

Algemene gegevens / General Information

Programma / Programme : **COVID-19 Programma**
 Subsidieronde / Subsidy round : **Bottom-up ronde COVID-19 aandachtsgebied 1**
 Projecttitel / Project title : **Altered IgG fucosylation driving pathologies in COVID-19: Relevance for diagnosis and therapeutics**
 Projecttaal / Project language : **Engels / English**
 Geplande startdatum / Planned start date : **30-07-2020**
 Geplande duur / Planned duration : **24 maanden / months**
 Datum indienen / Date of application : **16-06-2020**
 Projecttype / Project type : **Toegepast onderzoek**
 Vervolg eerder ZonMw-project / Continuation previously funded project : **Nee / No**
 ZonMw

Projectleden / Project members

5.1.2e

Functie / Position: Head of Immunoglobulin Research / PI AMC | *Opleiding / Education:*

Studierichting / Subject:

T: 5.1.2e | F: 5.1.2e | E: 5.1.2e @sanquin.nl

Sanquin Bloedvoorziening
 Postbus 9892
 1006 AN AMSTERDAM

5.1.2e

Functie / Position: Head of Immunoglobulin Research | *Opleiding / Education:*

Studierichting / Subject:

T: 5.1.2e | F: 5.1.2e | E: 5.1.2e @sanquin.nl

Sanquin Bloedvoorziening
 Postbus 9892
 1006 AN AMSTERDAM

5.1.2e

Functie / Position: Director of Research | *Opleiding / Education:*

Studierichting / Subject:

T: 5.1.2e | F: 5.1.2e | E: 5.1.2e @sanquin.nl

Sanquin Bloedvoorziening
 Postbus 9892
 1006 AN AMSTERDAM

5.1.2e

Functie / Position: Associate Professor | *Opleiding / Education:*

Studierichting / Subject:

T: 205668043 | F: 5.1.2e | E: 5.1.2e @amsterdamumc.nl

Amsterdam UMC - locatie AMC
 Laboratorium voor Experimentele Immunologie
 Meibergdreef 9
 1105 AZ AMSTERDAM ZUIDOOST

5.1.2e

Functie / Position: Associate Professor | *Opleiding / Education:*

Studierichting / Subject:

T: 5.1.2e | F: 5.1.2e | E: 5.1.2e @amsterdamumc.nl

Amsterdam UMC - locatie AMC
 Laboratorium voor Virologie
 Meibergdreef 15

1105 AZ AMSTERDAM ZUIDOOST

5.1.2e

Functie / Position: Head of Department | *Opleiding / Education:*

Studierichting / Subject:

T: 5.1.2e | F: | E: 5.1.2e @sanquin.nl

Sanquin Bloedvoorziening

Postbus 9892

1006 AN AMSTERDAM

5.1.2e

Functie / Position: Hoofd intensivist | *Opleiding / Education:*

Studierichting / Subject:

T: 5.1.2e | F: | E: 5.1.2e @amsterdamumc.nl

Amsterdam UMC - locatie AMC

Intensive Care Volwassenen

Postbus 22660

1100 DD AMSTERDAM ZUIDOOST

5.1.2e

Functie / Position: Head of Department | *Opleiding / Education:*

Studierichting / Subject:

T: 5.1.2e | F: | E: 5.1.2e @lumc.nl

Leids Universitair Medisch Centrum

Center for Proteomics and Metabolomics

Postbus 9503

2300 RC LEIDEN

Projectgegevens / Project information

Aandachtsgebieden / Focus

1.1 Thema's aandachtsgebied 1

- 5.1.2i Toelichting
- Virus, immuniteit, immuunrespons en pathogenese

1.3 Setting

- 5.1.2i Toelichting

Samenvatting / Summary

5.1.2i Toelichting

Trefwoorden / Keywords

5.1.2i Toelichting

Samenwerking / Collaboration

Samenwerking tussen onderzoek en praktijk / Cooperation between research and practice:

Ja / Yes

Organisaties

Rijksinstituut voor Volksgezondheid en Milieu (RIVM)
Centre for Immunology of Infectious diseases and Vaccines (IIV)
Postbus 1
3720 BA BILTHOVEN

Universitair Medisch Centrum Utrecht
Eijkman Winkler Instituut
Virologie

Financiële gegevens / Financial data**ZonMw budget**

	Jaar / Year								
Kostenpost	1	2	3	4	5	6	7	8	Totaal / Total
Personeel	5.1.1c								
Materieel									
Implementatie									
Apparatuur									
Overig									
Totaal / Total	5.1.1c								5.1.2i Toelichting

Co-financiering / Cofinancing

Naam co-financier / Name of cofinancier	Bedrag / Amount	Status
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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	5.1.2i Toelichting				
DEC					
WBO					

Onderschrijvingen / Assents

	Ja / Yes	Nee / No	N.v.t. / N.A.
Code biosecurity / Code Biosecurity	5.1.2i Toelichting		
Code openheid dierproeven / Code Transparency of Animal Testing			

Andere vergunningen / Other permits

APPLICATION FORM
FULL PROPOSAL
– BOTTOM-UP ROUND
COVID 19 programme

Submission deadline: 15 June 2020 (14:00 hours CEST)

**PLEASE CAREFULLY READ ALL INSTRUCTIONS IN THE ANNEX
"EXPLANATION SUBMISSION GRANT PROPOSAL" OF THE CALL TEXT!**

When you have completed the form:

1. Convert the form into a PDF file and check the details
2. Upload the entire form as an annex to your submission in ProjectNet
(Please note: there are two different links, only use 1 of the 2!)
ProjectNet: [Focus area 1 \(Predictive diagnostics and treatment\)](#)
ProjectNet: [Focus area 2 \(Care and prevention\)](#)

BASIC DETAILS (front page)

NAME OF THE MAIN APPLICANT:

5.1.2e

ORGANISATION:

Sanquin Research

ENGLISH PROJECT TITLE:

Altered IgG fucosylation driving pathologies in COVID-19: Relevance for prognosis and therapeutics

DUTCH PROJECT TITLE:

Veranderde antistof fucosylering bepaald ernst COVID-19: Implicaties voor prognose en behandeling

RESEARCH PROPOSAL max 8 pages A4 (including literature references)	(front page with basic details not included - font type Arial 10 pts)
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1. PROBLEM DEFINITION, URGENCY AND OBJECTIVE(S)

Substantiation problem definition, urgency and objective. Make objective SMART (specific, measurable, acceptable, realistic and time-related)

5.1.2i Toelichting

5.1.2i Toelichting

2. CURRENT RESEARCH

Briefly describe published research AND current national (and where possible international) research in this area and what your project adds to this. Click [here](#) for a list of possible portals.

5.1.2i Toelichting

3. ACTION PLAN (MOTIVATE CHOICES)

5.1.2i Toelichting

5.1.2i Toelichting

5.1.2e

5.1.2i Toelichting

5.1.2i Toelichting

4. ACTION PLAN (MOTIVATE CHOICES)

5.1.2i Toelichting

5. RELEVANCE

5.1.2i Toelichting

5.1.2i Toelichting

6. PROJECT GROUP MEMBERS AND THEIR ROLES

Demonstrate that in the project group, the relevant disciplines with the right expertise and intended target group(s) are represented. Make it clear which participants in the project group will have which role. You should preferably specify work packages.

5.1.2i Toelichting

7. KNOWLEDGE TRANSFER, IMPLEMENTATION, PERPETUATION

Describe how you will disseminate the knowledge acquired in your project, and how you will approach the further implementation of the results and/or products, for example by use in practice or in the formation of policy.

5.1.2i Toelichting

8. PARTICIPATION OF THE STAKEHOLDER(S) FINAL TARGET GROUPS

Describe which parties (who are possibly not co-applicants, for example patients, care professionals) will be involved in your project and how.

5.1.2i Toelichting

9. LITERATURE REFERENCES:

State here the references that substantively support your proposal and please avoid summaries of publications from your project group (members).

1. [REDACTED] et al. The SARS-CoV-2 receptor-binding domain elicits a potent neutralizing response without antibody-dependent enhancement. *bioRxiv* 2020; :2020.04.10.036418.
2. [REDACTED] et al. Anti-spike IgG causes severe acute lung injury by skewing macrophage responses during acute SARS-CoV infection. *JCI insight* 2019; 4.
3. [REDACTED] et al. A prominent lack of IgG1-Fc fucosylation of platelet alloantibodies in pregnancy. *Blood* 2014; 123:471–80.
4. [REDACTED] Decoding the human immunoglobulin G-glycan repertoire reveals a spectrum of Fc-receptor- and complement-mediated-effector activities. *Front Immunol* 2017; 8.
5. [REDACTED] Functional Attributes of Antibodies, Effector Cells, and Target Cells Affecting NK Cell-Mediated Antibody-Dependent Cellular Cytotoxicity. *J Immunol* 2019 203(12):3126–3135.
6. [REDACTED] et al. Natural variation in Fc glycosylation of HIV-specific antibodies impacts antiviral activity. *J Clin Invest* 2013; 123:2183–92.
7. [REDACTED] et al. IgG antibodies to dengue enhanced for FcγRIIIA binding determine disease severity. *Science* 2017; 355:395–8.
8. [REDACTED] Regulated glycosylation patterns of IgG during alloimmune responses against human platelet antigens. *J Proteome Res* 2009; 8:450–6.
9. [REDACTED] Glycosylation pattern of anti-platelet IgG is stable during pregnancy and predicts clinical outcome in alloimmune thrombocytopenia. *Br J Haematol* 2016; 174:310–20.
10. [REDACTED] et al. Symptomatic SARS-CoV-2 infections display specific IgG Fc structures. *medRxiv* 2020;2020.05.15.20103341.
11. [REDACTED] Afucosylated immunoglobulin G responses are a hallmark of enveloped virus infections and show an exacerbated phenotype in COVID-19. *bioRxiv* 2020;2020.05.18.099507. Available from: <http://biorxiv.org/content/early/2020/05/18/2020.05.18.099507>.
12. [REDACTED] Low anti-RhD IgG-Fc-fucosylation in pregnancy: A new variable predicting severity in haemolytic disease of the fetus and newborn. *Br J Haematol* 2014; 166:936–45.
13. [REDACTED] Antigen specificity determines anti-red blood cell IgG-Fc alloantibody glycosylation and thereby severity of haemolytic disease of the fetus and newborn. *Br J Haematol* 2017; 176:651–60.
14. [REDACTED] et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; 395:497–506.
15. [REDACTED] et al. The landscape of lung bronchoalveolar immune cells in COVID-19 revealed by single-cell RNA sequencing. *medRxiv* 2020;2020.02.23.20026690.
16. [REDACTED] receptor heterogeneity in leukocyte functional responses. *Front. Immunol.* 2017; 8:280.
17. [REDACTED] et al. Potent neutralizing antibodies from COVID-19 patients define multiple targets of vulnerability. *Science* 2020; **In Press**. Available from: <https://www.biorxiv.org/content/10.1101/2020.05.12.088716v1>
18. [REDACTED] A Targeted Liquid Chromatography-Mass Spectrometry Data Processing Package for Relative Quantitation of Glycopeptides. *J Proteome Res* 2016; 15:2198–210.

[illegible]

[illegible]

Specification staff

1.a Staff costs (based on salary scale)

nr	Function / Name	NFU / VSNU member / other staff ruling	Function/Scale	Months	Gross salary - based on table / 1 FTE	Monthly Gross salary (for Other	% fte (for the project)	Salary costs	Gross salary, 40% increment (for Other ruling only)	Overhead % (for Other ruling only)	Total
1	Postdoc (researcher C)	Other	Overig WP	24	5.1.1c					32%	5.1.2i Toelichting
2	Analist	Other	Overig WP	24						32%	
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										

1.b Staff costs (based on hourly rate)

The hourly rate should be acceptable, reasonable and fair

nr	Function	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		€ -		€ -

Titel: Altered IgG fucosylation driving pathologies in COVID-19: Relevance for diagnosis and therapeutics

Hoofdaanvrager: 5.1.2e

Dossier number: 5.1.2i Toelichting

Stukje onder relevance in aanvraag

**Why
Public
funding**

5.1.2i Toelichting

5.1.2i Toelichting

Altered IgG fucosylation driving pathologies in COVID-19: Relevance for prognosis and therapeutics

5.1.2e

Sanquin Research

Vragen uit vooraanmelding: Bij de uitwerking van de aanvraag dient u de volgende punten mee te nemen:

5.1.2i Toelichting

5.1.2i Toelichting

Met vriendelijke groet,

5.1.2e

1.

5.1.2e
5.1.2e
5.1.2e *bioRxiv*, in press, doi:10.1101/2020.05.18.099507.
2.

5.1.2e
5.1.2e A prominent lack of IgG1-Fc fucosylation of platelet alloantibodies in pregnancy. *Blood*. **123**, 471–480 (2014).
3.

5.1.2e 5.1.2e
5.1.2e Low anti-RhD IgG-Fc-fucosylation in pregnancy: A new variable predicting severity in haemolytic disease of the fetus and newborn. *Br. J. Haematol.* **166**, 936–945 (2014).
4.

5.1.2e 5.1.2e 5.1.2e
5.1.2e Prophylactic anti-D preparations display variable decreases in Fc-fucosylation of anti-D. *Transfusion*. **55**, 553–562 (2015).
5.

5.1.2e 5.1.2e
5.1.2e Glycosylation pattern of anti-platelet IgG is stable during pregnancy and predicts clinical outcome in alloimmune thrombocytopenia. *174*, 310–320 (2016).

Checklist

for Open science & FAIR data elements in the COVID-19 research programme

Version 1.1 26 May 2020

This checklist is for the first 4 out of 8 **requirements and recommendations** for the **activities for open science and FAIR data**. They relate to the preparation phase of a research project.

The checklist shows a number of options for open science and FAIR data. Please consult [Open science in COVID-19 research](#) for more information about what you can do, for recent updates on the guidance, new practices, and instructions.

Choose the options that suit your project best!

The purpose of the checklist is to fill in the options that you choose for your project. Discuss with your data steward (or other data expert) the options that suit your project best. If you have options that are not listed below, you may indicate this as well.

Please fill in the form and attach it to your grant application.

Requirements & Recommendations	Applicants must report as follows
The preparation phase: grant application	
Who is the data steward who supports the open science and FAIR data planning in your project? Check the website for ZonMw's webinars to inform and support data stewards.	☒ I involve a data steward: Name: 5.1.2e Institute: Sanquin Bloedvoorziening E-mail: 5.1.2e@sanquin.nl ☐ I do not have a data steward yet, because Klik of tik om tekst in te voeren.
Requirement 1: Alignment and reuse Please show the options for reusing data, biological materials, and/or other resources (from research or from practice) in your project. Check whether it is possible to use resources that are made in the context of COVID-19.	Name the existing resources that you plan to use: ☒ Data: Clinical parameters from COVID-19 biobanks ☒ Biological materials: COVID-19 biobank (AMC and Sanquin) ☒ Research software: LacyTools (https://github.com/Tarskin/LaCyTools) for extraction of IgG-glycosylation data; DOI: 10.1021/acs.jproteome.6b00171 ☐ Other resources, i.e. Klik of tik om tekst in te voeren. ☐ No, I will not use existing resources, because Klik of tik om tekst in te voeren. Please mark the resources that you indicated above in bold if it is a COVID-19 related resource
Requirement 2: preregistration of all animal studies (for all other studies, preregistration is strongly recommended) You are required (for animal studies) and recommended (for all other studies) to preregister your research	☐ In case of preregistration: Provide the link or registration code: Klik of tik om tekst in te voeren. ☐ For animal studies, the code at the Preclinical Trial Register is: Klik of tik om tekst in te voeren. ☐ No, I do not preregister my research proposal.

plan (including the protocols, methods, etc).	
Requirement 3: FAIR data within COVID-19 research community Choose the options that suit your project best! Here you can show the COVID-19 specific standards, technology or infrastructure for FAIR data that you have selected to apply during your project. Once your application is granted, you can use these to fill in your data management plan (DMP) (= requirement 5). Read for more information: Open science in COVID-19 research and 3.Creating FAIR data, tailored to COVID-19	Name the COVID-19 specific FAIR data standards, technologies or infrastructure that are applicable in your study, and you plan to use: ☐ eCRF of the WHO (machine actionable) ☐ A COVID-19 related or other FAIR data point ☒ COVID-19 research platform for data sharing ☐ Data will be recorded in RDF format ☐ I plan to use the metadata scheme that will be developed for COVID-19 research (planned in summer 2020) ☐ Other COVID-19 related standards, etc: Klik of tik om tekst in te voeren. ☐ Collaboration with COVID-19 data collection(s), namely Klik of tik om tekst in te voeren. ☐ A new standard, technology or infrastructure will be developed in the project with the COVID-19 research community, namely Klik of tik om tekst in te voeren. Comment on your choice(s) In the preposed work, both data and shareable research tools will be generated and made available. First reports will be shared directly on Open access prepublication servers (e.g. BioRxiv https://www.biorxiv.org/content/10.1101/2020.05.18.099507v1) ☐ None of the above. Comment: Klik of tik om tekst in te voeren. ☐ I did not decide yet.
Requirement 4: Budget for FAIR data and Open Access Publications You need to plan a budget for open science and research data management during your research project. This budget should include costs for data stewardship, and – if applicable - costs for additional services from data service providers (e.g. from Health-RI or other providers), or extra e-infrastructure.	Explain how you budgeted for open science and FAIR data in your project: ☒ I specified the costs in the budget form. ☐ I cannot specify the costs right now, and make a reservation of 5% maximum of my research budget for data stewardship. ☐ I did not budget the costs, because Klik of tik om tekst in te voeren. When you fill in the budget form, you could consider the following aspects: - o Data stewardship - o Data services providers - o Additional e-Infrastructure, exceeding the regular institutional infrastructure. - o Other open science and FAIR data related costs. o (Optional) Open access publication(s): ZonMw requires researchers within the covid-19 programme to make all publications resulting from scientific research, that is fully

	or partially subsidised by ZonMw, immediately (without embargo) open access available with an open license. You are allowed to include costs for <u>full gold</u> Open Access publications in the project budget up to a maximum amount of € 5000,- (specify with 'Open Access'). Immediate Open Access publishing via other routes is also permitted, but ZonMw does not provide financial resources for this. For the specific conditions we kindly refer to the programme texts.
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Verklaring akkoord indienen uitgewerkte subsidieaanvraag

Artikel 4:2 van de Algemene wet bestuursrecht bepaalt dat een uitgewerkte subsidieaanvraag wordt ondertekend. Een uitgewerkte subsidieaanvraag omvat een inhoudelijke beschrijving van het project alsmede een projectbegroting. Om aan de wettelijke verplichting te voldoen, is in artikel 8, lid 6 van de Algemene subsidiebepalingen van ZonMw bepaald dat de hoofdaanvrager en de bestuurlijk verantwoordelijke van de rechtspersoon een schriftelijke verklaring ondertekenen dat zij beiden akkoord zijn met het indienen van de uitgewerkte subsidieaanvraag. Deze verklaring dient een week na het aanvragen van de subsidie door ZonMw te zijn ontvangen.

Graag verzoek ik u aan deze wettelijke vereiste te voldoen. In het geval dat uw aanvraag in aanmerking komt voor honoreren en ZonMw heeft deze verklaring nog niet ontvangen, zal uw aanvraag op formele gronden niet worden toegekend.

Stuur de ondertekende verklaring binnen een week na indienen via email naar het betreffende programma secretariaat.

Titel aanvraag: Altered IgG fucosylation driving pathologies in COVID-19: Relevance for prognosis and therapeutics	
Dossiernummer: 5.1.2i Toelichting	
Hoofdaanvrager	Bestuurlijk verantwoordelijke
Naam: 5.1.2e	Naam: 5.1.2e
Functie: 5.1.2e	Functie: 5.1.2e
Handtekening: 5.1.2e	5.1.2e
Datum: 15-6-2020	Datum: 15/6/20