Screening of the immune repertoire of healthy volunteers for broadly reactive fusion-inhibiting antibodies directed against coronavirus S protein, including SARS-CoV-2

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To screen the immune repertoire of healthy volunteers for broadly reactive fusion-inhibiting antibodies directed against coronavirus S protein, including SARS-CoV-2 f and (if found) to isolate/clone and further characterize such antibodies with the...

Ethical review	Approved WMO
Status	Completed
Health condition type	Viral infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON49952

Source
ToetsingOnline

Brief title
Healthy volunteers blood sampling

Condition

- Viral infectious disorders

Synonym
Corona, COVID-19, SARS-CoV-2

Research involving
Human

Sponsors and support

Primary sponsor: Leyden Laboratories B.V.
Source(s) of monetary or material Support: Leyden Laboratories

Intervention

Keyword: Antibody, Blood sampling, COVID-19, SARS-CoV-2

Outcome measures

Primary outcome

* B-cell response as assessed by enzyme-linked immunosorbent assay (ELISA)

and/or enzyme-linked immunosorbent spot assay (ELISpot) and/or flow cytometry

methods

* Serology: peptide library scanning

Secondary outcome

* Prevalence of common cold as assessed by PCR-based assay for respiratory

pathogens panel

Study description

Background summary

Two processes are key to infection by any virus: attachment and entry. Viral attachment is achieved through binding of a protein on the surface of the viral particle to a specific receptor (i.e. protein or glycan structure) on the surface of a host cell, whereas entry is defined as the release of the viral proteins and genetic material in the cytosol of the host cell.
In the case of enveloped viruses, attachment and entry are mediated through distinct domains of a single surface protein. Typically, a globular *head* region of this protein contains the Receptor Binding Domain (RBD) while a membrane-proximal *stem* region contains the machinery that mediates viral entry by triggering fusion of the viral and host cell membranes, the so called *fusion domain* (1).
As the globular head region is much more exposed than the stem region, both natural infection and vaccination primarily induce antibodies that block

infection by binding to the RBD and prevent viral attachment. While such antibodies have high neutralizing potency, they are typically highly specific for one virus strain (or a small set of closely related strains) as a consequence of the fact that the RBD is prone to mutate and varies significantly between individual virus strains.
In contrast, the fusion domain is highly conserved among virus families. This is due to the fact that in order to trigger fusion of the virus* and host cell membranes, the fusion domain needs to undergo extensive conformational rearrangements. This molecular machine consists of many moving parts which imposes strong evolutionary constraints on many residues in the stem region (2).
For Coronaviruses, attachment and entry are mediated by the *Spike* (S) protein. The S1 subunit contains the variable RBD while the S2 subunit contains the conserved fusion machinery (3-5). There is ample evidence in the literature that the S2 domain of coronaviruses is antigenic, and antibodies able to inhibit membrane fusion by Coronavirus S proteins have been described (6-10).
In order to find human monoclonal antibodies with broad neutralizing activity, the current research will be focusing on interrogating the B-cell repertoire of healthy human donors for antibodies directed against the S, S1, and particularly the S2 domains of the coronavirus S protein able to block the membrane fusion process using state-of-the-art technology such as flow cytometry.
If broadly neutralizing antibodies are identified using the above-mentioned techniques, Leyden Labs will develop mAb-based fusion-inhibition product(s) for prevention of infection and respiratory disease by members of the corona virus family, including SARS-CoV-2.

Study objective

To screen the immune repertoire of healthy volunteers for broadly reactive fusion-inhibiting antibodies directed against coronavirus S protein, including SARS-CoV-2 f and (if found) to isolate/clone and further characterize such antibodies with the ultimate goal of developing an antibody for prophylactic and/or therapeutic use against coronavirus infections.

Study design

This is an exploratory study that is part of the development trajectory of a therapeutic antibody. A total of 20 healthy subjects will be enrolled. The study will consist of a single visit, the total duration of the study for each subject will not be more than half a day. During the visit, subject*s eligibility for this study will be assessed prior to sample collection, and blood will be collected for the study endpoints.

Study burden and risks

No investigational drug will be administered to the volunteers. The invasive

procedures under this protocol will be restricted to blood sample collection (venipuncture). The burden for the volunteer related to the study procedures is limited. Only well-established methods of sample collection will be applied, with a known and limited risk and no or mild discomfort for the volunteer. In addition, all collections will be performed by qualified medical staff.
No clinical benefit can be expected from this study for the participating subjects. A study population of 20 healthy volunteers (10 males; 10 females) is deemed appropriate to investigate in vitro the immune response for epitope based therapeutic SARS-CoV-2 antibody development.

Contacts

Public
Leyden Laboratories B.V.

Keizersgracht 290a
Amsterdam 1016EW
NL
Scientific
Leyden Laboratories B.V.

Keizersgracht 290a
Amsterdam 1016EW
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Participant must sign the study informed consent form prior to any

study-mandated procedure indicating that he or she understands the purpose, procedures and potential risks, and is willing to participate in the study;
2. Participant is male or female and between 40 and 65 years of age, inclusive, at the time of enrollment;
3. Participant is willing and able to complete the study procedures;
4. Participant has a primary care physician at the time of enrollment;
5. Participant is generally healthy in the investigator*s clinical judgment, as determined by medical history evaluation, including no clinically significant disorder, condition, infection or disease that would interfere with the study evaluation, procedures or completion.

Exclusion criteria

1. Participant has current clinical symptoms of COVID-19 (including, but not limited to: cough, fever, shortness of breath, sudden onset of anosmia, ageusia or dysgeusia). Note that a participant who reports a previous positive diagnostic test result for SARS-CoV-2 infection (serological testing or viral RNA detection by PCR testing) and who is recovered from COVID-19 for at least three weeks prior to blood sampling is allowed to participate in the study as deemed by the investigator;
2. Participant had recent close contact with a SARS-CoV-2 infected person or someone in their household tested positive for SARS-CoV-2, has travelled to a country/area that has been designated as a COVID-19 risk area according to the effective policies/guidelines of the National Institute for Public Health and the Environment (Dutch: RIVM) or otherwise meet criteria for home isolation;
3. Participant received immunosuppressive medication or other immunomodulating agents (including investigational drugs) in the 3 weeks prior to study blood sampling or received immunoglobulins or blood products in the 3 months prior to study blood sampling;
4. Participant with a whole blood donation or loss of >500 ml within 21 days before study blood sampling;
5. Any known factor, condition, or disease that might interfere with compliance, study conduct or interpretation of the results, as deemed by the investigator.

Study design

Design

Study type: Observational invasive
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	03-11-2020
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	28-10-2020
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 25763
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL75505.058.20

Study results

Date completed:	13-11-2020
Results posted:	03-05-2021

First publication
29-04-2021