health Commission.  |
| 7 Jan 2020    | <p>In an <a href="#">speech at the Politburo Standing Committee made on the 3rd Feb 2020</a> (and <a href="#">released on the 15th Feb 2020</a>), Mr. Xi mentioned he had "issued demands about the efforts to prevent and control" the coronavirus on the 7th Jan 2020, during a previous meeting of the Politburo Standing Committee, the highest council of the Communist Party, whose sessions are typically cloaked in secrecy.<br/>We should not overdo the session of the Standing Committee of the CPC Central Political Bureau on 7th Jan when Xi Jinping made a request to "to do a good job in epidemic prevention and control." This was just two days after the second-level emergency response was launched within the National Center for Disease Control and Prevention (National CDC). The report of the meeting actually does not mention epidemic prevention and control, according to this source: <a href="https://2newcenturynet.blogspot.com/2020/03/blog-post_3.html">https://2newcenturynet.blogspot.com/2020/03/blog-post_3.html</a>.<br/>Most likely Xi Jinping just mentioned it, but quite possibly with the hope that it could be dealt with quickly and not disturb the Chinese New Year. So effectively it was mentioned just to be better dismissed by Chinese New Year. Not a priority at the time.</p> |
| 8 Jan 2020    | The Wall Street Journal embarrasses China and the WHO <a href="#">by reporting that scientists had identified a new coronavirus</a> in samples from pneumonia patients in Wuhan, while still no official news is yet released by China. Behind the scene the Chinese CDC was <a href="#">allegedly positioned</a> to write the first paper announcing while all other labs were bound by the gag order.   |

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|               | The next day <a href="#">international pressure</a> starts building up on China.  |
| 8-18 Jan 2020 | The second group of experts from the National Health Commission arrived in Wuhan, after the first group of experts made their way to Wuhan on the morning of the 31st Dec 19.<br>During the period from January 8 to 18, 2020, when the <a href="#">second group</a> of experts was working in Wuhan, almost all relevant departments of the medical system in Wuhan were <a href="#">aware of the fact that medical staff were infected and "human-to-human"</a> transmission occurred, but no one reported to the expert group.   |
| 9 Jan 2020    | The "Wuhan Viral Pneumonia Pathogen Preliminary Evaluation Expert Group" , an expert team led by the CDC, made a preliminary conclusion that the disease was caused by a new strain of coronavirus, according to <a href="#">Chinese state broadcaster CCTV</a> .<br>Xu Jianguo (徐建国), of the Chinese Academy of Engineering, and <a href="#">leader of the expert team tasked with evaluating test results on the Wuhan pneumonia</a> , said on January 9 that that the preliminary conclusion they have arrived at was that the pathogen that had infected several people in Wuhan took the form of a coronavirus.<br>Chinese media <a href="#">start mentioning the outbreak</a> .   |
| 10 Jan 2020   | The Chinese Center for Disease Control and Prevention developed a diagnostic kit. The new coronavirus pneumonia virus can be detected by the kit and RT-PCR technology, so the "confirmed case" standard was added, requiring "positive virus test".<br>However getting test kits was really difficult and they had a high false negative rate.   |
| 10 Jan 2020   | Science <a href="#">published an article</a> announcing the findings of the Expert Group of the previous day.<br>At the same time the article raises doubt as to the absence of human-to-human transmission, given the high number of cases recorded so far (at least 59). quoting Daszak:<br>"I don't understand how you can get so many cases without human-to-human transmission," Daszak says. "This is something I have a red flag on."  |
| 11 Jan 2020   | The Wuhan Municipal Health Commission <a href="#">reduces the number of cases from 59 to 41</a> . <sup>23</sup><br>59 was 41 confirmed by RT-PCR + 18 suspected but without viral load.<br>Basically the suspected are not included any more - which may reject perfectly valid cases which were simply tested with RT-PCR 2 weeks plus after onset when viral load becomes difficult to detect.<br>Chinese authorities justified this by saying that <a href="#">genomic test kits rejected all these 18</a> .<br>The <a href="#">update from the National Health Commission</a> (NHC) reiterated that 'There have been no new cases since January 3. For the time being, the Mainland's investigation has neither identified any infection of healthcare workers nor definite evidence of human-to-human transmission'.   |
| 11 Jan 2020   | Farrar and Holmes force the release of the virus sequence to the world.   |
| 13 Jan 2020   | First case outside China, in Thailand, <a href="#">raising the likelihood of human transmission for international observers</a> .   |
| 14 Jan 2020   | The head of China's National Health Commission, Ma Xiaowei, laid out a grim assessment of the situation on Jan. 14 in a <a href="#">confidential teleconference with provincial health officials</a> . A memo states that the teleconference was held to convey instructions on the coronavirus from President Xi Jinping, Premier Li Keqiang and Vice Premier Sun Chunlan, but does not specify what those instructions were. "The epidemic situation is still severe and complex, the most severe challenge since SARS in 2003, and is likely to develop into a major public health event," the memo cites Ma as saying. Under a section titled "sober understanding of the situation," the memo said that "clustered cases suggest that human-to-human transmission is possible." It singled out the case in Thailand, saying that the situation had "changed significantly" because of the possible spread of the virus abroad.<br>See also <a href="https://www.cnbc.com/2020/04/15/china-didnt-warn-public-of-likely-pandemic-for-6-key-days.html">https://www.cnbc.com/2020/04/15/china-didnt-warn-public-of-likely-pandemic-for-6-key-days.html</a> |
| 15 Jan 2020   | Now two weeks have passed since the closure of the market. Any new case must be due to human-to-human infection due to max 2 weeks incubation period (estimated at the time).<br>"We have reached the latest understanding that <a href="#">the risk of sustained human-to-human transmission is low</a> ," Li Qun, the head of the China CDC's emergency center, told Chinese state television on Jan. 15. That was the same day Li was appointed leader of a group preparing emergency plans for the level one response, a CDC notice shows.  |
| 15 Jan 2020   | <a href="#">500 hospital staff had been confirmed infected by mid-January</a> , with a further 600 suspected, according to multiple sources and a slide from a CDC presentation. See also <a href="#">this source</a> .   |
| 16 Jan 2020   | Institut Pasteur Shanghai and some Shanghai labs sent an analysis in the form of a letter to the journal 'Science China - Life Sciences'. The analysis concludes that ' <b>To our surprise, despite replacing four out of five important interface amino acid residues, the Wuhan CoV S-protein was found to have a significant binding affinity to human ACE2</b> ' and that ' <b>The Wuhan CoV poses a significant public health risk for human transmission via the S- protein-ACE2 binding pathway</b> '. See <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7089049/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7089049/</a> .<br>This was before h2h transmission was properly acknowledged and while the official count of confirmed cases has not increased since the 5th Jan (it was actually decreased on the 11th Jan. The letter is published online on the 21st Jan 2020.  |
| 16 Jan 2020   | The National Health and Medical Commission released the <a href="#">first</a> version of the "Diagnosis and Treatment Plan for Novel Coronavirus Infected Pneumonia (Trial)", and the implementation of the "Trial Diagnosis and Treatment Plan" and "Inclusion and Exclusions Standards" of the 3rd Jan with their epi-link to the market were stopped   |

<sup>23</sup> See [https://web.archive.org/web/\\*/http://wjw.wuhan.gov.cn/front/web/showDetail/202001\\*](https://web.archive.org/web/*/http://wjw.wuhan.gov.cn/front/web/showDetail/202001*) for the archived updates for January 2020 from the Wuhan Health Commission.



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| 17 Jan 2020 | <p>On the last day of the 'two-sessions' of the party and more than two weeks after closure of the market, a total of 4 new patients were diagnosed for the first time since the 5th Jan 20.</p> <p>This is the very first <b>change up</b> since the 5th Jan 2020 (there was a <b>reduction</b> from 59 to 41 on the 11th Jan). In a release that will long be remembered, the <a href="#">Wuhan Municipal Health Commission stated</a>:<br/>         "An analysis of the epidemiological data of new coronavirus-infected pneumonia cases released in the previous period found that some cases have no history of exposure to the South China Seafood Wholesale Market. On the basis of standardising pre-examination and triage and fever diagnosis, the optimised detection kit was used to sample and monitor unexplained pneumonia cases isolated from fever diagnosis and treatment in the city, and 17 new coronavirus nucleic acid positive cases were detected".</p> |
| 17 Jan 2020 | <p>Yuan Guoyong, a member of the high-level expert group of the National Health and Health Commission, previously discovered a family aggregation case that returned from Wuhan to Shenzhen. One of the patients who had no history of Wuhan travel was also tested positive, so he inferred that the new coronavirus pneumonia can spread among people. On January 17, he notified Gao Fu, director of the Chinese Center for Disease Control and Guangdong Center for Disease Control <a href="#">through a written report</a>, and disclosed this information to other expert group members.</p>   |
| 18 Jan 2020 | <p>On the evening of January 18, 2020, the third group of experts from the National Health Commission led by Academician Zhong Nanshan rushed to Wuhan.</p>   |
| 18 Jan 2020 | <p>The Wuhan health commission resumed public notices about the outbreak, announcing that in the 24 hours of January 16, four new cases of the coronavirus had been discovered.</p>   |
| 18 Jan 2020 | <p>Wuhan's Baibuting district held its <a href="#">annual mass banquet</a>. On the 20th anniversary of the event, the organisers attempted to break a world record for the largest number of dishes served. Long tables in 10 locations were laid out with a total of 13,986 dishes, some bearing patriotic names such as Motherland in My Heart (cucumber and ham), and One Belt One Road (vegetable salad). 10,000 families were present at the banquet. At the same time Wuhan Culture and Tourism Bureau distributed <a href="#">200,000 local tourist activity vouchers</a>.</p>   |
| 19 Jan 2020 | <p>In the early morning of January 19, Wuhan City issued a notice saying that 17 patients had been found newly infected with the virus on January 17, raising the total number of confirmed cases to 62 (41 + 4 + 17). This is not 1/10 of the 757 confirmed cases to Jan 10 (onset date) later published by the CDC (17th Feb).</p>  |
| 19 Jan 2020 | <p>136 additional new cases were diagnosed as the epi-link to the market was no longer required (since 16th Jan), and cases were subsequently found in multiple hospitals and clinics across Wuhan.</p>   |
| 20 Jan 2020 | <p>Wuhan Culture and Tourism Bureau distributes <a href="#">200,000 local tourist activity vouchers</a>. News of cultural tourism activities during the Spring Festival <a href="#">was not only on the front page of Wuhan Evening News</a> on January 20, but also with a news guide below "No need to wear N95 masks to general public places" (meaning that ordinary one will do, as N95 were really needed for medical professionals). This was the acme of the <a href="#">gulf between Wuhan local authorities</a> playing the situation down and the rest of China reporting in a much more critical way.</p>   |
| 20 Jan 2020 | <p>For the first time, Wuhan health commission's announcement <a href="#">removed previous statements</a> that "limited person-to-person transmission cannot be ruled out," and that "the risk of continuous person-to-person transmission is relatively low."<br/>         Wang Guangfa, a member of the expert group, proved "human-to-human transmission" with personal infection. He became ill after returning to Beijing on January 16 and was diagnosed on January 20. In an interview in Beijing on the same day Zhong Nanshan affirmed the "human-to-human transmission" of the new crown pneumonia, and confirmed that medical staff were infected.</p>   |
| 20 Jan 2020 | <p>The China CDC would retrospectively report in their 'CDC Weekly' <a href="#">publication dated 17th Feb</a> that there had been 6,070 confirmed cases and 410+ deaths to the 20th Jan 2020.</p>  |
| 20 Jan 2020 | <p>6 days after the internal grim assessment of the situation during a confidential teleconference, <a href="#">President Xi Jinping warned the public on the 20th Jan</a>.</p>   |
| 20 Jan 2020 | <p>Shi Zheng-Li paper announcing the discovery of SARS-CoV-2, with sequencing and isolation at the WIV is sent for publication in Nature. It is published on the 3rd February 2020 (<a href="https://www.nature.com/articles/s41586-020-2012-7#article-info">https://www.nature.com/articles/s41586-020-2012-7#article-info</a>) but was first published as a preprint on the 23rd Jan 2020 (<a href="https://www.biorxiv.org/content/10.1101/2020.01.22.914952v2.article-info">https://www.biorxiv.org/content/10.1101/2020.01.22.914952v2.article-info</a>)<br/>         See also 25 Jan 2020 below</p>   |
| 21 Jan 2020 | <p>"The 2020 Hubei Province Spring Festival troupe theatrical performance was successfully held in Wuhan Hongshan Auditorium. The <b>Hubei Provincial Party Committee</b> The secretary, governor and other leaders attended the performance together with representatives from all walks of life in the province. [---]. More than 40 performers from Hubei Provincial National Song and Dance Troupe participated in many In the performance of this program, <a href="#">the actresses overcame multiple difficulties such as long-distance running, stuffy nose, cold, and physical discomfort, and after taking the stage, they performed with full firepower and performed perfectly when they were sick</a>. It created a festive, cheerful, and progressive festive atmosphere, and the performance was fully appreciated by the provincial leaders."</p>   |
| 22 Jan 2020 | <p>The <b>Central Committee of the Communist Party</b> of China required Hubei Province to implement comprehensive and strict control over the outflow of people.</p>   |
| 23 Jan 2020 | <p>Wuhan goes into lockdown.</p>  |

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| 25 Jan 2020 | A major paper is sent for publication in the English edition of the Chinese Medical Journal. That paper goes into detail of the careful identification and isolation of SARS-CoV-2. This critical paper was only published online on the 11th Feb 2020.<br><a href="https://journals.lww.com/cmj/Fulltext/2020/05050/Identification_of_a_novel_coronavirus_causing.3.aspx">https://journals.lww.com/cmj/Fulltext/2020/05050/Identification_of_a_novel_coronavirus_causing.3.aspx</a>  |
| 3 Feb 2020  | Dr. Zhang, a radiologist at Zhongnan Hospital in central Wuhan who had served on the front lines of SARS in 2003 <a href="#">took to her social messaging account to call for the use of chest X-rays in diagnosing Covid-19</a> , instead of lab tests that were resulting in so <b>many false negatives</b> . She raised the alarm on cross-infection within families, recommending the government make use of hotels and school dormitories to quarantine suspected cases.   |
| 5 Feb 2020  | The <b>National Health and Medical Commission</b> issued the <u>fifth</u> edition of the New Coronary Pneumonia Diagnosis and Treatment Plan, which stipulated that CT images should be used as clinical diagnostic criteria. Until then there was no confirmed case based on CT despite the absence of test kits (often unreliable anyway) in the early days   |
| 11 Feb 2020 | Academician Zhong Nanshan pointed out to the media: Wuhan City lost control of the virus in the early stage, and the work was not done well. The local government and health department should bear some responsibility.  |
| 12 Feb 2020 | 13,332 clinically diagnosed cases <a href="#">were retrospectively reported from Hubei</a> that day. This was the first time China has reported clinically diagnosed cases in addition to laboratory-confirmed cases.<br>Practically that meant many more patients could have a better chance of access to treatment, including hospital beds and quarantine locations as they opened up  |
| 14 Feb 2020 | The China CDC reported in their CDC Weekly publication (published Feb 17) that there had been 104 confirmed patients with onset of symptoms before Dec. 31. In addition, there were also 37 clinically-diagnosed patients in December, and 25 suspected, for a grand total of <b>166</b> .<br>This number, gathered before any in-depth retrospective search for cases and before the first WHO mission to China, is effectively still the official number for 2019 ( <b>174</b> cases released in the China-WHO mission report in Feb 2021).               |
| 21 Feb 2020 | The China CDC releases the <a href="#">Novel Coronavirus Pneumonia Prevention and Control Plan (Fifth Edition)</a>  |
| 3 Mar 2020  | As part of one of the last rounds of market decontamination, <a href="#">a family of 4 is found still living</a> in the dormitory of the market. They had been there for 43 days (so came back around the 20th Jan 2020 before the lockdown). The man in his 60s in the family was Gu Gangsheng, a former manager of the market, and merchants usually call him "Lao Gu". The dormitory where his family lived during the epidemic was located on the second floor of the East District of Huanan Seafood Market. Gu had lived in the dormitory since 2012. |
| 21 Feb 2021 | As part of the China-WHO mission report (first disclosed by CNN two weeks earlier), <b>174</b> confirmed cases for Dec 19 are published. This is essentially the same number as compiled by the Chinese CDC on the 14th Feb 2020, one year earlier and before any in-depth retrospective investigation.   |



### #1. Shotgun Metagenomics

The technology used by Vision Medicals for quickly screening for pathogens is called shotgun metagenomics, and is an application of metagenomics New Generation Sequencing (mNGS). The exact application of shotgun metagenomics developed by Vision Medicals was first marketed as [IDSeq™](#) around August 2019.

Here are some good articles co-authored or with contributions by Vision Medicals that explain the mNGS detection process and its place in the diagnostic landscape:

- 'mNGS in clinical microbiology laboratories: on the road to maturity' (Oct 2019): <https://www.tandfonline.com/doi/abs/10.1080/1040841X.2019.1681933>
- 'Multicenter assessment of shotgun metagenomics for pathogen detection' (Oct 2021): <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8608867/>
- 'Development and evaluation of a rapid CRISPR-based diagnostic for COVID-19' (Aug 20), for a comparison of mNGS, RT-PCR and CRISPR-based diagnostics for COVID-19: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7451577/>

### #2. NODE\_1\_length\_16579\_cov\_266.242859:

This is the name of a contig in SPAdes convention which was thus the software used for the assembly of the raw reads  
16579 is the contig length (a partial sequence of the virus obtained by automatically merging the overlapping short reads)  
Cov means coverage, 266.242859 is the mean coverage (the number of reads containing the Kmer with K the last one used for filtering the Bruijn graph)

### #3. On the two sequencing runs:

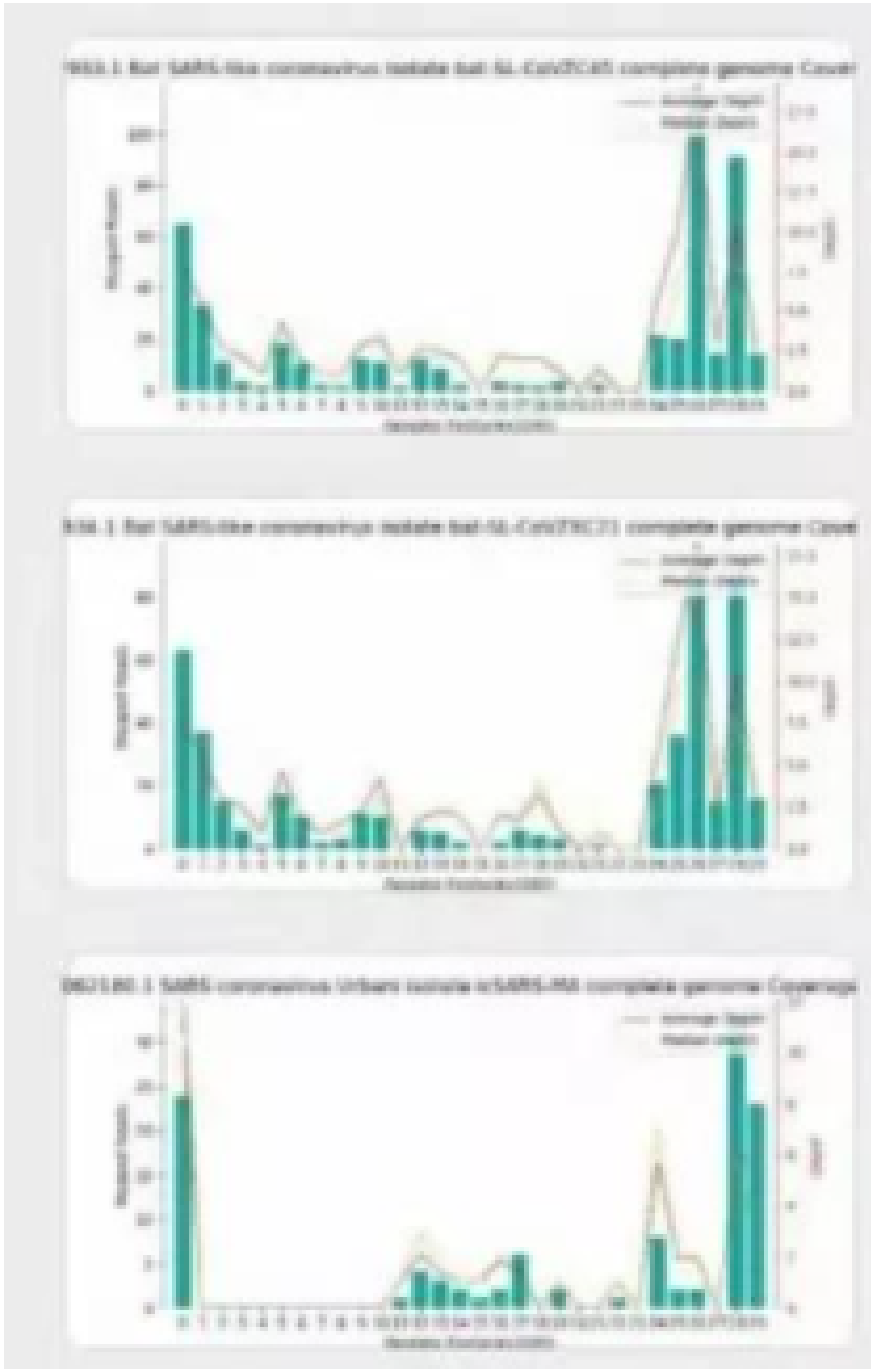
"Later, in-depth analysis was carried out from the gene level (orf1ab, S, N and other genes), and there was no significant discovery, mainly because the number of detected sequences was small, the coverage rate was too low, and they were all incomplete genes. Nothing"

"Retesting of complementary data for analysis was proposed at noon. Retesting allows for technical reproducibility validation, avoiding false positives due to contamination by some unknown factors, ensuring that the sample does have the pathogen, and additionally allows for more data to be analysed, such as the ability to assemble a complete genome, with more reliable analysis results and more in-depth analysis that can be done."

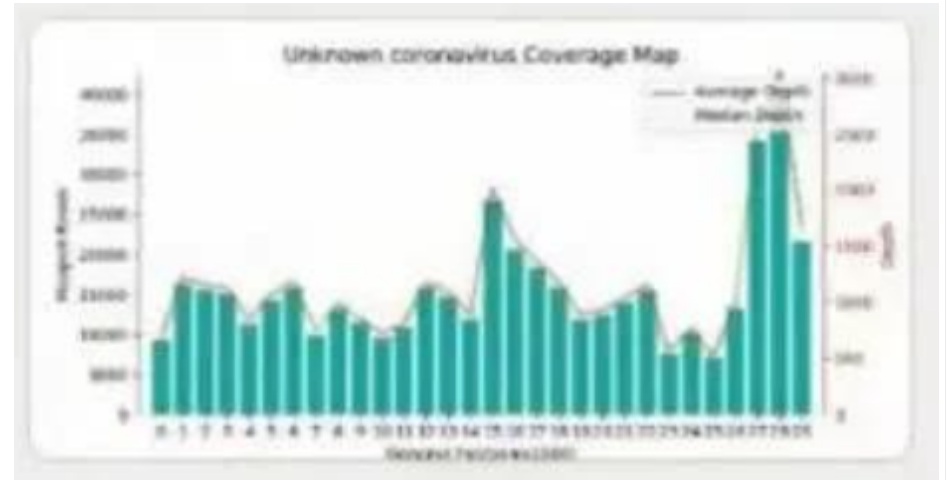
**"The next day (2019.12.27)**, after the data came out early in the morning, the assembly analysis was carried out quickly, and a nearly complete genome sequence was finally assembled. The data was also shared with other in-depth analyses of pathogens by the Chinese Academy of Medical Sciences. This time, the number of reads has increased from more than 500 to more than 470,000!"

Clear indication that there was a 2nd sequencing run (during the night between 26th December and 27th December) probably on a better machine. The first sequencing produced enough reads to indicate the presence of a new sarbecovirus but not enough to obtain a near complete genome, in contrast to the second run that was of high quality.

Bad genome coverage in the 1st sequencing run (x-axis is the genome coordinate, y-axis is the number of short reads mapping to it)



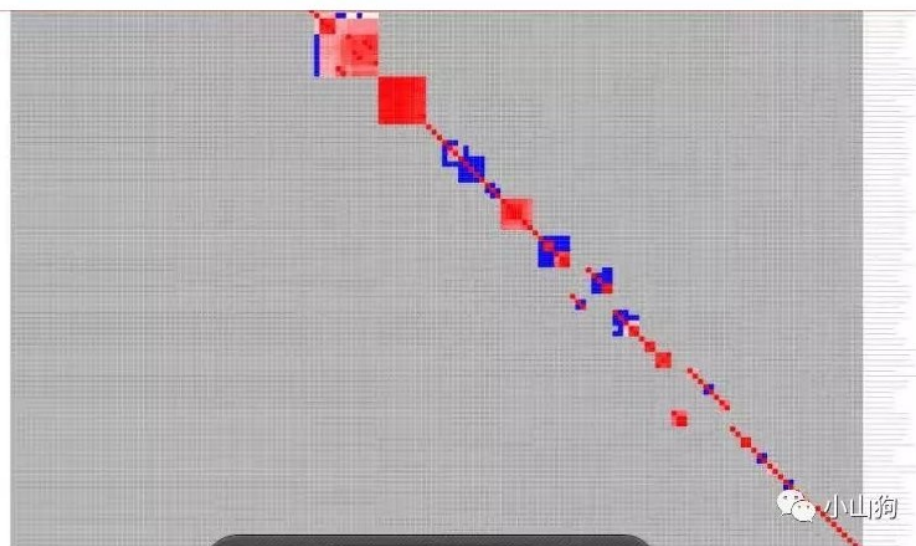
Very good coverage in the 2nd sequencing run



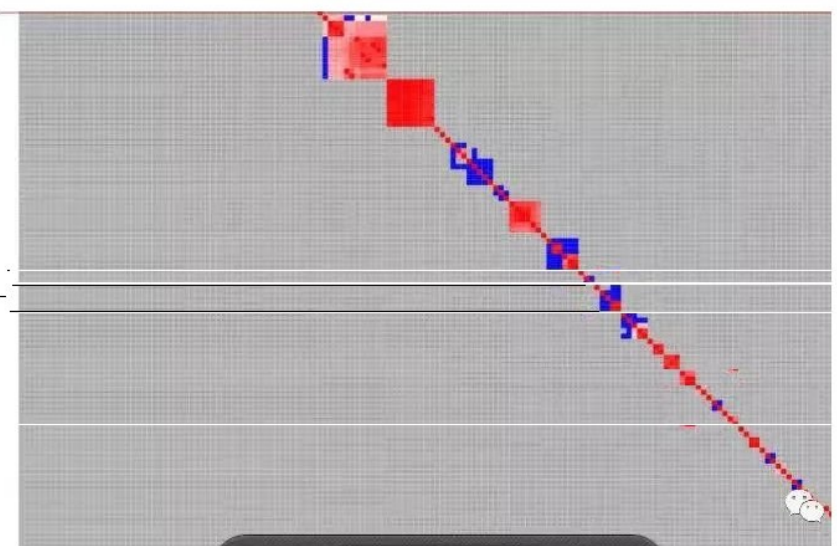
#### #4. Some issues with the plots

There are several pairwise similarity plots (of a fasta with 150 coronaviruses and the new sarbecovirus added). They look strange because they are not symmetric. For some unclear reason some rows are switched (not the same ordering as the columns) moving a few rows restores the symmetry which is what we expect for a pairwise similarity plot (image on the right produced by DRASTIC).

Original, some rows are switched making it non symmetric



Exchanging a few rows repairs the plot which is now a genuine pairwise similarity plot

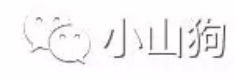
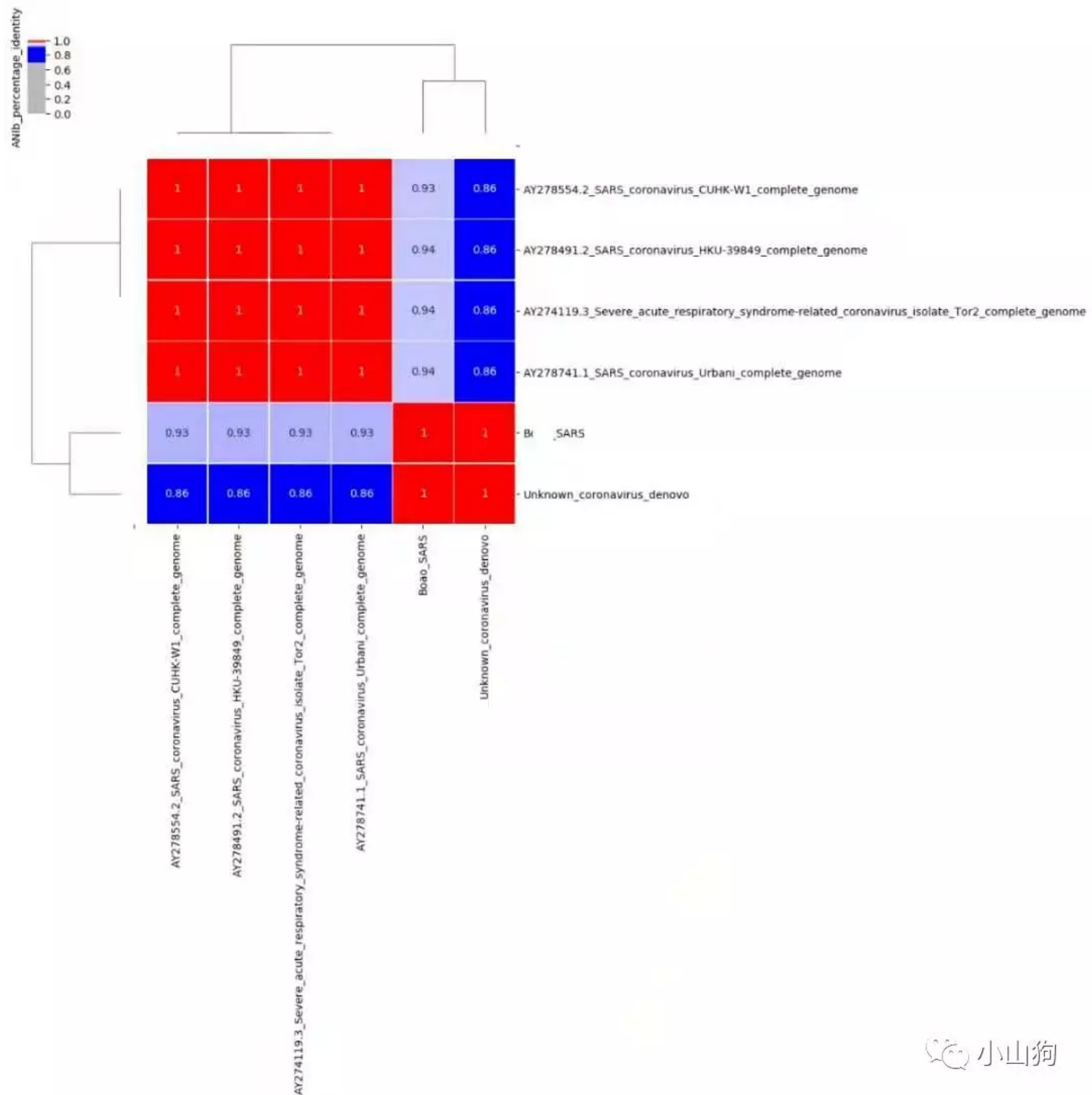




## #5. Comparison to the SARS virus sequence from Boao lab in Beijing:

We can see on the plot below that the new coronavirus obtained by Vision Medicals is near identical to another called Boao\_SARS [name partly blurred on image, but only on vertical line].

This refers to Beijing Boao medical laboratory, the one that sequenced the samples from the 41 year-old accountant whose whose (incorrect) "SARS" diagnostic leaked on wechat on the 30<sup>th</sup> Dec, becoming viral during the night as the whistle-giver (Ai Fen) and whistle blower (Li Wenliang) story.



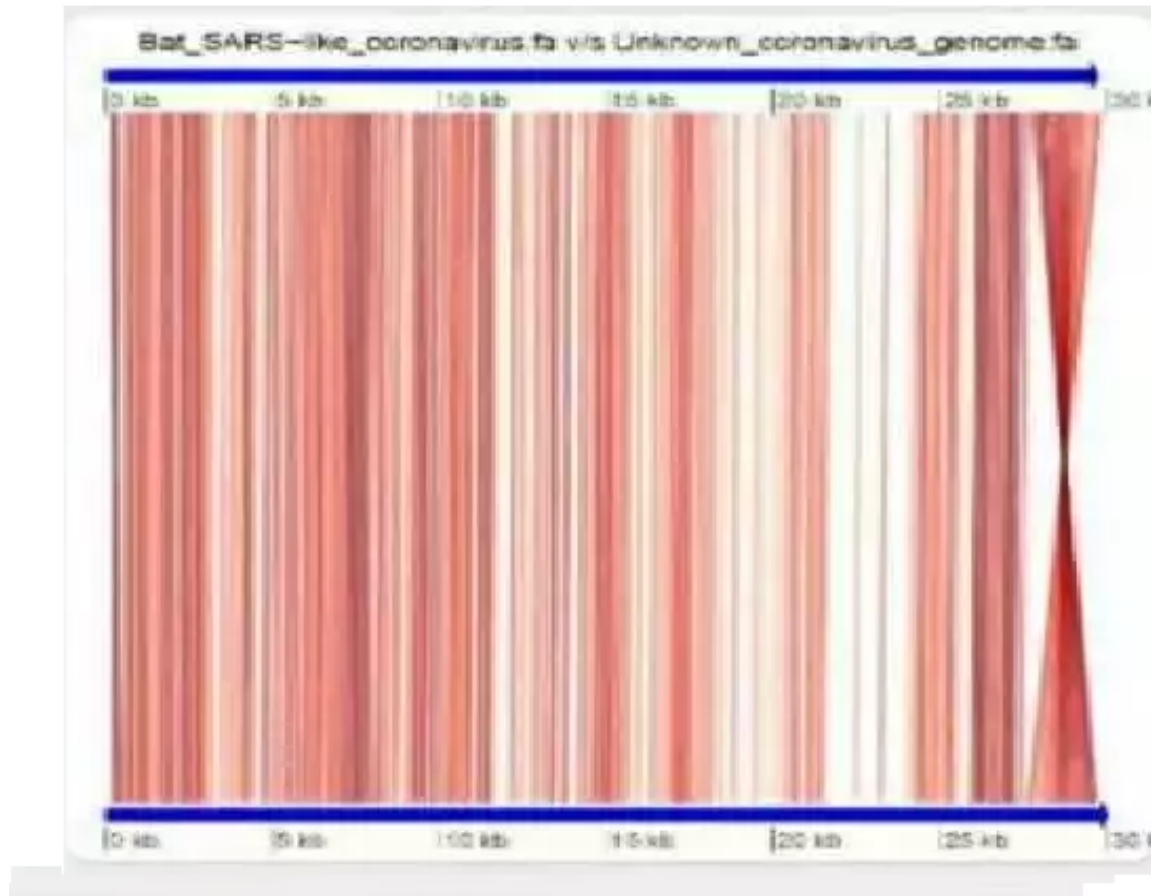
That patient lived in the dense residential district closest to the WIV new site in the south of Wuhan and after he transferred to the Wuhan Central Hospital on the other side of the river to the emergency department of Ai Fen where his uncle/aunt worked, as he was not improving in his local hospital.

As the Vision Medicals employee explains in her blog, she received that new sample in the early hours of the 30<sup>th</sup> Dec from some friend at Boao: "In the middle of the night on the 30<sup>th</sup>, I got the sequence from a friend's business for analysis."

Source Caixin report <https://web.archive.org/web/20200227094018/http://china.caixin.com/2020-02-26/101520972.html>

## #6. Inverted last contig:

In this plot the author merged the contig and plotted the identity to Bat SLCoV-ZC45 (red for higher identity) which showed that the last contig was inverted (minus sense, reverse complement). The simplot was added by DRASTIC for comparison



**Simplot - SARS-CoV-2 vs ZC45**

