



The Firestone Institute
for Respiratory Health

St. Joseph's
Healthcare Hamilton

McMaster
University

ing COVID Web, ECHO series

April 2026

ong Covid and immunology *focus on respiratory burden*

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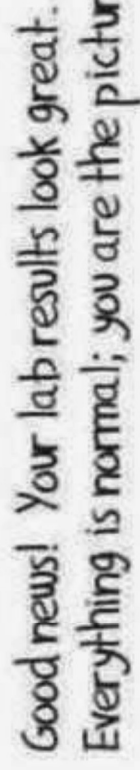
Acknowledgments

We acknowledge that St. Joseph's Healthcare Hamilton sits on the traditional territories of the Mississauga and the Haudenosaunee Nations and is within the lands protected by the "Dish With One Spoon" wampum agreement

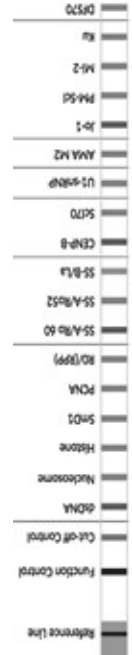
Disclosures

Disclosures	
Type	Company
Employment full time / part time	McMaster University
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Personal disclaimer	Personal Hx of Long COVID

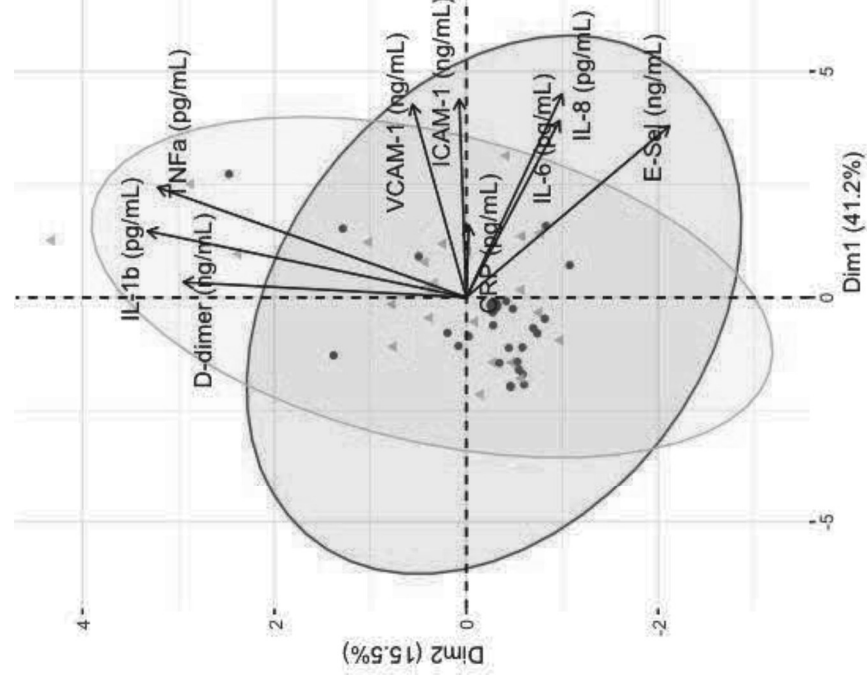
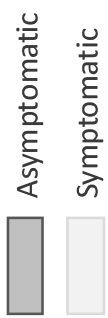
Long-term effects of COVID-19



evidence of immune dysfunction



- 12% shows de novo generation of autoantibodies at 12 months
- Anti-U1snRNP and anti-SS-B/La predicts fatigue and dyspnea, the most common PASC symptoms



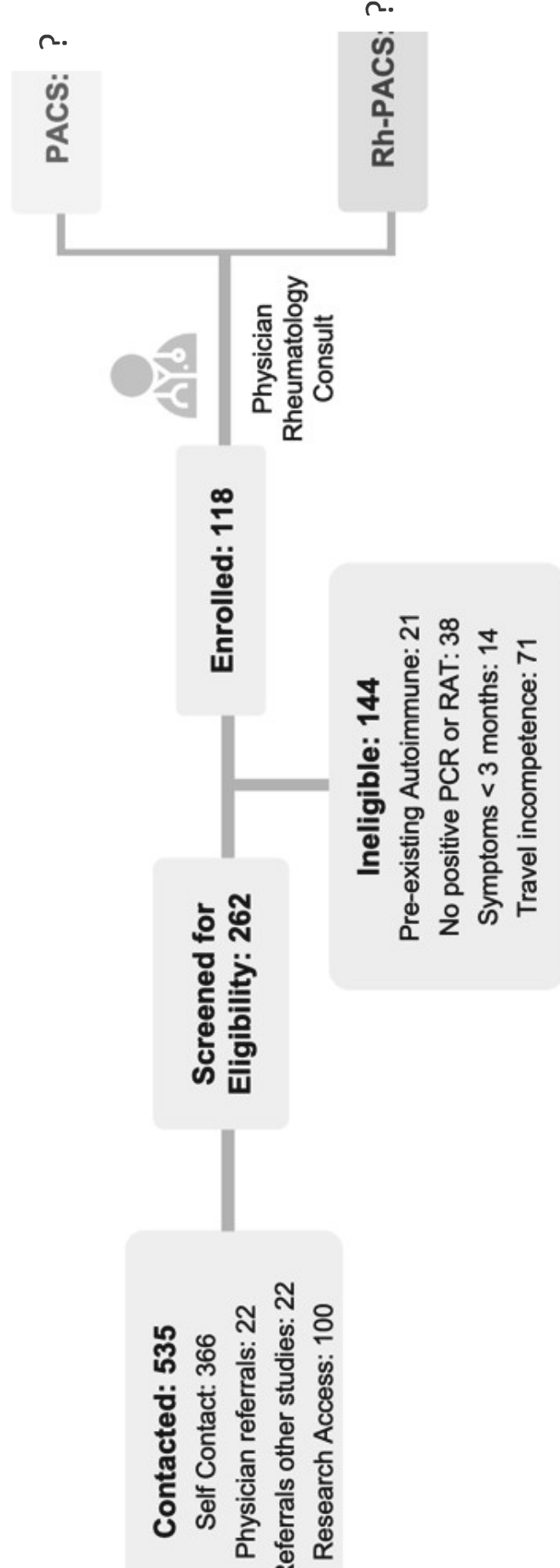
Flow diagram



Konstantinos Tselios
MD, PhD



Sarah Svenningsen
PhD



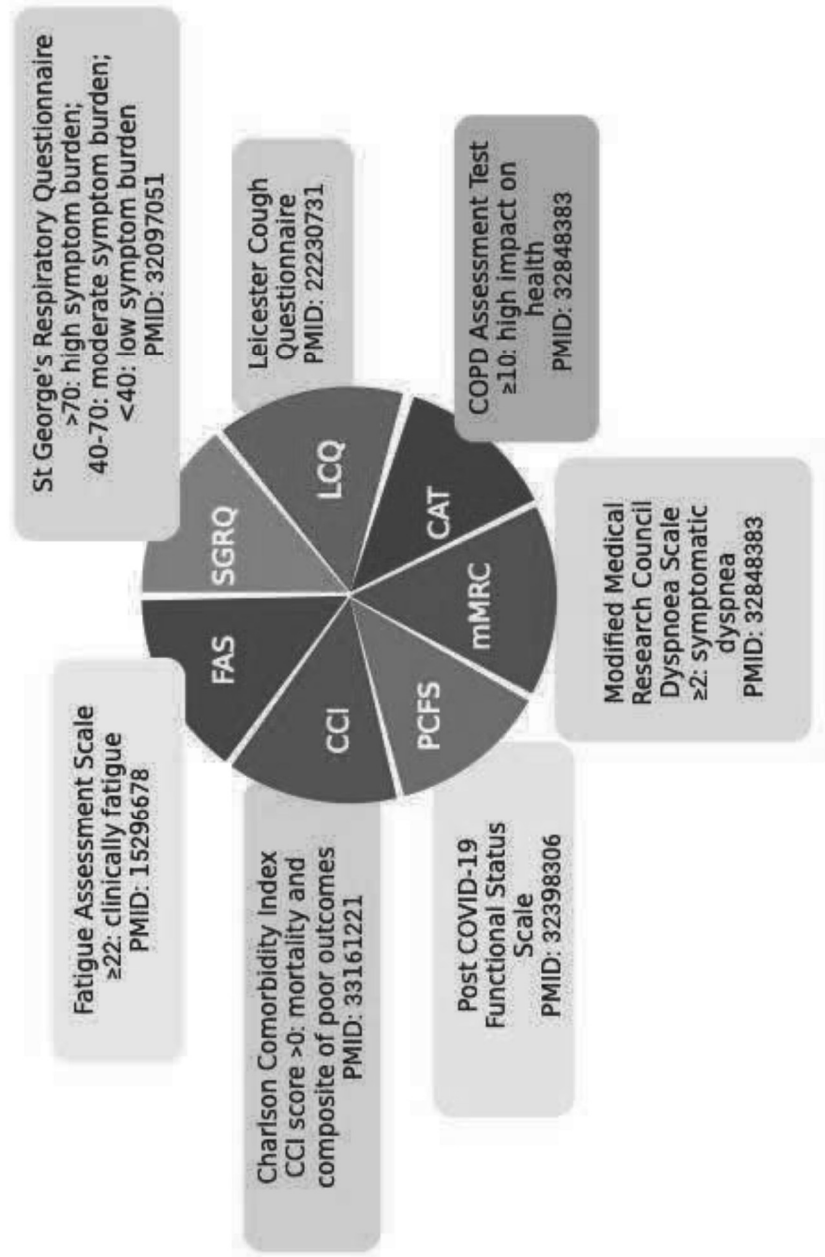
Outcomes: Clinical, molecular and patient reported

Molecular markers:

- Near Autoantibodies, Humatoid factor and (TPO, TSHR), adrenal, TTH antibodies
- Immatory Cytokines and Inflation mediators: Automated ELISA system
- Genotyping of B cells and T cells: Flow Cytometry
- Complete Blood Counts Differential Counts
- Hemoglobin Blood Testing

PACS
ished

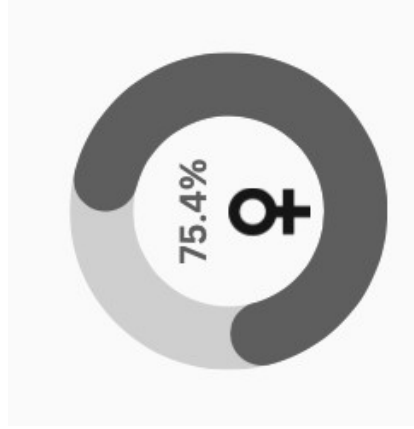
Patient reported outcomes and quality of life questionnaires:



- Functional tests
 - 6 Minute Walk Test
 - Pulmonary Function Spirometry, Oscillometry, Plethysmography and
 - Trail Making Test
- Imaging tests
 - Chest CT



Prevalence of common PACS symptoms

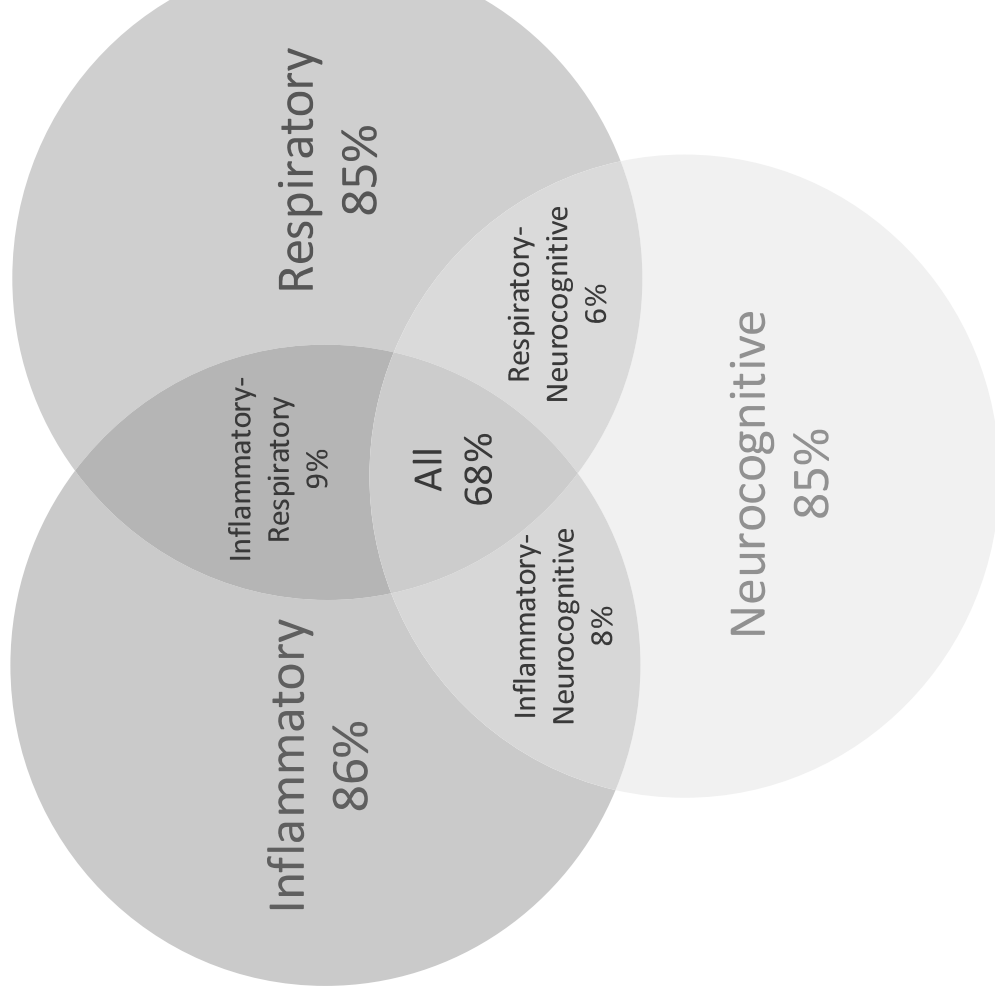


47

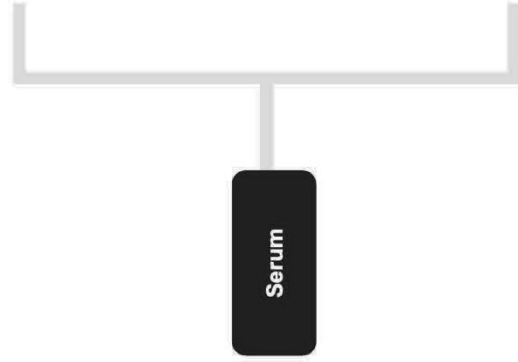
Mean Age (in years)

11

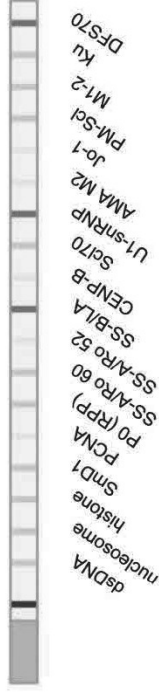
Months
since infection



B. Study Visit



Anti-Nuclear Antibody Immunoassay



dsDNA
nucleosome
histone
SMD1
PCNA
P0 (RPP)
SS-A/Ro 60
SS-A/Ro 52
SS-B/LA
CENP-B
Scl70
U1-snRNP
AMA M2
Jo-1
PM-Scl
MT-2
Ku
DFS70

Serum

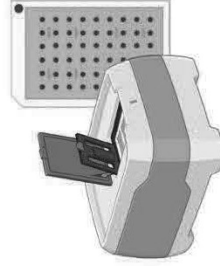
Elia™ Automated ELISA

Inflammatory cytokines and
chemokines:

CRP, CXCL10, TNF α , IL-1 β , IL-6, IL-8

Endothelial dysfunction markers:

D-dimer, E-selectin, ICAM-1, VCAM-1

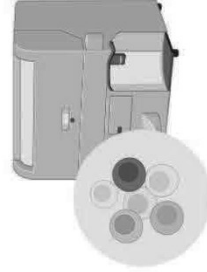


PBMCs

Immune

Phenotyping

B and T Cells Subsets



Questionnaires

Post-COVID Symptom Checklist
Acute COVID Symptom Checklist
Fatigue Assessment Scale

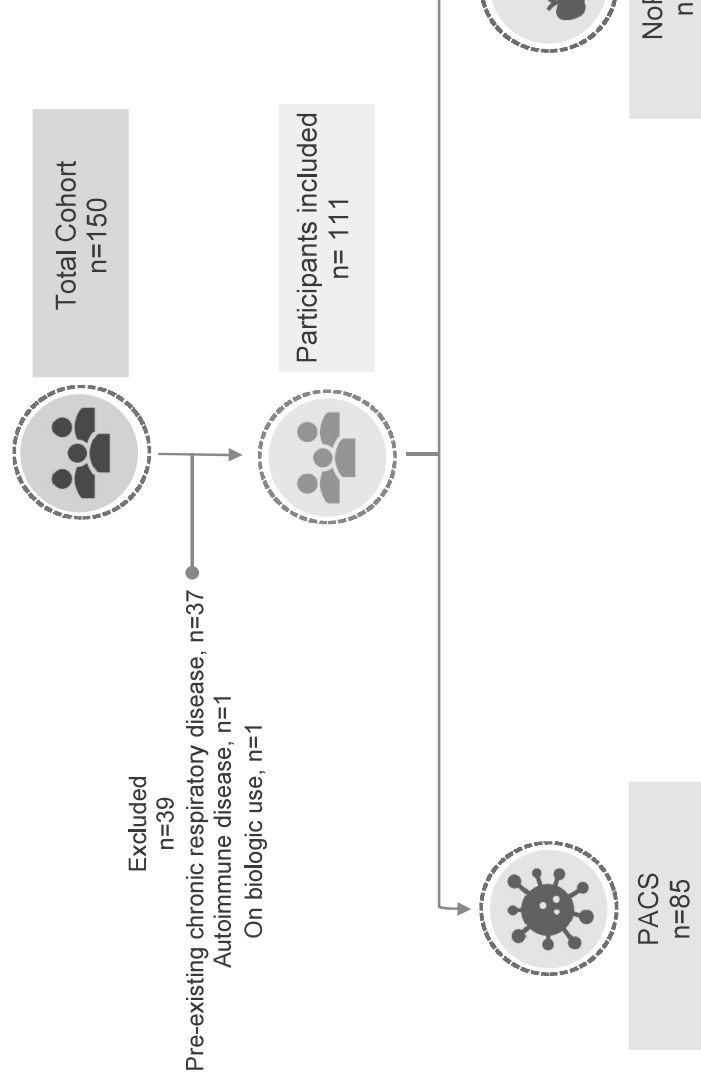
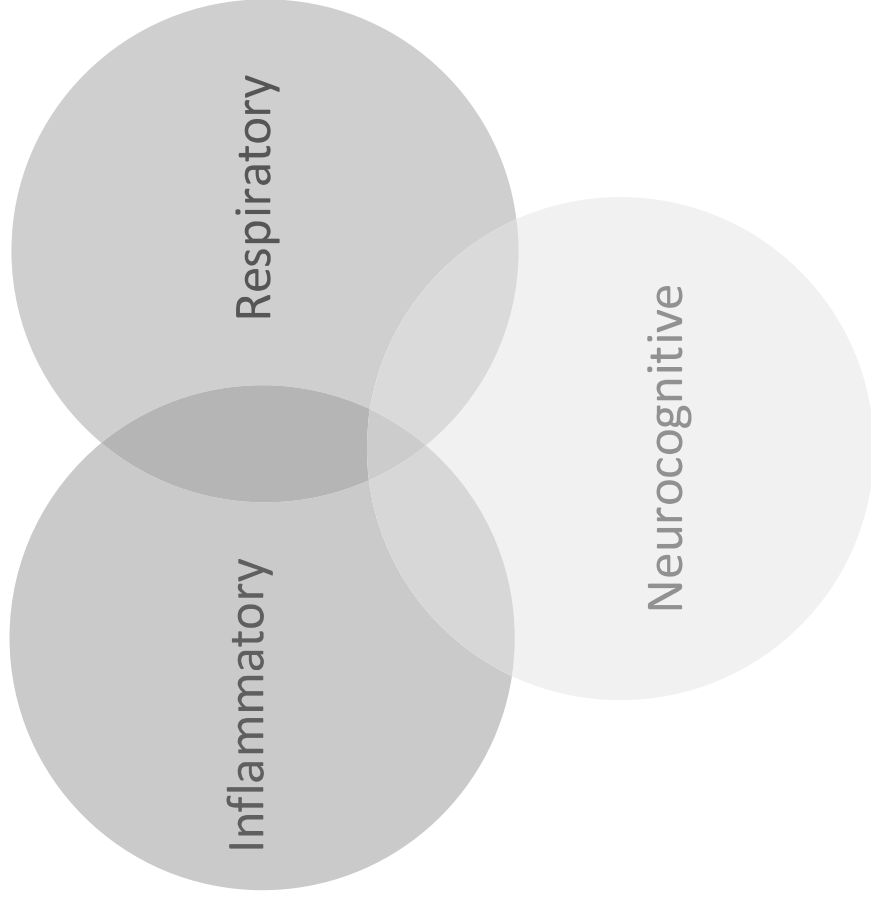
St. George's Respiratory Questionnaire
COPD Assessment Test
COVID Case Report Form
Leicester's Cough Questionnaire

Clinical Follow-Up

Diagnosis of incident Rheumatic Disease
Note of Rheumatic Complications
Assessment of Autoimmune Symptoms

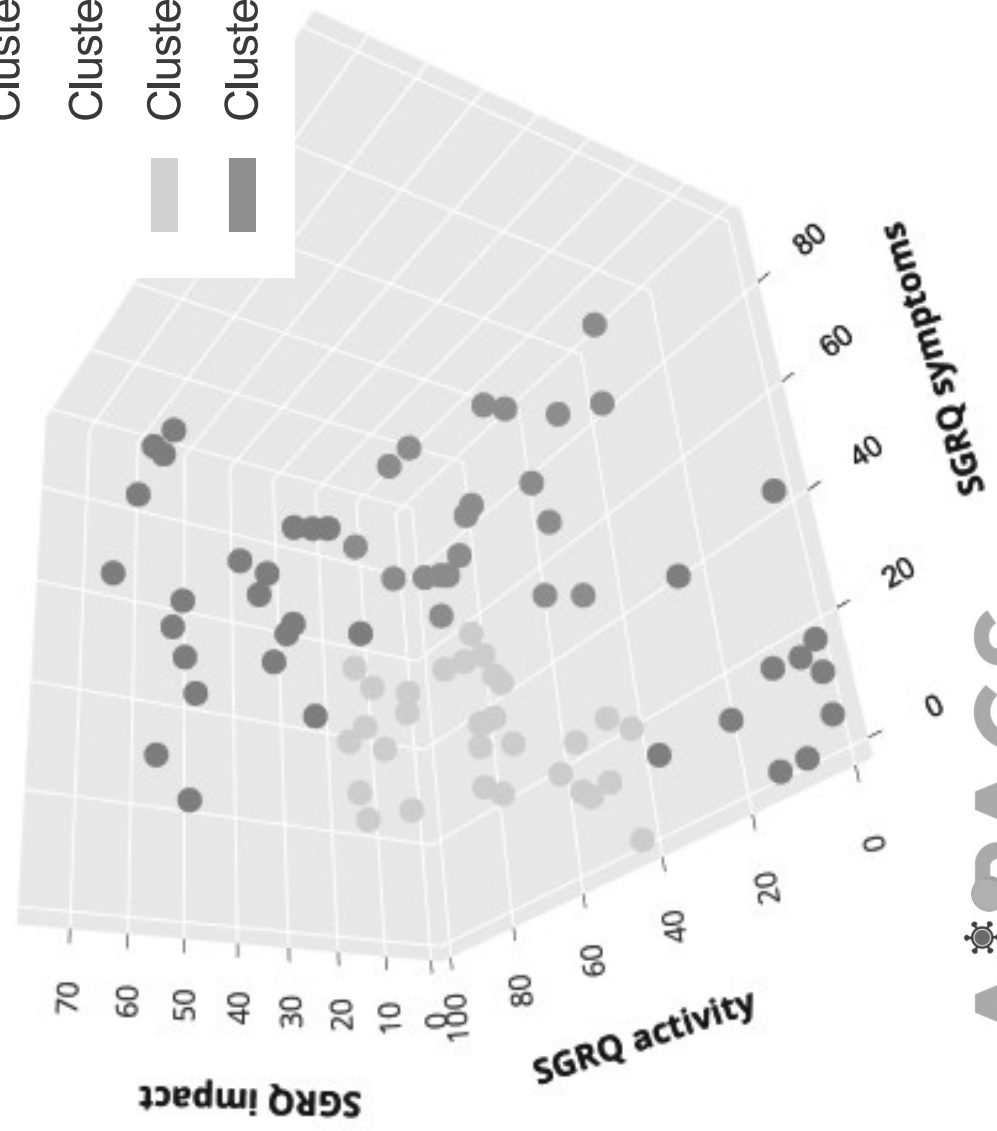
Respiratory Burden in Long COVID

Looking into respiratory phenotype and its change over time...



Respiratory Burden in Long COVID

- NoPACS
- Cluster 1
- Cluster 2
- Cluster 3
- Cluster 4



ST. GEORGE'S RESPIRATORY QUESTIONNAIRE
ORIGINAL ENGLISH VERSION

ST. GEORGE'S RESPIRATORY QUESTIONNAIRE (SGRQ)

This questionnaire is designed to help us learn much more about how your breathing is troubling you and how it affects your life. We are using it to find out which aspects of your illness cause you most problems, rather than what the doctors and nurses think your problems are.

Please read the instructions carefully and ask if you do not understand anything. Do not spend too long deciding about your answers.

Before completing the rest of the questionnaire:

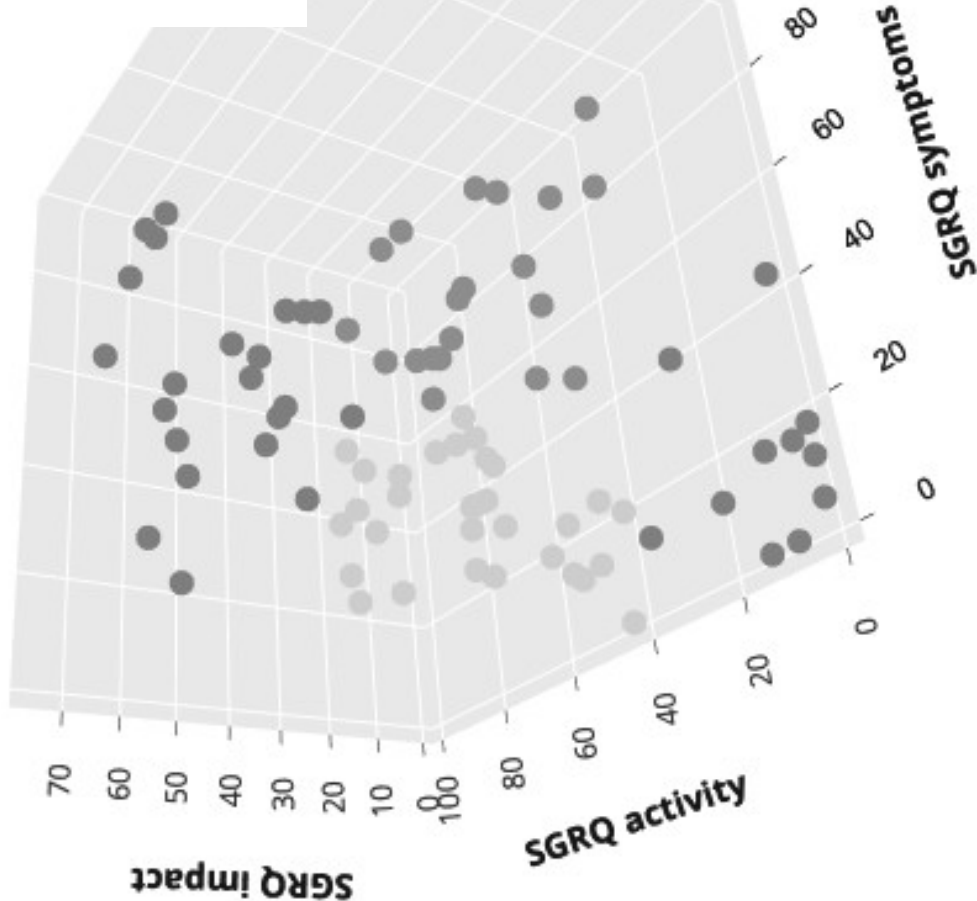
Please tick in one box to show how you describe your current health:

Very good	☐
Good	☐
Fair	☐



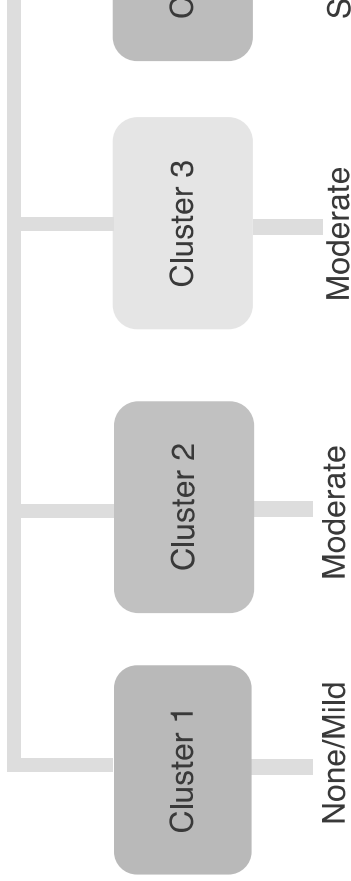
Respiratory Burden in Long COVID

- NoPACS
- Cluster 1
- Cluster 2
- Cluster 3
- Cluster 4



Respiratory Phenotypic Clusters

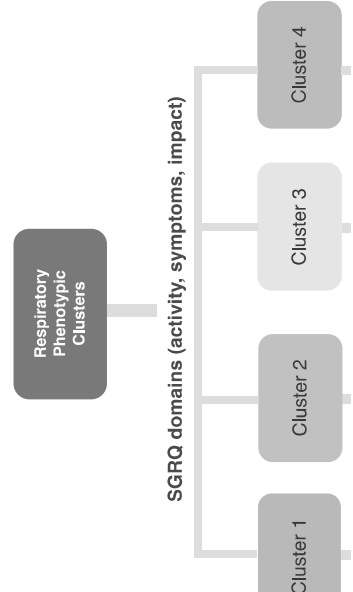
SGRQ domains (activity, symptoms, impact)



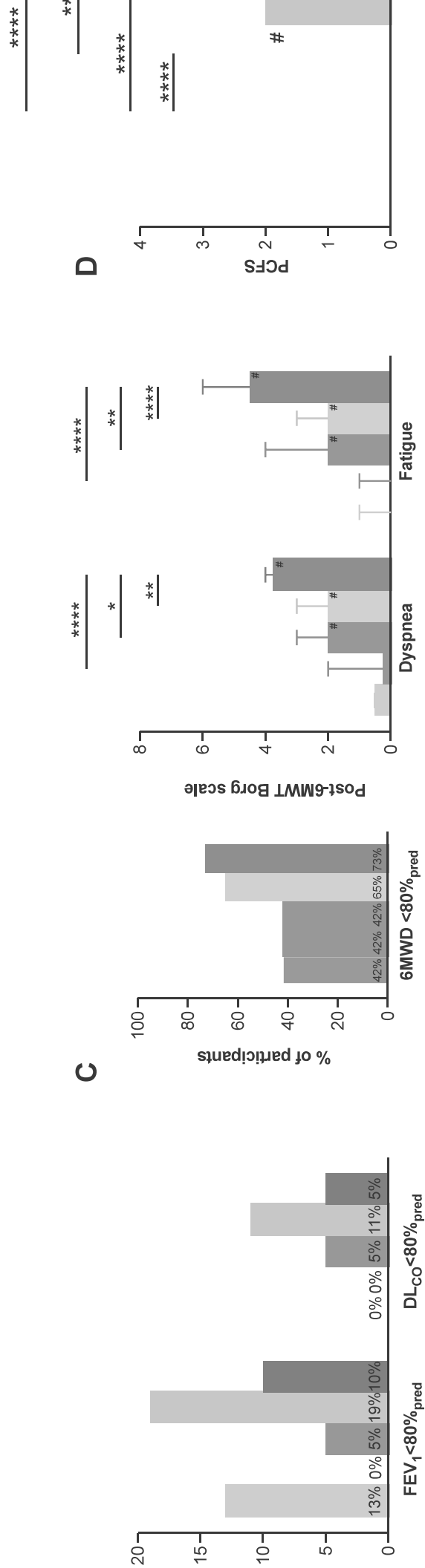
Respiratory Burden in Long COVID

	NoPACS	All PACS	p-value	PACS SGRQ Clusters			
				Cluster 1	Cluster 2	Cluster 3	Cluster 4
	n=26	n=85		n=12	n=20	n=31	n=22
Age, in years	45 ± 19	48 ± 13	0.37	55 ± 11	43 ± 14	48 ± 14	47 ± 7
Female sex, n (%)	16 (62%)	64 (75%)	0.17	6 (50%)	15 (75%)	23 (74%)	20 (91%)
BMI, in kg/m²	25 ± 3	30 ± 7	0.001	26 ± 6	29 ± 7	31 ± 7	31 ± 9
Smoking Status							
Never Smoked	22 (85%)	55 (65%)	0.05	9 (75%)	17 (85%)	18 (58%)	11 (50%)
Ex-Smoker	4 (15%)	28 (33%)	0.08	3 (25%)	3 (15%)	12 (39%)	10 (46%)
Current Smoker	0 (0%)	2 (2%)	0.43	0 (0%)	0 (0%)	1 (3%)	1 (4%)
Pack years	0 (0-12)	0 (0-38)	0.017	0 (0-4)	0 (0-4)	0 (0-35)	0.3 (0-38)
Months post-COVID	10 (3-32)	11 (3-28)	0.58	10 (4-28)	13 (3-21)	10 (4-24)	9 (3-22)

Respiratory Burden in Long COVID

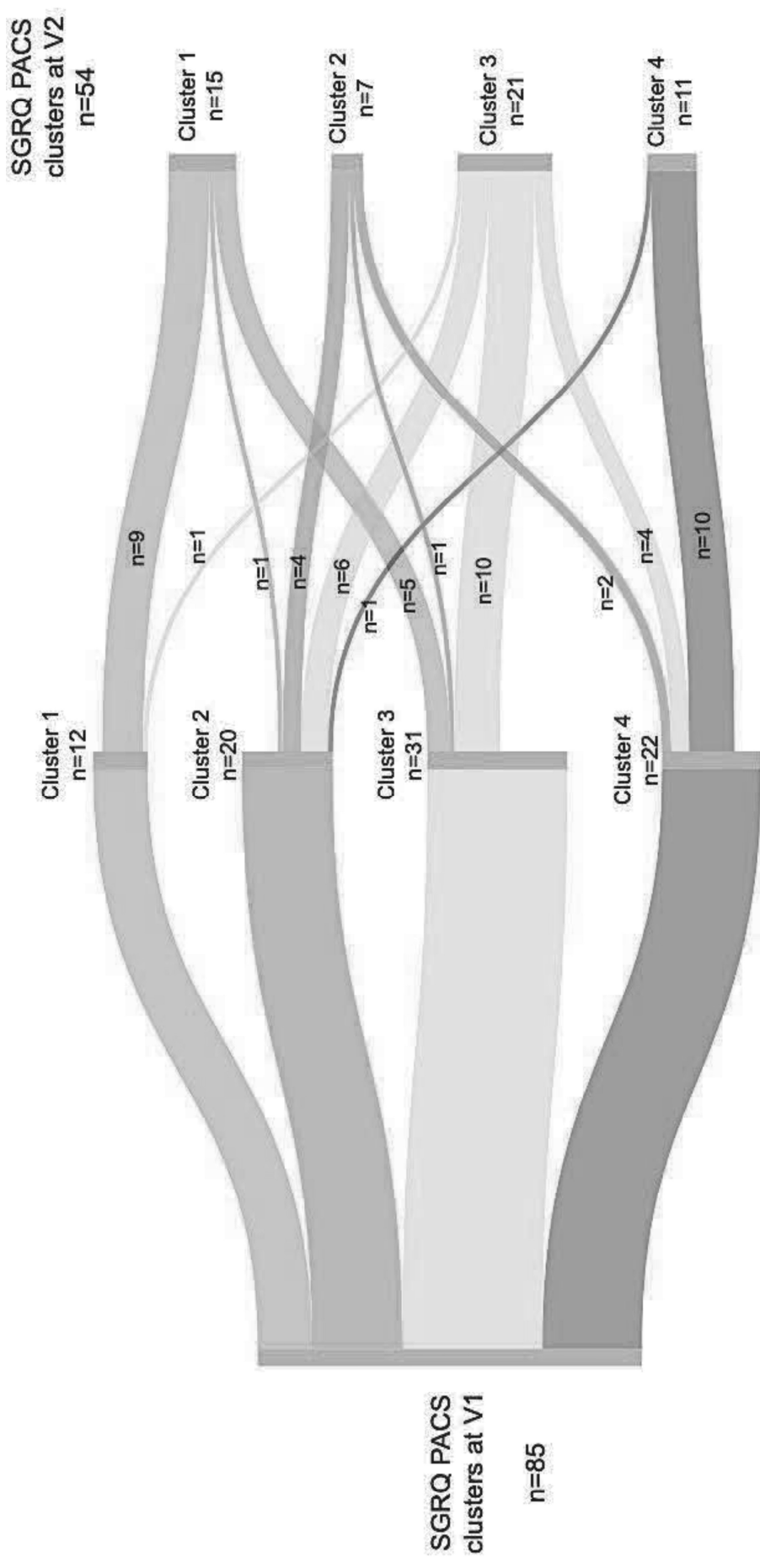


No changes in sputum differentials across clusters
(no airway inflammation!)



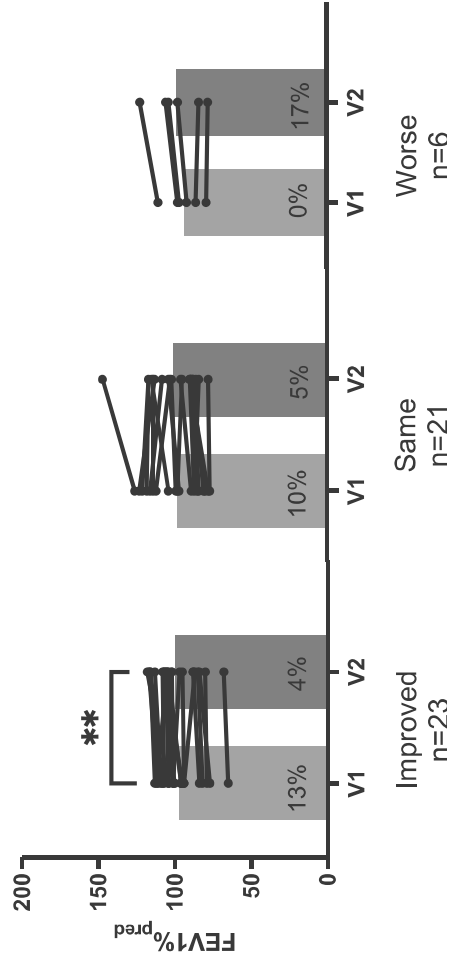
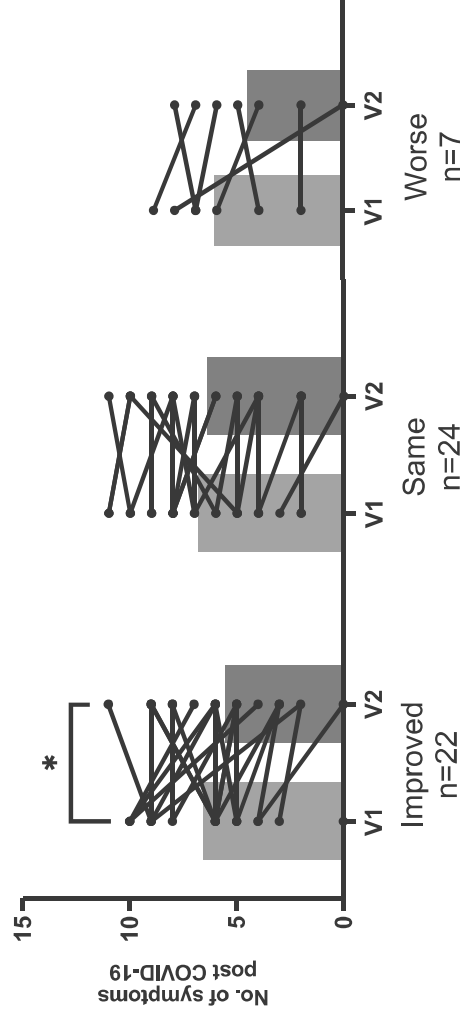
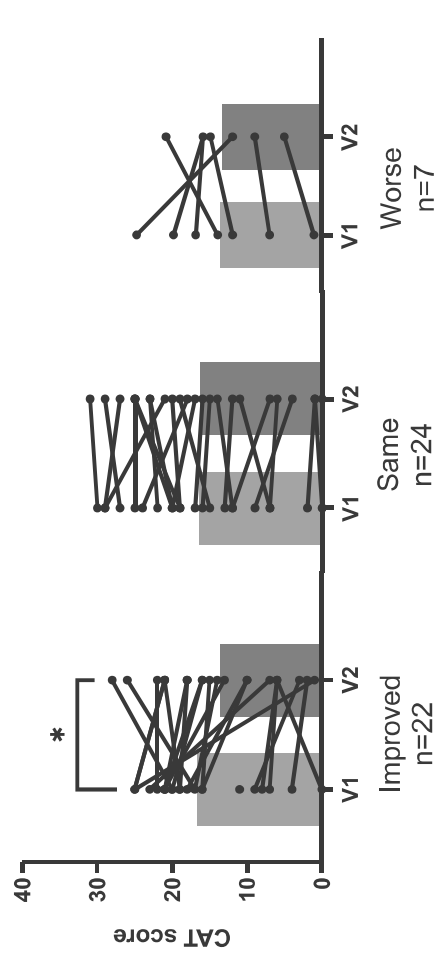
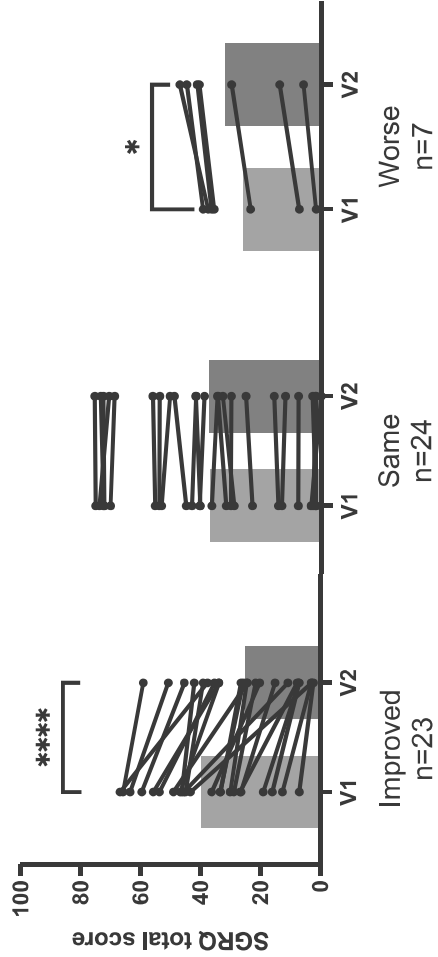
ers shown in median (95% CI). Significance to *-p value <0.05, **- p value <0.01, ***- p value <0.001.
St. George's Respiratory Questionnaire; FEV₁: forced expiratory volume in one second; DLCO: diffusing capacity for carbon monoxide; 6MWD:
e walk distance; PCFS: Post COVID-19 functionality status scale

tudinal SGRQ based cluster changes over 6-months

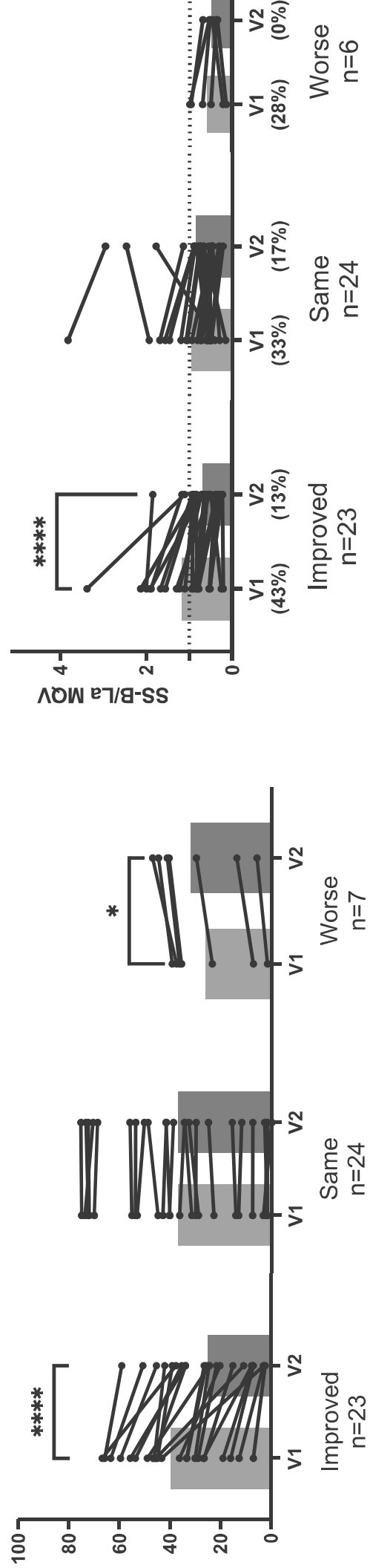


Heterogeneity and fluidity of symptomology within PACS

Improvement of Respiratory burden over 6 months



Improvement of Respiratory burden over 6 months



		Estimate	Standard Error	t value	p value
SS-B/La	Symptoms	-4.3953	7.7416	-0.568	0.57
	Activity	16.171	7.942	2.036	0.050
	Impact	13.0476	4.1157	3.170	0.003

Change in anti-SS-B/La predicts improvement in respiratory burden (SGRQ activity and impact scores)

tent neutrophil-associated immune signature rizes post-COVID-19 pulmonary sequelae

ge^{1,2}, Anna Reed^{1,2}, Sujal R. Desai^{1,2}, Anand Devaraj^{1,2}, Tasnim Sh
Man^{1,2,7}, Amama Kanwal⁵, Camille Esneau⁵, Michael K.C. Liu⁴, Faisal Kam
Man^{1,2,7}, Sundeep Kaul¹, Suveer Singh¹, Georgia Lamb¹, Fatima K.
iga⁵, Jane Read⁵, Thomas Burgoyne^{1,8}, Andreia L. Pinto¹, Jake Mic
as⁵, Julie Candiracci⁹, Mhammed Bougoussa⁹, Martelle Herzog⁹, La
aj-Shala², Stuart Turville¹⁰, Anupriya Aggarwal¹⁰, Hugo A. Farnes²
ria^{4,12}, Andrew D. Aswani^{13,14}, Francesca Patella¹⁵, Weronika E. Bi
ll¹², Nathan W. Bartlett⁵, Arran Dokal¹⁵, Xiao-Ning Xu⁴, Peter Kelle
641, Aran Singanayagam^{4,†}

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for the Advancement

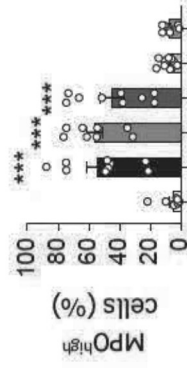
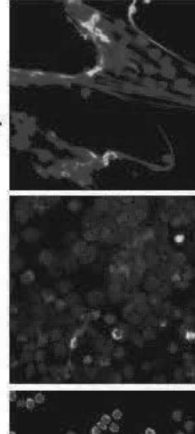
JCI insight

Autoantibodies stabilize neutrophil extracellular traps in COVID-19

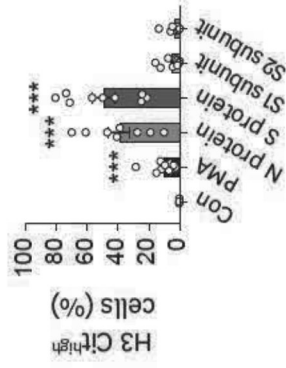
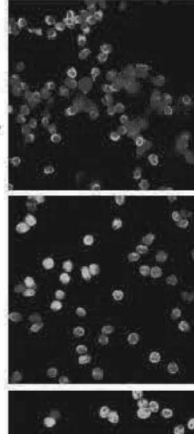
Yu Zuo, ... , Yogendra Kanthi, Jason S. Knight

JCI Insight 2021;6(15):e150111. <https://doi.org/10.1172/jci.insight.150111>.

PMA N protein



S1 subunit S protein



Immune Netw. 2021 Apr;21(2):e16
<https://doi.org/10.4110/in.2021.21.e16>
pISSN 1598-2629 · eISSN 2092-6685

Brief Communication

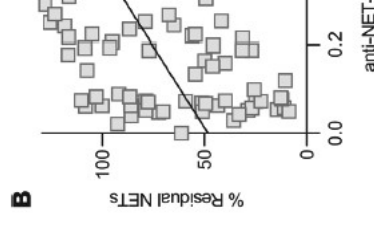
Check for updates

Nucleocapsid and Spike Protein of SARS-CoV-2 Drive Neutrophil Extracellular Trap Formation

Young-Jin Youn¹, Yu-Bin Lee¹, Sun-Hwa Kim¹, Hee K
Jae-sung Bae^{1,2}, Chang-Won Hong^{1,3}

¹Department of Physiology, School of Medicine, Kyungpook National University,
²Department of Laboratory Animal Medicine, College of Veterinary Medicine,
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41566, Korea

OPEN ACCESS



Summary

A significant subset of previously healthy PACS patients have clinically relevant respiratory burden as identified by unbiased SGRQ-domain analysis

Respiratory burden in PACS is associated with non-resolved systemic inflammation and autoantibodies

Clinical assessments

Dyspnea post 6 min walk test

SGRQ

Rheumatology assessment: constitutional symptoms

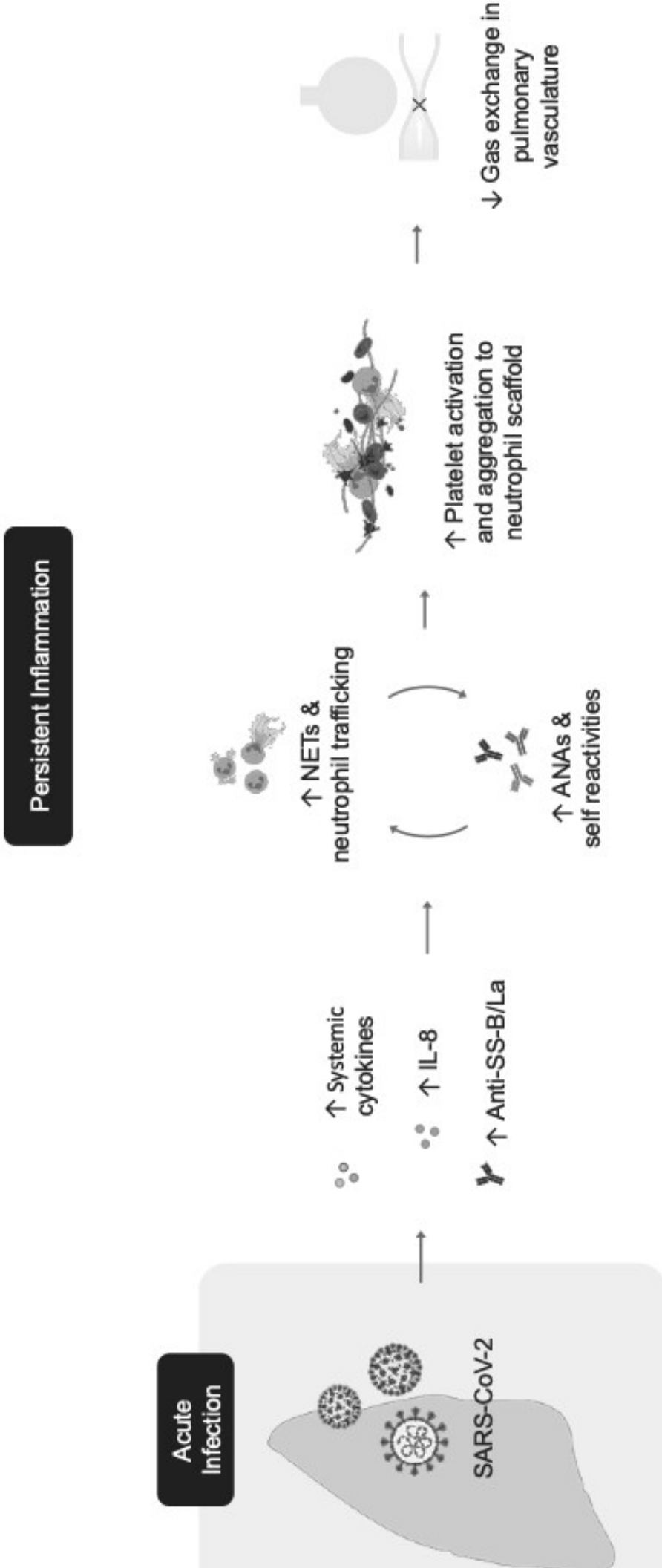
Rapid Assessment Clinical tests (under development)

TNFa

Anti-SSb-La antibodies

Neutrophil activation markers (?)

Circulating spike protein (?)



Useful predictive biomarkers for assessing long term complications post COVID

Clinical assessments

Dyspnea post 6 min walk test

Rheumatology assessment: constitutional symptoms

Rapid Assessment Clinical tests (under development)
TNFa

Anti-SSb-La antibodies

Altered B cell subset (Clinical Immunologist: flow)

Neutrophil activation markers (?)

Circulating spike protein (?)

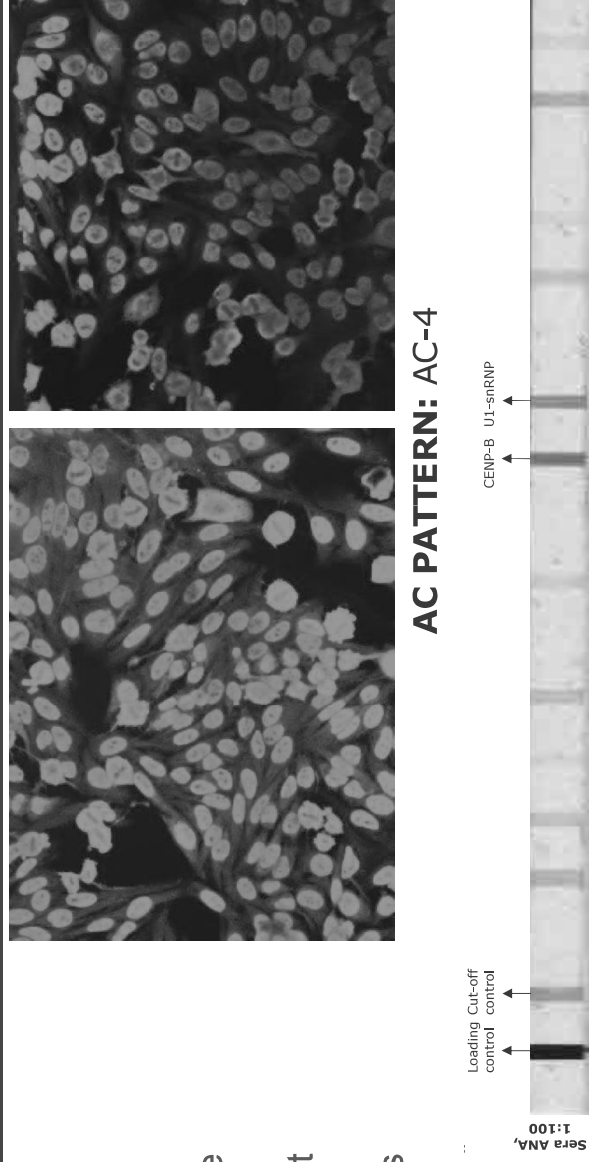
Study 1 (AIPACS)

Male (he/his), BMI 29.7, never smoker
16 months post- recovery
Previously healthy
COVID PCR+, prior to vaccination
Symptom-recovered, symptomatic acute phase (fever, sore throat, SOB, fatigue, diarrhoea, low pressure)
16 months, reporting of aches, fatigues, diarrhoea, chest pains, low pressure, loss of movement, swollen joints
CT normal, CT (normal), CBC normal, sputum differentials normal, 6MNW dyspnea (Borg 9) + fatigue
Family history of autoimmune: unremarkable
Initial investigations ANA+ , ANCA negative
ratory investigations (AIPAC 002)
dsDNA, SS-B/La, CENP positive (LIA)

ANAs evident at 1:320 titer (Hep-2 substrate slide)
IF and IL-8 high

Rheumatoid panel negative
Normal Immunoglobulin levels
Elevated B cell subset
16 months, post COVID

Myalgia rheumatica and trajectory to lupus
Hydroxychloroquine (Plaquenil 400mg/daily)
Joint assessment
Fatigue (FAS) Score 37 (visit 1) → 33 (visit 2) → 28 (visit 3)
Decrease in ANA titers, TNFa
Better managed, but active disease persists
Uninformed/diagnosed: SLE



AC PATTERN: AC-4

IMTEC-ANA-LIA XL		ITC92007 LOT		SS-A/Ro 52		SS-A/Ro 60		P0 (RPP)		PCNA		Smd1		Histone		Nucleosome		dsDNA	
Visit 1																			
2	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
IMTEC-ANA-LIA XL		ITC92007 LOT		SS-A/Ro 52		SS-A/Ro 60		P0 (RPP)		PCNA		Smd1		Histone		Nucleosome		dsDNA	
Visit 2																			
1	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
IMTEC-ANA-LIA XL		ITC92007 LOT		SS-A/Ro 52		SS-A/Ro 60		P0 (RPP)		PCNA		Smd1		Histone		Nucleosome		dsDNA	
Visit 3																			
17	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■

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Mukherjee

L A B O R A T O R Y

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Terence Ho**
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Mylinh Duong
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Susan Wasserman

Collaborating Scientists

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Ishac Nazy

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Katherine Radford
Melanie Kjarsgaard
Chynna Huang

Patient Partner and PWLE

Suzie Goulding
COVID Long-Haulers Support
Group Canada

Collaborating Investigators/Advisors

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Andrea Gershon (UHN, Toronto)
Simon Rousseau (McGill, BQC19)



COVID-19
IMMUNITY
TASK FORCE

GROUPE DE TRAVAIL
SUR L'IMMUNITÉ
FACE À LA COVID-19

CIHR



Canadian Institutes
of Health Research

The
Research
Institute
of St. Joe's Hamilton

St. Joseph's
Healthcare Hamilton

cyclomedica



Group by Suzie Goulding

COVID Long-Haulers Support
Group Canada

a Private group - 11.6K members



Hamilton Academic Health Sciences Organization



McMaster
University

St. Joseph's
Healthcare Hamilton



Keep Calm and Experiment on....

Summer of 2024



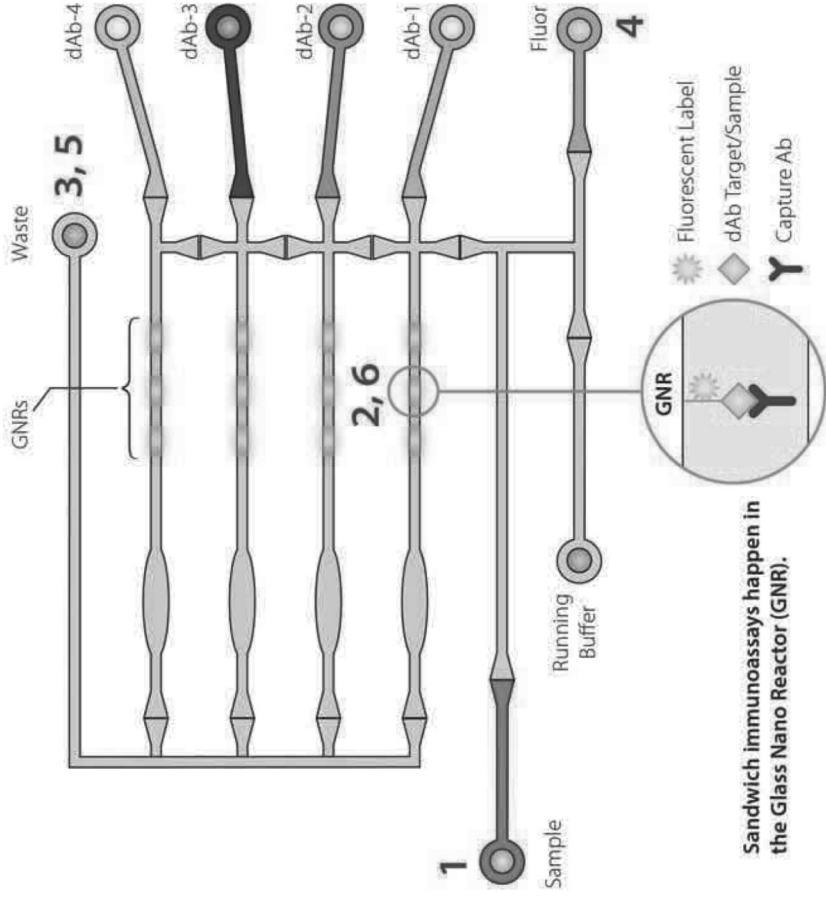
slides

Artise: Assessing the inflammatory micro-environment

Cytokines and inflammatory mediators

Artise™ automated ELISA

Sample types: sera, plasma, BAL, sputum



Sandwich immunoassays happen in the Glass Nano Reactor (GNR).

Cut-off thresholds established with age and sex matched healthy population

Artise: Autoimmune markers, cytokines, in vitro mechanisms towards Translation!

Can be used to monitor longitudinal outcomes over time

[illegible]