Identification of plasma biomarkers for risk stratification of hospitalised Covid-19 patients

Principal Investigators: Jacob Odeberg, KTH
Program research area: Biomarkers and systems immunology.
Collaborators: Charlotte Thålin, Karolinska Institutet and Danderyds Hospital; Lynn Butler, KI & KTH (SciLifeLab); Jochen Schwenk, KTH & SciLifeLab

May 2020

We aim to fast track the identification of early biomarkers that predict the likely course of individual COVID-19 disease progression. Specifically, we aim to identify plasma biomarkers predictive of:

1. Progression to severe disease in individuals initially presenting with moderate symptoms

2. Future deterioration in ICU patients. Such biomarkers could be used for risk stratification and clinical decision making, e.g. urgency of hospitalization and need for increased vigilance.

Patient material - The strategy is based on proteomic profiling of consecutive plasma samples repeatedly collected from hospitalized COVID-19 patients (n~1000). Demographic data, routine lab, comorbidity and on-going medical treatment will be collected from hospital records. In parallel, hospital employees will be recruited in a sub study, providing a control group that most likely will include a portion of individuals infected without knowledge.

We will use a biomarker screening suspension bead array of 380 antibodies targeting :

(i) endothelial enriched or specific proteins, that we identified as being expressed across all organ beds, or specifically in the lung vasculature (unpublished study), and

(ii) (ii) components and regulators of the coagulation and complement systems.

Systems immunology analyses of the cytokine storm in COVID-19

SciLifeLab

Principal Investigators: Petter Brodin Karolinska Institutet
Program research area: Biomarkers and systems immunology.
Collaborators: Yenan Bryceson, Clinical Immunology, Karolinska University Hospital, & MedH KI

May 2020

SARS-Cov2 infection is generally associated with mild disease, but a few individuals, mostly elderly or immunocompromised, develop severe disease. This is characterized by a hyperinflammatory state and development of acute respiratory distress syndrome, ARDS. This deadly complication is not caused by the virus itself but a consequence of an uncontrolled hyperinflammatory immune response to the virus.

To better guide such therapeutic efforts towards modulating hyperinflammation and ARDS, we need a better understanding of the cellular and molecular mechanisms involved.

All data will be published and shared publicly as soon as possible to allow clinicians in Sweden and abroad to better modulate the cytokine storm and learn what markers to monitor in their patients.

We would like to apply the methods Mass cytometry, plasma protein profiling, mRNA-sequencing, T-cell receptor repertoire sequencing and high-dimensional serology (VirScan), in two contexts:

1. A comparison of mild vs severe cases (~100 samples from KAW-funded biobank, Huddinge), and
2. Longitudinal samples from a fewer cases of younger individuals (< 50 years) with severe disease (requiring intensive care) and these samples we hope to collect at Karolinska University Hospital in Solna.

Prediction of severe disease in Covid-19

Principal Investigators: Lars-Magnus Andersson Department of Infectious Diseases, Institute of Biomedicine, Gothenburg University
Program research area: Biomarkers and systems immunology.
Collaborators: Magnus Gisslén, Ali Harandi, Ola Hammarström, Gothenburg University

May 2020

The study will be able to identify biomarkers that may predict disease severity and have the potential to greatly impact the management of patients in short and medium term. It will also provide understanding of myocardial dysfunction in Covid-19, which is an area were new data and biomarkers are urgently needed.

Severely ill patients seem to have high levels of viral replication and inflammatory markers are elevated to very high levels in many individuals. Accumulating evidence is also indicating that severely ill patients suffer from myocardial dysfunction and have elevated troponin levels.

mRNA transcriptomics will be performed on acute and convalescent blood samples.

Plasma levels of in >500 proteins will be analysed with proximity extension assay (PEA).

Cardiac troponin, NT-proBNP, suPAR, GDF15, cfDNA, and Cardiac specific Met-cfDNA will be analysed in serial samples from the same patient in the different groups.

Taking back the control of the SARS-CoV2 antiviral immune response as a mean to neutralize the COVID19 disease pathogenicity

Principal Investigators: Marie Larsson Linköping University
Program research area: Biomarkers and systems immunology.
Collaborators: Esaki Muti Shankar, Central University of Tamil Nadu, India; Mikael Sigvardsson, Linköping University/Lund University

May 2020

Project aims:
1. Elucidate the underlying mechanisms giving rise to a highly inflammatory response and impaired antiviral response SARS-CoV2.

2. Explore already existing drugs and new potential drugs ability to control viral infection and modulate the cytokine storm by enhancing the antiviral responses.

This study should provide a general picture over the initial COVID19 infection and how the SARS-CoV2 modulate the antiviral responses in favor of inflammation and display potential pathways and factors that can be targeted to restore the balance. It should also establish drugs with the ability to limit or block viral replication by enhancing antiviral responses and reducing the inflammation.

We will test the effect exerted by the SARS-CoV2 as early as 1h and up to 96h to test viral replication and antiviral and inflammatory responses by rtPCR, proteomics and RNA seq. Factors involved in inflammatory and antiviral signaling pathways such as STING, ERK, and STAT1 are of special interest.

Establishing a biobank of clinical specimens for studying evolution of viral diversity and development of immune respones, including inflammation, seroprevalence and protective antibodies, in SARS-Cov2 infection

Principal Investigators: Patrik Medstrand, Lund University
Program research area: Biomarkers and systems immunology.
Collaborators: Blenda böttiger, Thoas Fieretos, Ola Forslund, Marianne Jansson, Anna Nilsson, Mats Ohlin, Magnus Rasmussen, Kristian Riesbeck Anna Döerlund Strand and Anders Widell - Lund University; Ingvar Eliasson & Lisa Wasserstrom – Region Skåne

May 2020

1. Establish a biobank of clinical specimens.
2. Study viral evolution, viral population structure and diversity during infection using SciLifeLab infrastructure.
3. Investigate how SARS-Cov2 evolution is coupled to disease severity and inflammatory responses, including cytokine and inflammation marker profiles.
4. Evaluate to what extent bacterial and other viral superinfections contribute to the severity of disease.
5. Measure protective immunity in individuals who have recovered from SARS Cov-2 infection.
6. Study the development of immunity in the population of Skåne County.

We will fill several critical knowledge gaps of SARS-Cov2 infection that are of particular importance, e.g. how the longitudinal aspect of infection dynamics is coupled to the development of disease and protective immunity, which is critical for deeper understanding of the current pandemic.

Clinical specimens (nasopharynx, plasma, serum, whole blood and faeces) are collected from patients at admission and every three days during hospitalization.

Methods include:

- Targeted capture sequencing
- Ultrasensitive single genome sequencing
- NGS
- Inflammation markers will be assayed using Luminex.
- IgG detected by ELISA and studies of antibody effector functions will be performed on virus propagated in culture.

Dynamics and longevity of the specific adaptive immune response in COVID-19 patients

SciLifeLab

Principal Investigators: Davide Angeletti University of Gothenburg, Department of Microbiology and Immunology
Program research area: Biomarkers and systems immunology.
Collaborators: Mats Bemark (GU/SU), Kristina Nyström (SU), Magnus Lindh (SU), Nicolae Miron (SU), Anna Lundgren (GU/SU), Magnus Gisslén (SU), Per Sikora (SciLifeLab/GU), Adam Wheatly (Univ. of Melbourne), Florian Krammer (Ichan School of Medicine), Malin Bäckström (GU) Thomas Svensson (SciLifeLab/Chalmers), Jonathan Robinson (SciLifeLab/Chalmers)

May 2020

This project will elucidate the development of virus specific B cell (Bc) and T cell (Tc) responses over time in relation to clinical course and outcome and define the longevity of immunity tounderstand short- and long-term protection.
In detail we aim to:

1. Describe the expansion and longevity of antigen-specific Bc and Tc responses.
2. Identify viral mutations that promote antibody (Ab)-escape.
3. Determine immune cell signatures associated with disease severity.

Cytokine storm is a major cause for morbidity and mortality in patients with COVID-19, but the antigen specific immune response is nevertheless vital in clearing the infection. High titres of specific serum Abs are found in recovered patients and primate models suggest these are protective, supporting the idea that herd immunity can develop.

However, the longevity of SARS-CoV2 immunity has been questioned. Knowledge about the adaptive immune response is vital for handling the pandemic and in the development of vaccines.

This project critically depends on patient blood samples and clinical data from project “Building Capacity – the Sahlgrenska Covid-19 Biobank” which will be longitudinally collected during and after infection (up to 5 years) from hospitalized patients and less severe cases.