

Supplementary files



Figure S1. The composition of gut microbiota and discriminative genera observed in pairwise comparisons among juvenile, adult and old groups. (A) Bar plots showing the relative abundance of microbiota of three groups at phylum level. (B) 9 genera attributed to distinguishing adult from oldness. (C) 46 genera were responsible for distinguishing juvenile from adult. (D) 63 genera accounted for distinguishing juvenile from oldness. Differentiating

gut genera identified by LefSe with LDA effect size ≥ 2 and $P \leq 0.05$. Yo, juvenile, $n = 9$; Ad, adult, $n = 12$; Ag, oldness, $n = 15$.

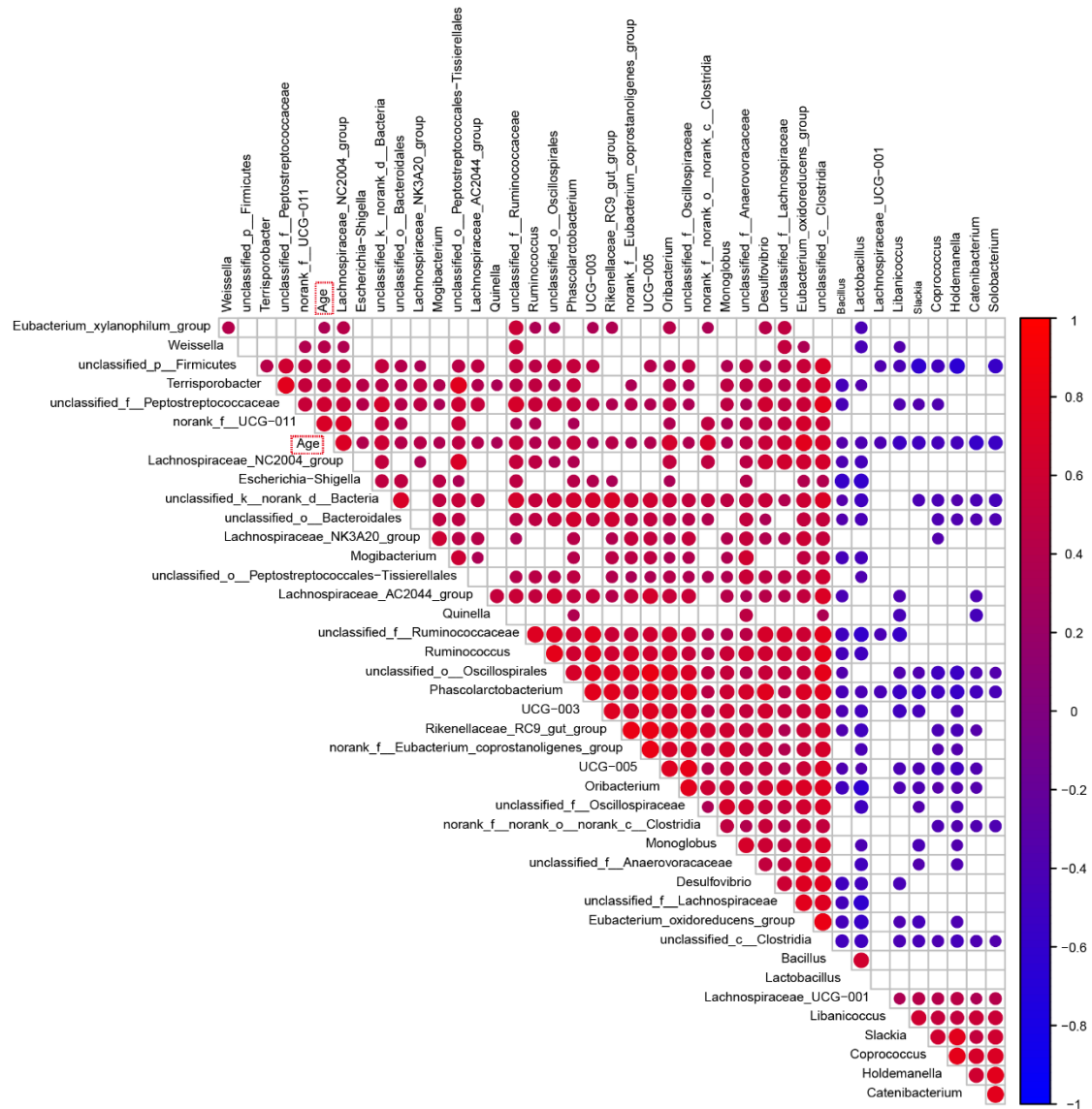


Figure S2. Correlation analysis of differential gut microbiota with age. The microbes used for correlation calculations met the criterion of significant differences between at least two age groups (see Figures S1B-D). In total, there are 41 discriminative microbes significantly correlated with age (the heatmap exclusively displayed age-related microbes). The size and color of each scatter plot point showed the p values of Spearman's correlation and correlation coefficient values (red points represented positive correlations, $P < 0.05$ and $R > 0.3$; blue points represented negative correlations, $P < 0.05$ and $R < -0.3$).

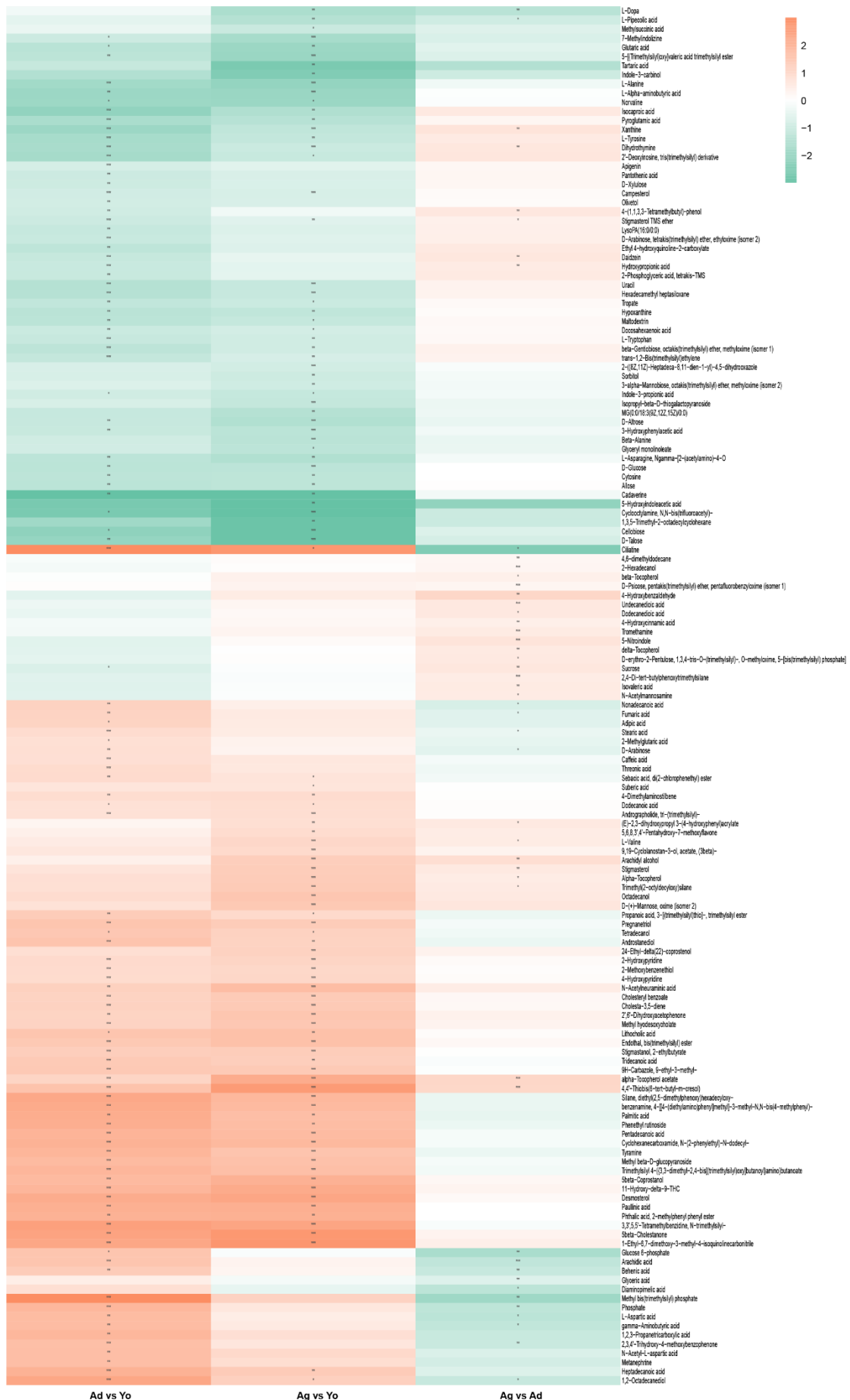


Figure S3. Changes in fecal metabolites discerned from pairwise comparisons among the juvenile, adult, and old groups. A total of 151 fecal metabolites showed significant differences between at least two age groups. The statistical significance was denoted on the squares ($*p < 0.05$ and $VIP > 1$; $**p < 0.01$ and $VIP > 1$; $***p < 0.001$ and $VIP > 1$). In pairwise comparisons, red squares indicate metabolites were significantly up-regulated in the higher-age group (logarithmic transformation of fold change values > 0), while green squares indicate those were significantly down-regulated (logarithmic transformation of fold change values < 0) compared to the lower-age group. Yo, juvenile, $n = 7$; Ad, adult, $n = 10$; Ag, oldness, $n = 13$.

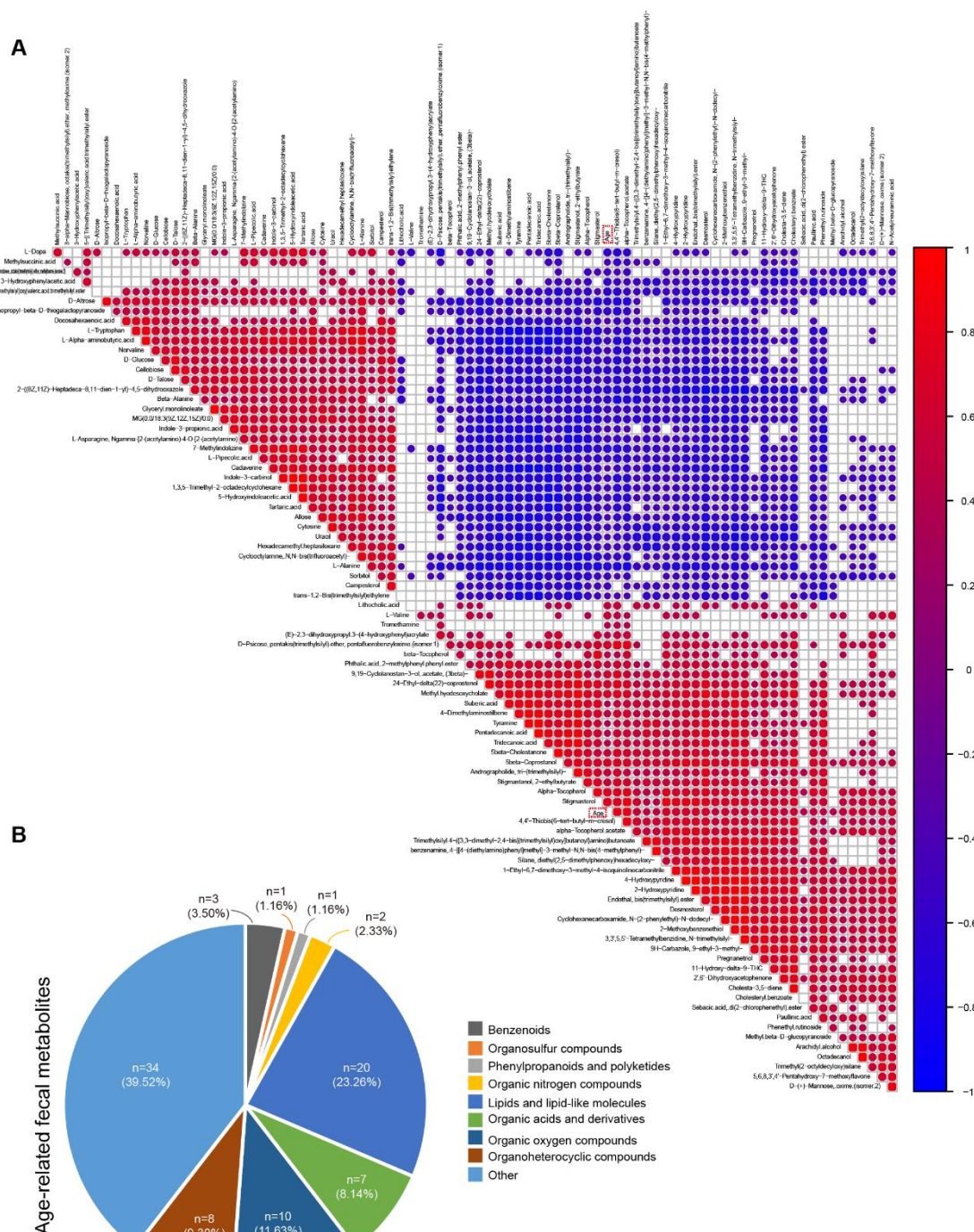


Figure S4. Correlation analysis of differential fecal metabolites with age. The metabolites used for correlation calculations met the criterion of significant differences between at least two age groups (see Figures S2). **(A)** There are a total of 86 differential metabolites significantly correlated with age (the heatmap exclusively displayed age-related metabolites). The size and color of each scatter plot point showed the p values of Spearman's correlation and correlation coefficient values (red points represented positive correlations, $P < 0.05$ and $R > 0.3$; blue points represented negative correlations, $P < 0.05$ and $R < -0.3$). **(B)** A pie chart illustrated the 86 age-related metabolites mainly belong to four categories: lipids and lipid-like molecules, organic oxygen compounds, organic acids and derivatives, and organoheterocyclic compounds.



Figure S5. Alterations in serum metabolites observed in pairwise comparisons among juveniles, adults and old groups. A total of 75 fecal metabolites showed significant differences between at least two age groups. The statistical significance was denoted on the squares (* $p < 0.05$ and $VIP > 1$; ** $p < 0.01$ and $VIP > 1$; *** $p < 0.001$ and $VIP > 1$). In pairwise comparisons, red squares indicate metabolites were significantly up-regulated in the higher-age group (logarithmic transformation of fold change values > 0), while green squares indicate those were significantly down-regulated (logarithmic transformation of fold change values < 0) compared to the lower-age group. Yo, juvenile, $n = 9$; Ad, adult, $n = 12$; Ag, oldness, $n = 15$.

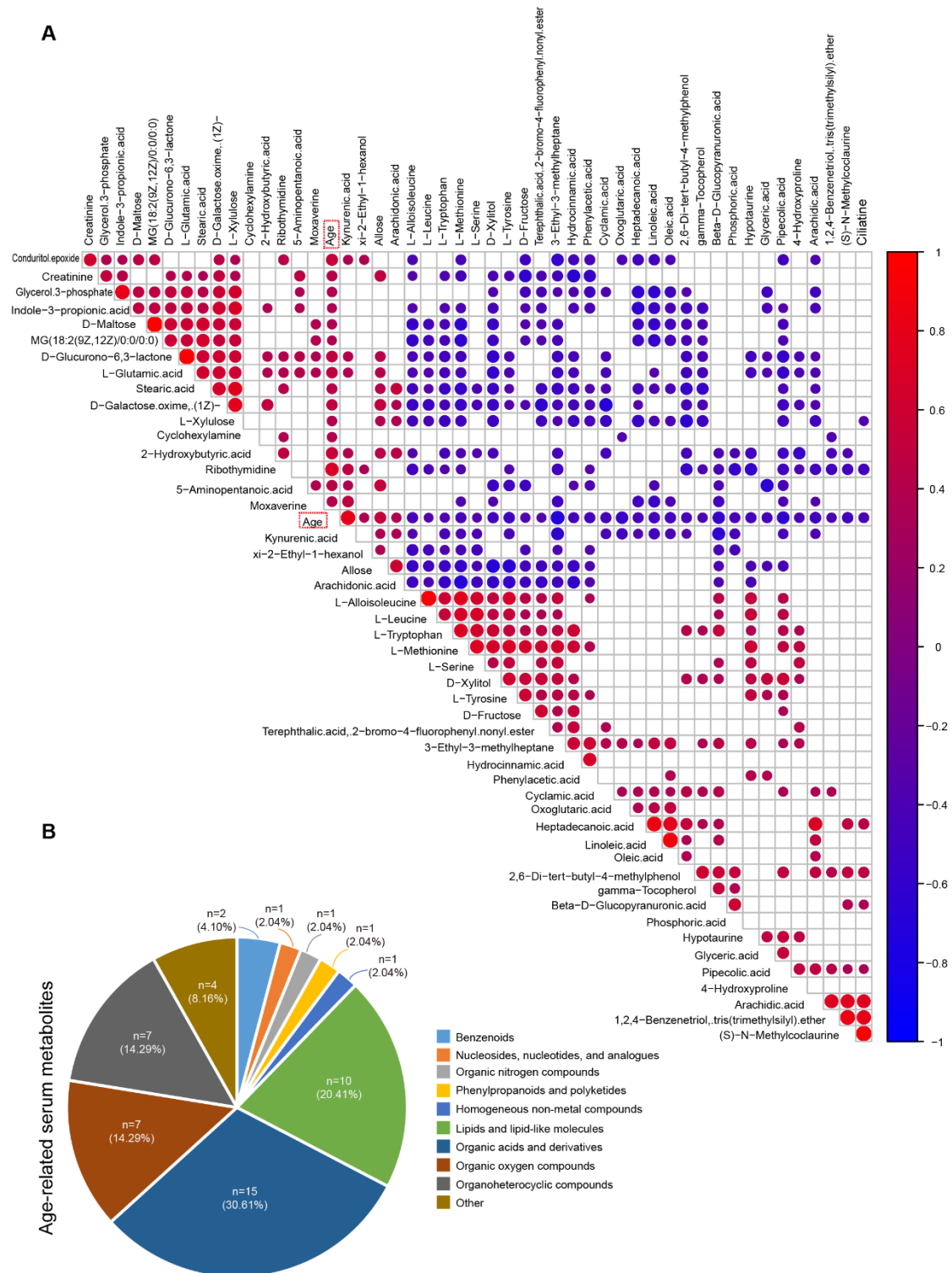


Figure S6. Correlation analysis of differential serum metabolites with age. The metabolites used for correlation calculations met the criterion of significant differences between at least two age groups (see Figures S3). (A) There are a total of 49 differential metabolites significantly correlated with age (the heatmap exclusively displayed age-related metabolites). The size and color of each scatter plot point showed the p values of Spearman's correlation and correlation coefficient values (red points represented positive correlations, $P < 0.05$ and $R > 0.3$; blue points represented negative correlations, $P < 0.05$ and $R < -0.3$). (B) Consistent with the fecal

metabolome, a pie chart revealed the 49 age-related metabolites mainly belong to four categories, which are organic acids and derivatives, lipids and lipid-like molecules, organic oxygen compounds, and organoheterocyclic compounds.

Table S1. The detail characteristics of the recruited rhesus macaques.

Sample ID	Gender	Age	Stage	Dugs-Free #	Health Status #	Host	Geographical Region *
Yo1	Male	3	Juvenile	Yes	Normal	Chinese	Xishan
Yo2	Male	3	Juvenile	Yes	Normal	Chinese	Xishan
Yo3	Male	3	Juvenile	Yes	Normal	Chinese	Xishan
Yo4	Male	3	Juvenile	Yes	Normal	Chinese	Xishan
Yo5	Male	3	Juvenile	Yes	Normal	Chinese	Xishan
Yo6	Male	3	Juvenile	Yes	Normal	Chinese	Xishan
Yo7	Male	3	Juvenile	Yes	Normal	Chinese	Xishan
Yo8	Male	3	Juvenile	Yes	Normal	Chinese	Xishan
Yo9	Male	3	Juvenile	Yes	Normal	Chinese	Xishan
Ad1	Male	9	Adult	Yes	Normal	Chinese	Xishan
Ad2	Male	9	Adult	Yes	Normal	Chinese	Xishan
Ad3	Male	11	Adult	Yes	Normal	Chinese	Xishan
Ad4	Male	11	Adult	Yes	Normal	Chinese	Xishan
Ad5	Male	9	Adult	Yes	Normal	Chinese	Xishan
Ad6	Male	12	Adult	Yes	Normal	Chinese	Xishan
Ad7	Male	13	Adult	Yes	Normal	Chinese	Xishan
Ad8	Male	8	Adult	Yes	Normal	Chinese	Xishan
Ad9	Male	10	Adult	Yes	Normal	Chinese	Xishan
Ad10	Male	10	Adult	Yes	Normal	Chinese	Xishan
Ad11	Male	8	Adult	Yes	Normal	Chinese	Xishan
Ad12	Male	15	Adult	Yes	Normal	Chinese	Xishan
Ag1	Male	26	Elderly	Yes	Normal	Chinese	Xishan
Ag2	Male	20	Elderly	Yes	Normal	Chinese	Xishan
Ag3	Male	23	Elderly	Yes	Normal	Chinese	Xishan
Ag4	Male	26	Elderly	Yes	Normal	Chinese	Xishan
Ag5	Male	16	Elderly	Yes	Normal	Chinese	Xishan
Ag6	Male	24	Elderly	Yes	Normal	Chinese	Xishan
Ag7	Male	23	Elderly	Yes	Normal	Chinese	Xishan
Ag8	Male	25	Elderly	Yes	Normal	Chinese	Xishan
Ag9	Male	23	Elderly	Yes	Normal	Chinese	Xishan
Ag10	Male	22	Elderly	Yes	Normal	Chinese	Xishan
Ag11	Male	24	Elderly	Yes	Normal	Chinese	Xishan
Ag12	Male	23	Elderly	Yes	Normal	Chinese	Xishan
Ag13	Male	22	Elderly	Yes	Normal	Chinese	Xishan
Ag14	Male	18	Elderly	Yes	Normal	Chinese	Xishan
Ag15	Male	16	Elderly	Yes	Normal	Chinese	Xishan

Confirmation based on veterinary diagnosis and quarantine records. * The region is located in the temperate zone and has a subtropical monsoon marine climate (E 120°19' 19"N 31° 07'05").