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SIREN

SARS-CoV2 Immunity & Reinfection Evaluation

SIREN Participants Newsletter
Issue 3
December 2021

Dear SIREN participants,

Please welcome the third issue of the SIREN study Participants' Newsletter!

As 2021 comes to its end and we start to dream of the next year, we would like to share with you SIREN achievements that were only possible thanks to your support.

These are the exciting news that you will find in this issue:

1. Latest SIREN insights

The SIREN team have been busy analysing the valuable data you provide, with two recent papers released, and several new analyses to be published over the coming weeks and months.

Our paper: Serological profile of first SARS-CoV-2 reinfection cases detected within the SIREN study, describes the serological profile of the first two confirmed cases of COVID reinfection within the SIREN cohort.

Both cases were seropositive (i.e. likely to have had COVID) on enrolment to SIREN with a history of COVID symptoms in March 2020, but no PCR test was performed at that time. They then tested positive by PCR in October 2020 and experienced mild symptoms. In both cases, we detected low or absent levels of neutralising antibodies at the time of reinfection with subsequent increases in antibody levels detected following the onset of symptoms. The hypothesis is that absence or low levels of neutralising antibody are likely to correlate with a lack of protection against COVID reinfection. This

finding has informed our ongoing analysis looking at a larger number of reinfections within SIREN, seeking to investigate which antibody levels are associated with protection. This information on 'correlates of protection' will help inform decisions on vaccination, for example, the timing of booster doses.

Thank you to all participants who have been flagged as 'Events of Interest' within SIREN, as the additional information you provide at the time of the event, including extra blood samples and swabs, provides crucial data for these analyses.

We are also delighted to inform you that the second SIREN interim analysis has been submitted for publication to a leading journal and we hope will be published in the coming weeks after peer-review. We have also published the manuscript on a pre-print server to ensure timely data sharing.

In this paper Effectiveness and durability of protection against future SARS-CoV-2 infection conferred by COVID-19 vaccination and previous infection, our goal was to better understand the protection acquired after infection and/or vaccination. We included data from over 35,000 SIREN participants, making this our largest analysis to date.

Key findings from this latest analysis include:

- Although there is some evidence of waning immunity after vaccination, protection against SARS-CoV-2 infection is higher following vaccination, regardless of prior infection status.
- This analysis was conducted during a Delta variant dominant period, and therefore shows that the BNT162b2 (Pfizer) and ChadOx1 (AstraZeneca) COVID-19 vaccines protect against Delta infections
- For participants who were previously infected with SARS-CoV2 and then vaccinated, vaccination provided additional protection, and these individuals had very high sustained protection even over 15-months after infection
- We also looked at protection following infection without vaccination. The vast majority of the period of follow-up for this analysis was before Delta emergence, and therefore this finding does not apply to the Delta period (i.e. the variant currently dominating) and there is no data available on Omicron
- In conclusion, our findings confirm that vaccination gives increased protection against SARS-CoV-2 infection, including the Delta variant, regardless of prior infection status.
- **This is key evidence that people should continue to get vaccinated to maximise their protection.**

In addition to the papers above, we are looking forward to sharing the results of our ongoing analyses with you in due course, with a number of exciting new papers to be released over the coming weeks and months. These analyses help shape future policy, and they are only possible thanks to you and your collaboration, so thank you so much for your support.

2. Participation in SIREN extension

Since the beginning in June 2020, almost 1,000,000 swabs and over 380,000 blood tests have been performed as part of SIREN. Despite the strain caused by the pandemic, the engagement and effort you have put into SIREN have been remarkable.

So far, the study extension has been launched at 80 SIREN sites, with at least 8 more expected to join. In England, just over 9,000 participants have now opted into the extension, and this number continues to steadily increase day by day. We have also seen great interest from Northern Ireland, Scotland and Wales, with all sites in Northern Ireland and Scotland offering the extension to their participants.

Thank you very much to everyone who has opted into the extended follow-up to date. There is lots for us still to learn together about the immune response to SARS-CoV-2 and COVID-19 vaccination, and this extended follow-up will enable us to assess the durability of protection over the longer term, and the impact of emerging variants like Omicron. If your site is offering the extension, you will receive your invitation to join as you reach your last month of your standard 12-months follow-up. We very much hope you consider continuing your participation in SIREN.

3. *NEW!* invitation to join the Patient and Public Involvement (PPI) panel

The SIREN consortium is pleased to invite **Expressions of Interest to join our Patient and Public Involvement (PPI) panel.** This panel will be vital to advising and informing our researchers, and to the continuation of the SIREN study. You will have the opportunity to provide open and honest feedback and reflections on the research project, discuss your thoughts on the wider implications, and provide input into activities aimed at informing and engaging the public. All Expressions of Interest will be reviewed individually and, although a relatively small number will be selected for this panel, there is also the opportunity to register your interest in being contacted about similar opportunities in the future as part of the SIREN study.

If you would like to learn more about this exciting opportunity, please click here for further information and to access the Expression of Interest form for completion. The closing date for registering interest is by **Monday 13th December 2021 at 5pm.** If you would like any further information, please contact Erika Aquino on E.Aquino@immunology.org.

The SIREN team are also keen to hear from participants with any feedback on our newsletter, videos, or webinars, or with any ideas of new ways we can engage with our participants. We really value your input and feedback so please contact our team on phe.siren.participants@phe.gov.uk.

4. PCR Update - Change in NHS Processes affecting some sites

We would like to make participants aware that some sites are changing the assay performed on SIREN PCR swabs. In these sites, the swab will continue to test for SARS-CoV-2 but also for influenza A, influenza B and respiratory syncytial virus, which are all common causes of winter respiratory illness.

SIREN will continue to receive only the SARS-CoV-2 results. Any other findings will be managed as per your local hospital policies – you may receive notification of your results.

If your site is changing their assay, you should receive a notification directly from your site.

5. SIREN & your professional learning

We're delighted with feedback we've been getting from sites that SIREN has been a valuable learning experience for finding out more about research and how it fits with your role. For some professions, such as nurses, midwives and doctors, it is possible to use this time toward a learning record for revalidation purposes or as evidence of continuous learning. You may therefore like to keep a log of attendance to SIREN events, like the upcoming webinar, reading results etc. All of these count towards your continued professional development and may be useful for future use, including updating your CV or job applications.

6. SIREN Science Corner - What is a PCR test?

PCR testing is now a regular everyday term that lots of us hear but I wonder how many of us really understand what it means? Well, the aim of Science Corner this month is to tell our lovely SIREN participants about this amazing test that you undertake every fortnight.

Part of SIREN is trying to see if the SARS-CoV-2 virus is present in your nose and throat swab. Just like you and me, viruses have genetic material; we have DNA and the SARS-CoV-2 virus has RNA. It is this viral RNA that we are trying to detect.

The first step when the swab gets to the lab is to make it safe for testing and to extract any viral nucleic acid (RNA).

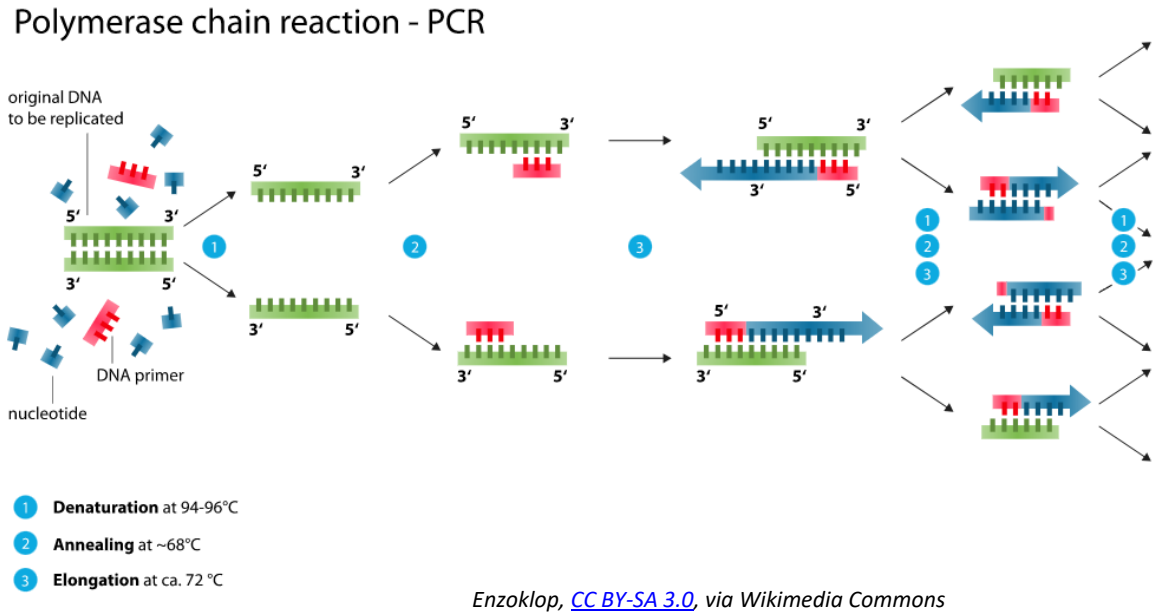
The viral RNA then needs to be converted to DNA using an enzyme called reverse-transcriptase. This reverse-transcriptase is sometimes abbreviated to RT, and when you see the word RT-PCR then it means reverse-transcriptase PCR. Sometimes RT-PCR also refers to real-time PCR – but more about that later!

Now we have the viral RNA converted to DNA we can do the actual PCR test. PCR stands for polymerase chain reaction and part of this reaction is to use another enzyme called DNA polymerase. The DNA polymerase is mixed with your extracted sample (which we call the template), along with the building blocks of DNA called nucleotides (lots of A, T, G and Cs) and special targets (primers) which are specially designed to only bind to SARS-CoV-2 genetic material.

We then put this mixture onto a PCR machine. DNA is double-stranded so we need to separate these strands by exposing the mixture to a really high temperature to split the DNA into two individual strands (denaturation). The temperature is then lowered so the primers bind to the specific areas on the template singe-stranded DNA (annealing). This only happens if the sample contains the virus. The nucleotides are then added to the primer by the DNA polymerase to make your single copy of DNA

into a double-strand again (extension / elongation). The cycle then repeats - a higher temperature separates the two strands of DNA, so these now become templates again when the temperature is cooled. Many cycles of this heating and cooling and making DNA from primers, nucleotides and DNA polymerase means that eventually there is enough DNA to be detected and show if you had the virus in your nose or throat. Detection is normally at the same time (real-time, RT-PCR) so the results are very fast.

Even though the PCR test is actually very quick there are lots of different steps the lab needs to take to keep them safe and to make sure you get the right results. The turnaround time is also affected by the large workload of samples being received in the laboratories for testing.



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7. Save the date: SIREN Participants live event + Q&A Thursday 9th of December 12:30pm - 1:30pm

We would like to invite you to the next SIREN Participants live event in December when we will be able to share some of our recent study findings, keep you updated on study changes, and most importantly answer any questions you may have. We look forward to seeing as many of you as possible on the 9th of December.

Add this to your calendar and click here to join the live event on MS Teams.

We look forward to seeing you then.

8. Remember to Enter the December SIREN Participant Prize Draw!

This month, we're celebrating your amazing contribution by holding a *Special Prize Draw!* **CLICK HERE TO ENTER** for a chance to win fantastic prizes (and treats). Winners will be announced live during the webinar.

All the best,
The SIREN team at UKHSA