Supplementary figure S1: Vaccination interval and the levels of SARS-CoV-2-specific antibodies induced by CoronaVac vaccine

Effect of different time intervals between the primary and second dose on the levels of SARS-CoV-2 IgM, IgG, IgA and nAb at 2 weeks after the 2nd dose of vaccine (T3) (A) and 2 weeks after the 3rd dose of vaccine (T5) (B). Each dot represents an individual subject. Bars represent the mean values with SEM. Statistics were calculated using Mann-Whitney U test (A, B). *P < 0.05; **P < 0.01; ns, not significant.
Supplementary figure S2: Polyclonal circulating CD4\(^+\) T cells.

(A) Representative plots illustrate the gating strategy of polyclonal CD4\(^+\) T cells. Lymphocytes were first gated, and doublets were excluded by FSC-H and FSC-A signals. Live cells were
identified by 7-AAD. CD4⁺ T cells were gated on CD3⁺CD19⁻TCRγδ⁻ cells. In particular, EM (CD45RA⁻CCR7⁻), CM (CD45RA⁻CCR7⁺) and naïve cells (CD45RA⁺CCR7⁺) are defined accordingly. T_REG (CD25⁺CD127low) and T_FR (CD25⁺CD127lowCXCR5⁺PD-1⁺) cells are gated accordingly. CD25 negative cells can be divided into cT_FH (CD45RA⁻CXCR5⁻) cells and T_H (CD45RA⁺CXCR5⁻) cells. Based on the expression of CXCR3 and CCR6, cT_FH cells were further divided into cT_FH1 (CXCR3⁺CCR6⁻), cT_FH2 (CXCR3⁻CCR6⁻) and cT_FH17 (CXCR3⁻CCR6⁺) cells, while T_H cells were divided into T_H1 (CXCR3⁺CCR6⁻), T_H2 (CXCR3⁻CCR6⁻), and T_H17 (CXCR3⁻CCR6⁺) cells. Longitudinal dynamics of polyclonal T_H1, T_H2, T_H17 (B) and T_REG (C) cells during three doses of vaccines at five timepoints. Each dot represents an individual subject. Bars represent the mean values with SEM. Statistics were calculated using Wilcoxon matched-pairs signed rank for comparison between timepoints (B, C). *, *P < 0.05; **, *P < 0.01; ***, *P < 0.001; ****, *P < 0.0001; ns, not significant.
Supplementary figure S3: Gating-strategy for spike-specific CD4$^+$ T and cTFH cells.

PBMCs were stimulated with SARS-CoV-2 spike protein (S1+S2, 2 ug/mL, SinoBiological) for 24h. Representative plots illustrate the gating strategy. CD4$^+$ T cells were driven from CD3$^+$CD19$^-$TCR$^{\gamma\delta}$ gating. Spike-specific CD4$^+$ T cells and spike-specific cTFH cells were defined as HLA-DR$^+$CD25$^+$CD4$^+$ and CXCR5$^+$ HLA-DR$^+$CD25$^+$CD4$^+$, respectively. Spike-specific CD4$^+$ T cells were further divided into memory and naïve cells. Spike-specific cTFH cells were further divided into cTFH1, cTFH2 and cTFH17 cells according to the expression of surface molecules CXCR3 and CCR6, and divided into AIM$^+$ cTFH-CM and cTFH-EM cells by CCR7 and PD1.
Supplementary figure S4: Gating-strategy and representative plots for spike-specific CD4\(^+\) T cells using ICS assay.

(A) Representative plots illustrate the gating strategy of spike-specific CD4\(^+\) T cells. CD4\(^+\) T cells were gating from live CD3\(^+\)CD19\(^-\) lymphocytes. T\(_H\)1 cells were defined as CXCR3\(^+\) CCR6\(^-\) CD4\(^+\) T cells. IFN-\(\gamma\)^\(+\) CD4\(^+\) T cells, IL-2\(^+\) CD4\(^+\) T cells, IFN-\(\gamma\)^\(+\) T\(_H\)1, IL-2\(^+\) T\(_H\)1 and IFN-\(\gamma\)^\(+\) IL-2\(^+\) T\(_H\)1 were further gated based on the cytokine production. Representative FACS plots of IFN-\(\gamma\)^\(+\) CD4\(^+\) T cells (B) and IL-2\(^+\) CD4\(^+\) T cells (C) were shown at five time points (T1-T5). DMSO and SEB were used as negative and positive controls, respectively.
Supplementary figure S5: Correlations between polyclonal CD4+ T cells and antibody responses following CoronaVac vaccination.
(A) Correlation heatmaps of the polyclonal CD4$^+$ T cell subsets and SARS-CoV-2 specific antibodies at two weeks post dose 2 (T3) and dose 3 (T5). Correlation analysis between the frequency of polyclonal cT$_{FH}$ cells (B), cT$_{FH}$1 cells (C), cT$_{FH}$2 cells (D), cT$_{FH}$17 cells (E) and SARS-CoV-2-specific IgG, IgM, IgA and nAb titers at two weeks post dose 3 (T5). Each dot represents an individual subject. The non-parametric Spearman’s rank correlation was used (A, B, C, D, E). *$P < 0.05$; **$P < 0.01$ (A). $P$ and R values were indicated (B, C, D, E).