MINISTRY OF HEALTH
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18 November 2020

[redacted]

By email: [redacted]
Ref: H202007576

Dear [redacted]

Response to your request for official information

Thank you for your request under the Official Information Act 1982 (the Act) on 5 October 2020 for information relating to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).

Under the Act, I will respond to each part of your request in turn.

1. *A valid peer reviewed empirical scientific study, confirming the identification, using either Koch's postulates or River's protocol, by isolation, visualisation and purification of SARS CoV-2.and/or Covid-19*

The following steps have been undertaken to provide assurance that SARS-CoV-2 is the virus that causes the severe respiratory illness known as COVID-19.

1. The full genome of the virus was sequenced which has enabled accurate identification of the type of virus as a coronavirus. Its RNA genome provides a way to explore its evolutionary links to other coronaviruses.
2. Culture of the virus (within a laboratory setting) was performed confirming the ability of the virus to infect and replicate in human cells.
3. Cell culture studies all demonstrated that the virus is able to cause damage to human cells (called the cytopathogenic effect or CPE)
4. Virus that is grown in culture is able to infect animals and cause disease.

Further information about studies into SARS-CoV-2 (with reference to Koch's postulates) can be found at the following link: www.biorxiv.org/content/10.1101/2020.02.07.939389v3.full.

2. *Scientific proof that an accurate diagnostic test is being used to identify a virus or disease (SARS CoV-2 and/or Covid-19) and not just RNA sequences, or Chromosome 8.*

The coronavirus SARS-CoV-2 has an RNA genome, therefore by definition it is "an RNA sequence". The published genome of the virus is distinct from other viruses and can easily be differentiated from Chromosome 8 if you are referring to the human genome. The 'scientific proof' is that the Polymerase Chain Reaction (PCR) test that has been designed to detect SARS-CoV-2 has been validated by labs around the globe to be specific for the viral target and not other genomic sequences. PCR tests have been sequenced to ensure they detect the intended target. The Institute of Environmental Science and Research (ESR) maintains the end-to-end system for testing, validating, analysing and reporting on COVID-19 in New Zealand. Further information on ESR's testing and validations can be found at the following link: https://www.esr.cri.nz/our-services/testing/novel-coronavirus/

3. *Proof that any test in use (Covid-19) has been compared to a gold standard.*

A 'gold standard' test is used in a laboratory setting to identify the best available test at the time. It is important to recognise that there is no perfect test. Each test will have been explored for its sensitivity and specificity.

In relation to COVID-19, the RT-qPCR test for viral RNA is considered as 'gold standard'. This test has been validated by several means including as a purified virus. However, the most definitive comparison is when PCR's are sequenced as they are mapped to the SARS-CoV-2 viral genome. This mapping is definitive proof that the test is picking up the target SARS-CoV-2 and no other samples.

Further information relating to SARS-CoV-2 and Koch's postulates is attached to this letter as Appendix One.

I trust this information fulfils your request. Under section 28(3) of the Act you have the right to ask the Ombudsman to review any decisions made under this request.

Please note that this response, with your personal details removed, may be published on the Ministry's website.

Yours sincerely

Rebecca Drew
Group Manager, COVID-19 Science and Insights
COVID-19 Health System Response

SARS-CoV-2 is the virus that causes COVID-19

The science behind the association of a specific microorganism with a specific disease has evolved considerably since Koch's postulates were published. Changes to the concept of infectious diseases, the role that host immunity plays in the development of symptomatology, and the revolution in laboratory testing and genome sequencing have replaced the requirement for infectious agents to cause disease in healthy humans in order to prove causation. Taken together, there is an overwhelming body of evidence (including satisfying Koch's postulates) that the disease known as COVID-19 is caused by the SARS-CoV-2 virus.

The relationship between SARS-CoV-2 and COVID-19

In late 2019 a cluster of cases of severe pneumonia in Wuhan, China, was identified through a local severe illness reporting system which was set up after the SARS outbreak. On 31 December the WHO China country office was informed of the cases and on 3 January 2020, 44 cases of pneumonia of unknown cause were reported of whom 11 were very ill. At that time the infectious agent had not been identified. Respiratory samples from the symptomatic individuals were tested and a corona virus, similar to SARS-CoV was identified in all the patients. The virus was named SARS-CoV-2. The following steps have been undertaken to provide assurance that SARS-CoV-2 is the virus that causes the severe respiratory illness known as COVID-19.

- The full genome of the virus was sequenced which has enabled accurate identification of the type of virus as a coronavirus. Its RNA genome provides a way to explore its evolutionary links to other coronaviruses.
- Culture of the virus (within a laboratory setting) was performed confirming the ability of the virus to infect and replicate in human cells.
- Cell culture studies all demonstrated that the virus is able to cause damage to human cells (called the cytopathogenic effect or CPE).

- Virus that is grown in culture is able to infect animals and cause disease.

Koch's Postulates

Approximately 200 years ago, a German physician named Robert Koch proposed that four conditions were required to demonstrate the causal relationship between a particular microorganism and disease.

These became known as Koch's postulates, which are as follows:

1. The microorganism must be found in diseased but not healthy individuals;
2. The microorganism must be cultured from the diseased individual;
3. Inoculation of a healthy individual with the cultured microorganism must recapitulated the disease; and finally
4. The microorganism must be re-isolated from the inoculated, diseased individual and matched to the original microorganism.

These criteria were further updated in 1937 by Rivers for viral diseases to allow for the fact that viruses are unable to survive without a host [1].

1. Regarding the first postulate, the concept of an infectious agent has markedly changed over the last 100+ years. In particular it is increasingly recognised that different individuals will have different responses to a particular micro-organism. While some people develop a life threating illness, others will remain without symptoms from a given illness. Koch himself recognised that there were asymptomatic cases of cholera. The risk of becoming ill from a particular microorganism then becomes a matter of probabilities, not an "all or none" phenomenon, as originally implied in Koch's postulates. Although not all individuals will develop symptoms of COVID-19, any individual infected with SARS-CoV-2 (asymptomatic or not) is able to pass the virus on to other individuals.

2. Most viruses can be cultured in specifically designed laboratory 'medium' that promotes their growth. Because viruses require a host cells to grow and reproduce, the type of cell required for culture will vary. However, viruses are not always easy to grow in culture and therefore to identify the presence of virus other means may be used which are more rapid, reliable and cost-effective. In particular, genetic tests are often used to identify sections of RNA which are unique to a specific virus.
3. The inoculation of a potentially deadly virus into healthy individuals is unnecessary to identify a particular virus as the cause of a disease. This step in Koch's postulates is usually determined by the observation of natural infection in groups of individuals, in cell culture or in animals. However, human challenge studies are being undertaken in young health individuals in order to accelerate the development of vaccines [2] and fulfils the third postulate.
4. The identification of the same virus in groups of infected individuals (clusters), as identified by genomic testing validates this point.

Supporting information/evidence

[1] Rivers TM. Viruses and Koch's Postulates. J Bacteriol. 1937;33(1):1-12. PubMed PMID: 16559982.
[2] Eyal N, Lipsitch M, Smith PG. Human Challenge Studies to Accelerate Coronavirus Vaccine Licensure. The Journal of Infectious Diseases. 2020;221(11):1752-6.