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.

Medical Hypotheses 140 (2020) 109752

Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy

The possible beneficial adjuvant effect of influenza vaccine to minimize the severity of COVID-19

To Editor

COVID-19, caused by the new corona virus (SARS-CoV-2), is an emerging, rapidly evolving disease that needs rapid intervention as it shows high spread mortality rates within very short time. Interestingly, the reported cases show different severity of symptoms, ranging from mild to severe with no symptoms in some cases. Although very limited studies investigated the immune responses toward COVID-19, a recent study conducted by researchers at the Peter Doherty Institute for Infection and Immunity in Australia, assessed the immune responses in the blood from a patient with COVID-19 disease with mild severity [1]. They looked at the cellular and humoral immune responses at different time points during the infection; i.e. before, during and after resolution of the disease and recovery of the patient. Their longitudinal analysis showed a robust immune response across different cell types associates with clinical recovery. These findings are similar to what the same group have reported before in patients with influenza infection [2,3], Accordingly, we suggest a link between the quality of the immunity and recovery from COVID-19, at least in part, in patients with mild symptoms.

Indeed, different susceptibilities to COVID-19 disease were observed between different age groups where children showed lower rate of infection than adults and elderly. Although the mechanism behind these differences in infection severity and susceptibility is not clear, one possible explanation could be the difference in the quality and quantity of the immune performance that is shaped by the history of recent infections and/or vaccinations. We present here the hypothesis that the resultant immunity against prior influenza infection would, at least in part, foster immunity against SARS-CoV-2. This hypothesis is supported by which the similarity in the quality of immunity toward both viruses. and by the previous studies showing cross reactivity of immunity between Flu and coronavirus [4] due to the similarity in their structures [5,6].

Besides the cross reactivity effect, the anti-Flu immune responses can induce bystander immunity [7] that is expected to non-specifically augment immunity against other viral infection such as SARS-CoV-2. Furthermore, influenza vaccination itself would generate sustained immunity that overall enhance immunity against SARS-CoV-2. This would explain why the rate of SARS-CoV-2 in children is low since they catch flu more than adults do [8]. As such, it is expected that their immune systems be often alarmed against influenza, generating bystander immunity that harness the immune responses against related viral infection. Under this setting, we hypothesize that children generate multifactorial immunity with the repeated influenza exposure that would offer bystander immune response in case they became infected with the new SARS-CoV-2. It might be possible also that individuals who received prior Flu vaccination might show mild severity of COVID-19 because of Flu-induced bystander effect of the generated immune responses which itself might cross react against SARS-CoV-2. Due to this cross reactivity between Flu and SARS-CoV-2, we suggest that the Flu-induced bystander immunity is more of beneficial effects to COVID-19 than those suggested by MMR and BCG vaccines [9,10]. Indeed, the zero COVID-19 patient (the Chinese patient suspected to be the first case infected with the new corona virus) who was released from the hospital couple of weeks after her diagnosis declared that the symptoms were almost like those of her repeated flu infection [11].

Given the safety of Flu vaccine in adult, we recommend the use of Flu vaccine, at least in part, as a bystander adjuvant to minimize the severity of COVID-19 disease.

We have no conflicts of interest to disclose.

References

[1] Thevarajan I, Nguyen THO, Koutsakos M, Druce J, Caly L, Van de Sandt CE, et al. Breadth of concomitant immune responses prior to patient recovery: a case report of non-severe COVID-19. Nat Med 2020;26:453–5.
[2] Ellebedy AH, Jackson KJ, Kissick HT, Nakaya HI, Davis CW, Roksin KM, et al. Defining antigen-specific plasmablast and memory B cell subsets in human blood after viral infection or vaccination. Nat Immunol 2016;17:1226–34.
[3] Koutsakos M, Wheatley AK, Loh L, Clemens EB, Sant S, Nüssing S, et al. Circulating TFH cells, serological memory, and tissue compartmentalization shape human influenza-specific B cell immunity. Sci Transl Med 2018;10(428):1–15.
[4] Zheng J, Perlman S. Immune responses in influenza A virus and human coronavirus infections: an ongoing battle between the virus and host. Curr Opin Virol 2018;28:42–52.
[5] Zeng Q, Langereis MA, van Vliet ALW, Huizinga EG, de Groot RJ. Structure of coronavirus hemagglutinin-esterase offers insight into corona and influenza virus evolution. Proc Natl Acad Sci 2008;105(26):9065–9.
[6] Abdella R, Aggarwal M, Okura T, Lamb RA, He Y. Structure of a paramyxovirus polymerase complex reveals a unique methyltransferase-CTD conformation. Proc Natl Acad Sci 2020;117(9):4931–41.
[7] Horns F, Dekker LC, Quake SR. Memory B cell activation, broad anti-influenza antibodies, and bystander activation revealed by single-cell transcriptomics. Cell Rep 2020;30:905–13.
[8] Kumar V. Influenza in children. Indian J Pediatr 2017;84(2):139–43.
[9] Salman S, Salem ML. The mystery behind childhood sparing by COVID-19. Int J Cancer Biomed Res 2020;5(1):11–3.
[10] Salman S, Salem ML. Routine childhood immunization may protect against COVID-19. Med. Hypotheses 2020;140:109689.
[11] Page J, Fan W, Khan N. How it all started: China's early coronavirus missteps. Wall Street J 2020.

Mohamed Labib Salem[a,b], Dina El-Hennawy[b,c,*]
[a] *Immunology and Biotechnology Unit, Department of Zoology, Faculty of Science, Tanta University, Tanta, Egypt*
[b] *Center of Excellence in Cancer Research, Tanta University Teaching Hospital, Tanta University, Tanta, Egypt*
[c] *First Health Office, Basyun Central Hospital, Basyun, AlGharbiya, Egypt*
E-mail addresses: mohamed.labib@science.tanta.edu.eg (M.L. Salem), Henawy.dt@gmail.com (D. El-Hennawy).

[*] Corresponding author at: Center of Excellence in Cancer Research, Tanta University Teaching Hospital, Tanta University, Tanta, Egypt.

https://doi.org/10.1016/j.mehy.2020.109752
Received 1 April 2020; Accepted 21 April 2020