Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Cross-reactivity towards SARS-CoV-2: the potential role of low-pathogenic human coronaviruses

The human body is capable of producing antibodies in response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, the causative agent of COVID-19. The principle of antigen-antibody reaction has been widely explored to develop enzyme immunoassays for studying seroprevalence. Kelvin Kai-Wang To and colleagues[1] found a seropositive rate of 2·73% (53 of 1938 serum samples) in SARS-CoV-2 enzyme immunoassays for individuals who had probably not been exposed to the virus. This finding raises the possibility of antibody cross-reactivity with other human coronaviruses.

There are seven types of coronaviruses that naturally infect humans. SARS-CoV-2, severe acute respiratory syndrome coronavirus (SARS-CoV), and Middle East respiratory syndrome coronavirus (MERS-CoV) can cause severe acute respiratory illnesses. By contrast, the four endemic genotypes, including 229E, NL63, OC43 and HKU1, usually only cause mild upper respiratory tract infections, and thus can be classified as low-pathogenic human coronaviruses. In total, there have been just over 10 000 cases of SARS-CoV and MERS-CoV. Because of their genetic relation with SARS-CoV-2 (appendix), the generation of cross-reactive antibodies is not surprising. However, as the population exposed to these two coronaviruses was very small and the outbreaks occurred some years ago, their effect on the global COVID-19 pandemic would be minimal.

Low-pathogenic human coronaviruses are continuously circulating among the global population. Globally, about 5% of acute respiratory tract infections are attributed to these pathogens. Because the incidence of respiratory infections is at multiple billion episodes per year worldwide[2] and antibodies can persist long term, a substantial proportion of the global population are expected to carry antibodies against low-pathogenic human coronaviruses. Genetically, these viruses are moderately related to SARS-CoV-2, although this relationship is more distal than that of SARS-CoV and SARS-CoV-2 (appendix). SARS-CoV-2-reactive immune responses have been detected in unexposed individuals who are IgG seropositive for OC43 and NL63.[3] This cross-immune reactivity mainly targets the viral 1AB polyprotein and S proteins,[3] and these regions consistently have high sequence similarity between low-pathogenic human coronaviruses and SARS-CoV-2 (appendix). Thus, such cross-reactivity cautions the interpretation of serological studies in the context of COVID-19.

If cross-neutralising activity also exists, this result could have a major effect on the global COVID-19 pandemic. Intriguingly, low-pathogenic human coronaviruses are more prevalent in young children (<5 years old), contrary to the clinical features of COVID-19 in which children are the least affected population.[4] This observation might also partly explain the potential benefits of intravenous immunoglobulin in treating patients with COVID-19.[5] With a pool of immunoglobulins from thousands of healthy donors, intravenous immunoglobulin must contain antibodies against low-pathogenic human coronaviruses. Future studies are needed to further validate whether cross-neutralising and cross-protective effects are present between low-pathogenic human coronaviruses and SARS-CoV-2.

We declare no competing interests.

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See Online for appendix