CMV CO-INFECTION AND T CELL EXHAUSTION IN LONG TERM CARE FACILITY RESIDENTS WITH COVID-19

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BACKGROUND

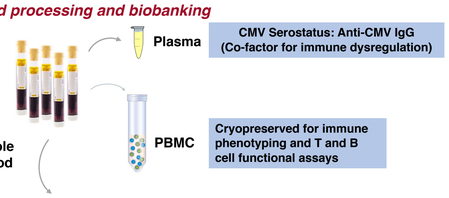
- Elderly long-term care facility (LTCF) residents have been disproportionately affected by COVID-19 and have suffered significant mortality and morbidity.
- Correlates of immunologic protection and susceptibility are not defined in highly vulnerable, advanced age, co-horted populations such as in LTCF.
- Elderly individuals are also often co-infected with cytomegalovirus (CMV), which can increase immune exhaustion and may impact SARS-CoV-2 immunity.

Objective: To examine immunity in highly exposed uninfected and SARS-CoV-2 infected LTCF residents in the context of CMV co-infection

METHODOLOGY

- Sample collection occurred during the peak of the Wave 1 COVID-19 outbreak at the Northwood long term care facility in Halifax, NS.
- Peripheral blood was collected at baseline and 1 month from 108 residents, following informed consent.
- SARS-CoV-2 infection was confirmed by real-time reverse transcriptase–polymerase chain reaction of nasopharyngeal swabs.
- Samples with Ct values <30 were set to the National Microbiology Laboratory for sequencing.
- Peripheral blood samples were collected during the peak of the outbreak and 30 days later.
- Plasma and PBMC were isolated for immunologic assays.

Blood processing and biobanking



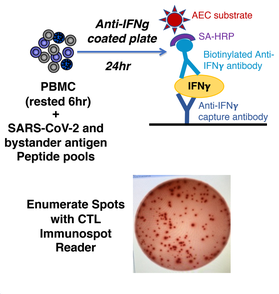
Direct ex vivo immune phenotyping by flow cytometry

T cells			B cells
CD3	CD57	*Activation and exhaustion markers*	CD20
CD4	PD-1	*In CD3+CD4+ and*	CD19
CD8	Tim-3	*CD3+CD8+ T cell subsets*	CD10
CD27	CTLA-4		CD21
CD28			CD27

Boolean gated B cell subsets	CD19	CD20	CD27	CD10	CD21
Immature transitional	+	+	-	+	-/+
Resting memory	+	+	+	-	+
Naïve	+	+	-	-	+
Activated memory	+	+	+	-	-
TLM	+	+	-	-	-
Plasma	+	-	+	-	-

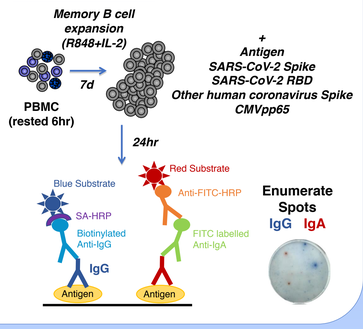
Functional Assays

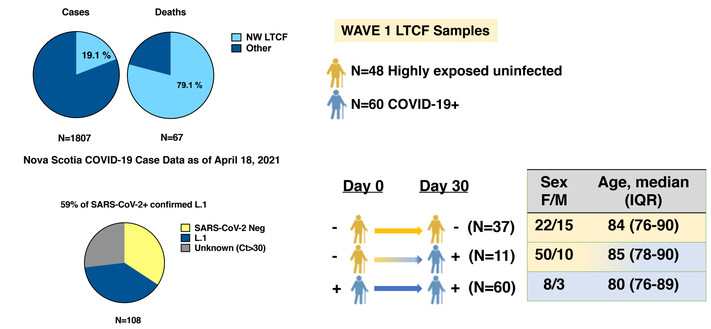
T Cell ELISPOT



Enumerate Spots with CTL Immunospot Reader

B Cell ELISPOT





Sex F/M	Age, median (IQR)
22/15	84 (76-90)
50/10	85 (78-90)
8/3	80 (76-89)

Figure 1: Wave 1 LTCF Cohort Characteristics. 79% of NS COVID-19 deaths occurred at the Northwood LTCF (NW LTCF). 108 residents were enrolled in study. 11/48 exposed COVID-19- individuals became positive by d30. 82% of COVID-19+ individuals were female. The SARS-CoV-2 L.1 lineage was the only lineage identified in the cohort.

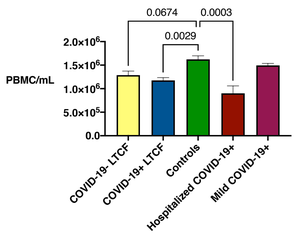


Figure 2: LTCF residents have fewer PBMC than healthy controls

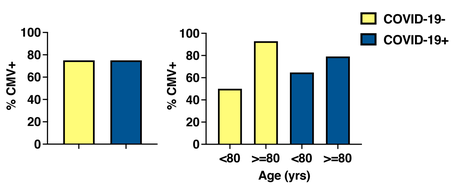


Figure 3: CMV infection is similar between COVID-19- and COVID-19+ individuals. Older individuals and COVID-19+ younger individuals are more frequently CMV+ than younger COVID-19- individuals (χ^2=12.77, P=0.0052).

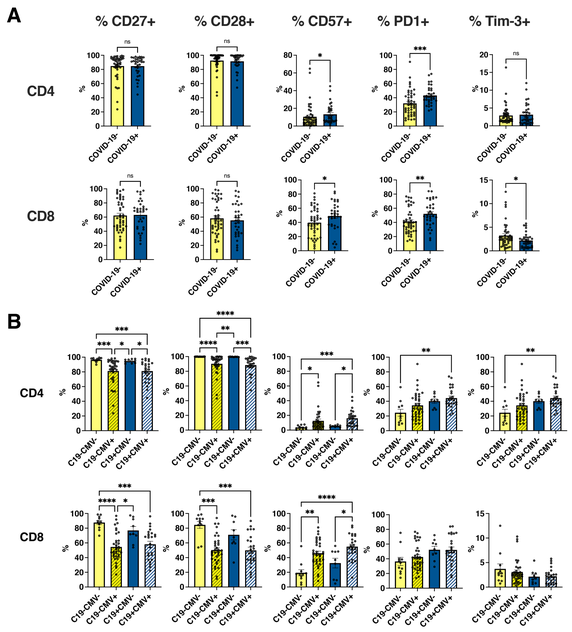


Figure 4: A) T cells in COVID-19+ LTCF residents have increased markers of exhaustion and senescence. B) Decreased T cell activation and increased T cell exhaustion was largely associated with CMV serostatus. Exhausted and senescent T cells were most frequent in the context of CMV and SARS-CoV-2 co-infection.

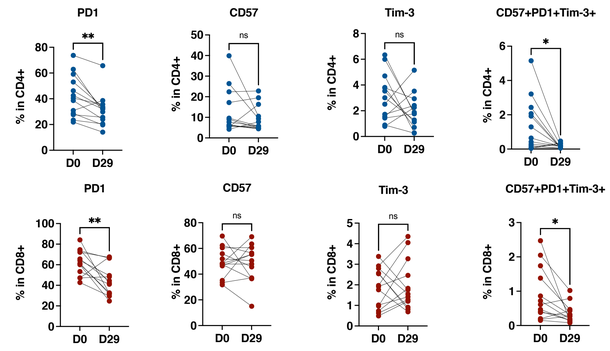
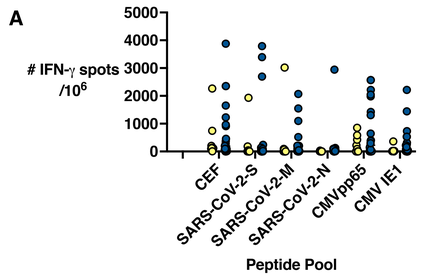


Figure 5: Markers of T cell exhaustion are decreased with COVID-19 recovery



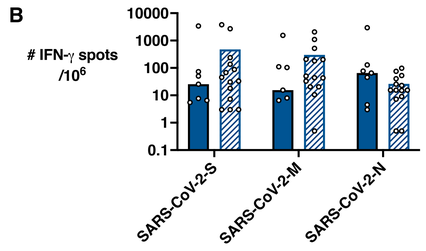


Figure 6: 1A) SARS-CoV-2 specific T cell responses are more frequent and of greater breadth in COVID-19+ LTCF individuals than exposed uninfected individuals. B) In COVID-19+ individuals, SARS-CoV-2 specific T cell IFNg responses did not significantly differ between CMV- and CMV+ individuals.

- CMV infection increases T cell exhaustion in LTCF residents and may exacerbate T cell exhaustion in COVID-19.
- Ongoing studies are comprehensively assessing global and SARS-CoV-2 humoral and cellular immunity in the context of biomarkers, frailty, disease severity, and clinical outcome.
- The persistence of immunologic memory in COVID-19 recovered LTCF residents and COVID-19 vaccine response in COVID-19 recovered, exposed uninfected and unexposed LTCF residents through longitudinal follow-up.
- Comprehensive evaluation is required to fully understand SARS-CoV-2 immunity in LTCF to inform rational COVID treatment and vaccination.

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