**Supplemental Data for:**

# A SARS-CoV-2 NSP7 homolog of a Treg epitope suppresses CD4+ and CD8+ T cell memory responses

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**Supplementary Table 1.** Healthy donors used in Bystander Supression Assays (BSA).

| Donor | Allele 1 | Allele 2 | Gender | Age | Donor | Allele 1 | Allele 2 | Gender | Age |
|-------|----------|----------|--------|-----|-------|----------|----------|--------|-----|
| EV202 | *0301 | *1501 | Female | 36 | EV327 | *0405 | *1401 | Male | 54 |
| EV229 | *0101 | *0301 | Male | 20 | EV329 | *1201 | *1501 | Female | 49 |
| EV277 | *1401 | *1501 | Male | 54 | EV354 | *0101 | *1301 | Male | 48 |
| EV279 | *0701 | *1101 | Male | 71 | EV366 | *0406 | *1601 | Female | 54 |
| EV285 | *0101 | *1302 | Female | 54 | EV375 | *0301 | *1501 | Female | 46 |
| EV292 | *0301 | *1301 | Male | 57 | EV381 | *0301 | *1303 | Female | 57 |
| EV299 | *0301 | *0701 | Male | 67 | EV545 | *0401 | *0701 | Male | 40 |
| EV318 | *0402 | *0701 | Male | 69 | EV546 | *1101 | *1501 | Female | 34 |
| EV320 | *0701 | *0701 | Male | 51 | | | | | |

**Supplementary Table 1.** Healthy blood donors collected from Rhode Island Blood Center from whom we have isolated PBMCs and stored at liquid N2 before use. The effect of Tregitope peptides and newly identified SARS-CoV-2-NSP7-homolog of 289 Tregitope were tested using our in vitro bystander suppression assays. HLA DRB1 of donor PBMCs were typed at American Red Cross in Dedham, MA. **41% percent of the donors were female, 59% were male. The age range of donors are 20 to 69.**

**Supplementary Table 2.** Convalescent COVID-19 donors used in CPI BSA.

| Donor | Allele 1 | Allele 2 | Gender | Age |
|-------|----------|----------|--------|-----|
| CV001 | *0701 | *1101 | Female | 56 |
| CV003 | *1502 | *1502 | Female | 57 |
| CV020 | *1301 | *1501 | Male | 40 |
| L009 | *0401 | *1201 | Female | 54 |
| L011 | *0301 | *1101 | Female | 28 |
| L013 | *0801 | *1303 | Female | 43 |
| L014 | *0101 | *1401 | Male | 37 |

**Supplementary Table 2.** List of the convalescent COVID-19 blood donors whom we have isolated PBMCs and stored at liquid N2 before use. The effect of Tregitope peptides and newly identified SARS-CoV2-NSP7-homolog of 289 Tregitope were tested using our in vitro CPI bystander supression assay. HLA DRB1 of donor PBMCs were typed at American Red Cross in Dedham, MA. **72% percent of the donors were female, 28% were male. The age range of donors are 28 to 57.**

CPI = a mixture of protein antigens from the cytomegalovirus, influenza, and parainfluenza.

**Supplement Figure S1.** Overview of Class II JanusMatrix Results of the SARS-CoV-2 NSP7- homolog of Tregitope 289 peptide.

| Input Sequence | Cluster Address (w/ Flanks) | Cluster Sequence | EpiMatrix Cluster Score (w/o Flanks) | Treg-Adj Cluster Score (w/o Flanks) | Number of HUMAN Matches | Janus Homology Score |
|---|---|---|---|---|---|---|
| NSP7_289HOMOLOG | 50 - 62 | EKMVSLLSVLLSM | 31.97 | 31.97 | 74 | 11.44 |

| Protein ID | Protein Description | Start Position | Sequence | Cluster Score | Number Of HUMAN Matches* | Janus HMLGY Score | DRB1 *0101 | DRB1 *0301 | DRB1 *0401 | DRB1 *0701 | DRB1 *0801 | DRB1 *0901 | DRB1 *1101 | DRB1 *1301 | DRB1 *1501 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| NSP7_289HOMOLOG | | 50 - 62 | EKMVSLLSVLLSM | 31.97 | 73 | 11.44 | DB Ver: April 02, 2023 | | | EpiMatrix Ver: 1.2 with DR9 | | | JMX Hit Threshold: 1.64 | | |
| | | 50 | EKMVSLLSV | | 0 | | 0.23 | 0.48 | 0.19 | 0.99 | 0.13 | 1.09 | 1.1 | 0.83 | 1.27 |
| | | 51 | KMVSLLSVL | | 0 | | -0.08 | 0.94 | -0.51 | 0.73 | -0.3 | 1.15 | 0.09 | 0.49 | 0.68 |
| | | 52 | MVSLLSVLL | | 20 | F52 | 3.12 | 2.25 | 2.42 | 2.97 | 2.18 | 2.08 | 1.74 | 2.43 | 2.84 |
| sp|Q9C0C7|AMRA1_HUMAN | Activating molecule in BECN1-regula... | 444 | SVSLLSVLR | | | | 1.79 | 1.61 | 1.48 | 1.17 | 1.67 | 0.83 | 0.74 | 1.8 | 1.49 |
| sp|O00206|TLR4_HUMAN | Toll-like receptor 4 | 635 | GVSVLSVLV | | | | 1.55 | 0.87 | 1.15 | 1.99 | 0.32 | 1.52 | 0.51 | 1.06 | 1.48 |
| sp|Q13873|BMPR2_HUMAN | Bone morphogenetic protein receptor... | 157 | SVSVLAVLI | | | | 1.71 | 1.57 | 0.91 | 1.8 | 0.71 | 1.77 | 0.41 | 1.74 | 1.57 |
| sp|P01861|IGHG4_HUMAN | Immunoglobulin heavy constant gamma... | 182 | VVSVLTVLH | | | | 1.68 | 1.85 | 2.42 | 1.38 | 2.1 | 1.9 | 1.67 | 2.02 | 1.52 |
| sp|P01860|IGHG3_HUMAN | Immunoglobulin heavy constant gamma... | 232 | VVSVLTVLH | | | | 1.68 | 1.85 | 2.42 | 1.38 | 2.1 | 1.9 | 1.67 | 2.02 | 1.52 |
| sp|P01857|IGHG1_HUMAN | Immunoglobulin heavy constant gamma... | 185 | VVSVLTVLH | | | | 1.68 | 1.85 | 2.42 | 1.38 | 2.1 | 1.9 | 1.67 | 2.02 | 1.52 |
| sp|Q8NGI9|OR5A2_HUMAN | Olfactory receptor 5A2 | 209 | IVSVLVLI | | | | 2.27 | 2.35 | 1.81 | 2.57 | 1.56 | 2.57 | 1.25 | 2.51 | 1.57 |
| sp|Q5XPI4|RN123_HUMAN | E3 ubiquitin-protein ligase RNF123 | 1078 | SVSLLRVLE | | | | 0.65 | 1.42 | -0.14 | 0.16 | 2.04 | -0.22 | 0.58 | 1.61 | 0.4 |
| sp|P78395|PRAME_HUMAN | Melanoma antigen preferentially exp... | 347 | SVSQLSVLS | | | | 1.9 | 1.59 | 2.04 | 0.85 | 1.42 | 0.46 | 1.29 | 2.27 | 1.69 |
| sp|Q05707|COEA1_HUMAN | Collagen alpha-1(XIV) chain | 690 | EVSLLAVLD | | | | 1.42 | 0.23 | 0.89 | 0.98 | 1.92 | 0.55 | 0.27 | 0.45 | 0.52 |
| sp|P49796|RGS3_HUMAN | Regulator of G-protein signaling 3 | 81 | HVSVLSVLS | | | | 1.86 | 1.31 | 1.92 | 1.45 | 1.21 | 1.59 | 1.32 | 1.49 | 1.64 |
| sp|Q9BXR5|TLR10_HUMAN | Toll-like receptor 10 | 70 | SVSKLVLI | | | | 0.62 | 1.76 | -0.86 | 0.98 | 1.63 | 0.53 | 0.33 | 2.17 | 0.37 |
| sp|Q8NCM8|DYHC2_HUMAN | Cytoplasmic dynein 2 heavy chain 1 | 3785 | VVSWLPVLE | | | | 0.47 | 1.25 | 1.45 | 1 | 1.29 | 0.83 | 0.27 | 2.21 | 0.61 |
| sp|Q5TH69|BIG3_HUMAN | Brefeldin A-inhibited guanine nucle... | 206 | VVSVLTVLC | | | | 2 | 1.24 | 1.81 | 1.77 | 1.42 | 1.73 | 1.03 | 1.42 | 1.84 |
| sp|O75746|S2512_HUMAN | Electrogenic aspartate/glutamate an... | 465 | RVSALNVLR | | | | 1.26 | 2.34 | 1.33 | 0.66 | 1.36 | 1.58 | 0.09 | 2.28 | 1.69 |
| sp|Q9HB89|NMUR1_HUMAN | Neuromedin-U receptor 1 | 103 | AVSDLLVLL | | | | 0.12 | 1.83 | 0.42 | -0.16 | 0.35 | 0.27 | -0.66 | 0.71 | 0.3 |
| sp|Q9GZQ4|NMUR2_HUMAN | Neuromedin-U receptor 2 | 88 | AVSDLLVLL | | | | 0.12 | 1.83 | 0.42 | -0.16 | 0.35 | 0.27 | -0.66 | 0.71 | 0.3 |
| sp|Q6NW34|NEPRO_HUMAN | Nucleolus and neural progenitor pro... | 179 | LVSRLWVLY | | | | 0.82 | 1 | 0.2 | 0.88 | 0.45 | 0.58 | -0.04 | 2.03 | 1.25 |
| sp|Q9Y5I1|PCDAB_HUMAN | Protocadherin alpha-11 | 705 | VVSSLLVLT | | | | 1.25 | 1.65 | 1.02 | 1.55 | 1.2 | 2.2 | 1.27 | 1.28 | 1.89 |
| sp|Q8NCA5|FA98A_HUMAN | Protein FAM98A | 49 | LVSELRVLC | | | | 1.99 | 1.63 | 0.86 | 1.24 | 1.13 | 0.9 | 1 | 1.38 | 0.92 |
| | | 53 | VSLLSVLLS | | 36 | F53 | 2.09 | 1.68 | 2.59 | 1.44 | 1.89 | 1.25 | 2.47 | 2.03 | 1.58 |
| sp|P30408|T4S1_HUMAN | Transmembrane 4 L6 family member 1 | 160 | VSLFSILLA | | | | 0.38 | 0.47 | 1.57 | 1.1 | 0.85 | 1.32 | 1.44 | 1.83 | 1.88 |
| sp|Q5VT06|CE350_HUMAN | Centrosome-associated protein 350 | 756 | GSLLSHLLS | | | | 0.8 | 0.68 | 1.21 | 0.16 | 1.07 | 0.04 | 1.68 | 1.04 | 1.49 |
| sp|Q9NX18|SDHF2_HUMAN | Succinate dehydrogenase assembly fa... | 19 | HSLLSPLLS | | | | 1.7 | 0.8 | 1.84 | 0.91 | 1.33 | 0.89 | 1.93 | 1.16 | 1.29 |
| sp|Q5JRX3|PREP_HUMAN | Presequence protease, mitochondrial | 346 | LSLLSSLLT | | | | 2.66 | 0.97 | 2.57 | 2.61 | 1.89 | 1.84 | 2.4 | 1.32 | 2.8 |
| sp|Q76KD6|SPERI_HUMAN | Speriolin | 193 | VSLSSPLLS | | | | 1.97 | 2.4 | 2.2 | 1.78 | 1.31 | 2.31 | 2.23 | 2.17 | 2.04 |
| sp|P13866|SC5A1_HUMAN | Sodium/glucose cotransporter 1 | 145 | LSLLSLLLY | | | | 0.93 | 1.99 | 0.95 | 0.44 | 0.99 | 1.22 | 1.78 | 2.33 | 1.88 |
| sp|Q96M86|DNHD1_HUMAN | Dynein heavy chain domain-containin... | 1568 | TSLLSALLV | | | | 1.76 | 0.38 | 1.46 | 1.74 | 0.71 | 0.94 | 1.38 | 0.75 | 1.34 |
| sp|Q9Y4D7|PLXD1_HUMAN | Plexin-D1 | 1410 | ISLFSSLLN | | | | 1.68 | 0.39 | 2.22 | 1.71 | 1.86 | 1.73 | 1.74 | 1.75 | 2.89 |
| sp|Q9GZU5|NYX_HUMAN | Nyctalopin | 414 | SSLLSKLLA | | | | 0.71 | 1.18 | 0.66 | -0.1 | 1.2 | 0.71 | 1.96 | 1.54 | 1.42 |
| sp|P59826|BPIB3_HUMAN | BPI fold-containing family B member... | 167 | ISLFSGLLP | | | | 1.07 | 0.06 | 1.78 | 0.83 | 0.88 | 1.68 | 1.22 | 1.43 | 1.85 |
| sp|P40197|GPV_HUMAN | Platelet glycoprotein V | 207 | VSLDSGLLN | | | | 1.33 | 1.35 | 1.89 | 0.4 | 0.79 | 0.84 | 0.24 | 0.39 | 0.91 |
| sp|A0A1B0GUA7|TEX51_HUMAN | Testis-expressed protein 51 | 142 | VSLSSALLL | | | | 2.3 | 2.4 | 1.89 | 2.81 | 1.07 | 2.45 | 1.75 | 2.18 | 2.44 |
| sp|P19021|AMD_HUMAN | Peptidyl-glycine alpha-amidating mo... | 391 | YSLLSKLLG | | | | 2.12 | 2.03 | 1.95 | 0.63 | 3.26 | 1.7 | 3.32 | 2.37 | 2.28 |
| sp|Q9C0I3|CCSE1_HUMAN | Serine-rich coiled-coil domain-cont... | 240 | SSLQSPLLS | | | | 1.25 | 1.1 | 1.55 | 0.32 | 0.92 | 0.14 | 1.58 | 1.95 | 1.27 |
| sp|Q96RG2|PASK_HUMAN | PAS domain-containing serine/threon... | 1225 | MSLVSGLLQ | | | | 1.63 | 1.03 | 1.96 | 1.62 | 0.96 | 1.26 | 1.81 | 1.37 | 1.88 |
| sp|O14497|ARI1A_HUMAN | AT-rich interactive domain-containi... | 1674 | MSLKSGLLA | | | | 1.1 | 1.12 | 1.02 | 1.05 | 1.15 | 0.91 | 1.22 | 1.7 | 0.97 |
| sp|Q6ZP01|RBM44_HUMAN | RNA-binding protein 44 | 683 | LSLESKLLS | | | | 1.49 | 2.42 | 1.72 | 0.28 | 1.3 | 1.19 | 2.44 | 2.31 | 1.4 |

| Protein ID | Protein Description | Start Position | Sequence | Cluster Score | Number Of HUMAN Matches* | Janus HMLGY Score | DRB1 *0101 | DRB1 *0301 | DRB1 *0401 | DRB1 *0701 | DRB1 *0801 | DRB1 *0901 | DRB1 *1101 | DRB1 *1301 | DRB1 *1501 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| sp\|Q9Y243\|AKT3_HUMAN | RAC-gamma serine/threonine-protein ... | 374 | KSLLSGLLI | | | | 1.95 | 0.75 | 1.19 | 1.51 | 0.7 | 1.02 | 0.89 | 1.11 | 1.55 |
| sp\|Q8NFD5\|ARI1B_HUMAN | AT-rich interactive domain-containi... | 1711 | MSLKSGLLA | | | | 1.1 | 1.12 | 1.02 | 1.05 | 1.15 | 0.91 | 1.22 | 1.7 | 0.97 |
| sp\|Q8N755\|S66A3_HUMAN | Solute carrier family 66 member 3 | 37 | LSLPSLLLE | | | | -0.95 | 1.1 | -0.09 | -0.45 | 1.02 | -0.42 | 0.16 | 1.89 | 0.74 |
| sp\|Q6ZS81\|WDFY4_HUMAN | WD repeat- and FYVE domain-containi... | 1481 | LSLFSHLLE | | | | 0.12 | 0.95 | 1.01 | 0.33 | 2.03 | 0.46 | 1.18 | 2.3 | 1.99 |
| sp\|Q5TEC3\|ZN697_HUMAN | Zinc finger protein 697 | 326 | FSLSSHLLS | | | | 1.93 | 2.7 | 2.4 | 1.88 | 1.95 | 2.33 | 2.86 | 2.47 | 2.64 |
| sp\|Q8TBY8\|PMFBP_HUMAN | Polyamine-modulated factor 1-bindin... | 13 | SSLNSKLLS | | | | 0.51 | 1.69 | 0.71 | -0.51 | 1.4 | 0.28 | 2.01 | 1.82 | 1.2 |
| sp\|P55290\|CAD13_HUMAN | Cadherin-13 | 697 | FSLPSVLLL | | | | 1.51 | 1.51 | 1.89 | 2.05 | 1.04 | 1.33 | 1.19 | 2.29 | 1.41 |
| sp\|Q4KMG0\|CDON_HUMAN | Cell adhesion molecule-related/down... | 85 | LSLNSSLLG | | | | 2.18 | 2.06 | 2.55 | 1.43 | 2.27 | 1.18 | 2.38 | 2.18 | 2.31 |
| sp\|A6ND91\|ASPDH_HUMAN | Aspartate dehydrogenase domain-cont... | 19 | QSLVSRLLA | | | | 0.73 | 0.74 | 0.31 | 0.74 | 0.62 | 0.89 | 1.68 | 1.08 | 0.89 |
| sp\|P55198\|AF17_HUMAN | Protein AF-17 | 541 | LSLESPLLG | | | | 2.01 | 1.79 | 2.27 | 0.91 | 1.09 | 1.17 | 1.75 | 1.69 | 1.13 |
| sp\|Q96MX3\|ZNF48_HUMAN | Zinc finger protein 48 | 368 | FSLSSTLLR | | | | 2.04 | 2.8 | 2.49 | 2.07 | 1.9 | 2.29 | 2.06 | 2.57 | 1.85 |
| sp\|Q9BV99\|LRC61_HUMAN | Leucine-rich repeat-containing prot... | 28 | FSLESILLL | | | | 1.73 | 1.77 | 1.99 | 2.62 | 0.62 | 1.62 | 1.54 | 1.67 | 1.13 |
| sp\|Q9NUD9\|PIGV_HUMAN | GPI mannosyltransferase 2 | 109 | LSLRSCLLI | | | | 0.78 | 0.68 | 0.82 | 1.26 | 0.99 | 0.67 | 0.65 | 1.88 | 1.1 |
| sp\|Q9UPM8\|AP4E1_HUMAN | AP-4 complex subunit epsilon-1 | 846 | FSLTSELLD | | | | 0.42 | 0.18 | 0.44 | 1.57 | 1.85 | 0.91 | 0.33 | 1.14 | 0.91 |
| sp\|Q68CQ1\|MROH7_HUMAN | Maestro heat-like repeat-containing... | 337 | LSLDSSLLF | | | | 1.19 | 2.71 | 2.57 | 1.6 | 1.27 | 1.57 | 1.02 | 1.73 | 1.15 |
| sp\|Q8NH41\|OR4KF_HUMAN | Olfactory receptor 4K15 | 206 | LSLSSFLLL | | | | 1.18 | 1.88 | 0.94 | 2.29 | 0.6 | 1.58 | 1.3 | 1.66 | 1.44 |
| sp\|O14771\|ZN213_HUMAN | Zinc finger protein 213 | 410 | FSLRSYLLD | | | | 1.22 | -0.31 | -0.11 | 1.23 | 1.75 | 0.43 | 0.36 | 0.91 | 1.16 |
| sp\|O43286\|B4GT5_HUMAN | Beta-1,4-galactosyltransferase 5 | 22 | FSLSSSLLY | | | | 2.24 | 2.94 | 2.29 | 2.33 | 0.92 | 2.94 | 2.03 | 2.71 | 2.31 |
| sp\|Q8N6C8\|LIRA3_HUMAN | Leukocyte immunoglobulin-like recep... | 208 | WSLPSDLLG | | | | 0.39 | 0.17 | 1.92 | 0.05 | 1.15 | -0.06 | 1.06 | 0.98 | 1.11 |
| | | 54 | SLLSVLLSM | | 17 | F54 | 0.08 | 1.81 | 0.03 | 0.58 | -0.44 | 1.52 | 0.74 | 1.6 | 1.25 |
| sp\|Q9Y6C5\|PTC2_HUMAN | Protein patched homolog 2 | 1105 | VLLPVLLSI | | | | 0.3 | 1.73 | 0.47 | 0.89 | 0.76 | 1.01 | 0.74 | 2.51 | 2.03 |
| sp\|O60241\|AGRB2_HUMAN | Adhesion G protein-coupled receptor... | 19 | LLLSVILSL | | | | 1.53 | 2.31 | 1.65 | 3.05 | 1.05 | 2.61 | 1.73 | 2.09 | 2.04 |
| sp\|Q9P2K9\|DISP3_HUMAN | Protein dispatched homolog 3 | 1207 | LLLPVLLSI | | | | 0.43 | 1.79 | 0.59 | 1.01 | 0.9 | 1.13 | 0.87 | 2.56 | 2.08 |
| sp\|Q86Y46\|K2C73_HUMAN | Keratin, type II cytoskeletal 73 | 419 | ELLSVKLSI | | | | 0.99 | 1.86 | 0.42 | 1.18 | 0.94 | 1.93 | 1.62 | 1.64 | 1.46 |
| sp\|O60423\|AT8B3_HUMAN | Phospholipid-transporting ATPase IK | 1189 | ILLVVLLSV | | | | 1.28 | 1.89 | 1.21 | 2.03 | 1.24 | 2.19 | 2.18 | 2.21 | 2.61 |
| sp\|A4D0T7\|SIM30_HUMAN | Small integral membrane protein 30 | 33 | LLLGVVLSI | | | | 1.65 | 2.2 | 1.76 | 1.98 | 1.01 | 1.68 | 1.18 | 1.86 | 1.59 |
| sp\|Q8IWT1\|SCN4B_HUMAN | Sodium channel subunit beta-4 | 23 | FLLPVTLSL | | | | 2.06 | 2 | 2.57 | 2.38 | 1.55 | 1.76 | 1.69 | 2.78 | 2.4 |
| sp\|Q15166\|PON3_HUMAN | Serum paraoxonase/lactonase 3 | 8 | VLLGVGLSL | | | | 2.11 | 1.79 | 1.73 | 1.92 | 0.69 | 1.45 | 1.05 | 1.46 | 2.4 |
| sp\|Q9NTG1\|PKDRE_HUMAN | Polycystin family receptor for egg ... | 8 | LLLGVGLSL | | | | 2.24 | 1.84 | 1.85 | 2.04 | 0.82 | 1.58 | 1.18 | 1.51 | 2.45 |
| sp\|Q9BUM1\|G6PC3_HUMAN | Glucose-6-phosphatase 3 | 153 | FLLAVGLSR | | | | 2.55 | 2.57 | 2.47 | 2.03 | 2.24 | 2.74 | 1.72 | 2.66 | 2.48 |
| sp\|Q86TG1\|T150A_HUMAN | Transmembrane protein 150A | 5 | ILLPVSLSA | | | | 1.56 | 1.72 | 2.33 | 1.73 | 1.07 | 1.56 | 1.62 | 2.5 | 2.42 |
| sp\|P04118\|COL_HUMAN | Colipase | 6 | ILLLVALSV | | | | 3.02 | 2.02 | 2.67 | 2.98 | 2.02 | 2.33 | 2.66 | 2.36 | 2.91 |
| sp\|H3BQJ8\|LY6L_HUMAN | Lymphocyte antigen 6L | 125 | LLLQVGLSL | | | | 2.82 | 1.91 | 2.25 | 2.25 | 1.56 | 1.44 | 1.95 | 2.74 | 2.61 |
| sp\|P39060\|COIA1_HUMAN | Collagen alpha-1(XVIII) chain | 534 | VLLGVKLSG | | | | 0.98 | 2.39 | 1.16 | -0.27 | 1.99 | 1.07 | 2.09 | 2.04 | 2.21 |
| sp\|O15120\|PLCB_HUMAN | 1-acyl-sn-glycerol-3-phosphate acyl... | 14 | LLLLVQLSR | | | | 1.85 | 1.82 | 1.29 | 1.4 | 1.95 | 1.44 | 1.78 | 2.16 | 1.4 |
| sp\|Q14667\|BLTP2_HUMAN | Bridge-like lipid transfer protein ... | 10 | VLLLVALSA | | | | 2.64 | 1.96 | 2.73 | 2.13 | 1.98 | 2.05 | 2.72 | 2.3 | 2.61 |
| sp\|O95994\|AGR2_HUMAN | Anterior gradient protein 2 homolog | 9 | FLLLVALSY | | | | 2.9 | 2.65 | 2.7 | 2.12 | 1.92 | 2.58 | 2.69 | 2.97 | 2.57 |

\* Count of HUMAN JanusMatrix matches found in the search database. With respect to a given EpiMatrix Hit (a 9-mer contained within the input sequence which is predicted to bind to a specific allele) , a Janus Matrix match is a 9-mer derived from the search database (typically the human genome) which is predicted to bind to the same allele as the EpiMatrix Hit and shares TCR facing contacts with the EpiMatrix Hit.

\*\* Janus Homology Score represents the average depth of coverage in the search database for each EpiMatrix hit in the input sequence. For example, an input peptide with eight EpiMatrix hits, all of which have one match in the search database, has a Janus Homology Score of 1. An input peptide with four EpiMatrix Hits, all of which have two matches in the search database, has a Janus Homology Score of 2.
The JanusMatrix Homology Score considers all constituent 9-mers in any given peptide, including flanks.

**Supplement Figure S1. JanusMatrix Analysis of the SARS-CoV-2 NSP7- homolog of Tregitope 289 peptide.** The JanusMatrix algorithm evaluates predicted MHC class II T cell epitopes for their homology to the human proteome. Here we observed that the NSP7 peptide (50-62) has shared homology to some common human protein sequences with a total of 73 human matches. Three epitopes were identified in frames 52, 53 and 54 that show significant cross-conservation. As shown in the above report frame 52 has 100% homology at the TCR-face (homologous amino acids are underlined) which corresponds to the well- characterized regulatory epitope, Tregitope 289, that is present in the constant region of human immunoglobin (the 9-mer epitope is shown in the green box). Tregitope regulatory epitopes are highlighted in green in this report, and frames that predict binding across multiple alleles (≥ 4) are considered promiscuous epitopes and have a higher likelihood to impact a larger global population. Additionally, there is cross-conservation in frames 53 and 54, having 36 and 17 human matches, respectively; these epitopes may be contributing to the HLA binding and the suppressive capacity observed in our bystander suppressive T cell assays for this peptide.

**Supplement Figure S2.** Flow cytometry gating strategy for CD4 T cell proliferation and activation in the bystander suppression assays.
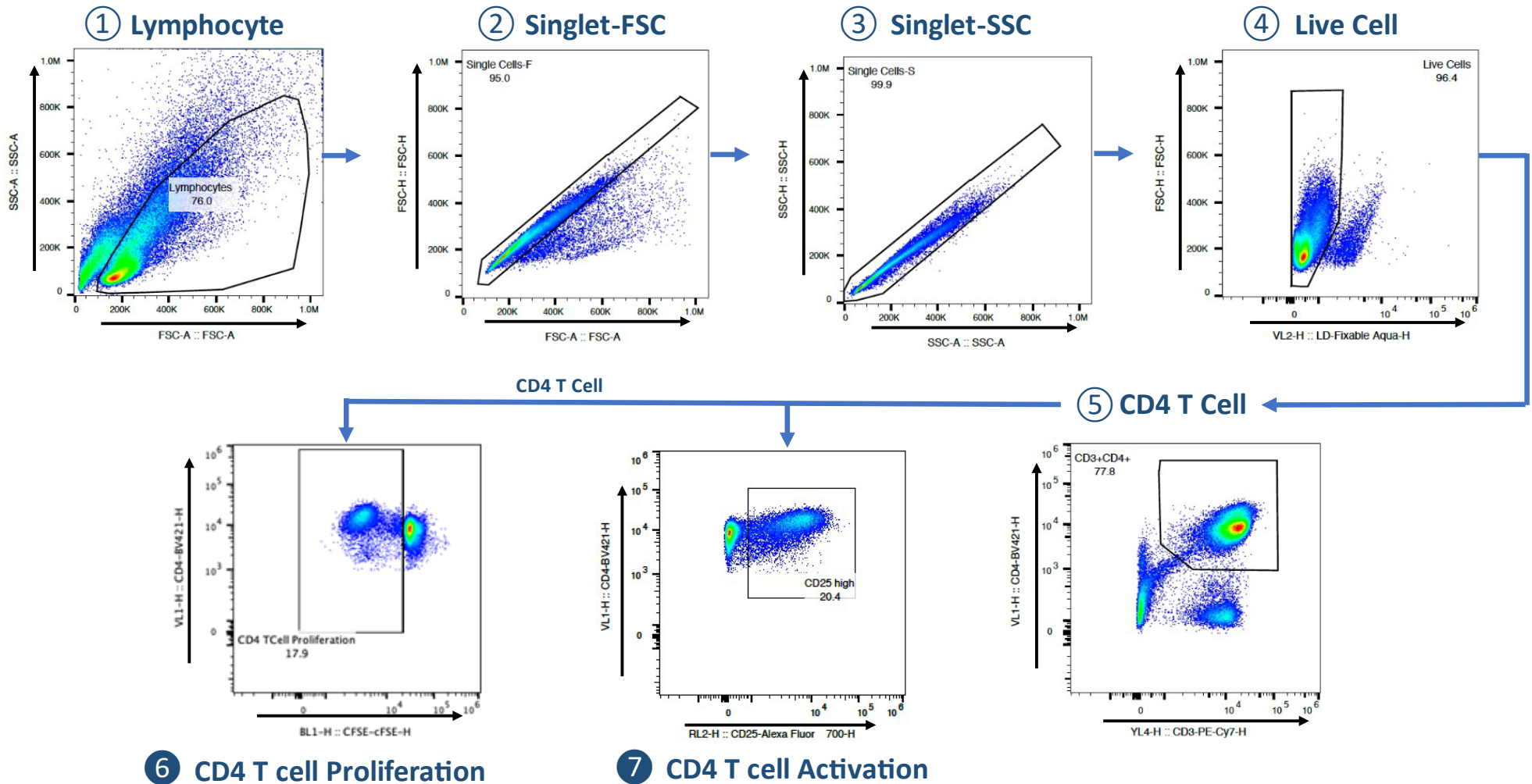


**Supplement Figure S2. Gating strategy for CD4 T cell proliferation and activation.** Healthy donors PBMCs were CFSE labelled at day0, then stimulated with 0.5 µg/ml of TT at day1, cultured for 6 days and stained with cell surface markers to identify CD4 T cell proliferation and activation. Initially lymphocyte populations were selected in side scatter (SSC) vs forward scatter (FSC) and doublets were excluded by flow scatter height vs area and side scatter height vs area plotting. Dead cells were then removed by live-dead staining. CD4 +T cells were selected by CD3+CD4+ positive markers and proliferation of CD4 T cells determined by CFSE dilution. Activation of CD4 T cells population was determined by the expression of CD25.

**Supplement Figure S3.** Representive FACS plot showing dose-dependent inhibition of CD4 T cell activation.
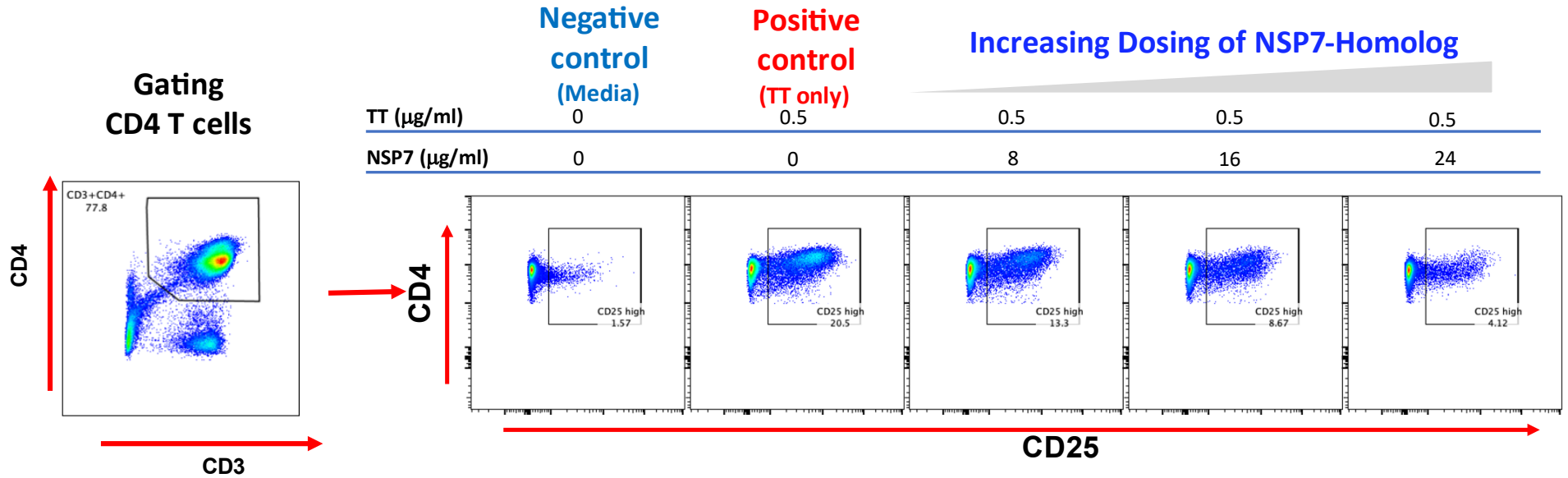


**Supplement Figure S3. FACS plot showing dose-dependent inhibition of CD4 T cell activation.** PBMC from healthy donors were stimulated with 0.5 ug/ml of TT with or without the addition of different concentrations of NSP7-Homolog peptide. Activation of CD4 T cells were measured six days post-stimulation by flow cytometry by the expression of activation marker CD25. FACS plot from a representative donor PBMC is shown here.