Abstract

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is a novel respiratory virus with a wide range of clinical presentations known collectively as COVID-19. The severe respiratory illness accounts for increased hospital admissions and high mortality. Understanding the immune response to COVID-19 is a pre-requisite to identifying clinical correlates of exposure and immunity. This is of particular importance in vulnerable patients such as those with immunodeficiency. Detecting the antibody response to COVID-19 is essential to diagnostic testing, however the antibody response may wane over time, or may not be detectable in patients with antibody deficiency necessitating an examination of the role of the cell-mediated immunity. There is already evidence to suggest an important role of cellular immunity. T cells may provide long-lasting immunity against the virus, and a T cell response has been detected in seronegative individuals post-COVID-19.

A simple and practical method is essential to assess the T cell response in the clinical setting. A functional [3H]-thymidine incorporation assay to assess the T cell response to SARS-CoV-2 was developed with the aim of analysing a cohort of primary immunodeficiency (PID) patients at Great Ormond Street Hospital. Proliferation of T cells in response to three SARS-CoV-2 antigens was investigated in healthy controls as well as in patients with PID post-vaccination/infection.

Structure of SARS-CoV-2

Testing methods for T cell response

• Heparinised blood is diluted with RPMI media and layered onto a Lymphoprep.
• PBMC separated from blood by density centrifugation.
• PBMC removed and wash with RPMI.
• PBMC resuspended in required RPMI.
• AB serum added.
• 96 well plates coated with Sars-Cov-2 antigens and PHA.
• Incubation of plates for 3-5 days.
• Pulsing with radioactive thymidine.
• Radioactivity measured on scintillation beta counter.
• Results analysed.

Subset of Results

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>CVID (n=6)</th>
<th>XLA (n=8)</th>
<th>XLA (n=1)</th>
<th>XLA (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-vaccination</td>
<td>1009 ± 67</td>
<td>2038 ± 75</td>
<td>952 ± 58</td>
<td>1267 ± 136</td>
</tr>
<tr>
<td>Post-vaccination</td>
<td>1500 ± 82</td>
<td>2505 ± 89</td>
<td>1000 ± 78</td>
<td>1625 ± 186</td>
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</tbody>
</table>

HC = 18 (8 pre vaccinated, 4 post infection, 6 post vaccination) Patients > more than 180 with different conditions.

Graphical representation of results obtained from the project.

HC, Healthy controls; CVID, common variable immunodeficiency; PID, primary immunodeficiency; XLA, X-linked agammaglobulinemia; OPM, counts per minute per suspension; BKG, background = unstimulated samples; PHA, Phytohaemagglutinin.

Conclusions

PHA proliferation (positive control) was normal in all patients tested. As expected healthy controls post-infection proliferated to all three COVID antigens while post-vaccination health controls showed a strong proliferative response to spike antigen alone. Patients with CVID and T cell disorders failed to proliferate to COVID antigens and had responses near-equivalent to background. The XLA patient had the highest T cell proliferation to antigen exposure of the entire cohort, and proliferation to antigen post-infection mimicked the pattern seen in healthy controls post-infection. Further analysis of XLA/B cell disorders patient is required to confirm this finding.

References