CROSS-IMMUNITY TO DISEASE

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The coronaviruses have an RNA genome; the SARS-CoV-2 has 4 structural proteins, consisting of the four structural proteins of SARS-CoV-2, which are: S peplomer protein, which looks like a spike on the viral capsid, E envelope protein, M matrix or membrane protein, and hemagglutinin esterase, which is another protein on the viral capsid that helps the virus attach to the host cell (Mateus et al, 2020). According to a study published in *Science* in 2020, coronaviruses express viral proteins, found in the epitope, and which they have similar protein sequences which cause them to be cross reactive because of their resemblance of peptide and genetic sequences. Although, the viruses are different, they are in the same family, and the epitope proteins expressed is what human T cells recognize on antigen presenting cells, and become cross-reactive to, because of their similarity (Mateus et al, 2020). In the article, it was found that other coronaviruses of the HCoV strain have been contracted by human's cohorts which cause them to develop antibodies to the antigen of the HCoV; these strains have been found to cause common colds and mild respiratory diseases which often go undiagnosed and fought off by the body easily (Mateus et al, 2020). The SARS-CoV-2 produces similar proteins presented on the epitope, which are presented in the common cold coronaviruses also, and therefore, humans may already have antibodies to the coronavirus of SARS-CoV-2; it is possible that the body has already reacted to other less obstructing coronaviruses in the family, that have been around for decades, and so if individuals are tested for Covid-19, then they are likely to have tested positive for the virus even if they have not contracted the actual SARS-CoV-2 virus (Mateus et al, 2020; Kumleben, 2020). Also, if individuals have received vaccinations against certain viruses like, influenza, pneumonia, tetanus, diphtheria, or pertussis, then the patient is likely to have cross-reactive immunity against SARS-CoV-2, because of similarities in their peptide sequences (Reche, 2020). The T cells don't recognize the whole virus; they recognize

viral peptides, derived from viral antigens that are remembered and presented on antigen presenting cells, in association with the major histocompatibility complex (Mateus et al, 2020).

Viruses in a certain family like for instance, coronaviruses, or herpes viruses, like herpes-simplex-virus compared to human papillomavirus may have significant resemblance in genetic sequences and proteins expressed in that certain family, but they also have resemblance of genetic sequences and peptides to other viruses that are not in the same family, and which may create cross-reactive immunity in certain populations towards SARS-CoV-2. Adaptive immunity of B and T cells allows for special immunity, involving recognizing antigens, or foreign proteins on antigen presenting cells, which may have been already remembered by the body. In a study to test cross-reactive immunity, *Frontiers of Immunology* have found that, vaccinations given to patients for meningitis B and DTP especially, has potential to cause cross-reactive immunity (Reche, 2020). The study involved analyzing blood samples from patients that have been vaccinated for different viruses; human pathogens including 18 viruses and 7 bacteria were then searched through BLAST for peptide matches, these pathogens also were common pathogens that we tend to vaccinate populations for, including some of the pathogens listed earlier (Reche, 2020). The researchers were interested in including viruses and bacteria that are commonly vaccinated against, in order to compare with peptide sequences to SARS-CoV-2, and make correlations to patients who received vaccinations for those viruses or bacteria, because they would obviously already have antibodies against those pathogens since they were vaccinated. Proteins found in the viruses matched for peptide sequences, are also expressed in SARS-CoV-2 and essentially, the body can recognize those same peptides and go ahead and activate immune cells and continue fighting. According to *Frontiers of Immunology*, Streptococcus pneumoniae, Neisseria meningitides, Haemophilus influenza, Clostridium Tetani (Cte), Corynebacterium

Diphtheriae (Cdi), and Bordetella pertussis (Bpe) all have hits of over 60 peptide matches; in a chart provided below, these pathogens evidently also caused the B cell, CD4+, and CD8+ reactivity to rise accordingly to the amount of peptide matches to SARS-CoV-2 (Reche, 2020).

This table shows the amount of peptide matches found of certain pathogens and the SARS-CoV-2 (Reche, 2020).

Figure 1.

Peptide Matches/Cell reactivity	SARS-Peptide Hits(1)	B(2)	CD8 T(3)	CD4 T(4)	Vaccine (5)
Bacille Calmette-Guérin (BCG)	120	41	21	11	Y
Bordetella pertussis (Bpe)	111	36	18	12	Y
Corynebacterium diphtheriae (Cdi)	83	33	14	5	Y
Clostridium tetani (Cte)	85	34	17	7	Y
Haemophilus influenzae (Hin)	53	16	6	5	Y
Neisseria meningitides (Nme)	60	23	9	3	Y
Streptococcus pneumoniae (Spn)	61	19	13	6	Y

The Table below are the Chosen Vaccine Agents of DTP and MenB with high peptide Matches to the SARS-CoV-2 (Reche, 2020).

Figure 2.

Vaccine Antigens	Proteins	SARS-Peptide Hits (1)	BCell(2)	CD8 T(3)	CD4 T(4)
D	340	24	6	5	2
T	601	28	13	8	2
aP	25	3	1	1	0
wP	1,852	67	23	10	5
MenB	267	10	3	2	1

Figure 1 & 2 (Reche, 2020) use information available from:

https://www.frontiersin.org/journals/immunology.

According to the data, Children could be more immune to SARS-CoV-2 yes, because of their immune systems, but not because they are just stronger, but possibly because they have been vaccinated for pathogens that express some of the same proteins found in the SARS-CoV-2, and more recently than elders. Required and recommended vaccinations for school and in newborns such as “DTP” and “Meningitis B” are reported to have high peptide matches and cell reactivity (Reche, 2020). The combination vaccine “DTwP” and “TDAP” are given many times to young aged children, and then it is not really required anymore after those ages; the vaccine antibodies and effects typically will decrease over time, and this could be the reason elders become less resistant to SARS-CoV-2 (Reche, 2020).In the study provided By *Science,* The SARS-CoV-2 produces similar proteins presented on the epitope, which are similar to the less obstructive common cold coronaviruses, on the spike (S) protein; according to *Frontiers of Immunology,* there were 16 SARS-CoV-2 peptide matches with DTP antigens, 14 of them were spike proteins of the membrane (Mateus et al, 2020; Reche, 2020).These findings suggest that the DTwP vaccine could be effective to prevent Covid-19, essentially because our T cells would recognize proteins on antigen presenting cells that are present in both SARS-CoV-2 and strains of Bordetella pertussis (Bpe), and which antibodies have been made from the DTP vaccine (Reche, 2020). This could be the reason the researchers found that children whom received DTP, TDAP, or “DTwP” vaccines recently are likely to show cross immunity to SARS-CoV-2 from T and B cell reactivity (Reche, 2020).

Limitations of the study could include not being able to actually test children cell reactivity from different populations, including American children and children that are required to receive TDAP immunizations for school; being able to compare data with children of third

world countries that may not receive vaccinations at all, compared with vaccinated children, could help further research of cross-immunity of immune cells.

This leads me to the conclusion that cross-immunity is very common from coronaviruses that have been around before SARS-CoV-2 pandemic, and also from other viruses that may have not been contracted, but however, a person will receive antibodies from vaccinations which causes them to become slightly immune and have weaker symptoms from Covid-19. This also proves my hypothesis that false positives could be the cause of this issue of cross-immunity. Cross-immunity is why Covid-19 testing must be specific for SARS-CoV-2, adjusting the number of antibodies required to determine a positive result has been a new testing technique to help give accuracy and prevent false positive (Kumleben, 2020). However, with there being false negatives as well, extensive testing will be needed to make sure the test isn't reacting from antibodies of other viruses that were already remembered by the body's adaptive immune cells.

References:

Kumleben, N et al., (2020). Test, test, test for COVID-19 antibodies: the importance of sensitivity, specificity and predictive powers. Public health (London), 185, pp.88–90

Mateus, Jose et al., (2020). Selective and cross-reactive SARS-CoV-2 T cell epitopes in unexposed humans. Science (American Association for the Advancement of Science), 370(6512), pp. eabd3871–94.

Reche, P.A., (2020). Potential cross-reactive immunity to SARS-CoV-2 from common human pathogens and vaccines. Frontiers in immunology, 11, p.586984.