Longevity and Neutralisation Activity of Secretory IgA following SARS-CoV-2 Infection

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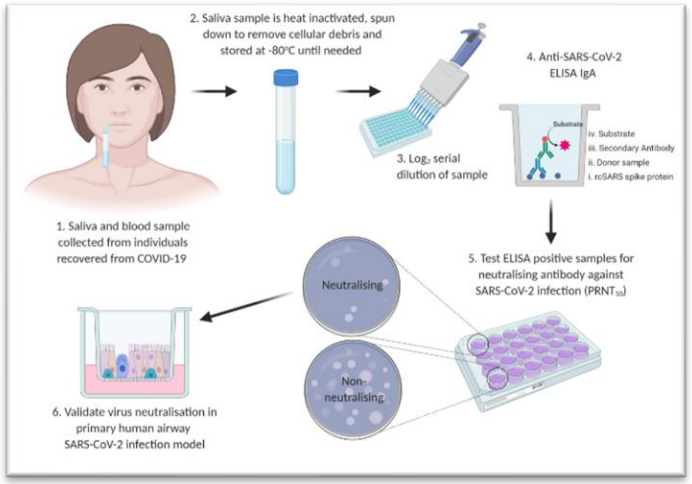
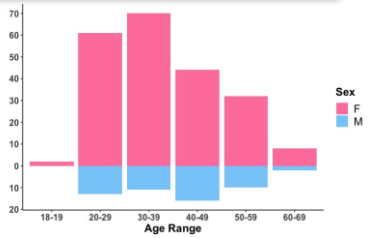
Study Design

Aim:
This project aims to determine whether SARS-CoV-2 infection induces a protective mucosal immunity through non-invasive testing for secretory IgA in saliva of GOSH staff who previously tested COVID-19+.

Main Objectives:
- Quantify levels and longevity of anti-SARS-CoV-2 IgA in saliva post-infection
- Determine neutralisation activity against SARS-CoV-2 infectivity using immortalised and primary cell culture models

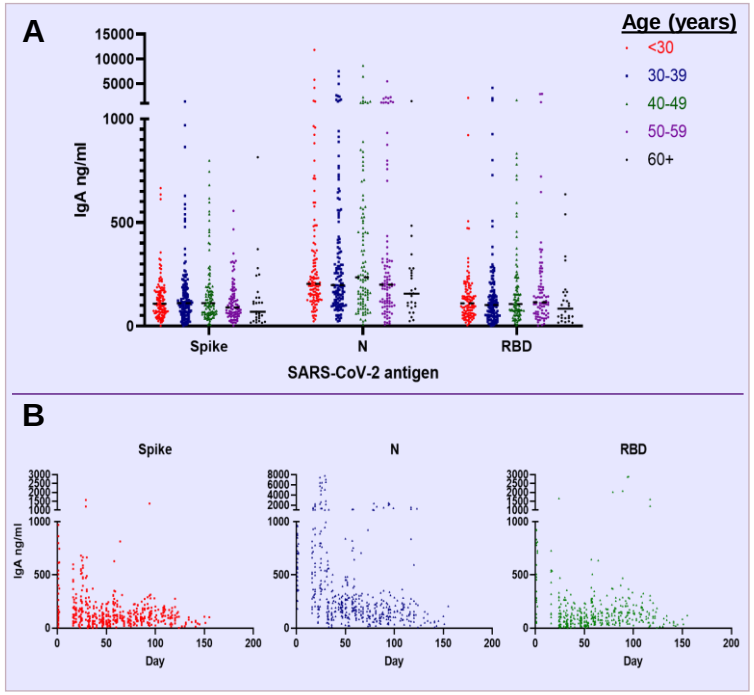


- 551 saliva samples collected from 292 participants between June and December 2020
- Age and sex demographics reflect staff population at GOSH



Mucosal IgA

- Saliva samples were screened for IgA using ELISAs for three SARS-CoV-2 protein antigens: whole trimeric **spike**, nucleocapsid (**N**), and spike receptor-binding domain (**RBD**)
- IgA level interpolated from standard curve of human IgA control



- Higher IgA levels observed for a subset of samples across all 3 antigens
- Frequency similar across age groups, but lower over 60 years (**A**)
- Detection of higher IgA concentrations decreased over time during the study window **(B),** suggesting mucosal IgA levels peak within first months post-infection, as reported previously for COVID-19 immune response **[1]**
- ELISA data being used for predictive decay modelling (in progress)

Neutralisation of SARS-CoV-2 infection

- Saliva samples were screened for neutralisation activity using a Vero E6 cell culture model – epithelial cell line expressing ACE2 receptor **[2]**
- SARS-CoV-2 virus pre-incubated 1 hr with sample or control, before incubation with cells for 48 hrs

- Pre-exposure of SARS-CoV-2 virus to some saliva samples greatly reduced infection of VeroE6 cells (representative sample shown in **C**)
- However, not all neutralising samples had high IgA levels against spike or RBD (**D**), suggesting other mucosal factors inhibiting the infection

Future Work

- ELISA IgA data is being analysed for differences between participant factors such as gender, ethnicity, & symptom severity
- SARS-CoV-2 neutralisation to be validated in an air-liquid interface cell culture model with primary respiratory epithelial cells
- Epitope analysis of IgA from neutralising mucosal samples
- Further ELISA experiments underway to test for cross-reactivity with seasonal coronavirus antigens
- Neutralising samples with low anti-SARS-CoV-2 IgA levels will be investigated for other innate immunity factors

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References:

[1] Isho B *et al.* Persistence of serum and saliva antibody responses to SARS-CoV-2 spike antigens in COVID-19 patients. Sci Immunol. 2020 Oct 8;5(52):eabe5511.
[2] Ogando NS *et al.* SARS-coronavirus-2 replication in Vero E6 cells: replication kinetics, rapid adaptation and cytopathology. J Gen Virol. 2020 Sep;101(9):925-940

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