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Supplemental information

Correlation of gut microbiota and metabolic functions with the antibody response to the BBIBP-CorV vaccine

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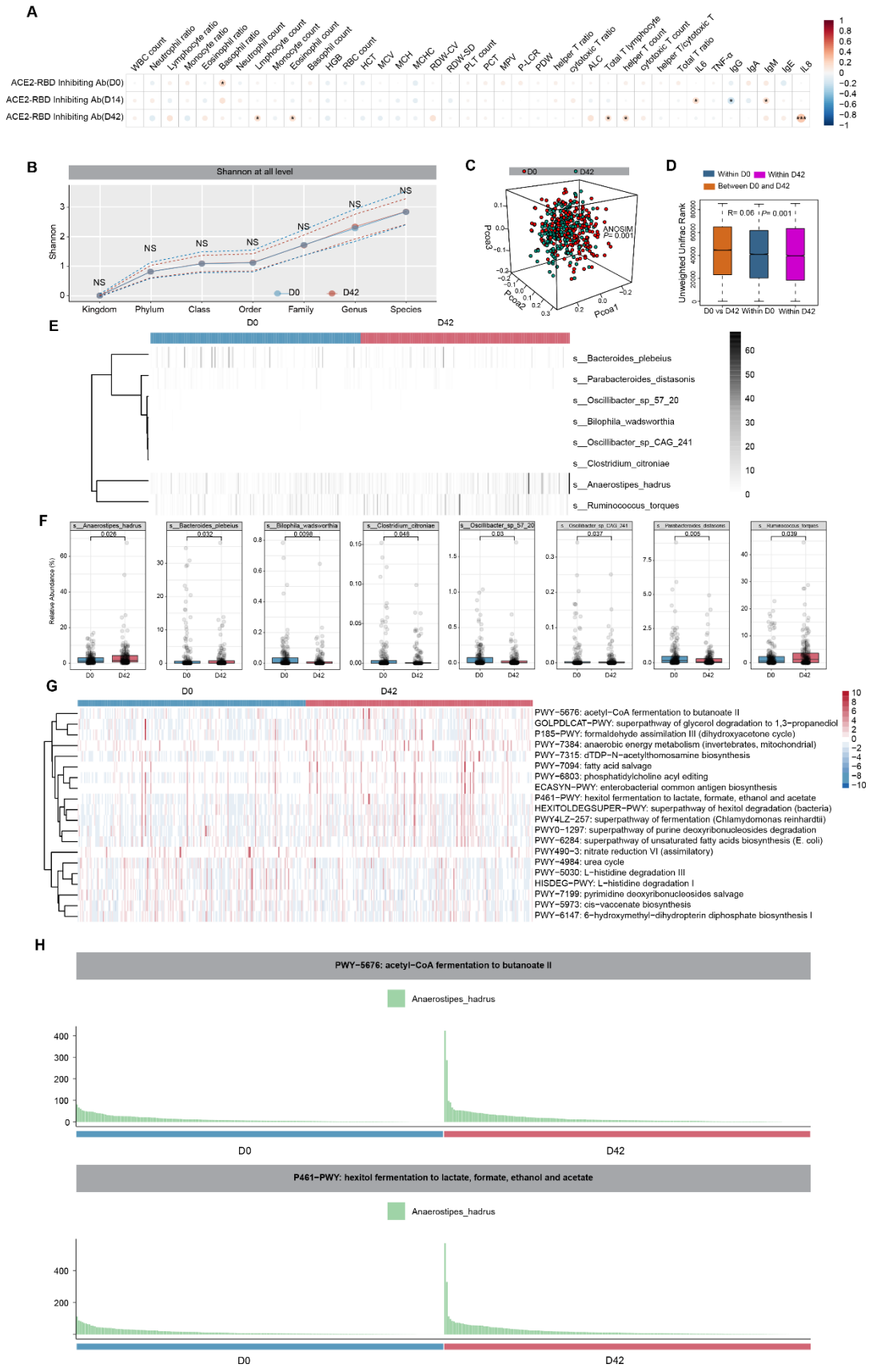

Figure S1. Correlation of clinical characteristics with antibody levels and altered gut microbiome and functional profile, Related to Figure 1 and Figure 2. (A) Correlation heatmap of baseline clinical

characteristics with ACE2-RBD inhibiting antibody levels at different timepoints (D0, D14, D42) (n=207). *P* values were determined by Pearson correlation analysis with FDR corrected. * *P*< 0.05, ***P* <0.01, ****P* < 0.001. (B) Comparison of alpha diversity (Shannon index) in samples at baseline (D0) and samples after the second injection (D42) (n=207). *P* values were determined by Mann-Whitney U test. (C) Unweighted Unifrac 3D PCoA (principal coordinate analysis) plot of samples at baseline (D0) and after the second injection (D42) (n=207). The ANOSIM test was used to calculate the significance of dissimilarity (ANOSIM, *P*=0.001). (D) Comparison of the Unweighted Unifrac range of samples between baseline (D0) and after the second injection (D42) (n=207). The ANOSIM test was used to calculate the significance of dissimilarity (ANOSIM, *P*=0.001). (E) Heatmap of differentially enriched bacteria between baseline samples (D0) and samples after the second injection (D42) (n=207). (F) Boxplots for comparison of the relative abundance of differentially enriched bacteria in baseline samples (D0) and samples after the second injection (D42) (n=207). *P* values were determined by Mann-Whitney U test. (G) Heatmap of differentially enriched MetaCyc pathways between baseline samples (D0) and samples after the second injection (D42) (n=207). *P* values were determined by Mann-Whitney U test. NS, no significance. (H) Contribution of differentially enriched bacteria to microbial pathways between baseline samples (D0) and samples after the second injection (D42) (n=207). The abundance of the microbial pathway was normalized based on relative log expression by DESeq2.

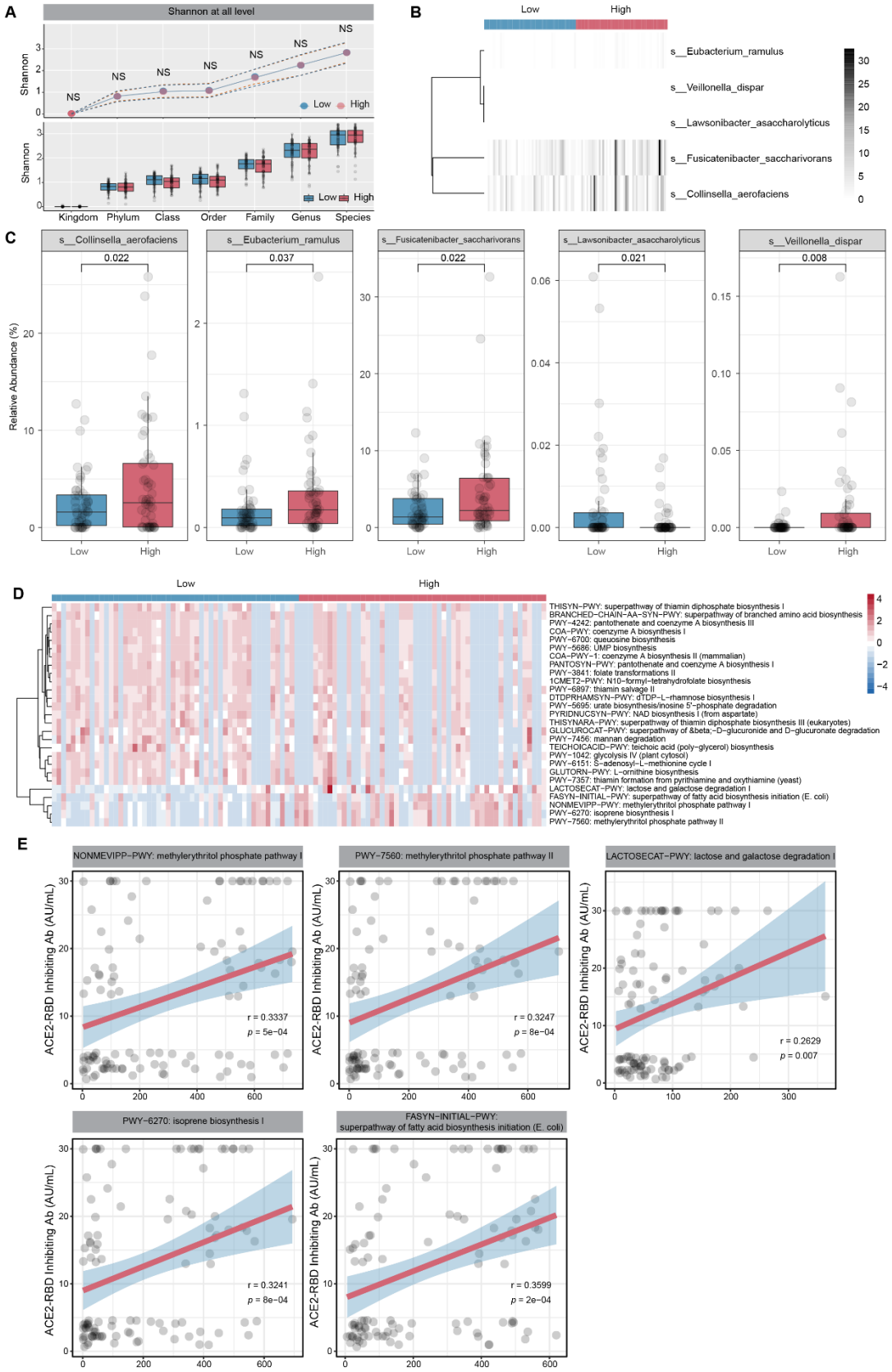

Figure S2. Altered gut microbiome and functional profile between samples of High and Low groups and correlation between MetaCyc pathways and antibody levels, Related to Figure 3. (A)

Comparison of alpha diversity at D0 (Shannon index) in samples from the High and Low groups (Low group, n=52; High group, n=52). *P* values were determined by Mann-Whitney U test. (B) Heatmap of differentially enriched bacteria between samples from the High and Low groups at D0 (Low group, n=52; High group, n=52). (C) Boxplots for comparison of relative abundance of differentially enriched bacteria in samples from the High and Low groups at D0 (Low group, n=52; High group, n=52). *P* values were determined by Mann-Whitney U test. (D) Heatmap of differentially enriched MetaCyc pathways between samples from the High and Low groups at D0 (Low group, n=52; High group, n=52). *P* values were determined by Mann-Whitney U test. (E) Correlation between differentially enriched MetaCyc pathways at D0 and the levels of ACE2-RBD inhibiting antibody at D42 (n=52). *P* values were determined by Pearson correlation analysis.

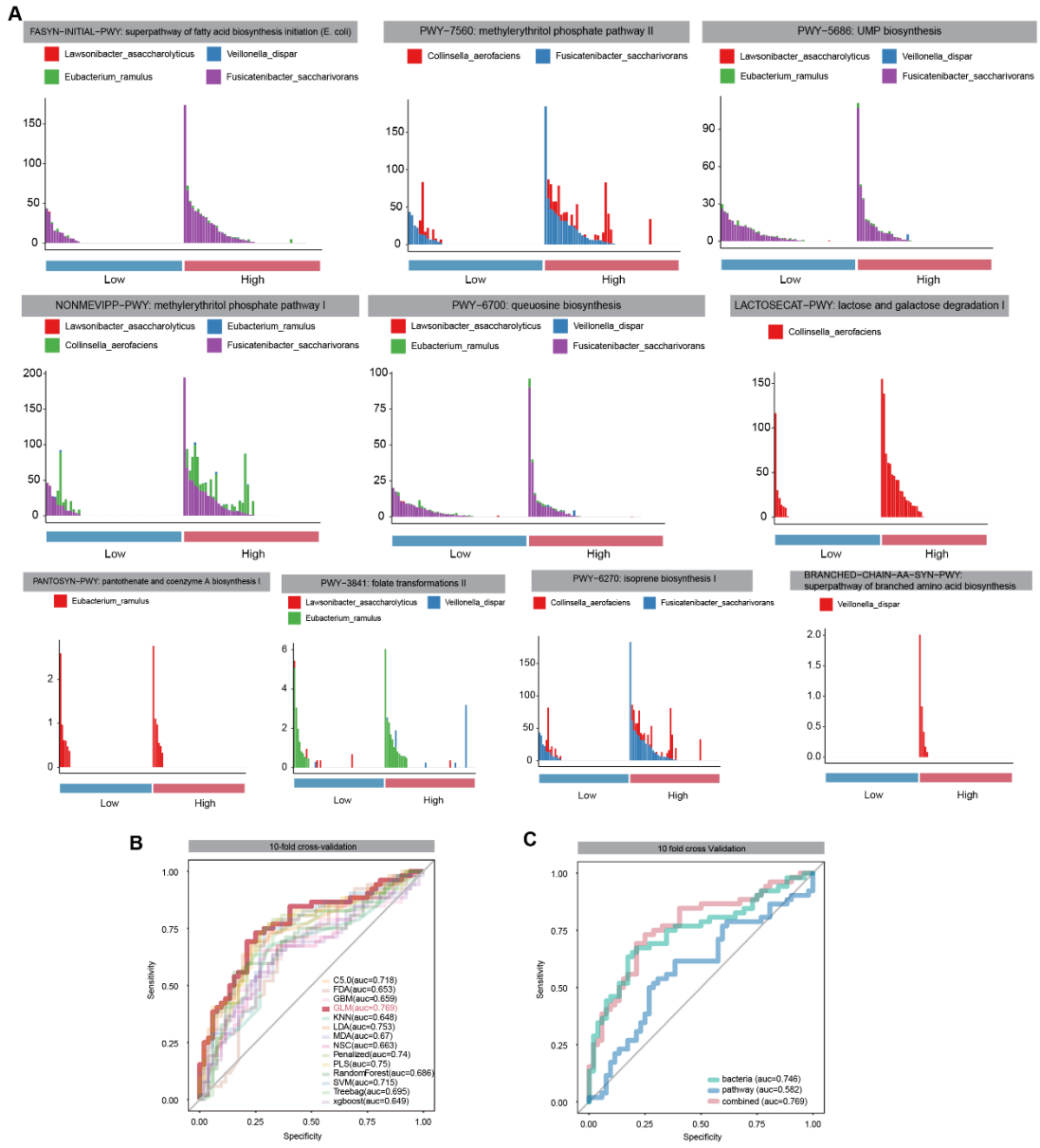

Figure S3. Contribution of differentially enriched bacteria to microbial pathways and role of gut microbial and functional pathways in predicting the antibody response, Related to Figure 3. (A) Contribution of differentially enriched bacteria to microbial pathways between samples of High and Low groups at D0 (Low group, n=52; High group, n=52). The abundance of the microbial pathway was normalized based on relative log expression by DESeq2. (B) ROC curves of different classifiers discriminating the High and Low groups by using differential bacteria and MetaCyc pathways at D0 as independent variables. (C) The ROC curves of the logistic regression models (one of Generalized Linear Models, GLM) for discriminating High and Low groups by using differential bacteria alone (green curve), using differential MetaCyc pathways alone (blue curve) and using combined differential bacteria and MetaCyc pathways (pink curve) at D0 as the independent variable of the model, respectively.

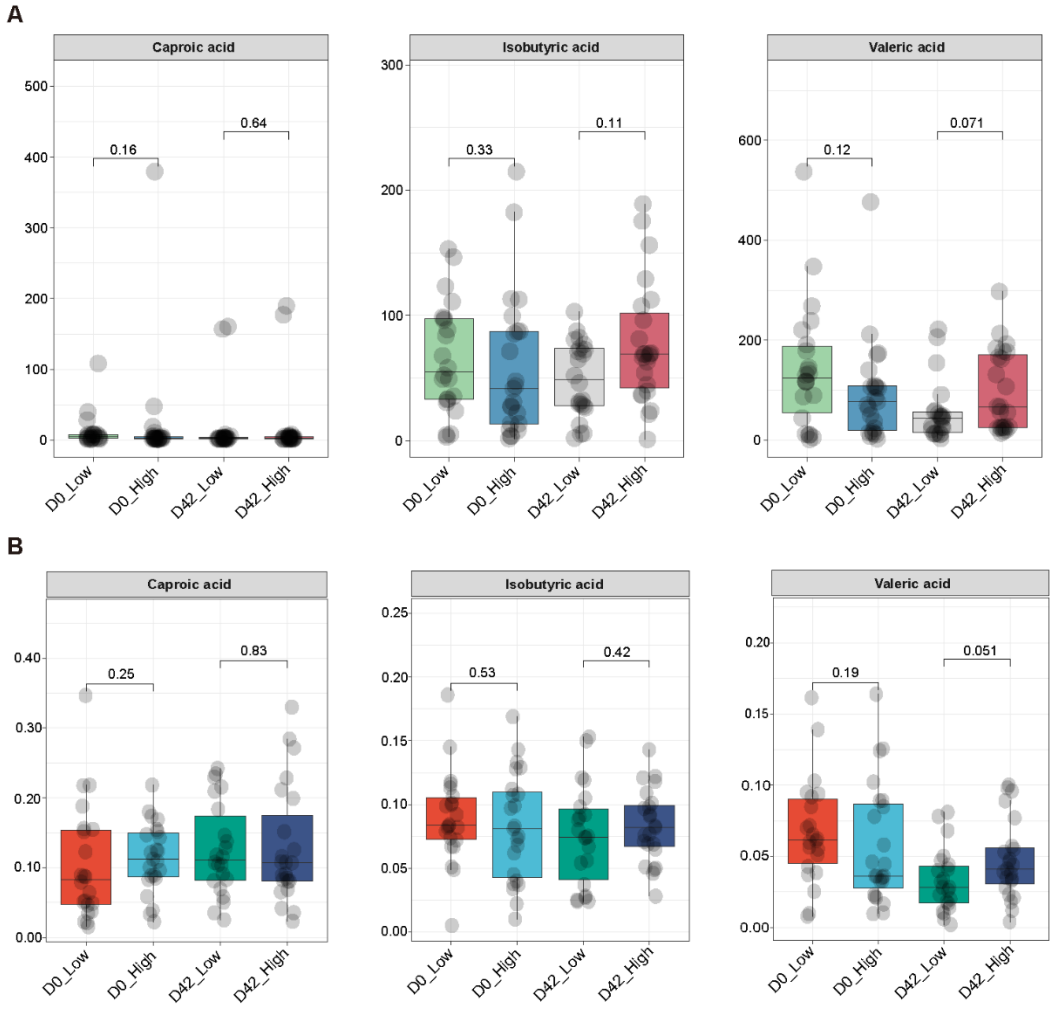

Figure S4. Levels of SCFAs in fecal and serum samples, Related to Figure 4. Boxplots for comparing short-chain fatty acids in fecal (A) and serum (B) samples between High and Low groups at D0 and D42 (Low group, n=52; High group, n=52). Comparisons between subgroups were performed using Mann-Whitney U test.

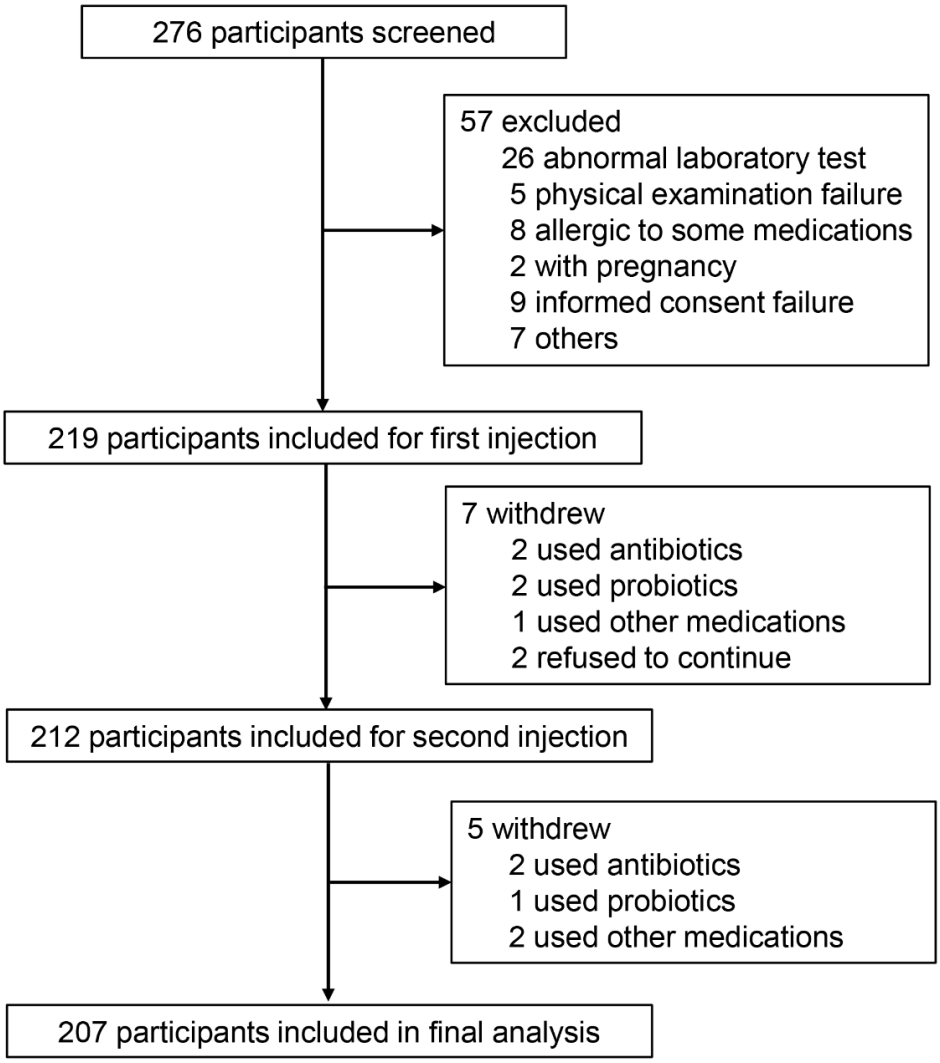

Figure S5. Flow of participants recruitment, Related to STAR Methods. 276 participants were screened. 57 participants were excluded including 26 abnormal laboratory test, 5 physical examination failure, 8 allergic history, 2 with early pregnancy, 9 informed consent failure, and 7 other reasons. 219 participants received the first vaccination, finished all safety visits, and provide blood and fecal samples at indicated timepoint. 7 participants quit the study before the second vaccination (2 with antibiotics use, 2 with probiotics use, 1 with other medications, and 2 refused to continue). 212 participants received the second vaccination and provide blood and fecal samples at indicated timepoint. During the follow-up, 5 participants were withdrawn because of antibiotics, probiotics and other medications use. 207 participants were included in the final analysis.