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An Insight towards the Role of Micro-Biota in Vaccine Development for COVID-19

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Abstract

The whole world is moving around to fight against corona virus (Covid19). In this present scenario, the study of gut-microbiota with vaccine development is studied. And it is tried to understand the role of gut microbiota in the immune response to the host. It is found that the diet is taken by the person of age, sex; patients will play a significant role in gut microbiota and show immune response towards vaccines. Many modern technologies of bioinformatics are applied to understand the diversity among gut microbiota with respect to age, sex, patients to immunity. It is recommended that these analyses will help to improve vaccine development against COVID19.

Keywords: Covid19; Corona Virus; Gut-microbiota; Vaccine; Bioinformatics

Abbreviations: HRV: Human Rotavirus; FOS: Fructooligosaccahride; GOS: Galactooligosaccaherides; NGS: Next-Generation Sequencing.

Introduction

Coronavirus, the big giant started eating all the humans from all over the world. It got its name COVID19 due to coronavirus originated in the year 2019. As it is moving from Wuhan to all over the world slowly but gradually. As it is one and first kind of virus which goes host body through touch or sneezing from an infected person basically having lung infection, becoming the world's largest killing disease [1]. Hence, scientists, researchers all over the world have now started the trials of the potential vaccine candidates to kill coronavirus. In this present scenario, the author makes an effort to take the opportunity to study the relationship between gut microbiota and vaccine development for covid19.

Microbiota and Vaccine Response

The microbiota constitutes a large and diverse group of micro-organisms. This microbiota performs essential functions including the nutrients metabolism, gut homeostasis maintenance, regulation of gut mucosal immunity, etc. Studies show that the profound effect of drugs may change the microbiota composition which leads to the consequences in metabolism and immune responses [2,3] of T-helper cells [4].

Vaccination reduces the disease progression burden in the world as it is safe and vaccine has no side effects. A vaccine characteristic includes:

- Vaccine formulation- it includes vaccine delivery systems, adjutants, and immunomodulators.
- Nature of antigen- it includes whole microbes, purified protein, polysaccharide, and nucleic acid.
- The dose: how much quantity is used for children, adults, and so on.
- The route of immunization- either it would be parental or mucosal.
- Vaccine schedule: what will be the vaccine schedule either homologous or heterologous prime-boost strategies,
- Time for vaccine doses- this includes gapping between vaccine doses if the boosting dose is there.

A vaccine induces B-cells to produce antigen-specific antibodies which can be booster doses as required for a

specific disease. Studies confirmed that if intestinal flora is not well flourished then inflammation and blunted immune response are observed [5,6]. In the developing world it is observed that due to poor sanitation, most of the vaccines get failed. This is associated with child growth with cognitive deficits [7].

This gut microbiota shows the reduced or absent population of certain commensal flora or overgrowth of microbes like Bifidobacteria, Lactobacillus, and Butyrate-producing Clostridia allows immune dysregulation of Bacteroides and Proteobacteria have an overgrowth [8]. Autoimmunity is regulated by gut microbiota [8] and immunity becomes hyperactive. The gut-brain axis is well studied which includes a connection between the vagus nerve, blood-brain barrier, lymphatic system, and newly discovered glymphatic system.

In recent years, it was shown that microbiota plays a significant role in the immune response to injectable and oral vaccines [9]. As soon as vaccination started during the birth of an individual, immune response and microbial community started developing. There is evidence that shows microbiota shows the immune response in both pre-clinical and clinical studies [10].

This microbial mutual relationship plays a critical role in the body's normal functions and maintaining homeostasis. Microbiota continues its work of modulating host immune functions after every vaccine doses. If microbial stimulation is not working there will be misbalanced in the intestinal immune system, i.e. the immune system will not work anatomically and functionally. Basically it is seen IgA and intraepithelial lymphocytes show improper balance in GFmice and more examples are studied [11].

Animal Model for Vaccine Development

Gnotobiotic animal models are the one best example to study gut microbiota on host responses towards vaccines [12]. Gunny pig model studies the effects of probiotics on the gut microbiome composition during human rotavirus (HRV) infection. This resembles human infant donors, so the study is easy to understand the immune response of vaccines in children. Gn models also studied to better understand gut dysbiosis [13-19]. Since pigs are similar to humans in physiologically, anatomically, and immunologically, they are chosen as a good animal model that is used in organ transplant [20]. It is recommended that Guinea pigs will be tested against childhood vaccines like Hepatitis B for being a success which requires microbiota like high proteobacteria, high Bacteroides, reduced or absent Bifidobacteria and lactobacillus, high or protective strains of Clostridia, healthy HGM.

Microbiota will play a continuous source of natural adjuvant which controls innate and adaptive immunity [21]. This endogenous adjuvant potential is being an inactivated influenza vaccine that showed that GF or antibiotic-treated mice had shown significant response [22]. This shows a strong correlation between the expression of TLR5 and the magnitude of the antibody response.

Diet and Microbiota

Nutritious diet directly interacts with microbes to promote or inhibit their growth. Dietary resources make our intestinal bacteria work more properly and efficiently [23,24]. Hence there would be a direct and indirect effect of diet in the microbiota. The nutrients also help in the protective functions of the intestinal barrier in many ways. This will affect the host-microbe interface and dysbiosis occurs.

Covid19 pandemic is the world's largest threatening disease in 2020. Everywhere in the world scientists are trying to combat the disease which appears more challenging. As soon as we understand the mechanism it is better to prepare a vaccine. The presence of SARSCov2 RNA in the stool of some patients and diarrhea suggests that there would be a connection joining the lung and the intestine. It is said that most of the asymptomatic children and adults may shed infectious virus particles in the stool leading to infection in others. The diverse nature of gut microbiota and other necessary microbes in the gut might be playing a significant act in describing the COVID19 disease. The immune-compromised patients mostly elders and patients with type-2 diabetes, cardiovascular disorders play fairly in fighting covid19. A very interesting fact is observed in murine models is that removal of certain gut bacteria by antibiotic leads to increased susceptibility to influenza virus infection in the lungs [25].

Prebiotics/Probiotics

Prebiotic agents are identified and tested in both mice and humans for their capacity to modulate the microbiota for host benefits. For example, whole grains and brown rice improved fecal bacterial diversity increased the firmicutes: Bacteroides ratio [26]. Sometimes medical practices also recommend prebiotics, implying to a microbiota-dependent mechanism for its anti-diabetic properties.

Since gut microbiota is ductile and very easily molded by diet, it can be said that personalized diet strategies could be implemented as a supplementary diet. Most important is that gut microbiota profiling in each and every patient by giving effective and recommended diet specialized with pre/probiotics such as fructooligosaccahride (FOS),

galactooligosaccaherides (GOS), and various lactobacilli strains to improve gut dysbiosis, which will improve the immune response of patients. It is seen that the lung-gut story will work for SARS-CoV-2 infection as most of the patients have respiratory symptoms. It is observed that all the probiotics are not the same, Lactobacilli and Bifidobacteria are the only two types of non-pathogenic bacteria that can balance the gut micro diversity in combating COVID-19 [27]. These are some indirect evidence found in the case of COVID19; still, there is a need to understand more about the SARS-CoV-2 and its effect on gut microbiota [27]. It is likely to be good potential for effective vaccine design for COVID19.

Bioinformatics and Vaccine Design

With the advancement of Next-generation sequencing (NGS) technologies, a new dimension to study microbiota is developed [28]. These studies characterize microbial communities, their specific environment, and interaction with humans. Comprehensive methods like 16S rRNA, short-gun metagenomics, and metatranscriptomics are presently available to study microbiota [29].

- 16S rRNA gene sequence analysis provides taxonomic content and community comparison and similarity analysis.
- In short-gun sequencing: Viromescan is an open-source tool, specifically developed to analyze virome taxonomy. This study will enrich viral reads from the metagenomic dataset and map them on a hierarchical viral data. This step informs the new virus detection for functional analysis of gene prediction. The short-gun metagenomics offers extensive knowledge of genomes of all the microbes consisting of the microbiota.
- Metatranscriptomics is the complete survey of the whole transcriptome of a microbial community. It is a good investigation of gene expression and possible function of the human microbiome in a specific tissue or specific organ with a particular condition [30].

These will reveal information about the human microbiome relation as per health and disease conditions. This study with respect to COVID-19 will better give insights for its prevention and cure. Vaccine efficacy and duration of protection could be highly recommended based on these modern technologies. The present scenario of COVID19 has given us a chance to again study microbes' diversity while vaccine candidate development [27]. Probiotics vaccine adjuvants are in the stage of development. Next generation sequencing, metagenomics and transcriptomics will play significant role in vaccine development of COVID19. As these experimental methods informs the taxonomic diversity and provide the information of microbes as functional profiles with various conditions. These analyses will have the power of showing the host immune response whether cell-mediated or humoral on vaccine. These system biology approaches apply important opportunity to integrate data related to both Microbiome and host response for vaccines. Diet, sex, age will also play a critical role for host- gut microbe interaction with respect to COVID19 [31].

Conclusion

Hence an effective nutritional strategy and particular food habits for each human which can enrich microbiota are the great need of an hour. Covid-19 pandemic teaches us to follow a dietary chart as per the symptoms appear and therapeutics given. Researches need to be conducted to examine the effect of COVID-19 on microbiota profiling especially gut microbes. Not only bacteria, fungi, and phages are also the gut niche. Lung microbiota is really needed to be investigated. These studies may further improve the way of Vaccine design against COVID19 and play a crucial role in taking pivotal measures in the near future. And it is the most exciting area of research this will open new insights for medicines in the modern world. Moreover very soon precision nutrition will be provided to each and every infected person.

References

1. Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R, et al. (2020) COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. Journal of Advanced Research 24: 91-98.

2. Hallander HO, Paniagua M, Espinoza F, Askelof P, Corrales E, et al. (2002) Calibrated serological techniques demonstrate significant different serum response rates to an oral killed cholera vaccine between Swedish and Nicaraguan children. Vaccine 21(1-2): 138-145.

3. Grassly NC, Jafari H, Bahl S, Durrani S, Wenger J, et al. (2009) Mucosal immunity after vaccination with monovalent and trivalent oral poliovirus vaccine in India. J Infect Dis 200(5): 794-801.

4. Seekatz AM, Panda A, Rasko DA, Toapanta FR, Eloe-Fadrosh EA, et al. (2013) Differential response of the cynomolgus macaques gut microbiota to Shigella infection. PLos One 8(6).

5. Huda MN, Lewis Z, Kalanetra KM, Rashid M, Ahmad SM, et al. (2014) Stool microbiota and vaccine responses of infants. Pediatrics 134(2): e362-372.

6. Collins N, Belkaid Y (2017) Do the microbiota influence vaccines and protective immunity to pathogens? Engaging our endogenous adjuvants. Cold Spring Harbor Perspectives Biology 10(2).

7. Watanabe K, William AP (2016) Environmental enteropathy: Elusive but significant subclinical abnormalities in developing countries. EBio Medicine 10: 25-32.

8. Xavier RJ, Vatanen T, Kostic AD, Siljander H, Franzosa EA, et al. (2016) Variation in microbiome Lps immunogenicity contributes to autoimmunity on Humans. Cell 165(4): 842-53.

9. Lynn DJ, Pulendrin B (2017) The potential of the microbiota to influence vaccine responses. J Leukoc Biol 103(2): 225-231.

10. Ciabitini A, Olivier R, Laazzari E, Medalini D (2019) Role of the Microbiota in the Modulation of Vaccine Immune Responses. Front Microbiol 10: 1305.

11. Aguiar-Pulido V, Huang W, Suarez-Ulloa V, Cickovski T, Mathee K, et al. (2016). Metagenomics, metatranscriptomics, andmetabolomics approaches for microbiome analysis. Evol Bioinform Online 12(Suppl 1): 5-16.

12. Dhar D, Mohanty A, (2020) Gut microbiota and Covid-19-possible link and implications. Virus Research 285: 198018.

13. Cram JA, Hager KW, Kublin JG (2018) Utilizing gnotobiotic models to inform the role of the microbiome in vaccine response heterogeneity. Curr Opin HIV AIDS 13(1): 1-8.

14. Wang H, Gao K, Wen K, Allen IC, Li G, et al. (2016) *Lactobacillus rhamnosus* GG modulates innate signaling pathway and cytokine responses to rotavirus vaccine in intestinal mononuclear cells of gnotobiotic pigs transplanted with human gut microbiota. BMC Microbiology 16: 109.

15. Wen K, Tin C, Wang H, Yang X, Li G, et al. (2014) Probiotic *Lactobacillus Rhamnosus* GG enhanced Th1 cellular immunity but did not affect antibody responses in a human gut microbiota transplanted neonatal gnotobiotic Pig model. PLos One 9(4): e94504.

16. Zhang H, Wang , H, H, Shepherd M, Wen K, Li G, et al. (2014) Probiotics and virulent human rotavirus modulate the transplanted human gut microbiota in gnotobiotic pigs. Gut Pathog 6: 39.

17. Liu F, Li G, Wen K, Wu S, Zhang Y, et al. (2013) *Lactobacillus Rhamnosus* GG on rotavirus-induced injury of ileal epithelium in gnotobiotic pigs. J Pediatr Gastroenterol Nutr 57(6): 750-758.

18. Hogenova HT, Stepankova R, Kozáková H, Hudcovic T, Vannucci L, et al. (2011) The role of gut microbiota (commensal bacteria) and the mucosal barrier in the pathogenesis of inflammatory and autoimmune diseases and cancer: contribution of germ free and gnotobiotic animal models of human diseases. Cell Mol Immunol 8(2): 110-120.

19. Planer JD, Peng Y, Kau AL, Blanton LV, Ndao IM, et al. (2016) Development of the gut microbiota and mucosal IgA responses in twins and gnotobiotic mice. Nature 534(7606): 263-266.

20. Saif LJ, Ward LA, Yuan L, Rosen BI, To TL, et al. (1996) The gnotobiotic piglet as a model for studies of disease pathogenesis and immunity to human rotaviruses. Arch Virol Suppl 12: 153-161.

21. Schirmer M, Smeekens SP, Vlamakis H, Jaeger M, Oosting M, et al. (2016) Linking the human gut microbiome to inflammatory cytokine production capacity. Cell 167(4): 1125-1136.

22. Cantarel BL, Lombard V, Henrissat B (2012) Complex carbohydrate utilization by the healthy human microbiome. PLOS One 7(6): e28742.

23. Nakaya HI, Clutterbuck E, Kazmin D, Wang L, Cortese M, et al (2016) System Biology of immunity to MF59-adjuvanted verses nonadjuvanted trivalent seasonal influenza vaccines in early childhood. Proc Natl Acad Sci USA 113(7): 1853-1858.

24. Pabst O, Honerf M (2014) Gut microbiota: a natural adjuvant for vaccination. Immunity 41(3): 349-351.

25. Eilam O, Zarecki R, Oberhardt M, Ursell LK, Kupiec M, et al. (2014) Glycan degradation analysis predicts mammalian gut microbiota abundance and host diet-specific adaptation. mBio 5(4): e01526-14.

26. Loof T, Allen HK (2012) Collateral effects of antibiotics on mammalian gut microbiomes. Gut Microbes. 3(5): 463-467.

27. Martinez I, Lattimer JM, Hubach KL, Case JA, Yang J, et al. (2013) Gut microbiome composition is linked to whole grain-induced immunological improvements. ISME J 7(2): 269-280.

28. Chen X, Liu H, Zhao Qi (2020) Editorial: Bioinformatics in Microbiota. Frontiers in Microbiology 11: 100.

29. D'Argenio V (2018) Human Microbiome Acquisition and Bioinformatics Challenges in Metagenomic Studies. Int J Mol Sci 19(2): 383.

30. Twitchell EL, Tin C, Wen K, Zhang H, Becker-Dreps S, et al. (2016) Modeling human enteric dysbiosis and rotavirus

immunity in gnotobiotic pigs. Gut Pathogens 8: 51.

31. Mak WYJ, Chan FKL, Ng SC (2020) Probiotics and COVID-19: one size does not fit all. Lancet Gastroenterol Hepatol 5(7): 644-645.