# The plasmablast response to COVID-19 in naïve individuals is dominated by IgA1 cells cross-reactive to other coronaviruses but memory formation is not

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## Abstract

The occurrence and subsequent spread of SARS-CoV-2 gave a rare opportunity to study the immune response to airway pathogens in antigen-naïve humans. During the first wave of infections in Sweden in 2020, a cohort of patients was selected for detailed analysis of fresh whole blood during the primary infection and memory development was subsequently followed in the group. During infection, we found a strong plasmablast response that was dominated by IgA1 producing cells but also contained many IgG1 and IgM cells. Most expressed the mucosal-associated integrin β1 and some also the gut-associated integrin β7, while a large proportion were $CCR9^{+}CCR10^{-}$, arguing for mucosal, but not gut, homing. Even 3 months after recovery, low levels of antigen-specific IgG producing plasmablasts were present in the circulation, but at 6 months these were largely gone. Interestingly, during the infectious phase, IgA and IgG produced from plasmablasts showed cross-reactivity against previously encountered coronaviruses, while neither 3 month plasmablasts or 6 month memory cells did. Single-cell RNASeq with BCR cloning from the early infectious stage until 12 months after infection showed that their different clones. Thus, infections with the original SARS-CoV-2 strain resulted in an early mucosal-targeted plasmablast IgA response that was likely derived from pre-existing memory B cells formed against other coronaviruses, but the response subsequently developed into a non-cross-reactive SARS-CoV-2 specific response based on other B cell clones.