FOI Request to Finland's Institute for Health and Welfare (THL)

and

subsequent complaint to

The Finnish National Board on Research Integrity

Hyvä vastaanottaja,

Tämä on julkisuuslakiin (http://www.finlex.fi/fi/laki/ajantasa/1999/19990621) perustuva tietopyyntö.

Vuonna 2020 WHO julisti maailmanlaajuisen koronaviruspandemian.
Pyydän nähtäväksi ja julkisesti julkaistavaksi todisteet koronaviruksen (Sars-Cov-2) täydellisestä eristämisestä, niin että virus on todella eristetty kaikesta muusta, soluista, kudoksista yms.
Lisäksi pyydän valokuvan eristetystä kyseisestä viruksesta, karakterisaatio sen biokemiallisesta rakenteesta, sen genomi sekvensoituna sekä määrittely mistä proteiineista kyseinen virus koostuu.
Samalla pyydän todisteet siitä, että juuri tuo kyseinen virus aiheuttaa ihmisissä oireita.

Pyydän toimittamaan aineiston jäljennöksen viivytyksettä sähköisessä muodossa liitetiedostona vastauksena tähän viestiin. Tietoaineistot avoimena rakenteellisena datana, eli .xls-, .csv-, .sql-, tai muussa rakenteellisessa muodossa. Dokumentit pyydän uudelleenkäytettävässä muodossa, kuten .doc, odf-, .ppt tai pdf/a-muodossa.
Olisi toivottavaa että aineisto olisi julkisuuslain 20 § mukaan vastedes saatavilla organisaationne web-sivulla.
Pyydän toimittamaan tiedot julkl 16 § mukaisesti pyydetyllä tavalla pyydetyssä muodossa tai perustelemaan sähköpostitse viivytyksettä mikäli on syy toimittaa toisella tavalla.
Huomioittehan että julkl. 34§ mukaan asiakirjan antamisesta ei peritä maksua, kun julkinen sähköisesti talletettu asiakirja lähetetään tiedon pyytäjälle sähköpostitse.
Pyydän toimittamaan tiedot viivytyksettä julkl. 14.4§ mukaisesti, enintään 2 viikon määräajan kuluessa, tai perustelemaan ensi tilassa mikäli tietojen toimittamiseen tarvitaan pidempi kuukauden toimitusaika.
Mikäli pyyntöä ei voida täyttää, pyydän 14.4§ mukaisessa 2 viikon määräajan kuluessa valituskelpoisen päätöksen.
Pyydän viivytyksettä kuittaamaan viestin vastaanotetuksi ja kertomaan asian diaarinumeron.

Ystävällisin terveisin,
[redacted]

Hyvä [redacted]

viitaten 6.9.2021 Terveyden ja hyvinvoinnin laitokselle (THL) lähettämäänne tietopyyntöön (THL/4635/3.10.00/2021), THL ilmoittaa vastauksenaan seuraavaa:

Viruksen eristämisestä puhutaan silloin, kun potilasnäyte istutetaan soluviljelmään ja virus alkaa siinä lisääntyä. Koronavirusdiagnostiikassa viruseristys ei ole rutiinitoimenpide. Viruseristys vaatii erityisturvatason laboratorion ja se on aikaa vievä toimenpide. Suomessa koronaviruksia on eristetty kuitenkin sekä diagnostiikan kehittämistarkoituksiin että virusten ominaisuuksien tutkimista varten. Ohessa tieteellinen julkaisu Suomen ensimmäisestä koronatapauksesta tammikuulta 2020, jolloin koronavirus eristettiin Suomessa ensimmäisen kerran. Sivulla 2 kappaleessa SARS-CoV2/Finland/1/2020 virus isolation kerrotaan erityisesti viruksen eristämisestä soluviljelmässä.

Elektronimikroskooppikuvia koronaviruksesta on runsaasti löydettävissä erilaisista kuvapankeista, esim. https://www.niaid.nih.gov/news-events/novel-coronavirus-sarscov2-images.

Tämän linkin kautta pääsette tarkastelemaan SARS-CoV-2 -viruksen rakennetta: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7164637/pdf/367_1260.pdf

Teillä on mahdollisuus saattaa asia viranomaisen ratkaistavaksi ilmoittamalla siitä sähköpostitse THL:n kirjaamoon kirjaamo@thl.fi, jolloin saatte asiasta valituskelpoisen hallintopäätöksen.

Ystävällisin terveisin

Hanna Kaarre

toimeksi saaneena

AUTO-TRANSLATION

Dear Recipient,

This is a request for information based on the Publicity Act (http://www.finlex.fi/fi/laki/ajantasa/1999/19990621).

In 2020, the WHO declared a global coronary virus pandemic. I request that evidence of complete isolation of the coronavirus (Sars-Cov-2) be seen and made public so that the virus is indeed isolated from all other cells, tissues, etc. In addition, a photo of the virus isolated that virus consists of. At the same time, I am asking for evidence that it is that virus that is causing the symptoms in humans.

Please provide a copy of the material in electronic form without delay as an attachment in response to this message. Data sets as open structured data, ie .xls, .csv, .sql, or other structured format. I request documents in a reusable format, such as .doc, odf, .ppt, or pdf / a.

It would be desirable for the material to be available on your organization's website from now on, in accordance with section 20 of the Public Access to Information Act.

If the request cannot be complied with, I will request an appealable decision within the 2-week period pursuant to section 14.4. Please acknowledge receipt of the message without delay and state the diary number.

Best regards,
[redacted]

Dear [redacted],

referring to your request for information sent to the National Institute for Health and Welfare (THL) on 6.9.2021 (THL / 4635 / 3.10.00 / 2021), THL replies as follows:

Virus isolation is when a patient sample is planted in a cell culture and the virus begins to multiply in it. In coronavirus diagnostics, virus isolation is not a routine procedure. Virus isolation requires a special level of security in the laboratory and is a time consuming operation. In Finland, however, coronaviruses have been isolated both for diagnostic development purposes and for studying the properties of the viruses. Attached is a scientific publication on the first corona case in Finland in January 2020, when the coronavirus was isolated for the first time in Finland. On page 2, section SARS-CoV2 / Finland / 1/2020 virus isolation describes in particular the isolation of the virus in cell culture.

Electron micrographs of the coronavirus can be found in abundance in various image banks, e.g., https://www.niaid.nih.gov/news-events/novel-coronavirus-sarscov2-images.

Use this link to view the structure of the SARS-CoV-2 virus:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7164637/pdf/367_1260.pdf

You have the opportunity to refer the matter to THL by e-mail to the registry office at kirjaamo@thl.fi, in which case you will receive an appealable administrative decision.

Yours sincerely,

Hanna Kaarre

Rapid communication

Serological and molecular findings during SARS-CoV-2 infection: the first case study in Finland, January to February 2020

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Citation style for this article:
Haveri Anu , Smura Teemu , Kuivanen Suvi , Österlund Pamela , Hepojoki Jussi , Ikonen Niina , Pitkäpaasi Marjaana , Blomqvist Soile , Rönkkö Esa , Kantele Anu , Strandin Tomas , Kallio-Kokko Hannimari , Mannonen Laura , Lappalainen Maija , Broas Markku , Jiang Miao , Siira Lotta , Salminen Mika , Puumalainen Taneli , Sane Jussi , Melin Merit , Vapalahti Olli , Savolainen-Kopra Carita . Serological and molecular findings during SARS-CoV-2 infection: the first case study in Finland, January to February 2020. Euro Surveill. 2020;25(11):pii=2000266. https://doi.org/10.2807/1560-7917.ES.2020.25.11.2000266

Article submitted on 06 Mar 2020 / accepted on 18 Mar 2020 / published on 19 Mar 2020

The first case of coronavirus disease (COVID-19) in Finland was confirmed on 29 January 2020. No secondary cases were detected. We describe the clinical picture and laboratory findings 3–23 days since the first symptoms. The SARS-CoV-2/Finland/1/2020 virus strain was isolated, the genome showing a single nucleotide substitution to the reference strain from Wuhan. Neutralising antibody response appeared within 9 days along with specific IgM and IgG response, targeting particularly nucleocapsid and spike proteins.

On 31 December 2019, a cluster of pneumonia cases of unknown aetiology was reported in Wuhan, Hubei Province, China [1]. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was isolated by Chinese scientists on 7 January 2020. To date, the SARS-CoV-2 virus causing the coronavirus disease (COVID-19) pandemic is spreading throughout the world.

Here we describe the timeline of events around the first COVID-19 case imported to Finland, and summarise the clinical, molecular and serological data. Successful SARS-CoV-2/Finland/1/2020 isolation enabled us to use the cytopathic effect (CPE)-based microneutralisation (MN) assay to detect SARS-CoV-2-specific neutralising antibody levels. Diagnostic serum samples of the case and three close contacts were analysed and compared with serum samples from the Finnish population collected in 2019.

Clinical presentation and laboratory confirmation of the case

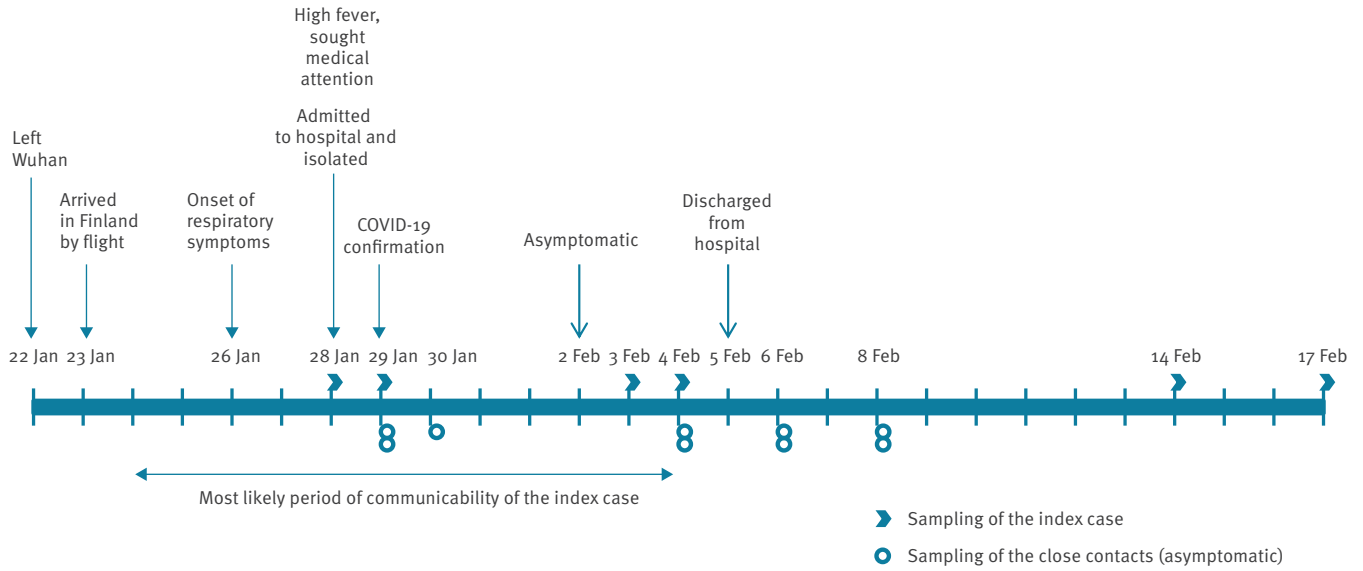
The first COVID-19 case in Finland was a female Chinese tourist in her 30s, who had left Wuhan on 22 January and arrived in Finland on 23 January. Her first symptoms were a runny nose on 26 January and nausea on 27 January. Because of high fever (39 °C), weakness and cough she sought medical attention on 28 January. Suspicion of COVID-19 led to her direct transfer to the Lapland Central Hospital in Rovaniemi, where she was isolated and sampled on 28 and 29 January for laboratory confirmation of SARS-CoV-2 infection (Figure 1). SARS-CoV-2 infection was confirmed from nasopharyngeal samples on 29 January by the Helsinki University Hospital Laboratory (HUSLAB), and further confirmed at the Finnish Institute for Health and Welfare (THL) (Table). Both laboratories performed real-time RT-PCR testing for three targets: the envelope (E), the RNA-dependent RNA polymerase (RdRp) and the nucleocapsid (N). Primers and probes were based on the Corman et al. method [2]. Cycle threshold (Ct) values above 37 were considered negative.

The case had mild symptoms throughout the isolation period. She was tested PCR-negative in 3 and 4 February samples and, as considered asymptomatic, discharged from hospital on 5 February. One additional sample for serology and PCR was taken on 14 and 17 February, respectively.

Altogether 21 close contacts were identified of whom we could reach 17. Fourteen were still in Finland and

Figure 1

Timeline of events around the first COVID-19 case imported to Finland, January–February 2020



COVID-19: coronavirus disease.

placed in quarantine for 14 days. Information about three close contacts that had left the country was communicated to the competent authorities in their respective countries. For the remaining four close contacts, we had no contact details. Two of the 21 close contacts were closely co-exposed and therefore sampled on Days 4, 10, 12 and 14 after the first symptoms of the index case. Follow-up of all contacts ended on 11 February without secondary transmission events.

SARS-CoV-2/Finland/1/2020 virus isolation

The SARS-CoV-2 virus SARS-CoV-2/Finland/1/2020 was isolated in a biosafety level 3 (BSL-3) laboratory in Vero E6 cells from the Day 4 nasopharyngeal swab (NPS) and nasopharyngeal aspirate (NPA) specimens (Table). The samples were inoculated into the cells for 1 h at 37 °C and 5% CO_2 and fresh culture medium (Eagle›s minimum essential medium (EMEM) supplemented with 2% fetal bovine serum (FBS), 0.6 µg/mL penicillin, 60 µg/mL streptomycin, 2 mM L-glutamine, 20 mM HEPES) were added for incubation. On the 4th day of incubation, half of the cultures were blind-passaged onto fresh Vero E6 cells and the rest of original passages were incubated further. After 4 days incubation a clear CPE was detected in the NPA-originated passage 2. The propagation of stock virus was done by passaging a low virus dose once again in Vero E6 cells, and virus culture was harvested on the 3rd day. Virus concentration was followed by RT-PCR. The Ct value for virus passage 1 on the 6th day of incubation was 17.65 and for passage 2 on the 2nd day, before any CPE was 20.63, whereas those of the NPS specimen remained at Ct values between 35 and 36.

SARS-CoV-2/Finland/1/2020 whole-genome sequencing

Nearly the complete coding region of SARS-CoV-2 (GenBank accession number: MT020781) was sequenced from the NPS collected on Day 4 (Table) and the complete coding region was sequenced from the virus isolate obtained after three passages in Vero E6 cells. The virus had 1 nt substitution C21707T compared with the reference strain Wuhan-Hu-1 collected in Wuhan China, December 2019 (NC_045512) [3] which had led to a histidine to tyrosine (H49Y) substitution in the N-terminal domain of the spike glycoprotein.

Antibody response during the SARS-CoV-2 infection

Serum samples were collected from the index case on Days 4, 9, 10 and 20 from onset of the first symptoms (Figure 1). Presence of serum IgM and IgG antibodies against SARS-CoV-2 was analysed by immunofluorescence assays (IFA) based on Vero E6 cells infected with passage 4 of the patient's isolate SARS-CoV-2/Finland/1/2020 virus and transferred onto microscope slides and fixed with acetone (Figure 2). Serum samples from the index case were serially diluted and incubated for 2 h for IgM and 30 min for IgG. Antibodies were visualised with fluorescein isothiocyanate (FITC)-conjugated anti-human IgM or IgG antibodies. While the antibodies were undetectable on Day 4 after onset of symptoms, IgG titres rose to 80 and 1,280 and IgM titres to 80 and 320 on Days 9 and 20, respectively (Table). Random serum samples from staff members of the University of Helsinki (n = 19) did not show specific binding at dilutions greater than 20 (Figure 2).

Mock- and SARS-CoV2-infected Vero E6 cells collected on Day 6 post infection were lysed in Laemmli sample

Table

Laboratory data of the first case of SARS-CoV-2 infection, Finland, January–February 2020

Sampling day Day since the first symptoms	Specimen	PCR done at	E	RdRp	N	MN	IgM	IgG
28 Jan 2020 Day 3	NPS	HUS	ND	ND	ND	NA	NA	NA
		THL	30.49	30.48	31.59			
29 Jan 2020 Day 4	NPA	HUS	31.18	27.56	28.29	NA	NA	NA
		THL	27.13	28.43	28.73			
	NPS	HUS	28.15	27.13	28.82	NA	NA	NA
		THL	29.59	30.87	31.78			
	Serum	THL	Neg	Neg	Neg	<4	<20	<20
		UH	Neg	Neg	Neg			
03 Feb 2020 Day 9	NPS	HUS	Neg	Neg	Neg	NA	NA	NA
		THL	Neg	Neg	Neg			
	Serum	UH	ND	Neg	Neg	60	80	80
04 Feb 2020 Day 10	NPS	HUS	Neg	Neg	Neg	NA	NA	NA
		THL	Neg	Neg	Neg			
	Serum	ND	ND	ND	ND	72	160	160
14 Feb 2020 Day 20	Serum	UH	Neg	Neg	Neg	160	320	1,280
17 Feb 2020 Day 23	NPS	HUS	Neg	Neg	Neg	NA	NA	NA
		THL	Neg	Neg	Neg			

E: envelope protein gene; HUS: Helsinki University Hospital Laboratory; IgG: immunoglobulin G; IgM: immunoglobulin M; MN: microneutralisation test; N: nucleocapsid protein gene; NA: not applicable; ND: not done; Neg: negative; NPA: nasopharyngeal aspirate; NPS: nasopharyngeal swab; RdRp: RNA-dependent RNA polymerase gene; RT-PCR: reverse-transcription PCR; THL: Finnish Institute for Health and Welfare; UH: University of Helsinki.

buffer, and Western blotting (WB) of lysates was performed as described previously [4]. At 1:200 dilution, the convalescent serum on Day 20 identified SARS-CoV2 N, S and E protein bands (Figure 3). At higher exposure, all bands were detectable even at 1:1,600 serum dilution (Figure 3).

SARS-CoV-2-specific neutralising antibody levels were measured in duplicate with the MN test in a BSL-3 laboratory. The serum samples were heat-inactivated at 56 °C for 30 min and 2-fold serially diluted starting from 1:4 in EMEM supplemented with 2% of heat-inactivated FBS and antibiotics. Fifty plaque□forming units (PFU) of the SARS-CoV-2/Finland/1/2020 strain were added to the serum dilutions and incubated for 1 h at 37 °C. Vero E6 cells (5×10^4/well) were added to the virus–serum mix, and the mixture was incubated in 96-well plates for 4 days at 37 °C with 5% CO_2. Neutralisation was assessed by CPE. The neutralisation endpoint was determined as the 50% endpoint of the serum that inhibited the SARS-CoV-2 infection observed by CPE of inoculated cells.

Diagnostic serum samples from the index case and her three asymptomatic close contacts were studied with the MN test. During the acute phase of infection, no neutralising antibodies were detected. The patient seroconverted for neutralising antibodies between Day 4 and 9, with the titre increasing to 160 on Day 20 (Table). The serum specimens were confirmed not to be toxic or infective to the cells as such.

Serum samples taken from the three close contacts tested negative in MN test. We also tested serum samples collected in 2019 from 83 Finnish subjects aged 4 to 89 years and all tested negative. Sera known to be positive for IgG against human coronavirus OC43 and 229E [5] and rabbit or guinea pig antibody against SARS-CoV N protein [6] could not neutralise the virus.

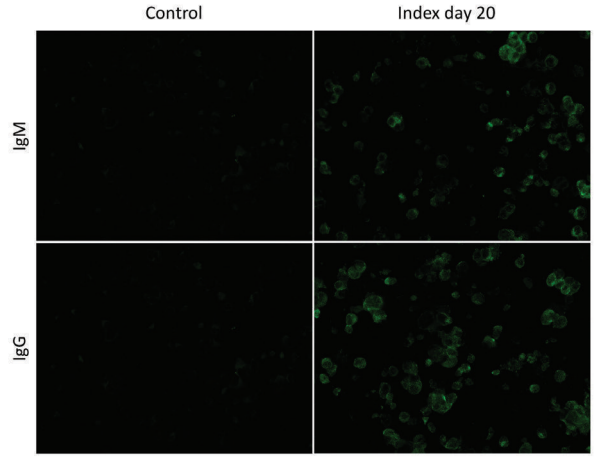
Ethical statement

The investigations were carried out in accordance with the General Data Protection Regulation (Regulation (EU) 2016/679 and Directive 95/46/EC) and the Finnish Personal Data Act (Finlex 523/1999) The Finnish Communicable Diseases Act (Finlex 1227/2016) allows sampling for diagnostic and surveillance purposes.

The convalescent serum sample was obtained on 14 February through informed consent of the patient and research permits (TYH2018322, TYH2019263) from the Helsinki University Hospital Laboratory.
Finnish population serum samples were collected during 2019. The study protocol was approved by the Ethics Committee of the Department of Medicine, Helsinki University Hospital (Permission 433/13/03/00/15).

Figure 2

Immunofluorescence assay of serum samples, COVID-19 index case, Finland, January–February 2020



COVID-19: coronavirus disease 2019.

Anti-SARS-CoV-2 IgM and IgG antibodies were detectable by immunofluorescence assay in samples from Days 9, 10 and 20 after onset of illness. Both IgM and IgG were found at a titre of 80 on Day 9, titres on Day 20 were 320 and 1,280. As an example, dilutions 1:20 and 1:160 from the Day 20 sample are shown for, respectively, IgM and IgG of the index case. Dilution 20 shown for the control serum.

Serum samples of University of Helsinki staff members were used under informed consent.

Discussion

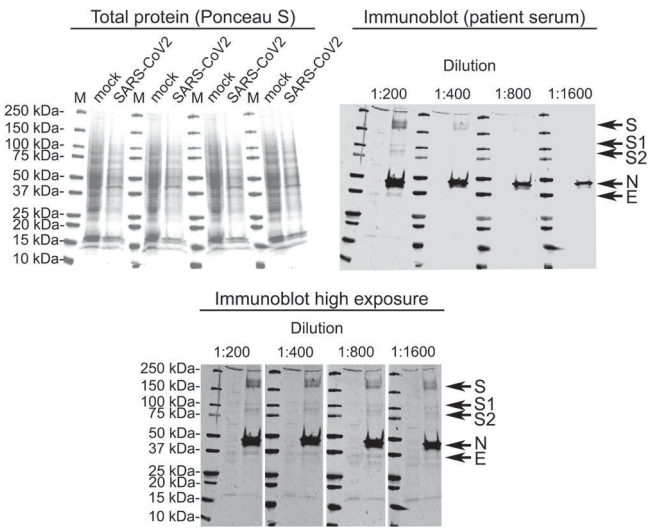
In the early phase of the COVID-19 outbreak, confirmed cases outside China were mostly imported among travellers from Wuhan [7]. The first case in Finland was detected on 29 January among the first imported cases in Europe. The case presented mild symptoms without pneumonia: runny nose, nausea, high fever, cough, muscular weakness and fatigue. No secondary transmission events were detected despite active follow-up by the Lapland Hospital district and THL.

As at 17 March 2020, 358 additional laboratory-confirmed cases of COVID-19 have been detected in Finland. Many of them are travel-related (mostly from northern Italy and Austria) but there is also local transmission from the travel-related cases. The risk of widespread national community transmission of COVID-19 infection in the European Union, European Economic Area and the United Kingdom in the coming weeks is considered high by the European Centre for Disease Prevention and Control [8].

The sequence of the viral genome of the patient was nearly identical to the reference strain from Wuhan, reflecting an early importation from China. Later sequence information in Finland (up to 2 March) showed clustering with strains circulating in Italy (see nextstrain.org/ncov) [9].

Figure 3

Western blot of mock- and SARS-CoV-2 infected Vero E6 cells using patient serum collected 20 days after onset of symptoms, Finland, January–February 2020



Top left panel: total protein staining (Ponceau S) of the nitrocellulose membrane before probing. Top right panel: strips probed with different dilutions of the patient serum at low exposure. Bottom panel: the same membranes individually contrasted for higher band intensity. The arrows indicate SARS-CoV-2 proteins, the labelling assumes that the migration of SARS-CoV-2 proteins was similar to that of Vero E6-expressed SARS-CoV proteins [23]. The bands migrating at ca 110 and 90 kDa probably represent S1 and S2, respectively. Marker M: Precision Plus Dual Colour Standards (Bio-Rad). The detection was done using Odyssey Infrared Imaging System (LI-COR) using goat anti-human IR800 conjugate at 1:10,000 dilution.

Current guidelines from the World Health Organization for testing COVID-19 recommend collection of both acute and convalescent serum samples from patients for serological testing, which can support the identification of the immune response to a specific viral pathogen [10]. The SARS-CoV-2 nucleic acid has been found also in anal swabs and blood [11], however we did not detect it in serum samples in this case. As yet, only limited data are available on antibody responses during SARS-CoV-2 infection [11,12]. Further studies are needed to better understand the seroprevalence of antibodies to different corona viruses in populations and the role of these antibodies in the risk of disease. In accordance with earlier findings [11], we found that both IgM and IgG titres were low or undetectable at on Day 4 (the second day after admission to hospital) yet increasing on Day 9–10, i.e. 5–6 days after the first sampling. Using other detection methods beyond IFA as well as recombinant antigens and analysing samples from a larger number of patients will shed more light on this. The time of first appearance of anti-SARS-CoV antibodies has ranged from Day 3 to 42 and Day 5 to 47 for IgM and IgG antibodies, respectively [13].

The WB of the serum sample collected at convalescence showed a prominent response against the N and S protein, confirming their role as main candidate

diagnostic targets for antibody tests. However, the patient serum appeared to recognise also the E protein and the processed S1 and S2 proteins. Although WB detects mainly linear epitopes, the strong antibody response against the S protein correlated well with the results of the MN assay.

Monitoring of the binding antibodies is suggested to be a more sensitive method than measuring functional neutralising antibodies for serological detection of human coronavirus (hCoV) infections [14]. However, hCoV OC43 and 229E samples can also cross-react with SARS-CoV ELISA testing [15]. The SARS-CoV-2 CPE-based MN test using live virus appeared to be very specific, while laborious to conduct requiring a BSL-3 laboratory. An increase of at least 4-fold in the neutralising antibodies indicating a positive response was detected at Day 9–10 after the first symptoms and at Day 20, the antibody levels were still increasing. Our findings indicate that the MN assay is specific for functional SARS-CoV-2 antibodies and could be applied in surveillance of population immunity for this virus. The assay can be used as confirmatory tool for SARS-CoV-2 specificity in the development of more accessible diagnostic tools such as assays based on detecting binding antibodies. Previous studies on patients with SARS-CoV infection indicated that the median time for seroconversion was 20 days, by which time 60–75% of patients had IgG against the virus [13,16]. That IgM and IgG antibodies were present within 2 weeks from the onset of symptoms in our study suggests that early convalescent patients may be suitable sources of therapeutic antibodies [17]. In accordance with our finding, a recent preprint report on patients admitted to hospital with confirmed SARS-CoV-2 infection in China indicated that the median time to seroconversion was 11–14 days, depending on the immunological assay used [18].

No neutralising SARS-CoV-2 antibodies were detected in the close contacts nor in the control population samples collected during 2019 in Finland. A low prevalence (0.21%) of antibodies against Middle East respiratory syndrome coronavirus was reported in the general population of Qatar [19]. A meta-analysis of seroprevalence to SARS-CoV among different human populations yielded an overall low seroprevalence (0.10%), although it was slightly higher (0.23%) among healthcare workers and others who had close contact with SARS patients [20]. Binding and neutralising HCoV antibodies were found to be higher in older adults [14]. In total 97% and 99% of serum samples from healthy adults had antibodies to HCoV-229E and HCoV-OC43, respectively [21], and 75% and 65% of the children in the age group 2.5–3.5 years were found to be seropositive for, respectively, HCoV-NL63 and HCoV-229E [22]. While it has been suggested that the late seroconversion in most SARS patients reduces the value of serological assays during the incubation and initial phases of SARS [13], serological testing is suggested for the confirmation of a SARS CoV-2 infection [11]. After understanding better the kinetics, specificity and sensitivity of the assays in development, the serological testing may help contact tracing of clusters and have a role in diagnosing acute and past SARS-CoV-2 infections.

Acknowledgements

We gratefully thank Mira Utriainen, Sanna Mäki, Minna Haanpää, Marja-Liisa Ollonen, Johanna Rintamäki, Hanna Valtonen, Riitta Santanen, Katri Keino, Alena Kaijalainen and Johanna Mustajoki for their expert technical assistance. Christel Pussinen and Mervi Nosa are thanked for their contribution to Finnish population sera collections. We also want to thank the anonymous patient for her help and collaboration throughout the study.

Funding: The study was supported by funds from the Finnish Institute for Health and Welfare (THL), Helsinki University Hospital (HUSLAB) and University of Helsinki. The funding organisations had no role in the study design, data collection and analysis, decision to publish or preparation of the manuscript.

Conflict of interest

LS is a co-investigator in an unrelated study, for which THL has received research funding from GlaxoSmithKline Vaccines. The other authors report no potential conflicts of interest.

Authors' contributions

All authors attest they meet the ICMJE criteria for authorship. All authors have contributed to, seen and approved the final version of the manuscript.

AH set up and performed MN tests, participated in laboratory confirmation of COVID-19 suspicions, coordinated and participated in the collections of the Finnish population sera, and wrote the manuscript.

TS performed the whole genome sequencing and genetic characterisation.

SK and JH performed the IFA and WB analysis, respectively.

PÖ isolated the virus and was responsible of the SARS-CoV-2 related biosafety level 3 laboratory work at THL.

MP, MS, TP and JS participated in THL COVID-19 situation monitoring group work of THL.

SB and MM participated in serological analysis planning group of THL. SB contributed in the interpretation of MN results.

ER set up the real-time RT-PCR method at THL and participated in laboratory confirmation of COVID-19 suspicions.

AK and TS participated in collection of the convalescent serum. AK had a significant role to organising convalescent serum sampling.

HKK, LM and ML were in charge of primary diagnostic of COVID-19 suspicions in HUSLAB. HKK and LM also set up

the real-time RT-PCR method at HUSLAB and participated in laboratory sample logistics from HUSLAB to THL.

MB was responsible for the care of the patient in hospital.

MJ and LS participated in interviewing the index case and contact tracing.

OV was responsible for virological and serological studies in HUSLAB and University of Helsinki, participated in the designing of the study and organising convalescent serum sampling.

NI and CSK were responsible of THL laboratory confirmation of COVID-19 suspicions, participated in COVID-19 situation monitoring group work of THL and laboratory sample logistics. CSK was also responsible for the collections of the Finnish population sera and participated in the designing of the study.

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Any supplementary material referenced in the article can be found in the online version.

Instructions for notification of alleged RCR violations

In Finland, alleged research misconduct and other violations of the responsible conduct of research (RCR) are investigated in accordance with the guidelines of the Finnish National Board on Research Integrity TENK *Responsible conduct of research and procedures for handling allegations of misconduct in Finland* (RCR 2012).

The guidelines state that allegations of violation of the responsible conduct of research may be notified on the following terms:

- The notification is to be sent to the organisation in which the research concerned is primarily being conducted/was primarily conducted or in which the researcher concerned was working at the time of the alleged violation.
- Violations of RCR may only be notified to organisations that have committed to follow the RCR guidelines, see the list of organisations on TENK's website.
- Notification must be sent directly to the highest authority at the organisation (e.g. the rector of a university).
- The person making the allegation does not need to be a researcher or a member of the research community.
- Notification may not be anonymous. In problematic situations, the person making the allegation may contact TENK's Secretary General in advance, see contact information on TENK's website.
- Making unfounded and malicious allegations of an RCR violation may in itself be an RCR violation.

Researchers may discuss suspicions of RCR violations in confidence with the Research Integrity Adviser at their own organisation. However, Research Integrity Adviser may not participate in the processing of allegations of RCR violations.

Notification may be made on this form. **The notification is to be sent directly to the rector/head of the organisation concerned.** The contact details of the rector/head of the organisation will be found on the organisation website.

The organisation receiving written notification of an alleged RCR violation sends this notification and the decisions reached in the case, with appended documentation, to TENK and the Research Integrity Adviser in their own organisation for information. Summaries of RCR violations identified in the RCR investigation process are published on TENK's website. TENK does not publish the names of the individuals concerned or the organisations which handled the case.

TENK's actions are guided by the Act on the Openness of Government Activities (1999/621). This being the case, anyone as a rule has the right to receive information about documents in the RCR process sent to TENK where these do not contain information that is to be kept secret (e.g. health data or business secrets).

Notification form

1. Contact details of the person/people submitting the notification

**) compulsory information*

An alleged RCR violation may be notified by one or more people. Where necessary, the details of other people submitting the notification may be given in section 9. Additional information.

Name* [redacted]	E-mail address* [redacted]
Address	
Post code and town	Phone number
Name [redacted]	E-mail address [redacted]
Name	E-mail address

2. Details of the person/people suspected of an RCR violation

An alleged RCR violation may concern more than one person. Where necessary, you may provide the details of other people suspected in section 4. Course of events.

Name Anu Haveri	E-mail address or other contact details (if known) anu.haveri@thl.fi
Title or position Researcher	Organisation THL
Name	E-mail address or other contact details (if known)
Title or position	Organisation
Name	E-mail address or other contact details (if known)
Title or position	Organisation

3. What violation of the responsible conduct of research (RCR) does the allegation primarily concern?

Please choose only one option. Definitions of the RCR violation categories are provided in *Responsible conduct of research and procedures for handling allegations of misconduct in Finland*, the RCR 2012 guidelines (pp. 32–33).

- ☐ fabrication
- ☐ falsification of observations
- ☐ plagiarism or misappropriation
- ☐ violation of authorship
- ☐ other negligence/misleading the research community
- ☐ exaggerating a CV
- ☐ inappropriately hampering the work of another researcher
- ☒ other, please state: scientific misleading and fraud

4. Course of events or description of alleged RCR violation

State briefly what the issue concerns. Additional details such as key evidence material regarding the case may be appended where necessary.

1. **On 6 September 2021, I made a request for information to THL in accordance with the Act on the Openness of Government Use. I asked for evidence of the complete isolation of the coronavirus (Sars-Cov-2) for viewing and public publication, so that the virus is isolated from everything else, as well as evidence of the virus's involvement in the symptoms, in addition to a photograph (note "photo" not "image" of the virus).**
2. **Thl responded to the request two days late on 22 September 2021, claiming as evidence a study carried out in Finland and a few links that can be found in the appendix file. [Annex 1]**
3. **They also claimed in their message that: "The isolation of the virus is talked about when a patient sample is implanted in a cell culture and the virus begins to multiply in it."**
4. **I replied by e-mail that the material they provided would not respond to my request.**
5. **The e-mail chain and other materials can be found in the attachments.**
6. **In addition to the person responsible for the investigation, Anu Haver, this suspicion of offence includes: Teemu Smura, Suvi Kuivanen, Pamela Österlund, Jussi Hepojoki, Niina Ikonen, Marjaana Pitkäpaasi, Soile Blomqvist, Esa Rönkkö, Anu Kantele, Tomas Strandin, Hannimari Kallio-Kokko, Laura Mannonen, Maija Lappalainen, Markku Broas, Miao Jiang, Lotta Siira, Mika Salminen, Taneli Puumalainen, Jussi Sane, Merit Melin, Olli Vapalahti, Carita Savolainen-Kopra**
7. **In addition, the National Institute for Health and Welfare for maintaining incorrect information and not correcting it.**

5. In which publication(s) did the alleged RCR violation occur or in which other context did the alleged violation became apparent?

Bibliographic details of the publication or description of other context. In cases of suspected plagiarism, show the text plagiarised.

Study: "Serological and molecular findings during SARS-Cov-2 infection: the first case study in Finland, January to February 2020" [Annex 2]

6. When did the alleged RCR violation take place?

Date or period of time in which the alleged RCR violation took place.

January to February 2020.

7. Grounds for the allegation

State here the reason why the course of events described above fulfils the criteria for an RCR violation. Use the guidelines *Responsible conduct of research and procedures for handling allegations of misconduct in Finland* to help you and refer to the applicable parts of the guidelines.

In response to the request for information, THL used the study in section 5 to prove the isolation, existence and inclusion of sars-cov-2 virus in the symptoms of a supposed coronavirus patient. However, the study does not prove that the coronavirus in question exists, nor that it causes symptoms. The study explains how to mix a patient's nasopharyndus sample with a cell culture with e.g. vero e6 cells (monkey kidney cells), penicillin (antibiotic), streptomycin (an antibiotic, which is toxic to the kidneys!) and l-glutamine (bovine fetal serum). In addition, the study used a PCR test to show patients had a "COVID-19 infection."

The authors and the THL in their response claim that the patient's sample is mixed with a cell culture as evidence of the virus, as described above. However, it is not a question of 'virus isolation' because

1. **The research method itself causes the destruction of the above cells and tissues used in cell culture, NOT the 'supposedly infected material'.**
2. **Virologists in this case, too, have flouted the basic rules of scientific work and have not carried out CONTROL tests.**
3. **Control tests show that the cells and tissues used in cell culture are completely degraded in the same way, even if the supposedly infected material is not added to the cell culture from patient samples.**
4. **Virologists compile a model of a virus that actually does not exist from short fragments (fragments) of scattered tissues and cells.**
5. **In a 2017 judgment of the German Supreme Court, the entire basis of virology was overturned in the so-called "measles virus trial". The court-appointed expert issued a statement indicating that the cell culture method used since 1954 to isolate the "virus" is not really proof that the "virus" exists. Molecular and marine biologist Tri. Stefan Lanka thus won a trial based on his €100,000 prize on whoever would prove the existence of the measles virus.**

The PCR tests used (and so on antibody tests) are therefore not indicative of any infection or virus, or part of the virus. Genetic virus tests (PCR) show only the body's own sequences (severity of the gene ring). Since the test only shows 'positive' when there are sufficient genetic specimens in the test sample, it is clear why there are also negative test results. Of course, it is clear that, especially in inflammatory events, the body releases more tissue material and with it genetic severities than in a healthy state or when the body at certain moments of healing does not release them at all. All you have to do is increase the amount of test sample (no matter what kind: a swipe sample, blood, mucus, semen, tissue sample, etc.) and so gets every human, every animal and probably even every plant a positive test result.
A more detailed written explanation of the explanatory statement can be found in the Annex [Annex 3]; "Statement on the isolation of the virus". We call on honest scientists, bioinformaticists and laborers to finally conduct and publish those control experiments that have never been conducted or published. We call for the suspicion of injury to be dealt with and for a response as a matter of emergency, because fraudulent virologists are to blame for the coronavirus crisis because they claim (intentionally or deliberately) to isolate viruses using a technique that is already a completely ridiculous and scientific fraud, even by layman's logic.
We also recommend watching a video of the link in the attachments with Tri. Stefan Lanka with his research on 21 April 2021, has refuted the entire fraudulent virology, which unfortunately is also represented by a research group set up by the National Institute for Health and Welfare. The fourth annex is the evidence summary "There are no viruses" by Vesa-Ilkka Laurio (retired MD). You might want to look into it very carefully. There are a lot of Dr. Stefan Lanka's clarifications on the deceitfulness of virology and also the measles virus trial we mentioned, which he won. We are happy to answer your questions if you need further clarification or additional information.

NOTIFICATION OF ALLEGED RCR VIOLATIONS

8. Handling of the matter by other organisations

State here if RCR notifications regarding the matter have been made in other research organisations and/or complaints have been made to other bodies (e.g. Parliamentary Ombudsman, Council for Mass Media, Administrative Court), the stage of processing that the case has reached and/or decisions made on the matter by other organisations.

Enter text by clicking or tapping here.

9. Additional information

Here you may state, for example, the details of other parties in the case or associated with the case.

Enter text by clicking or tapping here.

10. List of annexes

Material central to the case can be appended. Annexes must be numbered and must clearly support the alleged RCR violation reported above. The organisation receiving the notification may, where necessary, request additional information from the person making the notification.

Note: Both the RCR notification and the documents appended to it are public where these do not contain confidential data.

Enter text by clicking or tapping here.

11. Date and signature

Date	Person submitting the notification **First name Last name**	Title/profession (not compulsory) **Title or profession**

Terhi Kilpi

5.11.2021

[redacted]

[redacted]

Asia: Hyvän tieteellisen käytännön loukkausepäilyä koskeva ilmoituksenne 13.10.2021

Hyvät vastaanottajat

THL kiittää tutkijoittemme työtä kohtaan osoittamastanne kiinnostuksesta ja toteaa sen johdosta seuraavaa.

Ilmoituksenne kohdistuu tieteelliseen julkaisuun:
Haveri A, Smura T, Kuivanen S, Österlund P, Hepojoki J, Ikonen N, Pitkäpaasi M, Blomqvist S, Rönkkö E, Kantele A, Strandin T, Kallio-Kokko H, Mannonen L, Lappalainen M, Broas M, Jiang M, Siira L, Salminen M, Puumalainen T, Sane J, Melin M, Vapalahti O, Savolainen-Kopra C. Serological and molecular findings during SARS-CoV-2 infection: the first case study in Finland, January to February 2020. Euro Surveill. 2020 Mar;25(11):2000266. doi: 10.2807/1560-7917.ES.2020.25.11.2000266. Artikkelin kirjoittajat edustavat THL:n lisäksi Helsingin ja Zürichin yliopistoja, Helsingin yliopistollista sairaalaa (HUSLAB) ja Lapin keskussairaalaa.

Ilmoitatte epäilevänne artikkelin kirjoittajien syyllistyneen tieteelliseen harhaanjohtamiseen ja tieteelliseen petokseen. Ilmoitukseenne ja sen liitteisiin perehdyttyään THL toteaa, että tieteellistä harhaanjohtamista ja petosta koskeva epäilynne kohdistuu mikrobiologian koko tieteenhaaraan eikä tähän yksittäiseen tutkimukseen. Pääväittämänne, että SARS-CoV-2 -virusta ja viruksia ylipäänsä ei ole ollenkaan olemassa, poikkeaa radikaalisti tiedeyhteisössä laajasti hyväksytystä näkemyksestä. Tutkijaryhmän artikkeli on vertaisarvioitu, mikä tarkoittaa, että ainakin yksi riippumaton asiantuntija on tarkastanut kahdessa eri laboratoriossa viruksen osoittamiseksi tehdyt analyysit ja hyväksynyt viruksen osoitukseen käytetyt menetelmät ja tehdyt johtopäätökset.

Tutkimuseettinen ohjeistus *"Hyvä tieteellinen käytäntö ja sen loukkausepäilyjen käsitteleminen Suomessa"* (HTK-ohje) perustuu Tutkimuseettisen neuvottelukunnan ja tiedeyhteisön yhteistyönä laatimaan ohjeeseen, ja sitä noudattavat keskeiset tieteentekijät, myös THL. HTK-ohjeen mukaan *"[h]yvän tieteellisen käytännön loukkauksilla tarkoitetaan epäeettistä ja epärehellistä toimintaa, joka vahingoittaa tieteellistä tutkimusta ja pahimmillaan mitätöi sen tulokset"*. THL toteaa ettei ilmoituksessanne tai sen liitteissä ole mainintaa sellaisesta menettelystä, joka antaisi aiheen epäillä, että HTK-ohjeen mukaisia hyvän tieteen käytöntöjä ja keskeisiä lähtökohtia olisi loukattu.

Edellä esitetyn perusteella THL katsoo, että ilmoitettu loukkausepäily ei kuulu HTK-ohjeen soveltamisalaan, vaan kyse on muun tyyppisestä ongelmasta. THL ei näin ollen pidä esiselvityksen käynnistämistä aiheellisena.

Ystävällisin terveisin

Markku Tervahauta
Pääjohtaja

Terhi Kilpi
TKI-ylijohtaja

AUTO-TRANSLATION

5.11.2021

[redacted]

[redacted]

Subject: Report of suspected infringement of good scientific practice on 13.10.2021

Good recipients,

THL would like to thank and note the interest shown by our researchers in the work

next.

Your announcement is about a scientific study:

Haveri A, Smura T, Kuivanen S, österlund P, Hepojoki J, Ikonen N, Pitkäpaasi M, Blomqvist S,
Rönkkö E, Kantele A, Strandin T, Kallio-Kokko H, Mannonen L, Lappalainen M, Broas M, Jiang M, Siira
L, Salminen M, Puumalainen T, Sane J, Melin M, Vapalahti O, Savolainen-Kopra C. Serological and
molecular findings during SARS-CoV-2 infection: the first case study in Finland, January to February

2020. Euro Surveil[. 2020 Mar;25(11):2000266. doi:70.280711560-7917.ES.2020.25.17.2000266.
Artikketin kirjoittajat edustavat THL:n lisäksi Hetsingin ja Zürichin yliopistoja, Helsingin yliopistollista sairaalaa (HUSLAB) ja Lapin keskussairaalaa.

You suspect that the authors of the article are guilty of misleading and scientific fraud. After reviewing your report and its attachments, THL will state that the suspicion of deception and fraud is directed at the whole branch of microbiology and not for this single study. Your main claim is that the SARS-CoV-2 virus and viruses It does not exist at all, radically differs from what is widely accepted in the scientific community view. Peer-reviewed article from the research team, meaning that at least one has been tested by an independent expert in two different laboratories for the detection of the virus analyzes and accepted the methods used to detect the virus and the conclusions reached.

Research ethics guidelines "Good scientific practice already in the treatment of its trapping In Finland "(HTK guidelines) is based on the cooperation between the Research Ethics Advisory Board and the scientific community developed by key scientists, including the THL. HTK help according to "[t] he intrusion of scientific practice activity, either by scavenging scientific research and at worst measuring its results. ”THL notes there is no mention in your notice or its annexes of any such procedure suspect that the principles and key principles of good science in accordance with the HTK guideline have been violated.

In view of the above, THL considers that the alleged infringement does not form part of the HTK guidelines but this is another type of problem. THL does not therefore hold a preliminary investigation appropriate.

Regards

Markku Tervahauta
Pääjohtaja

TerhíKitpi

tKl CEO