Supplementary Information for

The Trans-omics Landscape of COVID-19

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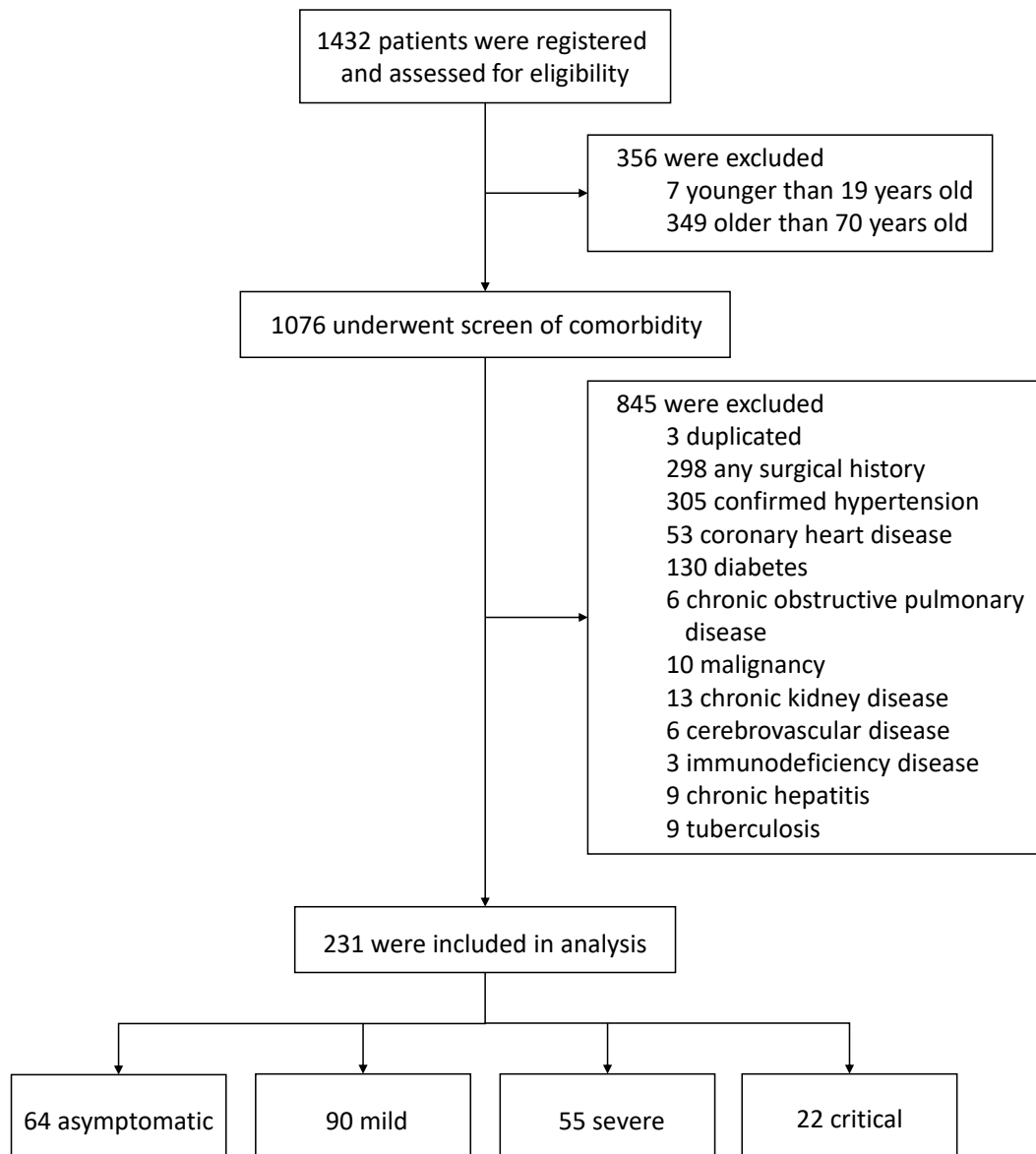
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Supplementary Fig. 1 Study design for multi-omics analysis

All COVID-19 patients (n = 1432) enrolled in this study were screened to exclude those

with selected complications, operation history, or aged younger than 19 or older than

70. After filtering, 231 patients were enrolled and grouped as asymptomatic (n = 64),

mild (n = 90), severe (n = 55), or critical (n = 22). Sample DNA, RNA, and total serum

proteins and lipids were isolated, followed by WGS, RNA-seq, and LC-MS analyses,

respectively, and multi-omics integration analysis.
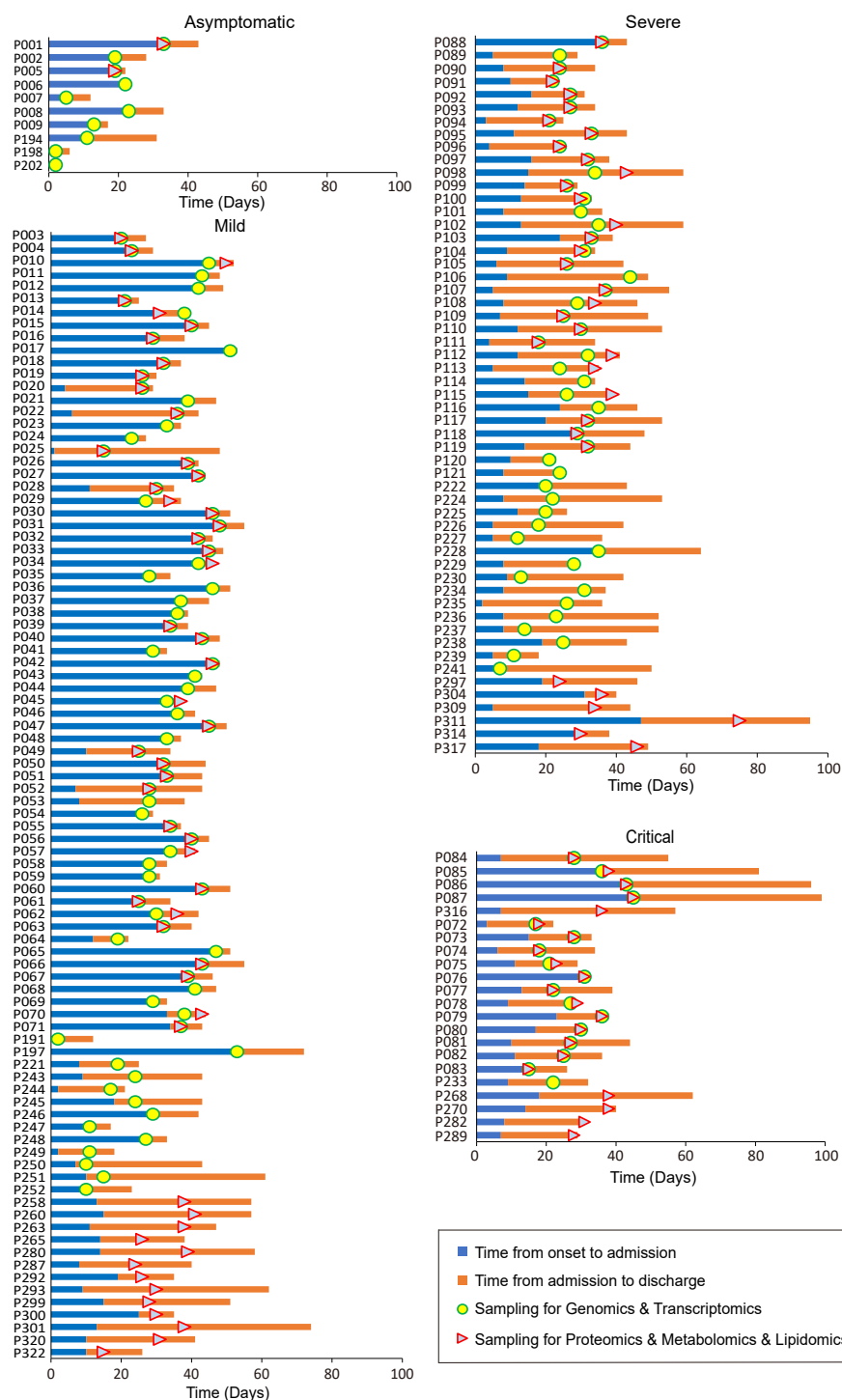
Supplementary Fig. 2 Clinical characteristics of enrolled patients

Summary of clinical characteristics of hospitalized COVID-19 patients, including asymptomatic, mild, severe, and critical. For asymptomatic patients, only 10 were hospitalized, with others diagnosed at the clinic and isolated at home. Patient IDs were labeled along y-axis.
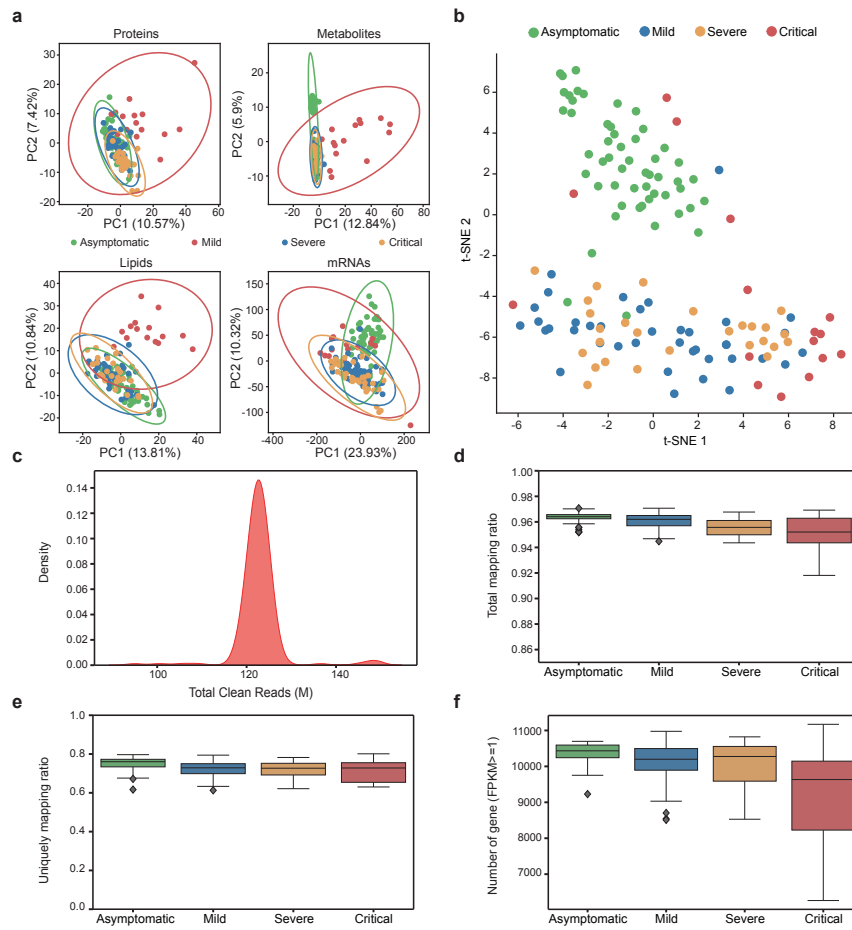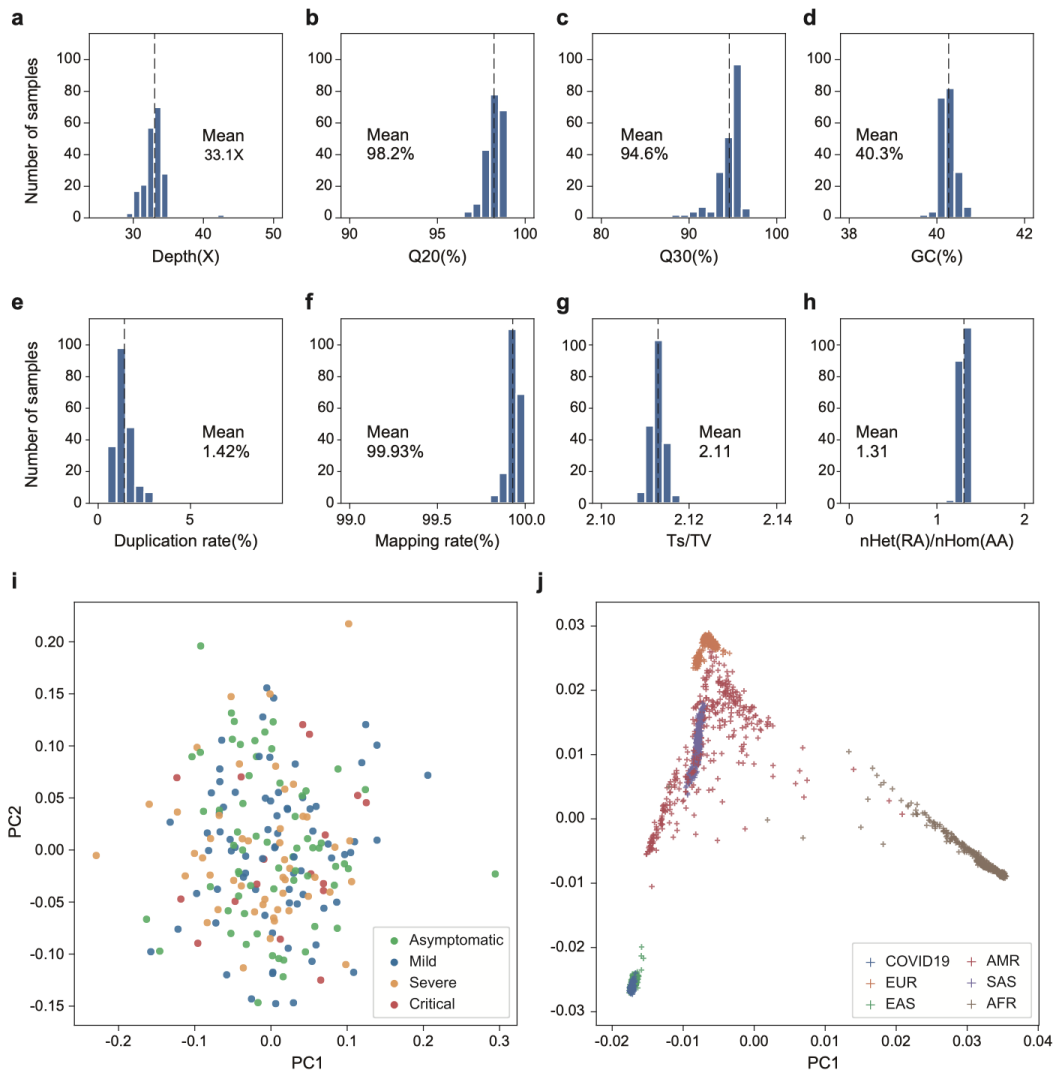
Supplementary Fig. 3 Quality control for data generation

a, Principal component analysis of proteomics, metabolomics, lipidomics, and transcriptomics. The transcriptomics analysis included asymptomatic (n = 64), mild (n = 64), severe (n = 34), and critical (n = 16) COVID-19 patients. The proteins, metabolites, and lipids analysis included asymptomatic (n = 53), mild (n = 54), severe (n = 33), and critical (n = 21) COVID-19 patients. **b,** 2D visualization of all multi-omics analytes using t-distributed stochastic neighbor embedding (tSNE) algorithm. Each dot represents a single sample. **c,** Density plot of total clean reads for all samples. **d,** Boxplot of total mapping ratio across four disease groups. **e,** Unique mapping ratio. **f,** Boxplot of detected gene numbers (FPKM ≥ 1) across four disease groups. The bold lines, upper boundaries and lower boundaries of notches represent the medians, 75th percentiles and 25th percentiles, respectively. Whiskers extend 1.5 times interquartile range (IQR). Data beyond the whiskers are considered as outliers and plotted as individual points.
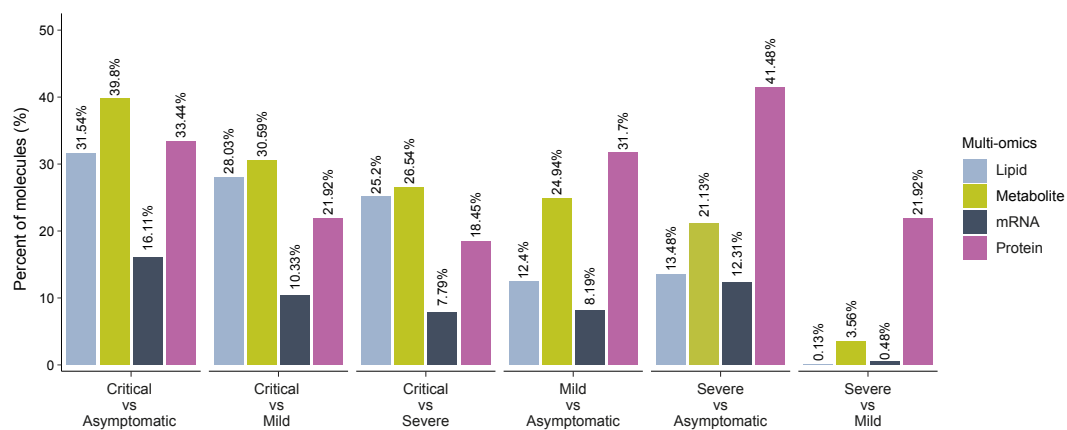
Supplementary Fig. 4 Bar graph representing proportion of analytes across molecule types showing significant differential expression between any two disease statuses

**Supplementary Fig. 5 Quality control of 203 sequenced genomes and principal component analysis (PCA)**

a-f, Quality control matrix for genome sequencing and mapping. **g-h,** Ratio of transitions to transversions (Ts/Tv) and ratio of heterozygous sites to non-reference homozygous sites for each patient. **i,** PCA based on genotype of 203 unrelated individuals, showing PC1 vs. PC2. **j,** PCA together with 2504 individuals from 1000 Genome Project, with all 203 COVID-19 patients grouped within the East Asian population.
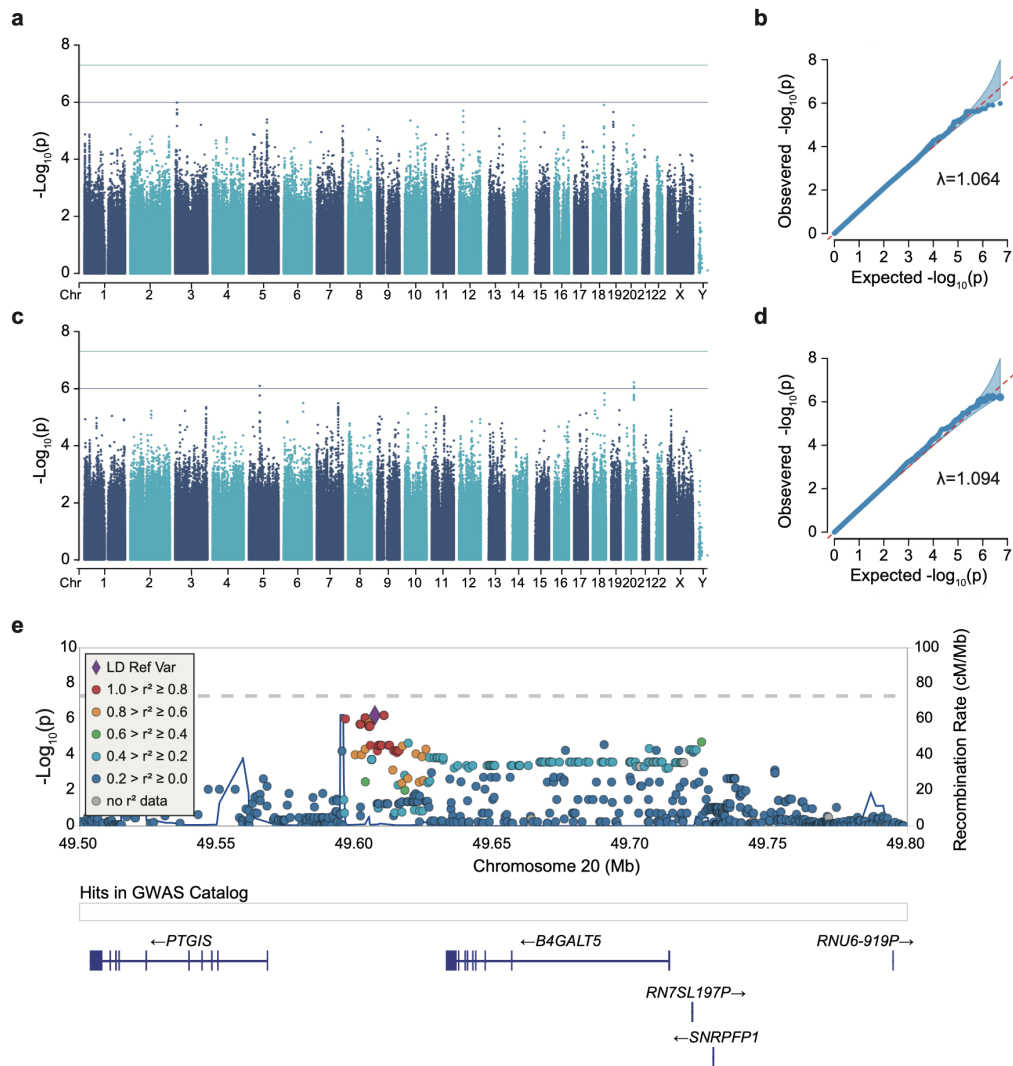
Supplementary Fig. 6 Association study results

Single-variant association test for common variants (MAF > 0.05). **a,** Manhattan plot and **b,** QQ-plot for severe and critical groups (n = 65) versus asymptomatic and mild groups (n = 138). P values were calculated using two-sided score test. **c,** Manhattan plot and **d,** QQ-plot for asymptomatic group (n = 63) versus symptomatic groups (n = 140). P values were calculated using two-sided score test. **e,** Locus zoom for genomic region flanking suggestive signal associated with absence of symptoms: showing chr20:49.5M-49.8M.
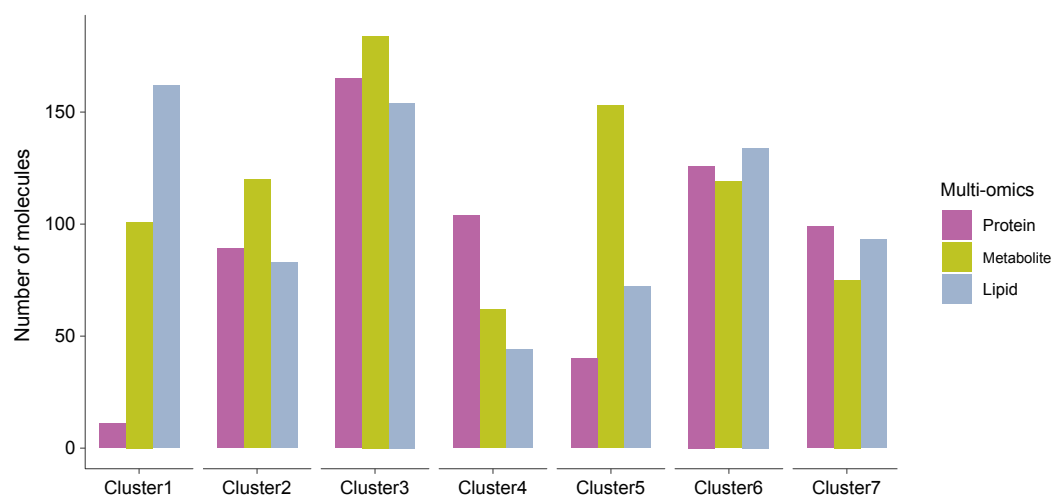
Supplementary Fig. 7 Cluster composition of proteins, metabolites, and lipids