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

COVID-19

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What we know.

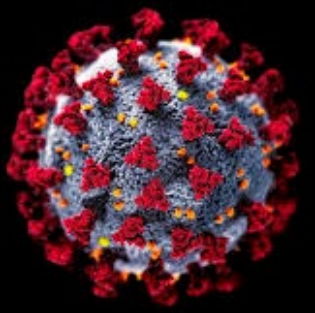
- To date, the cellular mechanisms underlying the immune response and disease severity of COVID-19 are still poorly understood
- A comprehensive overview of the inflammation processes of COVID-19 is still lacking
- There are significant variance in disease severity of COVID-19 with many unknowns on why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

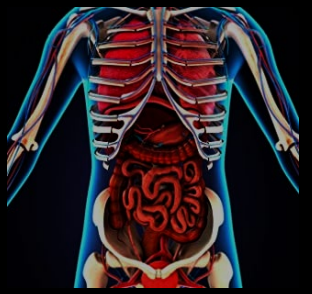
What we need.

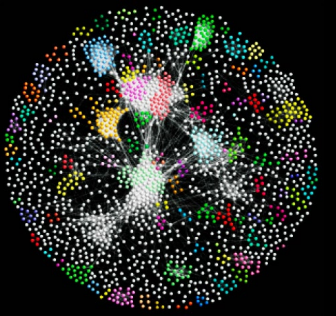
- Broaden our understanding of the pathophysiology behind COVID-19 with deep profiling of the inflammatory system
- Predictors of disease severity and ways to stratify patients in the context of outcomes
- Biomarkers correlative to viral load or subsequent viremia
- Understanding of therapeutic impacts 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 µl of blood







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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 [1]
Fibrosis	HGF, FGF21 upregulated in ICU patients	Long term fibrosis contributors[1]
Kinin-kallikrein system	DPP4, PCI/Serpina 5 downregulated in ICU patients	Disruption of coagulation[1]
Proinflammatory mediation	ENRANGE, TNFSF14, increase in severely ill patients	Lung inflammation, fibrosis, remodeling; ENRANGE, TNSFS14 or their receptors potential drug targets [2]
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 [3]

[1:] 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

[2]: 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

[3]: 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.

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A growing list of COVID-19 publications using Olink

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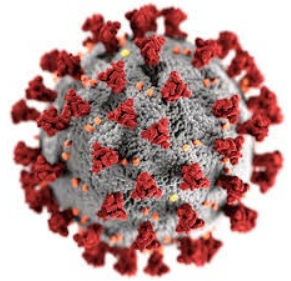
COVID-19 Technology Access Framework.

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.

1st 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)

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

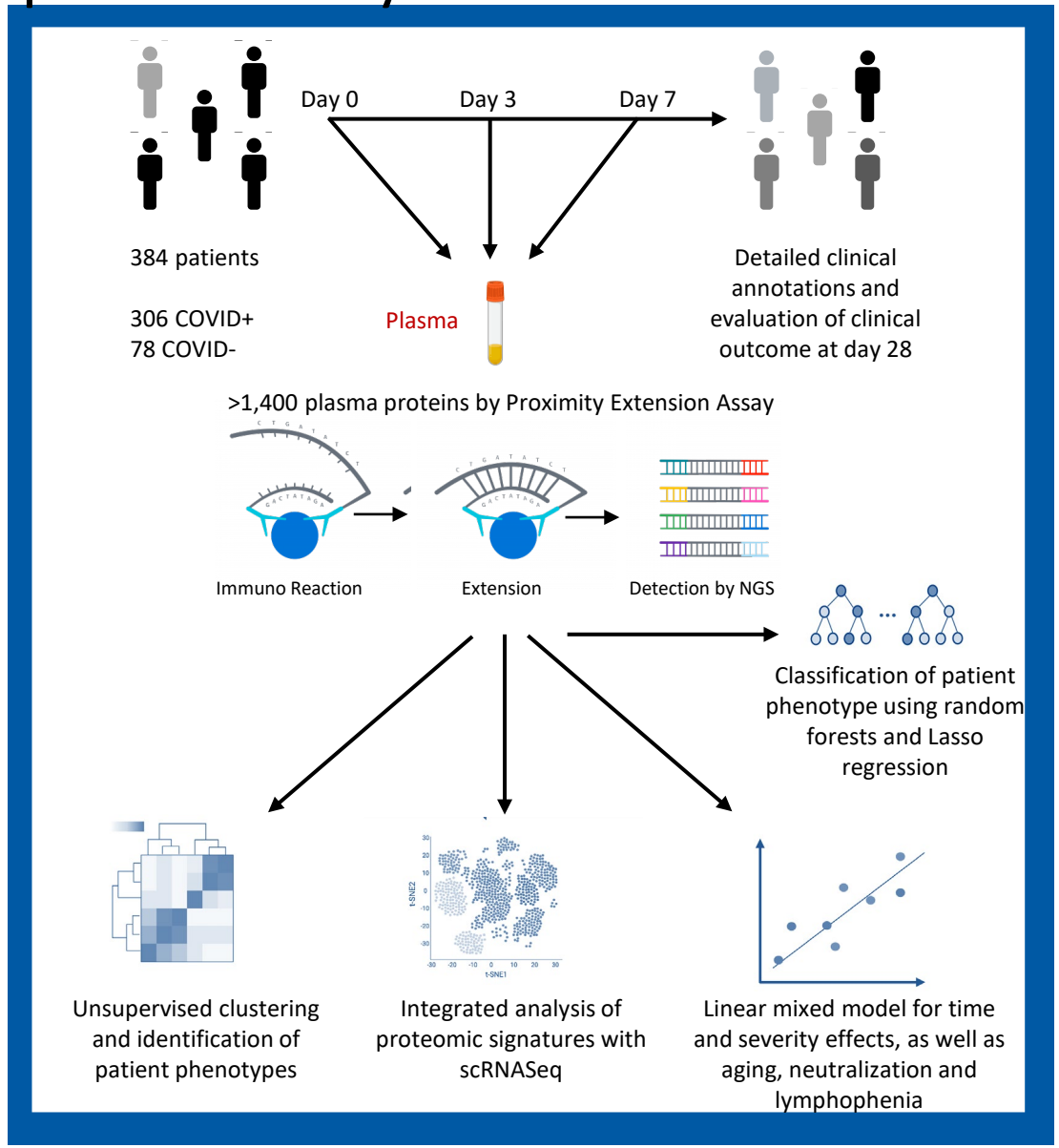
- As of 9/2020, COVID19 has caused over 1,000,000 deaths globally
- To date, the underlying **disease mechanisms are poorly understood**
- **Biomarkers are needed to** predict disease severity and outcomes, stratify patients, **guide therapy and drive drug/vaccine development**
- Using Olink Explore, **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."



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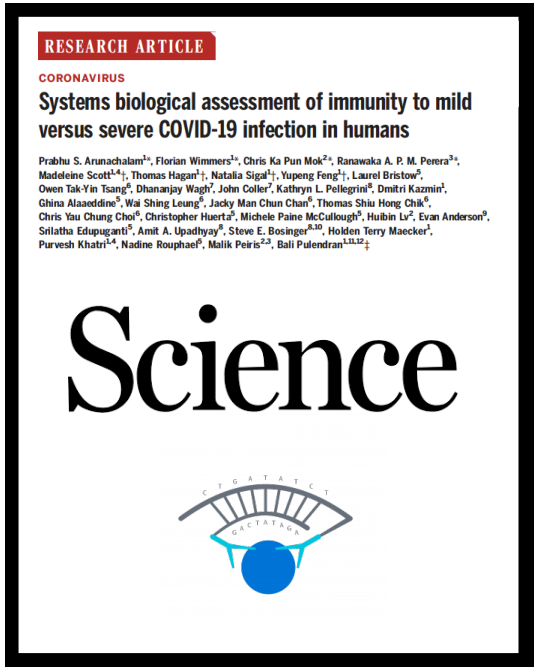
Novel Proinflammatory Pathways Discovered

- 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.


RESEARCH ARTICLE

CORONAVIRUS

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

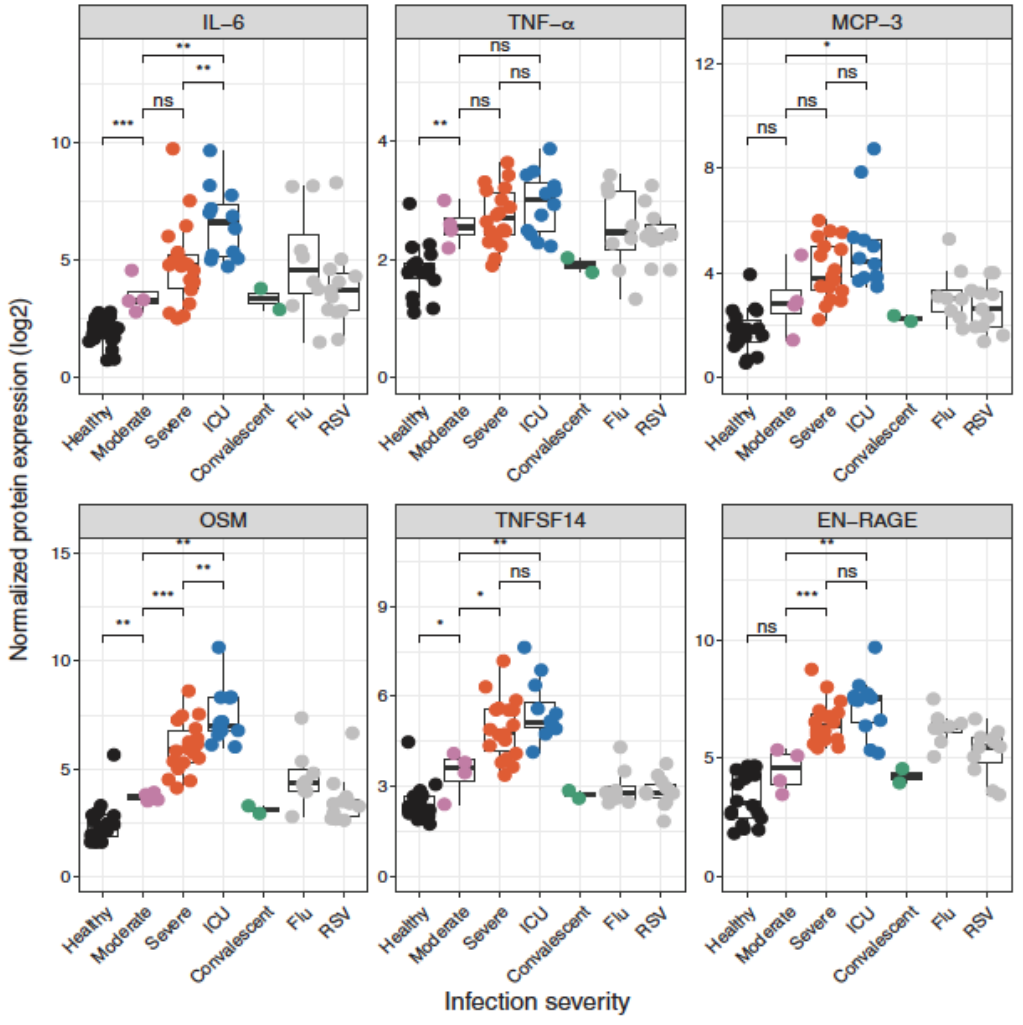
Prabhu S. Arunachalam[1]*, Florian Wimmers[1]*, Chris Ka Pun Mok[2]*, Ranawaka A. P. M. Perera[3]*, Madeleine Scott[1,4]†, Thomas Hagan[1]†, Natalia Sigal[1]†, Yupeng Feng[1]†, Laurel Bristow[5], Owen Tak-Yin Tsang[6], Dhananjay Wagh[7], John Coller[7], Kathryn L. Pellegrini[8], Dmitri Kazmin[1], Ghina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

Science


Bali Pulendran, Professor of Pathology, Stanford University

Stanford University

Cytokine levels of healthy or COVID-19 infected individuals



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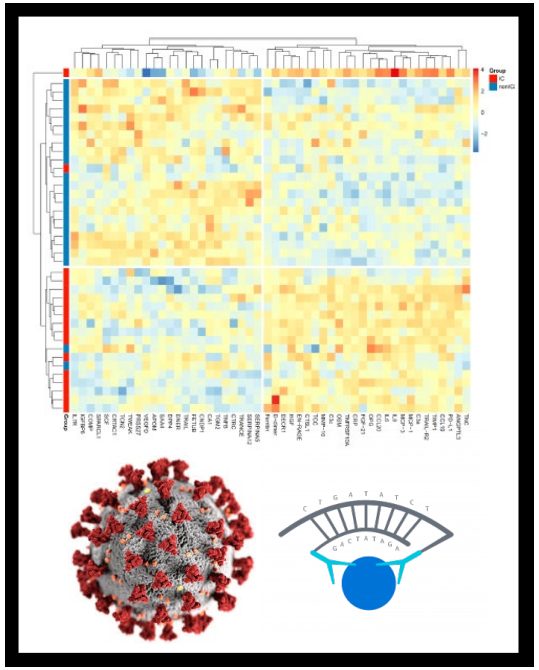
Increasing our Understanding of COVID-19 Severity

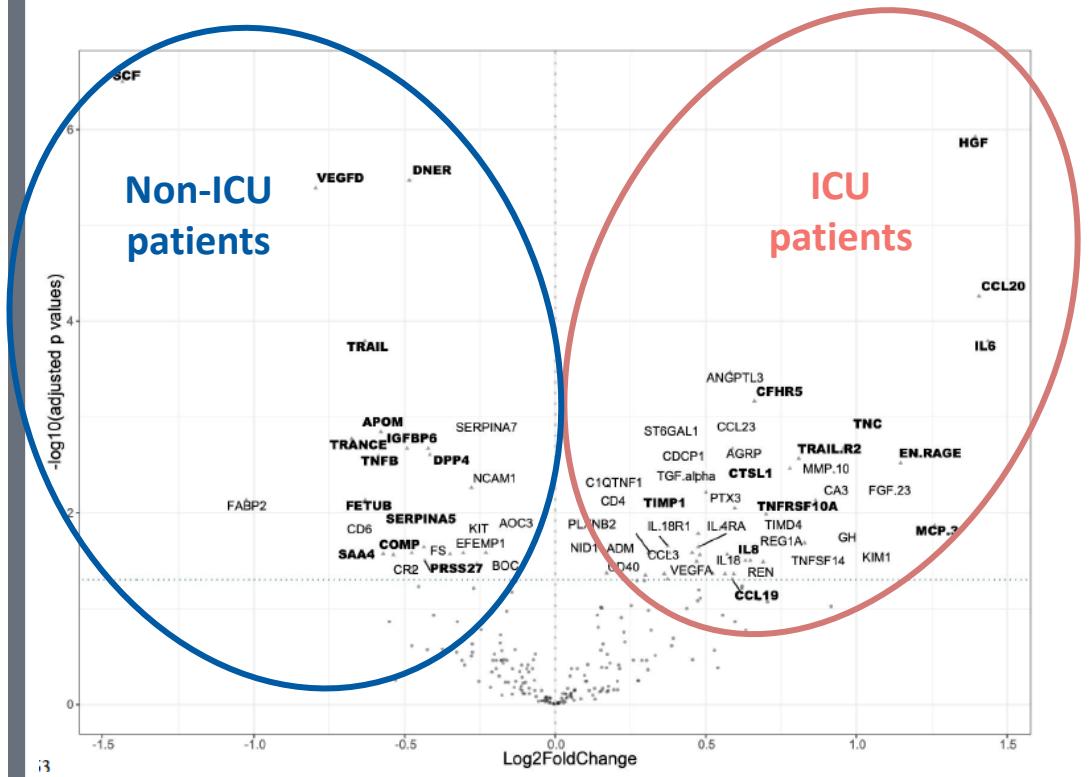
- Aimed to **find biomarkers of COVID-19 pathophysiology** to identify patients most at risk of developing severe lung inflammation
- **Identified important pathways** involved in dysregulation of inflammation in patients with severe COVID-19
- These findings indicate predictors of patient outcome and 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 r**epresent important therapeutic target in severe COVID-19** with acute respiratory distress syndrome

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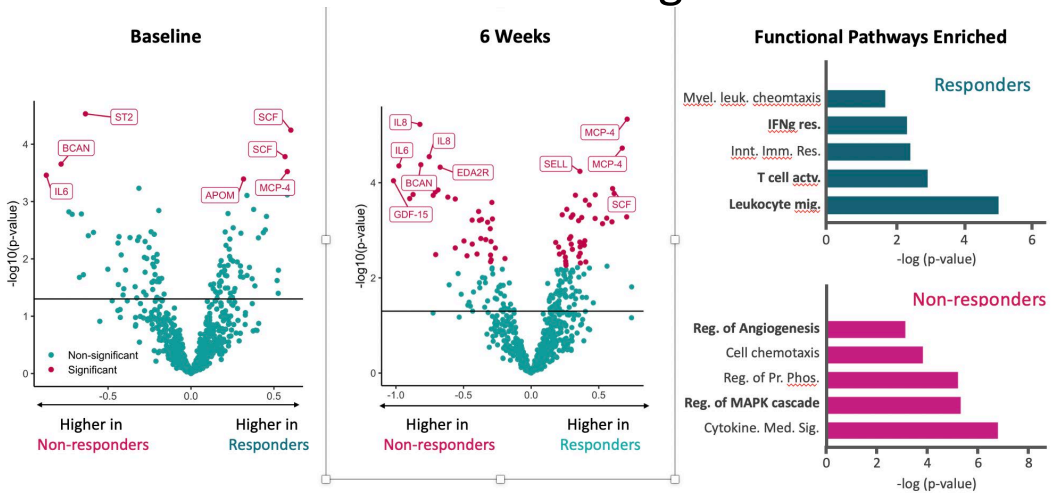
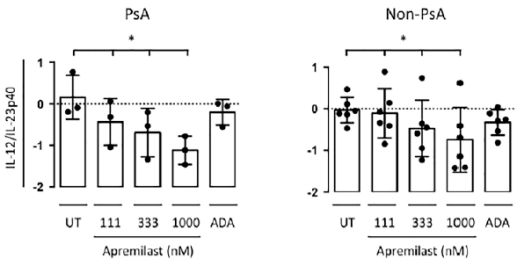
Olink Captures Response Signatures and Therapeutic Impacts on Biology

Predictive Biomarker Signatures



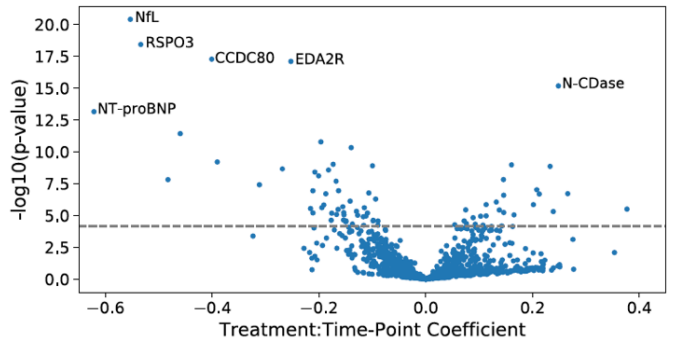
Mode of action biomarkers

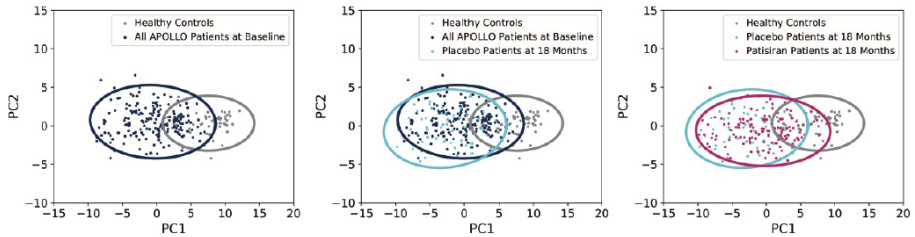


- In vitro study of downstream effects of therapy (Otezla®)
- Identification of pharmacodynamic biomarkers
- Findings hold promise for repositioning of the drug to other disease areas

Bristol-Myers Squibb
Celgene

Response biomarkers to therapy





- 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

Alnylam PHARMACEUTICALS

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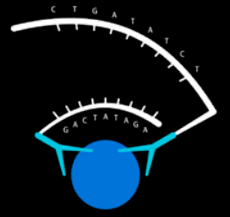
Proximity Extension Assay

COVID-19 samples

Small volume and matrix flexibility

Immuno Reaction

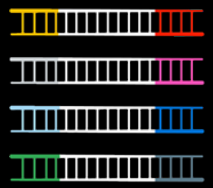


High sensitivity with no cross-reactivity

Extension Reaction

Analog to digital converter

Detection

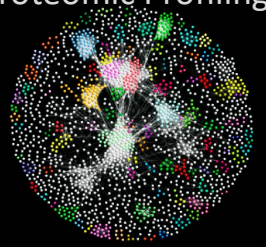


High multiplexing and throughput

QC & Data analysis

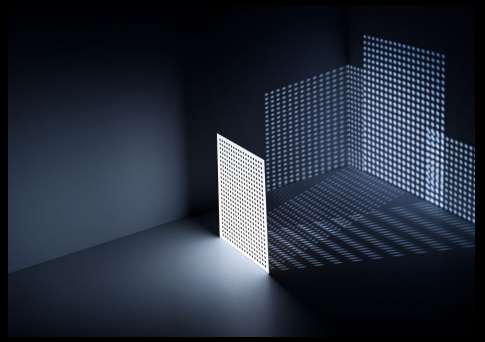
Robust and reproducible data to trust

Proteomic Profiling



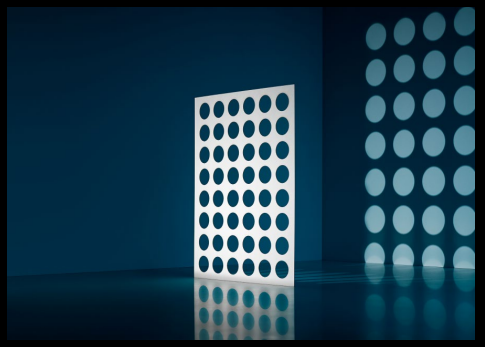
Actionable results driving your research forward

Olink Product Portfolio



Explore

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



Target 384

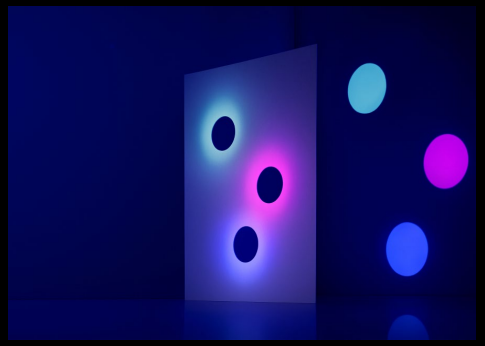
1µl and outstanding coverage of inflammatory cytokines

Target 96

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

Target 48

48-plex Cytokine panel with absolute quantification.

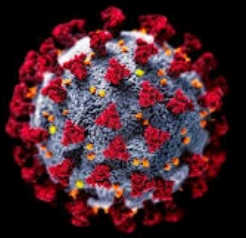


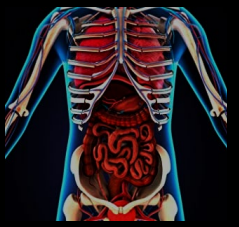
Focus

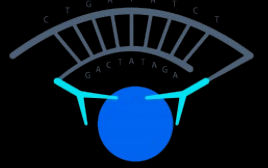
Measure up to 21 proteins simultaneously, selected based on your discoveries and needs

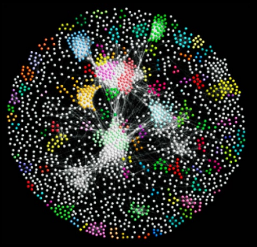
Conclusion

- 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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Reactions to open-access data

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

"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"

"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."

"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."

"Thanks for this initiative! This is amazing."

"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."