Dynamic changes in host immune system and gut microbiota are associated with the production of SARS-CoV-2 antibodies

Recently, we read the article by Ng et al with great interest, which identified several gut microbiota harbour the
potential to improve immune response and reduce adverse events following COVID-19 vaccines, and demonstrated that gut microbiota has the potential to complement the effectiveness of vaccines. Together with several recent studies, gut microbiota plays a key role in modulating immune responses of vaccination and is related to the severity of COVID-19 pandemic.

Furthermore, the comparison of the gut microbiota of healthy individuals who vaccinated with Sinovac vaccine and COVID-19 patients with different clinical diagnoses, without accounting for factors such as age, suggest that the alterations of gut microbiota during vaccination were not as substantial as those caused by SARS-CoV-2 infection (figure 1J).

Finally, our results showed that the correlations among gut microbiota, cytokines, lymphocytes and SARS-CoV-2 antibodies (figure 1K and online supplemental figures 2, 3). In particular, we found that several gut microorganisms have a significant association with SARS-CoV-2 antibodies production. For example, Prevotella copri was negatively correlated with IgG, whereas Clostridiurn leptum, Lactobacillus ruminis, Rumina-coccus torques, etc, presented a positive correlation with antibodies production (all p<0.01, figure 1K). Moreover, a variation partitioning analysis based on the metadata of body features and the compositions of gut microbial communities was performed, which showed that the production of antibodies is mainly affected by the gut microbiome (22%) and body features (18%, online supplemental table 5, online supplemental figure 4). These results suggest that gut microbiota plays an important role in the production of SARS-CoV-2 antibodies in young healthy individuals and the dynamic changes of immune system and gut microbiota and their associations with the production of SARS-CoV-2 antibodies in elderly population remain elusive and should be further investigated.

Overall, our study systematically investigated the dynamic changes of host, including lymphocytes, cytokines, gut microbiota and antibodies, and linked these factors to the production of antibodies. Our results provide an optional perspective for evaluating the safety and effectiveness of SARS-CoV-2 vaccines and settling the treatment of COVID-19 patients, and can alleviate the public’s concerns and fears about the vaccination.

Maozhen Han, Yixuan Huang, Hongya Gui, Xiyuan Xiao, Maozhang He, Jing Li, Xiujing Cao, Meijuan Zheng, Min Lu, Weihua Jia, Hui Li, Xiaoyan Wang, Na Zhang, Shu-an Kong, Xiaohui Liu, Yongguo Wu, Fengcheng Wu, Shenghai Huang.

1School of Life Sciences, Anhui Medical University, Hefei, Anhui, China
2Department of Clinical Medicine, The First School of Clinical Medicine, Anhui Medical University, Hefei, Anhui, China
3Department of Microbiology, The Key Laboratory of Microbiology and Parasitology of Anhui Province, The Key Laboratory of Zoonoses of High Institutions in Anhui, School of Basic Medical Sciences, Anhui Medical University, Hefei, Anhui, China
4Department of Epidemiology and Biostatistics, School of Public Health, Anhui Medical University, Hefei, Anhui, China
5Department of Clinical Laboratory, The First Affiliated Hospital of Anhui Medical University, Hefei, Anhui, China
6Hefei City Maternal and Child Health & Family Planning Service Center, Hefei, Anhui, China
7Department of Pediatrics, The First Affiliated Hospital of Anhui Medical University, Hefei, Anhui, China
8State Key Laboratory of Environmental Criteria and Risk Assessment, Chinese Research Academy of Environmental Sciences, Beijing, China
9Department of Nephropathy, The First Affiliated Hospital of Anhui Medical University, Hefei, Anhui, China

Correspondence to Professor Shenghai Huang; huangshh68@aliyun.com; Professor Fengcheng Wu; wufengcheng@vip.sjep.cn; Professor Yongguo Wu; wuyonggui@163.com

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Contributors. MHa and SH designed the study. MH, WJ and SH recruited the healthy volunteers from School of Life Sciences, Anhui Medical University. MHa, YX, MHe, HL, XL, NZ and SK collected the blood and fecal samples. MHa, YH, HG, YY, NZ and XC analysed the data of indicators obtained from routine blood tests, lymphocytes, cytokines and metagenomic sequencing data. HL and ML conducted the measurement of the indicators obtained from routine blood tests, lymphocytes and cytokines. MHa, YW, FW and SH organised the structure of the manuscript. MH, YH, HG and YY wrote the initial draft of the manuscript. All authors read, modified and approved the final manuscript.

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Figure 1  The response of healthy individuals during the vaccination of two dose of SARS-CoV-2 vaccine and the interplay between host immune systems and gut microbiota that contributes to the production of SARS-CoV-2 antibodies. (A) Study design for collecting the faecal and blood samples from 30 healthy individuals to explore the dynamics changes of host immune systems, gut microbiota and the production of SARS-CoV-2 antibodies. Dynamic changes in SARS-CoV-2 antibodies, cytokines, lymphocytes and indicators obtained from routine blood tests. (B) Concentrations of IgA, IgG and IgM detected at different time points during the vaccination process. The differences between different time-points were assessed by two-way ANOVA, and two-sided exact p values are reported. (C) Concentrations of IFN-γ, IL-2 and IL-4 measured at different time points during the vaccination process. (D) The levels of NK cells, B cells and CD4+T cells and the CD4+/CD8+ ratio are illustrated in chronological order. (E) Dynamic changes in the counts of white cell count, neutrophils (Neu), lymphocyte (Lym), monocytes (Mon) and eosinophils (EOSs) during the vaccination process. (F) The alpha diversities, including the Shannon and Simpson indices, of the human gut microbial communities did not significantly differ among different time points during the vaccination process. (G) A significant difference in the human gut microbial compositions was found among different time points during the vaccination process according to their Bray-Curtis dissimilarity at the species level. (H) Based on the taxonomic compositions of all 143 samples at the species level, LDA can successfully separate the human gut microbial communities at different time points during the vaccination process. (I) Compositional differences in the gut microbiota among different time points during the vaccination process visualised with the average relative abundances at the phylum level. (J) Comparison of the taxonomic structure of the human gut microbiota among unvaccinated healthy individuals, healthy individuals at different time points during the vaccination process, and COVID-19 patients with different clinical diagnoses. (K) Correlations between the production of antibodies against SARS-CoV-2 and gut microbiota.* p<0.05; ** p<0.01; *** p<0.001; ANOVA, analysis of variance; LDA, linear discriminant analysis.
informed consent to participate in the study before taking part.

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ORCID IDs Maozhen Han http://orcid.org/0000-0002-5958-1941
Shenghai Huang http://orcid.org/0000-0002-5699-8928

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