Vaccine Evaluation Center
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BC Children's Hospital Research Institute

UBC

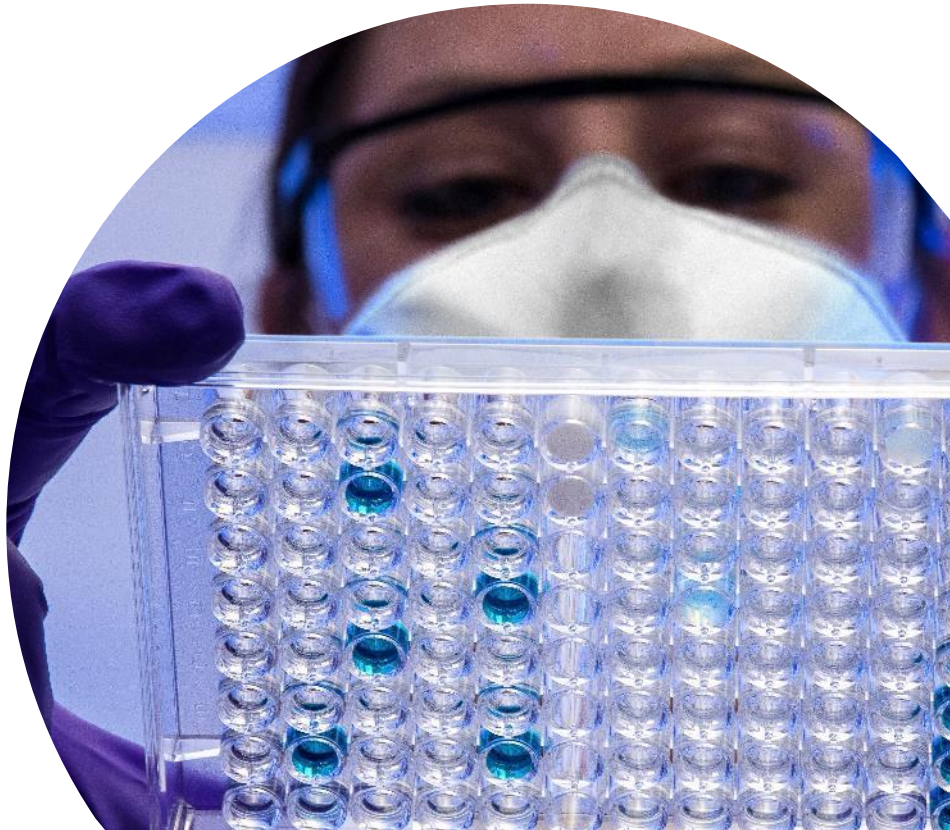
# COVID-19 Immunology Consortium-BC Symposium

November 5th, 2021

**Dr. Christopher Carlsten**

**Dr. Manali Mukherjee**

**Chad Poloni**



# Land acknowledgement

BC Children's Hospital Research Institute operates on the traditional, ancestral, and unceded territory of the Coast Salish peoples — xʷməθkʷəy̓əm (Musqueam), Sḵwx̱wú7mesh (Squamish), and Sə́l̓ílwətaʔ/Selilwitulh (Tsleil-Waututh) Nations.

# COVID-19 Immunology Consortium-BC

CIC-BC brings together researchers at all stages of their career to help facilitate collaborations with individuals who are interested in infectious disease immunology.

**As a member of CIC-BC, you have access to:**

- a community of over 100 researchers from across BC
- quarterly newsletters
- bimonthly research symposia
- student and trainee group.

# Today’s presenters

**Chad Poloni**

PhD Student, University of British Columbia

**Dr. Christopher Carlsten**

Professor and Division Head of Respiratory Medicine, University of British Columbia

**Dr. Manali Mukherjee**

Assistant Professor of Medicine, McMaster University

# Tracking the COVID-19 vaccine T cell response

Chad Poloni
Steiner Lab

CIC-BC Symposium

Nov 5, 2021

# Current COVID-19 vaccine T cell studies

**PREVENT Study**

*Definitions*
V1 - Day of COVID-19 vaccine, up to 24 hours prior to vaccination
V2 – 1 month post dose 1
V3 – Day of COVID-19 vaccine dose 2, up to 24 hours prior to vaccination
V4 – 1 month post series completion
V5 – 4 months post series completion
V6 – 7 months post series completion
V7 – 10 months post series completion
V8 – 13 months post series completion
V9 – 19 months post series completion

AIM assays N = 51  Ex vivo phenotyping N= 51

Individuals N = 18
**Individuals with V1, V2, V4, V5 N = 4**

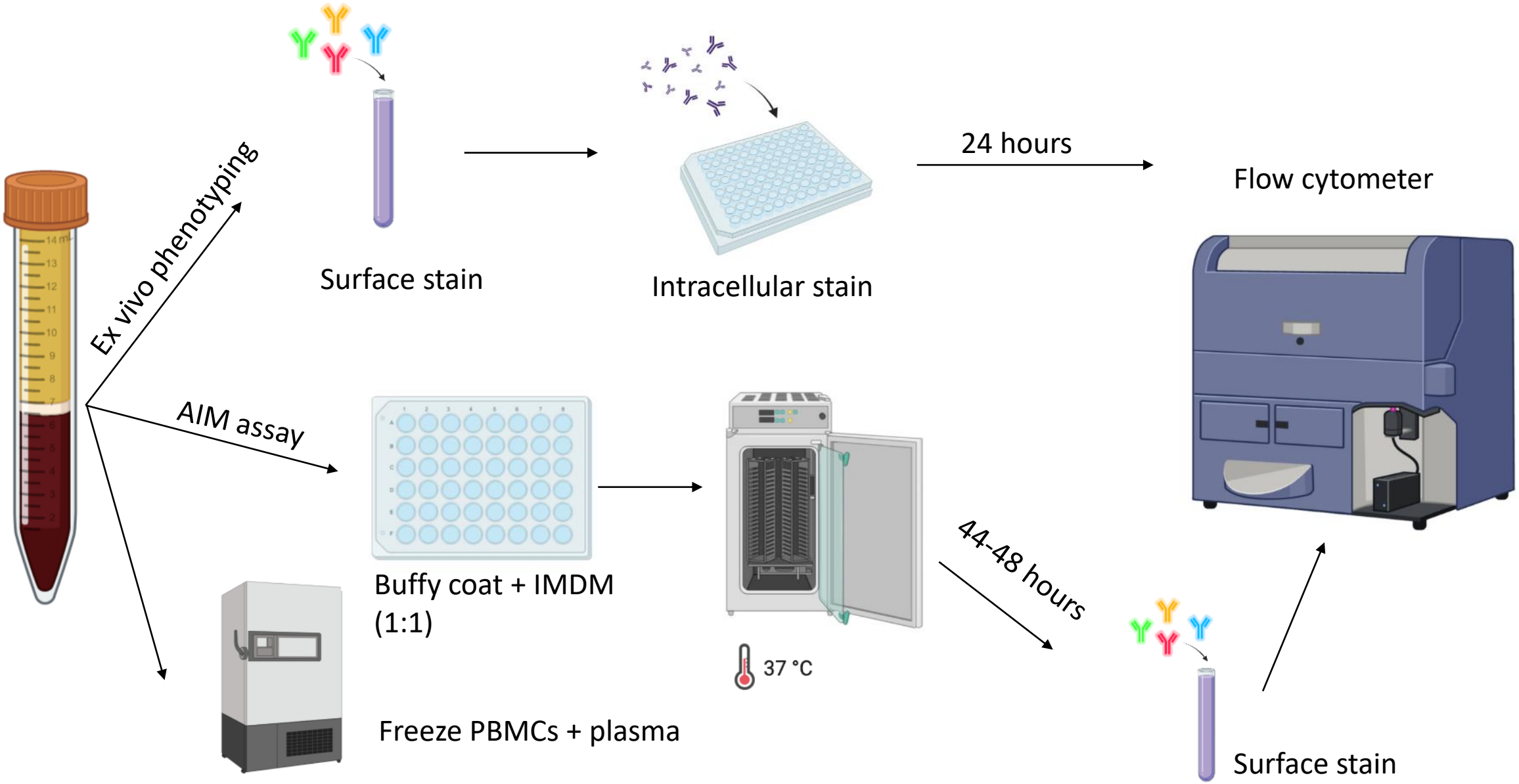
**PREVent-COVID – Transplant Study**
Total PBMCs collected N = 65
Total serum collected N = 115

| | |
|---|---|
| V1 PBMCs = 3 | V1 Serum = 3 |
| V2 PBMCs = 20 | V2 Serum = 21 |
| V3 PBMCs = 40 | V3 Serum = 80 |
| V4 PBMCs = 2 | V4 Serum = 11 |

**Blood Cancer Study – CSS**
Total PBMCs collected N = 220
Total AIM assays (fresh blood) N = 30

**Solid Tumor Study – CST**
Total PBMCs + AIM + ex vivo phenotyping N = 92
V1 = 29
V2 = 63

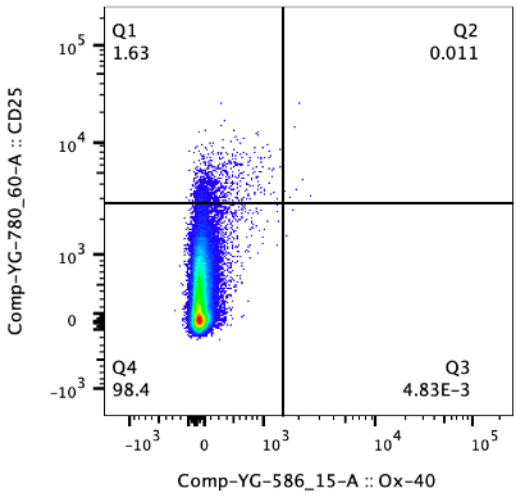
# Overview of sample processing



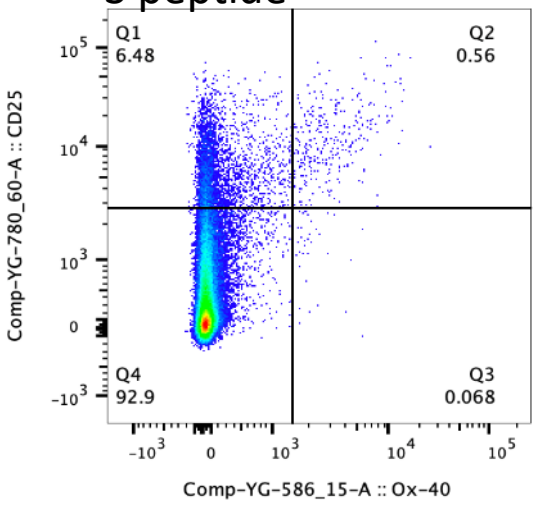
# The antigen-induced marker assay (AIM)

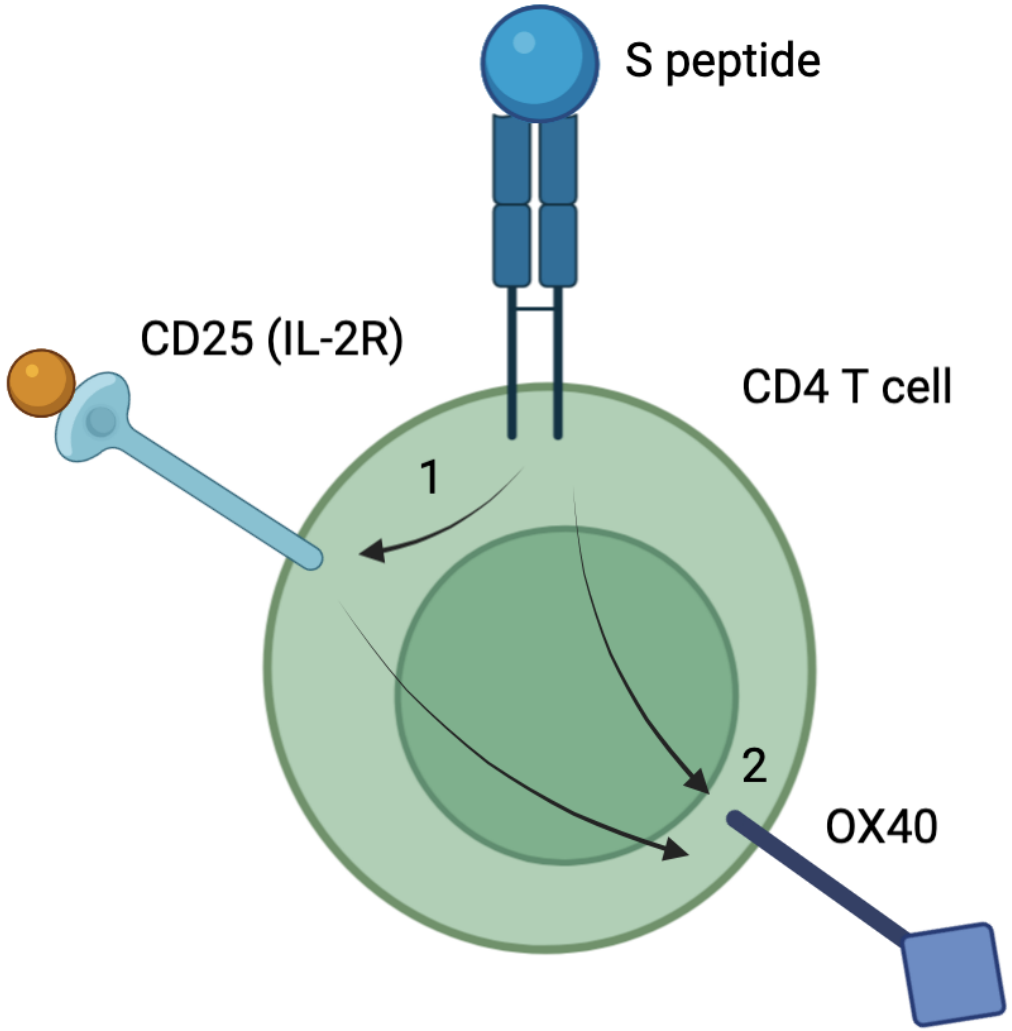
1. 100 ul buffy coat + 100 ul IMDM plated with antigen in 48-well plate
   - Unstimulated
   - S peptide
   - M peptide
   - N peptide
   - AgriFlu
   - Cytostim
2. Incubated for 44-48 hours at 37
3. Surface stain for CD4, CD8, and activation markers
   - CD25 + OX40 for CD4
   - CD69 + CD137 for CD8
4. Read on flow cytometer

Unstimulated



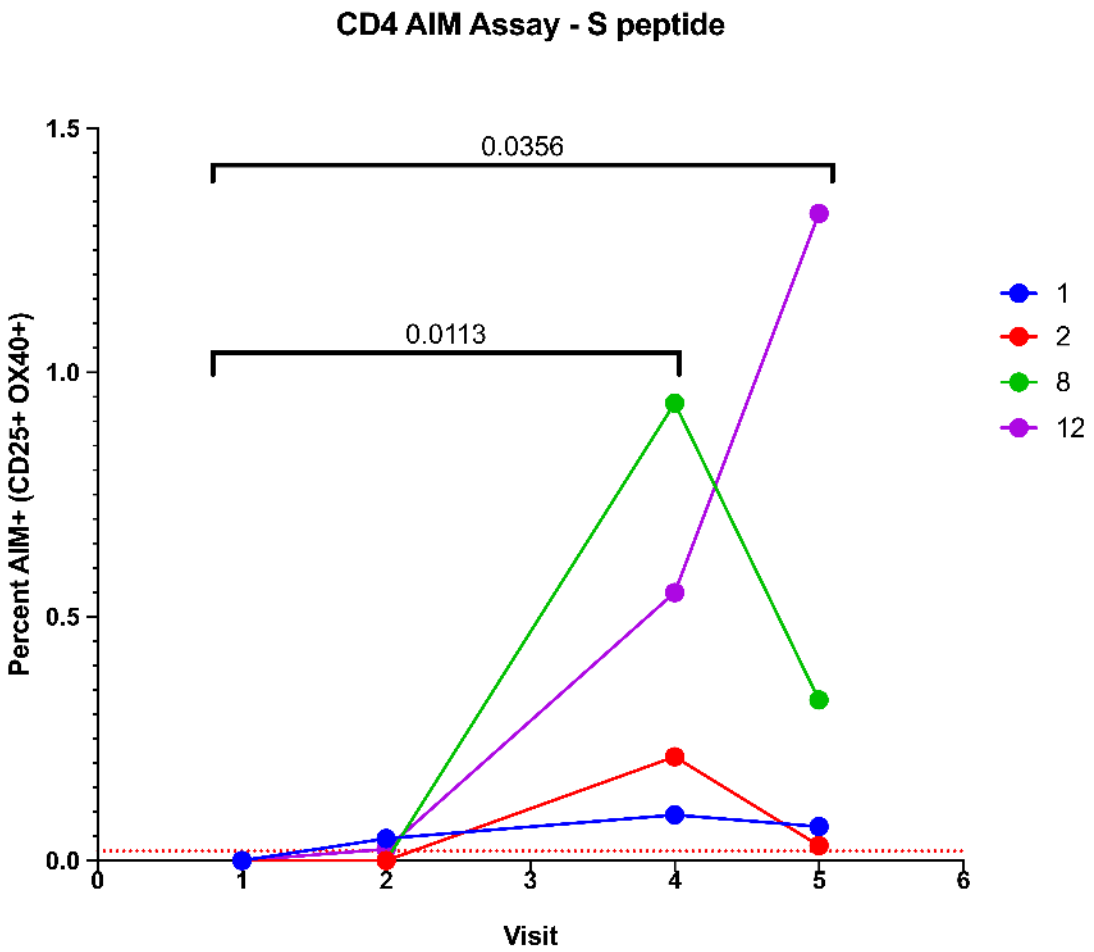

S peptide



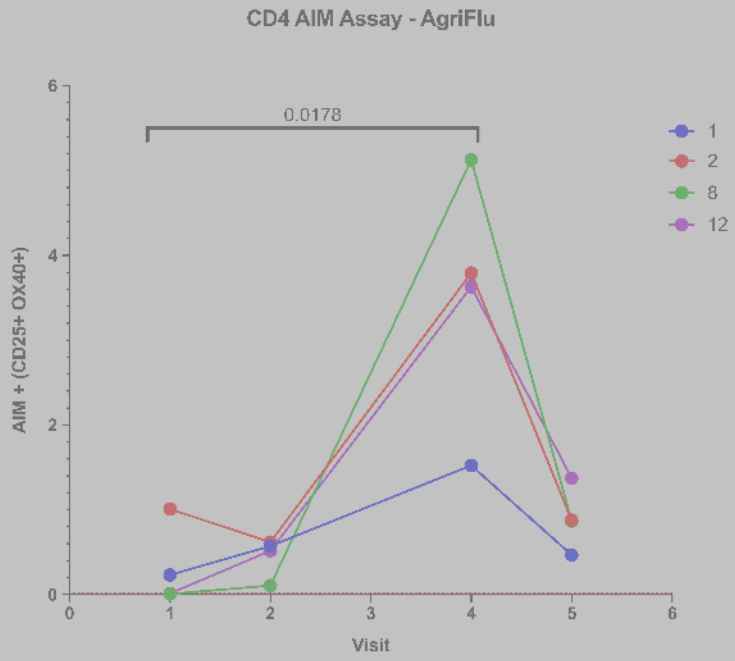




Created using Biorender

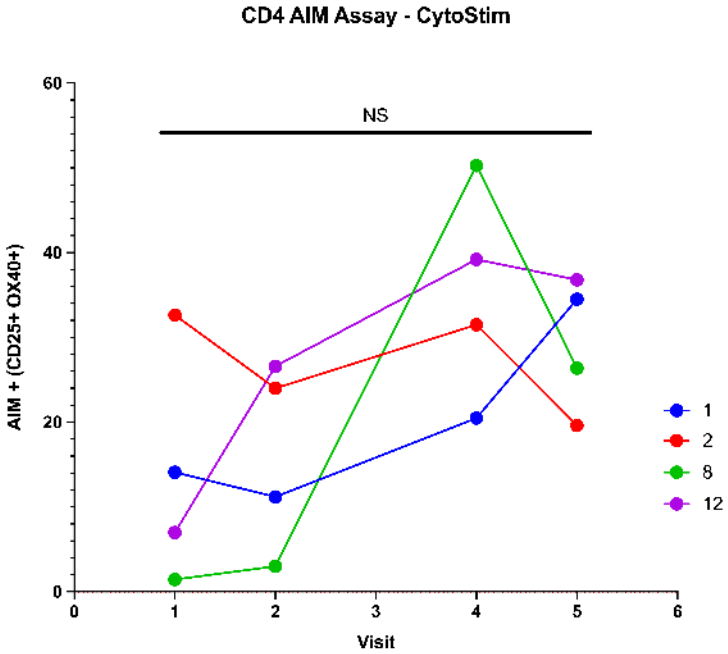
# CD4 T cell responses




N = 4
Kruskal-Wallis test: P = 0.0009
+ Dunn's multiple comparisons test

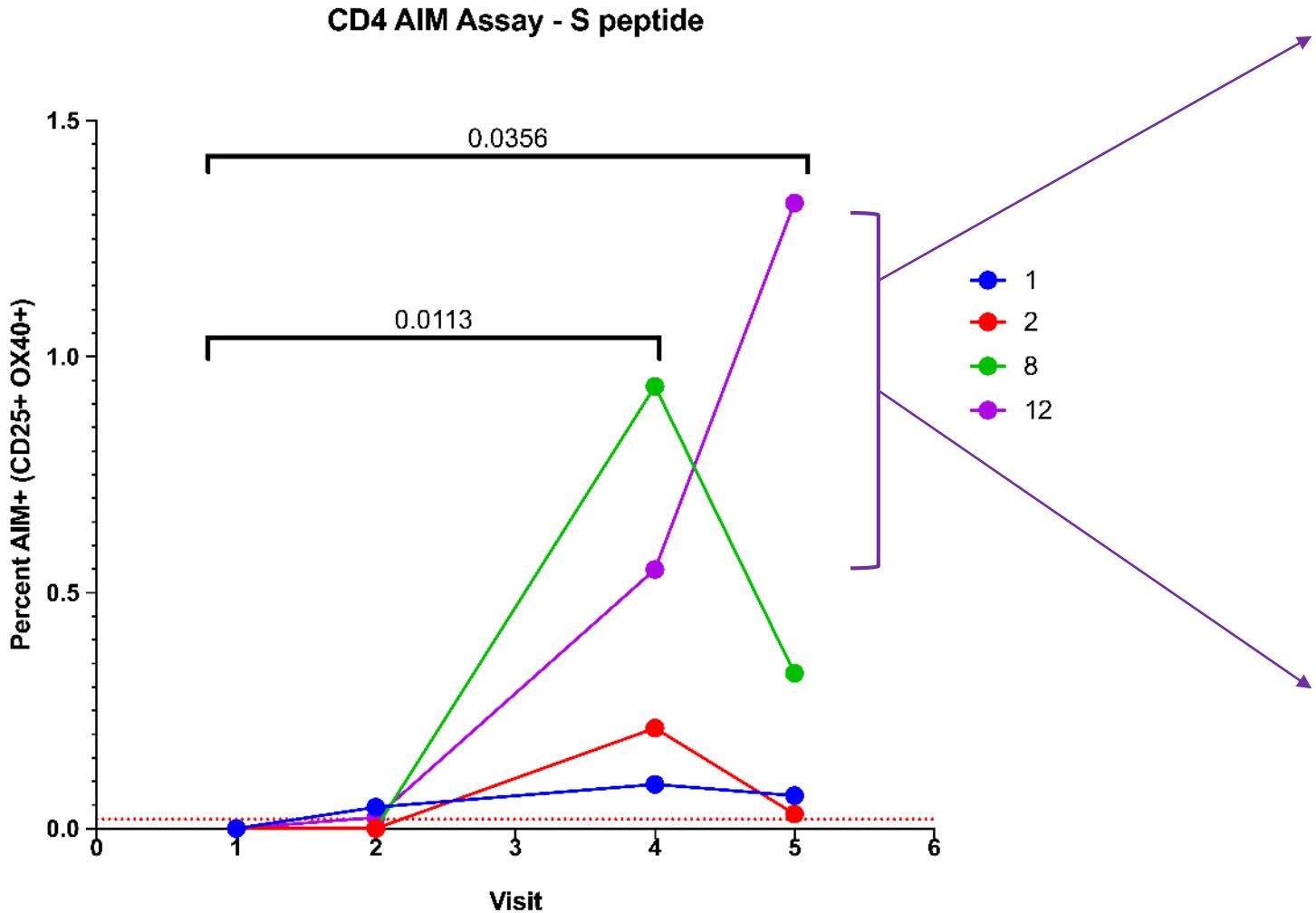


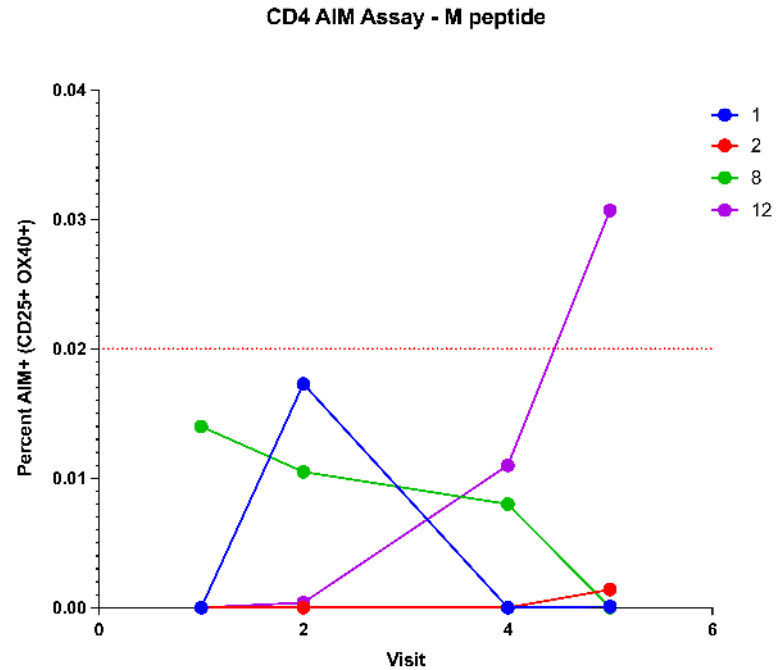

N = 4
Kruskal-Wallis test: P = 0.0033
+ Dunn's multiple comparisons test

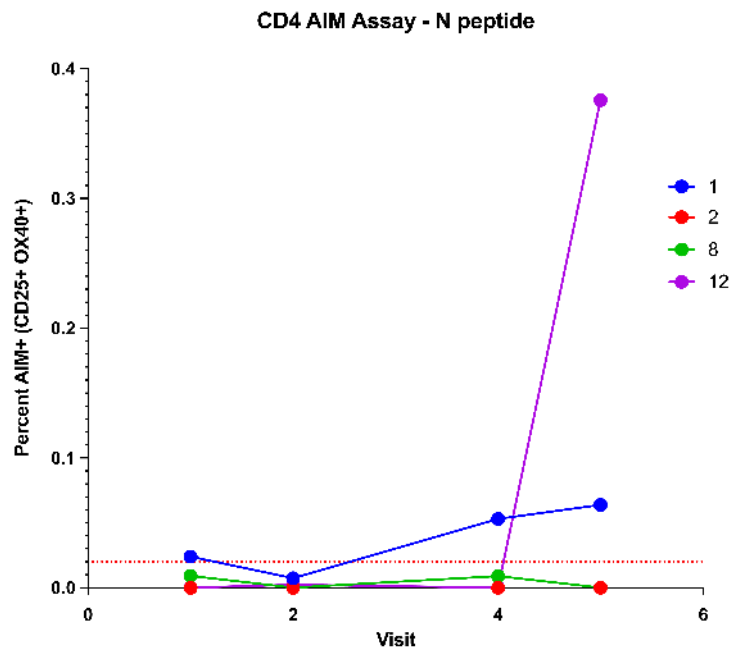



N = 4
Kruskal-Wallis test: P = 0.0955

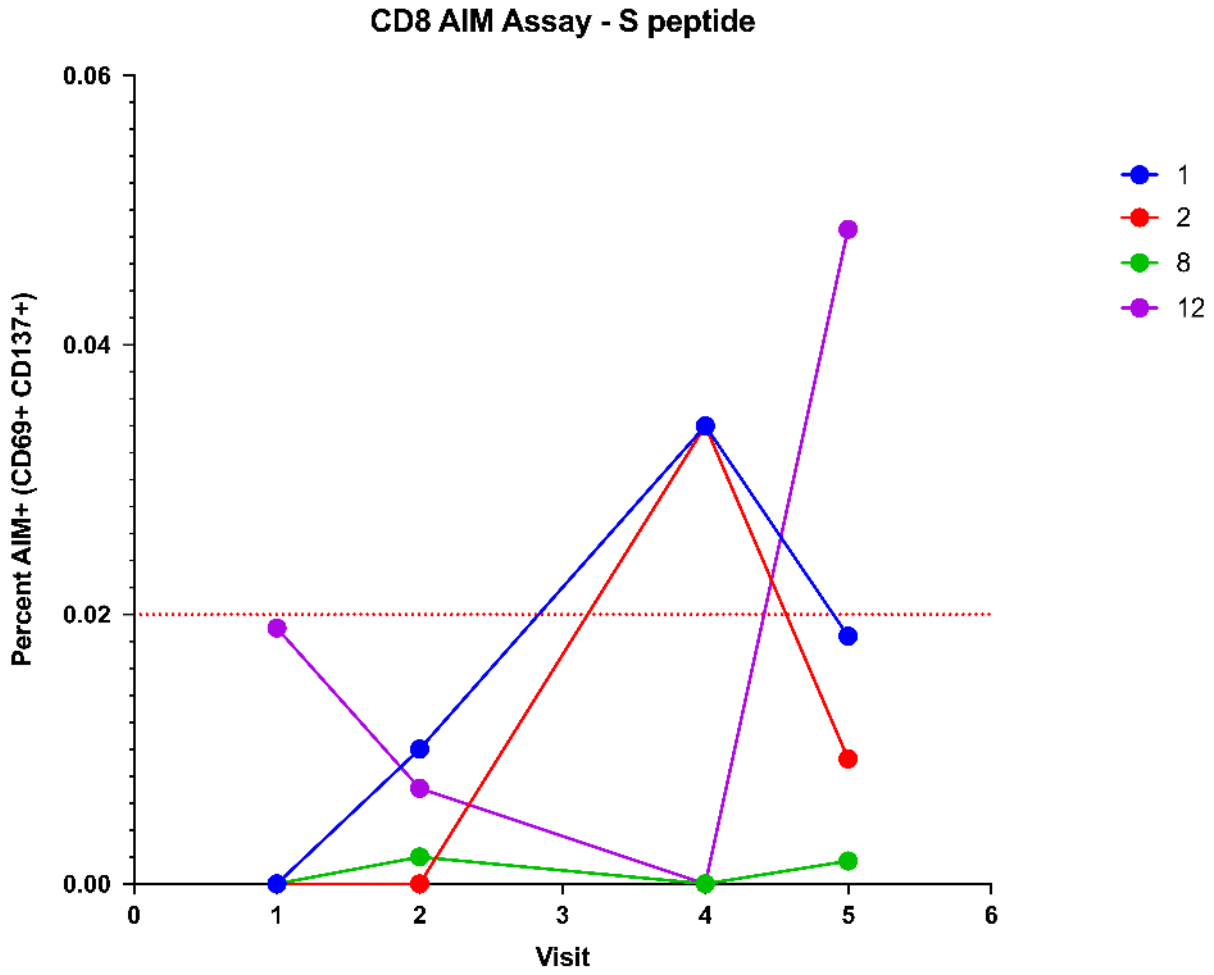
# CD4 T cell responses



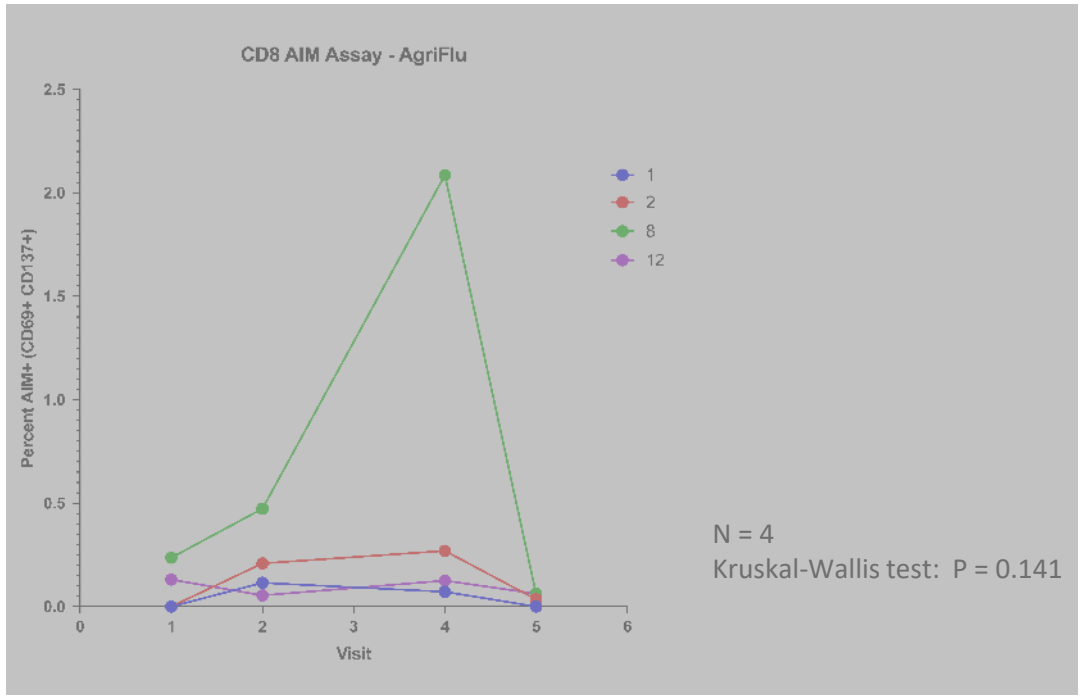



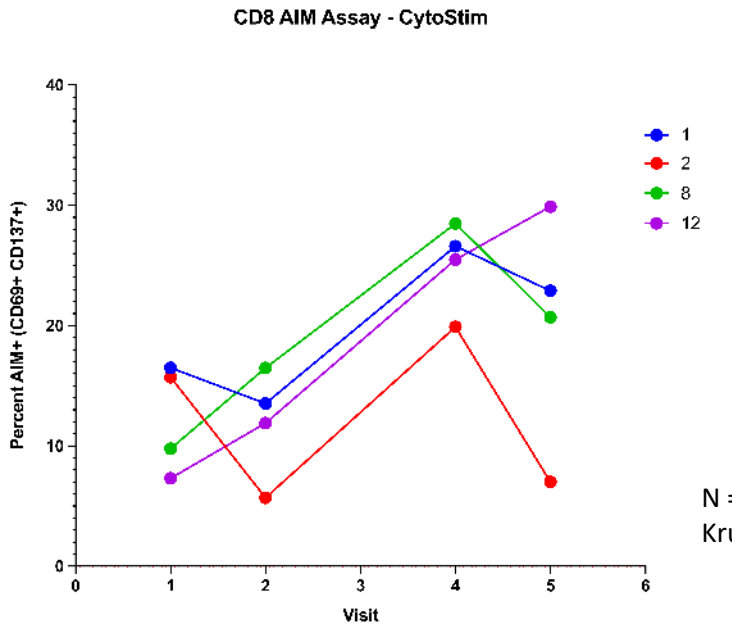
# CD8 T cell responses




N = 4
Kruskal-Wallis test: P = 0.448




N = 4
Kruskal-Wallis test: P = 0.141




N = 4
Kruskal-Wallis test: P = 0.0386

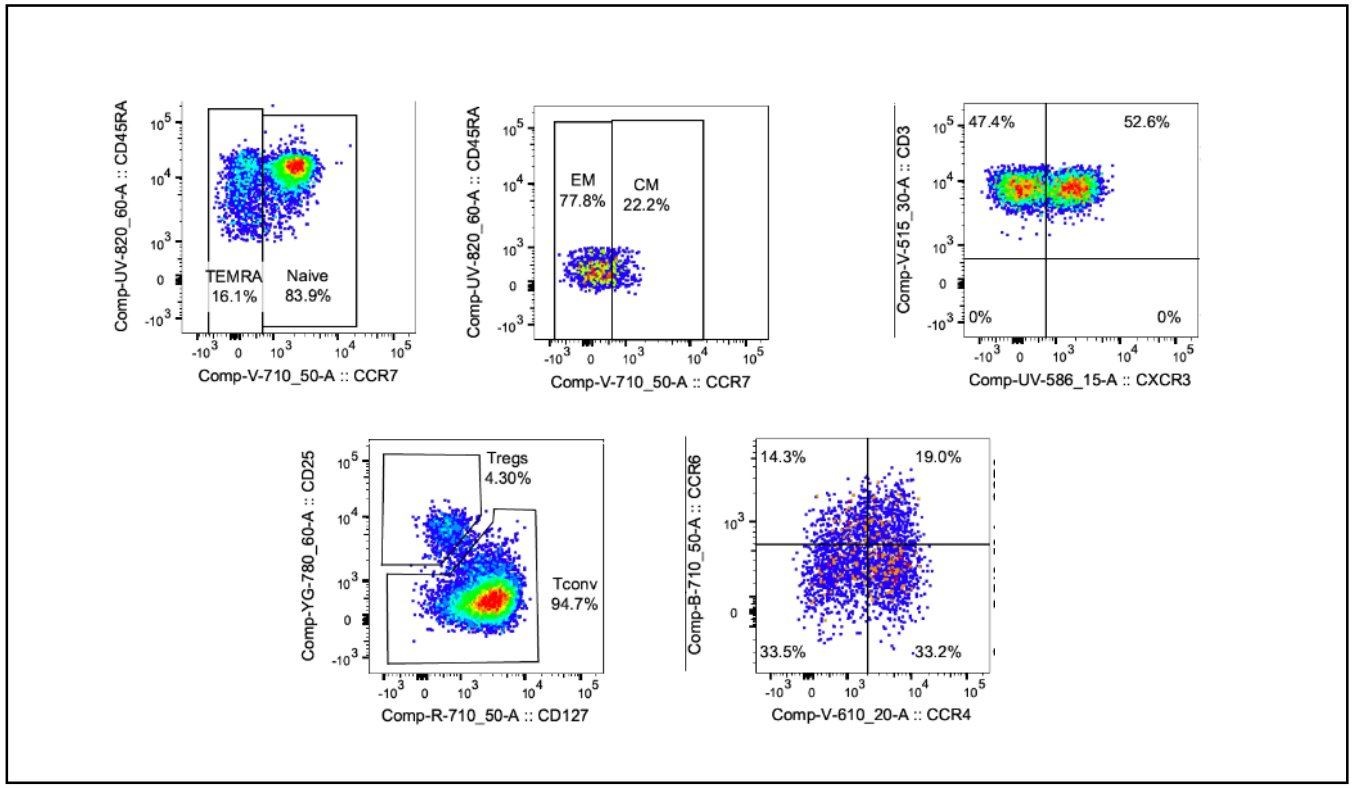
# Summary of T cell responses

- Antigen-specific S peptide CD4 T cell responses peak at visit 4 (1 month after series completion)
- CD4 T cell responses are still detectable at time point 5
- ID12 has suspected COVID-19 infection between V4 and V5 causing peak of CD4 T cell response at V5
  - T cell response to N and M peptides
- AgriFlu CD4 T cell response follows a similar pattern as the S peptide
  - Due to timing of Flu vaccination or ssRNA from COVID-19 vaccine acting as adjuvant to boost Flu-specific T cell response
- The magnitude of CD8 S-specific T cell responses is much lower than CD4 T cells

# Ex Vivo Phenotyping

- Phenotyping carried out on fresh whole blood

| Symphony | | Filter | Target |
|---|---|---|---|
| UV-355nm | 1 | 378/29 | CD45RO |
| | 2 | 515/30 | CD4 |
| | 3 | 586/15 | CXCR3 |
| | 4 | 610/20 | CD8 |
| | 5 | 670/30 | |
| | 6 | 740/35 | PD-1 |
| | 7 | 820/60 | CD45RA |
| | | | |
| V-403nm | 1 | 440/40 | CTLA4 |
| | 2 | 515/30 | CD3 |
| | 3 | 586/15 | |
| | 4 | 610/20 | CCR4 |
| | 5 | 670/30 | |
| | 6 | 710/50 | CCR7 |
| | 7 | 750/30 | |
| | 8 | 780/40 | CXCR5 |
| | | | |
| B-488nm | 1 | 488/10 | - |
| | 2 | 515/20 | CD39 |
| | 3 | 610/20 | |
| | 4 | 670/30 | |
| | 5 | 710/50 | CCR6 |
| | 6 | 780/60 | |
| | | | |
| YG-561nm | 1 | 585/42 | FOXP3 |
| | 2 | 610/20 | CCR5 |
| | 3 | 675/30 | |
| | 4 | 710/50 | |
| | 5 | 763/43 | CD25 |
| | | | |
| R-628nm | 1 | 660/10 | Helios |
| | 2 | 712/25 | CD127 |
| | 3 | 780/60* | HLA-DR |

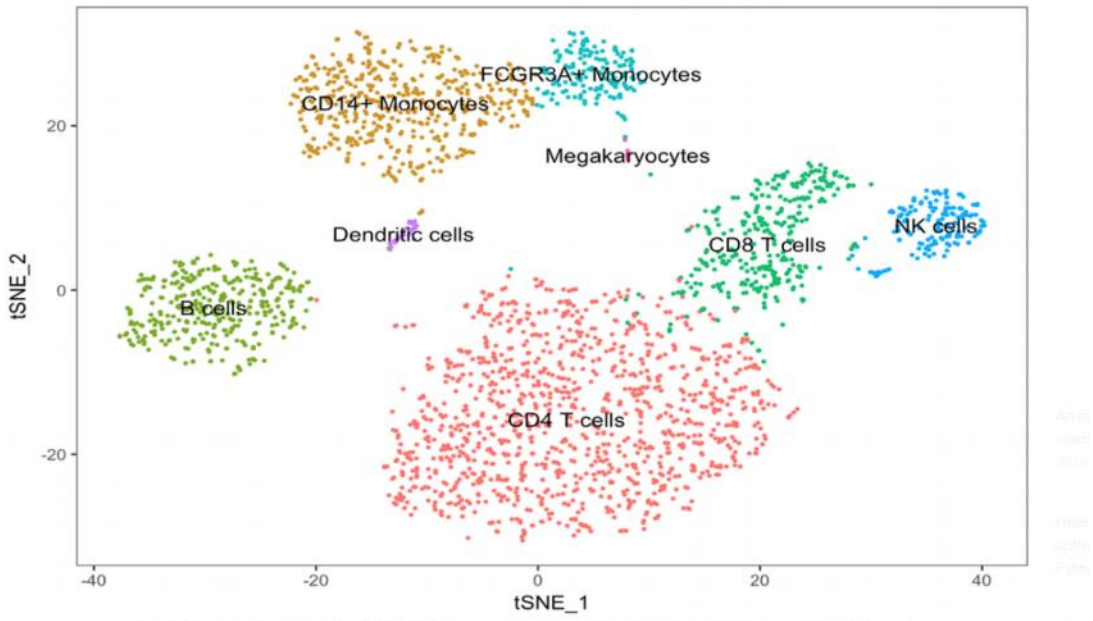



- Panel allows for traditional Boolean gating of CD4 and CD8 T cell subsets:
  - Naïve, effector memory, central memory follicular helper, Th1, Th2, Th17, Th1.17
- **Can utilize dimensionality reduction and clustering techniques to identify novel T cell subsets**

# Ex vivo phenotyping analyses

**tSNE – t-distributed stochastic neighbor embedding**

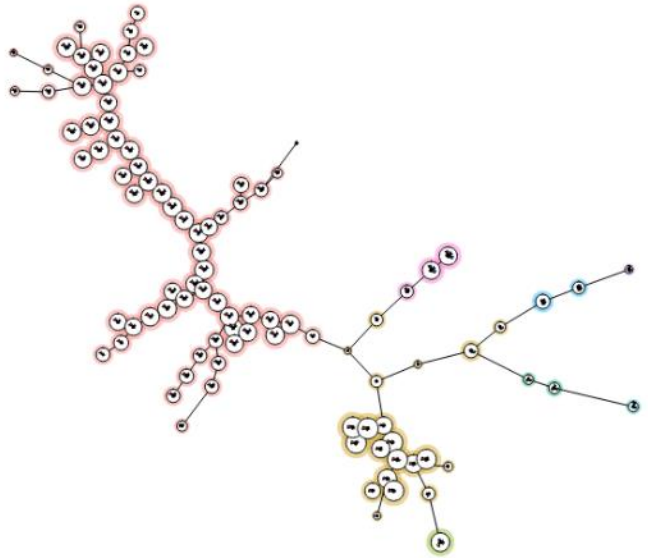
- Dimensionality reduction technique
- Visualization of high dimensional (parameter) datasets
- Gives each datapoint (cell) a position in 2D space
- Points are grouped by similarity




Source: https://towardsdatascience.com/how-to-tune-hyperparameters-of-tsne-7c0596a18868

**FlowSOM – t-distributed stochastic neighbor embedding**

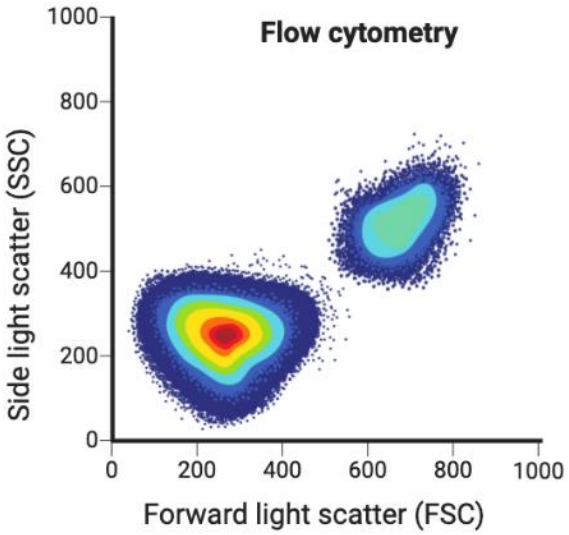
- Dimensionality reduction technique
- Visualization of high dimensional (parameter) datasets
- Generates self-organizing maps (SOM) of clusters based on markers, assigns each cluster to metacluster
- shows population abundances and marker expressions



Quintelier et al, 2021.

# Analysis pipeline

1. Clean up FCS files (gate single cells, CD3+)




2. Down-sample all visits and IDs to 8,000 events
   - Reduce number of events for tSNE and FlowSOM

3. Concatenate all sample visits into one FCS file


4. Run tSNE on single FCS file (hours – days)

5. Gate out each visit (using keywords), overlay on top of master tSNE to identify changes in T cell populations overtime

6. Perform FlowSOM of FCS file

7. Gate out visits for each FlowSOM population to determine which cluster is enriched for each visit

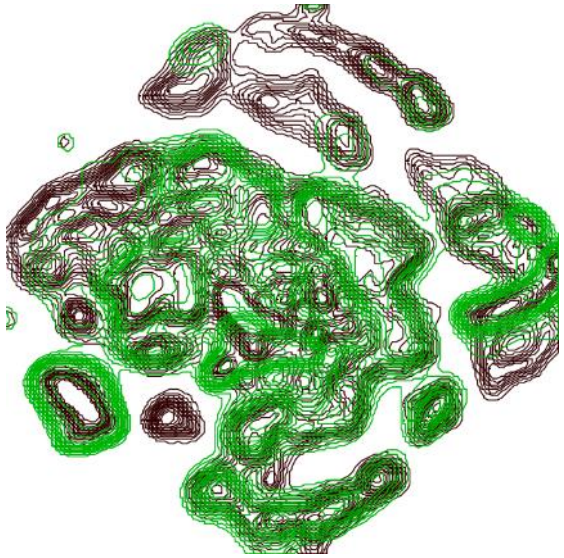
| | |
|---|---|
| FlowSOM.Pop19 | 1.26 |
| V1 | 0.099 |
| V2 | 99.2 |
| V3 | 0.30 |
| V4 | 0.40 |

Here pop 19 is almost exclusively from V2 events

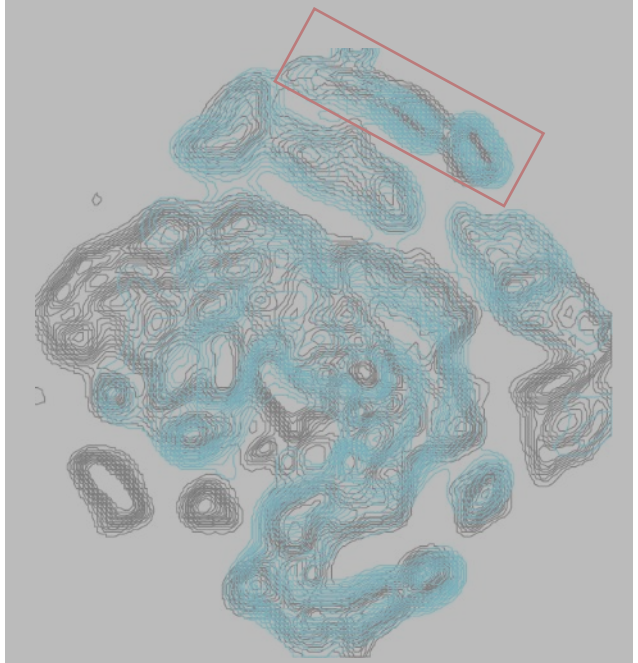
8. Overlay enriched FlowSOM populations on tSNE to determine the phenotype

# tSNE analysis of ex vivo phenotyping

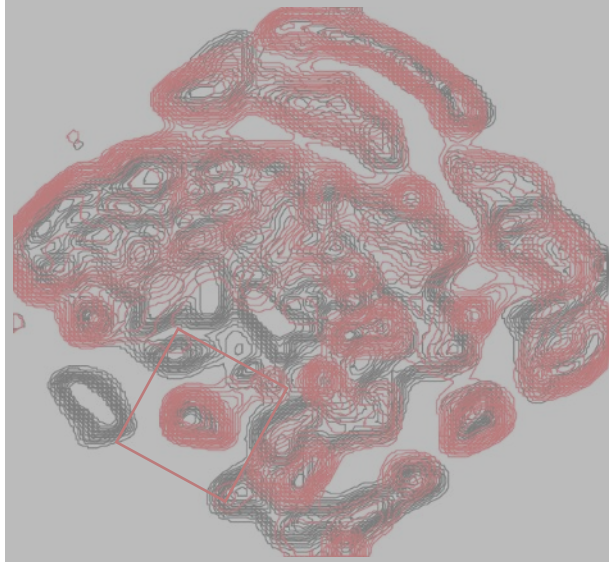
**Visit 1** – pre-dose 1



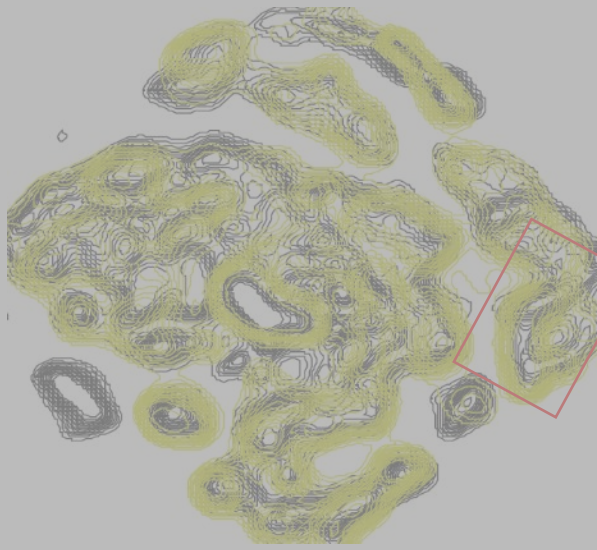
**Visit 2** – 1 month post dose 1



**Visit 4** – 1 month post series completion

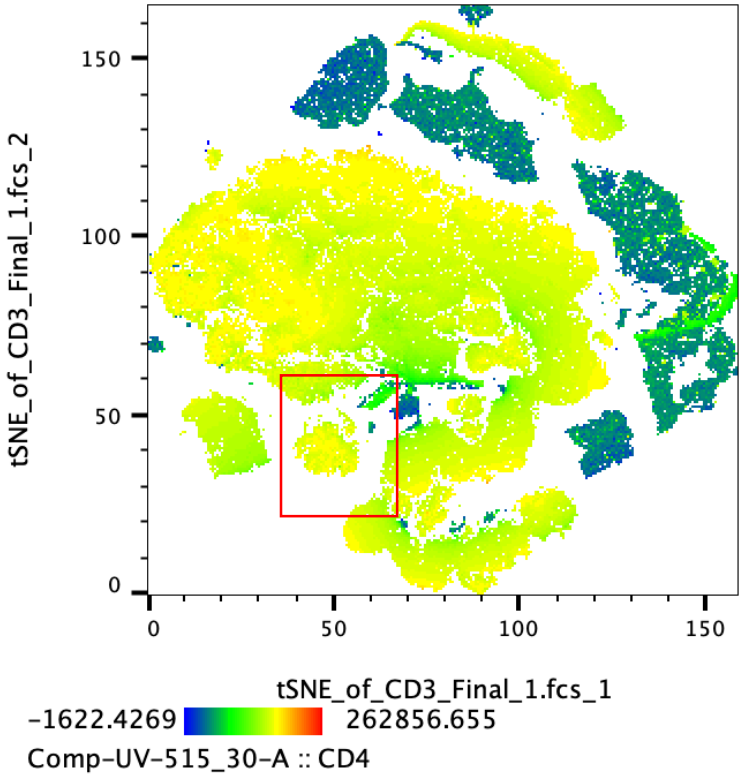


**Visit 5** – 4 months post series completion

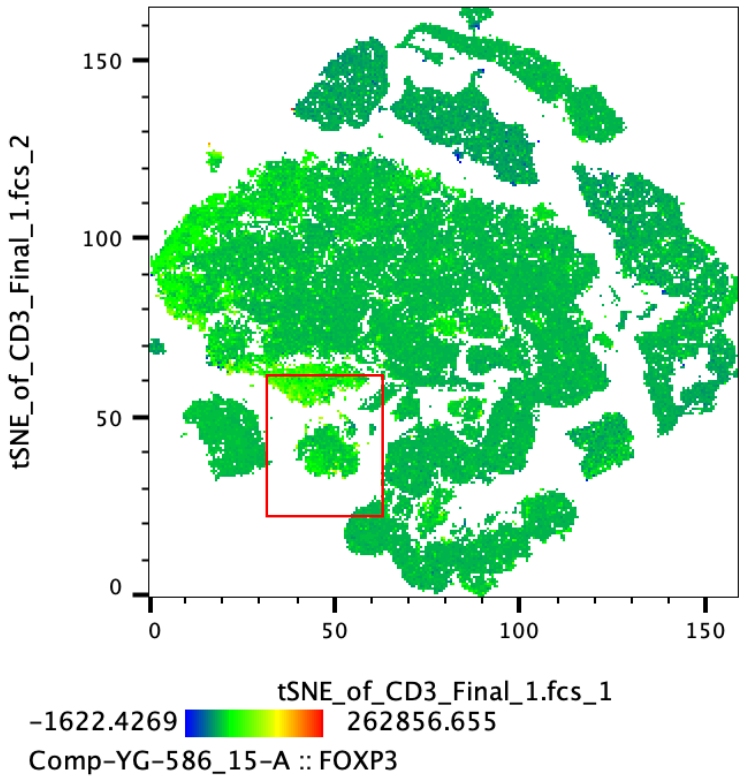


# tSNE analysis of ex vivo phenotyping – Visit 4

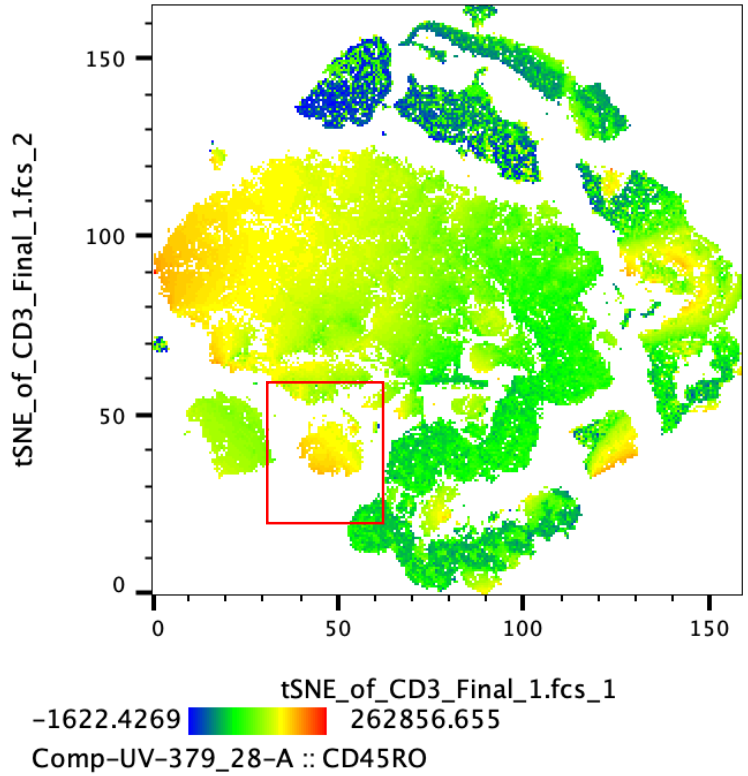
**CD4 heatmap**




**FOXP3 heatmap**

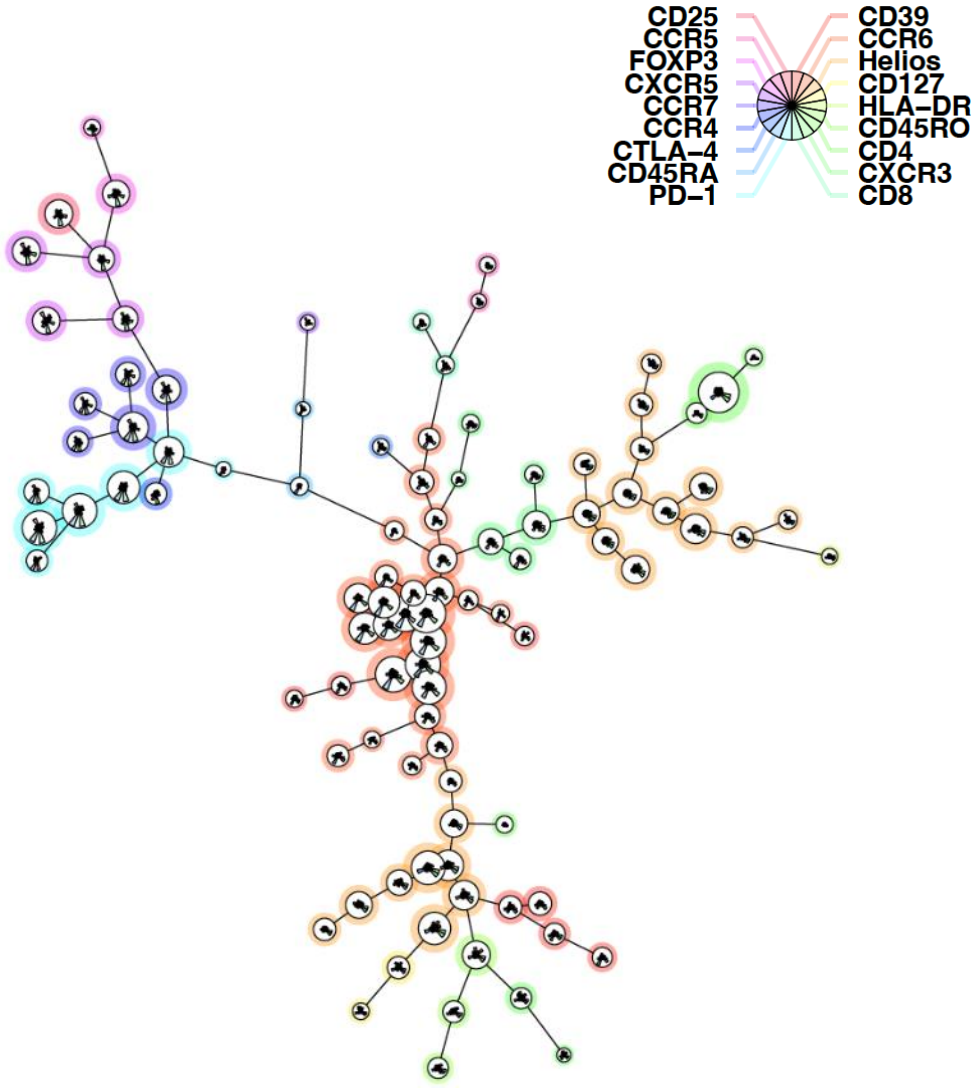


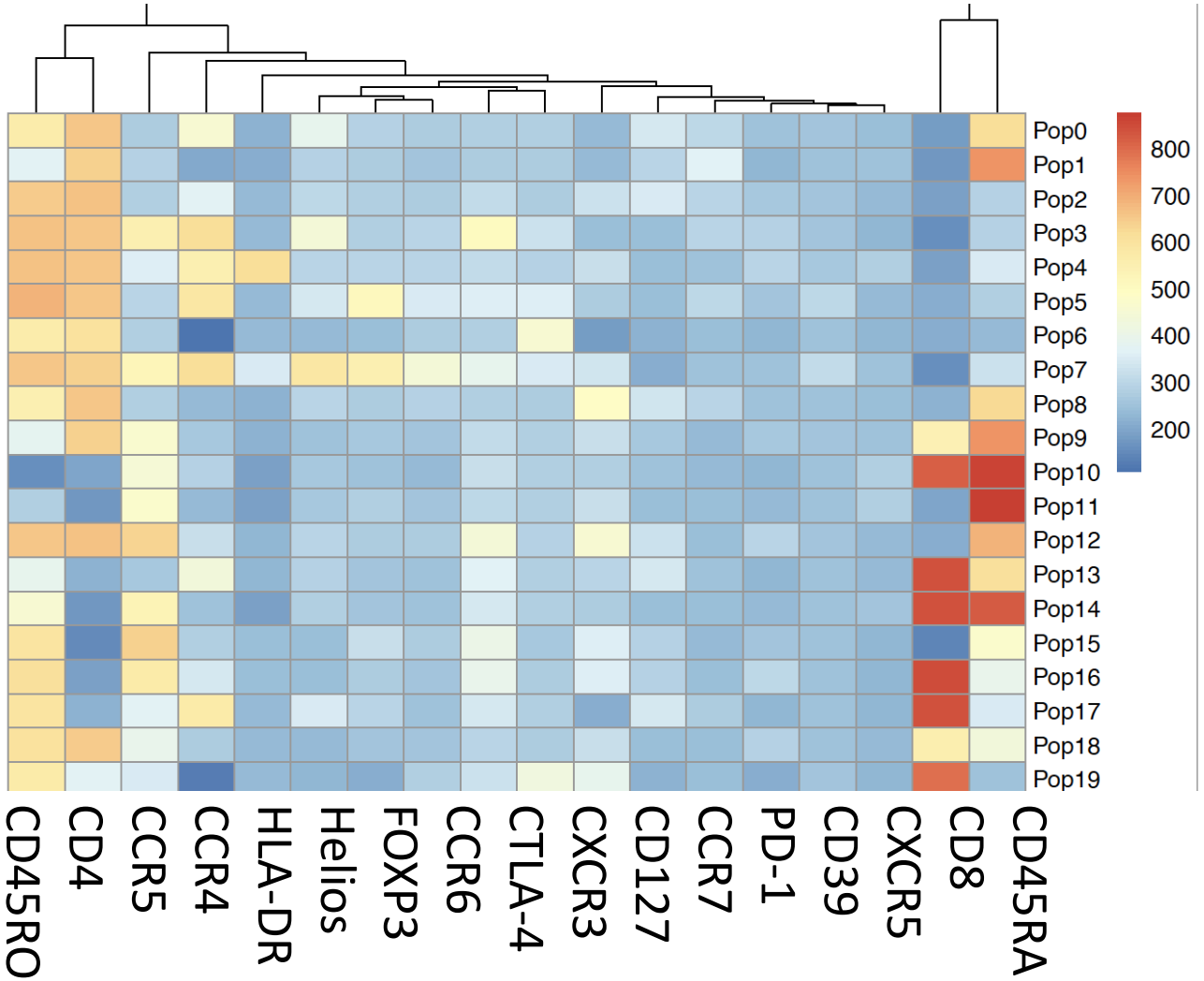

**CD45RO heatmap**




- tSNE cluster enriched during visit 4: CD4+ CD45RO+ FOXP3+

# Ex vivo clustering via FlowSOM



# FlowSOM T cell subset identification

## Populations enriched in V2

| | CD39 | CCR6 | Helios | CD127 | HLA-DR | CD45RO | CD4 | CXCR3 | CD8 | PD-1 | CD45RA | CTLA-4 | CCR4 | CCR7 | CXCR5 | FOXP3 | CCR5 | CD25 | V1 | V2 ▼ | V4 | V5 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| export CD3 Final 1 FlowSOM.Pop19.fcs | 127 | 531 | -107 | -66.8 | 11.6 | 3870 | 808 | 910 | 28207 | -92.5 | 82.2 | 1213 | -547 | 43.6 | -5.13 | 281 | 652 | -23.1 | 0.099 | 99.2 | 0.30 | 0.40 |
| export CD3 Final 1 FlowSOM.Pop6.fcs | 93.8 | 271 | 77.1 | -51.4 | 6.42 | 3568 | 4882 | -279 | -89.9 | -7.70 | 39.8 | 1526 | -676 | 71.9 | 0 | 207 | 261 | 21.8 | 0.55 | 97.1 | 1.11 | 1.24 |
| export CD3 Final 1 FlowSOM.Pop4.fcs | 195 | 414 | 350 | 60.4 | 5509 | 8117 | 7731 | 447 | -225 | 331 | 655 | 317 | 3126 | 95.1 | 274 | 331 | 707 | 339 | 23.8 | 39.4 | 13.8 | 23.1 |

## Populations enriched in V4

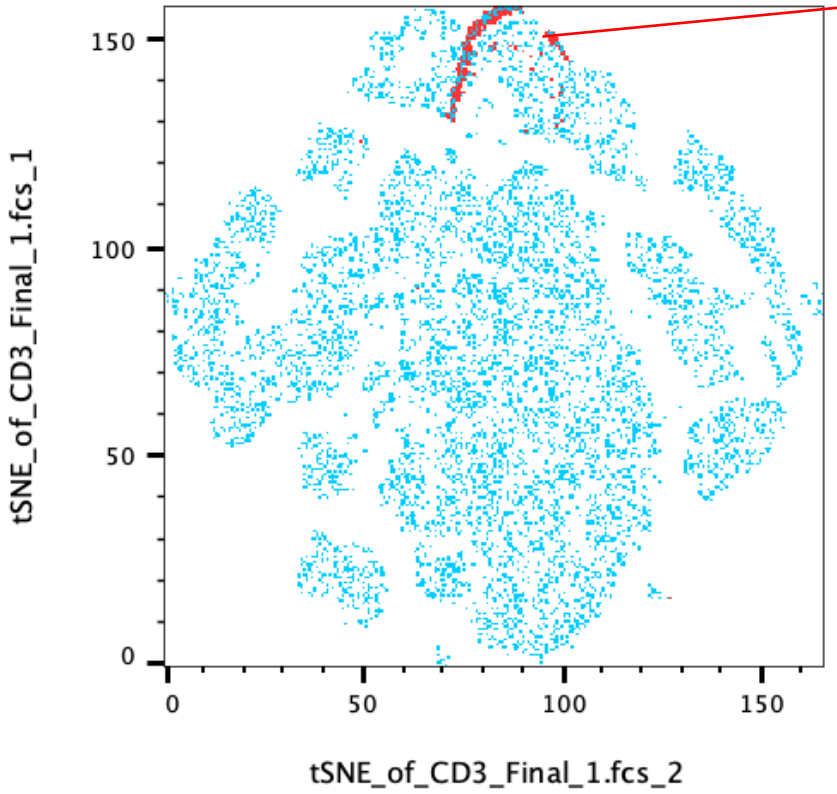
| | CD39 | CCR6 | Helios | CD127 | HLA-DR | CD45RO | CD4 | CXCR3 | CD8 | PD-1 | CD45RA | CTLA-4 | CCR4 | CCR7 | CXCR5 | FOXP3 | CCR5 | CD25 | V1 | V2 | V4 ▼ | V5 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| export CD3 Final 1 FlowSOM.Pop5.fcs | 367 | 710 | 2391 | 60.4 | 32.1 | 10650 | 7921 | 213 | -87.4 | 139 | 265 | 723 | 4290 | 383 | 2.57 | 665 | 337 | 596 | 15.1 | 16.6 | 54.2 | 14.1 |
| export CD3 Final 1 FlowSOM.Pop15.fcs | 114 | 1038 | 448 | 298 | 47.5 | 4537 | -423 | 692 | -483 | 135 | 1777 | 185 | 279 | 18.0 | 0 | 200 | 6703 | 69.4 | 18.2 | 19.8 | 36.0 | 26.0 |
| export CD3 Final 1 FlowSOM.Pop12.fcs | 134 | 1389 | 224 | 531 | -3.85 | 7800 | 8677 | 1555 | -116 | 332 | 10318 | 295 | 450 | 77.1 | 28.2 | 225 | 6404 | 347 | 28.9 | 3.39 | 35.1 | 32.7 |

## Populations enriched in V5

| | CD39 | CCR6 | Helios | CD127 | HLA-DR | CD45RO | CD4 | CXCR3 | CD8 | PD-1 | CD45RA | CTLA-4 | CCR4 | CCR7 | CXCR5 | FOXP3 | CCR5 | CD25 | V1 | V2 | V4 | V5 ▼ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| export CD3 Final 1 FlowSOM.Pop14.fcs | 102 | 599 | 152 | 66.8 | -212 | 1609 | -312 | 233 | 43169 | 23.1 | 36459 | 267 | 117 | 52.6 | 130 | 87.4 | 2888 | 240 | 9.64 | 5.06 | 23.9 | 61.4 |
| export CD3 Final 1 FlowSOM.Pop8.fcs | 117 | 263 | 207 | 556 | -48.8 | 3126 | 7834 | 1979 | -57.8 | 95.1 | 5812 | 220 | 24.4 | 356 | 65.5 | 282 | 250 | 344 | 24.9 | 7.80 | 29.8 | 37.4 |
| export CD3 Final 1 FlowSOM.Pop7.fcs | 438 | 933 | 3120 | -89.9 | 634 | 8063 | 6674 | 553 | -365 | 112 | 537 | 663 | 5592 | 107 | 80.9 | 1389 | 2676 | 4202 | 27.3 | 19.9 | 18.9 | 33.9 |
| export CD3 Final 1 FlowSOM.Pop12.fcs | 134 | 1389 | 224 | 531 | -3.85 | 7800 | 8677 | 1555 | -116 | 332 | 10318 | 295 | 450 | 77.1 | 28.2 | 225 | 6404 | 347 | 28.9 | 3.39 | 35.1 | 32.7 |

# tSNE + FlowSOM – Visit 2

FlowSOM population 19 (enriched in V2)



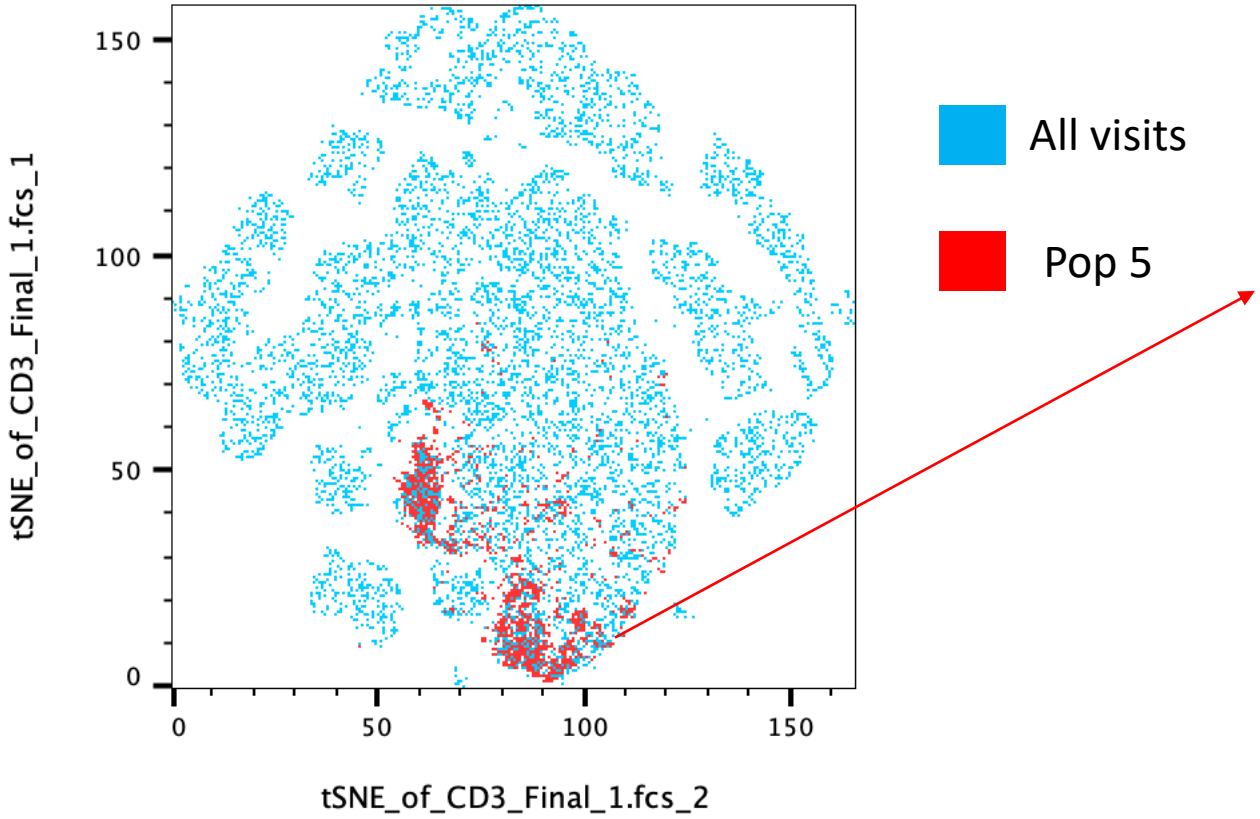

All visits

Pop 19


CD8+ CD45RO+ $CCR7^{low}$ = effector memory CD8+ T cells

# tSNE + FlowSOM – Visit 4

FlowSOM population 5 (enriched in V4)

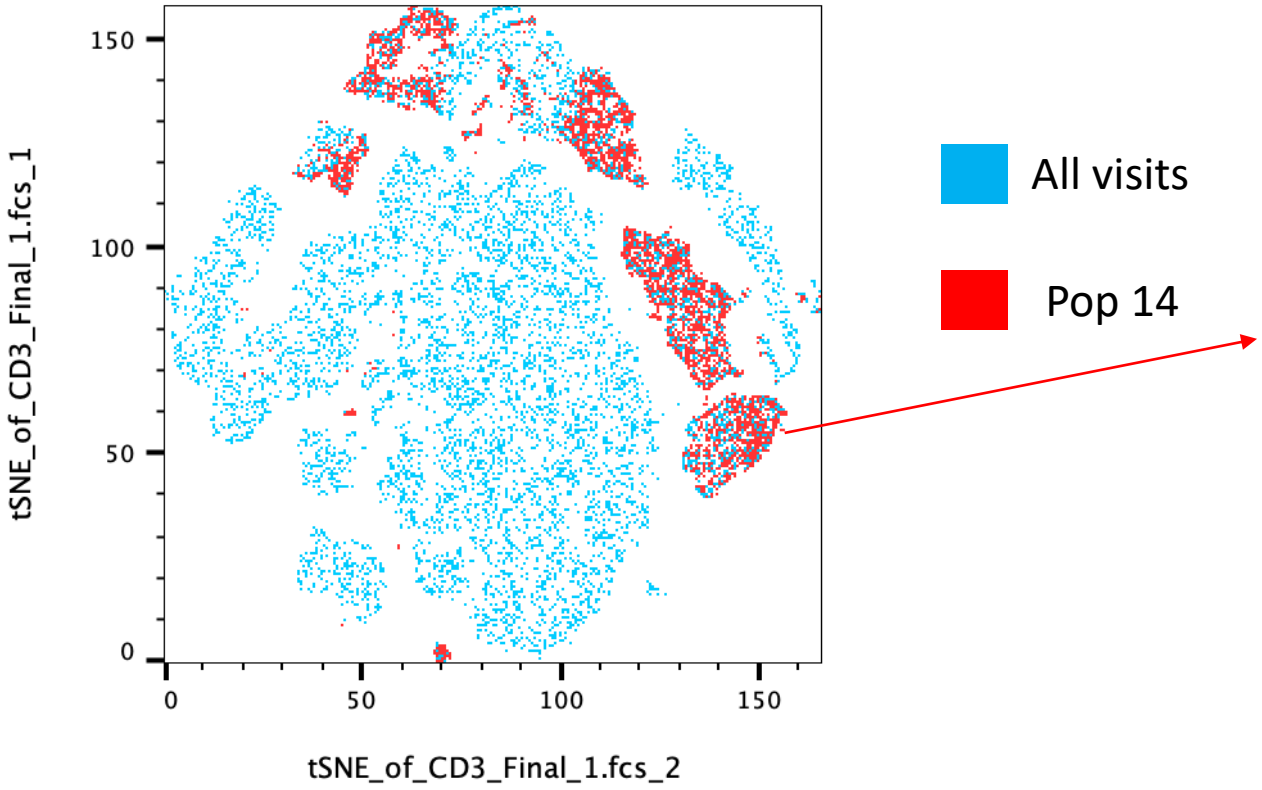


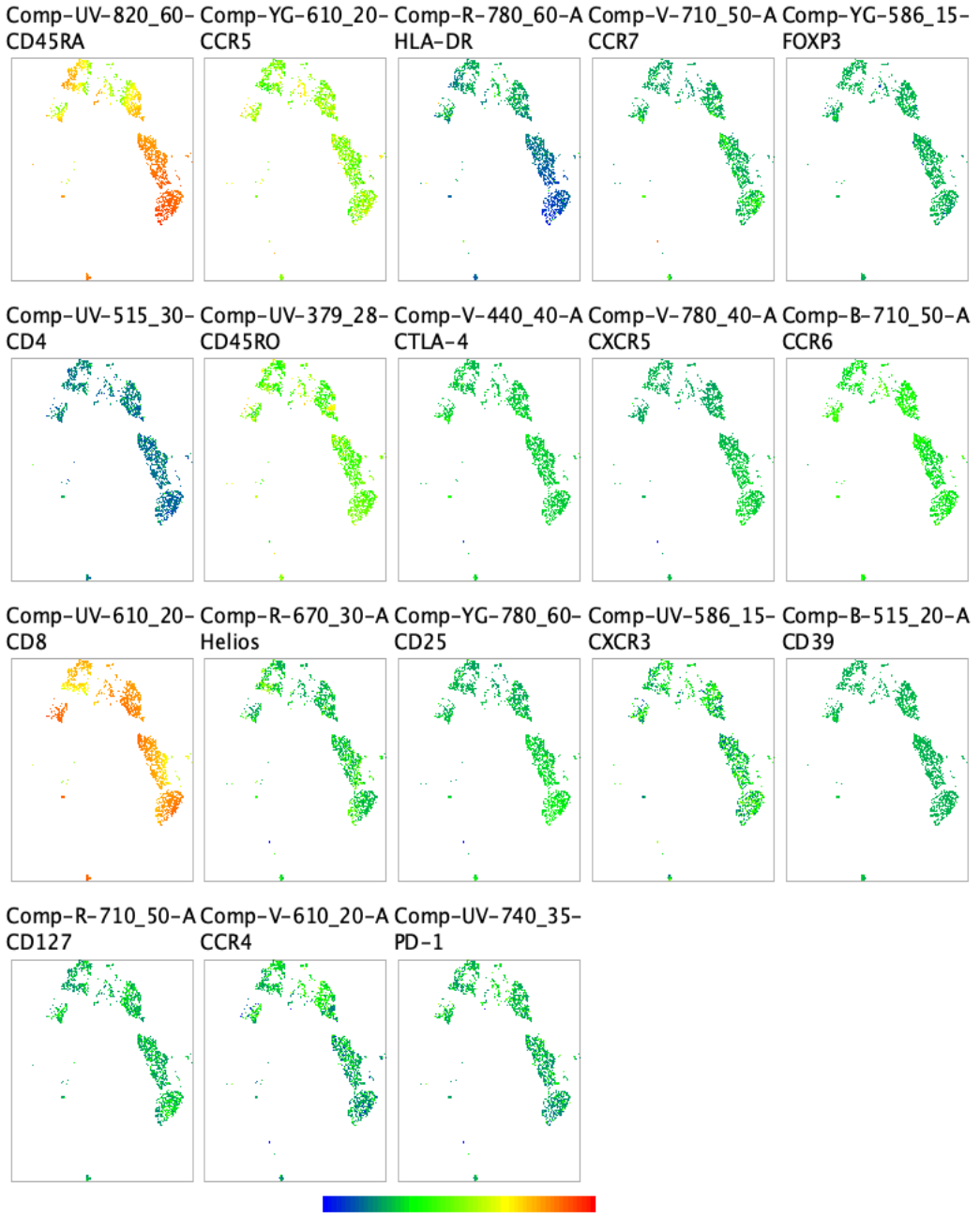


CD4+ CD45RO+ CCR4+ CCR7+/- FOXP3+ = CD4+ Treg humoral response?

# tSNE + FlowSOM – Visit 5

FlowSOM population 14 (enriched in V5)




CD8+ CD45RA+ CCR7- HLA-DR- = Naïve CD8 T cells

# Summary of Ex vivo phenotyping

- tSNE and FlowSOM allow for dimensionality reduction and overview of phenotypic data
- Visualization of all parameters to identify T cell subsets that could be missed during traditional Boolean gating
- V2: identification of CD8 T cell expansion
- V4: identification of potential Treg subset
- V5: resolution of initial vaccine response, majority naive CD8+ T cells with low/no activation markers (return to baseline)
- Need to confirm subset identification with traditional Boolean gating and statistics (clinical data needed)

# Future directions

- Generate tSNE and FlowSOM analyses using all timepoints (days-weeks of computing)
- Confirm populations using Boolean gates
- Correlate T cell subsets with T cell vaccine responses
  - Does an increased Treg subset at V4 correlate to decreased T cell responses at V5?
- Compare immunocompromised patient cohorts to PREVENT cohort
  - Blood cancer, solid tumour, transplant

# Acknowledgements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## Levings Lab

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Dr. Sabine Ivison

Rosa Garcia

## Sadarangani Lab

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Jennifer Mark

Neila Tong

Rebecca Lim

Tony Harn

## Dr. Stephen Chia

Alyssa Yeo

Shakhil Singh

## Dr. Heather Sutherland

Kaitlyn Le

Irene Wan

Arell Bryski

## Dr. Sara Belga

Gale

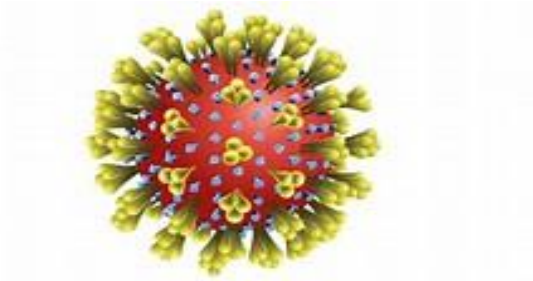
UBC Microbiology & Immunology

BC Children's Hospital

COVID-19 IMMUNITY TASK FORCE

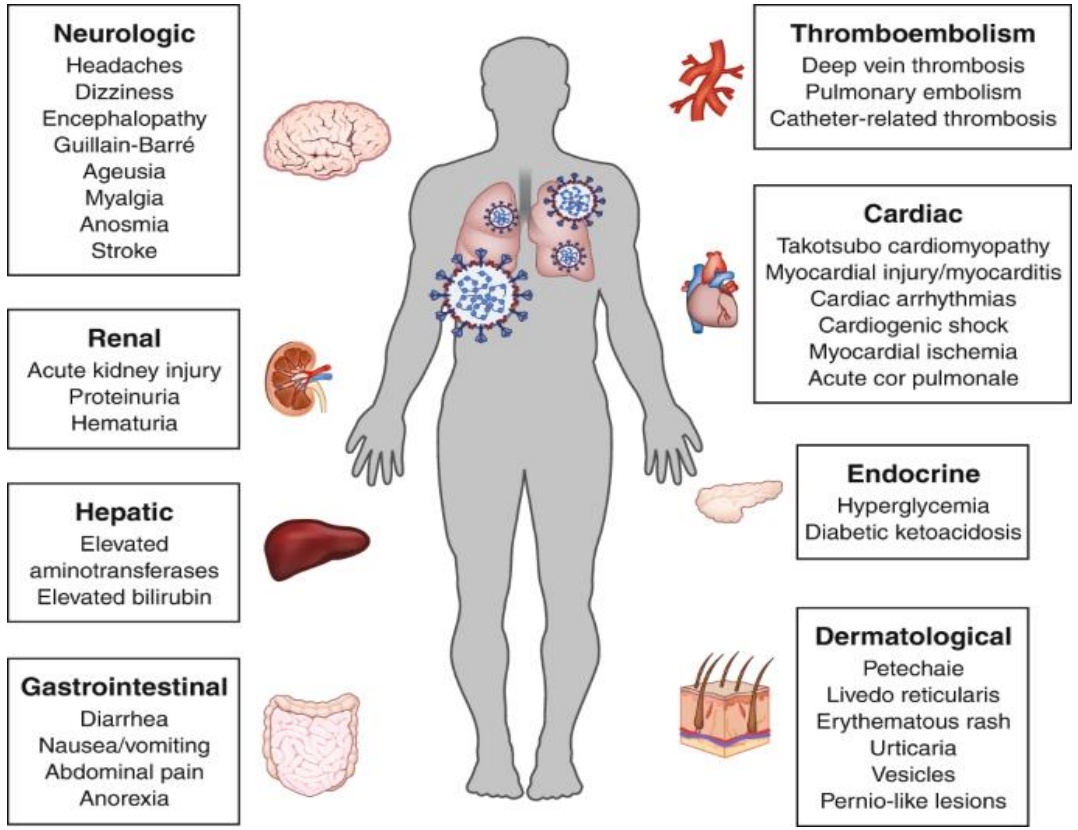
GROUPE DE TRAVAIL SUR L'IMMUNITÉ FACE À LA COVID-19

COVID-19 Immunology Consortium-BC (CIC-BC)



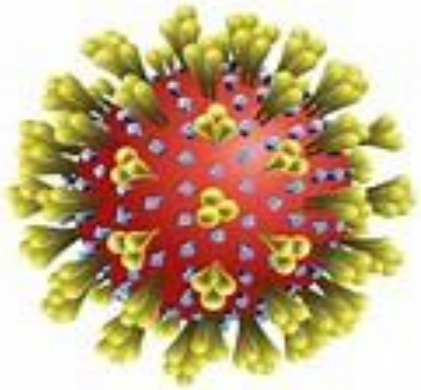
Post COVID-19
Interdisciplinary Clinical Care Network
Recovery | Care | Research | Education

# Life after COVID-19:
# Potential immunologic implications

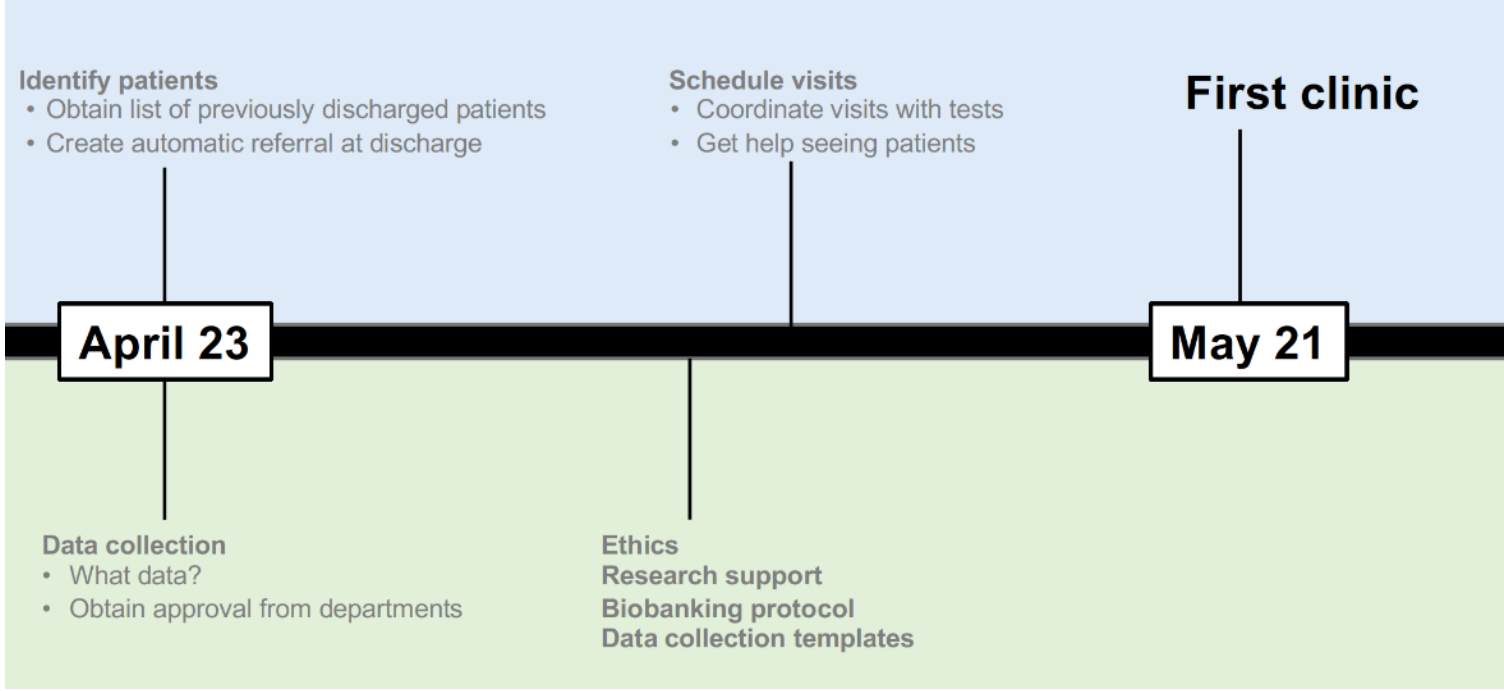


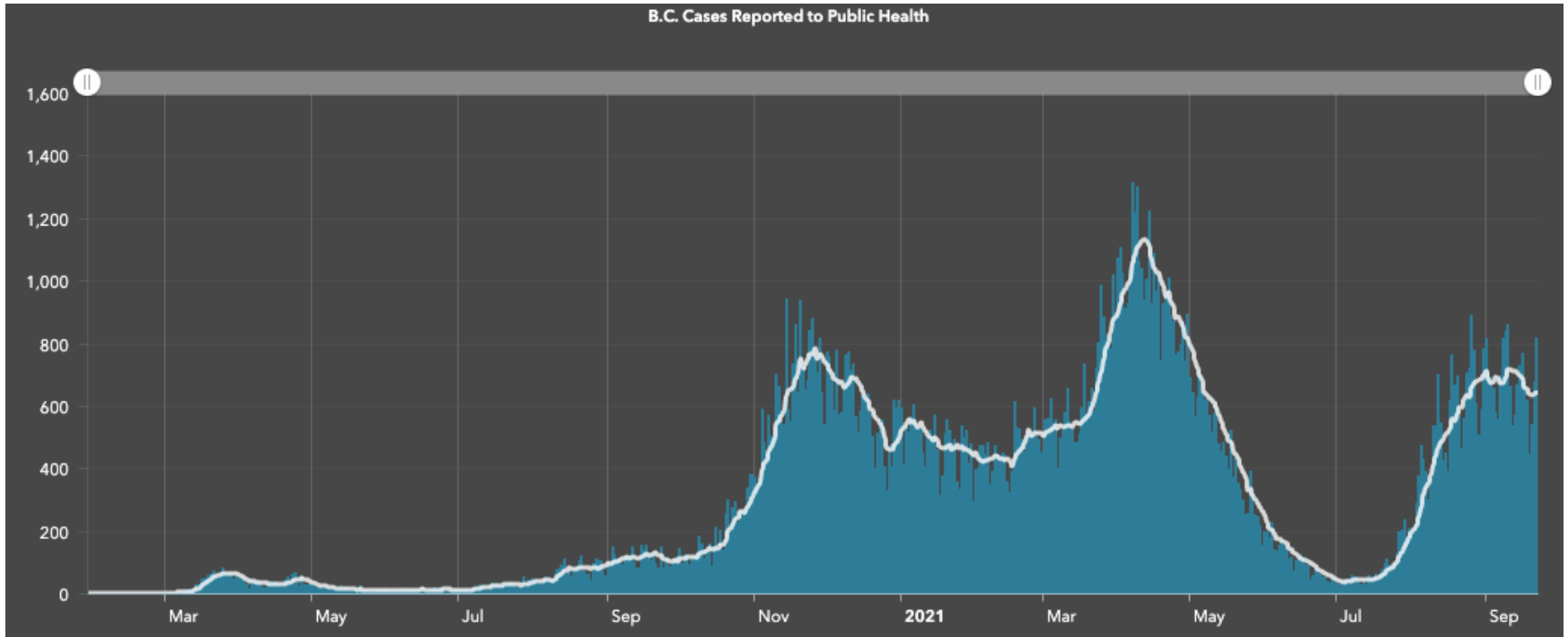

Chris Carlsten

Manali Mukherjee



# 2020


Identify patients
• Obtain list of previously discharged patients
• Create automatic referral at discharge
Schedule visits
• Coordinate visits with tests
• Get help seeing patients
First clinic
April 23
May 21
Data collection
• What data?
• Obtain approval from departments
Ethics
Research support
Biobanking protocol
Data collection templates


B.C. Cases Reported to Public Health
1,600
1,400
1,200
1,000
800
600
400
200
0
Mar
May
Jul
Sep
Nov
2021
Mar
May
Jul
Sep


Confirmed Deaths
1,922
Recovered
174,281

# A prospective study of 12-week respiratory outcomes in COVID-19-related hospitalisations

Aditi S Shah [1], Alyson W Wong,[1] Cameron J Hague,[2] Darra T Murphy [2], James C Johnston [1], Christopher J Ryerson [1], Christopher Carlsten [1]

***Thorax* 2021**

At least one pulmonary function variable was below 80% predicted in **58% of patients**

55% of patients had >10% of lung volume affected by either ground glass or reticulation

# **Patient reported outcomes** after COVID-19 @ 3 months

EUROPEAN RESPIRATORY *journal*
FLAGSHIP SCIENTIFIC JOURNAL OF ERS



## Patient-reported outcome measures after COVID-19: a prospective cohort study

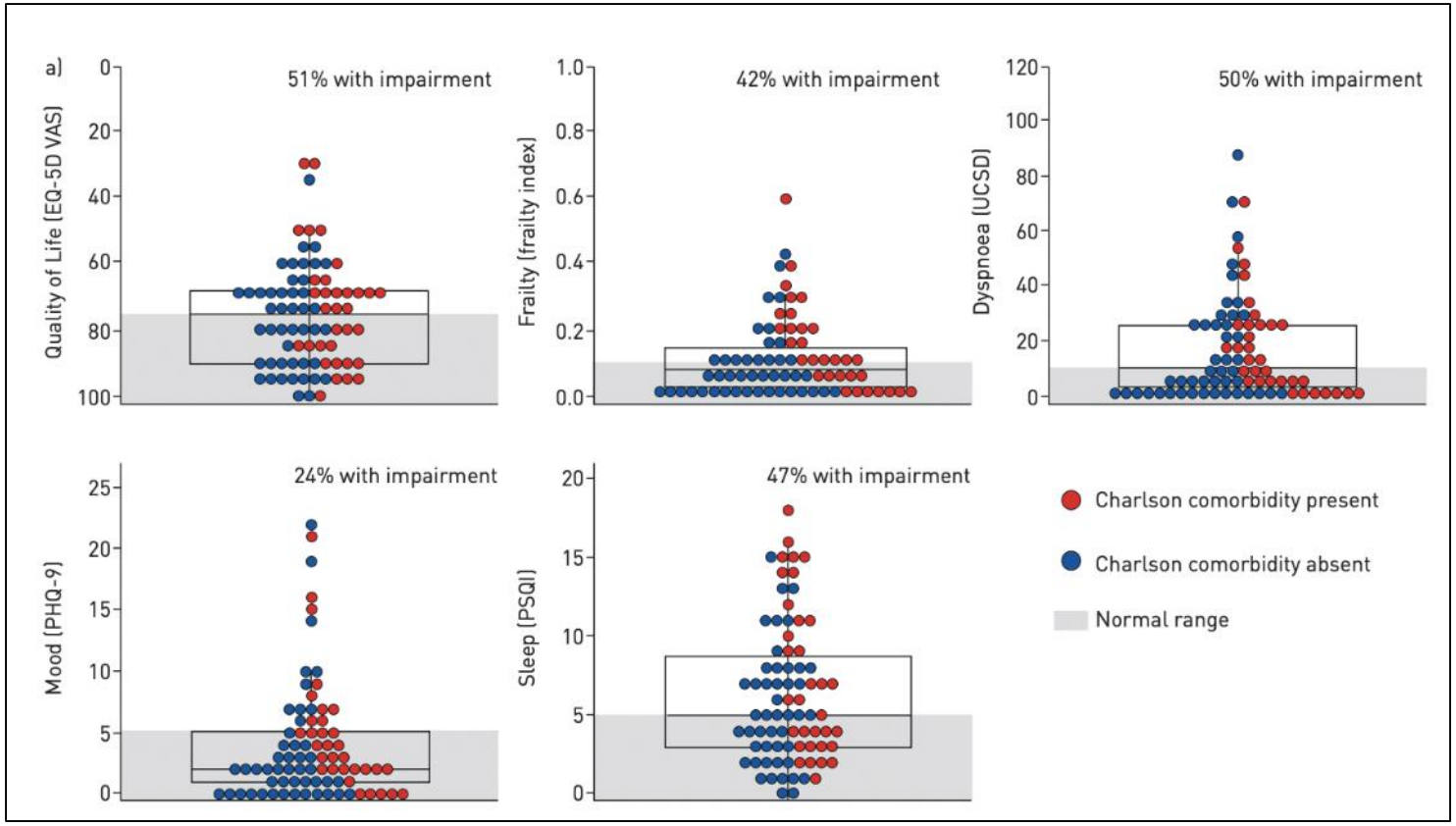
Alyson W. Wong, Aditi S. Shah, James C. Johnston, Christopher Carlsten, Christopher J. Ryerson

European Respiratory Journal 2020; **DOI:** 10.1183/13993003.03276-2020

# **Patient reported outcomes** after COVID-19 @ 3 months

Over 75% of patients had an abnormal PROM

The most frequently impaired outcomes were QoL and dyspnea



# Changes 3 → 6 months post-diagnosis

ERJ OPEN RESEARCH
ORIGINAL RESEARCH ARTICLE
A.S. SHAH ET AL.

## Changes in pulmonary function and patient-reported outcomes during COVID-19 recovery: a longitudinal, prospective cohort study

Aditi S. Shah [1], Min Hyung Ryu [1], Cameron J. Hague [2], Darra T. Murphy [2], James C. Johnston [3], Christopher J. Ryerson [4], Christopher Carlsten [1,5] and Alyson W. Wong [4,5]

# PFTs improved more than PFTs (3 to 6 months after diagnosis)

**TABLE 2** Respiratory symptoms, patient-reported outcome measures and pulmonary function at 3 and 6 months after coronavirus disease 2019 (COVID-19) symptom onset

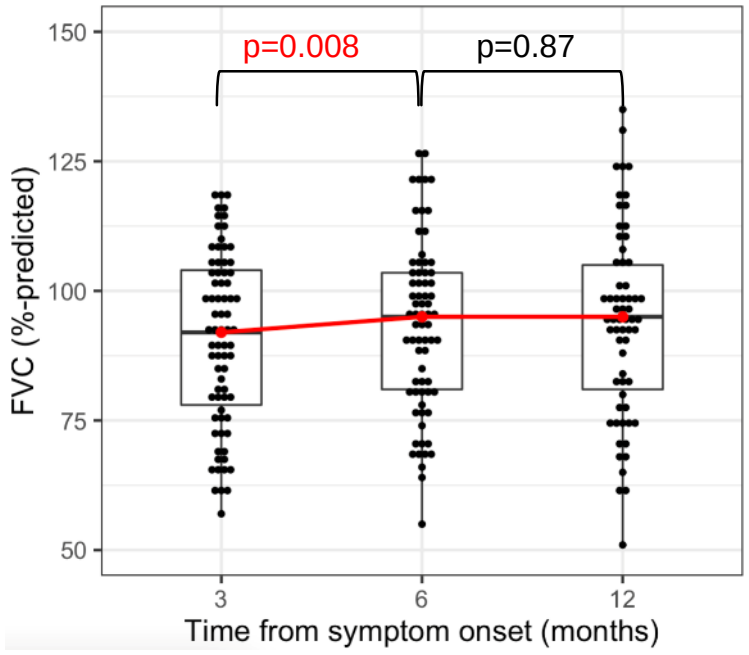
| | 3 months | 6 months | Mean or median difference | 95% CI | p-value |
|---|---|---|---|---|---|
| **Respiratory symptoms** | | | | | |
| UCSD dyspnoea score | 11 (3–26) | 9 (3–31) | −1.0 | −4.0–2.0 | 0.53 |
| Cough VAS | 28 (8–60) | 20 (10–35) | −4.6 | −18.7–8.4 | 0.41 |
| **Patient-reported outcome measures** | | | | | |
| PHQ-9 | 2 (1–6) | 1 (0–6) | 0.5 | 0–1.5 | 0.16 |
| PSQI | 5 (3–8) | 5 (2–9) | 0 | −1.0–1.5 | 0.81 |
| EQ-5D utility | 0.87 (0.79–0.95) | 0.90 (0.81–0.95) | −0.022 | −0.1–0.003 | 0.12 |
| EQ-5D VAS | 75 (68–90) | 80 (75–90) | 6.3 | 5.0–9.5 | **<0.001** |
| **Pulmonary function, % predicted** | | | | | |
| $FEV_1$ | 89±16 | 91±16 | 1.3 | −0.8–3.4 | 0.21 |
| FVC | 90±17 | 93±17 | 3.3 | 1.3–5.2 | **0.001** |
| $FEV_1$/FVC | 87±12 | 84±12 | −2.9 | −4.5– −1.3 | **0.001** |
| TLC | 83±14 | 87±13 | 3.8 | 2.2–5.5 | **<0.001** |
| $D_{LCO}$ | 74±17 | 80±17 | 5.7 | 3.6–7.8 | **<0.001** |

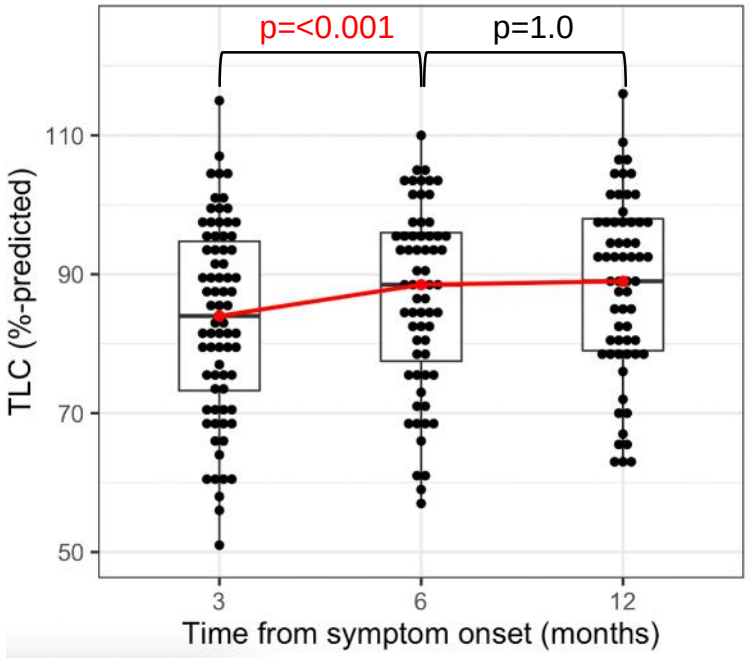
| Features | Overall cohort | Patients with dyspnoea at 6 months | |
|---|---|---|---|
| | | Unexplained dyspnoea | Dyspnoea |
| **Subjects n** | 73 | 13 | 15 |
| **Demographics** | | | |
| Age years | 65 (53–72) | 49 (34–67) | 66 (59–76) |
| Male sex n (%) | 44 (60) | 4 (31) | 9 (60) |
| Ever-smoker n (%) | 23 (32) | 2 (15) | 8 (53) |
| **Comorbidities n (%)** | | | |
| Hypertension | 27 (37) | 5 (39) | 8 (53) |
| Diabetes | 19 (26) | 3 (23) | 5 (33) |
| Chronic pulmonary disease[#] | 10 (14) | 0 | 4 (27) |
| Coronary heart disease | 7 (10) | 0 | 3 (20) |
| Malignancy | 8 (11) | 1 (8) | 1 (7) |
| Chronic kidney disease | 6 (8) | 1 (8) | 2 (13) |
| **Respiratory symptoms** | | | |
| UCSD dyspnoea score | 9 (3–31) | 31 (17–40) | 35 (23–46) |
| Cough VAS mm | 20 (10–37) | 10 (9–10) | 30 (16–44) |
| **Patient-reported outcome measures** | | | |
| EQ-5D health utility | 0.9 (0.8–0.9) | 0.83 (0.77–0.87) | 0.83 (0.76–0.87) |
| EQ-5D VAS | 80 (75–90) | 75 (70–90) | 75 (65–85) |
| PSQI | 5 (2–9) (n=72) | 9 (6–12) (n=12) | 7 (5–9) |
| PHQ-9 | 1 (0–6) | 6 (2–10) | 5 (1–7) |
| **Pulmonary function tests** | | | |
| $FEV_1$ % predicted | 91±15 (n=72) | 88±14 | 83±14 |
| FVC % predicted | 93±16 (n=72) | 93±11 | 81±15 |
| $FEV_1$/FVC % | 84±12 (n=72) | 84±13 | 84±11 |
| TLC % predicted | 87±13 (n=64) | 86±11 (n=12) | 77±13 (n=14) |
| $D_{LCO}$ % predicted | 79±18 (n=70) | 88±9 | 63±14 |

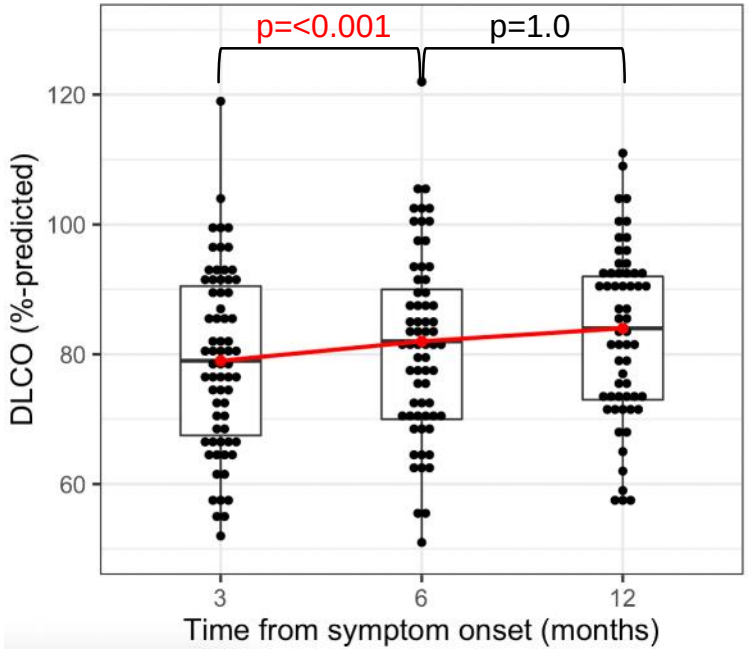
## Unexplained dyspnea
= UCSD > 10 and DLCO > 80% pred

## Dyspnea
= UCSD > 10 and DLCO < 80% pred

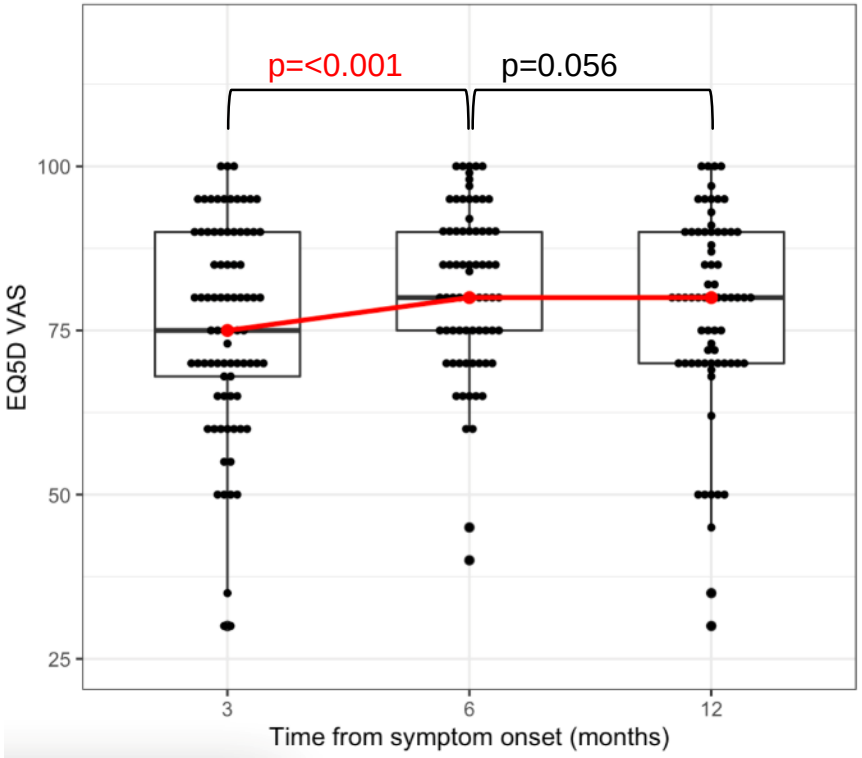
# **Preliminary** 12-month results: PFTs plateau ~6 months



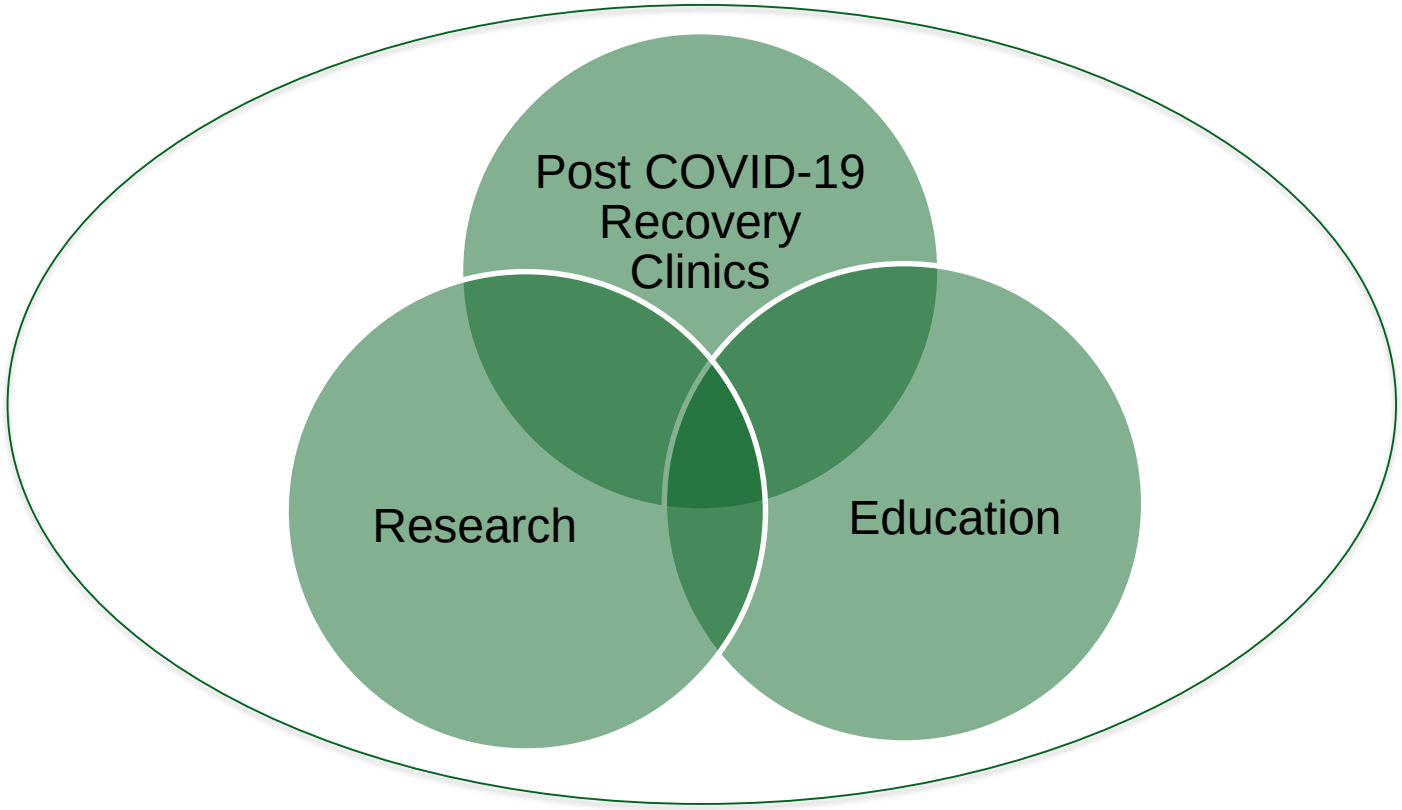



| PROMs | Normal | Median scores (IQR) | | | p-value |
|---|---|---|---|---|---|
| | | 3 months | 6 months | 12 months | |
| **Dyspnea (UCSD)** | <10 | 10 (3-25) | 9 (3-30) | 9 (2-22) | 0.262 |
| **Cough** | <17 | 30 (10-60) | 24 (10-35) | 15 (8-50) | 0.618 |
| **Frailty index** | <0.10 | 0.07 (0.02-0.14) | 0.07 (0.02-0.17) | 0.07 (0.02-0.14) | 0.987 |
| **Mood (PHQ-9)** | <5 | 2 (1-6) | 1 (0-5) | 2 (0-4) | 0.096 |
| **Sleep (PSQI)** | <5 | 5 (3-9) | 6 (3-9) | 5 (3-8) | 0.734 |
| **QoL (EQ5D VAS)** | >77 | 75 (68-90) | 80 (75-90) | 80 (70-90) | **<0.001** |

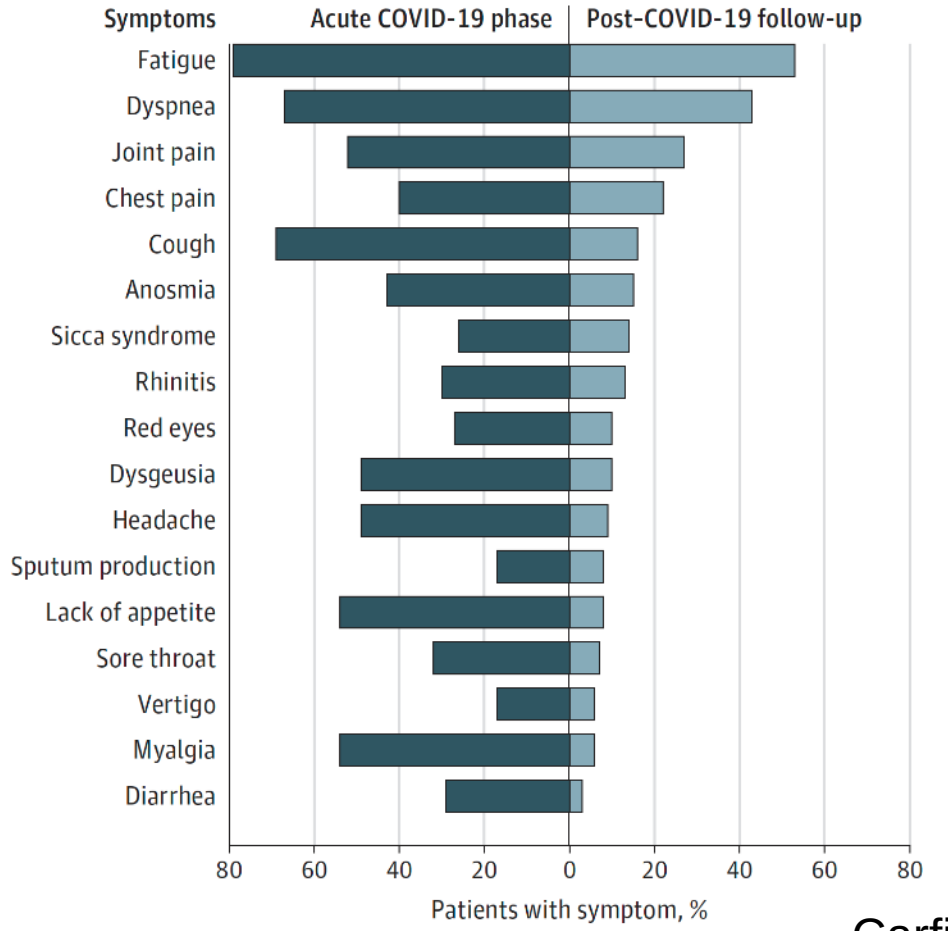



**Most PROMs did not improve within 12 months of symptom onset**

# *Coordinate care, research, and education for optimal outcomes for patients and health care systems*



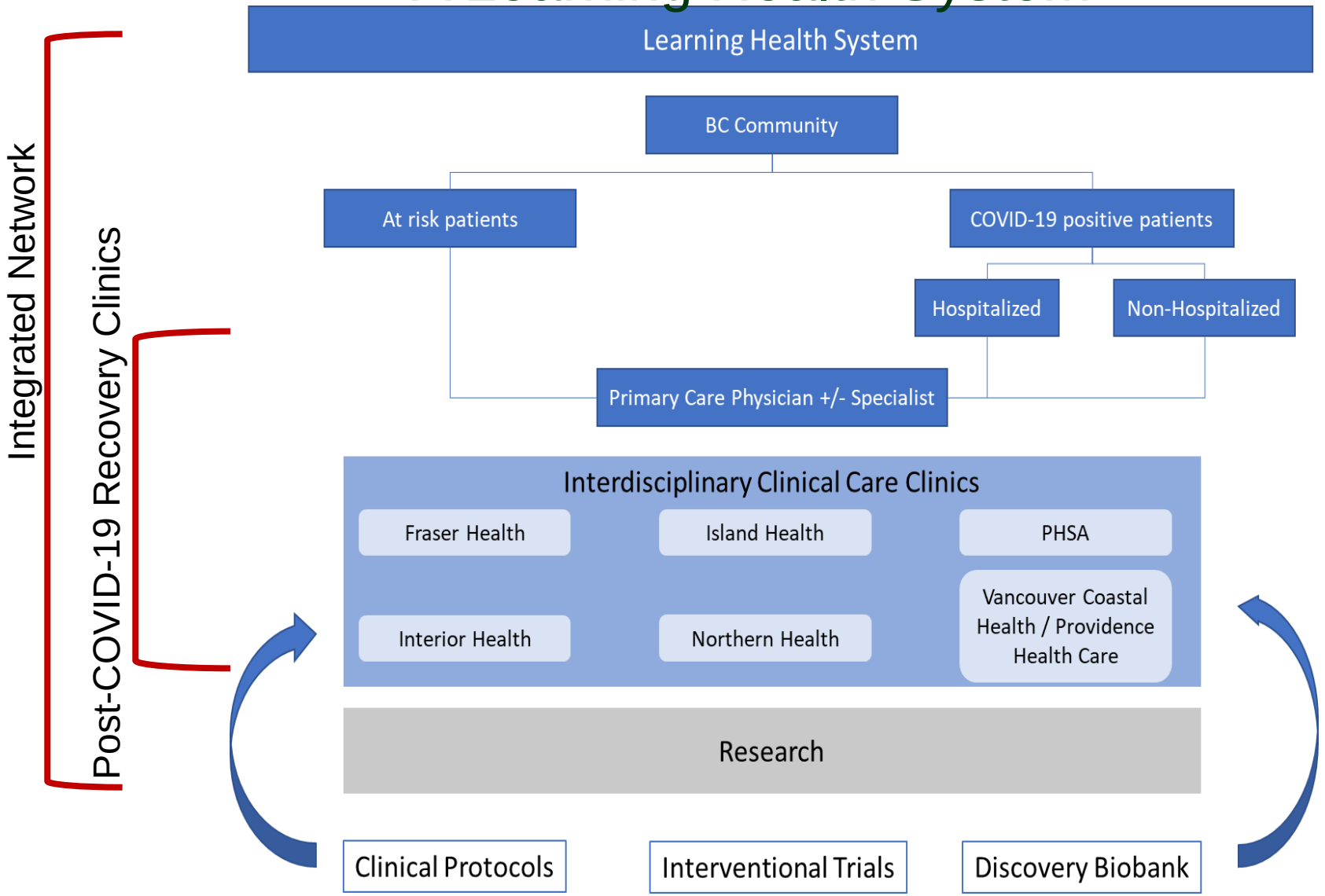

**Post COVID-19**
**Interdisciplinary Clinical Care Network**
Recovery | Care | Research | Education




Carfi
JAMA
2020

Provincial Health Services Authority
Province-wide solutions. Better health.
First Nations Health Authority
Health through wellness
fraserhealth
island health
Interior Health
northern health
Providence HEALTH CARE
Vancouver CoastalHealth
BC AHSN
British Columbia Academic Health Science Network
SFU
UBC

# Provincial Network of Post COVID-19 Recovery Clinics
## A Learning Health System



"Establish sustainable infrastructure for new conditions, post-hospital/ICU"

Post COVID-19
Interdisciplinary Clinical Care Network
Recovery | Care | Research | Education

# BC COVID-19 Biobank Network (BCCBN)

*BCCBN established in early 2021 to enable a provincial biobank network that facilitates and catalyzes strong interdisciplinary clinical and translational research initiatives related to the Covid-19 pandemic*

# Q & A discussion

# Thank you!