

12/2024 | CARE Biannual Newsletter CARE Biannual Newsletter



In this penultimate issue we talk about an impressive app developed by **AbbVie** to determine genetic factors related to COVID-19 risk... plus we share news of an exciting partnership between University of Dundee and Novartis that will take CARE activities to the next level for pandemic preparedness after the project finishes in March 2025. We also take a closer look our partner **Scifeon** and the important role they play in managing CARE's laboratory informatics

Introducing the COVID-19 QTL-GWAS colocalization explorer application

Led by AbbVie, a platform has been developed allowing easy query of summary statistics and visualization of the genomic context of significant COVID-19 gene links Dr. Meritxell Oliva

With the aim of understanding host response and prioritising treatment targets, the CARE partner AbbVie sought to identify human genes influencing genetically driven disease risk and severity, and to identify additional high-order phenotypes impacted by pleiotropic COVID-19-associated genomic loci.

The AbbVie team, led by Meri Oliva, published a paper aiming to identify genes and molecular phenotypes related to COVID-19 risk and severity.

As part of the work, a web application has been made available at https://covidgenes.shinyapps.io/shiny/. The application allows us to easily query summary statistics and visualize the genomic context of all significant COVID-19 gene links, stratified relevant molecular categories, and aids the identification of COVID-19 causal genes.

Meri Oliva describes the aim of the work: "While many efforts are being devoted to the characterization of the genetic architecture of COVID-19 effects on the human host, its underlying molecular basis has not been exhaustively explored across multiple molecular layers. To understand host response and to prioritize















Introducing the COVID-19 QTL-GWAS colocalization explorer application (Cont'd)

treatment targets, we sought to identify human genes influencing genetically-driven disease risk and severity. To this end, we performed ancestry-aware, translayer, multi-omic analyses by integrating recent (April 8, 2022) COVID-19 Host Genetics Initiative GWAS data from six ancestry endpoints - African, Amerindian, South Asian, East Asian, European and meta-ancestry - with functional maps and QTL catalogues.

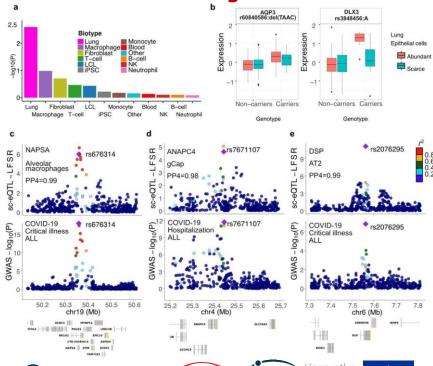
We explored 91 GWAS hits (p<5e-7), 28% of which were identified in a single ancestry. We analysed a comprehensive set of >300 cis QTL maps from ~100 biotype sources for colocalization, including disease-relevant biotypes and contexts; blood of COVID-19 patients, large airway epithelium, and lung cell contexts. Across all GWASs, QTL maps and molecular phenotypes, we identified thousands of colocalizations (PP4>0.75) involving >100 genes.

This provided repository hosts a R shiny app to interact with the results of the colocalization analysis."

Pulmonary cell of origin of COVID-19 linked genes

a) Enrichment (y axis) of COVID-19 loci in eQTL biotypes (x axis). b) Gene expression (y axis) of AQP3 and DLX3 genes by carrier status of corresponding COVID-19 severity allele (x axis). c-e) Genotype- phenotype association values of the NAPSA, ANAPC4 and DSP.

To learn more, click here: Integration of GWAS and multi-omic QTLs identifies uncharacterized COVID-19 gene-biotype and phenotype associations | medRxiv



















Collaboration between University of Dundee DDU and Biomedical Research Unit of Novartis announced

Continuing development of a CARE antiviral compound for future coronavirus pandemic preparedness



The University of Dundee's Drug Discovery Unit (DDU) and the Biomedical Research Unit of Novartis have announced a partnership to enable collaboration on a target-based project to develop a broad-spectrum antiviral compound for coronavirus preparedness. A lead chemical series developed in CARE

Work Package 3 has shown promising pan-coronavirus activity with low mutation and resistance risks. It will be taken forward by the partnership to conduct toxicology studies and complex virus efficacy models.

"We are very excited at the Dundee Drug Discovery Unit to be collaborating with Novartis, a world-leading pharmaceutical company, to push the frontier of coronavirus drug research and develop medicines for any future coronavirus pandemics". Dr Duncan Scott, Coronavirus Portfolio Lead, DDU University of Dundee

Working alongside Duncan, the DDU team in WP3 are Colin Robinson, Ian Gilbert, Irene Georgiou, Craig Smith, Sandra O'Neill, Shamshad Ahmad, Lesley-Anne Pearson, John Post, Suzanne Norval and Sean O'Byrne. The DDU is led by Prof Ian Gilbert and Dr Duncan Scott with funding by the Bill & Melinda Gates Foundation.

The Novartis team is part of the NIH-funded Antiviral Drug Discovery (AVIDD) Centers for Pathogens of Pandemic Concern which were set up to accelerate antiviral treatments for pandemic preparedness and will be bringing toxicology and virology expertise.

While attention in the healthcare sector has shifted away from COVID-19, the DDU and Novartis still recognize the risk of a future coronavirus pandemic and are prepared to continue to develop the work started in CARE WP3. This endeavour reinforces the value CARE has brought to pandemic preparedness, thus contributing to CARE'S legacy - through being a platform from which CARE's research can continue to bear fruit.

To learn more, click here for the Press Release and information about AViDD











Introducing Scifeon – a CARE SME organisation



Scifeon was set up in 2016 by **Thomas P. Boesen (PhD)** to help scientists have better, more flexible, adaptable and agile informatics support that can take them and their research to the next level.

Dr. Boesen's vision was to provide scientists with the next generation of research data management software to help them in their research.

Scifeon is a Software as a Service (SaaS) platform. This comprises the Electronic Laboratory Notebook (ELN), Laboratory Information Management System (LIMS) and Scientific Data Management System (SDMS). These systems collect, organize and securely store valuable research data for easier processing, better collaboration and faster results - giving scientists more time for science.



Thomas Boesen (PhD)
(Founder and CEO,
Scifeon)

Scifeon provides scientists with better informatics on a day-to-day basis. It is the next generation of research data management software specifically developed for scientists by scientists.

Why did Scifeon choose to get involved in CARE?

Scifeon recognised CARE's need for a flexible data management solution that could be adapted to its highly variable research effort. This involved the creation of CARE's data management plan as well as creating and operating the data management cloud platform, CARE-4-DATA.

In addition to Thomas, the Scifeon team includes



Stephan Boersma, M.Sc. Senior software engineer



Jakob Boysen, M.Sc., Principal Software Engineer, Scifeon











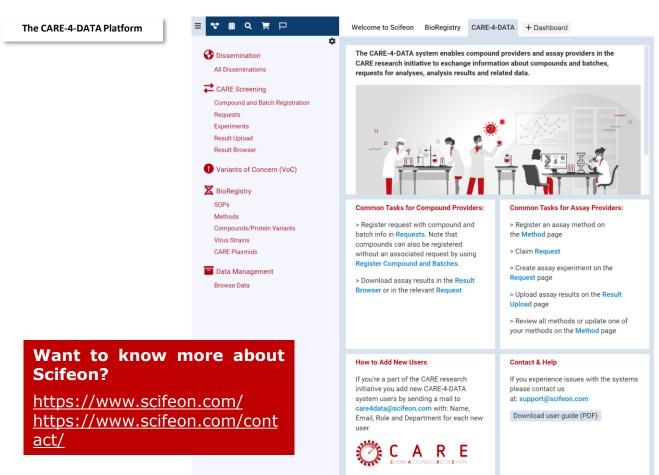




Introducing Scifeon (Cont'd)

What has Scifeon delivered for CARE?

The CARE-4-DATA platform houses protocols for several biochemical and cellular assays and allows researchers from different institutions to collaborate on testing compounds in these assays and sharing the results. It also contains a registry of virus strains and plasmids that are present at several of the CARE partner organisations.



What benefits has Scifeon enjoyed through participating in CARE?

Scifeon has seen its software platform grow and improve through incorporating feedback from CARE scientists.















CARE's Young Researchers: how this generation of scientists are contributing to the cause for pandemic preparedness. As shared on the CARE website and LinkedIn



Collins Owino, Postdoc

Utrecht University, WP5

Understanding how the coronavirus hijacks human host factors and processes, providing opportunities to develop therapies to inhibit viral replication



Emmely Treffers, Postdoc

LUMC, WP5

Proteomics of SARS-CoV-2 infected systems to grow knowledge of how virus and host interact, to find novel ways to disrupt viral life cycle or counteract potential pathogenic host responses



Grace Beirne, PhD Student

KU Leuven, WP8

Working in System Dynamics Modelling to help optimize the set-up of future consortia



Holly Kerr, PhD Student

University of Edinburgh, WP5

Understanding host response and resulting disease to help identify alternative or complementary approaches to direct-acting anti-virals by targeting the host



Manon Laporte, Postdoc

KU Leuven, WP1

Discovery of novel target in coronaviruses replication cycle and small molecule inhibitor to address that target, which may benefit future pandemic preparedness across many virus types



Oliver Debski-Antoniak, Postdoc

Utrecht University, WP4

Discovery and advancement of antibody treatments for existing and emerging coronavirus infections, helping prevent and alleviate economic and health strains caused by future endemics and pandemics



Thijs Steijaert, PhD Student

LUMC, WP5

Helping grow scientific knowledge of host pathways involved in replication and pathogenesis of the SARS-CoV-2 virus using proteomics and phosphoproteomics



Wenjuan Du, Postdoc

Utrecht University, WP4

Understanding more about conserved epitopes on the SARS-CoV-2 virus to make a valuable impact on future vaccine design



















Want to know more about our fantastic CARE Work Package teams?

During 2024, we have completed publishing a series of infographics about each of our Work Packages. The infographic provides an at-a-glance view on the team's objectives, collaborations, breakthrough moments and some impressive stats!

In 2025 we will produce an overview infographic, summarising all of CARE's achievements.

Please ensure you are following us on LinkedIn so that they appear in your feed, and please feel free to like/comment/repost our infographic posts when you see them.



Work Package 1	Anti-coronavirus drug discovery in phenotypic virus-cell-based assays
Work Package 2	Target based drug discovery & design
Work Package 3	Antiviral drug development: Hits to Leads
Work Package 4	Generation and characterisation of monoclonal antibodies against SARS-CoV-2 and related coronaviruses
Work Package 5	System Biology: identifying immune markers contributing to the host immune responses to SARS-CoV-2 infection and their correlations with clinical and virological outcomes
Work Package 6	From lead to pre-clinical candidate and proof-of-concept in small-animal and non-human primate models
Work Package 7	Clinical evaluation of repurposed or novel SARS-CoV-2 antivirals or antibodies
Work Package 8	Management, ethics, communication, dissemination and exploitation; focusing on laboratory and clinical data





management











All about CARE

CARE is one of <u>8 IMI EC funded consortia</u> playing a role in supporting efforts targeting coronavirus. It was launched in April 2020 and is Europe's largest scientific research initiative committed to tackling COVID-19.

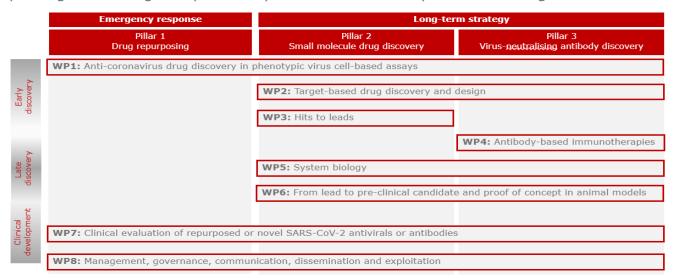


Its dual goals were firstly to find solutions to address the arising emergency; and secondly for future pandemic preparedness, exploring small molecule and antibody options.

CARE comprises 38 highly respected partners from around the globe, bringing together the relevant academic and industry expertise, with a budget of 76 million euro split between contributing EFPIA partners matched by the European Commission. It is led by Marnix Van Loock of Johnson & Johnson, with Ashley Roe representing Takeda as co-lead, and Professor Yves Lévy of VRI-Inserm as the project co-ordinator.



The consortium comprises three research pillars, addressed by eight work packages working independently and collaboratively towards our goals.



















Initial efforts in the emergency space did not yield results, but progress has steadily been made in the preparedness space in both small molecules and antibodies, with teams continually taking account of the evolving context as the virus yielded new variants.

The consortium is steadily building a pipeline of potential small molecule assets to move forward, with promising signs of differentiation from current standard of care. On the antibody front, two very promising candidates were developed with good breadth and potency across all currently known variants of concern, which are now being developed in the clinic, outside of CARE.

CARE is committed to serve society through science and collaboration. Its partners are dedicated to undertaking efforts to make potential new treatments accessible for broad populations including in low and lower-middle income countries at an affordable price. Naturally, the consortium is keen to focus its remaining resources towards the most promising candidates that will bring new benefit to patients.

More information: Go to the CARE website for more information about

















About this Newsletter

With many new discoveries and achievements under our belt, we share our progress every six months, each June and December via the newsletter; as well as more frequent posts being shared on LinkedIn. Our final external newsletter will be issued in March 2025, when the project will draw to a close.

All CARE partners will automatically receive a link to this newsletter. If you would like to be added to the distribution list please e-mail the <u>CARE Project</u> Management Office.

Reminders

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 101005077. The JU receives support from the European Union's Horizon 2020 research and innovation programme, EFPIA, BILL & MELINDA GATES FOUNDATION, GLOBAL HEALTH DRUG DISCOVERY INSTITUTE and UNIVERSITY OF DUNDEE.

The content of this publication only reflects the author's view and the JU is not responsible for any use that may be made of the information it contains.

In association with:













For more information

- www.IMI-CARE.eu
- Follow us on social media using <u>LinkedIn</u>
- Look for #CAREvsCOVID

Contact

- Click here to contact CARE















CORONA ACCELERATED R&D IN EUROPE

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