Multi-molecular phenotyping in a self-sampling population

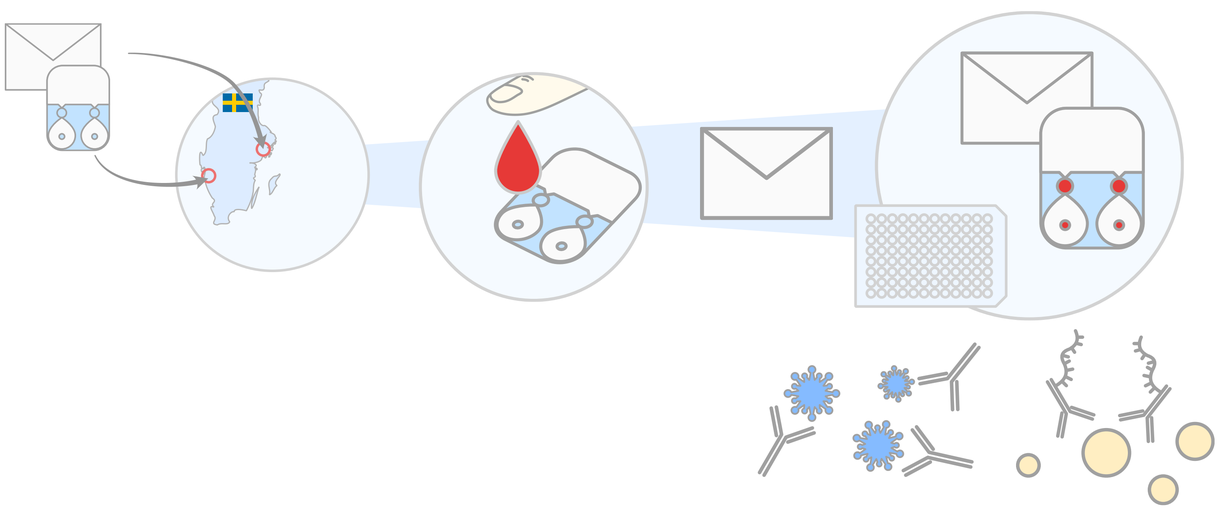
Leo Dahl, KTH Royal Institute of Technology
Department of Protein Science

Introduction

The COVID-19 pandemic has posed significant challenges to the healthcare systems. In response to the virus, new vaccines and technologies have been applied to induce, manage and understand the human immune response against the infection. Owing to the reactive capability of the proteome to respond to SARS-CoV-2 infections and vaccinations, many circulating proteins have been associated with severe states in hospitalized subjects. However, the proteomic responses to infection, vaccination and combinations thereof are still poorly studied in the general population.

Methods

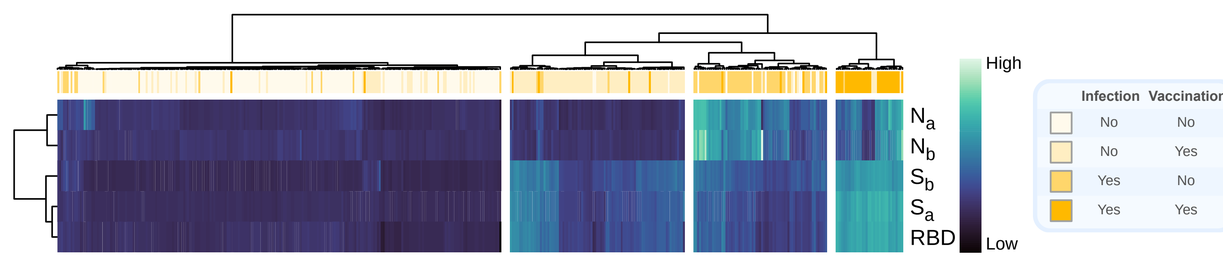
2000 DBS cards from Capitainer AB were sent out to randomly selected individuals in Stockholm and Gothenburg between May and September of 2021. An accompanying questionnaire about health, infection and vaccination was also filled out by each participant.



Samples from 440 participants were analysed in serological assays followed by proteomic profiling.
Serological assays used multi-analyte Luminex-based systems to measure human antibodies against two variants of the SARS-COV-2 S protein, two variants of the N protein, one variant of the RBD protein, and 22 interferons.
The proteomic assays used the Olink Explore and Alamar Biosciences platforms to measure >500 inflammation-related proteins.

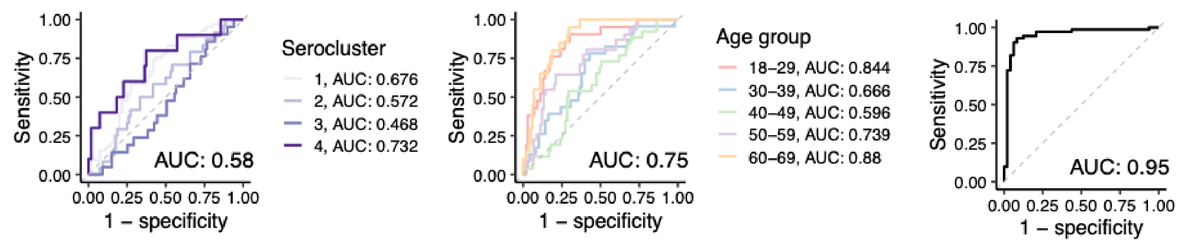
Serological assay results

Hierarchical clustering was performed on the anti SARS-CoV-2 antibodies. Cutting the resulting sample clustering into four groups revealed data-driven response phenotypes that were each dominated by different combinations of infection and vaccination. We found that the clusters agreed with self-reported infection and vaccination statuses, while more precisely capturing asymptomatic individuals and time between event and sampling.

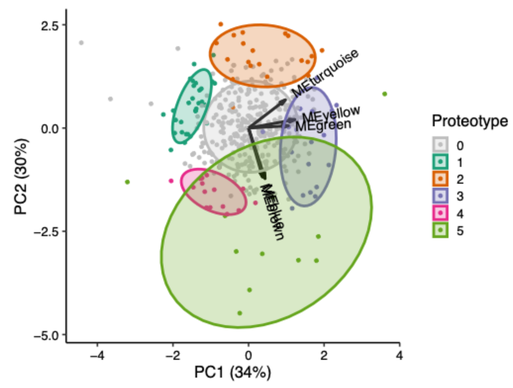


Proteomic assay results

Lasso regression was used to evaluate the predictive power of proteins on serology-based immune status. Proteins were found to predict sex well while predicting immune status poorly. This can be attributed to time from immune event and the more short-lived and dynamic nature of the circulating proteome compared to the immune response.



To analyse proteomics-specific phenotypes, the dimensions of the proteomics data were reduced using Weighted Gene Correlation Network Analysis (WGCNA). The samples were clustered using the resulting five dimensions in hierarchical clustering, revealing five proteomics clusters. These clusters were linked to different immune pathways or traits such as smoking or age, complementing the information gained from antibody levels.



Full author list

Leo Dahl[1], Annika Bendes[1], María Bueno Álvez[1], Vincent Albrecht[1], Hooman Aghelpasand[2], Sophia Björkander[3], Simon Kebede Merid[3], Anja Mezger[2], Max Käller[2], Claudia Fredolini[1,4], Åsa Torinsson Naluai[5], Olof Beck[6], Erik Melén[3,7], Stefan Bauer[8], Magnus Gisslén[9,10,11], Niclas Roxhed[12,13], and Jochen M Schwenk[1]

1. SciLifeLab, Department of Protein Science, KTH Royal Institute of Technology, Solna, Sweden.
2. SciLifeLab, Department of Gene Technology, KTH Royal Institute of Technology, Solna, Sweden.
3. Department of Clinical Science and Education, Södersjukhuset, Karolinska Institutet, Stockholm, Sweden
4. Affinity Proteomics Unit, SciLifeLab Infrastructure, KTH Royal Institute of Technology, Solna, Sweden.
5. Institute of Biomedicine, Sahlgrenska Academy at the University of Gothenburg, Gothenburg, Sweden.
6. Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden.
7. Sachs' Children and Youth Hospital, Södersjukhuset, Stockholm, Sweden.
8. TUM Technical University of Munich, Munich, Germany.
9. Department of Infectious Diseases, The Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden.
10. Sahlgrenska University Hospital, Gothenburg, Sweden.
11. Public Health Agency of Sweden, Solna, Sweden.
12. Department of Micro and Nanosystems, KTH Royal Institute of Technology Stockholm, Stockholm, Sweden.
13. MedTechLabs, BioClinicum, Karolinska University Hospital, Solna, Sweden.