SYSCID – A Systems medicine approach to chronic inflammatory diseases

SYSCID E-Newsletter No. 8/2021

We are pleased to present the 8th e-newsletter of the SYSCID consortium which unites internationally renowned experts from 9 countries with the ambition to pave the way for a systems medicine approach to chronic inflammatory diseases. We would like to provide you with a short update of our work progress and interesting news from the field. This includes:

- SYSCID work progress
- Recent publications
- News from the team: Science during COVID-19
- SYSCID annnual progress meeting

SYSCID work progress

The SYSCID project continues to actively contribute to the development of precision medicine by identifying a new molecular taxonomy of chronic inflammatory diseases. The project is now at its apex and develops predictive markers and mechanistic insights for clinical decision support. Results from the last year have identified first integrated molecular signatures, which may be able to predict the efficacy of anti-TNF therapy in inflammatory bowel disease, SLE and rheumatoid arthritis patients.

During the time of lockdowns and restrictions we have done lab work to generate significant knowledge on molecular processes involved in the pathogenesis of COVID-19. This was only possible as tools and methods had been already in place in SYSCID. Despite the delay from COVID-19 we will now finalize our integrative analyses on chronic inflammatory diseases in order to refine outcome and therapy predictor patterns. Our work thrives from the well-characterized patient cohorts with longitudinal molecular and clinical data, most of which are directly exported from electronic health records.

In the upcoming months, the SYSCID consortium will focus on

1. finishing cross-sectional analyses
2. finalizing ongoing single-cell related work and
3. work on longitudinal stability of obtained signatures.

Ultimately, SYSCID will help to develop molecularly defined disease endotypes and dynamic models of therapy response that will enable efficient patient stratification for future care of CID patients.

Recent publications

- Schulte-Schrepping, J., Reusch, N., Paclik, D. et. al.: Severe COVID-19 Is Marked by a Dysregulated Myeloid Cell Compartment. Cell (2020)
- Bernardes, J. P., Mishra, N., Tran, F. et. al. : Longitudinal Multi-omics Analyses Identify Responses of Megakaryocytes, Erythroid Cells, and Plasmablasts as Hallmarks of Severe COVID-19. Immunity (2020)
- Warnat-Herresthal, S., Schultze, H., Shastry, K.L. et al.: Swarm Learning for decentralized and confidential clinical machine learning. Nature (2021)

- Aschenbrenner, A.C., Mouktaroudi, M., Krämer, B. et al.: Disease severity-specific neutrophil signatures in blood transcriptomes stratify COVID-19 patients. Genome Med (2021)

News from the team: Science during COVID-19

SYSCID scientists were very active in COVID-19 research, as you can see in the testimonials from Comma Soft/University of Bonn, KCL and Genos below:

Comma Soft and University of Bonn: Online platform FASTGenomics supports scientists in combating the COVID-19 pandemic

Since the initial project phase, SYSCID partners Comma Soft and the University of Bonn worked on data storage and sharing solutions for the consortium based on FASTGenomics, an online platform for single-cell transcriptomics data analysis jointly developed by the two SYSCID partners. During the Pandemic, FASTGenomics quickly became a central platform to exchange data and analyses related to COVID-19 among collaborators and also to make it available to the public as supplementary information to publications. In addition, researchers were enabled to continue their work from home without access to their university infrastructure by using our analysis environments. Also, remote lectures and courses where successfully held with the support of the FASTGenomics platform.

Where needed, the functions of FASTGenomics were quickly adapted and extended to suit the needs of the researchers. More than 40 COVID-19 related datasets and corresponding analyses were published on FASTGenomics and several public projects were created that provide a quick and easy way to access, use and extend data and analysis from high-level publications. This saves valuable time, as everything can be found in one place and executed directly without the need to gather data and code, just to be faced with the problem that for some reason you cannot run it on your machine.

Notable examples for such projects, from the SYSCID consortium and associated partners, are listed below. Please also make sure to have a look at the exciting corresponding publications in the "Recent publications" sections of this newsletter.

- Schulte-Schrepping et al., 2020 - Severe COVID-19 is marked by a dysregulated myeloid cell compartment
- Bernardes_2020_COVID19_10x
- Warnat-Herresthal et al., 2021 - Swarm Learning for decentralized and confidential clinical machine learning
- COVID-19 whole blood transcriptome analysis 2021

TwinsUK: Our year of COVID-19 research

TwinsUK has been extremely busy int the past twelve months conducting ground-breaking COVID-19 research. Our COVID-19 studies this year have had the highest ever participation rates from TwinsUK members, reaching up to 80%.

- Serology home visits: We visited 512 twins who were within driving distance of TwinsUK at home to collect a range of samples. We visited twins who were asymptomatic or who had previously reported symptoms via the app and had completed their isolation period. Twins who tested positive for antibodies were visited a second time 6-8 weeks later, along with their co-twin.
- Cope study: All twins were asked to complete a questionnaire at set timepoints throughout the year to understand the consequences of COVID-19 has had on the mental and physical health of people.
- Immune response: We visited symptomatic twins in Greater London and South East England to collect viral swabs and blood samples within 3-5 days of reporting symptoms via the app. We then saw them again 2 weeks and 2 months later for follow-up visits.

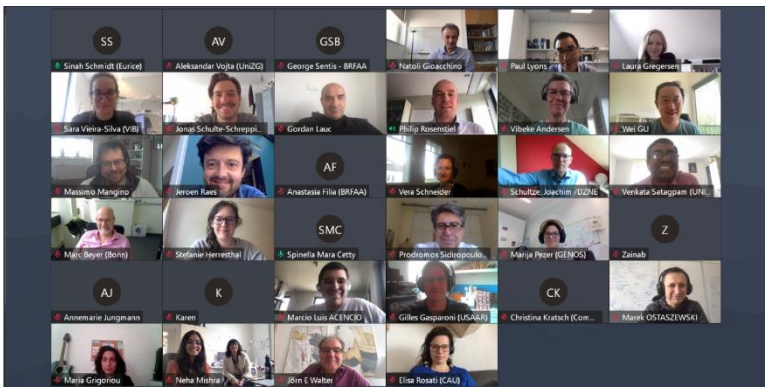
- T-cell home visits: We recruited a subset of twins from the home visits to collect a blood sample to find out if T-cells play a role in COVID-19 immunity.
- Antibody health study: We invited all twins to provide a finger-prick blood sample by post, to understand how many of our twins had developed antibodies to fight off a COVID-19 infection.
- Repeat blood collection: Twins who had tested positive from the second home visit were invited to complete a finger-prick blood collection and return it by post. This helped us study how antibody levels change over time.
- Long COVID home visits: We visited 20 twins at home to collect samples to investigate T-cells and immunity in people experiencing long COVID compared with short COVID.

COVID-19 research at Genos

Researchers in Genos were very active in the field of COVID-19. In spring 2020 they performed a large epidemiological study involving 7,000 hospitalised patients in Europe and China, as well as over 30,000 individuals reporting disease symptoms in UK. This study provided first strong evidence for the seasonal nature of COVID-19 and was the basis for very liberal policy of Croatia in spring 2020 (https://pubmed.ncbi.nlm.nih.gov/33553204/). Mucins in the mucosal barrier are an important first line of defence against all pathogens, including SARS-CoV-2. Indoor air humidity is a very important factor for proper function of our mucosal barrier, which is an acute problem in the winter season when heating results in very low indoor air humidity and contributes to the seasonal nature of COVID-19 (https://pubmed.ncbi.nlm.nih.gov/32373322/). Strategic focus of Genos are glycan biomarkers and they also performed the first study of glycans in COVID-19 that revealed significant biomarker potential of glycans as predictors of severe form of COVID-19 (https://pubmed.ncbi.nlm.nih.gov/33174592/).

SYSCID annual progress meeting

Since the restrictions related to the COVID-19 pandemic are still ongoing and the safe and health of the members of the SYSCID consortium are always a priority, the 4th annual meeting was conducted as a full virtual meeting on 18th May 2021.



SYSCID coordinator Philip Rosenstiel warmly welcomed the consortium members and pointed out that even though the COVID-19 pandemic had a high impact on the SYSCID consortium within the last year (e.g. due to lab closures and shortening of supplies) the scientists showed a great spirit of perseverance while facing the challenges of this pandemic. This spirit was also demonstrated in the following presentations held by the members of the consortium representing the work they had done in the past year. Although the meeting was held virtually, the working atmosphere and the scientific discussions were vivid yet efficient.

Since the SYSCID project has now entered its last phase, an important task for the future will be the publication of papers and everyone is having their fingers crossed that a face-to-face meeting in 2022 will be manageable.

Your contact persons

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