The Adaptive Immune Receptor Repertoire (**AIRR**) Community of The Antibody Society is pleased to announce a special event focused on AIRR-sequencing data and COVID-19. Due to the unprecedented nature of the COVID-19 pandemic and the need for rapid scientific progress, this virtual meeting will provide recent analyses of the B- and T-cell receptor repertoires of COVID-19 patients. In addition, we will explore a key objective of the AIRR Community in the context of the pandemic: *How the scientific response to the COVID-19 pandemic might be leveraged to promote the implementation of standards for AIRR-seq data.*

Day 1: Tuesday, September 8th – 8:00 – 11:00 PDT / 11:00 AM – 2:00 PM EDT / 5:00 – 8:00 PM CEST

8:00 – 8:10: Welcome and introduction to this AIRR Community special event: Nina Luning Prak, University of Pennsylvania, USA and Chair of the AIRR Community of The Antibody Society

Session Theme: *How T-cell receptor repertoire data inform the pathophysiology of COVID-19, implications for diagnostics, therapeutics, and/or vaccines*

8:10 – 8:15: Overview by Session Chair: Lindsay Cowell, UT Southwestern Medical Center, USA
This session will comprise four 23-min presentations, with each followed by a 7-min Q&A period. At the session's end there will be a 35-min panel discussion with prepared questions. In addition, attendees are invited to submit questions to the panel or specific members through the chat function.

8:15 – 8:45: Speaker 1: Aleksandra M. Walczak, Centre National Recherche Scientifique (CNRS), France
Title: *Dynamics of T-cell memory formation and reactivation after COVID-19*
Abstract: We used high-throughput T-cell receptor (**TCR**) sequencing to track concentrations and phenotypes of T-cell clones in longitudinal blood samples from each of two donors before and after mild COVID-19, and identified SARS-CoV-2-responding CD4+ and CD8+ T-cell clones. We found SARS-CoV-2-responding clonotypes at pre-existing timepoints, suggesting pre-existing immunity. We also identified characteristic motifs among TCR sequences of COVID-19-reactive clones.
Relevant DOI: https://doi.org/10.1101/2020.05.18.100545

8:45 – 9:15: Speaker 2: Donjete Simnica, Martin-Luther University, Germany
Title: *Shared T-cell clusters emerge over disease course in recovering COVID-19 patients*

Abstract: To understand the divergent manifestations of COVID-19, ranging from mild to severe/fatal disease, we analyzed the peripheral T-cell repertoire of patients from each disease course using next-generation sequencing. To identify clones that potentially recognize the same antigen, we used the algorithm, GLIPH2, to cluster T-cell clones based on local/global similarity. We found that the T-cell clusters present or enriched exclusively in the active (and mostly severe) disease group were predominantly public clonotypes (*i.e.*, they had a high probability of being generated by V(D)J recombination during T-cell development). In contrast, 31 T-cell clusters that were exclusive to the recovered group had a low generation-probability but were shared by several individuals, indicating their disease specificity. Analysis of longitudinal samples from a patient, taken during mild disease and recovery, identified 176 clones that steadily expanded over the course of disease until recovery. Some of these expanding clones share CDR3 amino-acid sequence similarity with clones from other COVID-19-recovered patients. Thus, we identified clonotype signatures that are likely associated with effective anti-viral T-cell responses, and hence may serve as a means of tracking effective vaccine responses.
Relevant DOI: https://doi.org/10.1016/j.immuni.2020.06.024

9:15 – 9:45: Speaker 3: Pandurangan Vijayanand, La Jolla Institute for Immunology, USA
Title: *Single-cell transcriptomic analysis of SARS-CoV-2 reactive CD4$^+$ T cells*

Abstract: The contribution of CD4$^+$ T cells to protective or pathogenic immune responses to SARS-CoV-2 infection remains unknown. Here, we present large-scale single-cell transcriptomic analysis of viral antigen-reactive CD4$^+$ T cells from 40 COVID-19 patients. In patients with severe disease compared to mild disease, we found increased proportions of cytotoxic follicular helper (T_{FH}) cells and cytotoxic T helper cells (CD4-CTLs) responding to SARS-CoV-2, and reduced proportion of SARS-CoV-2-reactive regulatory T cells. Importantly, in hospitalized COVID-19 patients, a strong cytotoxic T_{FH} response was observed early in the illness which correlated negatively with antibody levels to SARS-CoV-2 spike protein. Polyfunctional T helper (T_H)1 cell and T_H17 cell subsets were underrepresented in the repertoire of SARS-CoV-2-reactive CD4$^+$ T cells compared to influenza-reactive CD4$^+$ T cells. Together, our analyses provide so far unprecedented insights into the gene expression patterns of SARS-CoV-2-reactive CD4$^+$ T cells in distinct disease severities
Relevant DOI: https://www.biorxiv.org/content/10.1101/2020.06.12.148916v1

10-minute break

9:55 – 10:25 Speaker 4: Jonathan Carlson, Microsoft Research, USA
Title: *Magnitude and dynamics of the T-cell response to SARS-CoV-2 infection at individual and population levels*

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Abstract: As part of our ImmuneCODE efforts, to date we have sequenced >500 million TCRs from >1000 infected and convalescent patients, and mapped >100,000 TCRs from dozens of patients and healthy donors to hundreds of SARS-CoV-2-derived antigens. In this talk, I will describe some of our early observations, perhaps the most striking of which is that public disease-associated TCRs separate individuals who have been infected with SARS-CoV-2 from historical controls with high sensitivity and specificity.

10:25 – 11:00: Moderated Panel Discussion. The Session Chair will ask a few prepared questions of the speakers, such as:

(i) Please describe any overarching "take-home" conclusions regarding T-cell responses so SARS-CoV-2.

(ii) Are there assays that you might suggest for diagnosing and/or treating severe *vs*. milder cases of COVID-19, and especially for predicting severe *vs*. mild outcomes early-on in the disease process (*e.g*., following T-cell subsets or clonal expansions)? Or for monitoring for viral exposure or return to work?

(iii) Some COVID-19 patients who have experienced even mild infections have ongoing symptoms during convalescence (*i.e.,* after SARS-CoV-2 has presumably been cleared from the body). What is known about the immunological basis of those ongoing symptoms? Can you suggest a means of predicting or following, and perhaps treating or preventing, those ongoing symptoms?

(iv) What would the advantage be of inducing CD4+ and/or CD8+ T-cell responses *via* vaccination? If it's true, that induction of the strongest T-cell effector-memory occurs after moderate to severe (*vs*. mild or asymptomatic) COVID-19… What are the implications, if any, for whether strong, durable and protective effector-memory T-cell responses can be induced by vaccination?

(v) Based on the T-cell responses you've observed during COVID-19 and convalescence, what aspects of the T-cell response would you recommend be followed in a vaccine clinical trial (*e.g.,* cell phenotype, clonal expansion, epitope specificity)? How would those proposed assays help in identifying the most protective and durable vaccines and/or vaccination strategies?

Written questions from the audience will also be taken via the chat function, so please feel free to submit your own questions!

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Day 2: Wednesday, September 9th – 8:00 – 11:00 PDT / 11:00 AM – 2:00 PM EDT / 5:00 – 8:00 PM CEST

Session Theme: *How B-cell receptor repertoire data inform the pathophysiology of COVID-19, implications for diagnostics, therapeutics, and/or vaccines.*

8:00 – 8:10: Overview by Session Chair: Nina Luning Prak, University of Pennsylvania, USA
This session will comprise four 23-min presentations, with each followed by a 7-min Q&A period. At the session's end there will be a 35-min panel discussion with prepared questions. In addition, attendees are invited to submit questions to the panel or specific members through the chat function.

8:10 – 8:45: Speaker 1: Nina Luning Prak, University of Pennsylvania, USA
Title: *Antibody responses in SARS-CoV-2 infection*
Abstract: Since the SARS-CoV-2 pandemic came to Philadelphia, we have been studying humoral immune responses to the virus. In the serum, we have established clinical-grade assays for the detection of IgG and IgA antibodies that bind to the receptor binding domain (RBD) of the SARS-CoV-2 spike protein. We have also been studying B cells and immune repertoires. Many hospitalized patients with acute disease harbor massive plasmablast expansions in the blood and have correspondingly large expanded B-cell clones. Several of these expanded clones have long CDR-H3 sequences and some lack evidence of somatic hypermutation. While there is a mild bias towards VH3 family rearrangements, which may be enriched for spike protein binding based on other studies, in our global repertoire analysis we do not detect marked skewing towards specific VH genes or obvious public CDR-H3 motifs. In immunophenotyping experiments, we detect a low fraction of circulating B cells that bind to the RBD or the nucleocapsid, in spite of readily detectable serum antibodies in the same individuals. Taken together, our findings and those of others suggest that some B cells are recruited into an "all hands on deck" style extrafollicular response in severe disease. This response may be off-target and resemble immune responses that occur in flares of systemic autoimmunity.
Relevant DOI: https://doi.org/10.1101/2020.05.18.101717

8:45 – 9:15: Speaker 2: Charlotte Deane, University of Oxford, UK
Title: *Building databases and tools to aid in measuring vaccine efficacy, diagnosing exposure, and developing effective biotherapeutics for SARS-CoV-2.*

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Abstract: I will describe two interconnected efforts that aim to help characterise and understand how the natural immune system responds to SARS-CoV-2 infection and capture from all sources of anti-viral neutralising antibodies. Deep sequencing of B-cell receptor (**BCR**) heavy chain variable regions from a cohort of COVID-19 patients from the UK reveals a stereotypical naive immune response to SARS-CoV-2, which is consistent across patients and may be a positive indicator of disease outcome. Convergence was also demonstrated across wide geographies by comparison of data sets between patients from the UK, USA and China, further validating the disease association and consistency of the stereotypical immune response even at the sequence level. These convergent clonotypes provide a resource to identify potential therapeutic and prophylactic antibodies and demonstrate the potential of BCR profiling as a tool to help understand and predict positive patient responses. Alongside this analysis, we developed CoV-AbDab, which contains data on over 1400 published/patented antibodies and nanobodies known to bind to at least one betacoronavirus. This is a constantly updated resource that is free to access and download without registration at: http://opig.stats.ox.ac.uk/webapps/coronavirus.
Relevant DOIs: https://www.biorxiv.org/content/10.1101/2020.05.15.077313v1 and https://www.biorxiv.org/content/10.1101/2020.05.20.106294v1

9:15 – 9:45: Speaker 3: Kenneth Hoehn, Yale University, USA
Title: *B-cell lineage analysis and COVID-19*
Abstract: B cell somatic hypermutation and affinity-driven selection are crucial to the development of neutralizing antibodies in response to infection. These processes produce lineages of B cells related by point mutations to a common naïve B cell ancestor. Here, we show how lineage tree-based methods can be used to reveal important information about the dynamics of the B cell response in COVID-19.
Relevant DOIs: https://doi.org/10.1101/2020.07.16.20153437 and https://doi.org/10.1101/2020.05.30.124446

10-min break

9:55 – 10:25: Speaker 4: Bryan Briney, Scripps Research, USA
Title: *Rapid isolation of neutralizing antibodies against SARS-CoV-2*
Abstract: The development of countermeasures to prevent and treat COVID-19 is a global health priority. In under 7 weeks, we enrolled a cohort of SARS-CoV-2-recovered participants, developed neutralization assays to interrogate serum and monoclonal antibody responses, and adapted our high-throughput antibody isolation, production and characterization pipeline to rapidly screen over 1000 antigen-specific antibodies. In addition to the discovery of potential therapeutics and prophylactics, this work revealed the genetics of the humoral immune response to SARS-CoV-2.
Relevant DOI: https://doi.org/10.1101/2020.06.08.141267

10:25 – 11:00: Moderated Panel Discussion: The Session Chair will ask a few prepared questions of the speakers, such as:
(i) Please describe any overarching "take-home" conclusions regarding B-cell responses to SARS-CoV-2.
(ii) Are there any serologic or B-cell assays that you would recommend for clinical use in monitoring of viral exposure or return to work?

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(iii) Do you think that durable and protective antibody responses can be induced by infection or by vaccination? Do you think that individuals in high-risk groups will be able to respond to an active vaccine or will passive immunization be required?

(iv) Based on the B-cell responses you've observed during COVID-19 and convalescence, what aspects of the B-cell response would you recommend monitoring in a vaccine clinical trial?

(v) Some COVID-19 patients who have experienced even mild infections have ongoing symptoms during convalescence (*i.e.,* presumably after SARS-CoV-2 has been cleared from the body). What is known about the immunological basis of prolonged disease or these ongoing symptoms? Are there B-cell assays that you would recommend for the evaluation of potential sequelae of disease in individuals with ongoing symptoms?

Day 3: Thursday, September 10ᵗʰ – 8:00 – 11:00 PDT / 11:00 AM – 2:00 PM EDT / 5:00 – 8:00 PM CEST

Session theme: *COVID-19: A catalyst for the rapid implementation of the FAIR guiding principles* for AIRR-seq data*

8:00 – 8:10: Overview by Session Chair: Jamie Scott, Simon Fraser University, Canada

This session will be divided into three, 50-min panel discussions with a moderator and 2-4 invited members. Each panel member will give a brief overview of their involvement with the discussion topic. Then the panel will be asked prepared questions. *See the FAIR guiding principles for scientific data management and stewardship.

8:10 - 9:00: Panel 1 Topic: *State of FAIR 2020: Achievements, Catalysts, Obstacles and Risks*

Panel 1 Moderator: Christian Busse, German Cancer Research Center, Germany

Summary: The FAIR principles have become a central paradigm for research data management and Open Science. Seven years after their inception, we will discuss the most important achievements so far, the critical milestones to adoption, the major roadblocks ahead, and the potential risks of universal FAIRness.

Panel 1 Participants:
- Christine Choirat (Swiss Data Science Center / EOSC FAIR WG)
- Rob Hooft (Dutch Tech Center for Life Sciences / RDA COVID-19 Omics)
- Eva Maria Moar (EURAC Bolzano / EARTO)

10-min break

9:10 - 10:00: Panel 2 Topic: *How are database providers making COVID-19 data FAIR?*

Panel 2 Moderator: Bjoern Peters, La Jolla Institute for Immunology, USA

Summary: Database providers have had to address the challenge of making data related to COVID-19 rapidly accessible to their user communities. This need for immediacy can conflict with the goal of making data FAIR (findable, accessible, interoperable and re-usable). We will discuss the challenges encountered, approaches to engage user communities, and the lessons learned to prepare for the next pandemic.

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Panel 2 Participants:
- Bjoern Peters - IEDB
- Felix Breden - AIRR-C / iReceptor
- Patrick Dunn - IMMPORT
- Erica Ollmann Saphire - CoVIC-DB
- Darren Natale - UniProt / PRO

10-min break

10:10 - 10:55: Panel Topic: *Implementing policies to support FAIR data*
Panel 3 Moderator: Jamie Scott, Simon Fraser University, Canada
Summary: How journals, scientific societies, funding agencies and industry are envisioning the harmonization and sharing of data and software resources, including examples of their respective strategies and work in this area.

Panel 3 Participants:
- Journal perspective: **Sarah Callaghan**, Editor-in-Chief, Cell Press journal *Patterns*
- Scientific Society perspective: **Luis Eduardo Coelho Andrade**, Professor, Universidade Federal de São Paulo and Chair, Quality Assessment and Standardization Committee of the International Union of Immunology Societies (**IUIS**)
- Biomedical Research & Funding Agency perspective: **Joe Breen**, Immunoregulation Section Chief, Basic Immunology Branch, DAIT/NIAID/NIH
- Industry perspective: **Jake Glanville**, Co-founder and CEO, Distributed Bio and Centivax

Written questions from the audience will also be taken via the chat function, so please feel free to submit your own questions!

10:55 - 11:00 Concluding remarks ending this AIRR Community special event: Nina Luning Prak, University of Pennsylvania, USA and Chair of the AIRR Community of The Antibody Society

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