Early Antibody Responses to SARS CoV-2 Infection in Non-Human Primates

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Introduction

The widespread detrimental effects of the COVID-19 pandemic caused by SARS CoV-2 virus has made investigating the pathogenesis of infection and development of therapeutics a pressing matter. As of September 2020, COVID-19 has been linked to the deaths of over 200,000 Americans and infected over 7 million with the respiratory illness. Currently, antibody responses following COVID-19 infection are poorly understood. An increased understanding of antibody responses following infection may reveal implications for serological testing in early stages of COVID-19 infection.

Non-human primate (NHP) models for COVID-19 are needed to characterize virus-specific immune responses under controlled conditions. This project is the first to assess the earliest primary serum antibody responses that are generated in NHP after infection with the SARS CoV-2 virus.

Methods

6 Indian rhesus macaques were inoculated with 6 x 10⁶ infectious units of SARS CoV-2 by a combination of three routes:
- Intranasal (2 x 10⁶ infectious units)
- Intratracheal (2 x 10⁶ infectious units)
- Intraocular (2 x 10⁶ infectious units)

Serum samples were collected prior to inoculation and, at intervals, between days 2 and 10 then again at the time of necropsy to measure antibodies at each of these time points.

Results

Bioplex Antibody Assay: SARS-CoV-2 spike subunit 1 (S1), spike subunit 2 (S2), and nucleocapsid (NC) proteins were conjugated to magnetic beads, each embedded with a unique ratio of two infrared dyes (termed "regions"). Beads were incubated with serum samples from monkeys inoculated with virus. Bound SARS-specific antibodies were detected using biotinylated anti-rhesus IgG, IgM, or IgA secondary antibodies and fluorescent avidin-phycocerythrin (PE) in separate assays to measure the concentration of each antibody isotype present in each sample. A calibrated reference was included to generate a standard curve.

Conclusions

As noted in human studies, Spike-specific IgG and IgM antibodies appeared in serum simultaneously.

Both IgG and IgM antibody responses to Spike protein were readily detected 7 days after infection, but IgG antibodies to NC were very low and significant anti-NC IgM was not found at this time.

Significant IgG responses were not observed until day 10.

From day 10 to day 14, SARS-specific IgM declined but IgA increased, suggesting class-switching to IgA was occurring.

The antibody response to all viral proteins was dominated by IgG.

Overall, these results suggest that serological tests based on the presence antibodies to both Spike and NC proteins may not yield positive results until 10 days after infection.

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