



Olink  
Accelerating proteomics together

How plasma proteomics will help  
your drug repositioning and  
vaccine development programs for

# COVID-19





## What we know.

- To date, the cellular mechanisms underlying the immune response and disease severity of COVID-19 are still poorly understood
- A comprehensive overview of the inflammation processes of COVID-19 is still lacking
- There are significant variance in disease severity of COVID-19 with many unknowns on why some people are facing severe outcomes
- Multiple organ systems are impacted by the disease causing short- and long-term effects

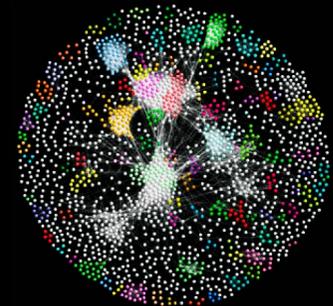
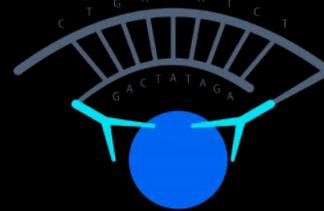
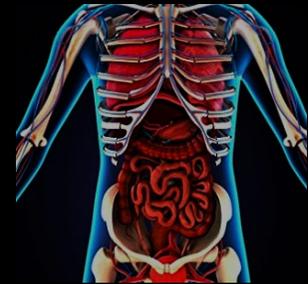
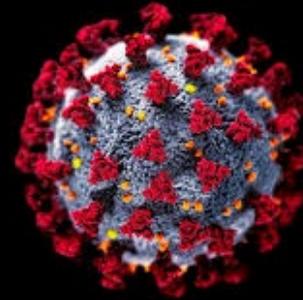
## What we need.

- Broaden our understanding of the pathophysiology behind COVID-19 with deep profiling of the inflammatory system
- Predictors of disease severity and ways to stratify patients in the context of outcomes
- Biomarkers correlative to viral load or subsequent viremia
- Understanding of therapeutic impacts on multiple organ systems and inflammatory biomarkers
- Identification of new therapeutic targets and methods to evaluate drug repositioning to treat COVID-19 patients

# How We Can Help



- Olink Explore provides a validated multi-organ system monitoring tool revealing insights into COVID-19
- Protein biomarkers associated with COVID-19 impacted organs
- Broad coverage of high-sensitivity inflammatory protein assays
- Our service provides insights into COVID-19 and therapeutic impacts across the body using just a few  $\mu\text{l}$  of blood





# Understanding COVID-19 by Olink

Some examples from published papers

Biological Pathways/ Mechanisms	Olink Protein Biomarker Changes in COVID-19 patients	Hypothesis/Outcomes
IL6/IL1 Inflammatory pathway	IL6 upregulation in Intensive Care Unit (ICU) patients	Homogenous endotype in severe disease (ICU patients) Tocilizumab (anti-IL6 rec) and Anakinra (IL-1 receptor antagonist) are potential treatment options <sup>1</sup>
Fibrosis	HGF, FGF21 upregulated in ICU patients	Long term fibrosis contributors <sup>1</sup>
Kinin-kallikrein system	DPP4, PCI/Serpina 5 downregulated in ICU patients	Disruption of coagulation <sup>1</sup>
Proinflammatory mediation	ENRANGE, TNFSF14, increase in severely ill patients	Lung inflammation, fibrosis, remodeling; ENRANGE, TNSFS14 or their receptors potential drug targets <sup>2</sup>
Inflammation, angiogenesis, Th1 immune response	IL-17A, IL6, CXL10, TWEAK, ADA	Multisystem Inflammatory Syndrome in Cov-2 infected children (MIS-C) differs from Kawasaki disease in the underlying immunopathology <sup>3</sup>

<sup>1</sup>: Frank L. van de Veerdonk, PhD, Nico A.F. Janssen, MD, Inge Grondman, MD. et al. **A systems approach to inflammation identifies therapeutic targets in SARS-CoV-2 infection (2020)** medRxiv preprint doi: <https://doi.org/10.1101/2020.05.23.20110916> medRxiv preprint

<sup>2</sup>: Arunachalam P, Wimmers F, Mok C, et. al. **Systems biological assessment of immunity to mild versus severe COVID-19 infection in humans.** (2020) Science, DOI: 10.1126/science.abc6261

<sup>3</sup>: Consiglio CR, Cotugno N, Sardh F, et. al. **The Immunology of Multisystem Inflammatory Syndrome in Children with COVID-19** (2020) Cell, 10.1016/j.cell.2020.09.016.

# A growing list of COVID-19 publications using Olink

**Original Clinical Report**

**Novel Outcome Biomarkers Identified With Targeted Proteomic Analyses of Plasma FN3 Critically Ill Coronavirus Disease 2019 Patients**

Douglas D. Fraser, MD, PhD<sup>1</sup>, Gediminas Cepkunas, DVM, PhD<sup>1</sup>, Eric K. Patterson, PhD<sup>1</sup>, Maral Slesarow, MD, MSc<sup>2</sup>, Claudio Martin, MD, PhD<sup>1</sup>, G. Mark Daley, PhD<sup>1,2</sup>, Matthew A. Patel, BS<sup>1</sup>, Michael R. Miller, PhD<sup>1</sup>, David R. Gorman, PhD<sup>1,2</sup>, Scott E. Gill, PhD<sup>1</sup>, Guillaume Faur, MD, MSc<sup>1</sup>, Jonathan Priddy, PhD<sup>1</sup>, Eleftherios Diamantidis, MD, PhD<sup>1</sup>, on behalf of the Lawson COVID-19 Study Team

**Lack of Association Between Gen Variants at ACE2 and TMPRSS2 Genes Involved in SARS-CoV-2 Infection and Human Quantitative Phenotypes**

Editorial A. Lopez Vera<sup>1</sup>, Adrian von der Grubbe<sup>1</sup>, Pauline Langlet<sup>1</sup>, Merve Ayar Gonen<sup>1</sup>, Arshwan Tan<sup>1</sup>, Albert Ramirez<sup>1</sup>, Luke Frasca<sup>1</sup>, Christopher Patrick Deaton<sup>1</sup>, Alessandro Zetteriani<sup>1</sup>, Severina Sanna<sup>2</sup> and Lillina Colucci<sup>1</sup>

**The Immunology of Multisystem Inflammatory Syndrome in Children with COVID-19**

Carina Svare Carlqvist<sup>1,2</sup>, Helle Carlqvist<sup>1,2</sup>, Fabian Sjöberg<sup>1,2</sup>, Christian Paul<sup>1,2</sup>, Daniela Annala<sup>1,2,3,4</sup>, Louise Kullander<sup>1,2</sup>, Zeynep Tuzi<sup>1,2</sup>, Ronita Zivon<sup>1,2</sup>, Alessia Roggero<sup>1,2</sup>, Giuseppe Palmieri Pascucci<sup>1,2</sup>, Veronika Santilli Tassi Camporini<sup>1,2</sup>, Yana Brykova<sup>1,2</sup>, Daniel Eriksson<sup>1,2</sup>, Jan Yngve<sup>1,2</sup>, Alessandra Mariani<sup>1,2</sup>, Tatjana Ljubanovic<sup>1,2</sup>, Anthonie Carpinus<sup>1,2</sup>, Alberto Villani<sup>1,2</sup>, Paolo Rossi<sup>1,2</sup>, the CAITUS Study Team, Niels Lankester<sup>1,2,3,4</sup>, Paolo Palmieri<sup>1,2</sup>, and Peter Donnelly<sup>1,2,3,4</sup>

**Coronavirus disease 2019 patients admitted to ICU show high mortality. The first retrospective analysis of COVID-19 has only been partially conducted, and prospective biomarkers have not been fully established. We performed targeted proteomics on critically ill coronavirus disease 2019 patients to better understand their pathophysiological mechanisms and to identify potential outcome biomarkers. We identified an elevated proinflammatory CD40 for mortality estimation to determine the plasma concentration of 1,161 proteins. Tumor necrosis factor- $\alpha$  and academic literature.**

**Coronavirus disease 2019 (COVID-19) shows a wide variation in expression and of symptoms, from very mild or no symptoms, to full-blown symptoms, and severe cases, to pneumonia, acute respiratory distress syndrome, and multi-organ dysfunction. Large differences in outcome have also been observed between males and females, and the cause for this variability are likely to be multifactorial, and to include the SARS-CoV-2 virus response for the infection, as well as host genetic factors. We performed a genome-wide association study (GWAS) for COVID-19 patients admitted to intensive care units (ICU) patients (classification accuracy 100%). The GWAS identified 19 new loci associated with COVID-19 severity. The most significant loci were associated with the ACE2 gene, which encodes the receptor for the SARS-CoV-2 virus. The GWAS also identified several loci associated with COVID-19 severity, including the ACE2 gene, which encodes the receptor for the SARS-CoV-2 virus. The GWAS also identified several loci associated with COVID-19 severity, including the ACE2 gene, which encodes the receptor for the SARS-CoV-2 virus.**

**Severe disease of SARS-CoV-2 is characterized by vigorous inflammatory responses in the lung, often with sudden onset after 7–12 days of initial disease. Efforts to modulate this hyperinflammatory response in the acute respiratory distress syndrome rely on the upregulation of the immune cell receptors and cytokines that drive this response. Given that severe disease is associated with a high degree of organ dysfunction, we investigated whether the inflammatory response in critical and systemic blood analyses and reported to capture cellular dysfunction. We report on a systems-level blood immunomonitoring study of 197 adult COVID-19 patients with COVID-19 and tested with a 1:1 blood samples from acute to recovery phases of the disease. We used a panel of 100 antibodies to identify high hyperinflammatory and changes in cell-cell communication during different stages of the disease. We also map immune trajectory during recovery that is seen among patients with severe COVID-19.**

**Systems-Level Immunomonitoring from Acute to Recovery Phase of Severe COVID-19**

Carina Svare Carlqvist<sup>1,2</sup>, Helle Carlqvist<sup>1,2</sup>, Fabian Sjöberg<sup>1,2</sup>, Christian Paul<sup>1,2</sup>, Daniela Annala<sup>1,2,3,4</sup>, Louise Kullander<sup>1,2</sup>, Zeynep Tuzi<sup>1,2</sup>, Ronita Zivon<sup>1,2</sup>, Alessia Roggero<sup>1,2</sup>, Giuseppe Palmieri Pascucci<sup>1,2</sup>, Veronika Santilli Tassi Camporini<sup>1,2</sup>, Yana Brykova<sup>1,2</sup>, Daniel Eriksson<sup>1,2</sup>, Jan Yngve<sup>1,2</sup>, Alessandra Mariani<sup>1,2</sup>, Tatjana Ljubanovic<sup>1,2</sup>, Anthonie Carpinus<sup>1,2</sup>, Alberto Villani<sup>1,2</sup>, Paolo Rossi<sup>1,2</sup>, the CAITUS Study Team, Niels Lankester<sup>1,2,3,4</sup>, Paolo Palmieri<sup>1,2</sup>, and Peter Donnelly<sup>1,2,3,4</sup>

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**Systems biological assessment of immunity to mild versus severe COVID-19 infection in humans**

Prabha S. Aravamudan<sup>1,2</sup>, Florian Wisniewski<sup>1,2</sup>, Chris Kai Pan Mok<sup>1,2</sup>, Runaway A. P. M. Perera<sup>1,2</sup>, Madhav Shivan-Narasimhan<sup>1,2</sup>, Xiaohu Zhang<sup>1,2</sup>, Yiqiang Feng<sup>1,2</sup>, Laurel Hillier<sup>1,2</sup>, Zheng-Jun Zhu<sup>1,2</sup>, Jihua Zhang<sup>1,2</sup>, Shao-Nan Zhou<sup>1,2</sup>, Yi Wang<sup>1,2</sup>, Yooni Lawani<sup>1,2</sup>, Talia H. Swartz<sup>1,2</sup>, Deepa Maddipati<sup>1,2</sup>, Avish S. Cohen<sup>1,2</sup>, Thomas U. Marron<sup>1,2</sup>, Hai-Hai, Manikam Kothari, Kevin Tullberg<sup>1,2</sup>, Olyver Olan<sup>1,2</sup>, Vasan Othman<sup>1,2</sup>, Aradhya Kulkarni<sup>1,2</sup>, Patricia Kowalek<sup>1,2</sup>, Judith A. Ables<sup>1,2</sup>, Eric Schacht<sup>1,2</sup>, Sundar Jagannathan<sup>1,2</sup>, Madhu Mazumdar<sup>1,2</sup>, Alexander Wu Chuan<sup>1,2</sup>, Adolfo Figo-Sotomayor<sup>1,2</sup>, Holden Terry Mackler<sup>1,2</sup>, Parvath Kishore<sup>1,2</sup>, Nadine Bousquet<sup>1,2</sup>, Math P. F. Bull<sup>1,2</sup>, Paul F. O'Keefe<sup>1,2</sup>

**Severe disease has revealed that the hyper-inflammatory response induced by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a major cause of disease severity and death. However, predictive biomarkers of pathogenic inflammation may help guide therapeutic immune pathways are critical findings. We implemented a rapid proteomic cytokine assay to measure severe inflammatory (IL-6, IL-8, IL-10, IL-17, IL-22, IL-27, IL-28, IL-30, IL-31, IL-32, IL-33, IL-34, IL-35, IL-36, IL-37, IL-38, IL-39, IL-40, IL-41, IL-42, IL-43, IL-44, IL-45, IL-46, IL-47, IL-48, IL-49, IL-50, IL-51, IL-52, IL-53, IL-54, IL-55, IL-56, IL-57, IL-58, IL-59, IL-60, IL-61, IL-62, IL-63, IL-64, IL-65, IL-66, IL-67, IL-68, IL-69, IL-70, IL-71, IL-72, IL-73, IL-74, IL-75, IL-76, IL-77, IL-78, IL-79, IL-80, IL-81, IL-82, IL-83, IL-84, IL-85, IL-86, IL-87, IL-88, IL-89, IL-90, IL-91, IL-92, IL-93, IL-94, IL-95, IL-96, IL-97, IL-98, IL-99, IL-100, IL-101, IL-102, IL-103, IL-104, IL-105, IL-106, IL-107, IL-108, IL-109, IL-110, IL-111, IL-112, IL-113, IL-114, IL-115, IL-116, IL-117, IL-118, IL-119, IL-120, IL-121, IL-122, IL-123, IL-124, IL-125, IL-126, IL-127, IL-128, IL-129, IL-130, IL-131, IL-132, IL-133, IL-134, IL-135, IL-136, IL-137, IL-138, IL-139, IL-140, IL-141, IL-142, IL-143, IL-144, IL-145, IL-146, IL-147, 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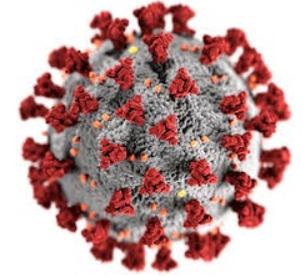
Olink  
Accelerating proteomics together



# COVID-19 Technology Access Framework.

Started by Harvard, MIT, and Stanford, now joined by 30 universities, aiming to combine data from the most critically important technologies that may help prevent, diagnose, or treat COVID-19 infections, and to share the findings openly to accelerate research, inform the public health response and help save lives.

1<sup>st</sup> data publicly released : >1 million NPX from Olink Explore



Dr. Michael Filbin (MGH)



Dr. Arnav Mehta  
(MGH & Broad Institute)



Dr. Alexandra-Chloé Villani  
(MGH & Broad Institute)



Dr. Nir Hacohen  
(MGH & Broad Institute)



Dr. Marcia Goldberg (MG)



Dr. Moshe Sade-Feldman (MGH)



# Initial findings from largest COVID-19 protein study from MGH Collaboratio

- As of 9/2020, COVID19 has caused over 1,000,000 deaths globally
- To date, the underlying **disease mechanisms are poorly understood**
- **Biomarkers are needed to predict disease severity and outcomes, stratify patients, guide therapy and drive drug/vaccine development**
- Using Olink Explore, **we successfully predicted** severity and outcome of COVID-19 infections in patients at the time of hospital admission



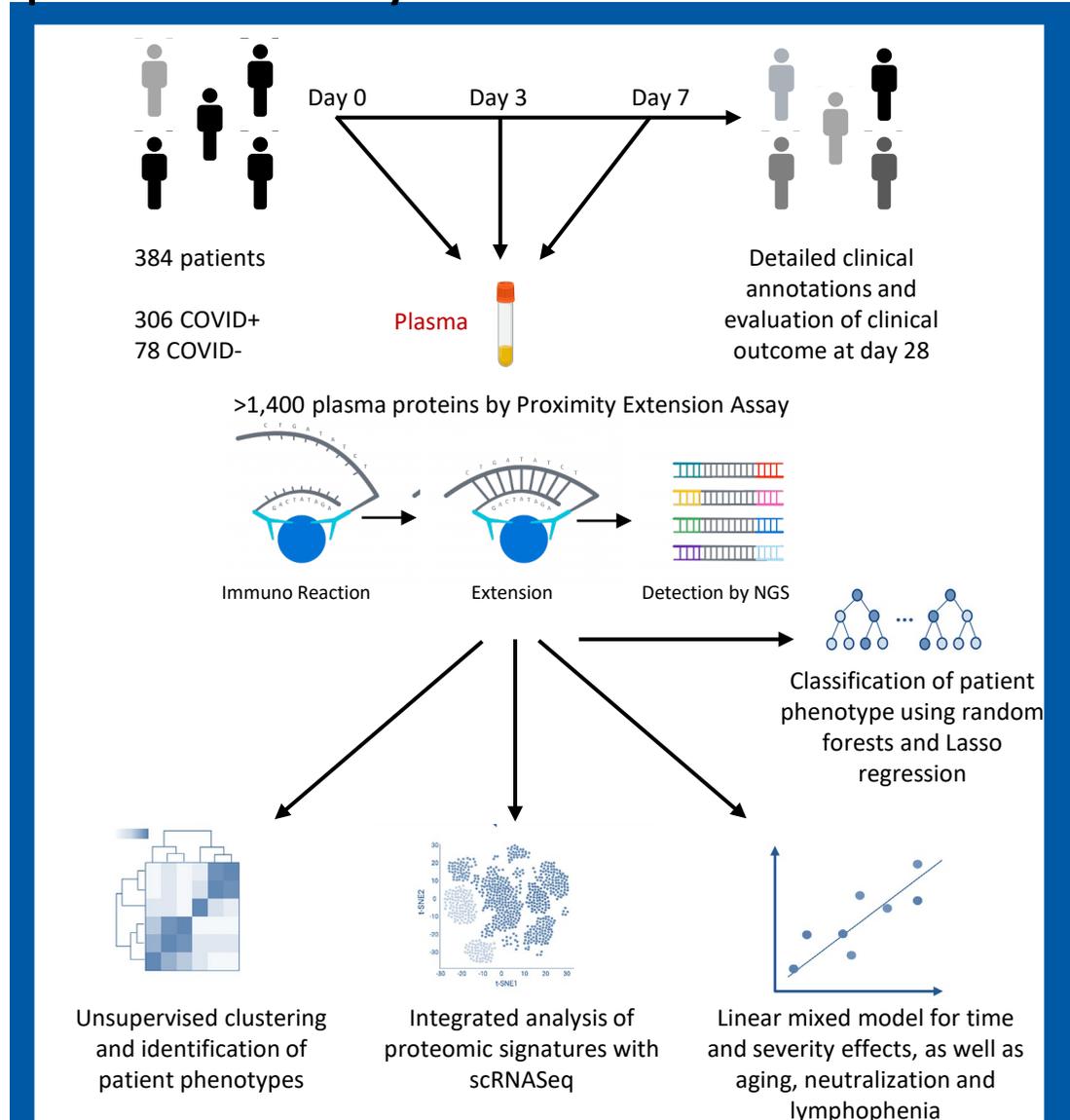
Dr. Michael Filbin, M.D.,  
M.S.  
Department of Emergency  
Medicine, MGH, Boston



“We are grateful to have entered this collaborative effort with Olink to investigate the plasma proteomic signatures of COVID-19 patients and with Olink’s help have profiled over 1400 plasma proteins in our entire cohort.

We hope together we can provide the clinical and scientific community with a rich dataset for further investigation of pathways underlying severe disease that may be the basis for early diagnosis and clinical intervention.

As such, we are eager to share our data broadly with the scientific community to augment others’ findings and to accelerate discovery that may lead to new therapies and a better understanding of the underpinnings of COVID-19.”

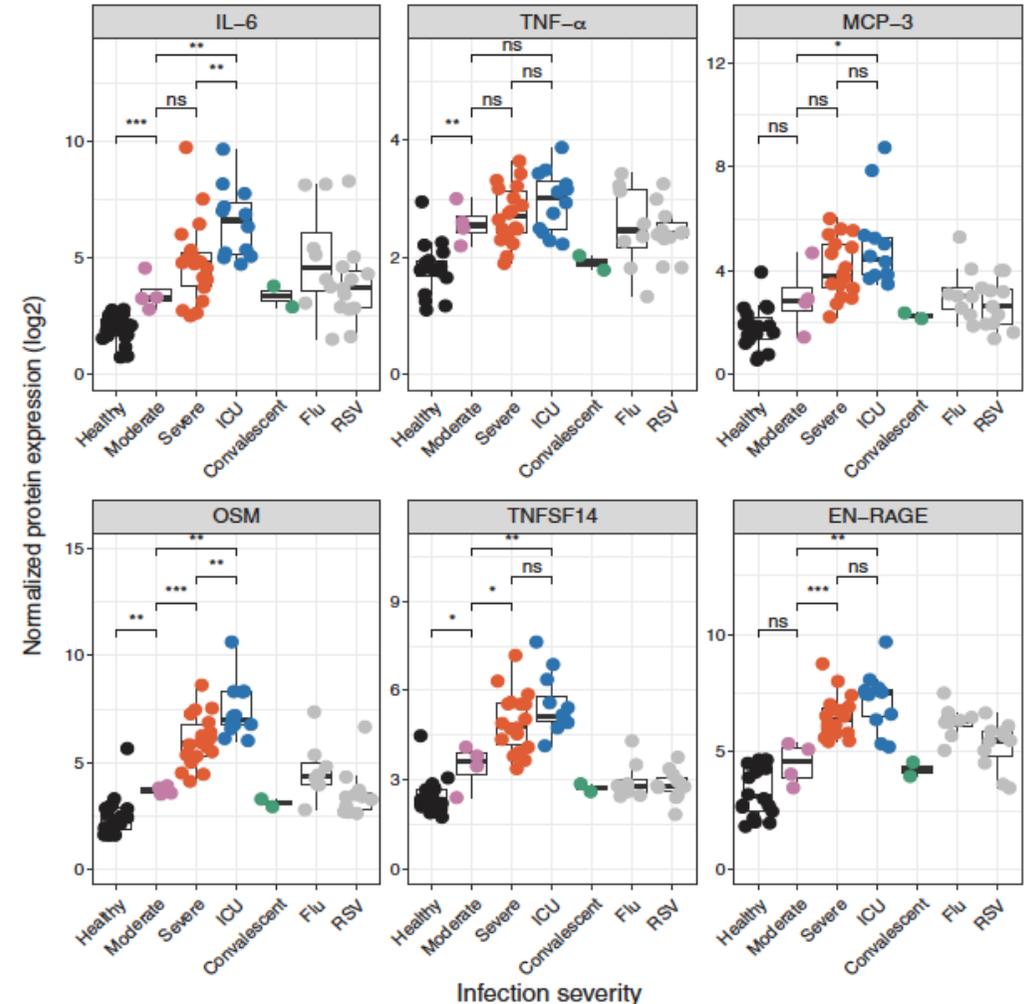




# Novel Proinflammatory Pathways Discovered

- Little is known about immunological mechanisms underlying severity
- **Multiplex analysis of cytokines** in plasma to assess the immune system and response of COVID-19 patients with mild-to-severe disease from two geographically distant cohorts.
- Revealed enhanced levels of several proinflammatory cytokines and strong association of the inflammatory mediators EN-RAGE, TNFSF14, and OSM with the clinical severity of the disease.
- These results **reveal mechanisms and potential therapeutic targets** for COVID-19.

Cytokine levels of healthy or COVID-19 infected individuals



RESEARCH ARTICLE

CORONAVIRUS

Systems biological assessment of immunity to mild versus severe COVID-19 infection in humans

Prabhu S. Arunachalam<sup>1,2</sup>, Florian Wimmers<sup>3,4</sup>, Chris Ka Pun Mok<sup>2,5</sup>, Ranawaka A. P. M. Perera<sup>2,6</sup>, Madeleine Scott<sup>1,7</sup>, Thomas Hagan<sup>1</sup>, Natalia Sigal<sup>1</sup>, Yupeng Feng<sup>2</sup>, Laurel Bristow<sup>8</sup>, Owen Tak-Yin Tsang<sup>9</sup>, Dhananjay Wagh<sup>7</sup>, John Collier<sup>7</sup>, Kathryn L. Pellegrini<sup>9</sup>, Dmitri Kazmin<sup>9</sup>, Ghina Alaaeddine<sup>9</sup>, Wai Shing Leung<sup>9</sup>, Jacky Man Chun Chan<sup>9</sup>, Thomas Shiu Hong Chik<sup>6</sup>, Chris You Chung Cho<sup>6</sup>, Christopher Huert<sup>2</sup>, Michele Paine McCullough<sup>10</sup>, Huibin Lv<sup>2</sup>, Evan Anderson<sup>9</sup>, Srilatha Eduguganti<sup>2</sup>, Amit A. Upadhyay<sup>2</sup>, Steve E. Bosinger<sup>2,10</sup>, Holden Terry Maecker<sup>2</sup>, Purvesh Khatri<sup>1,4</sup>, Nadine Rouphael<sup>2</sup>, Malik Peiris<sup>2,5</sup>, Bali Pulendran<sup>1,11,12</sup>

Science



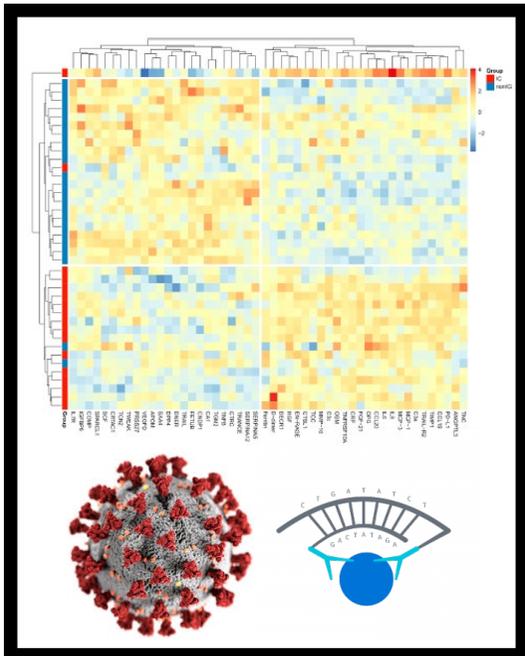
Bali Pulendran, Professor of Pathology, Stanford University





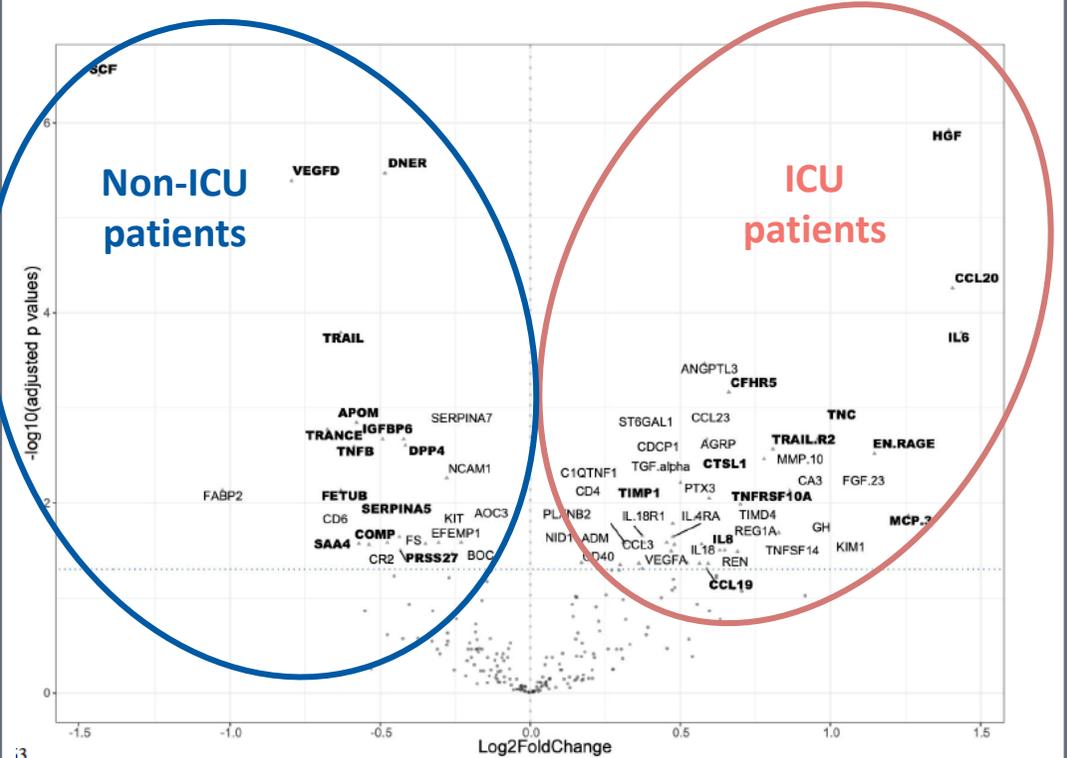
# Increasing our Understanding of COVID-19 Severity

- Aimed to find **biomarkers of COVID-19 pathophysiology** to identify patients most at risk of developing severe lung inflammation
- **Identified important pathways** involved in dysregulation of inflammation in patients with severe COVID-19
- These findings indicate predictors of patient outcome and identify **targets for potential immunotherapy treatment.**



Leo Joosten, Professor of Mechanisms of Inflammatory Disease at Radboudumc  
*"This is a very robust systems – it works across plasma, serum and supernatant"*

## Proteins assessing COVID-19 disease severity

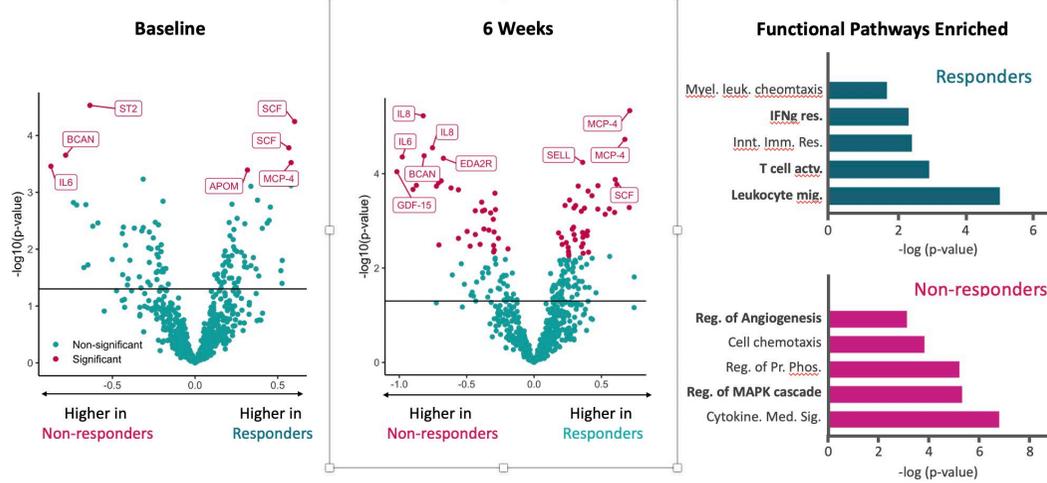


- Identified **several differences in patients that require intensive care**, e.g. IL-6, several chemokines and hepatocyte growth factor
- Stem cell factor and inhibitors of the kinin-kallikrein pathway were downregulated which may **represent important therapeutic target in severe COVID-19** with acute respiratory distress syndrome

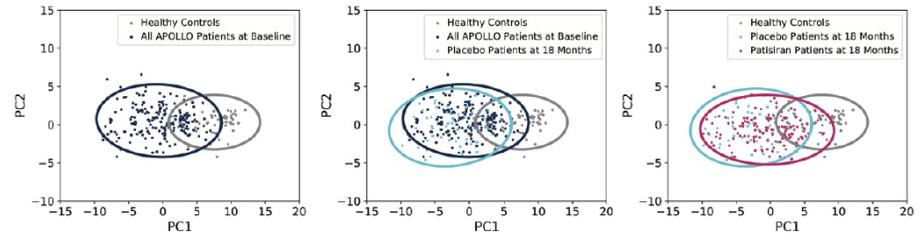
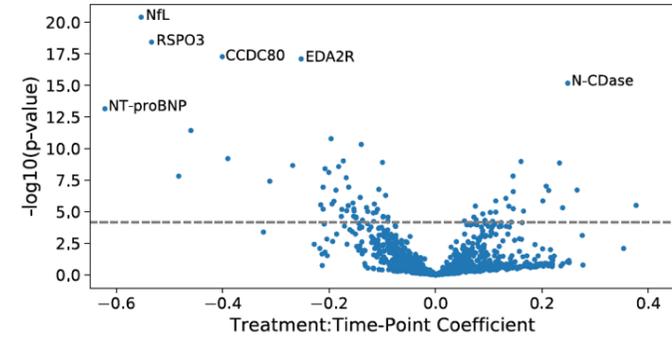


# Olink Captures Response Signatures and Therapeutic Impacts on Biology

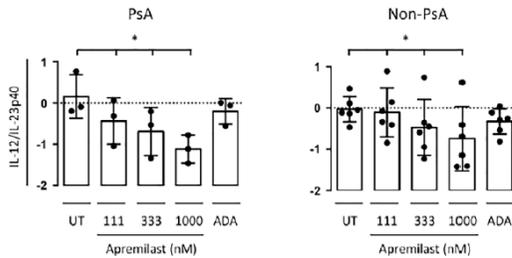
## Predictive Biomarker Signatures



## Response biomarkers to therapy



## Mode of action biomarkers



- In vitro study of downstream effects of therapy (Otezla®)
- Identification of pharmacodynamic biomarkers
- Findings hold promise for repositioning of the drug to other disease areas

- Phase 3 study (APOLLO) with patients receiving placebo or drug (patisiran)
- Significant change in 66 proteins in drug (Patisiran) vs. placebo
- The proteome of patients treated trended towards healthy individuals at 18 months



Olink  
Accelerating proteomics together

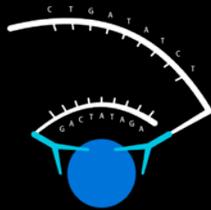
# Proximity Extension Assay

COVID-19 samples



Small volume and matrix flexibility

Immuno Reaction



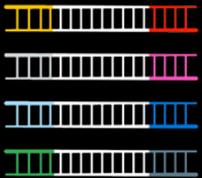
High sensitivity with no cross-reactivity

Extension Reaction



Analog to digital converter

Detection



High multiplexing and throughput

QC & Data analysis



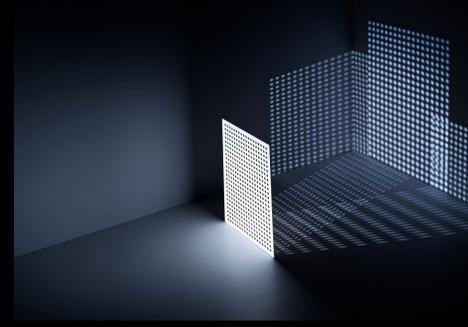
Robust and reproducible data to trust

Proteomic Profiling



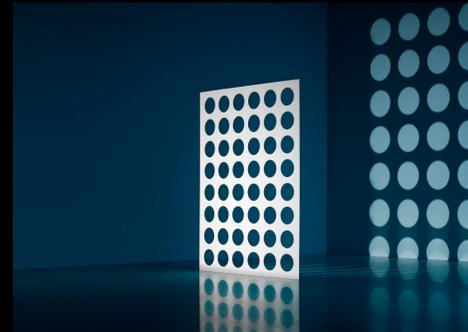
Actionable results driving your research forward

# Olink Product Portfolio



## Explore

Measure 1,536 proteins, Soon 3k and 4,5k proteins covering the dynamic plasma proteome.



## Target 384

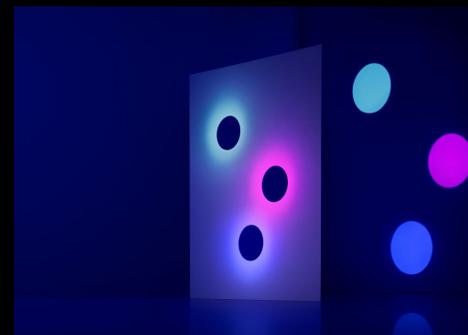
1µl and outstanding coverage of inflammatory cytokines

## Target 96

15 panels built for specific area of disease or biology process.

## Target 48

48-plex Cytokine panel with absolute quantification.



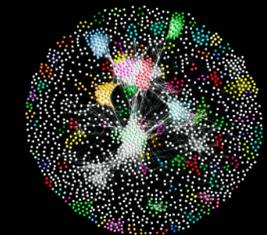
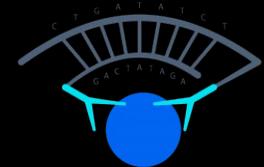
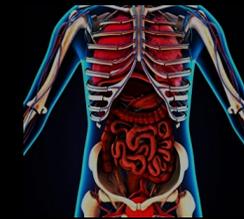
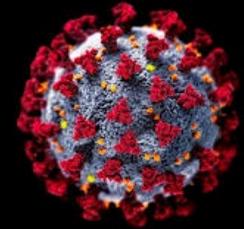
## Focus

Measure up to 21 proteins simultaneously, selected based on your discoveries and needs



# Conclusion

- With plasma proteomics, we can rapidly paint a comprehensive picture of how your therapeutic/vaccine strategy impacts multiple organ systems
- We provide the broadest high-quality coverage of inflammatory proteins driving cytokine storms
- We are the trusted provider to the COVID Technology Access Framework from the largest proteomics COVID project in the world
- Let us help with the analysis of your COVID-19 samples by offering
  - Inactivation of SARS-CoV-2 infected samples
  - Short turnaround time of sample analysis (4-6 weeks)
  - Access to results from largest proteomics dataset from extensive COVID-19 cohort



Where do you see Olink having the biggest potential impact on your COVID efforts?



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"Thank you for making these data available to the research community."

"Very much appreciate your free access data initiative. Hope the research community becomes open like this for the benefit of humanity even after the present pandemic completely resolves."

"We are doing a network-based analysis of the viral infection and it would be very interesting at looking at protein levels using the information provided here"

"Thanks for this initiative! This is amazing."

"I am working on multi-omics of population health. This data will be really useful for the science society. Thanks a lot for your contribution."

"I am very much interested by the technology, and by COVID pathology"

"We would like to utilise these tremendous resources to identify key biomarkers that associate with various health conditions."

"This is quite an impactful program."

"We would be interested to use Olink explore to monitor the therapeutic efficacy."

"Working on COVID and potentially using OLINK platform and am interested in results"

"Thank you for this MGH-Olink resource which can be instrumental in our efforts to understand and eradicate COVID-19."

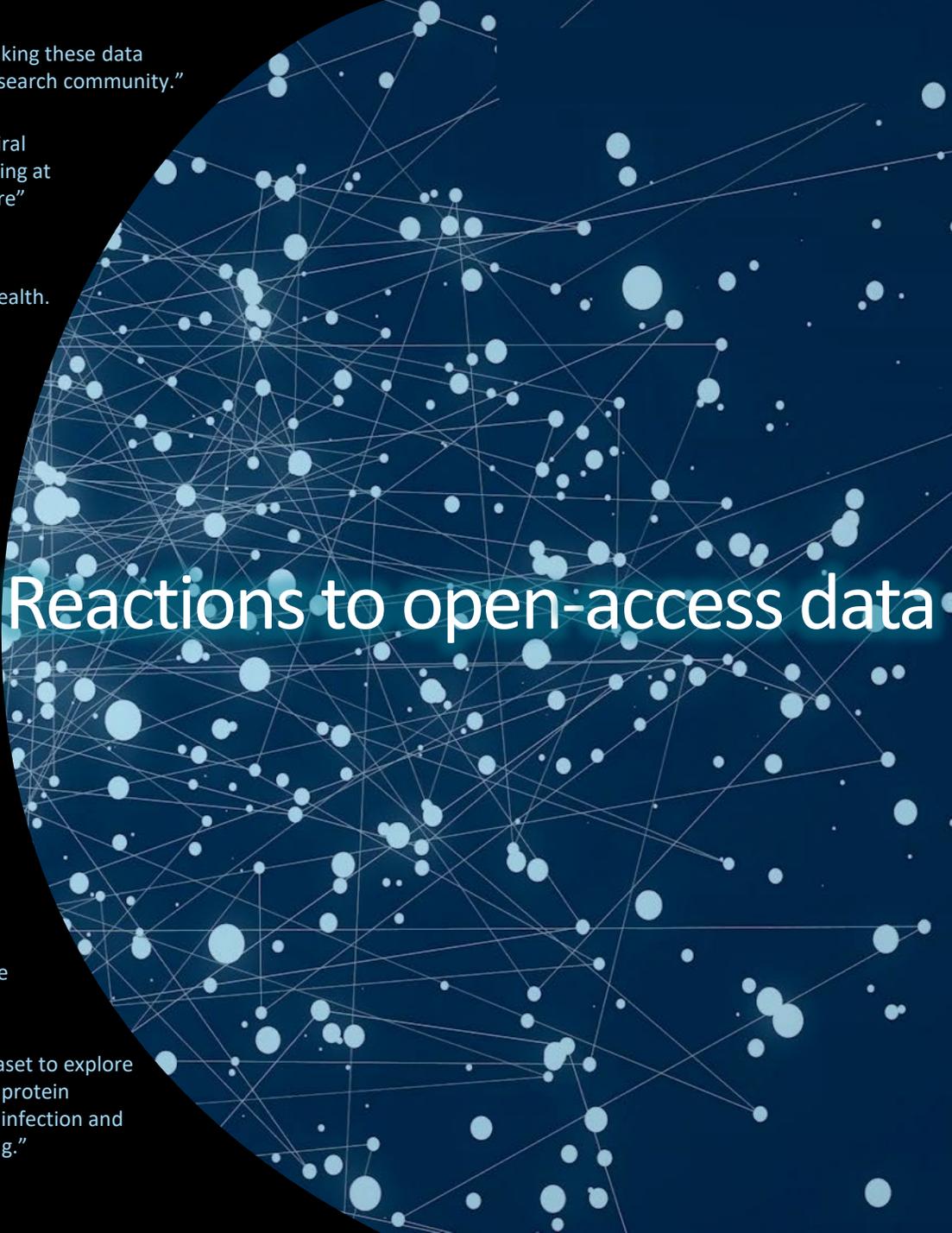
"Interested in large scale study using Olink platform"

"We are expert on Systems Immunology, and we have transcriptome data of COVID-19 patients. It would be really nice integrating this data with the Olink data."

"Thank you for sharing this tremendous resource with the scientific community."

"Accessing the protein profile linked with clinical data of patients is a valuable tool to identify possible therapeutic targets to treat COVID19."

"This is very interesting dataset to explore and relevant to understand protein expression during COVID19 infection and clearance. Thanks for sharing."



# Reactions to open-access data