Exclusive | Tracing to the Source of the Novel Coronavirus through Genome Sequencing: when did the alarm go off?

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[Caixin Network] (Reporters Gao Yu, Peng Yanfeng, Yang Rui, Feng Yuding, Ma Danmeng)

Tracing back to the source of the novel coronavirus which is similar to SARS and has caused more than 2,660 deaths and 77,000 confirmed infection cases as of February 24, when was it, discovered? Caixin reporters have put the information puzzles together and gradually shown the complete picture through multiple interviews, research and corroboration of relevant papers and database information.

Evidences 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. The genome sequencing showed that the pathogen was a type of SARS like coronavirus. These test results were returned to the hospitals and reported to the National Health Commission and the Chinese CDC system one after another. On January 9, CCTV reported that the Panel for the Preliminary Assessment of Wuhan Viral Pneumonia Pathogen Testing Results officially declared the pathogen as a "novel coronavirus".

The result of the first case came out as early as December 27

On December 15, 2019, a 65-year-old male delivery male from the Huanan Seafood Market started to develop a fever. On December 18, he went to the Emergency Department of Wuhan Central Hospital Main Campus (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, which main clinical symptoms include cough, with or without sputum, and chest pain.

On Dec. 22, the patient's condition deteriorated and was admitted to the ICU, where he failed to respond to the treatment with a variety of antibiotics. 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 sampled this patient's specimens via bronchoscope and sent the patient's bronchoalveolar lavage specimens to a third-party testing organization, Guangzhou Vision Medical Gene Technology Co. Ltd., for NGS testing, hoping to identify the pathogen through their metagenomic next-generation sequencing technology (mNGS) which is based on metagenomics. Alveolar lavage is a treatment to remove inflammatory secretions from the alveoli and improve respiratory function. For lower respiratory tract and lung diseases, the pathogen content of alveolar lavage fluid is higher than that of pharyngeal swabs.

Guangzhou Vision Medical Genetics Technology Co. Ltd. was established in June 2018. According to its recruiting advertisement, the company focuses on precision medicine in oncology and infection pathogenesis, and a sequencing platform based on metagenomic next-generation sequencing technology (NGS) is in their possession.

"Since the thriving of BGI Genomics with their sequencing technology, there have appeared many genome sequencing companies of all sized in China. At various medical seminars in recent years, mNGS technology has been introduced constantly, and these companies sent their sales representatives to major hospitals for promotion," Zhao Su told Caixin reporters. BGI Genomics (code at Shenzhen Stock Exchange:300676), or BGI Genomics Co., Ltd. in full, originally known as Beijing Huada Center for Genetic Research, was founded in 1999. The company has completed a number of internationally advanced genomic research work, including the Chinese section of the human genome project, the rice and giant panda genome projects. In July 2017, it was listed on the ChiNext exchange, labelled as the "first genome sequencing stock", and is the largest genomics research and development institution in the world.

According to one another doctor at Wuhan Union Hospital, "One test of 6 million base sequences costs CNY 3000. And this CNY 3000 can save a life if the test can find out which virus or bacteria causes the pathogen."

Generally speaking, the genome sequencing company was supposed to return the test result three days later, or on Dec. 27. But Vision Medical did not provide a written report. "They just notified us by phone, saying it was a novel coronavirus," said Zhao Su. By then, the patient was already transferred to Wuhan Tongji Hospital on Dec. 25.

On Feb. 21, 2020, the genetic test information of this case was disclosed in an article of the WeChat public account of Vision Medical. According to the article, the Chinese Medical Journal (English version) published a paper on January 27 about the discovery of the novel coronavirus, and Vision Medical participated in the early detection of the novel coronavirus.

The paper published in the Chinese Medical Journal (English version) refers to the article *Identification of a novel coronavirus causing severe pneumonia in human: a descriptive study*, published on January 29. The authors of the paper are from the Institute of Pathogen Biology of Chinese Academy of Medical Sciences/Beijing Union Medical College, China-Japan Friendship Hospital, Hubei provincial CDC, Wuhan Jinyintan Hospital, Wuhan Central Hospital, and Guangzhou Vision Medical Technology Co., Ltd. Vision Medical's CTO, Teng Xu, was one of the first co-authors, while the company's CEO Li Yongjun and COO Wang Xiaorui were among the signed authors. Li Yongjun once worked as a bioinformatics analyst at the Institute of Pathogen Biology of Chinese Academy of Medical Sciences.

According to the paper, the researching staff collected clinical data and bronchoalveolar lavage specimens from five patients with severe pneumonia at Wuhan Jinyintan Hospital of Hubei province, and performed pathogenic mNGS analysis. As a result, the specimens showed a coronavirus with 79.0% nucleotide similarity with the sequence of SARS. According to the paper, among the five patients, the first clinical specimen that went through genome sequencing was the one from a 65-year-old patient collected on December 24. The onset was on December 15 with symptoms of high fever and cough with small amount of sputum. He was admitted on the 18th, and was transferred to the ICU on December 22. He continued to have high fever after 16 days and developed severe shortness of breath.

The same high degree of consistency with the above information was also found in an article posted by a WeChat public account called Little Mountain Dog on January 28th, entitled Recording the Experience of the First Discovery of the Novel Coronavirus. In the comments section, the author claimed to be working in a private company in Huangpu district of Guangzhou. The article recorded that, "As soon as I arrived at work on December 26, 2019, as usual, I browsed through the automatic interpretation results of the day's mNGS pathogenic microorganism. Unexpectedly, I found that a specimen reported a sensitive pathogen - SARS coronavirus, with dozens of sequences, and there was only one such meaningful pathogen contained in this specimen. I was alerted and rushed to check the detailed analysis data in the back office and found that the similarity was not that high, only about 94.5%. In order to confirm the reliability of the results, I started a detailed analysis. The results of the exploratory version of the analysis suggested that this pathogen was most similar to Bat SARS like coronavirus, with an overall similarity of about 87%, while its similarity with SARS was about 81%."

According to the author, the patient's specimens was also collected on December 24. In the article, "according to the front-end, this patient was in seriously condition, and they were anxious for the test result. However, such a significant pathogen cannot be reported without caution. We had an urgent meeting with several leaders at noon and decided to continue the in-depth analysis and delay the release of the report. At the same time, the data was shared with the Pathogen Institute of the Chinese Academy of Medical Sciences for further analysis". The Pathogen Institute of the Chinese Academy of Medical Sciences is the Institute of Pathogen Biology of the Chinese Academy of Medical Sciences, where Li Yongjun, CEO of Vision Medical, one of the authors of the paper in Chinese Medical Journal (English version) quoted above, used to worked for. The President of the Institute's immediate superior organization - 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 genome sequence of the virus, while the data was also shared with the Institute of Pathogen of the Chinese Academy of Medical Sciences. "We can basically confirm that this patient's specimens did contain a new virus similar to Bat SARS like coronavirus," the article writes, "the information we were provided at the time indicated that the patient had returned to his hometown before that, and the possibility that he was exposed to bats could not be ruled out. Realizing the potential seriousness of the problem, the laboratory was fully cleaned and disinfected, while the specimens were put in harmless destruction, and the personnel involved in the lab operation were monitored accordingly. The result was communicated to the doctor before noon, and the patient was also isolated."

"It should be us who first discovered this novel coronavirus." The article by "Little Mountain Dog" also included a screenshot of the GISAID database, "From the submission of data to the GISAID database website, it was also us who collected the earliest specimen."

GISAID is a global platform for the sharing of influenza virus data where researchers can upload viral genetic sequences they extracted after registration. Each strain is given a unique serial number, and information such as time of collection, time of submission, and submitting laboratory are also recorded. Caixin reporters checked and found on GISAIDS that the earliest genome sequence of the novel coronavirus according to the specimen collection time was on December 24, 2019 and uploaded by the Institute of Pathogen of the Chinese Academy of Medical Sciences on January 11. By comparing the serial number and name, we found that it is the specimen sequence marked in the screenshot of the article by "Little Mountain Dog", for the testing their company participated in.

The article also mentioned that the company's leaders had phone communication with the hospital and the CDC on December 27 and 28, and they even personally went to Wuhan on the 29th and 30th to report and exchange face-to-face all the analysis results with the hospital and CDC leaders, "They covered both all our analysis results and the analysis results of the Institute of Pathogen of the Academy of Medical Sciences. Everything was under intense, confidential, and strict investigation (at this time, people at the hospital and the CDC already knew that there had been a number of similar patients; and the emergency response started after we communicated the test results).

The owner of the earliest known specimens on which the genome sequencing was completed later died at the Jinyintan Hospital. The results of this case, in which a new virus was detected on December 27, did not play any role at that time.

"SARS coronavirus" went viral on social media

In fact, in addition to the earliest known case, there had been specimens of two other patients with "pneumonia of unknown origin" from Wuhan Central Hospital, which were sent to different institutions for genome sequencing at the end of December 2019. The testing results of the two cases have had a significant impact on the public disclosure of the outbreak through different paths.

On December 27, a 41-year-old man surnamed Chen visited Wuhan Central Hospital Nanjing Road Campus. "He is an accountant who lives in Wuchang and has not been at all to Huanan Seafood Market in Hankou. It was probably on December 16 that, without obvious cause, he started to develop a fever as high as 39.5°C, accompanied by palpitations, chest tightness, breathing difficulties after activity, and significant loss of physical strength. He first saw a doctor at the First People's Hospital of Jiangxia District on December 22, but didn't get better." Zhao Su told Caixin reporter, "He is an acquaintance of a doctor at our hospital. He was transferred to our hospital on the 27th and was admitted to the emergency department." In the evening of December 27, the patient went through bronchoscopy sampling at the hospital's respiratory ICU, whose specimens were sent this time to another institution practicing NGS testing - Beijing CapitalBio MedLab Co., Ltd.

On December 30, Beijing CapitalBio MedLab sent the patient's test report back to the doctor, and the test result was simply "SARS coronavirus".

According to test report of the Beijing CapitalBio MedLab obtained by Caixin reporters, SARS coronavirus and pseudomonas aeruginosa were tested positive in this patient's specimens with high confidence. The SARS coronavirus was interpreted as a single-stranded positive-stranded RNA virus, which is transmitted by proximity droplet transmission or contacts with the patient's respiratory secretions, which can cause a special and significantly infectious pneumonia with possible involvement of multiple organ systems, also known as atypical pneumonia.

"Since their gene pool is not comprehensive enough, or maybe they didn't verify the result, they made a small mistake. It's actually a novel coronavirus instead of SARS," a genome sequencing expert told Caixin.

However, the test report, which contains a small mistake, caught the attention of Wuhan doctors, who blew a warning whistle to the public through social media, saving, to some extent, the lives of a considerable number of people.

On December 30, the test report from the Beijing CapitalBio MedLab appeared in WeChat messages of doctors at Wuhan Central Hospital. At 17:48 that evening, Li Wenliang, an ophthalmologist at Wuhan Central Hospital, released information in his classmate chat group, "Seven cases of SARS were confirmed at Huanan Fruit and Seafood Market, who are being quarantined at the emergency department of our hospital"; at 19:39, Liu Wen, a neurologist at Wuhan Red Cross Hospital, posted information in his work WeChat group "Union Red Cross Society Neurology", saying that: "just now, the Second Hospital (i.e. Wuhan Central Hospital) Houhu Campus confirmed a case of coronary infectious virus pneumonia, perhaps the surroundings of Huanan will be quarantined. It's basically determined that it's SARS. Dear nurses, stay put"; at 20:48, Xie Linka, a doctor at Oncology Center of Wuhan Union Hospital, posted a message in the WeChat group of the Oncology Center, saying "do not go to Huanan Seafood Market these days, as there are now many people suffering from pneumonia of unknown cause (similar to SARS) over there. Today, our hospital has admitted several pneumonia patients from Huanan Seafood Market. Everyone should pay attention to wear masks and ventilate". All these three doctors were then admonished by the police.

On the same day, the author of the "Little Mountain Dog" article", who was as far as in Huangpu district of Guangzhou, got also the above-mentioned news, and he recounted, "By December 30th, I heard the news that there were quite a few more patients with similar symptoms, which stretched again my nerves. In particular, I think it's in the afternoon of the 30th, a peer company may have detected the same virus in another patient's specimens. But they directly reported it as the detection of SARS coronavirus, which instantly made news go viral... The peer company shared the sequence for our analysis. And after I analyzed it; it was indeed the same virus! The first thought in my subconsciousness was 'this virus was contagious'!"

The information exposed by Li Wenliang and others made the story line of the gene companies' sequencing cross path with the story line of the clinicians' warning. While doctors at Wuhan Central Hospital were looking to gene sequencing companies for answers to the constantly appearing viral pneumonia patients who didn't respond to conventional treatments, Zhang Jixian, Director of the Department of Respiratory and Critical Care Medicine at Xinhua Hospital of Hubei Province which is adjacent to the Huanan Seafood Market, received four consecutive cases of pneumonia with unknown cause on December 26. On December 27, Zhang Jixian reported the discovery of four cases of "viral pneumonia with unknown cause" to the hospital leadership who then reported it to the CDC of Jianghan District.

On December 28 and 29, Xinhua Hospital admitted three more patients from Huanan Seafood Market who had similar symptoms of viral pneumonia. According to later reports such as in the Wuhan Evening News, at 1 P.M. on Dec. 29, Xia Wenguang, Vice President of Xinhua Hospital called together ten experts to discuss the seven cases, and all the experts agreed that the situation was unusual, and Xia Wenguang reported the cases directly to the Disease Control Division of the Health Commission at both the provincial and municipal levels. The Public Health Department of Wuhan Central Hospital also submitted their report on the same day. In the same afternoon, the Health Commission's Disease Control Divisions of Hubei Province and Wuhan Municipality notified the provincial, city and district level CDC that following the admission of a number of pneumonia patients with unknown cause at Xinhua Hospital, Wuhan Central Hospital Houhu Campus, who had a history of exposure to a seafood market, it's required to start the emergency response procedure. Hubei Provincial CDC, Wuhan Municipal CDC, in conjunction with CDCs of Jianghan District, Qiaokou District, Dongxihu District, started epidemiological investigation. Huang Chaolin, Vice President of Operations of Wuhan Jinyintan Hospital and others went to Xinhua Hospital to pick up six patients, while Wuhan Tongji Hospital also transferred the aforementioned patient who was the first to undertake genetic testing at the Wuhan Central Hospital to Jinyintan Hospital.

On December 30, the CDCs of the three levels drafted *Report on the Investigation and Handling of Multiple Pneumonia Cases at the Huanan Seafood Market as Reported by Hospitals*. On the same day, Wuhan Municipal Health Commission issued an internal circular mentioning that there had been multiple cases of pneumonia with unknown cause in a number of medical institutions in Wuhan, which were associated with Wuhan Huanan Seafood Wholesale Market, and requesting medical institutions to report similar patients of pneumonia with unknown cause they had received in the previous week.

Together with the WeChat alerts by doctors such as Li Wenliang who had access to the genome sequencing report, this *Urgent Notice on Good Management of the Treatment of Pneumonia of Unknown Cause*, issued by Wuhan Municipal Health Commission, which was triggered by Zhang Jixian's insistence on reporting, was soon exposed online, allowed information about the outbreak that started in Wuhan to reach the outside world for the first time.

Alerts from Shanghai

Another case's specimen of Wuhan Central Hospital came from their Houhu Campus, which is also adjacent to Huanan Seafood Market, and the admission of the patient was one day earlier. The patient, also surnamed Chen and native of Quanzhou of Fujian province, was a 41-year-old business owner at the seafood market, who, after catching a cold on December 20, developed a high fever of 40°C, accompanied with body aches and weakness, coughing and phlegm pus, chest tightness and shortness of breath. The patient was admitted to Wuhan Central Hospital's Houhu Campus on December 26 on the basis of "fever investigation and lung infection". The hospital took a specimen via bronchoscopy, took an extra specimen of his respiratory lavage fluid and kept it in the refrigerator at -80°C for storage.

"The reason why we kept an extra specimen is that we have been cooperating with Shanghai Public Health Clinical Center affiliated to Fudan University (hereinafter referred to as "Shanghai PHC") and Wuhan CDC on a major national science and technology project - China's Major Natural Focal Virus Resources – and the cooperation agreement has been renewed five years in a row. Wuhan CDC is responsible for the collection of clinical specimens and environmental samples in the central China region, which are sent regularly to Shanghai PHC for pathogen testing. They have a biosafety level 3 (BSL-3) laboratory with mNGS and bioinformatics analysis platform, while hospitals like ours are sentinel hospitals of the Wuhan CDC," explained Professor Zhao Su from the Department of Respiratory Medicine of Wuhan Central Hospital.

The specimens were picked up by a chief physician at the Wuhan CDC in the afternoon of December 30. On January 2, another researching staff member at the Wuhan CDC packed the specimen in multiple wraps such as dry ice, iron boxes and foam box before sending it by Railway express mailing to Shanghai, along with other animal specimens. The specimens were received by Professor Zhang Yongzhen's team at the Shanghai PHC on January 3. The Center is affiliated to Fudan University, and Zhang Yongzhen himself is a professor at the Institute of Infectious Disease Prevention and Control of the Chinese Center for Disease Control and Prevention (Chinese CDC), professor at the Institute of Biomedical Research of Fudan University and Shanghai PHC. Over the recent years, he has been engaged in scientific research work on zoonotic diseases and the investigation of major natural focal viral resources in China with the sponsorship of the National Natural Foundation of China, national major special projects and national key research and development programs. Members of his research team includes staff from several hospitals in Wuhan, including Wuhan Central Hospital, Wuhan CDC and the University of Sydney, Australia.

In the early morning of January 5, Zhang Yongzhen's research team detected a novel SARS-like coronavirus from the specimens and obtained the virus' full genome sequence through mNGS; the evolutionary tree drawn from the sequencing data also confirmed that the novel coronavirus discovered in Wuhan had never been seen in history. Shanghai PHC immediately reported it to the supervising departments on the same day, including Shanghai Municipal Health Commission and National Health Commission, reminding them that the new virus was homologous with SARS and should be transmissible via respiratory tract, while recommending appropriate disease control and epidemic prevention measures in public places. On January6, Chinese CDC initiated a level 2 internal emergency response procedure.

"We have been working with Wuhan CDC, Wuhan Central Hospital among others to collect new natural focal viruses, which is part of our major national project, and the use of the P3 laboratory was also accredited by China National Accreditation Service for Conformity Assessment." A professor at Shanghai PHC told Caixin, "When we are doing routine scientific research, if we happen to discover anything significant, we shall immediately report it to our upper-level authorities."

At least nine specimens were sampled and sent for testing before the end of last year

As confirmed by Caixin reporters, several other genome sequencing companies obtained specimens of pneumonia with unknown cause from hospitals in Wuhan, almost immediately after Guangzhou Vision Medical and Beijing CapitalBio MedLab, including the industry's leader, BGI Genomics, who received a genome sequencing order from a local hospital in Wuhan on Dec. 26, 2019. The specimen's gene sequencing results completed by BGI Genomics on Dec. 29 showed that the virus was 80% identical to the gene sequence of SARS, while it was a coronavirus previously unknown, instead of SARS. BGI Genomics also tested the case with their SARS test kit and the result was negative, confirming the elimination of SARS.

A staff member of BGI Genomics told Caixin that when they sequenced specimens from cases of viral pneumonia with unknown cause in late December, they were unaware that the virus had

clinically caused infection of many people, and there had even been aggregational infections in a same family. "We are a technology company that does genome sequencing. We receive many sequencing orders on a daily basis. We have been engaging with a large number of viruses, and we may find many new viruses. In the case of coronaviruses, there are many types. There were only six coronaviruses associated with people till then, including the SARS virus in the past. The only ones that are more infectious to human are SARS and MERS. At that time, we had no idea whether this virus was 'good' or 'bad'."

BGI Genomics cooperates with local hospitals in Wuhan year in year out. As per Caixin reports' investigation, local hospitals in Wuhan commissioned at least more than 30 specimens of difficult pneumonia cases to BGI Genomics in December 2019 for sequencing. Out of the specimens, BGI Genomics found a total of three cases of pneumonia that were identified as infection by the novel coronavirus, including this one case on December 26 along with the other two cases whose specimens were received on December 29 and 30 respectively. They mixed the three SARS-like coronaviruses, that is, they combined the fragments of the three virus genome sequences to form a mixed virus genome sequence. On January 1, the test report of the three specimens were submitted to Wuhan Municipal Health Commission, and on January 3, BGI Genomics performed high-depth full genome sequencing on the viruses in all three specimens.

Caixin reporters found that, as of January 19, 2020, there were new coronavirus genome sequences of 13 specimens uploaded onto the GISAID platform. Apart from three of them from Japan and Thailand, all the remaining ten were uploaded by Chinese research institutes. In terms of sampling time, the earliest one is the aforementioned case collected on December 24, 2019 and uploaded by the Institute of Pathogen of Chinese Academy of Medical Sciences, while eight other specimens were collected on December 30, which were respectively 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, Chinese CDC (2 entries). In addition, the Institute of Prevention and Control of Viral Diseases of Chinese CDC also uploaded a genome sequence of the specimen which was collected on January 1, 2020.

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

With an industry average testing cycle of three days, the genome sequencing results of the above eight specimens collected on December 30 should have been available by around January 2. In an open letter entitled "Wuhan Institute of Virology is fully engaged in scientific research on novel coronavirus pneumonia", Wuhan Institute of Virology of Chinese Academy of Sciences stated that the Institute of Virology received a specimen of the pneumonia with unknown cause from Jinyintan Hospital on the night of December 30, and after 72 hours of tackling of key issues, the full genome sequence of the novel coronavirus was determined on January 2, 2020 and was uploaded to GISAID on January 11.

The aforementioned paper published in Chinese Medical Journal (English version) also indicated that alveolar lavage fluid samples from the five patients were collected and sent for 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 Huanan Seafood Market.

In addition to the 65-year-old patient, the specimen of three of the five patients was collected on December 30, 2019. Among them, Patient #2, who was a 49-year-old woman working at Huanan Seafood Market, presented with high fever and dry cough on December 22, developed dyspnea and was admitted to the hospital five days later and was transferred to the ICU on December 29. Patient #3, also a female, 52 years old, was admitted to hospital because of symptoms on December 22 and

hospitalized on 29th, although she did not report any exposure to the seafood market. Patient #4 was a 41-year-old man who presented with high fever and dry cough starting from December 16 and was hospitalized on the 22nd. He, who had no known history of exposure to Huanan Seafood Market, is obviously the aforementioned Wuchang accountant who was received by Wuhan Central Hospital. Patient #5 had his bronchoalveolar lavage fluid sampled on January 1, 2020. The patient, a 61-year-old male who worked at Huanan Seafood Market, had chronic liver disease and abdominal myxoma, was admitted to a local hospital after 7 days of fever, cough, and dyspnea. He was given an emergency treatment using ECMO starting on January 2, and later died.

The paper claims that a novel coronavirus was thus identified in the laboratory, showing 79.0% nucleotide identity with the sequence of SARS virus; the virus is phylogenetically closest to a bat SARS-like coronavirus, but is in a separate clade, which falls under the β virus strain sequences. After conducting virus isolation for morphological confirmation and serological testing, the new pathogen was finally confirmed to be a novel coronavirus. The amino acid sequence of the virus' receptor-binding domain resembles that of SARS coronavirus, indicating that both viruses might bind to the same receptor on human cells.

Looking back at the days between the end of December 2019 and the beginning of January 2020, it should have been a critical period in determining the fate of countless people. But at that time, the public was still unaware of the consequences that this virus would later trigger.

A gene sequencing company source revealed that on January 1, 2020, he received a phone call from an official of Hubei Provincial Health Commission, informing him that testing of further novel coronavirus pneumonia case specimens commissioned by Wuhan must be stopped, and that existing case specimens must be destroyed, no information about the specimen shall be disclosed to the public, and no relevant papers and related data shall be released to the public, "if you detect it at a later date, you must report to us."

The General Office of the National Health Commission issued a circular on January 3rd, entitled Notice on Strengthening the Management of Biological Sample Resources and Related Scientific Research Activities in the Prevention and Control of Major Outbreaks of Infectious Diseases. This document, numbered NHC GO Science and Education (2020) No.3, stated that until further clarification of the pathogen information and based on the currently available information on etiology, transmission, pathogenicity and clinical data, the recent specimens of pneumonia cases in Wuhan shall be temporarily managed as highly pathogenic microorganisms (Class II). The transportation of related specimens should be carried out according to the requirements of the Regulation on the Transportation of Highly Pathogenic Microbes (Viruses) or Samples that are Infectious to Human Beings issued by the former Ministry of Health; pathogen-related experimental activities should be carried out in biosafety laboratories with corresponding protection levels.

Document No. 3 further stipulated that when all relevant institutions shall provide biological samples to designated pathogen testing institutions for pathogenic testing, and proper handover procedures should be followed in accordance with the requirements of the health and medical administrative authorities of provincial level and above; that biological samples and related information shall not be provided to other institutions and individuals without authorization or approval; institutions and individuals who have obtained biological samples of relevant cases from relevant healthcare institutions shall immediately destroy the samples on site or send the samples to the nationally designated storage facilities for safekeeping, while properly preserving the records of testing activities and information on the testing results, and during the epidemic prevention and control, the information generated by various institutions undertaking pathogenic testing tasks is regarded as a special public resource, no institution or individual may release information on pathogenic testing or experimental results without authorization, relevant papers and results must be published with the approval of the commissioning parties.

The document did not specify which institutions were regarded as the "designated pathogen testing institutions". A virologist revealed that even the Wuhan Institute of Virology of Chinese

Academy of Sciences was once requested to stop pathogen testing and destroy existing specimens, "because according to the current *Law on the Prevention and Control of Infectious Diseases*, to perform lab testing, diagnosis, pathogenic identification of infectious diseases is the legal responsibility of disease prevention and control agencies at all levels, and only the national and provincial level CDCs are authorized to perform pathogenic identification of infectious diseases. Wuhan Institute of Virology of Chinese Academy of Sciences is obviously not included in this list, let alone those unauthorized commercial research institutions".

Maybe for that reason, the Institute of Virology of the Chinese Academy of Sciences, who worked day and night after receiving the virus specimens on December 30, in order to isolate the virus on January 1, 2020, complete the genome sequencing of the virus on January 2, isolate the virus strain on January 5, and complete the national virus repository and standardized storage on January 9, only announced their research to the public until February, in a few isolated words and statements in the face of rumors and denunciations from the outside.

CCTV reported on January 9 that the Chinese CDC-led "Panel for the Preliminary Assessment of Wuhan Viral Pneumonia Pathogen Testing Results" determined that the pathogen was a novel coronavirus, "As of 21:00, January 7, 2020, a novel coronavirus was detected in the laboratory, and the full genome sequence of the virus was obtained. A total of 15 positive results for the novel coronavirus were detected with nucleic acid detection method, and the virus was isolated from one of the positive patient's specimens, indicating a typical coronavirus morphology under electron microscopy."

On January 11, Zhang Yongzhen's research team shared the virus genome sequence information on the website of the Virology Organization (Virologic.org) and GenBank, becoming the first team in the world to publish the virus sequence.

In the evening of the same day, the National Health Commission announced that China would share the genome sequence of the novel coronavirus with the WHO. Five other viral genome sequences from different patients were released by a team led by the National Health Commission on the platform of Global Initiative on Sharing All Influenza Data (GISAID). As for the question from which institution came this novel coronavirus genome sequence information shared with the WHO, Gao Fu, Director of Chinese CDC, responded to our Caixin reporter that the genome sequence came from three institutions, namely Chinese CDC, Chinese Academy of Medical Sciences and Chinese Academy of Sciences, and the task was tackled by joint efforts. According to the WHO, it has obtained further detailed information about viral pneumonia with unknown cause in Wuhan from China's National Health Commission, including information on the genome sequence of the novel coronavirus detected from the cases, 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 on the scientific crown, as 15 days have passed since the first case of the novel coronavirus identified through genome sequencing.

On January 11, Bulletin of Wuhan Health Commission, which had stopped updating for many days, changed for the first time the name of "viral pneumonia with unknown cause" to "novel coronavirus-infected pneumonia", and stated that, as of 24:00 on January 10, 2020, 41 cases had been preliminarily diagnosed as novel coronavirus pneumonia. On the same day, the provincial NPC and CPPCC of Hubei convened. By the time of the conclusion of the meetings on January 17, this number didn't increase.

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