

**Table S1.** Clinical and demographic characteristics of the study cohort

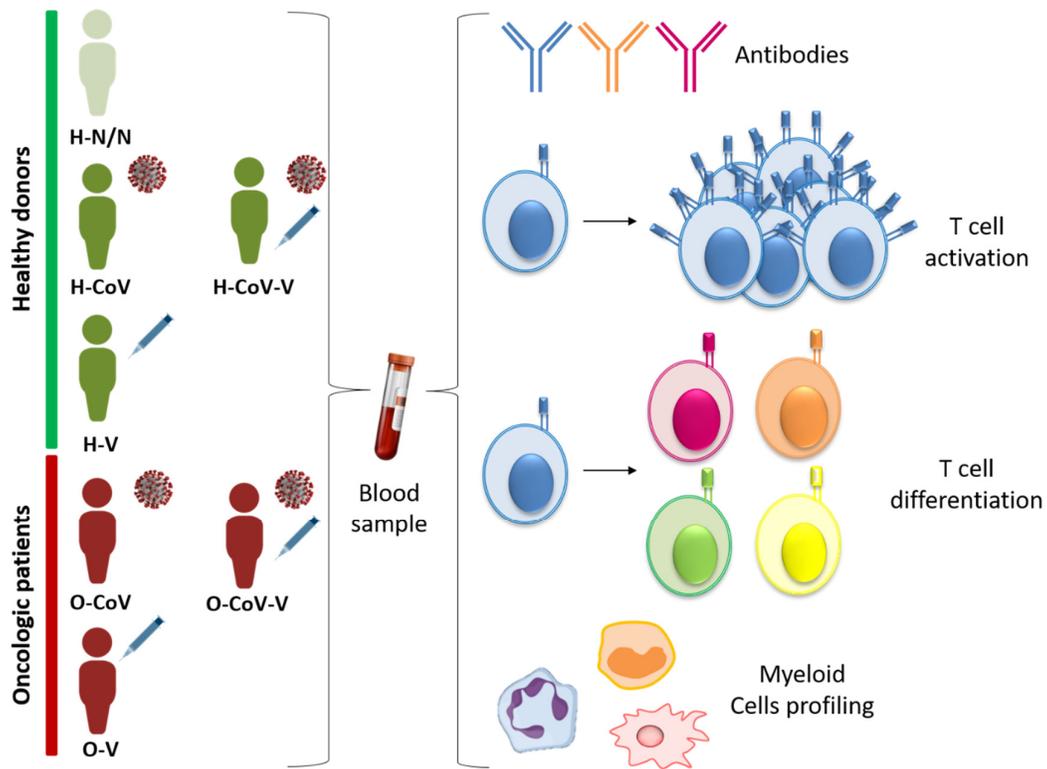
|  |        | Healthy donors   |                  |                 |                        | Oncologic patients  |                |                        |
|--|--------|------------------|------------------|-----------------|------------------------|---|----------------|------------------------|
|  |        | H-N/N<br>(n= 10) | H-CoV<br>(n= 15) | H-V<br>(n = 22) | H-CoV-<br>V<br>(n= 10) | O-CoV<br>(n = 10)   | O-V<br>(n= 20) | O-CoV-<br>V<br>(n =10) |
| Age (median, Q1,Q3)                              |        | 40 (25-58)       | 55 (53-61)       | 55 (42-61)      | 48 (34-61)             | 68 (61-75)  | 65 (60-71)     | 68 (57-74)             |
| Gender (n, %)                                    | Male   | 6 (60)           | 9 (60)           | 2 (9)           | 2 (20)                 | 8 (80)  | 8 (40)         | 5 (50)                 |
|  | Female | 4 (40)           | 6 (40)           | 20 (91)         | 8 (80)                 | 2 (20)  | 12 (60)        | 5 (50)                 |
| Comorbidities (n, %)                             | AHT    | 1 (11)           | 4 (29)           | 2 (9)           | 1 (10)                 | 4 (40)  | 8 (40)         | 6 (60)                 |
|  | DM     | 0 (0)            | 0 (0)            | 0 (0)           | 1 (10)                 | 3 (30)  | 3 (15)         | 3 (30)                 |
|  | DLP    | 1 (11)           | 5 (36)           | 4 (18)          | 2 (20)                 | 7 (70)  | 7 (35)         | 3 (30)                 |
|  | IC     | 0 (0)            | 0 (0)            | 0 (0)           | 0 (0)                  | 3 (30)  | 3 (15)         | 0 (0)                  |
|  | Neumo  | 0 (0)            | 3 (21)           | 1 (4,5)         | 0 (0)                  | 5 (50)  | 4 (20)         | 1 (10)                 |
| Type of cancer (n, %)                            |        |                  |                  |                 |                        | Pancreas<br>Colon/rectum 4 (40); breast 2 (20); pancreas, meso., lung, sarcoma 1 (10)<br>Breast, liver 5 (25); colon/rec tum 3 (15); ovary 2 (10); renal, gastric 1 (5)<br>Breast, pancreas, gastric 2 (20); meso., lung, ovary, salivary glands 1 (10) |                |                        |
| Cancer treatment during sample extraction (n, %) | NT     |                  |                  |                 |                        | 2 (20)  | 5 (25)         | 0 (0)                  |
|  | CT     |                  |                  |                 |                        | 5 (50)  | 10 (50)        | 5 (50)                 |
|  | IT     |                  |                  |                 |                        | 0 (0)   | 0 (0)          | 1 (10)                 |
|  | TKI    |                  |                  |                 |                        | 2 (20)  | 2 (10)         | 2 (20)                 |
|  | CT+TKI |                  |                  |                 |                        | 1 (20)  | 3 (15)         | 2 (20)                 |

CoV, SARS CoV-2 infection; vac, vaccinated; CT, chemotherapy; DLP, dyslipidaemia; DM, diabetes mellitus; AHT, arterial hypertension; IC, ischemic cardiopathy; IT, immunotherapy; meso., mesothelioma; Neumo., neumopathies; NT, non-treated; TKI, tyrosin-kinase inhibitors; Q1, quartile 1; Q3, quartile 3; vac, vaccinated.

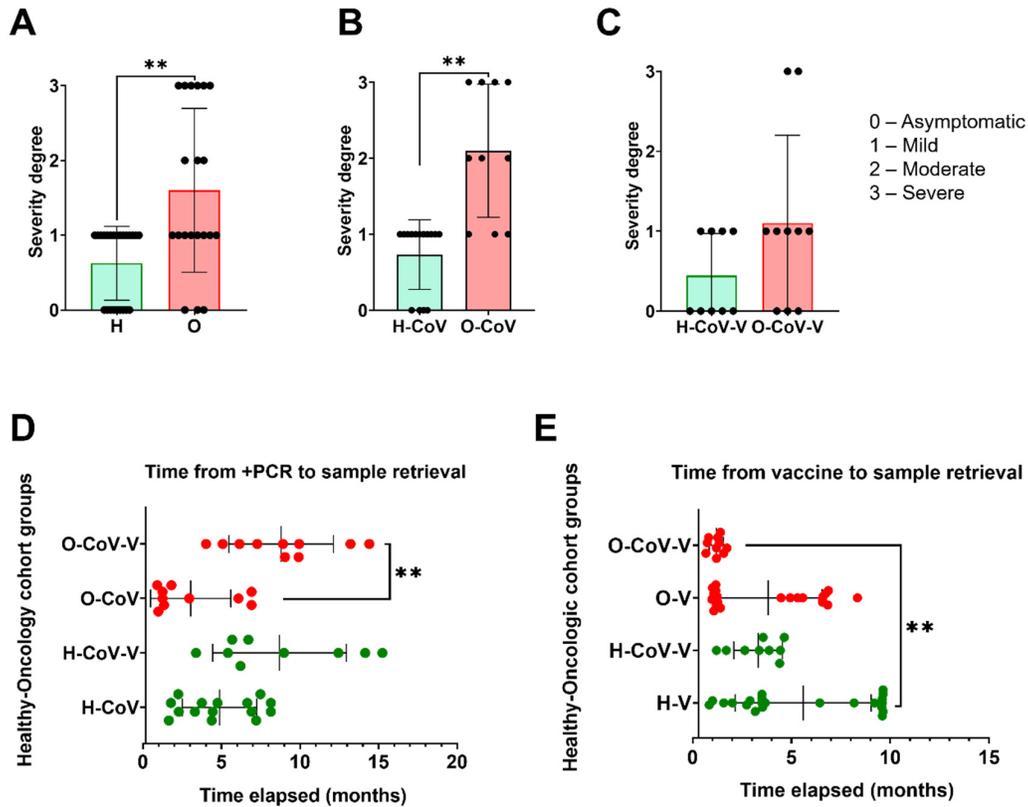
**Table S2.** SARS CoV-2- related parameters of the study cohort

|  |                                | Healthy donors   |                  |                 |                        | Oncologic patients |                |                        |
|--|--------------------------------|------------------|------------------|-----------------|------------------------|--------------------|----------------|------------------------|
|  |                                | H-N/N<br>(n= 10) | H-CoV<br>(n= 15) | H-V<br>(n = 22) | H-CoV-<br>V<br>(n= 10) | O-CoV<br>(n = 10)  | O-V<br>(n= 20) | O-CoV-<br>V<br>(n =10) |
| SARS                                       | 0                              |                  | 4(27)            |                 | 5 (56)                 | 0 (0)              |                | 3 (30)                 |
| CoV-2                                      | 1                              |                  | 11(73)           |                 | 4(44)                  | 3(30)              |                | 5(50)                  |
| infection                                  | 2                              |                  | 0(0)             |                 | 0(0)                   | 3(30)              |                | 0(0)                   |
| severity                                   | 3                              |                  | 0(0)             |                 | 0(0)                   | 4(40)              |                | 2(20)                  |
| Clinical                                   | Pneum.                         |                  | 0(0)             |                 | 0(0)                   | 9(90)              |                | 3(30)                  |
| manifest                                   | Complicatio<br>ns              |                  | 0 (0)            |                 | 0(0)                   | 4 (40)             |                | 0(0)                   |
| Time: infection-sample<br>months (mean±SD) |                                |                  | 4.7±2.4          |                 | 8.5±4.2                | 2.8±2.6            |                | 8.6±3.3                |
| Cancer                                     | NT                             |                  |                  |                 |                        | 3 (30)             |                | 6 (60)                 |
| treatmen                                   | CT                             |                  |                  |                 |                        | 4 (40)             |                | 2 (20)                 |
| t during                                   | IT                             |                  |                  |                 |                        | 0 (0)              |                | 1 (10)                 |
| SARS                                       | TKI                            |                  |                  |                 |                        | 2 (20)             |                | 1 (10)                 |
| CoV-2                                      |                                |                  |                  |                 |                        |                    |                |                        |
| infecctio                                  | CT+TKI                         |                  |                  |                 |                        | 1 (10)             |                | 0 (0)                  |
| n (n, %)                                   |                                |                  |                  |                 |                        |                    |                |                        |
| Type of                                    | BNT162b2<br>(Pfizer)           |                  |                  | 18 (82)         | 9 (90)                 |                    | 15 (75)        | 10 (100)               |
| vaccine                                    | mRNA-1273<br>(Moderna)         |                  |                  | 2 (9)           | 1 (10)                 |                    |                |                        |
| (n, %)                                     | Vaxzevria<br>(Astrazeneca<br>) |                  |                  | 2 (9)           | 0 (0)                  |                    | 5 (25)         | 0 (0)                  |
| Adverse events (n, %)                      |                                |                  |                  | 0(0)            | 0(0)                   |                    | 2 (10)         | 0 (0)                  |
| Time: vaccine-sample<br>months (mean±SD)   |                                |                  |                  | 5.1±3.7         | 3.1±1.3                |                    | 3.3±2.7        | 0.9±0.4                |
| Cancer                                     | NT                             |                  |                  |                 |                        |                    | 2 (10)         | 0 (0)                  |
| treatmen                                   | CT                             |                  |                  |                 |                        |                    | 11 (55)        | 2 (30)                 |
| t during                                   | IT                             |                  |                  |                 |                        |                    | 0 (0)          | 1 (10)                 |
| vaccinati                                  | TKI                            |                  |                  |                 |                        |                    | 3 (11)         | 3 (30)                 |
| on (n,<br>%)                               | CT+TKI                         |                  |                  |                 |                        |                    | 4 (20)         | 3 (30)                 |

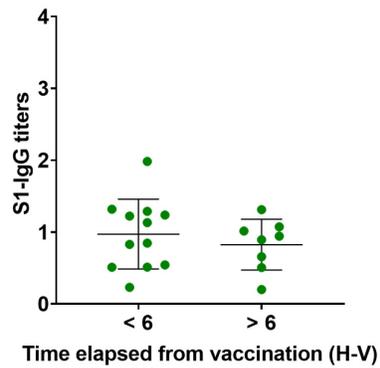
CoV, SARS CoV-2 infection; vac, vaccinated; CT, chemotherapy; IT, immunotherapy; NT, non-treated; SD, standard deviation; TKI, tyrosin-kinase inhibitors; Q1, quartile 1; Q3, quartile 3; vac, vaccinated.



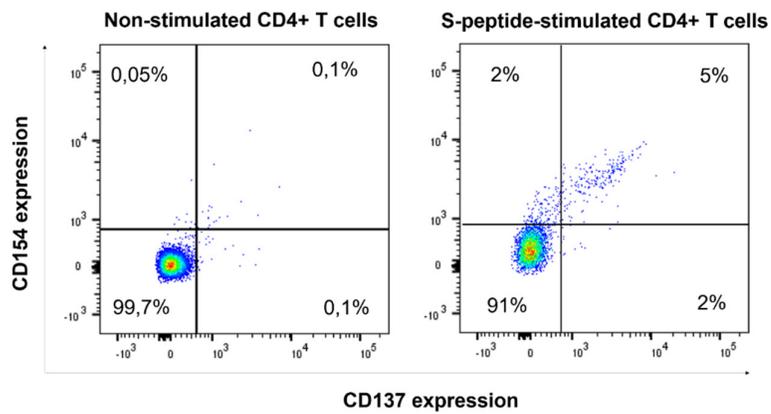
**Figure S1.** Schematic representation of the study cohort and design. Samples from healthy donors and cancer patients naturally infected by SARS CoV-2 and vaccinated with/without previous SARS CoV-2 infection were collected. A group of non-infected non-vaccinated healthy donors was included as control responses. Blood samples were retrieved following informed consent and analysed for antibody titers, T cell activation and differentiation, and characterization of systemically circulating myeloid cell subsets.



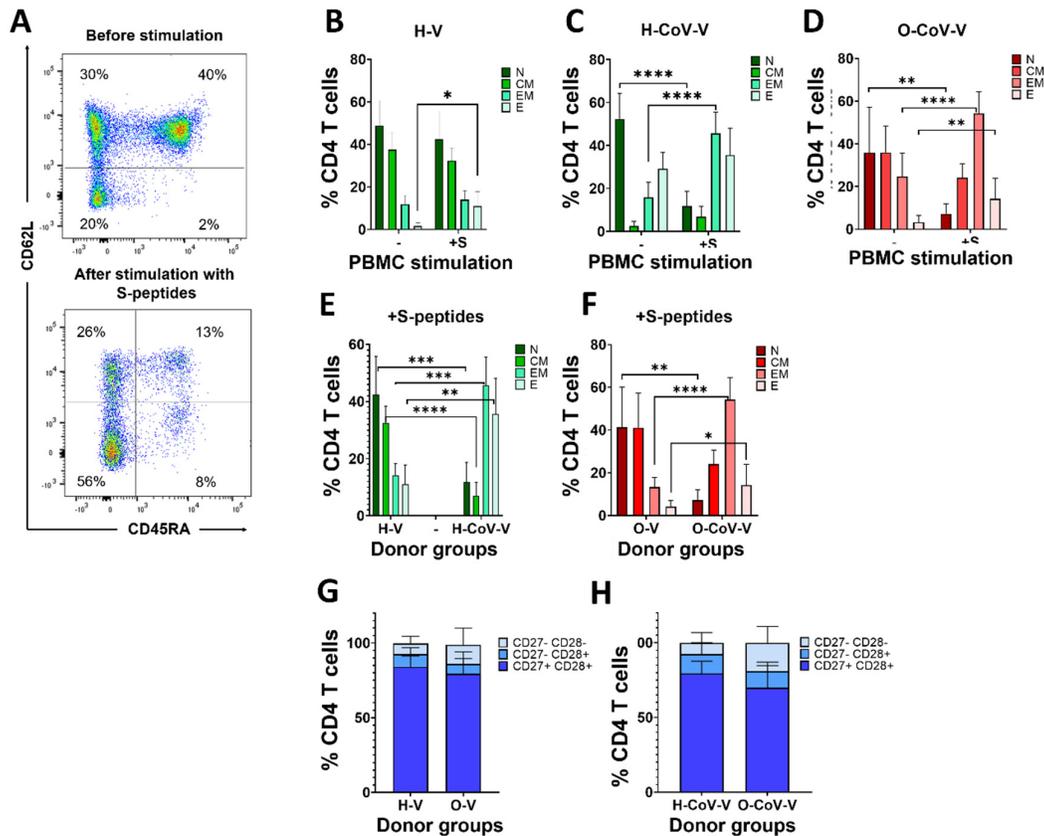
**Figure S2.** COVID-19 severity degree and time elapsed from SARS CoV-2 infection and/or vaccination to sample collection. **(A, B, C)** COVID-19 severity degree according to the NIH guidelines in all the indicated groups of healthy donors and oncologic patients. The U of Mann-Whitney test was used to evaluate significance. **(D, E)** Time elapsed from SARS CoV-2 diagnosis to sample collection and from vaccination to sample collection in the indicated groups of healthy donors and cancer patients. Kruskal-Wallis test was used for multiple comparisons followed by Dunn's test for pair-wise comparison. H-CoV, healthy donors with previous COVID-19 infection; H-V, vaccinated healthy donor; H-CoV-V, vaccinated healthy donor with previous COVID-19; O-CoV, oncologic patient with previous COVID-19; O-V, vaccinated oncologic patients; O-CoV-V, vaccinated oncologic patients with previous COVID-19; \*, \*\*, \*\*\* and \*\*\*\* indicate significant ( $p < 0.05$ ), very significant ( $p < 0.01$ ) and highly significant ( $p < 0.001$ ) differences, respectively.



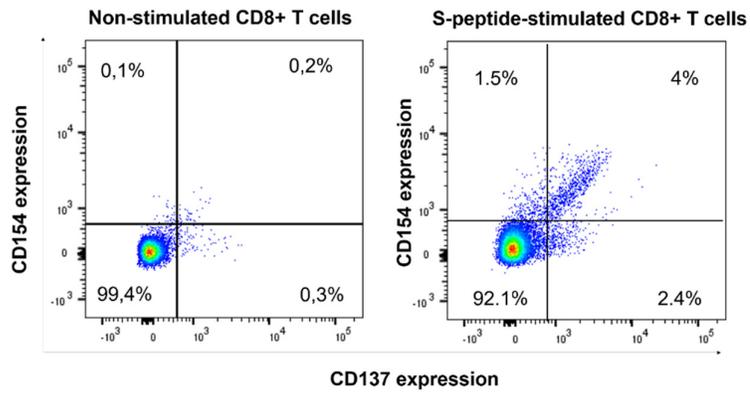
**Figure S3.** Dynamics of S-specific IgG titres. S specific IgG antibody titres in vaccinated healthy donors without previous infection (V-H) from samples collected less than 6 months and more than 6 months after vaccination. The U of Mann-Whitney test was used for statistical significance giving a non-significant result ( $P>0.05$ ).



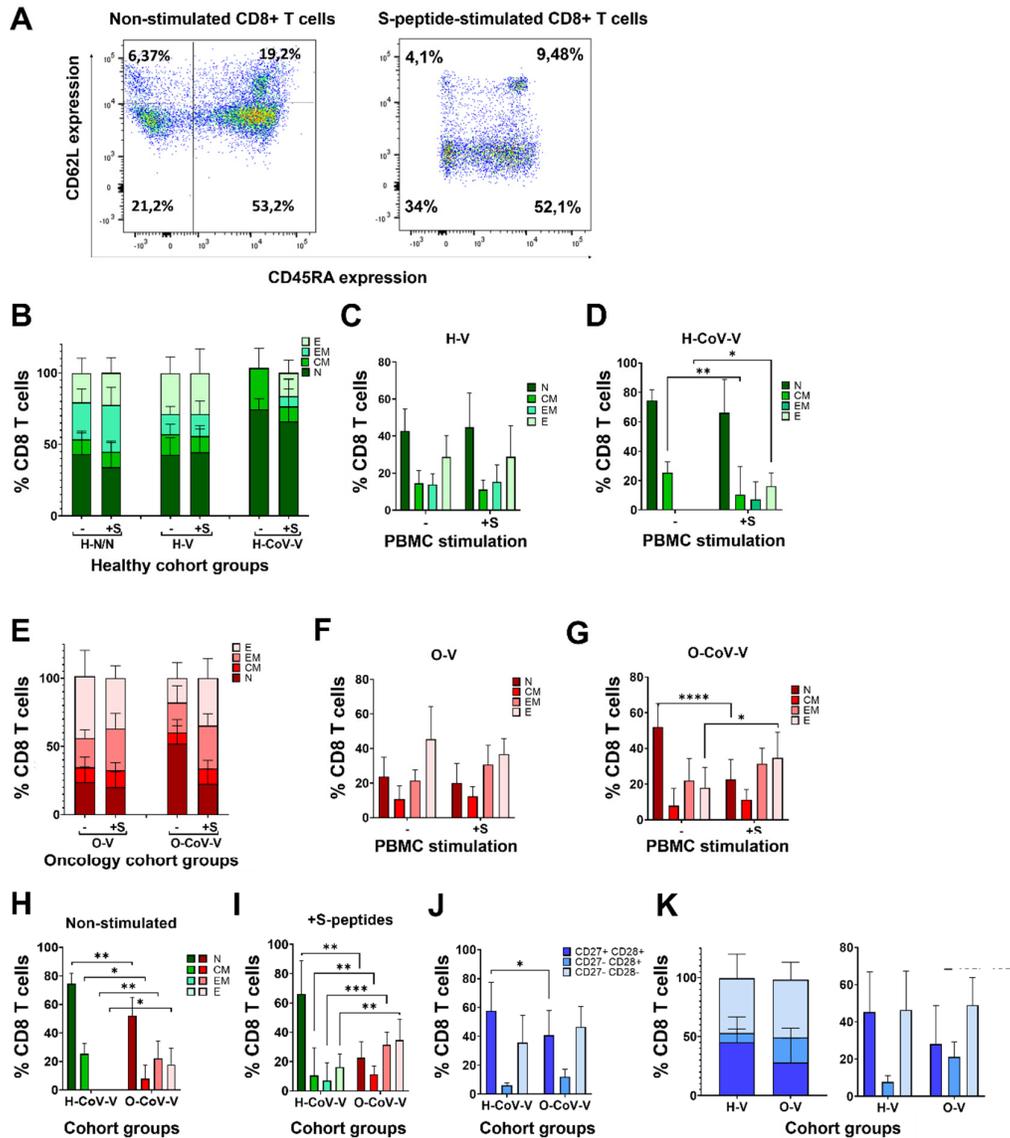
**Figure S4.** Flow cytometry and gating strategy for quantification of activated CD4 T cells. Representative flow cytometry density plots of CD154 and CD137 co-expression profiles in CD4 T cells from donors before and after stimulation with S-peptides, as indicated.



**Figure S5.** CD4 T cell phenotypes after stimulation with S peptides. **(A)** Representative flow cytometry density plots with CD62L-CD45RA co-expression profiles in CD4 T cells before and after the stimulation with S-peptides. Quadrants were established with unstained controls. Percentages of the corresponding populations are shown within the quadrants. **(B, C)** CD4 T cell phenotypic changes in H-V and H-CoV-V donors. (-) and (+S), non-stimulated and S-peptide stimulation. N, CM, EM and E, indicate naïve-stem cell (CD62L+ CD45RA+), central memory (CD62L+ CD45RA-), effector memory (CD62L- CD45RA-) and effector (CD62L- CD45RA+) phenotypes. **(D)** Phenotypic changes in CD4 T cells within O-CoV-V before and after stimulation with S-peptides. **(E,F)** Effects of previous CoV infection in vaccinated healthy donors and oncologic patients over T cell phenotypes after stimulation with S-peptides. **(B-F)** Relevant statistical comparisons are indicated by ANOVA followed by pair-wise comparisons with Tukey's test. **(G, H)** Relative percentages of CD4 T cell differentiation phenotypes in H-V and O-V and in H-CoV-V and O-CoV-V. CD27+ CD28+, CD27- CD28+ and CD27- CD28- indicate poorly differentiated, intermediate differentiated and highly differentiated T cell phenotypes. U of Mann-Whitney was used to test for significance. H-N/N, non-vaccinated, non-COVID-19 donors; H-CoV, healthy donors with previous COVID-19 infection; H-V, vaccinated healthy donor; H-CoV-V, vaccinated healthy donor with previous COVID-19; O-CoV, oncologic patient with previous COVID-19; O-V, vaccinated oncologic patients; O-CoV-V, vaccinated oncologic patients with previous COVID-19; \*, \*\*, \*\*\* and \*\*\*\* indicate significant ( $p < 0.05$ ), very significant ( $p < 0.01$ ) and highly significant ( $p < 0.001$ ) differences, respectively.

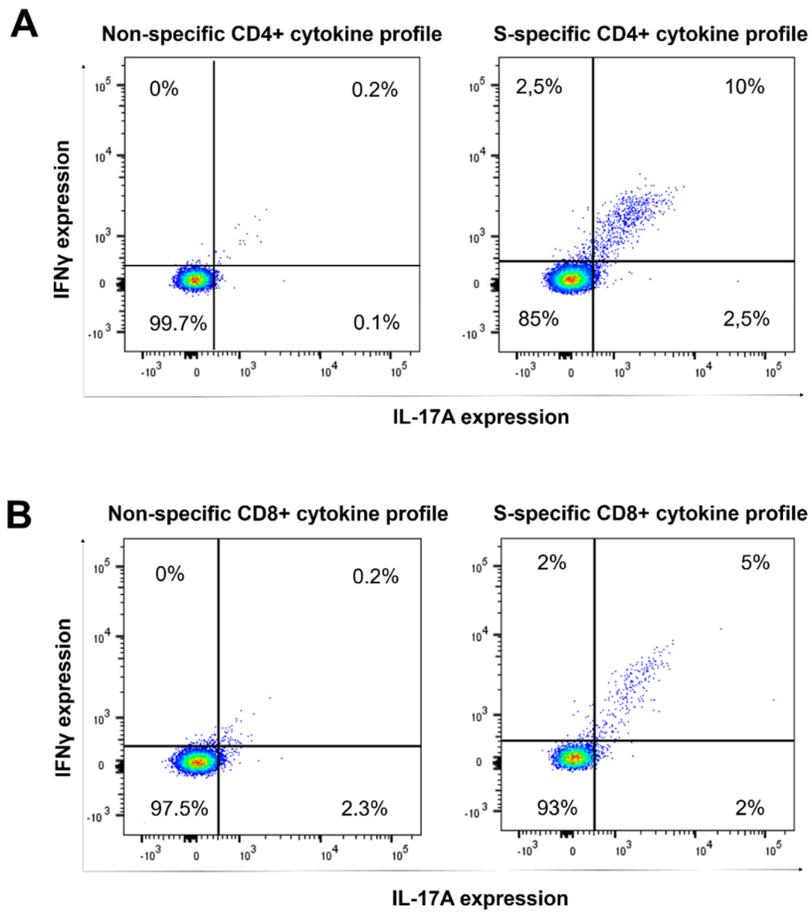


**Figure S6.** Flow cytometry and gating strategy for quantification of activated CD8 T cells. Representative flow cytometry density plots of CD154 and CD137 co-expression profiles in CD8 T cells from donors before and after stimulation with S-peptides, as indicated.



**Figure S7.** Differentiation phenotypes in CD8 T cells. **(A)** Representative flow cytometry density plots with CD62L-CD45RA co-expression profiles in CD8 T cells before and after the stimulation with S-peptides. Quadrants were established with unstained controls. Percentages of the corresponding populations are shown within the quadrants. **(B, C, D)** Relative percentages of CD8 T cell differentiation phenotypes from the indicated healthy donors and oncologic patient. Means and error bars (standard deviations) are shown. N, CM, EM and E, indicate naïve-stem cell (CD62L+ CD45RA+), central memory (CD62L+ CD45RA-), effector memory (CD62L- CD45RA-) and effector (CD62L- CD45RA+) phenotypes. **(E, F, G)** Relative percentages of CD8 T cell differentiation phenotypes from the indicated healthy donors and oncologic patients. **(H, I)** Relative percentages of CD8 T cell differentiation phenotypes in H-CoV-V and O-CoV-V groups before and after stimulation with S-peptides. **(J, K)** Relative percentages of CD8 T cell differentiation phenotypes in V-H-CoV, V-O-CoV, H-V and O-V groups as indicated in the graphs. CD27+ CD28+, CD27- CD28+ and CD27+ CD28+ indicate poorly differentiated, intermediate differentiated and highly differentiated T cell phenotypes. **(B-K)** Statistical significance was tested by ANOVA followed by Tukey's pair-wise comparisons. H-N/N, non-vaccinated, non-COVID-19 donors; H-CoV, healthy donors with previous COVID-19 infection; H-V, vaccinated healthy donor; H-CoV-V, vaccinated healthy donor with previous COVID-19; O-CoV, oncologic patient with previous COVID-19; O-V, vaccinated oncologic

patients; O-CoV-V, vaccinated oncologic patients with previous COVID-19; \*, \*\*, \*\*\* and \*\*\*\* indicate significant ( $p < 0.05$ ), very significant ( $p < 0.01$ ) and highly significant ( $p < 0.001$ ) differences, respectively.



**Figure S8.** Flow cytometry and gating strategy for quantification of cytokine expression within activated T cells. **(A, B)** Representative flow cytometry density plots with the expression of INF $\gamma$  and IL-17 before and after stimulation with S peptides in CD4 T cells **(A)** and in CD8 T cells **(B)**.