ZonMw

COVID-19 / COVID-19
Dossier nummer / Dossier number: 50-55700-98-904
DEFINITIEF

Algemene gegevens / General Information

Programma / Programme	:	**Infectieziektebestrijding 3 2019-2023**
Subsidieronde / Subsidy round	:	**Incidentiële subsidie COVID-19**
Projecttitel / Project title	:	**Monitoring the evolution, spread and transmission of SARS-CoV-2 through whole genome sequencing to enable fast genotype to phenotype prediction**
Projecttaal / Project language	:	**Engels / English**
Geplande startdatum / Planned start date	:	**24-04-2020**
Geplande duur / Planned duration	:	**12 maanden / months**
Datum indienen / Date of application	:	**02-04-2020**
Projecttype / Project type	:	**Toegepast onderzoek / Applied research**

Projectleden / Project members

5.1.2e 5.1.2e **(Main applicant)**
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Projectgegevens / Project information

Samenvatting / Summary

Emerging viral infections, once established in the human population, may evolve with continued circulation. The evolution of SARS-CoV-2 in the Netherlands will be monitored throughout the phases of the pandemic with close to real-time whole genome sequencing, allowing fast responses in case of remarkable genomic changes, and providing a reference database for investigation of community outbreaks. Bioinformatic tools will be developed to rapidly identify changes that may impact ability to detect, treat and prevent infections. In case novel lineages start to emerge, the effects on transmission dynamics will be further investigated using in vitro and in vivo studies to specifically look at the receptor binding properties, pathogenicity and other relevant virus properties. The results will directly inform precise public health decision making to control the outbreak.

Samenwerking / Collaboration

Samenwerking tussen onderzoek en praktijk / Cooperation between research and practice:
Nee / No

Organisaties

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Inhoud / Content

Relevantie / Relevance

Evaluation of SARS, MERS, Ebola, Zika and other emerging infectious disease (EID) outbreaks has highlighted the critical need for laboratory support at all stages of an outbreak, from initial detection via development of diagnostics, to the assessment of the evolution and transmission of outbreak strains. A further characterization of essential properties related to the virus-host interactions, pathogenesis, origin of infections and modes of transmissions is needed to monitor the progress of outbreak. To this point, control activities need to be coordinated.

Presumably in the beginning of December an outbreak of a novel coronavirus started in a seafood and live animal market in Wuhan, China (Zhu, Zhang et al. 2020). This novel virus was tentatively named SARS-CoV-2 (Coronaviridae, Intern. Comm. on Taxonomy 2020) and rapidly spread throughout the world. By March 24th the virus spread to 169 different countries and infected over 410,000 people causing 18,240 deaths (Dong, Du et al. 2020). In the Netherlands, the first COVID-19 case was diagnosed on the 27nd of February and as of March 31st, 12,595 patients with SARS-CoV-2 have been diagnosed and 1039 patients have died because of COVID-19 in the Netherlands (RIVM).

The emergence and fast spread of a recently introduced virus into the human population asks for extensive tracking and monitoring of possible changes. Since the start of the pandemic, virus whole genome sequencing (WGS) by the ErasmusMC project team has been used to support public health decision making in the Netherlands and abroad. Using methods developed through an EU funded consortium COMPARE, a pipeline of near to real-time WGS was developed in which sequence data was linked with epidemiological data, such as contact tracing and travel history, collected as part of the national public health effort.

The observed diversity of virus sequences found by March 2nd reflected widespread independent incursions rather than ongoing epidemic spread from a single isolate. Subsequent analyses of SARS-CoV-2 infected healthcare workers confirmed widespread community circulation of multiple lineages, and was used as a basis for investigation of clusters at request of colleagues throughout the country. These observations were used directly to inform public health decision making, as mentioned in the press conference of the RIVM on the 15th of March and during the briefing for the House of Representatives on the 25th of March (hhttps://www.tweedekamer.nl/sites/default/files/atoms/files/20200325_briefing_coronavirus_tweede_kamer_presentatie_rivm.pdf). The project team was also recognised for this effort internationally, since at a given point over 30% of publicly available SARS-CoV-2 sequences were from the Netherlands (GISAID). At present, the project team is drafting a protocol for guidance of the use of WGS for the global laboratory reference network of WHO.

Since its emergence, the global spread of SARS-CoV-2 led to rapid diversification into lineages that reflect ongoing chains of transmission in specific geographic regions in the Netherlands. This diversification provides the basis for the use of WGS to investigate possible transmission chains in healthcare settings, providing essential information for infection control and prevention. Moreover, even if complete suppression of the current circulation is successful, SARS-CoV-2 will (sporadically) re-emerge and discrimination between novel introductions versus prolonged local circulation is important to inform appropriate public health decision. In addition, due to genomic mutations, the phenotype and the transmission dynamics of the virus might change during time. Therefore close monitoring of the behavior of the virus is essential.

Our project aims to provide a novel laboratory approach to deploy in the early stages of new disease outbreaks by combining the possible applications of real-time sequencing for diagnostic purposes, with profiling of virulence factors, and transmissibility markers, within the same laboratory test and with rapid turnaround. If successful, this would bring the advantages of pathogen research to the fingertips of both the clinician and the public health doctor, because information that currently is collected over the course of weeks or months will be available as soon as the diagnostic results are produced. This will also provide training

materials for WGS for SARS-CoV-2 as part of the national response to the pandemic.

As a WHO reference laboratory and a partner of the national COVID-19 response team, the proposed project team of department of Viroscience of Erasmus MC has a unique opportunity to link data from different sources and researchers from different disciplines to gain more insight in the evolution, spread and transmission of SARS-CoV-2. The proposed project team combines competitive expertise in basic and applied clinical, molecular and public health research, respectively, which is a unique combination in the world.

Kennisoverdracht, implementatie, bestendiging / Knowledge transfer, Implementation Consolidation

To have an immediate impact on the current outbreak in the Netherlands, and beyond, the following strategy for knowledge transfer is proposed. This strategy ensures rapid sharing of the specific results of this project with relevant stakeholders, as indicated below.

All generated sequences will be publicly available via GISAID, making this data available for researchers word-wide. In addition, raw sequence data will be deposited in the newly formed COVID-19 research data infrastructure, using data hubs specifically developed for this effort (https://www.ebi.ac.uk/about/news/announcements/embl-ebi-leads-international-collaboration-share-covid-19-research-data). For this effort, we will closely collaborate with our collaborating partner The European Bioinformatics Institute (Dr. 5.1.2e), with whom we have closely collaborated in the development of the data hub in the EU funded projects COMPARE and VEO.

Updates of sequencing activities and more detailed analyses will be shared in the appropriate networks, such as the Dutch SARS-CoV-2 outbreak team, national and international laboratory networks, such as EVD labnet and reference laboratory networks. Notable changes in behaviour or genome of the virus will be reported immediately to the RIVM and the WHO. Participating hospitals will receive a regular report with relevant analysis, which can be used for infection control and prevention measures, or changes in patient care (if, for example, changes in the virus may have an effect on drug susceptibility or pathogenicity). Furthermore, there will be a continuous discussion with other ZonMw proposals funding under this call, especially where the application of WGS to specific settings can have a substantial benefit for outbreak control. The lead applicants of these proposals are therefore “co-applicants” for this proposal.

Results will be presented at national and international virology and public health meetings. Resulting manuscripts will be published in peer-reviewed open access journals allowing global access to this essential research.

Finally, results will also be rapidly shared with the EU as well as EU funded initiatives dedicated to COVID-19. This will be ensured directly through participation of the lead applicant and project team members in projects as VEO and RECOVER, but also through the dedicated platform under the DG SANTE coordinated “health policy platform” (HPP), which is called “COVID – Research to policy action”. The “HPP/ COVID – Research to policy action” aims to ensure the rapid contribution of relevant research findings to public health policy for the pandemic response in Europe.

Doelstelling / Objective

To detect potential sequence variations that might occur in time, continued monitoring of viral genome variations is needed. After initial characterization of the viral genomes, an integrative approach to determine critical pathogen properties like the pathogenicity of the virus and the disease it causes is required, particularly focusing on platforms that allow rapid characterization of novel variants.

The overall aim is to gain in depth understanding of the evolution, spread and transmission of SARS-COV-2 during the coming phase of the pandemic, and the potential impact of genomic changes that may affect our ability to detect, treat or prevent SARS-CoV-2 (infection).

Objectives are:
1. To provide a reliable workflow, analytical tools and training materials for WGS for SARS-CoV-2 as part of the national response to the pandemic.
2. To design a suite of bioinformatic tools and in vitro validation methods to perform fast genotype to phenotype predictions during the current SARS-CoV-2 outbreak.
3. To analyse the genomic diversity of SARS-CoV-2 throughout the pandemic in the population as a whole, as well as in patients.
4. To develop a workflow to rapidly assess potential phenotypic changes of SARS-CoV-2, based on data from genomic monitoring
5. To provide advice to Public Health Authorities on the potential consequences of genomic and phenotypic changes for diagnostics, therapeutics, and vaccine development.

We will answer the following research questions:

1. What are the routes and risk factors for SARS-CoV-2 spread in the Netherlands?
2. Does SARS-CoV-2 spread lead to phenotypic changes that may affect diagnostics, treatment, control or prevention?
3. What are genomic markers that could predict such changes?
4. How can the findings be translated for public health and clinical decision making?

Plan van Aanpak / Strategy

To achieve the objectives as set out under "doelstelling", we have identified four specific tasks. Most notably, for this project, we will link with the other relevant ZonMW proposals funding under this COVID-19 call. One of the proposals is aiming to perform in depth studies on hospital transmission of SARS-CoV-2. When a SARS-CoV-2 positive healthcare worker (HCW) at one of the participating hospitals is enrolled in that study, a subset of samples will also be shared with Erasmus MC for WSG, meaning that sequencing can be performed on patient (HCW) samples, with extensive metadata, from 12 hospitals distributed over the Netherlands. This collaboration will also provide opportunities to include patients with divergent or unexpected disease presentations, and patients that have been infected for a long duration of time, to study possible relevant mutations. In addition, we will link with another ZonMW proposal looking at household transmissions, for which samples will be shared with Erasmus MC for WGS. In particular, we will collaborate with 5.1.2e 5.1.2e (UMC Utrecht, Julius Center for Health Sciences and Primary Care), Prof Dr 5. 5.1.2e (together with 5.1.2e and 5.1.2e UMC Utrecht, medical microbiology & Julius Center for Health Sciences and Primary Care), and Prof Dr 5.1.2e (AMC, medical microbiology, co-lead PREPARE COVID cohort study).

Task 1: Reliable workflow, analytical tools and training materials for WGS for SARS-CoV-2

Sub task 1.1 Sample collection (start month April 2020, end month April 2021)

A selection of laboratories and hospitals, including the co-applicant organisations, at locations geographically spread throughout the Netherlands have agreed to share a selection of SARS-CoV positive samples at a monthly basis, which will be processed for whole genome sequencing. From this collection, 120 samples will be sequenced each month from April 2020 till April 2021 (13 months). This will allow for a representative sample set to monitor the circulation of SARS-CoV-2 strains in the Netherlands. In addition, in collaboration with the other ZonMw proposals, samples will be sequenced for the HCW and household settings (1500 samples anticipated). In total, we anticipate sequencing of 3000 samples. Metadata such as the date of the sampling, residence and recent travel history will be collected by the participating institutes, in compliance with GDPR (AVG) rules. RIVM will collect the majority of this information, and standardize and harmonize this data for analysis. A dedicated (confidential) data sharing platform to allow rapid and real-time exchange of data between Erasmus MC and RIVM will be set up for this purpose.

Sub task 1.2 Analytical tools and training materials for WGS for SARS-CoV-2 (start month April 2020, end month end month April 2021)

We have established and validated a SARS-CoV-2 specific amplicon-based Nanopore sequencing protocol to enable low-cost and near to real-time sequencing. This protocol has already been published, using Usutu virus as an example (Oude Munnink, Munger et al. 2020) and (Oude Munnink, Kik et al. 2019). We continue to keep on working on improving the protocol to reduce the time to results. In addition, we will further develop analytical tools to increase speed of analysis to allow for fast data sharing and responses. The generated data will also be shared using data hubs specifically developed for this effort, as described in the section "kennisoverdracht". At request of our collaborating partners and hospitals proving samples, or researchers working on SARS-CoV-2, we will provide training on the protocol for SARS-CoV-2 WGS, as well as data visualization and interpretation.

Task 2: To design a suite of bioinformatic tools and in vitro validation methods to perform fast genotype to phenotype predictions during the current SARS-CoV-2 outbreak. (start month April 2020, end month April 2021)

If sequences with specific mutations are detected, methods are needed for rapid characterisation of possible relevance of the observed changes to the virus properties (genotype to phenotype prediction). Methods include basic characterisation of in vitro growth properties in different cell lines and organoids, representative of the known tissue tropism of COVID-19, to look for possible changes in virus behavior. It also includes cross neutralisation assays using reference sera from immunized animals, as well as monoclonal antibody panels, to study possible antigenic changes. Although we do not expect to see significant drift over the course of the project duration, we consider it important to develop methods to be able to rapidly assess such changes, using our extensive expertise on influenza evolution and coronaviruses as a reference. A suite of methods will be developed and piloted using a panel of virus isolates reflecting the currently known global diversity of SARS-CoV-2 viruses (Hadfield et. al. 2018).

Task 3: Analysis of the genomic diversity of SARS-CoV-2 throughout the pandemic (start month April 2020, end month April 2021)

We aim to analyse the SARS-CoV-2 sequences from the selected patients described above for the duration of at least 12 months (April 2020 - April 2021) to monitor and analyse sequence diversity and spread. This will be done in collaboration with international reference centres involved in the global tracking of SARS-CoV-2. Global sequence diversity will be analysed using models to assess phylogenetic relationships, but also phylogeographical models and time-resolved phylogenetic analysis that are able to combine the collected metadata with the sequence information that was generated, such as Maximum Likelihood trees, BEAST analysis (Suchard et. al. 2018) and Nextstrain (Hadfield et. al. 2018).

Task 4: Analyse consequences of genomic and phenotypic changes for diagnostics, therapeutics, public health and vaccine development (start month May 2020, end month December 2020)

The sequences generated, in addition to the global analyses in task 3 will be analysed for specific markers that could indicate changes relevant for diagnostics, treatment of prevention. All generated whole genomes will be checked in silico to monitor the

performance of diagnostic primers using a user-friendly web-based tool (Nieuwenhuijse et al. under review). In case of newly evolving lineages or viruses with mutations in sites that could have potential relevance for receptor binding, treatment a.o, the samples from which these sequences were generated will be used for cell culture isolation and in vitro analysis of strain properties using the tools described in task 2. Following the results of the phenotype predictions in task 2, a risk assessment will be performed to assess possible consequences (potential escape from diagnostics, potential escape from treatment, potential escape from vaccines) in practice.

Finally, in line with the fourth research question, Erasmus MC and RIVM, and where needed with the collaborating partners, will discuss the interpretation of the results and their translation into immediate advice for public health and clinical decision making.

Expected results:
1. Detailed overview on how SARS-CoV-2 spread throughout the Netherlands
2. Early detection of potential changes in the virulence of SARS-CoV-2
3. Detailed overview on the global evolution of SARS-CoV-2

Referenties / References

Coronaviridae Study Group of the International Committee on Taxonomy of, V. (2020). "The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2." Nat Microbiol 5(4): 536-544.

Dong, E., et al. (2020). "An interactive web-based dashboard to track COVID-19 in real time." Lancet Infect Dis.

Hadfield J. et. al. (2018) "Nextstrain: real-time tracking of pathogen evolution." Bioinformatics 34(23): 4121-4123.

Oude Munnink, B. B., et al. (2019). "Towards high quality real-time whole genome sequencing during outbreaks using Usutu virus as example." Infect Genet Evol 73: 49-54.

Oude Munnink, B. B., et al. (2020). "Genomic monitoring to understand the emergence and spread of Usutu virus in the Netherlands, 2016-2018." Sci Rep 10(1): 2798.

Suchard M. A. et. al. (2018). "Bayesian phylogenetic and phylodynamic data integration using BEAST 1.10" Virus Evolution 4(1).

Zhu, N., et al. (2020). "A Novel Coronavirus from Patients with Pneumonia in China, 2019." N Engl J Med 382(8): 727-733.

Financiële gegevens / Financial data

ZonMw budget

	Jaar / Year								
Kostenpost	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	**Totaal / Total**
Personeel	5.1.1c	0	0	0	0	0	0	0	5.1.1c
Materieel		0	0	0	0	0	0	0	
Implementatie		0	0	0	0	0	0	0	
Apparatuur		0	0	0	0	0	0	0	0
Overig		0	0	0	0	0	0	0	0
Totaal / Total	5.1.1c	**0**	**0**	**0**	**0**	**0**	**0**	**0**	5.1.1c

Co-financiering / Cofinancing

Naam co-financier / Name of cofinancier	Bedrag / Amount	Status

Bijzondere gegevens / Additional information

Vergunningen / Permits

	Verklaring nodig / Statement required?		Status verklaring / Statement status		
	Ja / Yes	Nee / No	Verkregen / Acquired	Aangevraagd / Applied	Nog niet aangevraagd / Not applied yet
METC		X			
DEC		X			
WBO		X			

Onderschrijvingen / Assents

	Ja / Yes	Nee / No	N.v.t. / N.A.
Code biosecurity / Code Biosecurity			X
Code openheid dierproeven / Code Transparency of Animal Testing			X

Andere vergunningen / Other permits

Historie subsidieaanvraag / History grant application

Deze aanvraag is ook ingediend bij organisatie / This grant application has also been submitted to organization:

ZonMw Budget Format

Name organisation	Type of organisation	Quoted costs	Quoted co-funding	Requested budget
Erasmus MC	Research Organistion	5.1.1c	-	5.1.1c
RIVM	Other		-	
		-	-	-
		-	-	-
		-	-	-
		-	-	-
		-	-	-
		-	-	-
		-	-	-
	Total	5.1.1c	-	5.1.1c

Staff costs

Position / Name (will be filled based on "staff"sheet)	Description of activities within project	Organisation (dropdown menu)	Costs	Own contribution / 3rd party co-funding	Requested budget ZonMw
PI (prof)/ 5.1.2e	Hoofdaanvrager en projectleider	Erasmus MC	€ 5.1.1c	€ -	€ 5.1.1c
Postdoc/ B. 5.1.2e	Lead sequencing work (development of workflow, analytical tools and training materials for	Erasmus MC	€	€ -	€
PhD student	public health/ bio-informatics and data visualization/ in vitro analysis of phenotypic	Erasmus MC	€	€ -	€
technician	sample preparation, sequence work	Erasmus MC	€	€ -	€
Senior Postdoc	lead in vitro analysis of phenotypic changes/ data scientist	Erasmus MC	€	€ -	€
Senior Postdoc/ epidemiologist	collecting, harmonizing and standardization of metadata for analyses, interpretation and translation of findings into policy advise	RIVM	€	€ -	€
0			€ -	€ -	€
0			€ -	€ -	€ -
to be specified			€ -	€ -	€ -
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to be specified			€ -	€ -	€ -
			€ 5.1.1c	€ -	€ 5.1.1c

Specification staff

1.a Staff costs (based on salary scale)

nr	Position / Name	NFU / VSNU member / other staff ruling	Position/Scale	Months in project	Gross salary - based on table / 1 FTE	Monthly Gross salary (for Other ruling only)	% fte (for the project)	Salary costs	Gross salary, 40% increment (for Other ruling only)	Overhead % (for Other ruling only)	Total
1	PI (prof)/ 5.1.2e	NFU	PostDoc	12	5.1.1c		5%	€ 5.1.1c	€ -		€
2	Postdoc/ 5.1.2e	NFU	PostDoc	12			50%	€	€ -		€
3	PhD student	NFU	Promovendus	12			50%	€	€ -		€
4	technician	NFU	NWP-HBO	12			100%	€	€ -		€
5	Senior Postdoc	NFU	PostDoc	12			10%	€	€ -		€
6	Senior Postdoc/ epidemio	Other	Overig WP	12		5.1.1c	5%	€	€ 5.1.1c		€
7					€ 0			€ -	€ -		€ -
8					€ 0			€ -	€ -		€ -
9	to be specified				€ 0		100%	€ -	€ -		€ -
10	to be specified				€ 0		100%	€ -	€ -		€ -
11	to be specified				€ 0		100%	€ -	€ -		€ -
12	to be specified				€ 0		100%	€ -	€ -		€ -
13	to be specified				€ 0		100%	€ -	€ -		€ -
14	to be specified				€ 0		100%	€ -	€ -		€ -
15	to be specified				€ 0		100%	€ -	€ -		€ -

1.b Staff costs (based on hourly rate)

The hourly rate should be acceptable, reasonable and fair

nr	Position	Activity / Actions	Hourly rate	number of hours	Total
1	to be specified		€ -		€ -
2	to be specified		€ -		€ -
3	to be specified		€ -		€ -
4	to be specified		€ -		€ -
5	to be specified		€ -		€ -
6	to be specified		€ -		€ -
7	to be specified		€ -		€ -
8	to be specified		€ -		€ -
9	to be specified		€ -		€ -
10	to be specified		€ -		€ -
11	to be specified		€ -		€ -
12	to be specified		€ -		€ -
13	to be specified		€ -		€ -
14	to be specified		€ -		€ -
15	to be specified		€ -		€ -

Material, equipment & consumer goods (itemised)

What item(s)	Used for	Organisation (dropdown menu)	Costs	Own contribution / 3rd party co-funding	Requested budget ZonMw
Consumables for WGS sequencing 5.1.2b	WGS sequencing	Erasmus MC	€ 5.1.1c	€ -	€ 5.1.1c
Software licenses and (data and cloud) access fees	Data analysis and visualization	Erasmus MC	€	€ -	€
Consumables for in vitro work phenotypic changes	in vitro work phenotypic changes	Erasmus MC	€	€ -	€
			€	€ -	€
			€ -	€ -	€ -
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			€ -	€ -	€ -
			€ -	€ -	€ -
			€ 5.1.1c	€ -	€ 5.1.1c

Other costs (itemised)

Description	Used for (dropdown menu)	Organisation (dropdown menu)	Costs	Own contribution / 3rd party co-funding	Requested budget ZonMw
Open access publications (3 - 4 publications)	Open access	Erasmus MC	€ 5.1.1c	€ -	€ 5.1.1c
Communication and implementation (other than open access publications)	Others, please specify in description	Erasmus MC	€	€ -	€
incl expert meetings, presentation at (inter)national conferences			€	€ -	€
and tools for data management			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
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			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ 5.1.1c	€ -	€ 5.1.1c

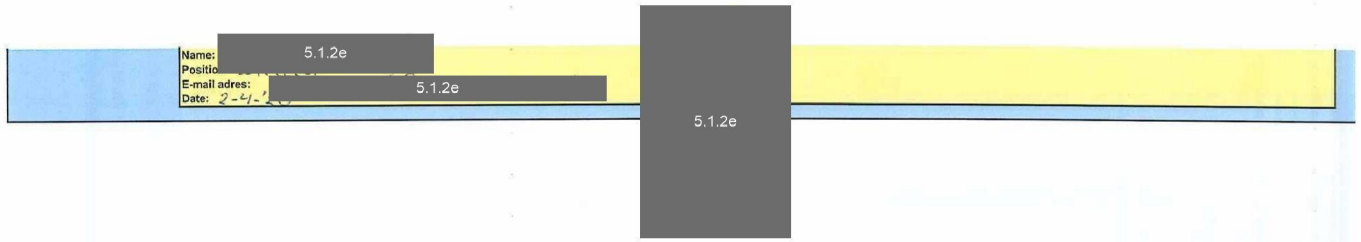
Total costs project	€ 5.1.1c	
Own contribution / co-funding		€ -
TOTAL REQUETED BUDGET ZONMW		€ 5.1.1c

Additional explanation for budget
See document "toelichting op de begroting"

Approval financial responsible receiving organisation

Receiving organisation

5.1.2e


Name:
5.1.2e
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E-mail adres:
5.1.2e
Date: 2-4-2
5.1.2e

Toelichting op de begroting

Monitoring the evolution, spread and transmission of SARS-CoV-2 through whole genome sequencing to enable fast genotype to phenotype predictions
Hoofdaanvrager: Prof. 5.1.2e, Erasmus MC Rotterdam

Personeel

We request funding for the following project team members, whose specific expertise on this topic and experience in this work is imperative for achieving the aims of this project in such a timely manner that it has an immediate impact on the current outbreak.

PI prof. 5.1.2e for 5% of her time for 12 months. Her specific expertise on public health virology and outbreak control is necessary amongst others for the interpretation of the results and translation into policy advice and public on health measures. We request funding for 50% of the time of 5.1.2e for 12 months, post-doc, who will be responsible for the WGS work, development of the workflow, analytical and bio-informatics tools, and training material for WGS, as well as analyses of the WGS work. We request 100% senior technician for 12 months, who will perform the WGS work, including sample and library preparation, sequencing work, etc.

10% Postdoc for 12 months include 5.1.2e, group leader Coronaviruses and lead for in vitro work on phenotypic changes (5% for 12 months), as well as 5.1.2e (data scientist and bio-informatician), who is responsible for data management (5% for 12 months). Their specific expertise on Coronaviruses and data management, respectively, are necessary to perform this project. We also request funding for 50% PhD student for 12 months. This includes 5.1.2e, group leader public health (15% for 12 months), 5.1.2e 5.1.2e bio-informatic analysis and data visualization (30% for 12 months), and 5.1.2e (5% for 12 months) who will perform the in vitro work on phenotypic changes.

Finally, we request funding for a senior post-doc/epidemiologist from RIVM for the collection, harmonizing and standardization of metadata for the analyses, as well as interpretation and translation of findings into policy recommendations (together with 5.1.2e).

Materieel

We request 5.1.1c for consumables for WGS sequencing. This also includes the consumables costs for preparation of the samples for WGS (e.g. nucleic acid extraction). Costs for this are 5.1.1c per genome, aiming for at least 3000 genomes. Furthermore, we request 5.1.2b for software licenses for the data analysis and visualization. Finally, we request 5.1.1c for consumables for the in vitro work for genotypic to phenotypic changes.

Communicatie en implementatie

We request 5.1.1c or open access publications, aiming for at least 3 publications. Furthermore, we request 5.1.1c for communication and implementation costs to cover costs amongst others for expert meetings, presentations at international and national conferences, as well as tools necessary for data management. Given the aim of this project proposal, the measures applicable in the Netherlands as set by our government (and the likelihood there will be no gatherings such as conferences for the coming months) and the duration of 12 months, we deem it justified to not fully comply with the 5% budget rule for communication and implementation.