Direct SARS-CoV-2 Antibody Detection in Clinical Samples Using a Portable Surface Plasmon Resonance Method and a Reference ELISA Assay

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Introduction

Enzyme-linked immunosorbent assay (ELISA) is considered the gold standard in immunological tests aimed at detecting and quantifying SARS-CoV-2 antibodies in blood samples. While ELISA remains a sensitive and reliable technique, it has a slow turnaround time and is a labor-intensive method requiring highly qualified personnel. The development of portable and fast sensing technologies may become pivotal in gaining relevant knowledge on the current immunity state of populations in pandemic situations. This study aims at comparing the analytical performances of an established ELISA assay and a surface plasmon resonance (SPR) technique for anti-SARS-CoV-2 antibodies detection in serum, plasma and dried blood spot (DBS) samples obtained from COVID-19+ patients.

Methods

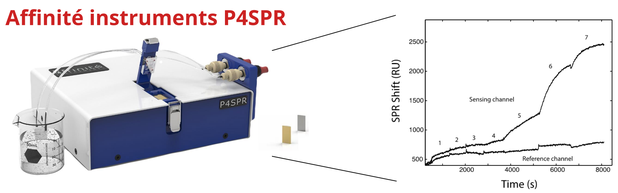
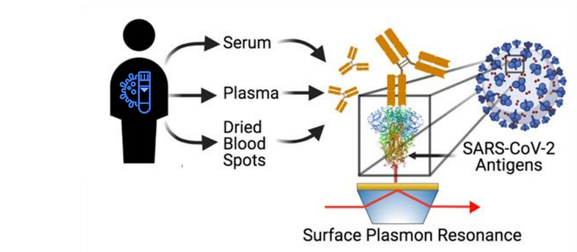


Figure 1 – A typical SPR sensorgram. A plot of SPR response vs time is generated from a portable SPR instrument and reveal whether there is a binding event between an analyte (e.g. antibody) and a ligand (e.g. protein) and whether the binding is specific. RU = Resonance units.



Scheme I – Blood was collected 4 and 16 weeks post-diagnosis (n=32) or from negative individuals (n=8). SPR sensors were prepared by surface immobilization with SARS-CoV-2 antigens (nucleocapsid, RBD or spike) over a gold (d=50 nm)-coated glass prism. IgG antibodies quantification from different blood products were performed with SPR and reference ELISA method.[1]

Results

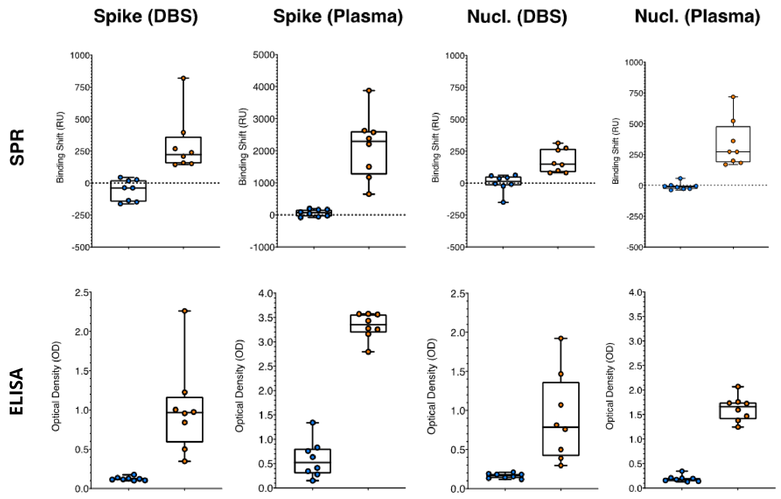


Figure 2 – Statistical comparison of the SPR and in-house ELISA responses obtained for the positive (right side, orange symbols) and negative (left side, blue symbols) detection of human anti-spike and anti-nucleocapsid antibodies in DBS and in plasma. All means were statistically different with p<0.01. Nucl. = Nucleocapsid. (n = 3 for ELISA and n = 1 for SPR).

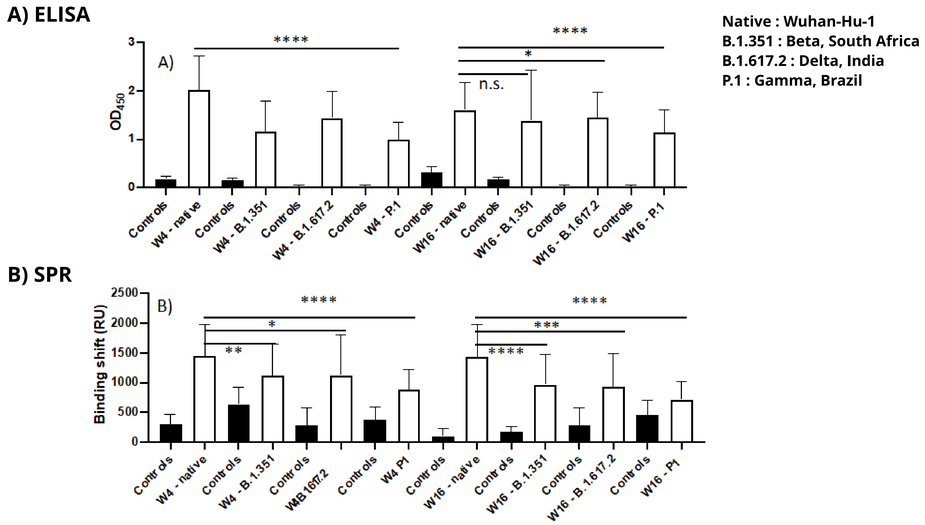


Figure 3 – Average ELISA OD_{450} (A) and SPR binding shifts (B) for the detection of anti-spike IgG in SARS-CoV-2-positive sera (n = 32) and negative controls (n = 8) at week 4 (W4) and week 16 (W16) post-diagnosis for the native, B.1.351, B.1.617.2 and P.1 spike proteins. Error bars represent one standard deviation. n.s. not statistically significant, * p < 0.05, ** p < 0.01, *** p < 0.001, and **** p< 0.0001.

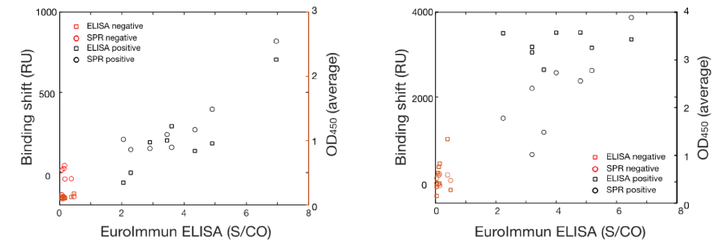


Figure 4 - Cross-validation assays between the commercial EuroImmun SARS-CoV-2 anti-spike in the x-axis and SPR in the left y-axis (open circles, n = 1 per sample) and in-house ELISA (OD_{450}, n = 3 per sample) in the right y-axis (open squares) for positive (black symbols) and negative (red symbols) samples. The Pearson's coefficients were all above 0.85, showing collinearity of the data. S/CO refers to the signal to cut-off of the ELISA measurements.

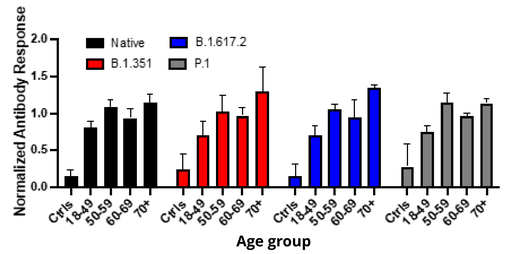


Figure 5 – Average normalized antibody binding stratified by age group for human anti-IgGs targeting the native (black), B.1.351 (red), B.1.617.2 (blue) and P.1 (gray) spike proteins among variant-naïve, non-hospitalized individuals. SPR and ELISA data from weeks 4 and 16 post-diagnosis were normalized to the mean of the overall cohort and pooled.

Conclusion

Portable SPR devices could be deployed on the field to conduct seroprevalence studies or to monitor the effectiveness of vaccination. This report provides the development process blueprints of an SPR-based antibody sensing method that can perform direct antibody detection in clinical samples.

References

[1] Djaileb et al. Cross-validation of ELISA and a portable surface plasmon resonance instrument for IgG antibody serology with SARS-CoV-2 positive individuals. Analyst. 2021 Jul 26; 146(15):4905-4917.