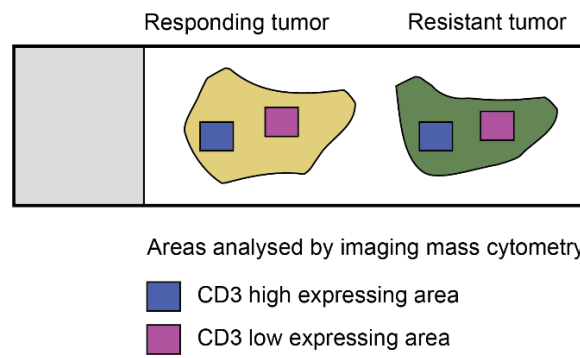


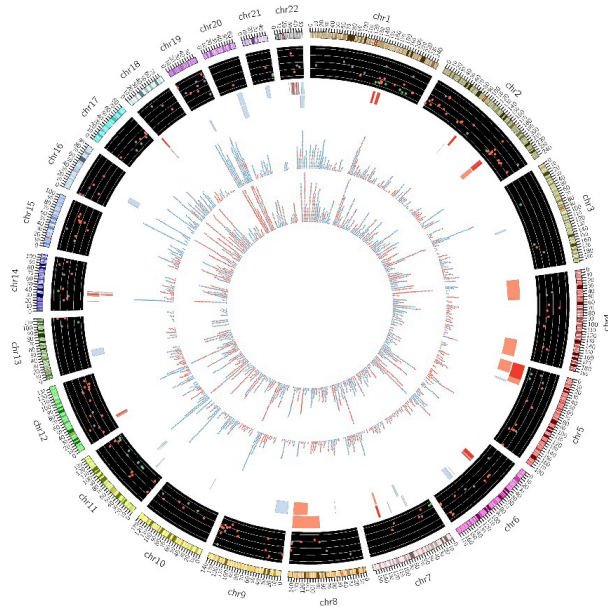
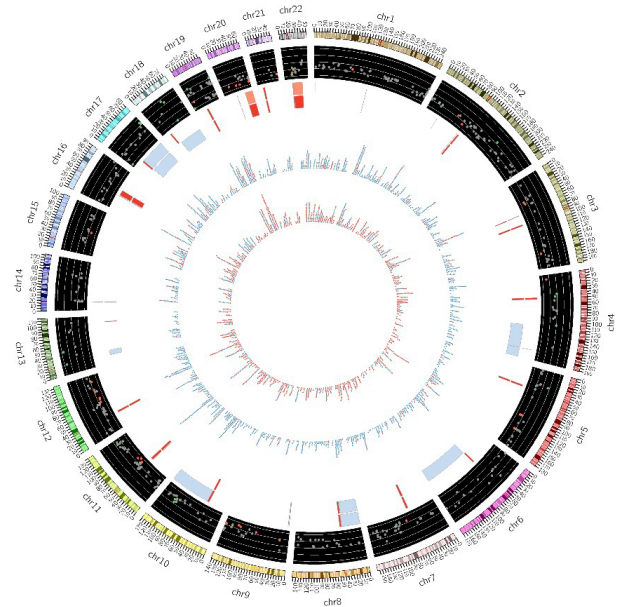
**Supplemental information for the manuscript:**

**Acquired resistance to anti-PD1 therapy in patients with NSCLC associates with immunosuppressive T cell phenotype**

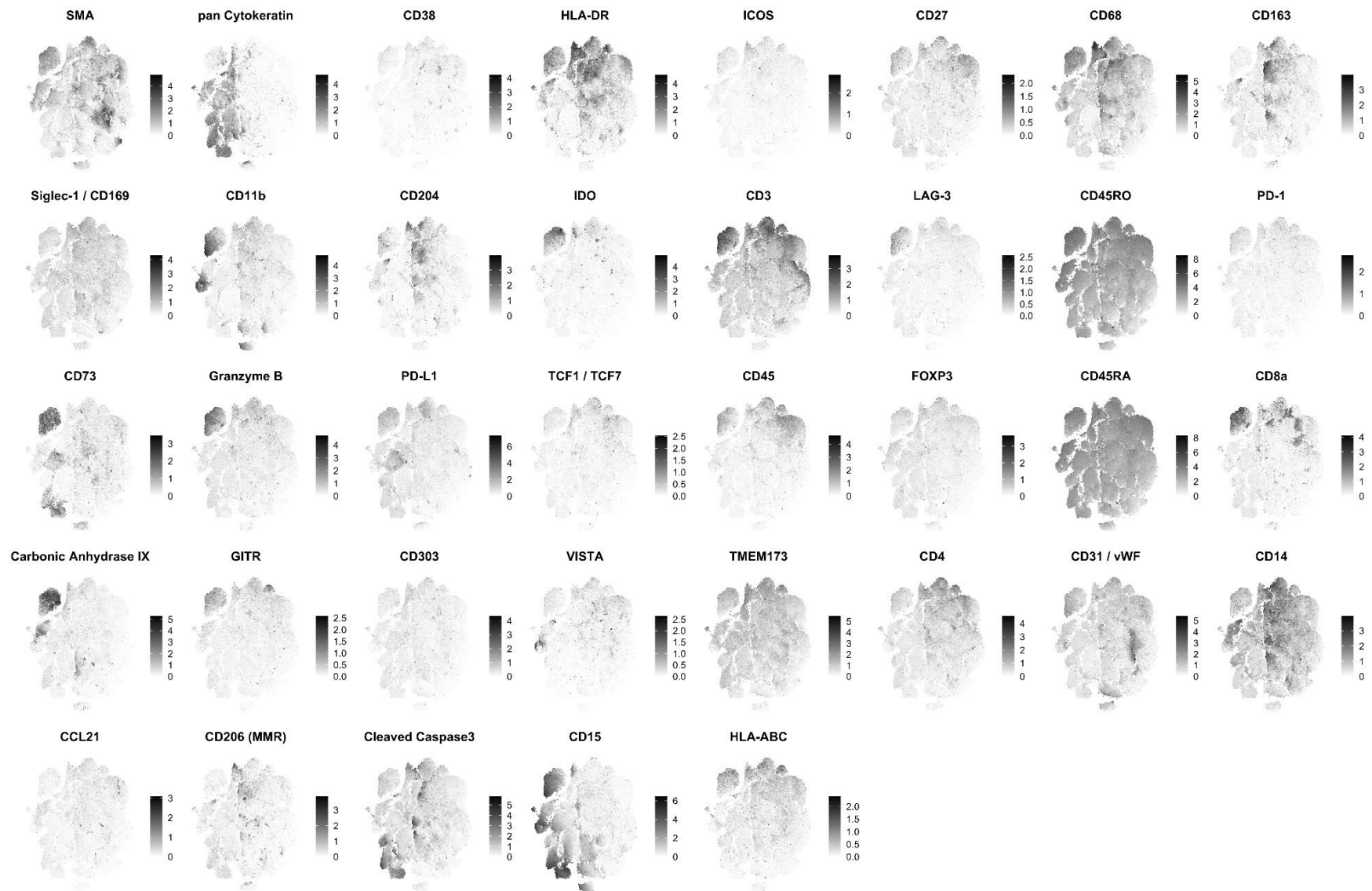
Stefanie Hiltbrunner<sup>1,2,3,4</sup>, Lena Cords<sup>4,5,6,7</sup>, Sabrina Kasser<sup>2,4</sup>, Sandra N. Freiburger<sup>8</sup>, Susanne Kreutzer<sup>9</sup>, Nora C. Toussaint<sup>10,11</sup>, Linda Grob<sup>10,11</sup>, Isabelle Opitz<sup>12</sup>, Michael Messerli<sup>3,13</sup>, Martin Zoche<sup>8</sup>, Alex Soltermann<sup>8</sup>, Markus Rechsteiner<sup>8</sup>, Maries van den Broek<sup>4,14</sup>, Bernd Bodenmiller<sup>4,5,6</sup>, and Alessandra Curioni-Fontecedro<sup>1,2,3,4,15\*</sup>



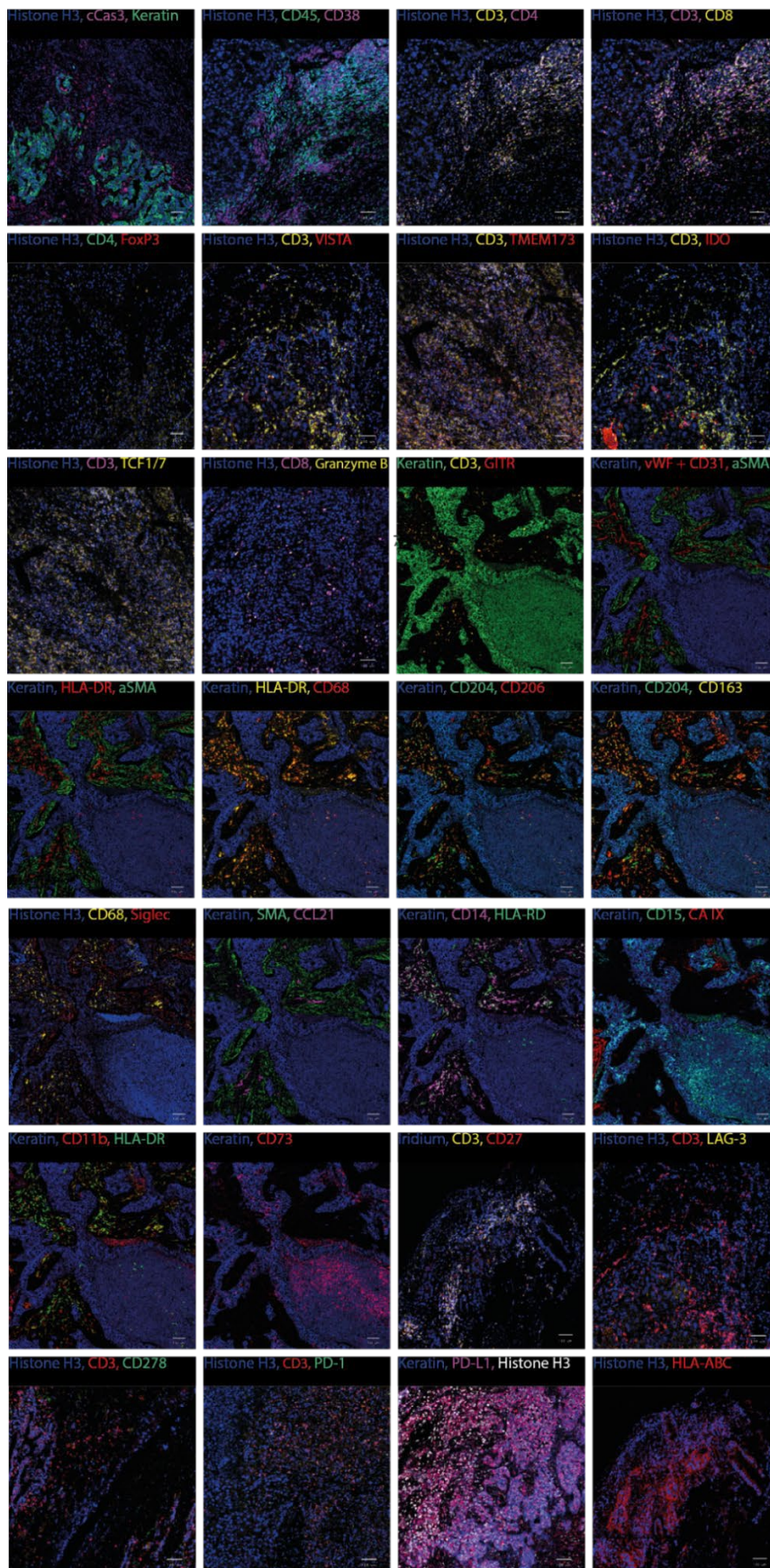
**Supplementary Fig. 1:** Schematic overview on the analyzed areas by IMC. In the responding and resistant tumors a CD3 high and a CD3 low area were selected.

**a****b**

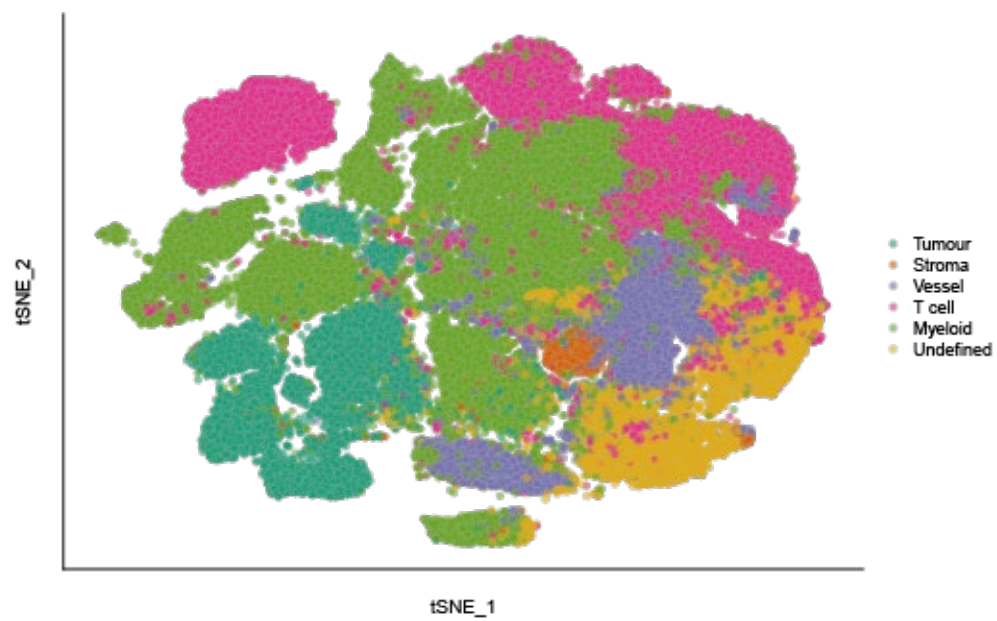
**Supplementary Fig. 2:** Overview on sequencing data from (a) patient 1, (b) patient 7. The black outer ring indicates all SNVs plotted according to their frequency, green dots mutations only at response, red dots mutations only at resistance. The ring in the middle indicates all CNVs, inner ring at response, outer ring at resistance, dark red: copy number > 4, light red: copy number > 2, light blue: copy number < 2, dark blue: copy number = 0, the two rings in the center represent RNA sequencing data, red: overexpression, blue: underexpression, inner ring at response, outer ring at resistance, data related to the TCGA cohort.



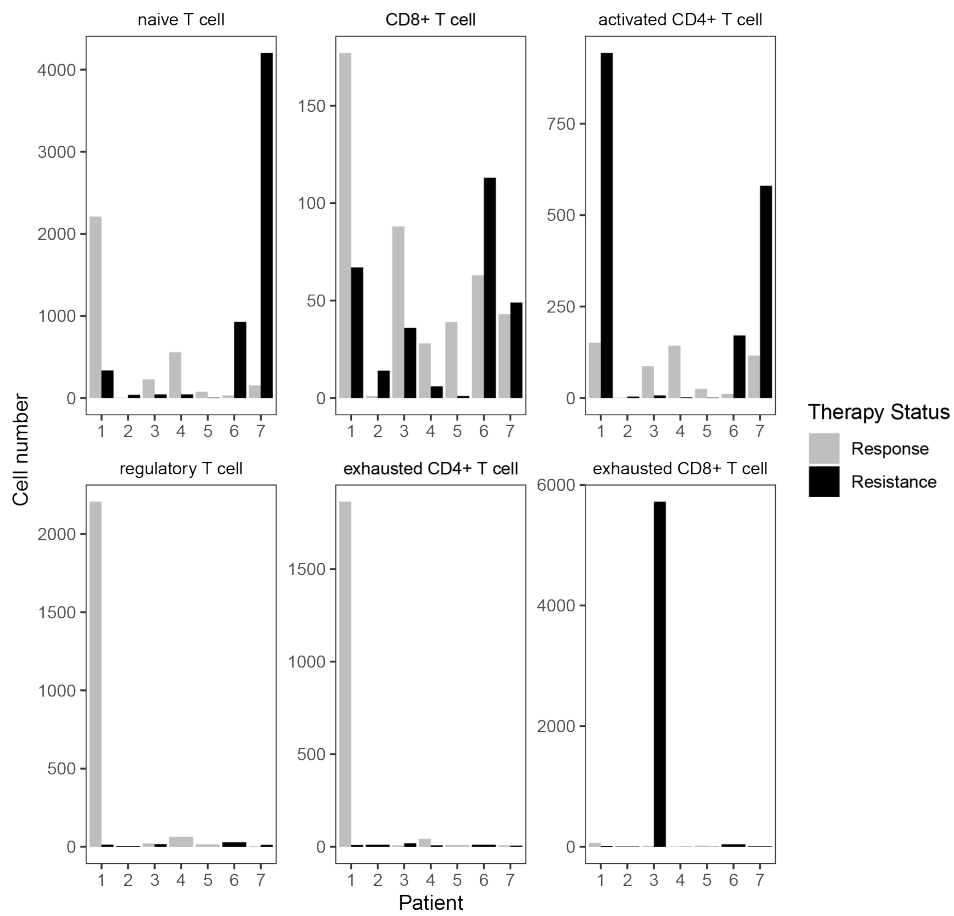
**Supplementary Fig. 3: t-SNE plots over all cell markers used in the study**



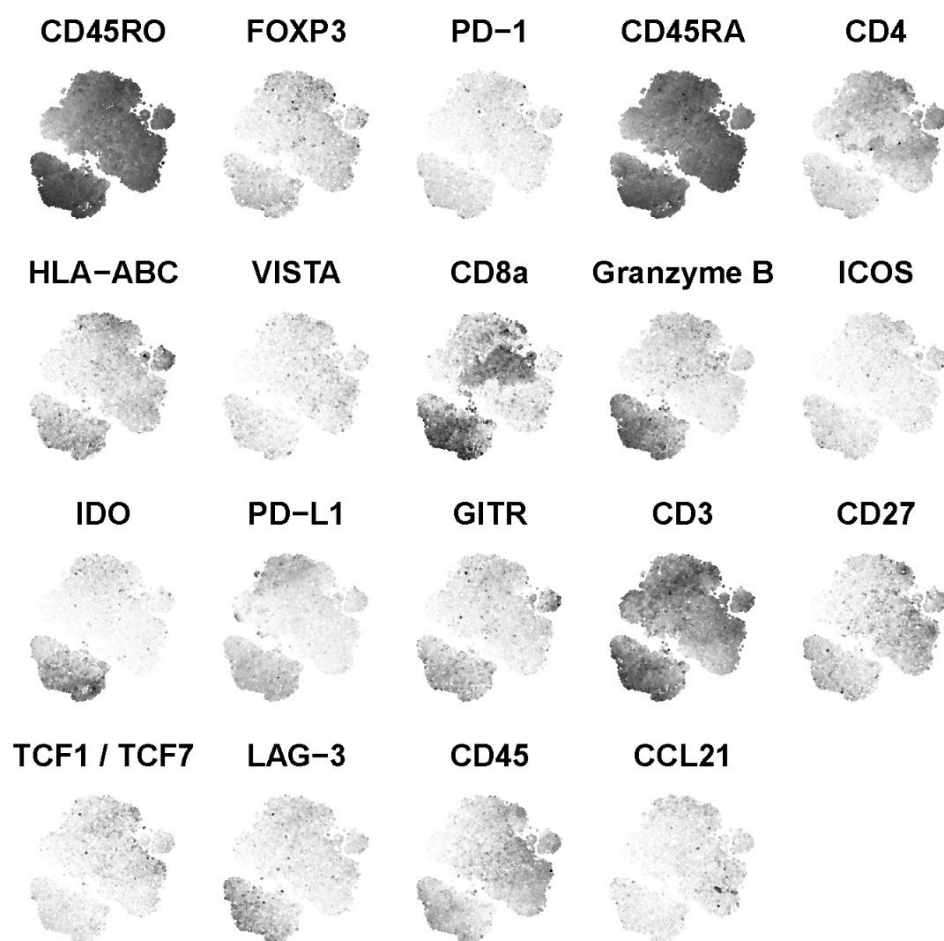
**Supplementary Fig. 4:** Representative immunofluorescence stainings of all IMC antibodies used in the study.



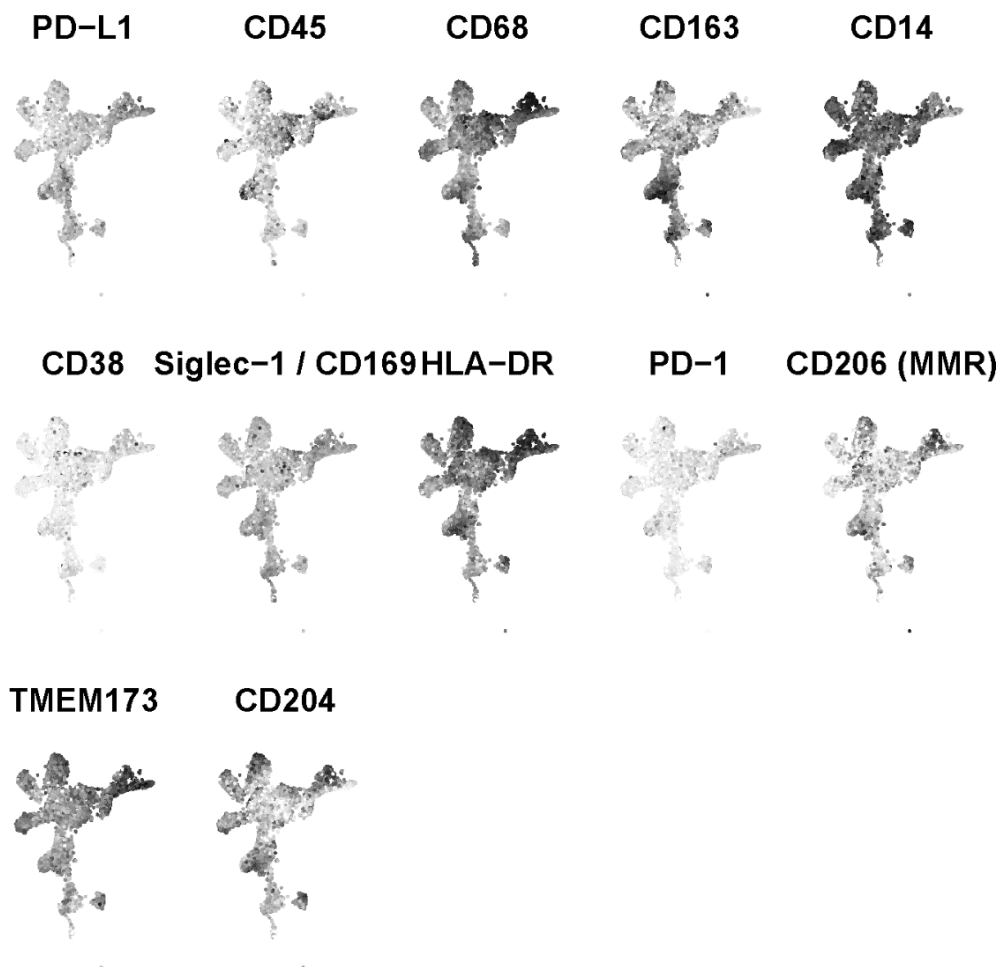
**Supplementary Fig. 5:** t-SNE plot colored-coded to the cell subtypes depicts clear separation between the different subtypes, related to Fig. 4 and 5



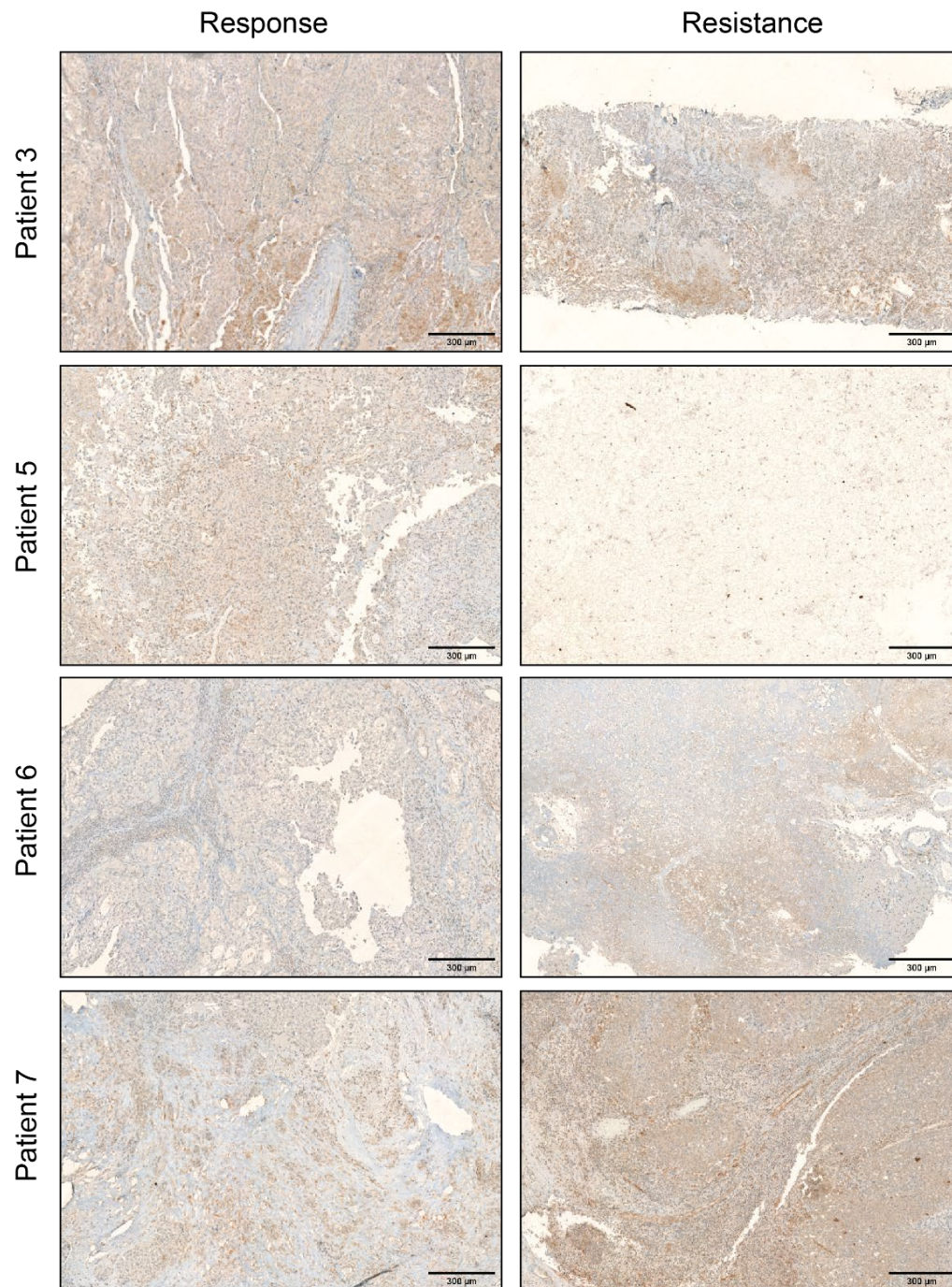
**Supplementary Fig. 6:** Numbers of T cell subsets at response and resistance, related to Fig. 3



**Supplementary Fig. 7:** t-SNE plots over all T cell markers, related to Fig. 4



**Supplementary Fig. 8:** t-SNE plots over all macrophage cell markers, related to Fig. 5



**Supplementary Fig.9:** IHC of Tim-3 at response and at resistance in patients 3, 5, 6 and 7, magnification 4x, scale bar 300  $\mu$ m, one tumor per patient for each time point was analyzed.

**Supplementary Table 1.** Patient history

|                  | Stage at diagnosis and histology | Treatment lines           | Time of resistance after start of CPI, months (m) |
|------------------|----------------------------------|---------------------------|---------------------------------------------------|
| <b>Patient 1</b> | IIIB (Ad)                        | CRT → anti-PD1            | 10m                                               |
| <b>Patient 2</b> | IV (Ad)                          | CRT → anti-PD1+anti-CTLA4 | 6m                                                |
| <b>Patient 3</b> | IV (Ad)                          | TKI → anti-PD1            | 7m                                                |
| <b>Patient 4</b> | IV (Ad-Sq)                       | CRT → Ch → anti-PD1       | 9m                                                |
| <b>Patient 5</b> | IV (Ad)                          | Anti-PD1                  | 8m                                                |
| <b>Patient 6</b> | IV (Ad)                          | CRT → anti-PD1            | 8m                                                |
| <b>Patient 7</b> | IV (Ad)                          | Ch → anti-PD1             | 15m                                               |

Ad: Adenocarcinoma; Ad-Sq: Adenosquamous; CRT: Chemoradiotherapy; Ch= Chemotherapy; CPI: checkpoint inhibitors

**Supplementary Table 2.** Genes with short variants of patient 7 only present at resistance

| Chromosome | Position  | Change | Frequency | Genes                                                                                                                                                      | Annotation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|------------|-----------|--------|-----------|------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| chr1       | 82409203  | G>T    | 34.2      | ADGRL2                                                                                                                                                     | ADGRL2:c.948G>T p.Met316Ile                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| chr2       | 67631048  | G>T    | 31.6      | ETAA1                                                                                                                                                      | ETAA1:c.1234G>T p.Asp412Tyr                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| chr9       | 18775811  | T>C    | 29.6      | ADAMTSL1                                                                                                                                                   | ADAMTSL1:c.2468T>C p.Leu823Pro                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| chr9       | 126214571 | T>A    | 26.3      | DENND1A                                                                                                                                                    | DENND1A:c.1283A>T p.Lys428Met                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| chr19      | 7523450   | C>G    | 23.1      | ARHGEF18                                                                                                                                                   | ARHGEF18:c.1670C>G p.Ala557Gly;ARHGEF18:c.1196C>G p.Ala399Gly                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| chr12      | 97051883  | A>T    | 22.2      | CFAP54                                                                                                                                                     | CFAP54:c.5324A>T p.His1775Leu                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| chr12      | 120106195 | C>T    | 21        | PRKAB1                                                                                                                                                     | PRKAB1:c.146C>T p.Ser49Phe;PRKAB1:c.146C>T                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| chr5       | 108207909 | G>T    | 20        | FER                                                                                                                                                        | FER:c.919G>T p.Val307Leu;FER:c.394G>T p.Val132Leu                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| chr5       | 140803085 | C>G    | 19.3      | PCDHGA11;PCDHGB8P;PCDHGB7;PCDHGA1;PCDHGA2;PCDHGA3;PCDHGB1;PCDHGA4;PCDHGB2;PCDHGA5;PCDHGB3;PCDHGA6;PCDHGA7;PCDHGB4;PCDHGA8;PCDHGB5;PCDHGA9;PCDHGB6;PCDHGA10 | PCDHGA11:c.2291C>G p.Ser764Trp;PCDHGB8P:n.-2768C>G ;PCDHGB7:c.*3232C>G ;PCDHGA1:c.2422-71289C>G ;PCDHGA2:c.2425-71289C>G ;PCDHGA3:c.2425-71289C>G ;PCDHGB1:c.2409+70849C>G ;PCDHGA4:c.2514+65897C>G ;PCDHGB2:c.2421+60962C>G ;PCDHGA5:c.2421+56767C>G ;PCDHGB3:c.2415+50709C>G ;PCDHGA6:c.2424+47011C>G ;PCDHGA7:c.2424+38195C>G ;PCDHGB4:c.2397+33237C>G ;PCDHGA8:c.2424+28281C>G ;PCDHGB5:c.2397+22994C>G ;PCDHGA9:c.2424+18142C>G ;PCDHGB6:c.2418+12898C>G ;PCDHGA10:c.2436+7907C>G ;PCDHGB7:c.2415+3244C>G ;PCDHGA11:c.1878+413C>G |
| chr9       | 71679882  | G>T    | 17.9      | FXN                                                                                                                                                        | FXN:c.413G>T p.Gly138Val;FXN:c.413G>T                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| chr9       | 140481452 | C>T    | 17.9      | ZMYND19                                                                                                                                                    | ZMYND19:c.326G>A p.Arg109Gln                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| chr7       | 73119495  | G>A    | 17.4      | STX1A                                                                                                                                                      | STX1A:c.268C>T p.Arg90Cys                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| chr20      | 16021914  | G>T    | 16.7      | MACROD2                                                                                                                                                    | MACROD2:c.1222G>T p.Gly408Cys;MACROD2:c.517G>T p.Gly173Cys                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| chr15      | 49074401  | G>A    | 16.5      | CEP152                                                                                                                                                     | CEP152:c.1348C>T p.Gln450*                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| chr12      | 72029263  | C>A    | 16.4      | ZFC3H1                                                                                                                                                     | ZFC3H1:c.2198G>T p.Gly733Val                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| chr21      | 46078009  | T>A    | 16        | KRTAP12-3;KRTAP12-4;TSPEAR                                                                                                                                 | KRTAP12-3:c.113T>A p.Val38Glu;KRTAP12-4:c.-3478A>T ;TSPEAR:c.82+53339A>T ;TSPEAR:c.-123+32451A>T                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| chr12      | 78400279  | T>C    | 15.5      | NAV3                                                                                                                                                       | NAV3:c.961T>C p.Ser321Pro                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| chr3       | 51378776  | G>C    | 15.4      | DOCK3                                                                                                                                                      | DOCK3:c.3875G>C p.Gly1292Ala                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| chr12      | 81283136  | G>A    | 14.9      | LIN7A                                                                                                                                                      | LIN7A:c.95C>T p.Ala32Val;LIN7A:c.-12-41035C>T ;LIN7A:n.276-41035C>T ;LIN7A:n.288C>T                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| chr2       | 84936633  | G>T    | 14.3      | DNAH6                                                                                                                                                      | DNAH6:c.9215G>T p.Gly3072Val                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| chr4       | 9785030   | C>A    | 13.8      | DRD5                                                                                                                                                       | DRD5:c.1377C>A p.Cys459*                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| chr9       | 107289445 | C>T    | 13.8      | OR13C4                                                                                                                                                     | OR13C4:c.46G>A p.Gly16Arg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| chr22      | 17670893  | G>T    | 13.6      | CECR1                                                                                                                                                      | CECR1:c.911C>A p.Ser304Tyr;CECR1:c.188C>A p.Ser63Tyr;CECR1:c.785C>A p.Ser262Tyr;CECR1:c.551C>A p.Ser184Tyr                                                                                                                                                                                                                                                                                                                                                                                                                             |
| chr11      | 74632266  | C>T    | 13.3      | XRRA1                                                                                                                                                      | XRRA1:c.625G>A p.Ala209Thr;XRRA1:c.-75G>A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| chr5       | 108673054 | C>T    | 12.5      | PJA2                                                                                                                                                       | PJA2:c.2005G>A p.Gly669Arg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| chr20      | 60902010  | C>T    | 12.3      | LAMA5                                                                                                                                                      | LAMA5:c.5125G>A p.Gly1709Ser                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| chr11      | 62295656  | A>T    | 12.2      | AHNAK                                                                                                                                                      | AHNAK:c.6233T>A p.Val2078Asp;AHNAK:c.342+6819T>A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |

|       |           |     |      |         |                                                                                                                                                                                         |
|-------|-----------|-----|------|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| chr20 | 31815368  | C>A | 11.6 | BPIFA3  | BPIFA3:c.710C>A p.Thr237Asn;BPIFA3:c.602C>A p.Thr201Asn                                                                                                                                 |
| chr20 | 40113115  | G>A | 11   | CHD6    | CHD6:c.2134C>T p.Arg712Cys                                                                                                                                                              |
| chr9  | 112141911 | G>T | 10.8 | PTPN3   | PTPN3:c.2667C>A p.Ser889Arg;PTPN3:c.1806C>A p.Ser602Arg;PTPN3:c.1671C>A p.Ser557Arg;PTPN3:c.2274C>A p.Ser758Arg;PTPN3:c.2139C>A p.Ser713Arg;PTPN3:c.2532C>A p.Ser844Arg;PTPN3:n.1549C>A |
| chr3  | 164906102 | G>T | 10.7 | SLITRK3 | SLITRK3:c.2517C>A p.His839Gln                                                                                                                                                           |
| chr11 | 69063836  | C>A | 5.4  | MYEOV   | MYEOV:c.919C>A p.Leu307Ile;MYEOV:c.745C>A p.Leu249Ile                                                                                                                                   |

**Supplementary Table 3.** Genomic characteristics of all patients included in the study (Foundation One analysis)

| Patient | Sex    | Histology | Time point | Status    | Specimen    | Short Variants                                                                                        | Copy number alteration                                                                                                  | Rearrangements              | TMB-Status |
|---------|--------|-----------|------------|-----------|-------------|-------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|-----------------------------|------------|
| 1       | male   | AC        | Response   | na        | Lung        |                                                                                                       |                                                                                                                         |                             |            |
|         |        |           | Resistance | Completed | Soft Tissue | <i>ARID1A</i> , <i>ATR</i> , <i>CTNNB1</i> , <i>KRAS G12C</i> , <i>MUTYH</i> splice site, <i>TP53</i> | <i>GNAS</i> , <i>KRAS G12C</i> , <i>MCL1</i> , <i>MET</i> , <i>NFKBIA</i> , <i>NKX2-1</i> , <i>RAD21</i> , <i>VEGFA</i> |                             | 13 Muts/Mb |
| 2       | male   | AC        | Response   | na        | Liver       |                                                                                                       |                                                                                                                         |                             |            |
|         |        |           | Resistance | Completed | Soft Tissue | <i>DNMT3A</i> , <i>KRAS G12V</i> , <i>NFKBIA</i>                                                      |                                                                                                                         | <i>CDKN2A-CDKN2A</i> fusion | 8 Muts/Mb  |
| 3       | male   | AC        | Response   | Completed | Lung        | <i>KRAS G13C</i> , <i>NF1</i> splice site, <i>NF1</i> , <i>SMARCA4</i> , <i>TP53</i> , <i>U2AF1</i>   |                                                                                                                         |                             | 34 Muts/Mb |
|         |        |           | Resistance | na        | Lung        |                                                                                                       |                                                                                                                         |                             |            |
| 4       | female | SCC       | Response   | Completed | Lung        | <i>KRAS G13D</i> , <i>NFE2L2</i> , <i>PIK3CB</i> , <i>TP53</i> splice site                            | <i>RICTOR</i>                                                                                                           |                             | 4 Muts/Mb  |
|         |        |           | Resistance | na        | Lung        |                                                                                                       |                                                                                                                         |                             |            |
| 5       | male   | AC        | Response   | Completed | Soft Tissue | <i>MAP2K1</i> , <i>TP53</i>                                                                           | <i>NFKBIA</i>                                                                                                           |                             | 19 Muts/Mb |
|         |        |           | Resistance | Completed | Lymph Node  | <i>MAP2K1</i> , <i>SMARCA4</i> , <i>TP53</i>                                                          |                                                                                                                         |                             | 14 Muts/Mb |
| 6       | female | AC        | Response   | Completed | Brain       | <i>KRAS G13C</i> , <i>NOTCH1</i> , <i>STK11</i> , <i>TP53</i>                                         | <i>MCL1</i> , <i>RPTOR</i>                                                                                              |                             | 11 Muts/Mb |
|         |        |           | Resistance | na        | Brain       |                                                                                                       |                                                                                                                         |                             |            |
| 7       | male   | AC        | Response   | Completed | Pleura      | <i>CREBBP</i> , <i>FANCA</i> , <i>TP53</i>                                                            |                                                                                                                         |                             | 8 Muts/Mb  |
|         |        |           | Resistance | Completed | Lymph Node  | <i>CREBBP</i> , <i>FANCA</i> , <i>TP53</i>                                                            | <i>ARFRP1</i> , <i>AURKA</i> , <i>CRKL</i> , <i>GNAS</i> , <i>MAPK1</i> , <i>ZNF217</i>                                 |                             | 6 Muts/Mb  |

AC: Adenocarcinoma, SSC: Squamous cell carcinoma

**Supplementary Table 4.** Genes with copy number alterations (from WGS) in sample from tumor from patient #7 isolated at resistance

| Gene      | Chromosome | Start     | End       | Copy Number | Call Type | p value    | log2 ratio |
|-----------|------------|-----------|-----------|-------------|-----------|------------|------------|
| JB175072  | chr16      | 33964385  | 34196972  | 6.4         | 2         | 1.78E-05   | 1.67401    |
| LOC646813 | chr11      | 50323722  | 55026423  | 4.7         | 2         | 0.00014859 | 1.23908    |
| TRNA_Lys  | chr11      | 50323722  | 55026423  | 4.7         | 2         | 0.00014859 | 1.23908    |
| OR4A5     | chr11      | 50323722  | 55026423  | 4.7         | 2         | 0.00014859 | 1.23908    |
| OR4C46    | chr11      | 50323722  | 55026423  | 4.7         | 2         | 0.00014859 | 1.23908    |
| DQ579288  | chr4       | 49093177  | 52661966  | 4.1         | 2         | 0.00205358 | 1.03634    |
| DQ583161  | chr4       | 49093177  | 52661966  | 4.1         | 2         | 0.00205358 | 1.03634    |
| DQ579969  | chr4       | 49093177  | 52661966  | 4.1         | 2         | 0.00205358 | 1.03634    |
| DQ593719  | chr4       | 49093177  | 52661966  | 4.1         | 2         | 0.00205358 | 1.03634    |
| DQ596206  | chr4       | 49093177  | 52661966  | 4.1         | 2         | 0.00205358 | 1.03634    |
| AK097814  | chr1       | 1645990   | 1943347   | 3.8         | 2         | 0.0031059  | 0.930962   |
| CALML6    | chr1       | 1645990   | 1943347   | 3.8         | 2         | 0.0031059  | 0.930962   |
| TMEM52    | chr1       | 1645990   | 1943347   | 3.8         | 2         | 0.0031059  | 0.930962   |
| C1orf222  | chr1       | 1645990   | 1943347   | 3.8         | 2         | 0.0031059  | 0.930962   |
| SLC35E2   | chr1       | 1645990   | 1943347   | 3.8         | 2         | 0.0031059  | 0.930962   |
| GNB1      | chr1       | 1645990   | 1943347   | 3.8         | 2         | 0.0031059  | 0.930962   |
| KIAA1751  | chr1       | 1645990   | 1943347   | 3.8         | 2         | 0.0031059  | 0.930962   |
| CDK11B    | chr1       | 1645990   | 1943347   | 3.8         | 2         | 0.0031059  | 0.930962   |
| NADK      | chr1       | 1645990   | 1943347   | 3.8         | 2         | 0.0031059  | 0.930962   |
| ACTR3BP5  | chr10      | 38772322  | 42818239  | 3.6         | 2         | 0.00520024 | 0.853701   |
| ANXA10    | chr4       | 169076438 | 169077537 | 0           | -2        | 6.00E-05   | -6.1742    |

**Supplementary Table 5.** Most up- and downregulated genes of patients #1 and #7

| Downregulated genes<br>* downregulated in both patients |                    |           |                    | Upregulated genes<br>*upregulated in both patients |                    |            |                    |
|---------------------------------------------------------|--------------------|-----------|--------------------|----------------------------------------------------|--------------------|------------|--------------------|
| Patient 1                                               |                    | Patient 7 |                    | Patient 1                                          |                    | Patient 7  |                    |
| Gene Name                                               | Fold Change (log2) | Gene      | Fold Change (log2) | Gene                                               | Fold Change (log2) | Gene       | Fold Change (log2) |
| HAGHL                                                   | -3.68              | PLA2G7    | -1.36              | TFPI2                                              | 5.43               | CCDC80     | 1.74               |
| TIFAB                                                   | -3.69              | ATP2A3    | -1.36              | CXCL14                                             | 5.42               | COL11A1*   | 1.71               |
| IL27                                                    | -3.70              | IL7R      | -1.36              | COL11A1*                                           | 5.42               | ZFH4       | 1.71               |
| MS4A4E                                                  | -3.71              | SNORA49   | -1.36              | MEG3*                                              | 5.30               | MEG3*      | 1.67               |
| CARD11                                                  | -3.71              | ITGA4     | -1.36              | PTGS2                                              | 5.29               | HTRA3*     | 1.66               |
| SRPK3                                                   | -3.71              | INPP5D    | -1.37              | MXRA5                                              | 5.06               | COL6A6     | 1.59               |
| PPARG                                                   | -3.72              | HLA-DQA1  | -1.37              | IGFBP5                                             | 5.02               | MAPK4      | 1.58               |
| AVPR2                                                   | -3.72              | MST1R     | -1.38              | MMP11                                              | 4.95               | COL8A1     | 1.57               |
| LOC105379051                                            | -3.74              | SNORA36C  | -1.39              | THBS2*                                             | 4.94               | ADAMTS17   | 1.57               |
| ZBP1                                                    | -3.74              | CYTH4     | -1.39              | PXDN                                               | 4.94               | SLC2A3     | 1.57               |
| BLID                                                    | -3.75              | FUCA1     | -1.39              | RUNX1T1                                            | 4.93               | PLOD2      | 1.53               |
| CSNK1G2-AS1                                             | -3.76              | ARHGEF6   | -1.39              | FAM227A                                            | 4.85               | COL1A1     | 1.52               |
| ZNF366                                                  | -3.77              | SAMSN1    | -1.39              | MMP1                                               | 4.82               | MBOAT2     | 1.51               |
| FBXL15                                                  | -3.77              | PRRG3     | -1.40              | SULF1                                              | 4.79               | MMP2       | 1.50               |
| IL20RB                                                  | -3.77              | GIMAP4    | -1.40              | PDGFRA                                             | 4.74               | POU6F1     | 1.50               |
| TRPV3                                                   | -3.77              | MYH14     | -1.40              | DIO2                                               | 4.71               | ZIC5       | 1.48               |
| TAF6L                                                   | -3.79              | JAK3      | -1.40              | COL12A1                                            | 4.67               | CLDN3      | 1.47               |
| IZUMO4                                                  | -3.79              | FGD2      | -1.40              | HMCN1                                              | 4.64               | PPP1R9A    | 1.46               |
| LIME1                                                   | -3.79              | LAPTM5    | -1.41              | HOXD1                                              | 4.62               | P2RX2      | 1.46               |
| POU5F1                                                  | -3.79              | CCL2      | -1.41              | TRPM8                                              | 4.62               | AFAP1      | 1.46               |
| OASL                                                    | -3.79              | LCK       | -1.41              | HEY1                                               | 4.61               | DNAH14     | 1.45               |
| ODF3B                                                   | -3.80              | SNORD17   | -1.41              | PDLIM3                                             | 4.59               | PRG4       | 1.45               |
| UCA1*                                                   | -3.80              | GIMAP5    | -1.42              | HOPX                                               | 4.58               | PROSER2    | 1.45               |
| XIRP2                                                   | -3.81              | ARHGAP25  | -1.42              | DDIT4L                                             | 4.57               | CBS        | 1.42               |
| ATG9B                                                   | -3.81              | CPNE4     | -1.42              | TMPRSS4                                            | 4.55               | MEIS2      | 1.42               |
| PAQR6                                                   | -3.82              | OAS1      | -1.42              | MAGI2-AS3                                          | 4.54               | CCDC8      | 1.42               |
| SLC26A1                                                 | -3.82              | FCRL5     | -1.43              | STC1                                               | 4.52               | TRHDE-AS1  | 1.41               |
| PNPLA7                                                  | -3.82              | SPN       | -1.43              | PDPN                                               | 4.52               | PRKAA2     | 1.40               |
| UNC5A                                                   | -3.83              | DDX60     | -1.43              | CTSE                                               | 4.49               | COL1A2*    | 1.39               |
| PLD4                                                    | -3.84              | STAT1     | -1.44              | MMP13                                              | 4.49               | RNF144A    | 1.39               |
| PSTPIP1                                                 | -3.84              | DOCK2     | -1.44              | CACHD1                                             | 4.48               | TSPYL5     | 1.38               |
| NKG7                                                    | -3.84              | FCER1G    | -1.44              | ADAMTS12                                           | 4.47               | LAMA1      | 1.38               |
| MTRNR2L2                                                | -3.85              | GBP2      | -1.45              | SLC7A2                                             | 4.42               | CYP26B1    | 1.38               |
| FCER2                                                   | -3.86              | HLA-DPA1  | -1.45              | PRODH                                              | 4.42               | HCAR2      | 1.37               |
| ZNF296                                                  | -3.86              | STC1      | -1.45              | MPDZ                                               | 4.41               | PCLC       | 1.37               |
| SAA1                                                    | -3.87              | SPI1      | -1.46              | POSTN                                              | 4.38               | LINC00641  | 1.37               |
| CR2                                                     | -3.88              | IQGAP2    | -1.46              | ABCC9                                              | 4.37               | ACOX3      | 1.37               |
| FLT3LG                                                  | -3.89              | RNU5D-1   | -1.46              | CLDN2                                              | 4.36               | COL9A3     | 1.36               |
| TSPAP1-AS1                                              | -3.89              | C1QB      | -1.47              | LAMA4                                              | 4.35               | AFAP1-AS1  | 1.36               |
| PHOSPHO1                                                | -3.89              | LSP1      | -1.47              | IBSP                                               | 4.34               | SLIT3      | 1.36               |
| CARMIL2                                                 | -3.90              | TSPAN7    | -1.47              | TSPAN12                                            | 4.33               | SLIT2      | 1.36               |
| APOB                                                    | -3.90              | RASAL3    | -1.47              | CTGF*                                              | 4.33               | ESYT3      | 1.35               |
| PIK3CD-AS2                                              | -3.90              | PRKCB     | -1.47              | PI15                                               | 4.33               | WDR87      | 1.35               |
| VWA2                                                    | -3.90              | CD38      | -1.48              | MYBPH                                              | 4.30               | LMTK3      | 1.34               |
| MUC4                                                    | -3.91              | HLA-DRA   | -1.48              | COL6A5                                             | 4.30               | ATRNL1     | 1.34               |
| AMH                                                     | -3.91              | ADAMDEC1  | -1.48              | IGSF3                                              | 4.29               | TDRP       | 1.33               |
| EPHB6                                                   | -3.91              | SCARNA13  | -1.49              | ESM1                                               | 4.25               | MYO3A      | 1.33               |
| BRSK2                                                   | -3.92              | GPRIN3    | -1.49              | ADGRD1                                             | 4.25               | TMEM117    | 1.33               |
| LINGO3                                                  | -3.93              | CORO1A    | -1.50              | HSPB8                                              | 4.25               | THBS2*     | 1.32               |
| DTX1                                                    | -3.94              | CD3E      | -1.50              | ETFRF1                                             | 4.24               | CCDC149    | 1.31               |
| TMPRSS9                                                 | -3.95              | NCKAP1L   | -1.51              | SGIP1                                              | 4.23               | NRCAM      | 1.31               |
| PRF1                                                    | -3.95              | SRGN      | -1.51              | RGS16                                              | 4.22               | PLA2G12A   | 1.30               |
| CRACR2B                                                 | -3.96              | CTSC      | -1.51              | SNORD113-8                                         | 4.21               | CGNL1      | 1.30               |
| TSPAN32                                                 | -3.97              | PIK3AP1   | -1.51              | GJA1                                               | 4.21               | ATP7B      | 1.30               |
| GMPR                                                    | -3.97              | HLA-F     | -1.52              | GGTLC1                                             | 4.20               | PLAGL1     | 1.30               |
| LINC00612                                               | -3.97              | SNORA36A  | -1.52              | KCNJ8                                              | 4.20               | PTPN3      | 1.30               |
| CD22                                                    | -3.97              | PLEK      | -1.52              | COL1A2*                                            | 4.20               | TCHH       | 1.30               |
| SHANK2                                                  | -3.98              | SP140     | -1.53              | SYT7                                               | 4.18               | CTGF*      | 1.30               |
| CARD9                                                   | -4.01              | CAPN8     | -1.53              | COL5A1                                             | 4.18               | SNX7       | 1.29               |
| P2RY8                                                   | -4.02              | JCHAIN    | -1.53              | PKHD1                                              | 4.17               | PLEKHG3    | 1.29               |
| FAM30A                                                  | -4.02              | ITGB2     | -1.53              | PGM5                                               | 4.17               | STARD13-AS | 1.29               |
| SAA2                                                    | -4.03              | LCP2      | -1.54              | PRRX1                                              | 4.16               | MAML3      | 1.28               |
| VPS9D1                                                  | -4.03              | MIR142*   | -1.55              | HTRA3*                                             | 4.14               | DCN        | 1.28               |
| MIR3687-2                                               | -4.04              | TNC       | -1.55              | MAP1B                                              | 4.14               | CTSV       | 1.28               |
| CD72                                                    | -4.05              | GVINP1    | -1.55              | FGF7                                               | 4.13               | MARVELD1   | 1.28               |
| CD79A                                                   | -4.07              | SNORA54   | -1.55              | COL15A1                                            | 4.13               | CC2D2A     | 1.28               |
| APOBEC3A                                                | -4.09              | SAMHD1    | -1.56              | PDGFRB                                             | 4.13               | ZNF185     | 1.27               |
| CACNA1I                                                 | -4.10              | BANK1     | -1.57              | CPXM1                                              | 4.13               | SLC6A2     | 1.27               |
| JAKMIP1                                                 | -4.10              | IFIT3     | -1.57              | FREM2                                              | 4.11               | COL3A1*    | 1.27               |
| MIR3648-2                                               | -4.12              | SNORD66   | -1.57              | SHROOM4                                            | 4.09               | GJB2       | 1.27               |

|          |       |          |       |
|----------|-------|----------|-------|
| MIR205   | -4.14 | IFI6     | -1.58 |
| PTGER2   | -4.15 | IKZF3    | -1.58 |
| FCRL1    | -4.16 | ITGAX    | -1.58 |
| PLIN4    | -4.16 | CXCL10   | -1.59 |
| LY9      | -4.17 | TRIM22   | -1.59 |
| PTPRCAP  | -4.19 | C1QA     | -1.60 |
| FAM129C  | -4.25 | CCL21    | -1.60 |
| PRKCQ    | -4.27 | BST2     | -1.61 |
| HBB      | -4.29 | FYB      | -1.62 |
| MTRNR2L8 | -4.30 | SERPINA1 | -1.62 |
| FGA      | -4.33 | XAF1     | -1.62 |
| HKDC1    | -4.34 | SLA      | -1.62 |
| NAPSB    | -4.37 | CXCL13   | -1.62 |
| PLIN5    | -4.38 | MS4A1    | -1.63 |
| LIMD2    | -4.38 | PTPRC    | -1.64 |
| RASGRP2  | -4.39 | CYFIP2   | -1.64 |
| ALB      | -4.43 | RSAD2    | -1.65 |
| RP1      | -4.43 | RELN     | -1.65 |
| SCML4    | -4.45 | CTSS     | -1.66 |
| ORM1     | -4.50 | SNHG12   | -1.66 |
| PF4      | -4.58 | IFI44    | -1.67 |
| TUBB1    | -4.59 | OAS2     | -1.67 |
| ABCC2    | -4.60 | SPOCK2   | -1.68 |
| MIR142*  | -4.62 | SNORA71D | -1.69 |
| CRP      | -4.63 | UCA1*    | -1.69 |
| RUFY4    | -4.66 | DNAJC6   | -1.69 |
| NCF1     | -4.68 | NLRC5    | -1.70 |
| IRX2     | -4.71 | LCP1     | -1.70 |
| HP       | -4.96 | SNORA55  | -1.72 |
| AZGP1    | -5.21 | ITGAL    | -1.79 |

|              |      |           |      |
|--------------|------|-----------|------|
| LINC01021    | 4.08 | DOCK3     | 1.26 |
| UNC5C        | 4.08 | FAM149A   | 1.26 |
| RASSF8       | 4.07 | MARK1     | 1.26 |
| ITGA11       | 4.06 | PNMA5     | 1.25 |
| LONRF2       | 4.04 | IQCA1     | 1.25 |
| PRR26        | 4.03 | SLC18A3   | 1.25 |
| COL3A1*      | 4.03 | SFRP2     | 1.24 |
| SCIN         | 4.03 | DGKH      | 1.22 |
| KCNJ12       | 4.02 | C2orf61   | 1.22 |
| GPC6         | 4.02 | PLSCR4    | 1.22 |
| ADAMTS1      | 4.02 | CHN2      | 1.22 |
| GLI3         | 4.02 | MIR30B    | 1.21 |
| ACTG2        | 4.01 | STXBP6    | 1.21 |
| EGFL6        | 4.01 | PQLC3     | 1.21 |
| SNORD114-1   | 4.01 | ALDH1A2   | 1.21 |
| PPP1R1B      | 3.99 | LINC00442 | 1.21 |
| CXCL5        | 3.98 | PLEKHA5   | 1.21 |
| FBN1         | 3.98 | PODN      | 1.21 |
| PAEP         | 3.98 | PALM2     | 1.21 |
| LUM          | 3.98 | PTPN13    | 1.21 |
| KCNE4        | 3.96 | PCDHGA2   | 1.20 |
| DLC1         | 3.96 | DLGAP2    | 1.20 |
| CLIC6        | 3.96 | MET       | 1.20 |
| PTHLH        | 3.95 | KIF26B    | 1.19 |
| PTK7         | 3.95 | KIAA1324  | 1.19 |
| LOC101929705 | 3.94 | FKBP10    | 1.19 |
| RCAN2        | 3.94 | CTHRC1    | 1.19 |
| FAP          | 3.93 | COL4A5    | 1.19 |
| BICC1        | 3.93 | KL        | 1.18 |
| LAPTM4B      | 3.92 | MISP      | 1.18 |

**Supplementary Table 6.** GO terms of the 100 most up- and downregulated genes in patient #1 and #7**Downregulated genes (GO terms)**

| <b>Patient 1</b>                                                               |                     |                    |          |             |
|--------------------------------------------------------------------------------|---------------------|--------------------|----------|-------------|
| Gene Set Name                                                                  | # Genes in Gene Set | # Genes in Overlap | p-value  | FDR q-value |
| GOBP_DEFENSE_RESPONSE                                                          | 1816                | 27                 | 6.39E-15 | 6.75E-11    |
| GOBP_INFLAMMATORY_RESPONSE                                                     | 850                 | 19                 | 1.06E-13 | 5.62E-10    |
| GOBP_IMMUNE_RESPONSE                                                           | 1940                | 24                 | 1.32E-11 | 4.66E-08    |
| GOBP_BIOLOGICAL_PROCESS_INVOLVED_IN_INTERSPECIES_INTERACTION_BETWEEN_ORGANISMS | 1722                | 22                 | 6.03E-11 | 1.59E-07    |
| GOBP_DEFENSE_RESPONSE_TO_OTHER_ORGANISM                                        | 1178                | 18                 | 2.57E-10 | 5.43E-07    |
| GOBP_CELL_ACTIVATION                                                           | 1150                | 17                 | 1.41E-09 | 2.49E-06    |
| GOBP_REGULATION_OF_IMMUNE_SYSTEM_PROCESS                                       | 1523                | 19                 | 2.21E-09 | 3.34E-06    |
| GOBP_REGULATION_OF_IMMUNE_RESPONSE                                             | 918                 | 15                 | 3.84E-09 | 5.07E-06    |
| GOCC_INTRINSIC_COMPONENT_OF_PLASMA_MEMBRANE                                    | 1795                | 19                 | 3.10E-08 | 3.45E-05    |
| GOBP_INNATE_IMMUNE_RESPONSE                                                    | 921                 | 14                 | 3.27E-08 | 3.45E-05    |
| <b>Patient 7</b>                                                               |                     |                    |          |             |
| Gene Set Name                                                                  | # Genes in Gene Set | # Genes in Overlap | p-value  | FDR q-value |
| GOBP_IMMUNE_RESPONSE                                                           | 1940                | 53                 | 2.84E-43 | 3.00E-39    |
| GOBP_REGULATION_OF_IMMUNE_SYSTEM_PROCESS                                       | 1523                | 45                 | 1.97E-37 | 1.04E-33    |
| GOBP_POSITIVE_REGULATION_OF_IMMUNE_SYSTEM_PROCESS                              | 966                 | 37                 | 2.47E-34 | 8.69E-31    |
| GOBP_CELL_ACTIVATION                                                           | 1150                | 38                 | 6.11E-33 | 1.61E-29    |
| GOBP_DEFENSE_RESPONSE                                                          | 1816                | 43                 | 1.23E-31 | 2.59E-28    |
| GOBP_LYMPHOCYTE_ACTIVATION                                                     | 841                 | 31                 | 4.70E-28 | 8.27E-25    |
| GOBP_REGULATION_OF_IMMUNE_RESPONSE                                             | 918                 | 31                 | 6.55E-27 | 9.88E-24    |
| GOBP_BIOLOGICAL_PROCESS_INVOLVED_IN_INTERSPECIES_INTERACTION_BETWEEN_ORGANISMS | 1722                | 37                 | 2.04E-25 | 2.69E-22    |
| GOBP_DEFENSE_RESPONSE_TO_OTHER_ORGANISM                                        | 1178                | 32                 | 6.72E-25 | 7.88E-22    |
| GOBP_REGULATION_OF_CELL_ACTIVATION                                             | 720                 | 27                 | 1.41E-24 | 1.49E-21    |

**Upregulated genes (GO terms)**

| <b>Patient 1</b>                                                             |                     |                    |          |             |
|------------------------------------------------------------------------------|---------------------|--------------------|----------|-------------|
| Gene Set Name                                                                | # Genes in Gene Set | # Genes in Overlap | p-value  | FDR q-value |
| GOBP_EXTERNAL_ENCAPSULATING_STRUCTURE_ORGANIZATION                           | 324                 | 23                 | 2.88E-27 | 3.04E-23    |
| GOCC_EXTERNAL_ENCAPSULATING_STRUCTURE                                        | 575                 | 26                 | 9.93E-26 | 5.24E-22    |
| GOCC_COLLAGEN_CONTAINING_EXTRACELLULAR_MATRIX                                | 434                 | 21                 | 1.92E-21 | 6.75E-18    |
| GOBP_TISSUE_DEVELOPMENT                                                      | 1998                | 35                 | 4.35E-21 | 9.15E-18    |
| GOMF_EXTRACELLULAR_MATRIX_STRUCTURAL_CONSTITUENT                             | 173                 | 16                 | 4.89E-21 | 9.15E-18    |
| GOBP_CIRCULATORY_SYSTEM_DEVELOPMENT                                          | 1211                | 29                 | 5.20E-21 | 9.15E-18    |
| GOBP_CELL_ADHESION                                                           | 1541                | 28                 | 3.62E-17 | 5.45E-14    |
| GOBP_TUBE_DEVELOPMENT                                                        | 1155                | 24                 | 5.09E-16 | 6.72E-13    |
| GOBP_ANIMAL_ORGAN_MORPHOGENESIS                                              | 1058                | 23                 | 8.73E-16 | 1.02E-12    |
| GOBP_ANATOMICAL_STRUCTURE_FORMATION_INVOLVED_IN_MORPHOGENESIS                | 1244                | 24                 | 2.61E-15 | 2.76E-12    |
| <b>Patient 7</b>                                                             |                     |                    |          |             |
| Gene Set Name                                                                | # Genes in Gene Set | # Genes in Overlap | p-value  | FDR q-value |
| GOCC_COLLAGEN_CONTAINING_EXTRACELLULAR_MATRIX                                | 434                 | 19                 | 9.76E-19 | 1.03E-14    |
| GOMF_EXTRACELLULAR_MATRIX_STRUCTURAL_CONSTITUENT                             | 173                 | 14                 | 9.20E-18 | 3.35E-14    |
| GOCC_EXTERNAL_ENCAPSULATING_STRUCTURE                                        | 575                 | 20                 | 9.52E-18 | 3.35E-14    |
| GOBP_EXTERNAL_ENCAPSULATING_STRUCTURE_ORGANIZATION                           | 324                 | 16                 | 9.93E-17 | 2.62E-13    |
| GOMF_EXTRACELLULAR_MATRIX_STRUCTURAL_CONSTITUENT_CONFERRING_TENSILE_STRENGTH | 41                  | 8                  | 7.72E-14 | 1.63E-10    |
| GOCC_COLLAGEN_TRIMER                                                         | 86                  | 9                  | 7.56E-13 | 1.33E-09    |
| GOBP_ANIMAL_ORGAN_MORPHOGENESIS                                              | 1058                | 20                 | 8.92E-13 | 1.35E-09    |
| GOBP_TISSUE_DEVELOPMENT                                                      | 1998                | 25                 | 7.40E-12 | 9.77E-09    |
| GOMF_STRUCTURAL_MOLECULE_ACTIVITY                                            | 808                 | 17                 | 1.05E-11 | 1.23E-08    |
| GOCC_COMPLEX_OF_COLLAGEN_TRIMERS                                             | 22                  | 6                  | 1.23E-11 | 1.30E-08    |

**Supplementary Table 7. Antibodies used for IMC**

| Metal Tag | Target                            | Antibody Clone            | Lot            | Host   | Clonality  | Vendor                   | Catalogue number | Final Concentration |
|-----------|-----------------------------------|---------------------------|----------------|--------|------------|--------------------------|------------------|---------------------|
| Nd150     | CD204                             | J5HTR3                    | 4338161        | Mouse  | Monoclonal | eBioscience              | 14-9054-82       | 5 ug/mL             |
| Tm169     | VISTA                             | D1L2G                     | 2              | Rabbit | Monoclonal | Cell Signal Technologies | 64953            | 3 ug/mL             |
| Pr141     | pan Cytokeratin                   | AE1                       | 2341224        | Mouse  | Monoclonal | Milipore                 | MAB1612          | 2 ug/mL             |
| Pr141     | Keratin Epithelial                | AE3                       | 2607604        | Mouse  | Monoclonal | Milipore                 | MAB1611          | 2 ug/mL             |
| In113     | Histone H3                        | D1H2                      | 15             | Rabbit | Monoclonal | Cell Signal Technologies | 4499BF           | 1 ug/mL             |
| Nd142     | CD38                              | EPR4106                   | GR3251769-4    | Rabbit | Monoclonal | Abcam                    | ab176886         | 3 ug/mL             |
| Sm149     | CD11b                             | SP330                     | GR3258740-1    | Rabbit | Monoclonal | Abcam                    | ab241408         | 4 ug/mL             |
| Eu151     | Indoleamine 2-3-dioxygenase (IDO) | SP260                     | GR3259345-2    | Rabbit | Monoclonal | Abcam                    | ab245737         | 5 ug/mL             |
| Yb172     | CD31                              | EPR3094                   | GR3229164-2    | Rabbit | Monoclonal | Abcam                    | ab207090         | 4 ug/mL             |
| Yb173     | CD14                              | SP192                     | GR3245776-1    | Rabbit | Monoclonal | Abcam                    | ab230903         | 2 ug/mL             |
| Y89       | HLA-ABC                           | EMR8-5                    | 565292         | Mouse  | Monoclonal | BD Biosciences           | 565292           | 4 ug/mL             |
| Gd158     | CD134                             | Ber-ACT35 (ACT35)         | B247739        | Mouse  | Monoclonal | BioLegend                | 350002           | 2.5 ug/mL           |
| Ho165     | CD8a                              | C8/144B                   | 2003078        | Mouse  | Monoclonal | EBioscience              | 14-0085-82       | 2 ug/mL             |
| Yb172     | vWF                               | poly vwf                  | 3239865        | Rabbit | Polyclonal | Milipore                 | AB7356           | 4 ug/mL             |
| In115     | SMA                               | 1A4                       | 2033287        | Mouse  | Monoclonal | Ebioscience              | 14-9760-82       | 0.25 ug/mL          |
| Nd146     | CD68                              | KP1                       | 2071775        | Mouse  | Monoclonal | EBioscience              | 14-0688-82       | 3 ug/mL             |
| Dy161     | TCF1/TCF7                         | C63D9                     | 9              | Rabbit | Monoclonal | Cell Signal Technologies | 2203             | 4 ug/mL             |
| Nd143     | HLA-DR                            | TAL 1B5                   | GR3222279-4    | Mouse  | Monoclonal | Abcam                    | ab20181          | 1 ug/mL             |
| Lu175     | CD206 (MMR)                       | 685645                    | CEZR0217061    | Mouse  | Monoclonal | R&D Systems              | MAB25341         | 4.5 ug/mL           |
| Gd156     | CD73                              | D7F9A                     | 2              | Rabbit | Monoclonal | Cell Signal Technologies | 13160BF          | 4 ug/mL             |
| Yb176     | Cleaved Caspase3                  | C92-605                   | 6074683        | Rabbit | Monoclonal | Bectin Dickinson         | 559565           | 3 ug/mL             |
| Bi209     | CD15                              | HI98                      | B265372        | Mouse  | Monoclonal | BioLegend                | 301902           | 5 ug/mL             |
| Dy163     | FOXP3                             | 236A/E7                   | 2049450        | Mouse  | Monoclonal | EBioscience              | 14-4777-82       | 5 ug/mL             |
| Er166     | Carbonic Anhydrase IX             | polyclonal_CA9_AF2188     | VNQ0218041     | Goat   | Polyclonal | R&D Systems              | AF2188           | 3 ug/mL             |
| Er167     | GITR / TNFRSF18                   | D5V7P                     | 2              | Rabbit | Monoclonal | Cell Signal Technologies | 10419            | 10 ug/mL            |
| Sm147     | CD163                             | EDHu-1                    | 149022a        | Mouse  | Monoclonal | Novus Biologicals        | NB110-40686      | 4.5 ug/mL           |
| Gd155     | CD279 (PD-1)                      | D4W2J                     | 4              | Rabbit | Monoclonal | Cell Signal Technologies | 86163BF          | 5 ug/mL             |
| Sm152     | CD3                               | polyclonal_A0452          | 20068606       | Rabbit | Polyclonal | Dako                     | 20068606         | 6 ug/mL             |
| Yb171     | CD4                               | EPR6855                   | GR3215375-27   | Rabbit | Monoclonal | Abcam                    | ab181724         | 5 ug/mL             |
| Eu153     | LAG-3                             | D2G4O                     | 5              | Rabbit | Monoclonal | Cell Signal Technologies | 15372BF          | 10 ug/mL            |
| Tb159     | Granzyme B                        | D6E9W                     | 3              | Rabbit | Monoclonal | Cell Signal Technologies | 46890BF          | 5 ug/mL             |
| Nd145     | CD27                              | Polyclonal_CD27 / TNFRSF7 | AXS0418031     | Goat   | Polyclonal | R&D Systems              | AF382            | 10 ug/mL            |
| Nd148     | Siglec-1 / CD169                  | SP213                     | GR3259343-1    | Rabbit | Monoclonal | Abcam                    | ab245735         | 5 ug/mL             |
| Sm154     | CD45RO                            | UCHL1                     | 95787-13291511 | Mouse  | Monoclonal | Biolegend                | 304202           | 3 ug/mL             |
| Dy162     | CD45                              | 2B11                      | 2069169        | Mouse  | Monoclonal | eBioscience              | 14-9457-82       | 4 ug/mL             |
| Er170     | TMEM173                           | SP339                     | GR3245429-1    | Rabbit | Monoclonal | Abcam                    | ab238796         | 4 ug/mL             |
| Yb174     | CCL21 / 6Ckine                    | Polyclonal_CCL21 / 6Ckine | AYJ218071      | Goat   | Polyclonal | R&D Systems              | AF366            | 5 ug/mL             |
| Nd144     | CD278 (ICOS)                      | D1K2T                     | 4              | Rabbit | Monoclonal | Cell Signal Technologies | 89601BF          | 5 ug/mL             |
| Dy164     | CD45RA                            | HI100                     | 95783-13291513 | Mouse  | Monoclonal | BioLegend                | 304102           | 5 ug/mL             |

|       |                     |                                   |             |        |            |             |          |         |
|-------|---------------------|-----------------------------------|-------------|--------|------------|-------------|----------|---------|
| Gd160 | CD274 (B7-H1-PD-L1) | 73-10                             | GR3237208-3 | Rabbit | Monoclonal | Abcam       | ab226766 | 5 ug/mL |
| Er168 | CD303               | Polyclonal_DLEC / CLEC4C / BDCA-2 | IDL0218101  | Goat   | Polyclonal | R&D Systems | AF1376   | 3 ug/mL |

**Supplementary Table 8.** Antibodies used for immunohistochemistry

| Target | Antibody Clone | Vendor          | Catalogue number | Detection            |
|--------|----------------|-----------------|------------------|----------------------|
| PDL1   | E1L3N          | Cell Signaling  | 1368S            | OptiView Kit Ventana |
| CD8    | C8/144B        | DAKO/Agilent    | M7103            | OptiView Kit Ventana |
| CD3    | LN10           | Leica/Biosystem | NCL-L-CD3-565    | OptiView Kit Ventana |
| TIGIT  | TG1            | Dianova         | DIA-TG1          | HRP Refine Kit Leica |
| Tim3   | 4C4G3          | Proteintech     | 60355-1-Ig       | OptiView Kit Ventana |