The story of COVID-19 – chapter 8

Open questions to the Pasteur Institute, France.

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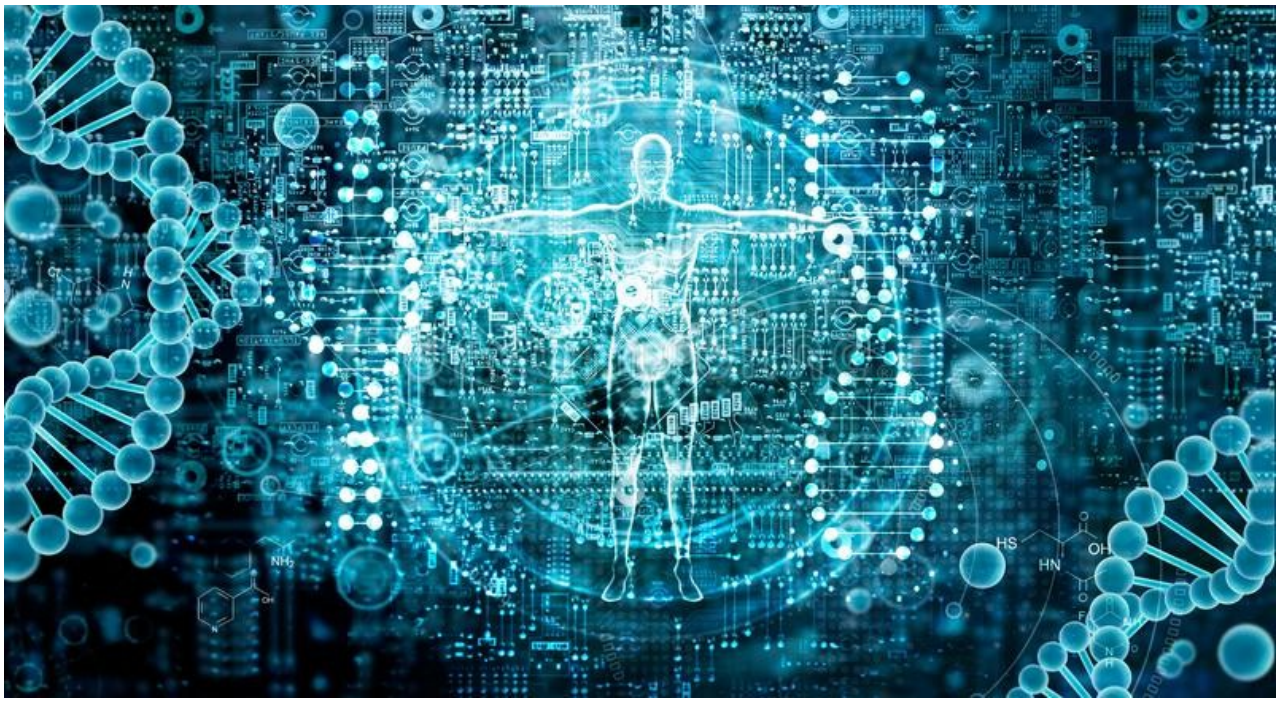

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Part 3. Li-Meng Yan in the spotlights with embarrassing questions to some world-renowned scientists and to expert virologists of the Pasteur Institute

Summary for the hurried reader : in this part 3 of chapter 8, we have deepened the initial work of Li-Meng Yan to demonstrate that she is indisputably right on two crucial issues that demonstrate the artificiality of SARS-Cov2. Firstly, we show that the three viruses : SARS-Cov2 (human), RaTG13 (bat) and Pan-Cov-GD (Pangolin-Cov-2020), supposedly from pangolin, share both the EcoRI and BsTEII restriction enzyme sites flanking the receptor binding motif (RBM) of their spike (S) protein. We show that at the end of 2019, the statistics on SARS-Like coronaviruses deposited in Genbank allowed for estimating the odds that this happens simultaneously, in 3 a priori unrelated natural viruses, as about 1 chance in 1.7 billion. Thus, SARS-Cov2 and Pan-Cov-GD are directly related to RaTG13, a virus kept since 2013 at the Wuhan Institute of Virology (WIV). Secondly, comparing the S protein ratio of synonymous versus non-synonymous mutations between the RaTG13/SARS-Cov2 supposed bat-to-human species crossing

pair with the natural RsSHC014/SARS-Cov and Rs3367/SARS-Cov bat-to-human pairs, we demonstrate further the non-natural relationship between SARS-Cov2 and its closest parent RaTG13, pointing to a laboratory manipulation.

Is Li-Meng Yan a whistle blower, a political refugee or a double-agent ?

Let's see now what Li-Meng Yan, the young post-doctoral researcher from Hong-Kong exiled in USA since April 28, tells us about the receptor binding motif (RBM) in the spike protein of SARS-Cov2. She landed on an American airport in California pretending to the immigration officers that the SARS-Cov2 virus was not of natural origin but man-made. She affirmed it was artificially elaborated from two viruses ZC45 and ZXC21 issued from the Chinese military research. She was very assertive claiming she detained proofs of that. The story was reported in the press and televisual media in USA. In France, the press has insinuated that she was close to the President Trump administration. A bad-faith article published in Libération, a large audience newspaper, brushed with prejudice the portrait of Li-Meng Yan as “a self-proclaimed whistle blower”. However, some other articles such as that of the site profession-gendarme.com, took seriously the possibility of a virus manipulated at the Wuhan Institute of Virology (WIV) in the Hubeï province of China mainland. According to New Tang Dynasty (NTD), a pro Trump-administration alternative TV-channel broadcasting information on China, the mother of Li-Meng Yan was arrested in China.

Being considered that the press declarations of Li-Meng Yan can be regarded as being “enthusiastically” convoluted with some conspiracy theory, we sketch a rapid portrait of her that may look unfair but is necessary to summarize the criticisms against her that are opinion driven prejudices rather than based on science.

The way the “dissent” of Li-Meng Yan was presented to the public reminds us of the scientist heroes fleeing the Warsaw pact countries during the cold war era. An authorized study travel to a conference was the opportunity for them to make shattering declarations and find refuge in the West. She said the pressure exerted has forced her to leave Hong Kong. Let's recall that Hong Kong has become a special administrative region of the People's Republic of China since its handover to China by the United Kingdom in 1997. The question of the circumstances of her departure from Hong Kong in April 2020, during the first epidemic pic in USA, does not raise politically because only the restrictions due to Covid-19 could have prevented her from traveling, the special political status of Hong Kong authorizing it. This makes her quality of political refugee somewhat relative. But, we must admit that she is very brave when she affirms strongly that : “We can see immediately who does not want to hear the hypothesis of a manipulated virus and it tells a lot on who we are dealing with...”.

She acted probably in good faith, rebelling against the widespread scientific omerta and the soothing statements of many interviewed virologists such as those issued by the Pasteur Institute of France. If we confront the facts, in the light of the arm-wrestling match between USA and China, one can ask oneself whether there wasn't a mind manipulation or at least an encouragement to Li-Meng Yan from politicized contacts in the Chinese diaspora in the USA. These two dominating nations are equally guilty in terms of gain-of-function (GOF) research on viruses, although China seems to be now largely ahead of USA, not technically speaking, but at the level of what is commonly called “the psychology of no-limit”. In brief, what Li-Meng Yan says seems to be inspired more with intuition and some politically recuperated sincerity than just a will of misinforming the public with a savvy mixing of true and false arguments. For instance, we can ask ourselves whether her determination in affirming that SARS-Cov2 was fabricated based on the ZC45 military virus would not, in fine, distract the international attention away from the laboratory of Shi Zheng Li at the Wuhan Institute of Virology (WIV), where extreme GOF experiments have been carried out on bat coronaviruses. In any case, as we will show it, she shows strong determination in maintaining her shattering declarations with intelligence despite her relatively modest scientific curriculum. Her seditious talk against the mandatory single way of thinking, imposed by the international oligarchy, has earned her to have her twitter account suspended.

But what is out-mostly interesting with Li-Meng Yan is that we are not dealing with a prominent scholar like in the soviet era of the cold war. She has just terminated her studies with a MD degree (Medical Doctorate) of the School of Public Health at the University of Hong-Kong. She has also pursued a thesis in virology at the WHO Collaborating Centre for Infectious Disease and Epidemiology affiliated to the same university. Her scientific production in terms of publications is freely accessible on PubMed, the NCBI internet site where most published research works are referenced. We can find that since 2012, the year of her first publication, she published 7 articles of which only 2 as first authors and 3 as second authors. From that point of view, she is just a regular student, freshly graduated and without post-doctoral training. Therefore, she cannot be considered a confirmed researcher.

Elements that she considers as pieces of evidence of the manipulated origin of SARS-Cov2 are exposed in two freely written articles. Although they have not been peer reviewed these texts present a scientific character; she names them “reports” and signs them as first author. They are accessible online on the site of the association Rule of Law Society & Rule of Law Foundation based in New York. Other persons, that Li-Meng Yan calls “her team”, are present as coauthors. They are all Chinese-American members of the same association and they apparently own Ph.D. titles although it is impossible to determine their real university affiliations. The Law Society & Rule of Law Foundation is an American political association whose goal is to promote democracy in China, or at least

launch alerts on its violations of human rights. Without being too harsh, we must recognize there an instrument of political propaganda just as the NTD TV-channel. However, despite their obvious drawbacks, these alternative media are very useful in palliating information deficiencies in twisted democracies. They sometimes reveal the crude reality of certain problems purposely ignored by the mainstream press and media controlled by private financial interests. For instance, during the last presidential election in USA, the NTD TV-channel was the only televisual media to inform the public on the possibility of a massive electoral fraud by manipulation of the voting machines,.

The first report of Li-Meng Yan was semi-officially reviewed by a panel of experts of the Massachusetts Institut of Technolgy (MIT). It was composed of prominent scientists such as the renowned Professor Gallo (a world expert in virology). The outcome was negative as the panel has rejected the arguments of Li-Meng Yan on the ground of “severe methodological defects and errors” in the data provided and their analysis. They concluded their review stating the report of Li-Meng Yan was only disinformation, although it is very unclear how they have scientifically reached this conclusion. However, the result of their pseudo review was propagated in France by the site French China Org which purpose is to develop and maintain a good image of China.

We agree we should not accept disinformation. This is why we are proceeding here to a thorough analysis of the essential elements presented in her reports.

Li-Meng Yan is not such a bad student.

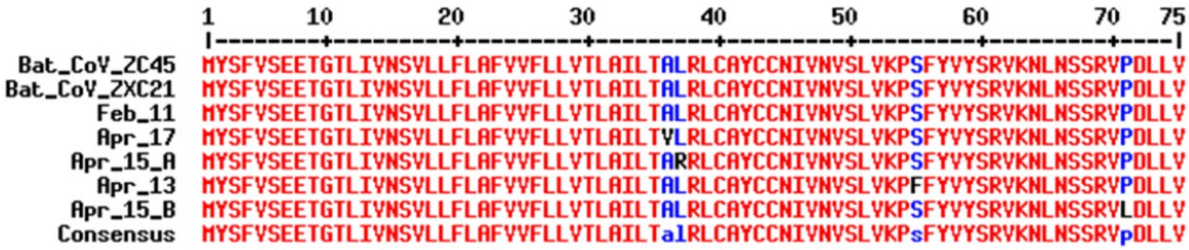
Despite all what we wrote previously, the reports of Li-Meng Yan must be read and understood. Her first report was published on Sept. 14, 2020 on the Zenodo internet site with the title : “Unusual Features of the SARS-CoV-2 Genome Suggesting Sophisticated Laboratory Modification Rather Than Natural Evolution and Delineation of Its Probable Synthetic Route”.

Undoubtedly, this report in the format of a scientific article deserves particular attention. It was accessed more than 1 million times and downloaded 744 000 times, more than enough to make any researcher of renown green with envy. Indeed, usually a scientific article is considered successful when it is cited a few dozens of times and downloaded several hundred times. In very rare cases, an article may be cited thousands of times revealing a planetary scientific interest. Thus, all the scientific articles claiming the natural origin of the SARS-Cov2 virus cannot be compared with the staggering success of the first report of Li-Meng Yan. They are often written in the esoteric jargon belonging to science masking a lack of real insight. Their underlying moto is to state systematically that all

unusual observations related to SARS-Cov2 are necessarily of natural origin, being considered “inconceivable” that it might be otherwise. An elliptic and dogmatic reasoning that reminds us of the pops time. Unfortunately, this dogma has caused scientific ravages all along the Covid-19 pandemics. It has been constantly affirmed implicitly despite the overwhelming reality of gain-of-function (GOF) manipulations of SARS-like coronaviruses during the last 15 years. We agree with Li-Meng Yan when she writes that all scientific journals have censured any contradictory opinion on the natural origin of SARS-Cov2, and that the articles produced in this direction were forced to remain at the stage of preprints.

It would be too cumbersome to proceed to a complete analysis of her report. We present here only the 5 key issues she raises in her assessment of the artificial origin of SARS-Cov2. Since these points are essential we would like to have explanations from expert virologists of the Pasteur Institute. We cordially invite them to answer to this article.

(1) Firstly, Li-Meng Yan draws attention on the fact that the amino acid sequence (aa) of the envelop protein E is 100% conserved between SARS-Cov2, RaTG13, Pan-Cov-GD (Pangolin-Cov-2020; GenBank:MP789) and the two viruses ZC45 and ZXC21. According to her, this is not consistent with the fact that mutations of the E protein were observed during the first months of the pandemics. Indeed, this may seem particularly strange since an absolute 100% conservation of protein E may not be necessary to preserve its function. She writes that it is all the more true since no other known coronavirus shares 100% of aa identity with the protein E of ZC45 and ZXC21.



It is true that the E protein seems to be 100% or quasi 100% conserved in coronaviruses that are related. For instance, Rs3367 collected in 2012, the closest parent to SARS-Cov (2003) with 96.7% of overall nucleotide (nt) sequence identity, shares 100% aa identity regarding the E,M,N, and Orf6 proteins, although 9 years of evolution separate them. The virus RsSHC014, collected in 2011, the second closest to SARS-Cov Urbani, with also 96.7% nt identity, shares 98.7% aa identity for protein E, that is to say only 1 aa mutation since E is 76 aa long.

Overall the two viruses, Rs3367 and RsSHC014, share more than 98.5% aa identity with SARS-Cov and 98.9% nt identity between each-other. It is therefore very intriguing to consider that the ZC45 and ZXC21 viruses, quite distant from the SARS-Cov2, with only 88% nt identity, still share a 100% conserved E protein even though the identity at the gene level is only 86.7%. But one thing for sure is that the Pan-Cov-GD and RaTG13 with more than 99% identity at the gene level for their 100% conserved proteins E are indisputably directly related to SARS-Cov2, which is more difficult to assert for ZC45 and ZXC21.

Thus, 3 virus originating from various locations in China maybe abnormally linked in a way that cannot be explained by regular evolutionary science unless they are very closely related. We note that the E protein is an essential factor for the effective propagation of the virus in the epithelial and neuronal cells (propagation in the lungs and the central nervous systems).

Table 1. Nucleotide sequence identity among the whole genome, each gene or region of pangolin-Cov-2020 and other representative coronaviruses against SARS-Cov-2

	Nucleotide sequence identity (%)						
	Whole genome	S	RBD	E	M	N	ORF1ab
Pangolin-CoV-2020	90.32	84.52	86.64	99.11	93.24	96.18	90.36
Bat-CoV-RaTG13	96.18	93.15	86.19	99.56	95.93	96.90	96.52
Bat-CoV-ZXC21	88.04	76.74	67.32	86.67	93.39	91.17	89.12
Bat-CoV-ZC45	88.06	77.14	68.64	86.67	93.39	91.09	89.15
SARS-CoV	79.75	74.05	73.30	94.67	84.92	88.62	80.02

	RdRp	ORF3a	ORF6	ORF7a	ORF7b	ORF8	ORF10
Pangolin-CoV-2020	91.31	93.21	95.70	93.39	91.47	91.82	99.15
Bat-CoV-RaTG13	97.80	96.24	98.39	95.59	99.22	96.99	99.15
Bat-CoV-ZXC21	86.99	88.85	95.16	89.62	95.35	88.53	100.00
Bat-CoV-ZC45	86.70	87.76	95.16	89.31	94.57	88.53	99.15
SARS-CoV	88.58	75.67	76.88	82.65	86.18	52.87	93.16

Source Ping Liu et al. - Plos Pathogens, May 14, 2020

(2) Secondly, she points out rightly that the gene coded by Orf8 corresponds to a function unknown before the pandemics. Some results recently established show that this gene may allow SARS-Cov2 to escape the adaptive immunity of its host by suppressing (down regulating) the activity of the MHC-I major histocompatibility complex, which is an ultra-essential component of the immune system. This certainly helps the virus to prevent antibodies production and thus could contribute to explain its high replication rate. Li-Meng Yan underlines also that normally the Orf8 is only weakly conserved among coronaviruses. The Orf8 protein of the ZC45/ZXC21 pair share 94.2% of identity with the Orf8 protein of SARS-CoV-2

whereas other coronaviruses do not share more than 58% of identity with it. This type of proximity for an accessory protein is highly unusual. It must be noted also the same very high percentage of identity for the Orf8 protein of the viruses RaTG13 (bat) and Pan-Cov-GD (pangolin), which strengthens our certitude of a close relationship between these three viruses. The presence of an accessory gene, not necessary to the virus viability, seems to have had a dramatic impact on the emergence of a world-broad pandemics. Li-Meng Yan suspects that this gene may have been the target of GOF manipulations. Indeed, the progressive loss of the Orf8 gene, via the deletion by mutation of some of its fragments was associated with the intermediate and final phases of the SARS-Cov pandemics in 2002-2004, where the replication capacity of the virus was divided by 20. These spectacular results on the conditions of emergence and ending of an epidemics were known after their publication in Nature on October 11th, 2018.

Table 2. Protein sequence identity among the whole genome, each gene or region of Pangolin-Cov-2020 and other representative coronaviruses against SAR-Cov-2

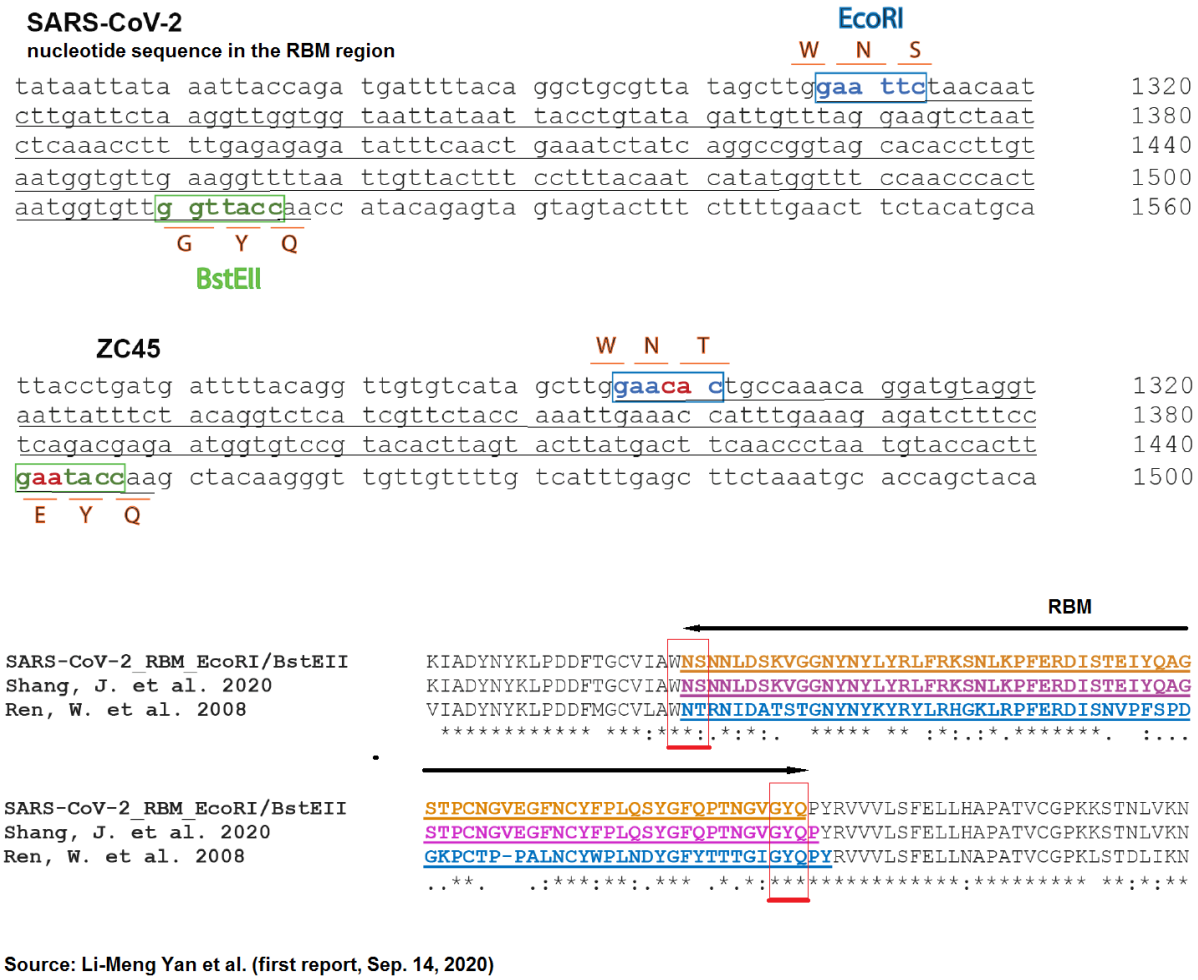
	Amino acid sequence identity (%)						
	Whole genome	**S**	**RBD**	**E**	**M**	**N**	**ORF1ab**
Pangolin-CoV-2020	96.00	90.18	96.80	100.00	98.18	97.83	96.73
Bat-CoV-RaTG13	98.43	97.69	89.56	100.00	99.09	99.04	98.55
Bat-CoV-ZXC21	93.45	79.66	66.35	100.00	98.64	94.10	95.56
Bat-CoV-ZC45	93.59	80.36	66.35	100.00	98.64	94.10	95.71
SARS-CoV	83.39	74.54	70.17	95.92	89.01	90.49	85.57

	RdRp	**ORF3a**	**ORF6**	**ORF7a**	**ORF7b**	**ORF8**	**ORF10**
Pangolin-CoV-2020	99.35	97.05	96.67	97.49	95.24	94.12	97.33
Bat-CoV-RaTG13	99.57	97.79	100.00	97.49	97.65	94.91	97.33
Bat-CoV-ZXC21	95.69	91.66	93.22	87.70	92.77	94.04	100.00
Bat-CoV-ZC45	96.03	90.47	93.22	86.77	92.77	94.04	97.33
SARS-CoV	96.48	68.02	62.68	84.86	84.18	40.00	82.31

Source Ping Liu et al. - Plos Pathogens, May 14, 2020

(3) As for the RBM of SARS-Cov2, she shows that it is flanked with great precision, at both extremities, with distinct restriction-enzyme sites unique in the whole gene S. This allows the easy exchange of the RBM. The two restriction sites, EcoRI and BsTEII, imply 6 nucleotides which makes their occurrence rare (chap. 7 part 1). They occur randomly on average every 4096 nucleotides, but their distribution along a genome is not regular. Over the 29.903 nucleotides of the SARS-Cov2 genome, the EcoRI site appears 9 times and the BstEII site 4 times. They appear uniquely in the ORF (open reading frame) of the S gene of SARS-Cov2 that is 3822 nt long (from position 21563 to 25384) which is statistically consistent.

However, remarkably they are exactly located at positions allowing the RBM manipulation. Thus, microbiologists who would like to work on the properties of the SARS-Cov2 RBM have their task greatly facilitated. It is not every day that Mother Nature offers such a possibility. Let's point out that expert virologists of the Pasteur Institute have declared in early 2020 that if SARS-Cov2 had been genetically manipulated one should find the traces of restriction enzyme sites at some key locations in its genome...



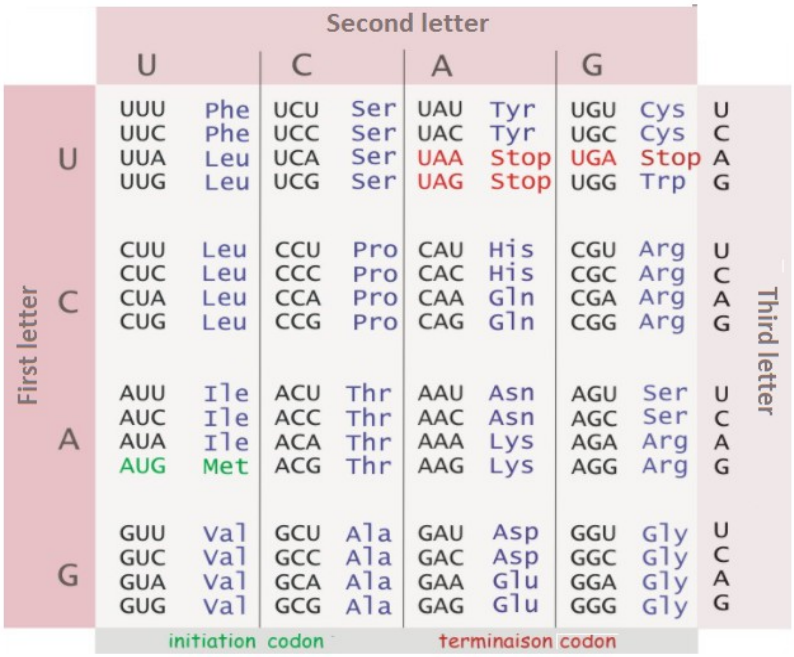
Source: Li-Meng Yan et al. (first report, Sep. 14, 2020)

(4) Li-Meng Yan brings to the fore that the SARS-Cov2 genome has a furin cleavage site at the level of the S protein (precisely at the intersect of the S1 and S2 domains). She raises the fact that this site is absent in “this class of coronavirus”. She meant the evolutionary branch of 2b betacoronaviruses that covers 69 viruses of the SARS type. Her argument was dismissed by Pr Gallo who replied that “this class of coronavirus” is too reduced to allow a conclusion to be drawn. He was implicitly referring only to the two viruses having lead to the SARS syndrome in humans (i.e. SARS-Cov2 and SARS-Cov). But it is obvious that this cleavage site is

absent from this same very precise location in a large number of other betacoronavirus identified as being of the SARS type according to the characteristics of their RBM, such as the bat viruses RsSCH014, Rs3337, RaTG13 and the pangolin viruses Pan-Cov-GX and Pan-Cov-GD that have killed pangolins smuggled in China. The ZC45 and ZXC21 viruses also induced SARS in laboratory rats. None of these coronaviruses possesses a furin cleavage site between the S1 and S2 sub-domains. It also does not exist in the human alpha-coronavirus HCoV229E responsible of common cold symptoms neither in many other coronaviruses. It is however found in the human beta 2a coronaviruses HCov-OC43 and HCov-HKU1 that may cause severe respiratory pathologies.

Therefore, the presence of this site raises a controversy among virologists because, without being essential, it has conferred to SARS-Cov2 a gain of infectious character. Alexandra Henrion-Caude, geneticist and former director of research at CNRS, points out that the insertion of the furin cleavage site is covered by a patent in the domain of virus genetic manipulation. In part 4 of this chapter, we develop this issue with the doctorate thesis that Ariane Bonnin has carried out at the Pasteur Institute of Lille. Her thesis deals with the artificial insertion of the furin cleavage site in the common cold coronavirus HCoV-229E.

(5) Finally, the last point of concern that we select out of the work of Li-Meng Yan is the very strange observation she notes about the Ks/Ka ratio of synonymous versus non-synonymus mutations (also noted dS/dN) between the SARS-Cov2 and RaTG13, its closest parent. Sometimes, the terms silent and non-silent mutations are used but the meaning is the same. One must know that when a genome mutates some point mutations of nucleotides occur that do not translate into a change in the amino-acid sequence of the proteins expressed. For instance, the amino acid glutamine (Q) is coded by two possible codons *caa* and *cag* so that if *caa* is mutated in *cag* then no change takes place at the level of the protein expression. Many amino acids are coded by 2 possible codons, some correspond to 4 possible codons (valine, proline, alanine,...), leucine and serine correspond to 6 possible codons. For this reason, mutations that do not result in a change at the protein level are called synonymous and those inducing changes are called non-synonymous (chapter 6 part 3). Only non-synonymous mutations may generate a modification in the functioning of an organism (here a coronavirus) and, in general, they are more rarely beneficial than deleterious. Being considered that, they are largely less frequent than synonymous mutations that have a neutral effect. However, during species adaptation non-synonymous mutations can become more frequent than the synonymous ones. This adaptive phenomenon is called “positive selection”, the inverse phenomenon called “purifying selection”.



Nota Bene: Uracil (U) for RNA corresponds to Thymine (T) for DNA

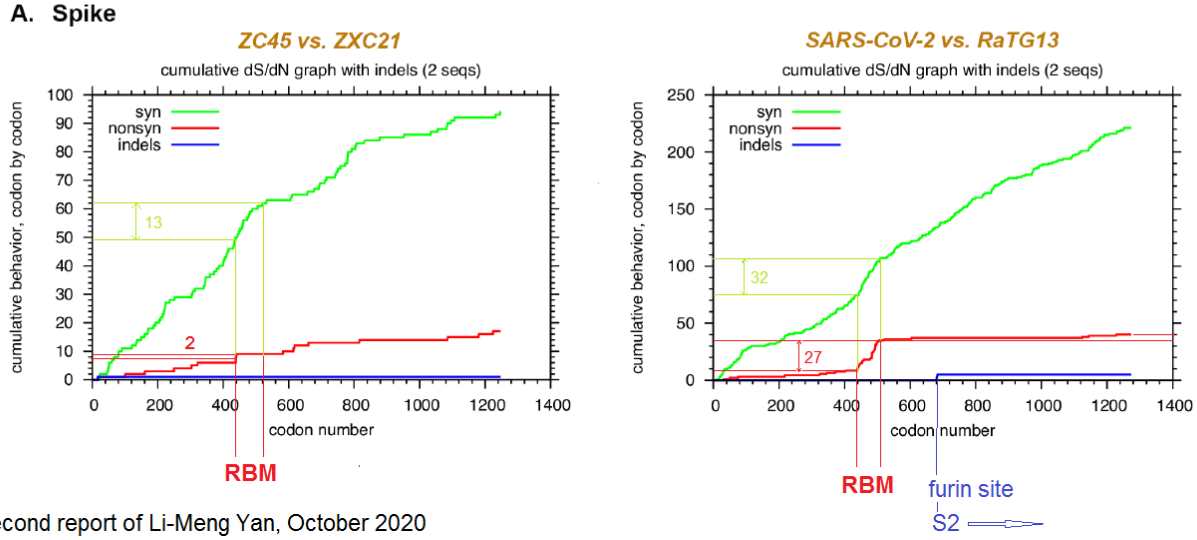
Adapted from: la traduction du code génétique | Trikapalanet Fr par Amélie
https://www.trikapalanet-fr.com/10/le-code-genetique/

Li-Meng Yan establishes a comparison with the twin viruses ZC45 and ZXC21. She calculates that the SARS-Cov2/RaTG13 pair has a ratio Ks/Ka = 44. at the level of the S2 domain (see table and figure below). On the contrary, the overall ratio of the S protein is 5.4, which is according to her consistent with respect to a normal situation between closely related viruses. She is wrong on that point, since as we will see in the next section the overall ratio should be around 1. for a species crossing pair. She affirms that a ratio of 44. for the S2 domain is totally aberrant indicating a manipulation of the virus sequence to obtain an overall ratio around the value 5. We shall note here that Jean-Claude Perez and Pr Luc Montagnier (who received the Nobel prize for the discovery of HIV) made the same observation in their update of their article in Granthaalayah deposited on ResearchGate in April 2020. Nevertheless, this observation was swept away by a panel of expert virologists without any explanation because these people are jealous of their knowledge. Their conclusion echoed in the press, were that the second report of Li-Meng Yan was only a propaganda manisfesto. However, like Montagnier and Perez, Li-Meng Yan has pointed out another critical issue about SARS-Cov2 that we examine in detail in the following section.

Ratio of synonymous/non-synonymous mutations observed in SARS-Cov2 with respect to its closest parent - comparison with the twin viruses ZC45 and ZXC21

Protein	*ZC45 vs. ZXC21*	*SARS-CoV-2 vs. RaTG13*
S2	5.4:1	44.0:1
Spike	5.5:1	5.4:1
Orf1a	2.7:1	5.0:1
Orf1b	7.1:1	10.8:1
N	4.3:1	6.8:1

A. Spike



Second report of Li-Meng Yan, October 2020

A deepened re-investigation of the Ks/Ka ratio of SARS-Cov2 with respect to its closest parent RaTG13 confirms Li-Meng Yan is right on this point

First of all, we shall mention that very high Ks/Ka ratios can be observed (conditions of extreme purifying selection). We have dedicated part3 of chapter 6 to a detailed demonstration of how molecular clocks were informing us on the differential pressure evolution can exert depending on which section of the genome of a virus is considered. For instance, in the poliovirus, that is also a RNA virus, the capside gene has a very high rate of mutations, with a ratio Ks/Ka = 30. This is because the capside proteins share several essential roles in: (1) coating the viral genome with a protective capside, (2) assembling the viral external envelope in a very complex geometrical volume, and (3) triggering cellular penetration. These 3 functions are so perfectly arranged with respect to each-others that only a restricted number of real (non-synonymous) mutations are allowed. Similarly, the study of Lau et al. (2010) has measured that the S (spike) proteins of SARS-like bat coronavirus exhibited a Ks/Ka ratio close to 20 (18.5) due to their evolutionary culmination in this reservoir. In bats, the S protein essential to the virus

survival is optimized by evolution and, accordingly, can only tolerate a few non-synonymous mutations.

One must also realize that the Ks and Ka clocks can be determined reliably only from a phylogenetic tree that possesses a well established temporal reference. In that respect, values deduced by Li-Meng Yan in her pair comparison do not take into account the real evolution between the viruses. That is to say they are not necessarily direct descendants or ascendants but the offspring of some unidentified common ancestors. Consequently, we do not know exactly the number of evolution years separating them. Using three different molecular clocks, established for SARS-Cov2 and bat SARS-like coronaviruses, we have calculated that the common ancestor of SARS-Cov2 and RaTG13, if it ever existed, should be situated in a relatively large time period from 2008 to 2015. We refer the reader to chapter 6 part 3 for more ample details. That is all what should be said about the criticisms that make the point raised by Li-Meng Yan unduly ignored by the scientific establishment. The truth is that when a virus crosses the species barrier some parts of it must adapt so that it can optimally propagate in its new host. This process leads to a Ks/Ka ratio that decreases (bias towards positive selection). In 2010, Lau et al. have measured that this ratio decreased to 1.0 (not 5. as Li-Meng Yan asserted it) for the S protein of SARS-Cov when it crossed the barrier species to adapt to humans.

Li-Meng Yan was therefore unskillful because she used for the purpose of her comparison the virus pair ZC45 and ZXC21, that are both bat viruses, whereas it would have been scientifically correct to take a pair similar to SARS-Cov2 and RaTG13, implying the crossing of the species barrier. Obviously, the viruses SARC-Cov and its closest SARS-Bat-Covs coronaviruses, Rs3367 and RsSHC014, identified by Shi Zheng Li in 2011-2012 were ideal for appropriately comparing mutation rates. Indeed, approximately the same number of evolution years (8 to 10 years) separate SARS-Cov2 from RaTG13 and SARS-Cov from Rs3367 and RsSCH014. The genomic identity differences between SARS-Cov/Rs3367 (Urbani: 3.3 %, GZ02: 4%) and SARS-Cov/RsSCH014 (Urbani: 3.3%, GZ02:4.2 %) are in the same range of that of SARS-Cov2 and RaTG13 (3.8 %), opening the possibilities of relevant comparisons. The S protein of the Rs3367 virus has a 93% identical RBM, in terms of amino-acid (aa) composition, to the SARS-Cov and as for RsSCH014 the RBM is only 53.5% aa identical. The value of 77.8 % identity (aa) of the RBM between SARS-Cov2 and RaTG13 falls in the middle of this range which allows methodical interpretation.

We could reproduced the results of Li-Meng Yan for the SARS-Cov2/RaTG13 pair and we performed an identical calculation on the two other pairs involving species crossing. We observe first, as Lau et al. have evidenced in 2010, that the overall S protein Ks/Ka ratio is around 1 (and not 5.). Furthermore, there is strong adaptive evolution (positive selection)

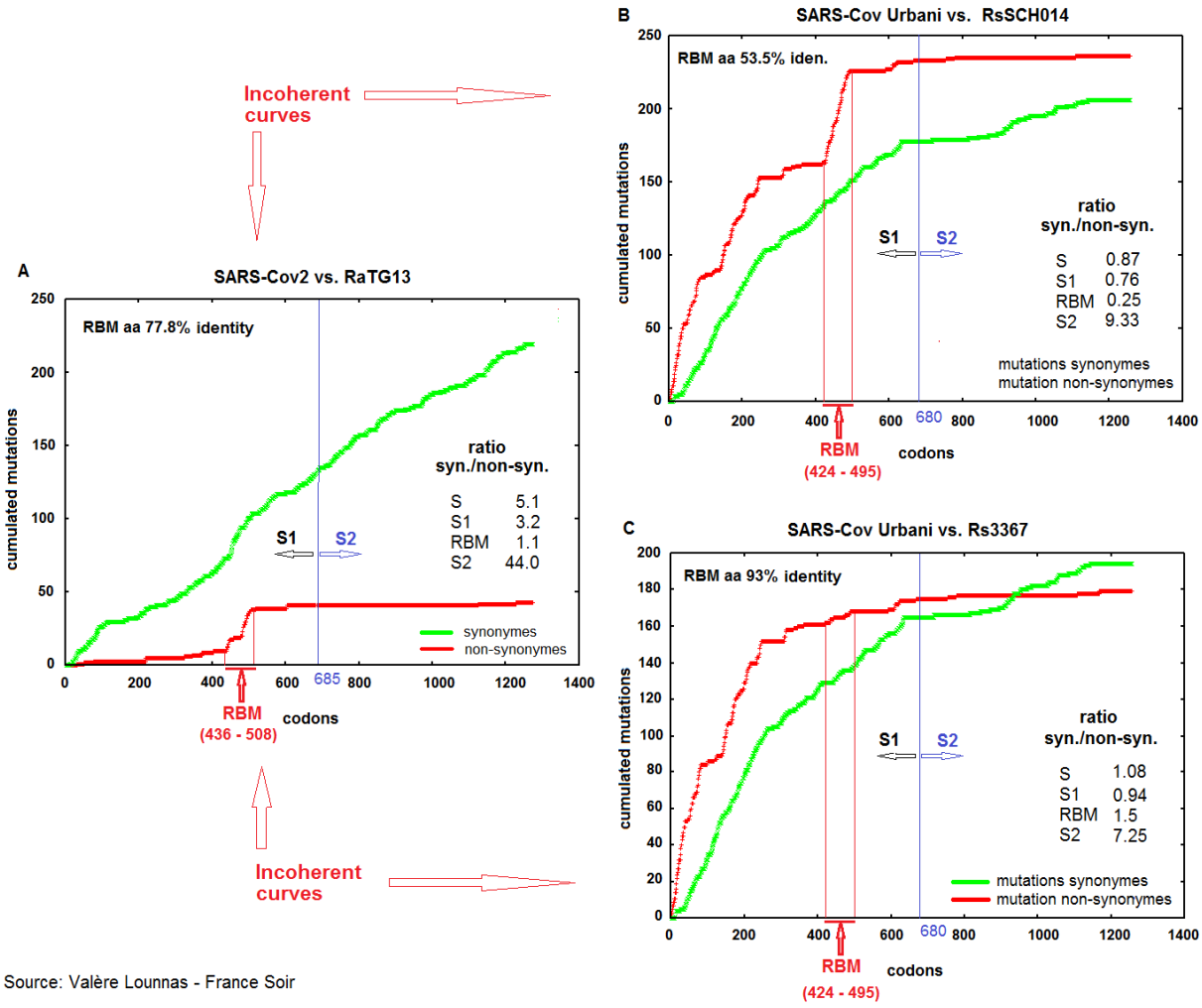
with Ks/Ka < 1. between SARS-Cov and RsSHC014, for the overall sub-domain S1 and even more pronounced for the RBM (Ks/Ka = 0.25). This necessity of adaptation is less marked for the S protein of Rs3367 closer to SARS-Cov (aa 92.2%) than that of RsSHC014 (aa 90%) with a ratio Ks/Ka = 1.5 for the RBM of the pair SARS-Cov/Rs3367. All that is perfectly coherent and logical.

Now, if we appreciate what is happening for the SARS-Cov2/RaTG13 pair compared with the two other pairs we realize that only for the RBM with 77.8% of aa identity for SARS-Cov2/RaTG13 the ratio Ks/Ka has a consistent value (1.1) with respect to the RBM of the two other pairs of viruses. But the number of non-synonymous mutations (red curve) on the domain S1 that adapt to the new host should be higher than the number of synonymous mutations (green curve), which is not the case...

The 98.4 % aa identity of the SARS-Cov2 S protein with the one of RaTG13 is much higher than the percentages of identity for the 2 other pairs (92.2 and 90 %) despite a similar higher percentages of aa identity (96.7%) at the level of their whole genomes. Such a proximity for the SARS-Cov2/RaTG13 pair prevents a high number of non-synonymous mutations elsewhere than the RBM were they are all grouped. These observations are very unlikely natural and underline the incoherence between the SARS-Cov2/RaTG13 pair and the naturally evolved pairs.

In fact, 66% (20/30 aa) of the differences between the S proteins of SARS-Cov2 and RaTG13 occur in the RBM and at the level of the furin cleavage site. Beside these two loci the percentage of aa identity is 99.1% (98.8% for the sub-domain S1 and 99.7 % for S2) revealing an extraordinary proximity of the S protein that does not seems natural at all, being considered that about 8 years of evolution and host species separate the two viruses. We have shown in part 2 that the systematic comparison of Bat-SARS-Cov coronaviruses shows that the S1 sub-domain of the S protein, in particular in the S1 N-terminal region and the RBM, is naturally the most divergent section of their genomes.

Comparison of the synonymous/non-synonymous mutation ratios of the SARS-Cov2/RaTG13 pair with respect to SARS-Cov/RsSHC014 and SARS-Cov/Rs3367 species crossing pairs



Source: Valère Lounnas - France Soir

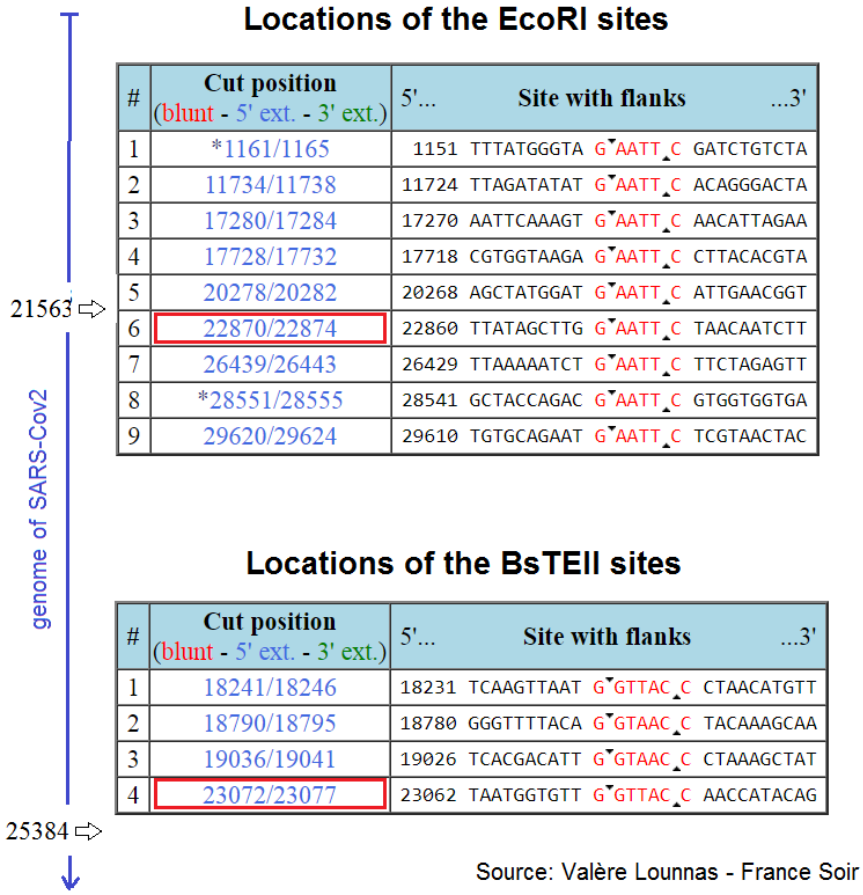
As calculations show for the naturally evolving pairs SARS-Cov/Rs3367 and SARS-Cov/RsSCH014, when crossing the species barrier the S protein is very adaptive in its S1 sub-domain (Ks/ka ≤ 1.) and has only a little adaptive potential in its S2 sub-domain (Ks/Ka much higher than 1.) which drives the structural overall stability of the its trimeric assembly. The values of the ratio for the S2 sub-domain are therefore relatively elevated although without exceeding 10. (9.33 for SARS-Cov/RsSHC014). Consequently, a value of Ks/ka = 44. for the SARS-Cov2/RaTG13 pair appears statistically aberrant.

Cyphers do not lie. Due to her lack of experience Li-Meng Yan has not pushed her reasoning sufficiently far, but she is right when she affirms that there is a lack of coherence in the calculated ratio of mutations between SARS-Cov2 and RaTG13, not only for S2 but at the level of the overall protein S sequence as well. With only about ten changes over the 1273 amino-acids that compose it, the SARS-Cov2 S protein is simply that of RaTG13 whereon evolution would have grafted a new RBM and the furin site.

Li-Meng Yan has put her finger on the presence of restriction enzyme sites ideally located for genetically manipulating the virus infectious character

A careful study of the restriction enzyme sites evidences the virus artificiality in connection with RaTG13 and Pan-Cov-GD. Considering a random distribution of nucleotides along a genome sequence we can infer the probability that two particular restriction sites co-occur at the precise locations indicated by Li-Meng Yan. We find a probability of $(1/4)^{12}$ that is 1 chance over 16.7 millions. However, if we consider that about fifteen restriction sites implying 6 nucleotides exist the probability that two sites randomly selected occur in particular locations drop to 1 chance per 74 000. It means that on average the sequence of one coronavirus in 74 000 coronaviruses would be naturally ready for the genetic manipulation of its RBM by microbiologists.

The calculation would be right if the RBM sequence was randomly variable at its extremities, however this is not actually the case. RBMs of SARS-type coronaviruses have the particularity to present highly conserved triplets of amino acids at their extremities. They are WNT on the N-terminal side and GYQ or GHQ on the C-terminal side.



Source: Valère Lounnas - France Soir

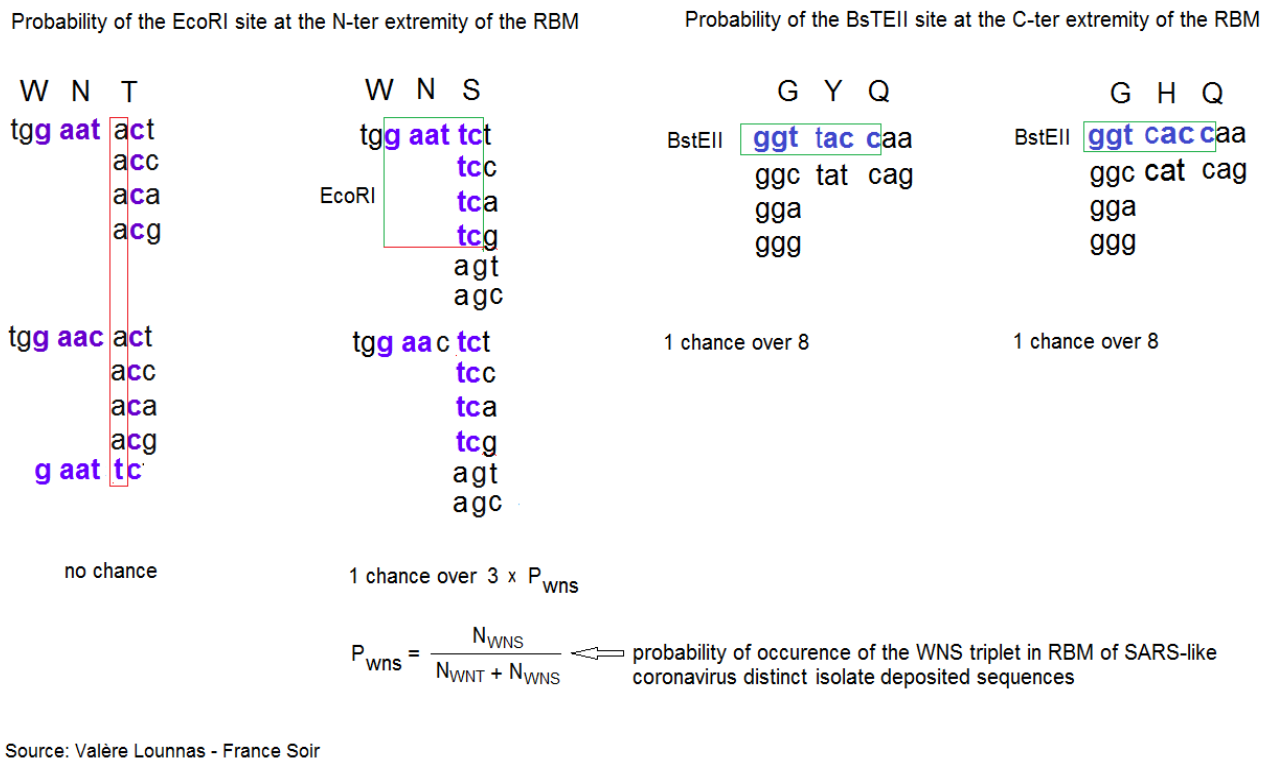
It must be pointed out that the triplet WNT corresponds to 8 possible ways of chaining 9 nucleotides excluding the possibility of having *gaattc* of the EcoRI restriction site. On the contrary, GYQ and GHQ are triplets that may correspond to the sequence *ggtnacc* of the BsTEII site. But this is far from occurring systematically because G (glycine) corresponds to 4 possible codons and, Y (tyrosine) and H (histidine) to 2 possible codons which gives 1 chance over 8 (P_{ggt} x P_{tac} x P_c = ¼ x ½ x 1) to have the BsTEII site directly at this place with these two triplets. However, with 1 or 2 synonymous point mutations one can obtain the BsTEII site without modifying the amino acids composition of the RBM extremity, which is extremely interesting for the purpose of accurately studying the function of the RBM. For example, in the SARS-Cov S gene only one mutation is sufficient (gg**c**tacc to gg**t**tacc). Astonishingly, the 3 viruses SARS-Cov2, RaTG13 and Pan-Cov-GD present directly the BsTEII site at the level of the GYQ triplet. The probability that it occurs simultaneously on randomly selected unrelated coronaviruses bearing the WNT triplet at the C-ter extremity of their RBM is 1 chance over 512 ($P_{BsTEII} = 8^{-3}$).

With BLAST, the sequence alignment online software, we have extracted all Bat-SARS-like coronavirus and Bat-coronavirus sequences contained in GenBank. We used the RBM aa sequences of RsSCH014 (71 aa) and ZC45 (52 aa) to match all coronaviruses sequences of these types. This allowed us to retrieve a complete set of sequences. On the C-terminal side the omnipresent triplet is GYP for RBMs of 70-72 aa length, except in 1 or 2 cases where GHQ or NYQ are found. This ensures the possibility of having, naturally or via a reduced manipulation, the BsTEII site for coronaviruses with such a RBM. As for coronaviruses with RBMs of a shorter length one find essentially the EYQ triplet (possible exceptions being NYQ or AYQ) which never allows the natural presence of the restriction site, although it may be easily introduced. To establish proper statistics all redundant sequences (corresponding to multiple sequencing of the same viruses) are to be eliminated although they are indicative of mutations that may occur, eliminating the over-abundant SARS-Cov2, SARS-Cov and palm civet sequences, as well as the X-ray, electron microscopy (EM) structures and synthetic and recombinant constructs. Multiple identical isolates of the same viruses were to be eliminated as well. Indicatively, we have identified about 62 unique sequences covering long and short RBMs, corresponding to really distinct virus isolates, comparable to the 53 distinct 2b betacoronaviruses according to Hoffman et al 2020.

On the N-terminal side of the RBM, irrespective of its short or long length, the WNT triplet is 100% conserved except for only SARS-Cov2, RaTG13, Pan-Cov-GD (Pan-Cov-GX as well) and a mysterious fourth coronavirus isolated in Japan that bear the WNS triplet. A very small fragment of its genome (0.6%) was deposited in GenBank in September 2019. This fragment covers its RBM that presents the WNS triplet. When a virus protein bears this triplet it implies 1 chance over 3 to have the EcoRI site at the level of the nucleic sequence. W is coded by a unique codon, N by 2 possible codons, and S corresponds to 6

codons, 4 of which may correspond to the EcoRI restriction site. Only the amino acid sequence of the Japanese virus was deposited so that we do not know whether the WNS triplet corresponds to the EcoRI site (*gaattc*).

Therefore, we can consider that, statistically, the probability to directly encounter a coronavirus with the EcoRI site at the N-ter extremity of its RBM is P_{EcoRI} = 0.5*(4/6)*$Freq_{WNS}$, with $Freq_{WNS}$ being the frequency of the WNS triplet that we estimate to 1/(51) (since only the Japanese virus bears it). We exclude the 3 viruses SARS-Cov2, RaTG13 et Pan-Cov-GD from the count of Hoffman et al. Pan-Cov-GX (collected in 2017-2018 but sequenced in 2020) that was not included by Hoffman but differ from Pan-Cov-GD (whole genome 85% identity) although it bears the WNS triplet. Therefore we place ourselves from the perspective of calculating the probability before the epidemics outbreak in December 2019, that is to say before the sudden publication within a few months of the sequencing of 4 closely related viruses with the WNS triplet (SARS-Cov2, RaTG13, Pan-Cov-GD and Pan-Cov-GX).



Source: Valère Lounnas - France Soir

Finally, the odds that the RBM of the 3 viruses be flanked simultaneously by the EcoRI and BsTEII sites at both their extremities is expressed by the formula (P_{bsTEII} xP_{EcoRI})**3 = [(0.5*(4/6)*$Freq_{WNS}$)]**3x(1/512) which is 1 chance over 1.72 billion with $Freq_{WNS}$ = 1/50. If we include the four viruses SARS-Cov2, RaTG13, Pan-Cov-GD, Pan-Cov-GX (considering them as totally unrelated) in the $Freq_{WNS}$ estimate (4/54) the odds are still 1 in 34 millions.

Although our result is dependent on the estimate of $Freq_{WNS}$, which could be made more accurately, it raises questions. Without the sequence of the Japanese virus deposited in GenBank in September 2019, the odds would have been just zero. It would be of interest in the coming years to systematically collect samples of bat feces and search by PCR RBM sequences (< 220 nt) matching a N-ter motif with the WNS triplet.

During the year 2020, the confidential watchword of the international research was to do the sequencing of all the collected bat-feces samples stored in research laboratories. The official goal was to identify a close parent of SARS-Cov2. But it is a research of fools because the closest parent of SARS-Cov2 is RaTG13 and identifying an even closer virus and the supposed intermediate host could have been made only in relation with the wet markets or the wild animal farms in the Hubeï province around Wuhan. Perhaps the untold goal was actually to formally prove Li-Meng Yan wrong when she affirmed the artificial presence of the EcoRI site in the SARS-Cov2. This site is also found in its presumed cousin RaTG13 and as well in Pan-Cov-GD, a virus most probably carried by wild animal traffickers (chapter 6 part 4). Li-Meng Yan affirms also that RaTG13 and Pan-Cov-GD would be viruses fabricated to distract the international attention from the ZC45 virus issued from the Chinese military research. Beside her point #1 raised about protein E, which is indeed very troubling, we do not find other solid evidence to follow her in this direction. However, we must admit that the obvious embarrassment of the microcosm of virologists and microbiologists, and their reluctance in providing clear explanation to the questions raised, confirms that the proximity between at least three viruses is not natural.

It may seems odd to find the WNS triplet instead of WNT in a fragment of 186 aa including the RBM (50 aa) of the S protein, representing 0.6% of a coronavirus, deposited in GenBank (GenBank: BBJ35999.1) in September 2019 by Japanese researchers (Murakami,S. and Horimoto,T.) under the title “Novel coronaviruses harbored by wild bats in Japan”. On November 5th 2020, they have deposited again in GenBank (code: BCG66627.1) the complete sequence (1235 aa) of the S protein of this new virus along with an article entitled “Detection and characterization of bat sarbecovirus phylogenetically related to SARS-CoV-2, Japan.” It may inspire a conspiracy feeling that this fragment was deposited in September 2019... dismissing in advance the claim of the impossibility of having the WNS flanking a bat coronavirus RBM. This is puzzling but one must realize that since the WNS leads obviously to very viable viruses the real question is why was it not observed before in other coronaviruses ? Evolution should allow it since it is a viable combination. The fact that the Japanese team has published this very short RBM sequence showing the WNS triplet proves that this was a unique observation and important finding, worth being deposited in priority in GenBank. It confirms the impossibility that 3 viruses, originating from the same geographical area within a few months (RaTG13 was in the laboratory of Shi Zheng Li since 2013 but sequenced in 2018), with ≥ 90% sequence identity share this same characteristic without being intimately related.

Our probability calculations show that Li-Meng Yan has put her finger on the very disturbing fact that the EcoRI site presence is absolutely not in conformity with a natural virus. The natural quasi-absence of the WNS triplet in the RBM of coronaviruses is very astonishing because mutations of threonine (T) to serine (S) are generally authorized, these two amino acids being relatively close in terms of the physico-chemical interactions implied. However, contrary to serine, threonine bears a methyl chemical group that could explain its quasi-unique specificity mediated by some particular interaction. But, since WNS is obviously very viable, its scarcity cannot be only explained either by the necessity of double nucleotide mutation or a loss of function. Only an in-depth study of the RBM three-dimensional structure could possibly demonstrate the reason.

The EcoRI site was artificially introduced by the team of Shi Zheng Li at the Wuhan Institute of Virology to substitute the RBM of the SARS-Cov virus.

Li-Meng Yan tells us that as early as 2008 Shi Zheng Li and her team had introduced a point mutation to obtain the EcoRI site uniquely on the SARS-Cov S gene to allow its RBM to be grafted on other bat coronaviruses. Their published article specifies that the BamHI restriction site was used at the other RBM extremity without specifying whether it was introduced there artificially. We cannot find it in the SARS-Cov strain (BJ01-S) they used. Their purpose was to manipulate the RBM region of the virus to explore its infectious capability with respect to the human receptor ACE2. In their experiment, they inserted the SARS-Cov S protein RBM (aa position 424 to 494) on a pseudo-typed HIV virus, expressed in a plasmid. Subsequently, they could exchange the RBM with RBMs of other bat coronaviruses of the type SL-Cov (SARS-Like coronavirus) to study their capacity to activate the human cell penetration ACE2 receptor (hACE2). This research work of Shi Zheng Li et al. was as usual published in Nature. Their conclusion was that the insertion of a minimal section (aa position 310 to 518) encompassing the RBM of SARS-Cov was sufficient to induce the binding to hACE2 of a bat SL-Cov coronavirus unable to do it before hand. This was absolutely remarkable, demonstrating how to simply create an infectious virus able to cross the species barrier to humans. But that demonstration was not sufficient for her since she re-iterated it in 2015 in a collaborative work with R Baric from Chapel Hill University (North Carolina), substituting the RBM of a mouse adapted SARS-Cov virus with that of RsSHC014 demonstrating the chimeric virus was highly infectious on human lung-cell cultures at the same level of replication as in alveolar extracts of hospitalized patients from 2002-2003.

In any case, it is really extraordinary that the two closest viruses to SARS-Cov2 share, in addition to the BsTEII at the RBM C-terminal extremity, the EcoRI site at its other extremity

on the N-ter side making it easily exchangeable. This two sites are unique on the S gene overall length, thus allowing targeted manipulation avoiding the possibility of several cleavages along the S gene, which is an essential condition. In the case of the pangolin virus, the EcoRI site is present at another location on the S gene, but it can be specifically protected by methylation, allowing cleavage only at the RBM N-terminal extremity. The Pan-Cov-GD RBM seems to have been exchanged with that of RaTG13 to create the S1 sub-domain of the SARS-Cov2 S gene. “Fate is a good provider” should we say, except that Mother Nature does not need the presence of restriction sites to recombine viruses...

Bat coronavirus RaTG13, complete genome

Sequence ID: MN996532.2 **Length:** 29855 **Number of Matches:** 8

Range 1: 22867 to 23082 GenBank Graphics ▼ Next Match ▲

Alignment SARS-Cov2 RBM (query) with RaTG13 RBM (Sbjct)

Score	Expect	Identities	Gaps	Strand
122 bits(152)	6e-31	162/218(74%)	4/218(1%)	Plus/Plus

```
Query  1      GAATTCTAACAATCTTGATTCTAAGGTTGGTGGTAATTATAATTACCTGTATAGATTGTT  60
              ||||||||||  || |||||  | ||  |  || |||||||  ||| || ||  |   | ||
Sbjct  22867  GAATTCTAAGCATATTGATGCAAAAGAGGGCGGTAATTTTAACTATCTTTACCGTCTCTT  22926
```

EcoRI restriction site unique in ORF S

```
Query  61     TAGGAAGTCTAATCTCAAACCTTTTGAGAGAGATATTTCAACTGAAATCTATCAGGCCGG  120
              |||  ||   ||||||| |||||  |||||||| |||||  ||||||||||| || ||  ||
Sbjct  22927  TAGAAAAGCTAATCTTAAACCCTTTGAGAGGGATATCTCAACTGAAATTTACCAAGCAGG  22986

Query  121    TAGCACACCTTGTAATGGTGTTGAAGGTTTTAATTGTTACTTTC--CTTTACAATCATAT  178
               ||||  |||||||||||||       |||  |  |||||  ||||   |  |||||  |    ||||
Sbjct  22987  CAGCAAACCTTGTAATGGTCAAACTGGTCTAAATTGCTACTACCCACTTTATA--GATAT  23044

Query  179    GGTTTCCAACCCACTAATGGTGTTGGTTACCAACCATA  216
              ||  ||   |  ||  |||  ||||||||||| ||||||| ||
Sbjct  23045  GGATTTTACCCTACTGATGGTGTTGGTCACCAACCTTA  23082
```

BsTEII restriction site unique in ORF S

Pangolin coronavirus isolate MP789, complete genome

Sequence ID: MT121216.1 **Length:** 29521 **Number of Matches:** 1

Range 1: 22716 to 22931 GenBank Graphics ▼ Next Match ▲ Pr

Score	Expect	Identities	Gaps	Strand
245 bits(307)	1e-60	191/216(88%)	0/216(0%)	Plus/Plus

```
Query  1      GAATTCTAACAATCTTGATTCTAAGGTTGGTGGTAATTATAATTACCTGTATAGATTGTT  60
              |||||||||||| ||||||||||||||||||||||||||||||  |||||  ||||||||||||
Sbjct  22716  GAATTCTAACAACCTTGATTCTAAGGTTGGTGGTAATTATAACTACCTTTATAGATTGTT  22775

Query  61     TAGGAAGTCTAATCTCAAACCTTTTGAGAGAGATATTTCAACTGAAATCTATCAGGCCGG  120
              |||  |||||  ||  ||||||||||||||   ||||  |||||  ||  |||||  ||  ||  ||
Sbjct  22776  TAGAAAGTCCAACCTCAAACCTTTTGAACGAGACATTTCTACAGAAATATACCAAGCTGG  22835

Query  121    TAGCACACCTTGTAATGGTGTTGAAGGTTTTAATTGTTACTTTCCTTTACAATCATATGG  180
              |||  |||||  ||  |||||  ||||||||||||||  ||||||||||||  ||||||  |||||
Sbjct  22836  TAGTACACCCTGCAATGGGGTTGAAGGTTTTAACTGTTACTTTCCTCTACAATCTTATGG  22895

Query  181    TTTCCAACCCACTAATGGTGTTGGTTACCAACCATA  216
              ||||||  ||  ||||||||||||||||||||||  ||
Sbjct  22896  TTTCCACCCTACTAATGGTGTTGGTTACCAACCTTA  22931
```

BsTEII restriction site unique in ORF S

Credit: Valère Lounnas - France Soir

The E protein argument is counter productive

Although, it is very disturbing to observe that the E protein is strictly conserved across the five coronaviruses (SARS-Cov2, RaTG13, Pan-Cov-GD, ZC45 and ZC21) Li-Meng Yan should not affirm without a formal proof that SARS-Cov2 was created by manipulation from the virus ZC45, even-though 100% conservation of protein E is intriguing. As we showed previously, at the nucleotide level, the E protein of ZC45 and ZXC21 is actually quite distant, with 88% identity from that of SARS-Cov2. On the contrary, RaTG13 and Pan-Cov-GD have > 99% nt identity for the E protein. This protein is small (76 aa) and due to its very precise function it is probably highly constrained by evolution, authorizing only little variations of its sequence. This is why that specific argument made by Li-Meng Yan on the E protein is counter-productive with respect to the two main indisputable observations on the ratio of synonymous vs non-synonymous mutations and the joint presence of the restriction sites EcoRI and BsTEII at both ends of the SARS-Cov2 RBM. Their simultaneous presence in 3 randomly selected unrelated virus would be an event statistically quasi-impossible.

Answers from the Institut Pasteur are awaited

We have scientifically established that SARS-Cov2 is undoubtedly related to RaTG13 (that comes from the laboratory of Shi Zheng Li), but it is also related to the Pan-Cov-GD virus. What a surprise! In chapter 6 part 4 and part 5 we have developed a long list of arguments demonstrating that the Pan-Cov-GD origin could not be the pangolin. Li-Meng Yan strongly affirms the same conclusion in her second report, specifying that it is impossible that a coronavirus supposedly originating from pangolins may have the same RBM as SARS-Cov2 (quasi 100% of identity). Indeed, on the one hand the pangolin ACE2 receptor is evolutionary distant from the human one (chapter 6, part 4 and part 5) and on the other hand, no trace of coronavirus was found in the Malayan pangolin samples collected between 2009 and march 2019.

We may be mislead and we therefore invite the virologists of the Pasteur Institute to answer us in FranceSoir. This is with pleasure that a forum will be opened for them and we await their reply. Let's note that on the technical level there are exactly 210 nucleotides between the two restriction sites (including them). We are here at the extreme limit of what chemical nucleo-synthesis allows. Beyond a length of 200 nt the synthetic reaction yield becomes null. Synthesis errors are about 1 to 2% which is also a limitation. These technical aspects explain the necessity of having restriction sites as close as possible to substitute a RBM for a synthetic RBM with a sequence that can be optimized at will at the conceptual level.

A second report that is a firebrand against China

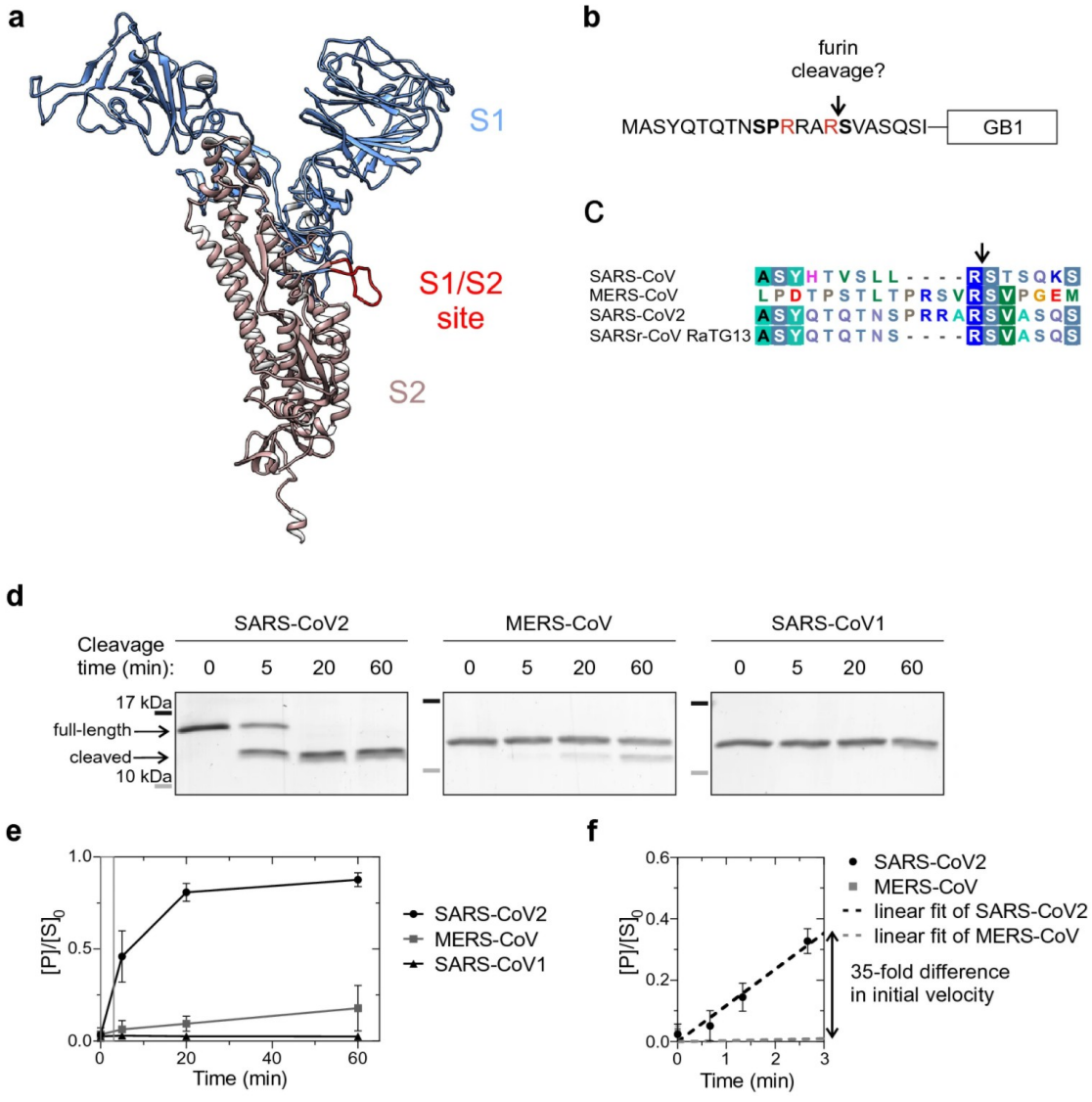
The second report of Li-Meng Yan : “SARS-CoV-2 Is an Unrestricted Bioweapon: *A Truth Revealed through Uncovering a Large-Scale, Organized Scientific Fraud”, was* published also on the internet site Zenodo, short after the her first report, on October 8, 2020. She makes no concession to China. Her article is punctuated at intervals by words such as : *fraudulent, fabricated, suspect, genetic evidence*... about the viruses RaTG13 and Pan-Cov GD supposed to prove the natural origin of SARS-Cov2. The fabrication of these viruses would allow, according to her, the creation of a diversion with respect to the twin military viruses ZC45 and ZXC21 and at the same time make their proximity to the SARS-Cov2 looks more distant. We cannot follow her on the conclusion that China has purposely let a lethal pandemic virus spread over the world. But there is no doubt that the responsibility of China is engaged in a way or another. Li-Meng Yan has the merit and the courage to denounce loudly a number of truths on the irresponsible attitude of China and the endless GOF virus manipulations that have taken place for many years at the Institute of Virology of Wuhan. The Western world is paralyzed by fear and refuses to hold China and WHO accountable for this planetary catastrophe.

To conclude

SARS-Cov2 cannot have evolved naturally from RaTG13 or another virus close to it. Cyphers show unquestionably the incoherence in term of natural evolution between these two viruses that have an identical S protein besides the RBM and the furin cleavage site that ensures multi-organ infection. Cyphers and observations do not match knowledge on SARS-like coronaviruses. The furin site that considerably strengthens the penetration capacity of the virus appears as a pure gain of function because it is useless for SARS coronaviruses inter-species crossing and adaptation to humans. It appears also at the S1/S2 domain intersect in the Middle East Respiratory Syndrome (MERS) the intermediate host of which (the camelidae) is well identified. It probably contributes to make the MERS a very lethal virus but MERS is not yet a virus highly transmissible between humans, as contact with camels is needed in most cases. Additionally, the furin cleavage site seems much more optimal in SARS-Cov2 as it is dramatically more efficient in vitro compared with MERS.

Figure 1

From: The sequence at Spike S1/S2 site enables cleavage by furin and phospho-regulation in SARS-CoV2 but not in SARS-CoV1 or MERS-CoV



Source: Mihkel örd et al., Nature - Scientific Report, Oct. 9, 2020

The SARS-Cov2, RatG13 and Pan-Cov-GD viruses are undoubtedly related to each others due to the common presence on the S gene of the EcoRI and BsTEII restriction sites flanking their RBMs with clock-master precision. Additionally, the SARS-Cov2 and Pan-Cov-GD have exactly the same RBM. All these observations may explain why an intermediate host has not been identified. Although they cannot be denied they cannot constitute a formal proof because true science is not accessible to mass media and too many scientists are ignorant of these facts, afraid of speaking loud or simply in denial. In the absence of direct concrete physical evidence that could be collected at the WIV this gives China the benefit of the doubt.

The accumulation of the abnormal features in SARS-Cov2 beyond reasonable coincidence deserve real explications from the renown virologists of Institut Pasteur - France who for some obscure and ill-motivated (political) reasons refuse to do it. It maybe in connection with the implication of France in the construction and funding of the P4 lab of Wuhan (a copy of the P4 in Lyon-Gerland). Let's also mention that Shi Zheng Li, the head of the special pathogens laboratory of the Wuhan Institute of Virology (WIV), has obtained her Ph.D. in microbiology at the University of Montpellier 2 (France) in 2000 and that the Merieux-Sanofi consortium has trained the Wuhan P4 lab technicians in Lyon, before France was evicted from the official collaborative program agreement signed with China in 2004 (chapter 2 part 2).

The conviction of Li-Meng Yan in her declarations on the involvement of the viruses originating from the Chinese military research may have lured the world with a counter productive excess of political incorrectness by far too embarrassing for Western world diplomacy, diverting attention from the WIV and subsequently detrimental to the truth. As a matter of fact, we don't know to which extent civil and military researches are interconnected at the WIV, but there are indications that it may well be the case. Li-Meng Yan was intuitively attempting to proclaim loudly what may be a reality. But it was unskillful, and it would have been better to keep concentrated on indisputable scientific arguments.

The logical consequence of all the facts we have analyzed in detail in chapter 6 (part 1 to 5) and this part of chapter 8 point towards the possibility of one or several laboratory leakages at the WIV, following GOF experiments on bat coronaviruses collected in the Yunnan province. Wild animals markets have played a role still to be elucidated. Anyhow, that the epidemics be the result of activities around the markets or an accident of laboratory, China is accountable for it and owes a credible explanation to the world. The hypothesis that mink farms could be at the origin of the virus has arisen incongruously in the media recently, after a year of categorical refusal from China to accept international investigations carried out by mandated virologists on its soil.

Wild animals such as palm civets and raccoon dogs (5 millions) are massively produced in farms that are now in the collimator of some epidemiologists. This industry, representing 3 000 production sites for a total amount of 50 millions animals, is a considerable economical asset for China. According to an article of Reporterre published on January 8 2021, the “colossal” Chinese branch of this industry weights more than 20 billions dollars annually. It is inconceivable that samples have not been collected systematically in the farms of the Hubeï province as early as January 2020 and that the coronaviruses that could have been extracted were not sequenced and compared with SARS-Cov2. Now, it is by far too late. Viruses 99.9% identical to SARS-Cov2 or the corresponding antibodies

may be found. But being considered the time interval of one year since the epidemic outbreak, it will be meaningless besides confirming the fact that its point zero is indeed actually somewhere in Wuhan... The world is being manipulated by China that prevents any serious inquiry, leads and controls all scientific researches and publications conducted on its territory. Not only because of China but also because of the Western countries governments, the world has entered an era of Orwellian disinformation. The Reporterre article tells us that the Chinese Academy of Sciences, the Chinese CDC (Center of Disease Control) and of course the WIV are very favorable to the mink farms hypothesis. Of course, the international acceptation of this theory would be a lesser evil for China. But this cannot change scientific analysis and conclusions drawn on (1) the circulation between 2017 and 2019, of SARS-like coronaviruses in the microcosm of wild animal vendors and traffickers (chapter 6 part 4), and on (2) the comparison of the virus SARS-Cov2, RaTG13 and Pan-Cov-GD.

An exhaustive audit of the WIV which conceals other bat coronaviruses close to RaTG13 should have been the priority on the agenda of UNO. A mission of a small dozen of international experts was recently mandated by the World Health Organization (which is a weak body of UNO controlled by China) for a period of 6 weeks two of which will be spent in quarantine, leaving only 4 weeks for investigation. Such a short period seems out of place and in line with the diplomatic manipulations that China has orchestrated via WHO since the epidemics outbreak in Wuhan one year ago. A field mission in the search of “scientific answers to the face-to-face confrontation between humans and animals” has declared a top WHO functionary... What a mockery! Maybe, would it be better to investigate the face-to-face confrontation between human populations and research laboratories. But we wish them good luck. A subsidiary goal of this mission is to determine the measures to be taken so that such a world pandemics does not occur again in the future. Unfortunately, the same wishful thinking and international guaranties were given by the Chinese authorities after the first SARS epidemics of 2002-2003 originating from Canton.

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