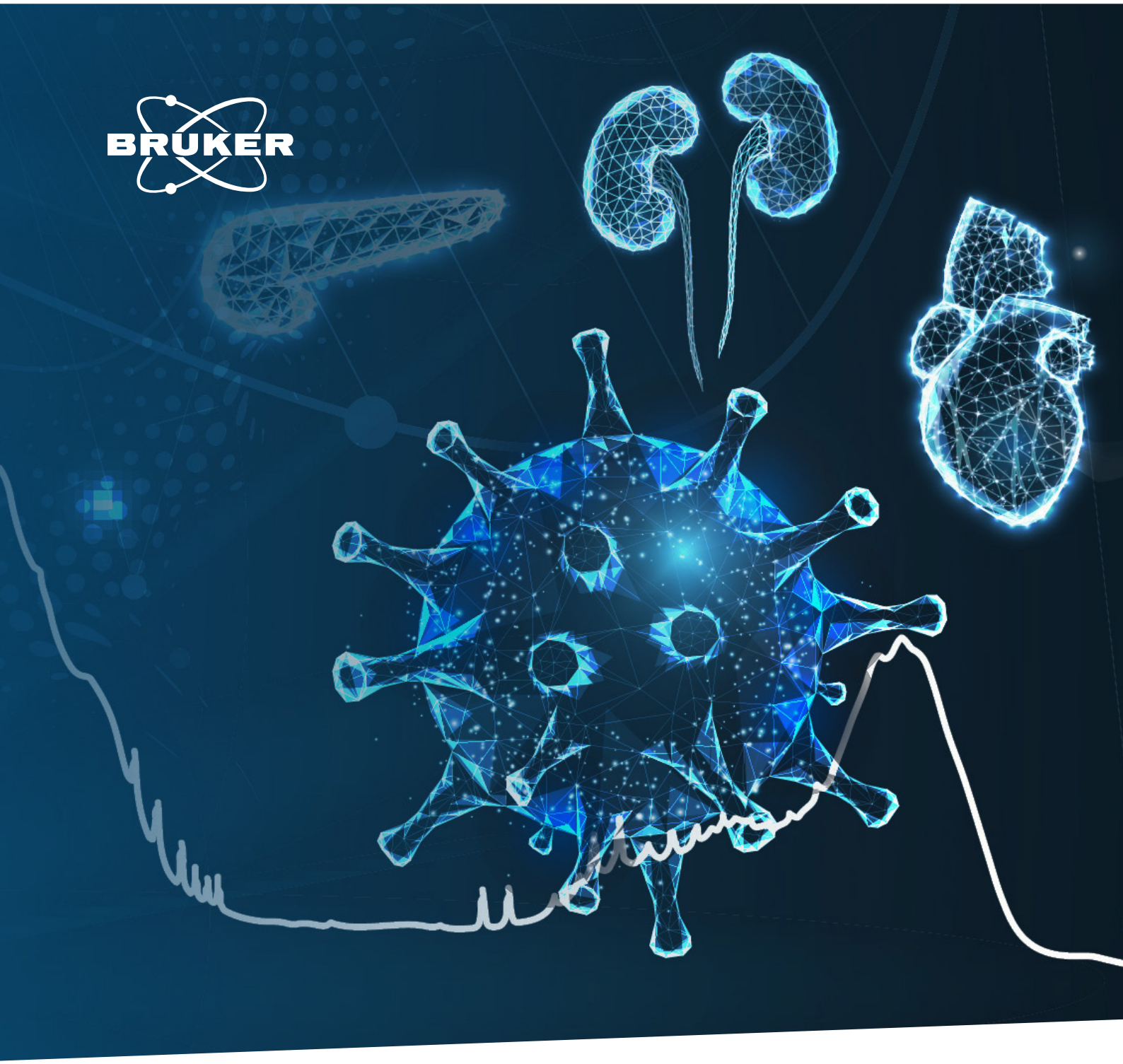


NMR CLINICAL RESEARCH SOLUTIONS

# PhenoRisk Post Acute COVID-19 Syndrome RuO*

## Molecular Phenomic Multi-Organ Risk Screening in PACS Research With PhenoRisk PACS™ RuO*

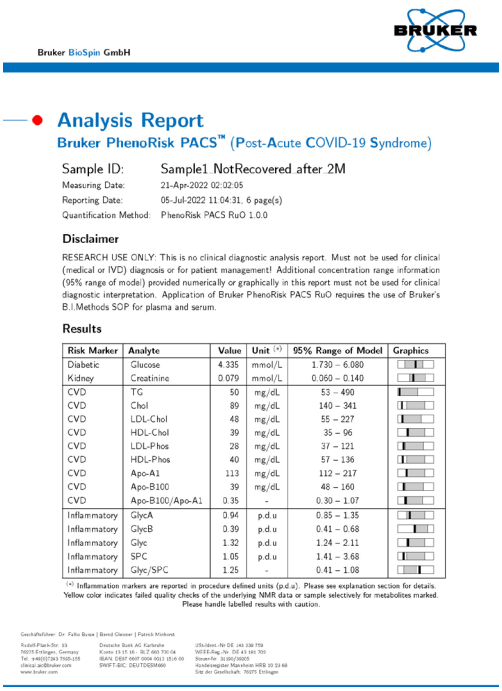
Innovation with Integrity

# A Powerful Solution for Supporting Researchers in the Understanding Of Long-Term Effects in COVID

PhenoRisk PACS™ RuO* delivers a unique metabolomic biomarker panel within a single laboratory test analyzing human plasma samples[1]. It is enabling highly reproducible quantitative multiplexed testing to help researchers in the early detection of clinically well-characterized risk markers of cardiovascular disease, diabetes, and kidney dysfunction, thus. has the potential to provide the clinical researchers with insights in personalized risk information which may assist in longitudinal follow-up of COVID patients.

The new module provides an RuO solution supporting research activities for in-depth characterization of pathomechanisms in SARS-CoV-2 infections and PACS even in subjects with mild symptoms or asymptomatic individuals.

PhenoRisk PACS™ seamlessly expands the clinical research solution suite for the standardized and automated Bruker Avance IVDr NMR platform by adding innovative RuO inflammation biomarkers, which are exclusively assessable by nuclear magnetic resonance (NMR) technology. Results are produced in less than 20 minutes from just one measurement on a single instrument run which may provide the basis for a multi-risk screening for organ dysfunction after SARS-CoV-2 infection.



Bruker BioSpin GmbH

**Analysis Report**

**Bruker PhenoRisk PACS™ (Post-Acute COVID-19 Syndrome)**

Sample ID: Sample1 NotRecovered after 2M
Measuring Date: 21-Apr-2022 02:02:05
Reporting Date: 05-Jul-2022 11:04:31, 6 page(s)
Quantification Method: PhenoRisk PACS RuO 1.0.0

**Disclaimer**

RESEARCH USE ONLY: This is no clinical diagnostic analysis report. Must not be used for clinical (medical or IVD) diagnosis or for patient management! Additional concentration range information (95% range of modal) provided numerically or graphically in this report must not be used for clinical diagnostic interpretation. Application of Bruker PhenoRisk PACS RuO requires the use of Bruker's B.I.Methods SOP for plasma and serum.

**Results**

| Risk Marker | Analyte | Value | Unit (*) | 95% Range of Model | Graphics |
|---|---|---|---|---|---|
| Diabetic | Glucose | 4.335 | mmol/L | 1.730 – 6.080 | |
| Kidney | Creatinine | 0.079 | mmol/L | 0.060 – 0.140 | |
| CVD | TG | 50 | mg/dL | 53 – 490 | |
| CVD | Chol | 89 | mg/dL | 140 – 341 | |
| CVD | LDL-Chol | 48 | mg/dL | 55 – 227 | |
| CVD | HDL-Chol | 39 | mg/dL | 35 – 96 | |
| CVD | LDL-Phos | 28 | mg/dL | 37 – 121 | |
| CVD | HDL-Phos | 40 | mg/dL | 57 – 136 | |
| CVD | Apo-A1 | 113 | mg/dL | 112 – 217 | |
| CVD | Apo-B100 | 39 | mg/dL | 48 – 160 | |
| CVD | Apo-B100/Apo-A1 | 0.35 | - | 0.30 – 1.07 | |
| Inflammatory | GlycA | 0.94 | p.d.u | 0.85 – 1.35 | |
| Inflammatory | GlycB | 0.39 | p.d.u | 0.41 – 0.68 | |
| Inflammatory | Glyc | 1.32 | p.d.u | 1.24 – 2.11 | |
| Inflammatory | SPC | 1.05 | p.d.u | 1.41 – 3.68 | |
| Inflammatory | Glyc/SPC | 1.25 | - | 0.41 – 1.08 | |

(*) Inflammation markers are reported in procedure defined units (p.d.u). Please see explanation section for details.
Yellow color indicates failed quality checks of the underlying NMR data or sample selectively for metabolites marked.
Please handle labelled results with caution.

## Unmet need for tools to support researchers' investigation to understand Post-Acute COVID Syndrome (PACS)

A better understanding of COVID is urgently needed to improve the management of long-term disease risks after acute SARS-CoV-2 infection at the individual and global level. More than 1 in 5 adult COVID survivors may develop long-term impairment, thus millions of patients suffer from PACS, also commonly known as Long COVID. PACS involves damage to a variety of organ systems (e.g. lungs, heart, kidneys, pancreas), along with mental health impairment. There is an emerging consensus in recent scientific publications that an individual's NMR metabolomic signature might deliver reliable insight into PACS. The NMR-based Bruker's PhenoRisk PACS™ metabolomic investigation could possibly enable researchers to the monitoring of PACS patients and might indicate secondary disease as early as possible.

## Molecular Phenomics for unlocking research in the Post-Acute Covid Syndrome

SARS-CoV-2 infection causes a complex range of immunologically driven systemic effects, which manifest in multiple biochemical pathway disruptions, causing changes in the metabolic signature. PhenoRisk PACS™ may bring value in the study of SARS-CoV-2 -triggered metabolic phenoconversion, defined as transient or persistent systemic changes of the molecular signatures in human blood related to SARS-CoV-2 infection, which may also persist post-acute infection. This molecular phenoconversion is present during acute infection and up to months after the acute disease. In addition, a subsequent phenoreversion indicated by normalization of the metabolic signature and detected by PhenoRisk PACS™ may help to mark SARS-CoV-2 recovery. The metabolo-phenomic monitoring may help in the discrimination of SARS-CoV-2 / PACS patients from healthy or recovered individuals, may provide the basis to reveal disease progression but may also assist researchers in providing a measure of a patient's partial recovery, or of emerging chronic PACS risk. As well it may allow definition of treatment outcome, which is important, amongst others, for translational research on new treatment approaches[2].

## PhenoRisk PACS™: Unique NMR-based Biomarker Panel

The SARS-CoV-2 infection dysregulates the metabolomic and lipidomic profiles of serum by abnormal concentrations of Apo-A1, Apo-B100, Creatinine, Glucose, GlycA, GlycB and SPC**. The breadth of the disturbed pathways indicates a systemic signature involving dyslipidemia, diabetes, kidney disorders and inflammation. In a scientific publication done by researchers at the Australian Phenome Center it was shown that the pattern of disturbed molecular markers persisted in some patients after the virus became undetectable in their blood, indicating an incomplete systemic recovery and metabolic phenoreversion in PACS.[4]

Amongst studying lipoproteins and small molecules, PhenoRisk PACS™ is used to quantify a set of composite signals for groups of glycoproteins (Glyc A and B) and phospholipids (SPC) which are either elevated or reduced in SARS-CoV-2. This supports the clinical researchers with detection of a potential inflammation and cardiovascular disease risk. The new, unique biomarker Supramolecular Phospholipid Composite (SPC) is a total composite NMR signal from terminal head groups, from terminated choline headgroups in phospholipids that are associated with HDL and LDL subfractions[4].

These analytes show excellent discrimination of SARS-CoV-2 from healthy controls. Particularly the SPC/Glyc ratio is proposed as sensitive molecular marker for SARS-CoV-2 that could effectively augment current SARS-CoV-2 research [4].

| Secondary Disease | Analyte & Ratio |
|---|---|
| **Cardiovascular Disorders** | ApoA1<br>ApoB<br>ApoB/ApoA1<br>TG<br>Chol, LDL-Chol, HDL-Chol,<br>LDL-Phos, HDL-Phos |
| **Prediabetes or Diabetes Type II** | Glucose |
| **Kidney Disorders** | Creatinine |
| **Inflammation (NMR only analytes)** | GlycA<br>GlycB<br>Glyc<br>SPC*<br>Glyc/SPC |

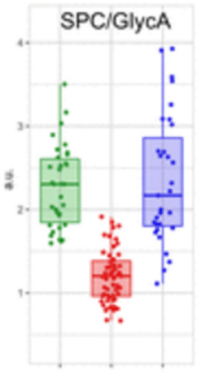



**Figure 1** Follow-up after acute Sars-CoV-2-infection.
Healthy Controls
Acute COVID, day 3
Follow-up after 6 months

**Glycoproteins** are significantly increased in patients tested positive for SARS-CoV-2. GlycA has originally been identified as an NMR-only detectable biomarker potentially indicating acute systemic inflammation and is described as being associated with cardiovascular disease risk[4]. **SPC**** signals (NMR-only) when lowered, may indicate a phenoconversion of the metabolome associated with inflammation. Ratios of GlycA/GlycB and SPC components are particularly sensitive to PACS according to recent publications.[2,3] **Apo-B** and **Apo-A1** are known risk indicators of coronary heart disease, and their ratio is described as a marker of atherogenicity. Apo-B/Apo-A1 ratio is clinically used to assess cardiovascular disease risk. In PACS, high Apo-B/Apo-A1 ratio are apparent, with much lower levels of major HDL class particles. **Glucose** and **Creatinine** levels are abnormal in PACS.

**Results**

| Risk Marker | Analyte | Value | Unit (*) | 95% Range of Model | Graphics |
|---|---|---|---|---|---|
| Diabetic | Glucose | 4.335 | mmol/L | 1.730 – 6.080 | |
| Kidney | Creatinine | 0.079 | mmol/L | 0.060 – 0.140 | |
| CVD | TG | 50 | mg/dL | 53 – 490 | |
| CVD | Chol | 89 | mg/dL | 140 – 341 | |
| CVD | LDL-Chol | 48 | mg/dL | 55 – 227 | |
| CVD | HDL-Chol | 39 | mg/dL | 35 – 96 | |
| CVD | LDL-Phos | 28 | mg/dL | 37 – 121 | |
| CVD | HDL-Phos | 40 | mg/dL | 57 – 136 | |
| CVD | Apo-A1 | 113 | mg/dL | 112 – 217 | |
| CVD | Apo-B100 | 39 | mg/dL | 48 – 160 | |
| CVD | Apo-B100/Apo-A1 | 0.35 | - | 0.30 – 1.07 | |
| Inflammatory | GlycA | 0.94 | p.d.u | 0.85 – 1.35 | |
| Inflammatory | GlycB | 0.39 | p.d.u | 0.41 – 0.68 | |
| Inflammatory | Glyc | 1.32 | p.d.u | 1.24 – 2.11 | |
| Inflammatory | SPC | 1.05 | p.d.u | 1.41 – 3.68 | |
| Inflammatory | Glyc/SPC | 1.25 | - | 0.41 – 1.08 | |

(*) Inflammation markers are reported in procedure defined units (p.d.u). Please see explanation section for details. Yellow color indicates failed quality checks of the underlying NMR data or sample selectively for metabolites marked. Please handle labelled results with caution.

**Figure 2** Result Screen PhenoRisk PACS™ RuO

## PhenoRisk PACS™ can help researchers' understanding Of COVID

PhenoRisk PACS™ RuO, based on well-proven, advanced NMR technology, is comprised of hardware, software and consumables, and may help PACS researchers to deepening the understanding of the multisystemic nature of COVID. The solution may improve basic, as well as translational clinical research, and may provide the basis of the development of impactful treatments by:

- Enabling highly reproducible quantitative multiplexed testing with a high dynamic range to support researchers in the early detection of risk markers of cardiovascular disease, diabetes, kidney dysfunction and inflammation.
- Delivering insight into unique biomarkers, exclusively assessable by NMR technology (Glyc A and B, SPC).
- Providing easy to operate and non-destructive, label-free multiplexed testing with minimal hands-on time. The test is performed in less than 20 min in a single human plasma/serum sample with solely one test run under highly standardized conditions at affordable costs.
- Seamlessly complementing Bruker's RuO biomarker panel portfolio, providing in-depth understanding of lipoprotein profiles (B.I.LISA, 112 analytes) and quantification of small metabolites (B.I.Quant PS 2.0, 40 metabolites)A and B, SPC).

*** Bruker NMR Instruments are for Research Use Only. Not for Use in Clinical Diagnostic Procedures**
**** SPC Supramolecular Phospholipid Composite**


[1] Cuttler D.M. et al.; JAMA Health Forum.2022;3(5):e221809.
[2] Lodge S. et al., Anal Chem. 93(8): 3976–3986
[3] Kimhofer T et al., J Proteome Res, 6;19(11):4442-4454.
[4] Otvos, J.D. et al., Clin. Chem. 2015, 61, 714{723.





**Bruker BioSpin**
info@bruker.com

bruker.com

**Worldwide offices**
bruker.com/

**Online information**
bruker.com/