

New studies suggest possible cross-immunity between common cold and Covid-19

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Photo: - coronapathology.com/immunology/

Recently, some very interesting scientific articles have been published (so far, only available in online archives and awaiting peer-review) hinting to important discoveries regarding Covid-19, - its prevalence, severity of its course, population immunity, and vaccine development.

At least two groups of scientists have confirmed that there may be some immunity to the new coronavirus - SARS-Cov-2 in individuals who are thought to have had in past several strains (229E, NL63, OC43 and HKU1) of human coronaviruses (HCoV), an infection known as seasonal (nonspecific) flu or "common

cold." According to the US Centers for Disease Control (CDC), most people get infected with one (or more) of these less virulent coronaviruses at least once in their lifetime. Characteristic signs of common cold are: wheezing, sore throat, headache, fever, cough, general weakness; rarely - damage to the bronchi or lungs.

The first article submitted for publication in the journal *Cell* on April 20, belongs to the group of American scientists - Alba Grifoni and co-authors (La Jolla Institute of Immunology, University of San Diego, CA, North Carolina Medical School, NC, Mount Sinai Medical School, NY). They examined CD4 and CD8 lymphocytes in 20 patients convalescent from Covid-19, 20-35 days after the disappearance of symptoms, when immune response was already developed. The control group examined the cellular material of blood donors taken in 2015-2018 which could not have had Covid-19 then, instead they most likely have had seasonal cold-causing coronaviruses. Patients convalescent from Covid-19 were found to have SARS-CoV-2-specific CD4 (100%) and CD8 (70%) lymphocytes. At the same time, the authors found similar SARS-CoV-2-reactive CD4 T cells (40-60%) in controls that could not have had history of Covid-19, and suggested that there was cross-reactivity of T-cells in humans with circulating seasonal colds and the new coronavirus (SARS-CoV-2) causing Covid-19.

The second article, posted online on May 15, belongs to a group of English scholars Kevin Ng and co-authors representing the Francis Crick Institute, University College London and its hospitals, and Imperial College London. They also found that people not infected with the new coronavirus still could have some immunity to the virus. The authors examined several study groups - including those infected with Covid-19 and those who were not diagnosed with SARS-CoV-2 but were either diagnosed (or likely to have) a seasonal cold coronavirus (HCoV) infection, and a control group with neither CoV-2 nor HCoVs confirmed.

Studies in Covid-19 patients confirmed, as expected, all three classes of antibodies to SARS-CoV2 (IgG, IgM, and IgA). However, individuals who were exposed to seasonal cold-inducing HCoVs coronaviruses were also found to have antibodies to Covid-19 coronavirus (SARS-CoV2) in their blood, but only of the IgG class (with relatively lower titers and somewhat different characteristics, with different subtypes of the virus). Most importantly, the sera of individuals exposed to seasonal colds (HCoVs) possessed the ability to neutralize the new coronavirus SARS-CoV2 (S-pseudotypes) in sample tubes, what was comparable to the ability of antibodies from Covid-19 convalescent patients. According to the authors, this may be explained by assumption that exposure to seasonal cold coronaviruses presumably also determines some of these individuals' pre-existing humoral (antibody-based) immunity to Covid-19 as well.

Therefore, to date, we have preliminary data (which, hopefully, further studies will confirm) that pandemic-causing new coronavirus can have both cellular (lymphocytic) and humoral (antibody-dependent) cross-immunity due to numerous circulating infections of the Human coronaviruses (HCoVs) for years causing the so-called "Common cold". Numerous cases of seasonal flu or seasonal (general) colds, the vast majority of which have a much milder clinical course, or a more frequent non-symptomatic course, than Covid-19. If this view of cross-immunity is confirmed, it will have a number of practical implications, as well as several new questions may arise:

1. It was difficult to explain why there is a sharp difference in mortality rates in different regions. It is likely that the above-mentioned 4 strains of seasonal cold HCoVs may unequally affect different

geographical areas over subsequent years, and one of the results of this may be that during the Covid-19 pandemic Australia, New Zealand, Taiwan and China itself were limited to relatively less severe cases and lower lethality.

2. There are more cases of seasonal colds in children (especially in kindergarten and lower grade pupils) and some of them sometimes go so easily that they are not detected at all. Instead, the cross-immunity acquired at this time may be the protective shield that protects most children (though not all of them) from the development of a Covid-19 infection, as well as from its severe complications. The above-mentioned factor may also apply to children's parents and teachers.

3. Not only abroad, but also in our country, there have been cases where family members either carried over the Covid-19 infection particularly easily, or, despite the generally high risk of infection with the new coronavirus, some family members did not become infected at all, despite long, continuous and close contact with the infected. The reason here, too, may have been the previous infections by seasonal HCoV coronaviruses inducing common cold which presumably led to cross-immunity against SARS-CoV-2, either protecting these persons from Covid-19, or causing only mild course of the disease.

4. It is known that a particularly high percentage of deaths of elderly patients were observed in nursing homes. Interesting question is, what are the rates of co-infection and lethality in the same age group for those, who had close contact with their grandchildren during last years and, presumably, a seasonal cold could also have been carried over in past, with possible current cross-immunity to Covid-19. So far there are no studies clarifying this issue.

5. Regarding doubts of specificity of rapid antibody tests against the new coronavirus, is their questionable specificity as to whether these tests reflect true SARS-nCoV2 antibodies, or may be also "catch" cross-reactivity with HCoVs? If this is the case, then until sufficient specificity is guaranteed, it makes no sense to perform such rapid tests, as they may often discover past history of common colds due to infection by seasonal coronaviruses (HCoVs) instead of Covid-19.

6. A number of mathematical calculations indicated that the development of population immunity (so called "herd immunity") to the new coronavirus would take a very long time. It is now accepted that if there is still some pre-existing immunity in the population, it may be related not so much to the number of Covid-19 transmissions (which, assuming unidentified cases, would still be a relatively small segment), but to the last year (or – to last few years?) cases of less dangerous HCoV infection with seasonal colds which summarily could be higher than the number of Covid-19 carriers, and thus hopefully might lead to sooner achievement of needed level of herd immunity.

7. Finally, if cross-immunity confirms the potential for coronavirus neutralization in more extensive studies, and not only in vitro, then the HCoV strains, which only induce non-lethal seasonal flu could be used to treat lymphocytes and/or plasma of Covid-19 patients. It is possible that such studies will help us in terms of developing a vaccine (maybe a polyvalent coronavirus vaccine?)

However, it should be noted that so far the above studies are based on very limited materials - related to the study of several dozen patients and our optimism may not be justified.

Until we have more multiple and thorough studies, caution, adherence to hygienic norms (hand washing, facemask wearing) and physical distancing are essential! Overconfidence and premature recognition of hypotheses might prove to be dangerous.

<https://www.cell.com/action/showPdf?pii=S0092-8674%2820%2930610-3>

<https://www.biorxiv.org/content/10.1101/2020.05.14.095414v1?fbclid=IwAR3IC72lOPIppxxjZqOjV01hfdsXDyrGbIZz5pNZpB3rcBeokDOtkgMu2Y8>

<https://www.cdc.gov/coronavirus/general-information.html>