inoviv

Inoviv-Charité Predictive COVID-19 Disease Severity Test

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PREDICTIVE COVID-19 DISEASE SEVERITY TEST

The test measures **host response to COVID-19** and, based on it, classifies and predicts disease severity.

It predicts whether the patients (1) are **likely to develop severe disease**, (2) will need **invasive ventilation** and (3) are likely to **survive if they have severe disease.**
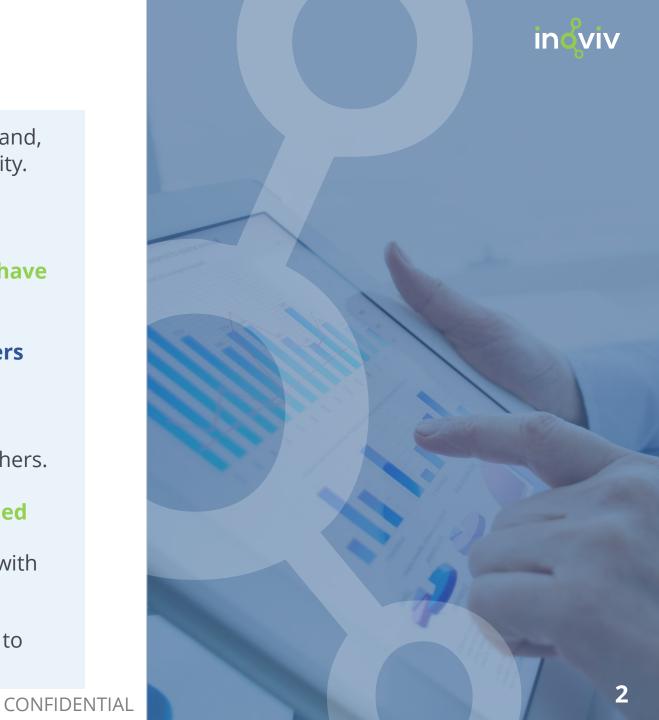
The test monitors **31 plasma protein biomarkers** simultaneously which span multiple aspects of COVID-19, including proteins that function in **inflammation**, **coagulation and vascular dysfunction, the complement cascade** and others.

This predictive biomarker signature was **identified** through **proteome screening** of **thousands of patient samples** at Charité University Hospital with **longitudinal** follow up.

Assay is being used on COVID-19 clinical studies to **demonstrate treatment efficacy**

INOVIV-CHARITÉ COVID-19 BIOMARKER PANEL

Disease Process/ Biomarker Category	Biomarker Name	Biomarker Name Abbreviation	Rationale for Inclusion in Panel	References
Inflammation	Complement C3	C3	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	C-reactive protein	CRP	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Monocyte differentiation antigen CD14	CD14	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Alpha-2-HS-glycoprotein	AHSG	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Lysozyme C, EC 3.2.1.17	LYZ	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Inter-alpha-trypsin inhibitor heavy chain H1	ITIH1	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
Immune Response	Proteoglycan 4	PRG4	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Immunoglobulin heavy variable 5-51	IGHV5-51	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Alpha-1-antichymotrypsin	SERPINA3	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Complement C1q subcomponent subunit C	C1QC	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022

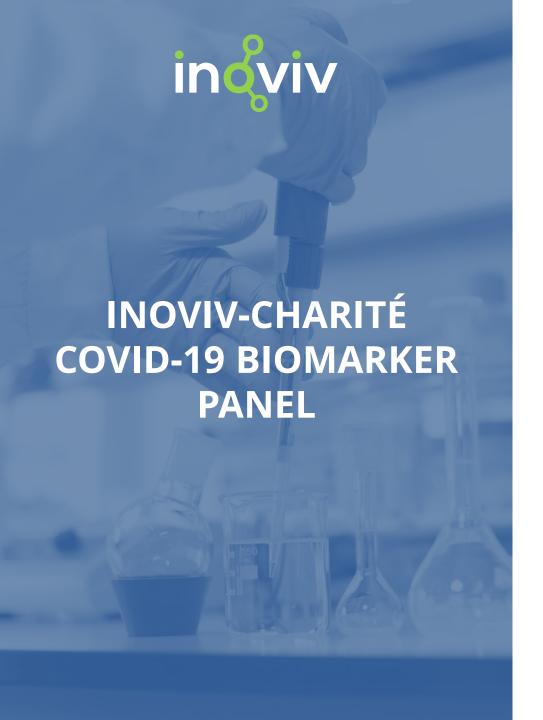# INOVIV-CHARITÉ COVID-19 BIOMARKER PANEL

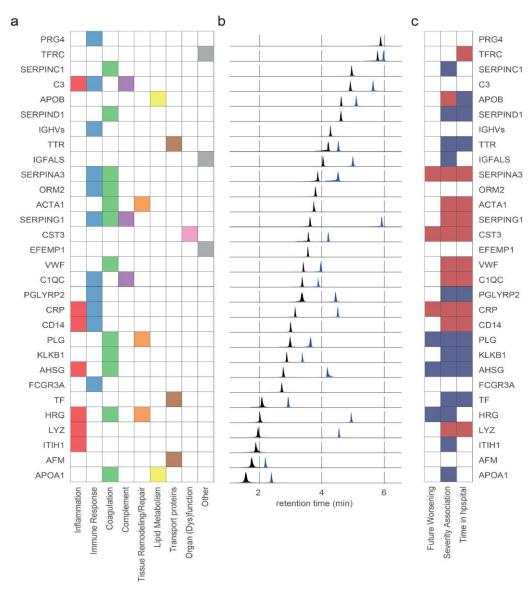| Disease Process/ Biomarker Category	Biomarker Name	Biomarker Name Abbreviation	Rationale for Inclusion in Panel	References
Immune Response	N-acetylmuramoyl-L-alanine amidase, EC 3.5.1.28	PGLYRP2	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Low affinity immunoglobulin gamma Fc region receptor III-A	FCGR3A	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Beta-2-microglobulin	B2M	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
Coagulation & Vascular Dysfunction	Antithrombin-III	SERPINC1	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Heparin cofactor 2	SERPIND1	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Protein ORM2	ORM2	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Histidine-rich glycoprotein	HRG	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Plasma protease C1 inhibitor	SERPING1	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	von Willebrand factor	VWF	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Plasma kallikrein, EC 3.4.21.34	KLKB1	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022

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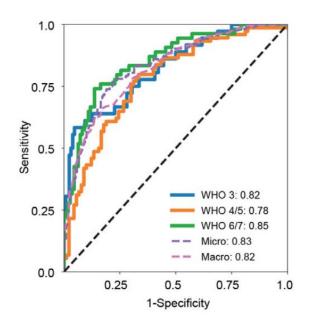| Disease Process/ Biomarker Category	Biomarker Name	Biomarker Name Abbreviation	Rationale for Inclusion in Panel	References
Tissue Remodelling / Repair	Actin, aortic smooth muscle; Actin, cytoplasmic 1; Actin, cytoplasmic 2; Actin, gamma-enteric smooth muscle	ACTA2;ACTB;ACTG1; ACTG2	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Plasminogen, EC 3.4.21.7	PLG	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
Lipid Metabolism	Apolipoprotein A-I	APOA1	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Apolipoprotein B-100	APOB	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
Transport Proteins	Serotransferrin	TF	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Transthyretin	TTR	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Afamin	AFM	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
Organ Dysfunction	Cystatin-C	CST3	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
Other Proteins Related to COVID-19	EGF-containing fibulin-like extracellular matrix protein 1	EFEMP1	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Insulin-like growth factor-binding protein complex acid labile subunit	IGFALS	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022
	Transferrin receptor protein 1	TFRC	Inoviv generated data	Messner et al., 2020; Demichev et al., 2021; Wang et al., 2022

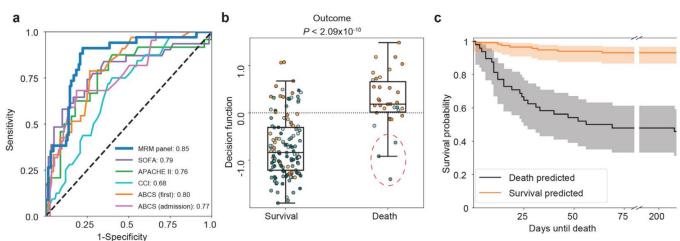# INOVIV-CHARITÉ COVID-19 BIOMARKER PANEL

Wang et al., 2022

PREDICTIVE COVID-19 DISEASE SEVERITY TEST

- ✓ ROC curves for the prediction of the WHO severity group from the first time point measured for every patient

- ✓ (n=36 (WHO 3), n=47 (WHO 4), n=27 (WHO 5), n=16 (WHO 6), n=38 (WHO7)

- ✓ Outperformed current clinical assessments for survival prediction

SCIEX TECHNICAL NOTE

High throughput LC-MS/MS stratification of plasma proteome response to SARS-CoV-2 infection

Using the SCIEX Triple Quad 7500 system, powered by SCIEX OS software

Catherine S. Lane[1], Daniel Blake[1], Adam Cryar[2], Jacob Harris[2], Ernestas Sirka[2], Markus Ralser[3], Ziyue Wang[3], Johannes Hartl[3], Michael Mülleder[4]
[1]SCIEX, Alderley Edge, UK, [2]Inoviv, London, UK, [3]Institute of Biochemistry, Charité Universitätsmedizin Berlin, Germany, [4]Core Facility - High-Throughput Mass Spectrometry, Charité Universitätsmedizin Berlin, Germany

Multi-faceted research into the nature of the COVID-19 disease caused by the SARS-CoV-2 virus is ongoing, as scientists strive to increase understanding of the disease and stratify and predict the impact it has on everyday life globally. One important area of research is to investigate the severity of the disease and
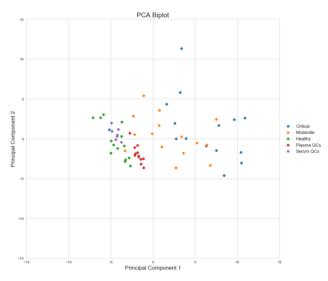
Figure 2 PCA Biplot of quantification results from all 52 peptides monitored, showing disease state stratification.