

## SUPPLEMENTARY TABLE TITLES AND LEGENDS

**Supplementary Table 1: Tumor Sample WES coverage**

| Exome Sequencing Coverage |        |         |            |
|---------------------------|--------|---------|------------|
| Patient ID                | Normal | Primary | Metastatic |
| ST_001                    | 148    | 244     | 251        |
| ST_002                    | 136    | 258     | 309        |
| ST_004                    | 79     | 388     | 225        |
| ST_007                    | 139    | 231     | 274        |
| ST_009                    | 97     | 325     | 267        |
| ST_011                    | 113    | 179     | 180        |
| ST_013                    | 131    | 365     | 234        |
| ST_014                    | 101    | 248     | 246        |
| ST_015                    | 259    | 309     | 559        |
| ST_016                    | 114    | 266     | 271        |
| ST_017                    | 107    | 309     | 272        |
| ST_018                    | 146    | 235     | 316        |
| ST_019                    | 157    | 279     | 295        |
| ST_020                    | 131    | 279     | 390        |
| ST_021                    | 145    | 231     | 306        |
| ST_022                    | 127    | 264     | 350        |
| ST_023                    | 142    | 384     | 309        |
| ST_025                    | 150    | 272     | 356        |
| ST_026                    | 112    | 250     | 266        |
| ST_027                    | 237    | 258     | 266        |
| ST_028                    | 117    | 279     | 339        |
| ST_029                    | 131    | 230     | 279        |
| ST_030                    | 65     | 331     | 139        |
| LT_031                    | 133    | 244     | 442        |
| LT_033                    | 226    | 300     | 316        |
| LT_034                    | 169    | 428     | 248        |
| LT_035                    | 142    | 278     | 355        |
| LT_036                    | 210    | 299     | 332        |
| LT_037                    | 213    | 263     | 336        |
| LT_038                    | 120    | 344     | 288        |
| LT_039                    | 175    | 389     | 218        |
| LT_041                    | 167    | 275     | 319        |
| LT_042                    | 186    | 338     | 181        |
| LT_043                    | 90     | 439     | 364        |
| LT_044                    | 241    | 331     | 278        |
| LT_045                    | 138    | 396     | 344        |
| LT_046                    | 187    | 283     | 331        |

Exome sequencing coverage for each patient's normal, primary, and metastatic tumor. Coverage is expressed as the number of times a base would be covered by sequencing reads.

**Supplementary Table 2** BRCA1 Somatic Mutations

| <b>Patient ID</b> | <b>Clonal Variant</b> | <b>Variant Type</b>  | <b>Nucleotide Position</b> | <b>Amino Acid Change</b> | <b>Primary VAF</b> | <b>Metastatic VAF</b> | <b>ClinVar Clinical Significance</b> |
|-------------------|-----------------------|----------------------|----------------------------|--------------------------|--------------------|-----------------------|--------------------------------------|
| ST_009            | yes                   | missense             | c.5344A>C                  | p.F1782V                 | 72.48              | 46.46                 | not provided                         |
| ST_015            | yes                   | frame-shift deletion | c.2419                     | p.A807fs                 | 36.96              | 42.76                 | pathogenic                           |
| LT_039            | no                    | missense             | c.3419C>G                  | p.S1140T                 | 56.67              | NA                    | uncertain significance               |
| LT_042            | yes                   | frame-shift deletion | c.2284                     | p.R762fs                 | 92.04              | 75.77                 | pathogenic                           |

All BRCA1 somatic mutations identified in tumor cohort for WES with a VAF>30. Nucleotide position and amino acid changes are based on GRCh37.

**Supplementary Table 3** BRCA1 Germline Mutations

| Patient ID | Variant Type | Nucleotide Position | Amino Acid Change | VAF   | ClinVar Clinical Significance                |
|------------|--------------|---------------------|-------------------|-------|--|
| ST_021     | missense     | c.4798G>C           | p.P1600A          | 53.77 | conflicting interpretations of pathogenicity |
| ST_027     | missense     | c.1487C>T           | p.R496H           | 43.96 | benign                                       |
| ST_027     | missense     | c.455A>G            | p.L152P           | 59.51 | conflicting interpretations of pathogenicity |
| ST_029     | missense     | c.4931G>C           | p.A1644G          | 51.67 | pathogenic/likely pathogenic                 |
| LT_031     | nonsense     | c.2035T>A           | p.K679*           | 57.81 | pathogenic                                   |
| LT_031     | missense     | c.736A>C            | p.L246V           | 55.29 | benign                                       |
| LT_037     | missense     | c.5396T>C           | p.D1799G          | 42.86 | conflicting interpretations of pathogenicity |
| LT_044     | nonsense     | c.2138G>C           | p.S713*           | 37.01 | pathogenic                                   |

All BRCA1 germline mutation identified in patient cohort from WES with a VAF>30. Nucleotide position and amino acid changes are based on GRCh37.

**Supplementary Table 4** BRCA2 Germline Mutations

| Patient ID | Variant Type | Nucleotide Position | Amino Acid Change | VAF   | ClinVar Clinical Significance |
|------------|--------------|---------------------|-------------------|-------|-------------------------------|
| LT_039     | missense     | c.3568C>T           | p.R1190W          | 47.89 | benign                        |

All BRCA2 germline mutations identified in patient cohort from WES with a VAF>30. Nucleotide position and amino acid changes are based on GRCh37.

**Supplementary Table 5** Somatic TP53 mutations

| Patient ID | Clonal Variant | Variant Type          | Nucleotide Position         | Amino Acid Change         | p53 Protein Domain | Primary VAF | Metastatic VAF |
|------------|----------------|-----------------------|-----------------------------|---------------------------|--------------------|-------------|----------------|
| ST_001     | yes            | missense              | c.536T>C                    | p.H179R                   | DNA-binding domain | 55.70       | 23.85          |
| ST_002     | yes            | missense              | c.423G>C                    | p.C141W                   | DNA-binding domain | 76.04       | 55.11          |
| ST_007     | yes            | mssense               | c.707T>C                    | p.Y236C                   | DNA-binding domain | 49.59       | 36.27          |
| ST_009     | yes            | missense              | c.659T>C                    | p.Y220C                   | DNA-binding domain | 72.30       | 50.00          |
| ST_011     | yes            | missense              | c.818C>T                    | p.R273H                   | DNA-binding domain | 92.86       | 64.00          |
| ST_013     | yes            | frame shift deletion  | C.636A>-                    | p.R213fs                  | DNA-binding domain | 92.54       | 78.82          |
| ST_014     | yes            | missense              | c.818C>T                    | p.R273H                   | DNA-binding domain | 47.57       | 25.00          |
| ST_015     | yes            | frame shift deletion  | c.250del                    | p.A84fs                   | NA                 | 38.18       | 29.93          |
| ST_015     | no             | 5' UTR                | c.-7579816G>T               | NULL                      | NA                 | 6.59        | NA             |
| ST_016     | yes            | frame shift deletion  | c.297_294GGAA>-             | p.S99fs                   | DNA-binding domain | 65.69       | 39.93          |
| ST_017     | yes            | missense              | c.487A>T                    | p.Y163N                   | DNA-binding domain | 53.65       | 77.71          |
| ST_018     | yes            | frame shift insertion | c.371_370->A                | p.C124fs                  | DNA-binding domain | 53.23       | 50.00          |
| ST_019     | yes            | in-frame deletion     | c.478_473TGGCGC>-           | p.RAM158in_f<br>rame delL | DNA-binding domain | NA          | NA             |
| ST_020     | yes            | missense              | c.830C>A                    | p.C277F                   | DNA-binding domain | 21.28       | 72.41          |
| ST_021     | yes            | splice site           | c.560-1C>T                  | e5-1                      | NA                 | 30.63       | 25.90          |
| ST_023     | yes            | nonsense              | c.499G>A                    | p.Q167*                   | DNA-binding domain | 18.60       | 50.00          |
| ST_025     | yes            | missense              | c.490T>C                    | p.K164E                   | DNA-binding domain | 49.77       | 62.31          |
| ST_026     | yes            | missense              | c.580G>A                    | p.L194F                   | DNA-binding domain | 53.37       | 55.75          |
| ST_027     | yes            | frame shift deletion  | c.1024G>-                   | p.R342fs                  | tetramer           | 51.16       | 54.20          |
| ST_028     | no             | splice site           | c.376-2T>C                  | e4-2                      | NA                 | 95.05       | NA             |
| ST_029     | yes            | missense              | c.764A>C                    | p.I255S                   | DNA-binding domain | 76.10       | 89.09          |
| ST_030     | yes            | missense              | c.817G>A                    | p.R273C                   | DNA-binding domain | 76.00       | 22.22          |
| LT_031     | yes            | missense              | c.722G>A                    | p.S241F                   | DNA-binding domain | 63.24       | 46.01          |
| LT_033     | yes            | missense              | c.524C>T                    | p.R175H                   | DNA-binding domain | 73.97       | 67.80          |
| LT_033     | yes            | intronic              | c.96+41_96+34<br>CTCCAGGT>- | e2+41                     | NA                 | NA          | NA             |
| LT_034     | yes            | missense              | c.818C>T                    | p.R273H                   | DNA-binding domain | 23.85       | 15.97          |
| LT_035     | yes            | splice site           | c.672+1C>1                  | e5+1                      | NA                 | 57.79       | 45.45          |
| LT_036     | yes            | missense              | c.584A>G                    | p.I195T                   | DNA-binding domain | 90.16       | 81.64          |
| LT_037     | yes            | nonsense              | c.493G>A                    | p.Q165*                   | DNA-binding domain | 67.61       | 80.99          |

|        |     |                       |                              |          |                    |       |       |
|--------|-----|-----------------------|------------------------------|----------|--------------------|-------|-------|
| LT_038 | yes | missense              | c.743C>T                     | p.R248Q  | DNA-binding domain | 83.19 | 61.97 |
| LT_039 | yes | nonsense              | c.592C>A                     | p.E198*  | DNA-binding domain | 70.54 | 41.90 |
| LT_041 | yes | missense              | c.748G>A                     | p.P250S  | DNA-binding domain | 62.39 | 53.60 |
| LT_041 | yes | missense              | c.747C>A                     | p.R249S  | DNA-binding domain | 62.39 | 53.28 |
| LT_041 | no  | intronic              | c.96+41_96+3CTCCAGGT>-       | e2+41    | NA                 | NA    | NA    |
| LT_042 | yes | frame shift deletion  | c.366_350CACAGACTTGGCTGTCC>1 | p.G117fs | DNA-binding domain | NA    | NA    |
| LT_043 | yes | frame shift deletion  | c.801C>-                     | p.N268fs | DNA-binding domain | 82.26 | 83.78 |
| LT_043 | yes | intronic              | c.96+41_96+34CTCCAGGT>-      | e2+41    | NA                 | NA    | NA    |
| LT_044 | yes | missense              | c.488T>G                     | p.Y163S  | DNA-binding domain | 41.98 | 96.08 |
| LT_045 | yes | missense              | c.638C>A                     | p.R213L  | DNA-binding domain | 81.82 | 77.00 |
| LT_046 | yes | frame shift insertion | c.853_852->T                 | p.E284fs | DNA-binding domain | 66.67 | 17.59 |

Somatic TP53 mutations identified in tumor cohort from WES.

**Supplementary Table 6** INTEGRATE Recurrent Gene Fusions

| Recurrent gene fusions unique to ST survivors | Number of samples | Number of patients | Number of primary samples | Number of met samples |
|---|-------------------|--------------------|---------------------------|-----------------------|
| LINC01176>>ZNRF2                              | 11                | 10                 | 4                         | 7                     |
| ZRANB1>>AL731577.2                            | 10                | 9                  | 4                         | 6                     |
| CCDC32>>CBX3                                  | 9                 | 9                  | 6                         | 3                     |
| AC060766.7>>SLFN12                            | 9                 | 9                  | 5                         | 4                     |
| AL035409.1>>ST6GALNAC5                        | 9                 | 8                  | 5                         | 4                     |
| TIAM2>>SCAF8                                  | 10                | 8                  | 6                         | 4                     |
| SLC35A1>>AL109930.1/AL354993.1                | 7                 | 6                  | 3                         | 4                     |
| SLC35A1>>AL354993.1                           | 6                 | 5                  | 2                         | 4                     |
| AC025178.1>>GOLPH3                            | 5                 | 5                  | 3                         | 2                     |
| BMPR1B>>PDLIM5                                | 4                 | 4                  | 3                         | 1                     |
| AL049697.1/SLC35A1>>AL109930.1/AL354993.1     | 3                 | 3                  | 2                         | 1                     |
| SLC35A1>>AL109930.1                           | 4                 | 3                  | 1                         | 3                     |
| BACH1-IT1>>BACH1                              | 3                 | 3                  | 2                         | 1                     |
| FP236383.1>>PDE3A                             | 3                 | 3                  | 2                         | 1                     |
| HYDIN>>AC239809.3                             | 3                 | 3                  | 2                         | 1                     |
| AL596220.1>>C1orf27                           | 3                 | 3                  | 1                         | 2                     |
| PPP1CB>>PLB1                                  | 3                 | 2                  | 2                         | 1                     |
| COL14A1>>DEPTOR                               | 3                 | 2                  | 1                         | 2                     |
| CCDC6>>ANK3                                   | 2                 | 2                  | 1                         | 1                     |
| SLC35A1>>AL354993.1/AL109930.1                | 2                 | 2                  | 1                         | 1                     |
| TRIO>>ARHGEF3                                 | 3                 | 2                  | 2                         | 1                     |
| FP236383.1>>COL6A1                            | 2                 | 2                  | 0                         | 2                     |
| RNU6-4P>>SNORA20/TCP1                         | 2                 | 2                  | 1                         | 1                     |
| ERBB4>>IKZF2                                  | 2                 | 2                  | 1                         | 1                     |
| TPTE2>>MRPS31P2                               | 2                 | 2                  | 2                         | 0                     |
| CATSPERB>>TC2N                                | 2                 | 2                  | 2                         | 0                     |
| PSPC1>>ZMYM5                                  | 3                 | 2                  | 1                         | 2                     |
| RNU6-2>>SNORD10                               | 2                 | 2                  | 2                         | 0                     |
| COL4A2>>COL4A1                                | 2                 | 2                  | 1                         | 1                     |
| NCALD>>GRHL2                                  | 2                 | 2                  | 2                         | 0                     |
| LINC00032>>EQTN                               | 2                 | 2                  | 1                         | 1                     |
| MECOM>>PHC3                                   | 2                 | 2                  | 2                         | 0                     |
| RAD9A>>KDM2A                                  | 2                 | 2                  | 2                         | 0                     |
| SKIL>>PRKCI                                   | 2                 | 2                  | 1                         | 1                     |
| CYP1B1-AS1>>RMDN2                             | 2                 | 2                  | 2                         | 0                     |

Chart showing the recurrent gene fusions predicted by INTEGRATE for the ST survivor tumor samples. The chart displays a breakdown of number and types of samples each gene fusion was identified among the ST survivors.



**Supplementary Table 7** Predicted Collagen Gene Fusions

| Gene fusion (5'>>3')     | Patient sample | Encompassing and spanning reads detected in sample | In-Frame prediction |
|--------------------------|----------------|--|---------------------|
| COL1A1>>7SK/RN7SK        | ST.015.M.FF    | 8  | out-of-frame        |
| COL1A1>>GSN              | ST.001.M.FF    | 4  | in-frame            |
| BROX>>COL1A1             | ST.015.M.FF    | 2  | in-frame            |
| MALAT1>>COL1A2           | ST.018.M.FFPE  | 76   | in-frame            |
| COL1A2>>NEAT1            | ST.029.M.FFPE  | 40   | out-of-frame        |
| C3>>COL1A2               | ST.027.P.FF    | 20   | in-frame            |
| RPS11>>COL1A2            | ST.018.P.FF    | 9  | in-frame            |
| COL1A2>>PABPC1           | ST.001.M.FF    | 7  | in-frame            |
| COL1A2>>PCBP2/AC023509.1 | ST.002.M.FF    | 4  | in-frame            |
| AC093752.1>>COL1A2       | ST.001.M.FF    | 3  | in-frame            |
| COL1A2>>TBC1D4           | ST.018.P.FF    | 3  | out-of-frame        |
| COL1A2>>PCBP2            | ST.002.M.FF    | 2  | in-frame            |
| COL1A2>>TBCCD1           | ST.001.M.FF    | 2  | in-frame            |
| COL1A2>>YWHAB            | ST.029.P.FF    | 2  | in-frame            |
| HM13>>COL1A2             | ST.021.P.FF    | 2  | in-frame            |
| MALAT1>>COL3A1           | ST.028.M.FFPE  | 169  | in-frame            |
| FN1>>COL3A1              | ST.018.P.FF    | 54   | in-frame            |
| COL3A1>>RN7SL2           | ST.001.M.FF    | 52   | out-of-frame        |
| COL3A1>>RMRP             | ST.021.P.FF    | 10   | out-of-frame        |
| CLU>>COL3A1              | ST.029.P.FF    | 4  | in-frame            |
| STX7>>COL3A1             | ST.029.P.FF    | 3  | out-of-frame        |
| HAX1>>COL3A1             | ST.018.P.FF    | 3  | in-frame            |
| MAP2>>COL3A1             | ST.018.P.FF    | 3  | in-frame            |
| COL4A2>>COL4A1           | ST.001.M.FF    | 5  | in-frame            |
|                          | ST.011.P.FF    |  | in-frame            |
| RPL15>>COL4A2            | ST.030.M.FF    | 2  | out-of-frame        |
| FP236383.1>>COL6A1       | ST.023.M.FFPE  | 15   | out-of-frame        |
|                          | ST.028.M.FFPE  | 28   |                     |
| COL6A3>>ARID1B           | ST.021.P.FF    | 3  | out-of-frame        |
| COL6A2>>FP236383.3       | LT.041.M.FFPE  | 7  | out-of-frame        |
| ORC4>>COL6A3             | ST.011.M.FF    | 2  | out-of-frame        |
| COL6A6>>TTLL9            | ST.027.P.FF    | 6  | out-of-frame        |
| RPS24>>COL12A1           | ST.018.P.FF    | 4  | out-of-frame        |

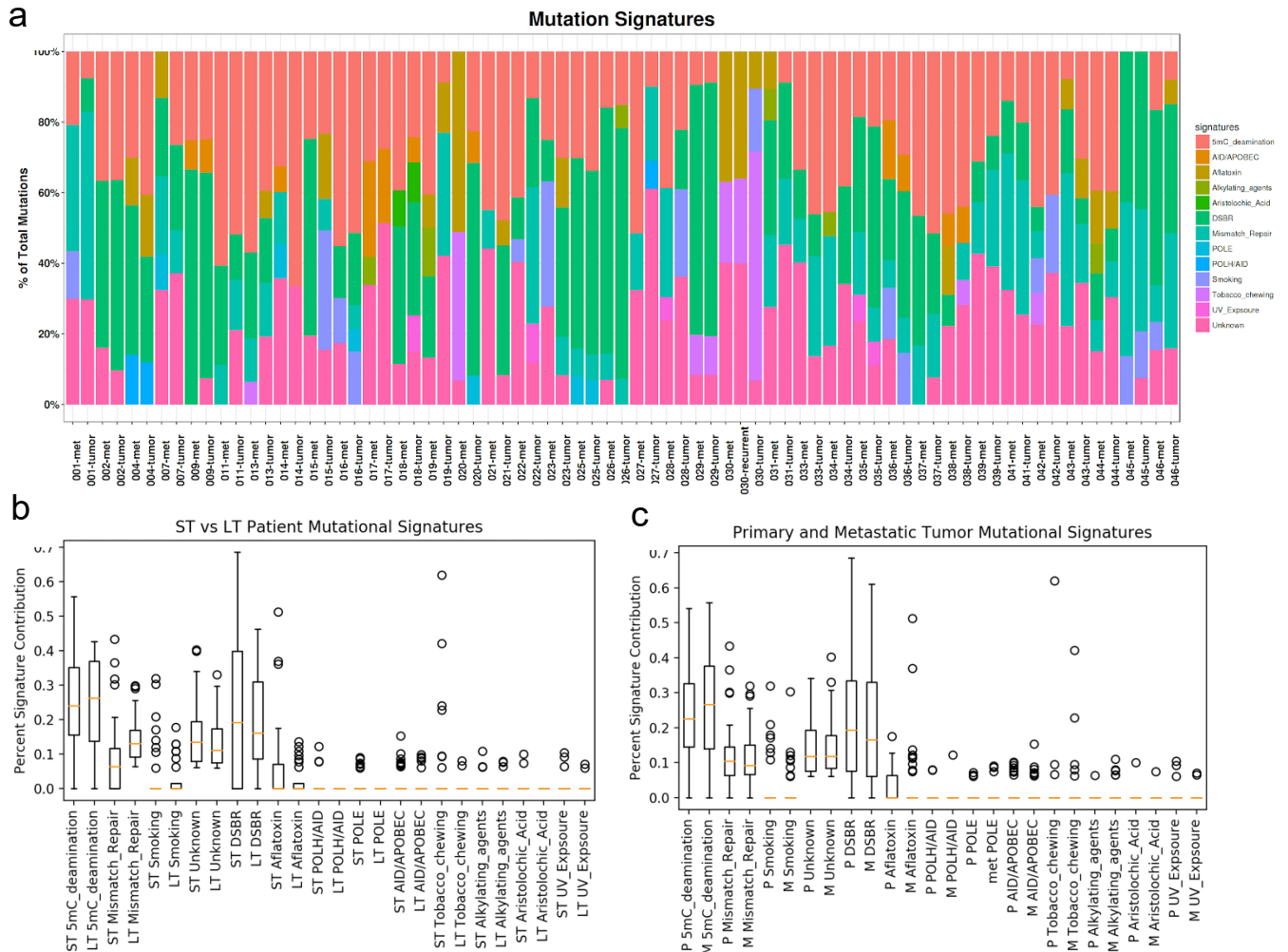
|                 |   |               |          |
|-----------------|---|---------------|----------|
| COL14A1>>DEPTOR | ST.007.P.FF<br>ST.007.M.FF<br>ST.030.M.FF | 49<br>3<br>39 | in-frame |
| TFDP2>>COL18A1  | ST.013.M.FF                               | 3             | in-frame |

Chart displaying the 33 gene fusions involving collagen genes, the sample the fusion was identified in, the number of encompassing and spanning reads that identified the fusion, and INTEGRATE's prediction if the reads were in- or out-of-frame.

**Supplementary Table 8: CIBERSORT immune cell fraction statistics**

| Immune cell type             | ST v LT survivors      |                | Primary (P) v Metastatic (M) |                 | ST survivors - PvM |                | LT survivors - PvM |                | Primary tumors - ST v LT |                | Metastatic tumors - ST v LT |                 |
|------------------------------|------------------------|----------------|------------------------------|-----------------|--------------------|----------------|--------------------|----------------|--------------------------|----------------|-----------------------------|-----------------|
|                              | Mann-Whitney Statistic | p-value        | Wilcoxon Statistic           | p-value         | Wilcoxon Statistic | p-value        | Wilcoxon Statistic | p-value        | Mann-Whitney Statistic   | p-value        | Mann-Whitney Statistic      | p-value         |
| B cells naive                | 690                    | 0.282<br>22397 | 51                           | 0.3793<br>74669 | 32                 | 0.582<br>91955 | 3                  | 0.465<br>20882 | 177                      | 0.370<br>74399 | 167                         | 0.5937<br>86144 |
| B cells memory               | 647                    | 0.722<br>85701 | 196                          | 0.2035<br>40906 | 82                 | 0.600<br>87101 | 24                 | 0.132<br>95729 | 164                      | 0.753<br>43757 | 158                         | 0.9094<br>58667 |
| Plasma cells                 | 696.5                  | 0.241<br>82612 | 52                           | 0.4080<br>44206 | 32                 | 0.582<br>91955 | 4                  | 0.715<br>00065 | 189.5                    | 0.118<br>64898 | 157                         | 0.9229<br>74403 |
| T cells CD8                  | 733                    | 0.176<br>80624 | 187                          | 0.0360<br>35175 | 49                 | 0.010<br>32448 | 45                 | 0.972<br>12533 | 154.5                    | 1              | 217.5                       | 0.0407<br>89302 |
| T cells CD4 naive            | 784                    | 0.002<br>87582 | 23                           | 0.6464<br>62203 | 23                 | 0.646<br>4622  | NA                 | NA             | 189                      | 0.062<br>65679 | 203                         | 0.0227<br>49719 |
| T cells CD4 memory resting   | 690                    | 0.395<br>8775  | 312                          | 0.7414<br>58844 | 104                | 0.482<br>59115 | 24                 | 0.078<br>49121 | 208                      | 0.082<br>55079 | 133                         | 0.5059<br>06885 |
| T cells CD4 memory activated | 658                    | 0.379<br>63095 | 2                            | 0.0250<br>61844 | 1                  | 0.046<br>39946 | 0                  | 0.179<br>71249 | 161                      | 0.458<br>84883 | 169                         | 0.4959<br>12321 |
| T cells follicular helper    | 356                    | 0.002<br>71976 | 259                          | 0.3590<br>21078 | 100                | 0.590<br>0638  | 34                 | 0.267<br>57813 | 84                       | 0.024<br>11617 | 93                          | 0.0495<br>61507 |
| T cells regulatory (Tregs)   | 375                    | 0.002<br>98062 | 144                          | 0.2796<br>41534 | 43                 | 0.861<br>30426 | 12                 | 0.008<br>54492 | 53                       | 0.000<br>4148  | 145                         | 0.7706<br>23805 |
| T cells gamma delta          | 658                    | 0.166<br>19833 | 1                            | 0.2850<br>49407 | 1                  | 0.285<br>04941 | NA                 | NA             | 161                      | 0.458<br>84883 | 168                         | 0.2699<br>00195 |
| NK cells resting             | 581                    | 0.658<br>98278 | 141                          | 0.7970<br>68494 | 26                 | 0.172<br>95492 | 4                  | 0.009<br>92549 | 205.5                    | 0.059<br>63849 | 80                          | 0.0098<br>23086 |
| NK cells activated           | 490.5                  | 0.147<br>8352  | 259                          | 0.9255<br>10561 | 75                 | 0.420<br>90992 | 27                 | 0.196<br>05096 | 105                      | 0.114<br>21541 | 149                         | 0.8837<br>53087 |
| Monocytes                    | 676                    | 0.491<br>60656 | 301                          | 0.6151<br>48209 | 119                | 0.823<br>72856 | 40                 | 0.463<br>13477 | 168                      | 0.660<br>61466 | 164                         | 0.7578<br>58154 |
| Macrophages M0               | 691                    | 0.388<br>08951 | 202                          | 0.0641<br>9212  | 67                 | 0.054<br>24547 | 39                 | 0.649<br>64403 | 181                      | 0.389<br>21972 | 163.5                       | 0.7690<br>31965 |
| Macrophages M1               | 505                    | 0.196<br>18414 | 223                          | 0.3042<br>32069 | 68                 | 0.277<br>24064 | 48                 | 0.807<br>73926 | 109                      | 0.133<br>85961 | 150.5                       | 0.9222<br>738   |
| Macrophages M2               | 499                    | 0.178<br>38381 | 321                          | 0.8504<br>63631 | 115                | 0.726<br>18389 | 41                 | 0.501<br>58691 | 134                      | 0.526<br>85427 | 115                         | 0.2115<br>46541 |
| Dendritic cells resting      | 664                    | 0.413<br>30065 | 34                           | 0.6948<br>86602 | 15                 | 0.674<br>42407 | 5                  | 1              | 162                      | 0.707<br>75726 | 170                         | 0.4666<br>76921 |
| Dendritic cells activated    | 452                    | 0.053<br>03165 | 227                          | 0.9099<br>30768 | 72                 | 0.556<br>57941 | 29                 | 0.432<br>76758 | 134                      | 0.511<br>25239 | 93                          | 0.0464<br>126   |
| Mast cells resting           | 606                    | 0.901<br>55873 | 111                          | 0.8757<br>10309 | 25                 | 0.151<br>95619 | 6                  | 0.092<br>89194 | 139.5                    | 0.605<br>13707 | 166                         | 0.6768<br>59087 |
| Mast cells activated         | 625                    | 0.916<br>40813 | 137                          | 0.2115<br>55387 | 75                 | 0.943<br>39206 | 6                  | 0.028<br>41686 | 124.5                    | 0.324<br>55326 | 183.5                       | 0.3012<br>92617 |
| Eosinophils                  | 715                    | 0.240<br>89382 | 180                          | 0.8288<br>12374 | 85                 | 0.982<br>62729 | 19                 | 0.678<br>40238 | 174                      | 0.516<br>89552 | 182                         | 0.3542<br>47644 |
| Neutrophils                  | 587.5                  | 0.717<br>91202 | 78                           | 0.0396<br>72486 | 21                 | 0.047<br>98975 | 22                 | 0.575<br>06213 | 155                      | 0.984<br>13058 | 143                         | 0.7187<br>26623 |

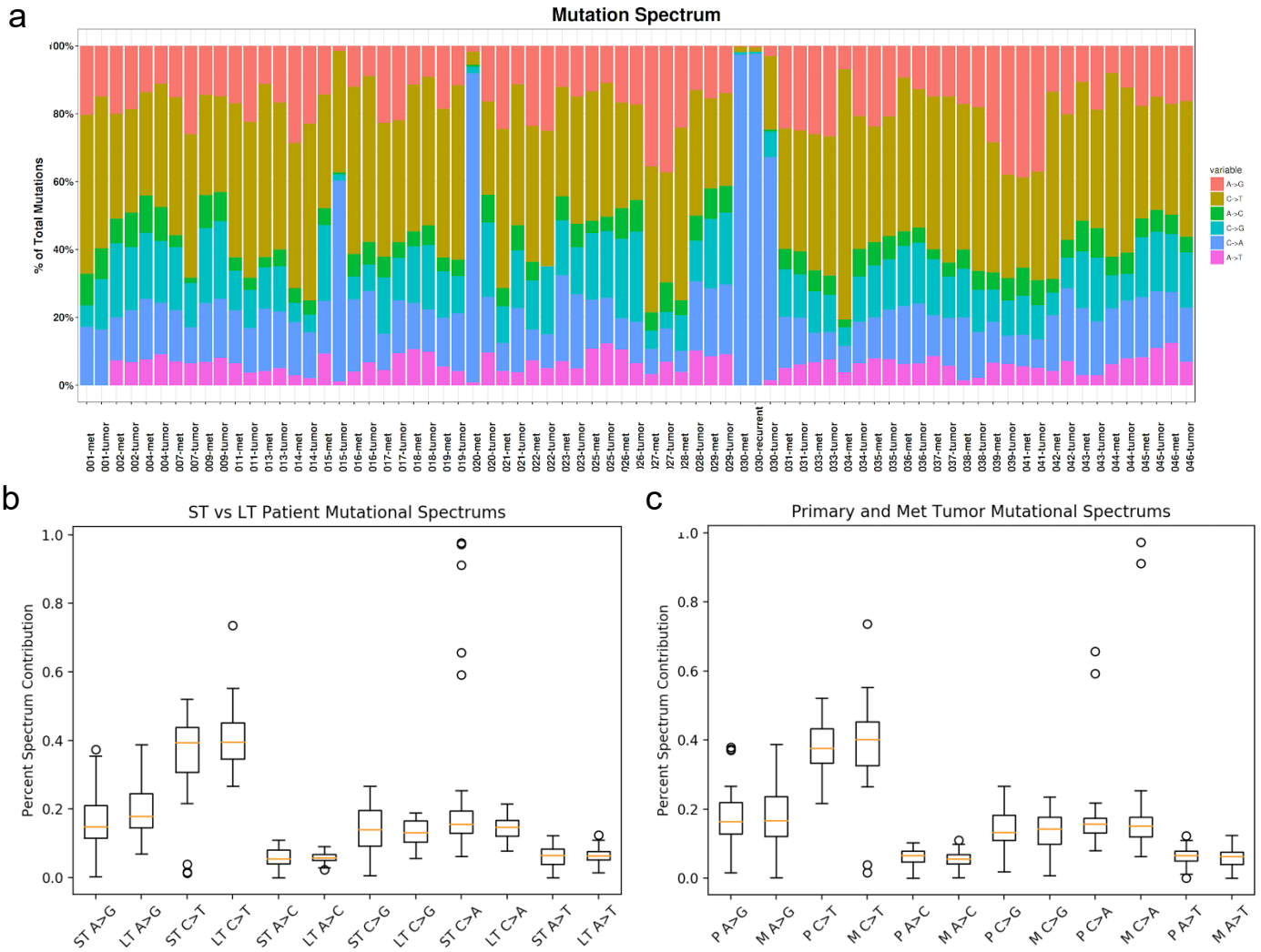
Table listing the Mann-Whitney or Wilcoxon Statistic and corresponding p-values for comparisons between ST and LT survivors and Primary and Metastatic tumor for each of the 22 immune cell types



**Supplementary Fig 1 Mutational Signatures**

a. Stacked bar plot displaying the percent of total mutations that fit into the mutational signatures shown on the right. Each patient is ordered by patient number and their metastatic and primary tumor with ST survivors on the left (001-met – 030 tumor) and LT survivors on the right (031-met – 046-tumor).

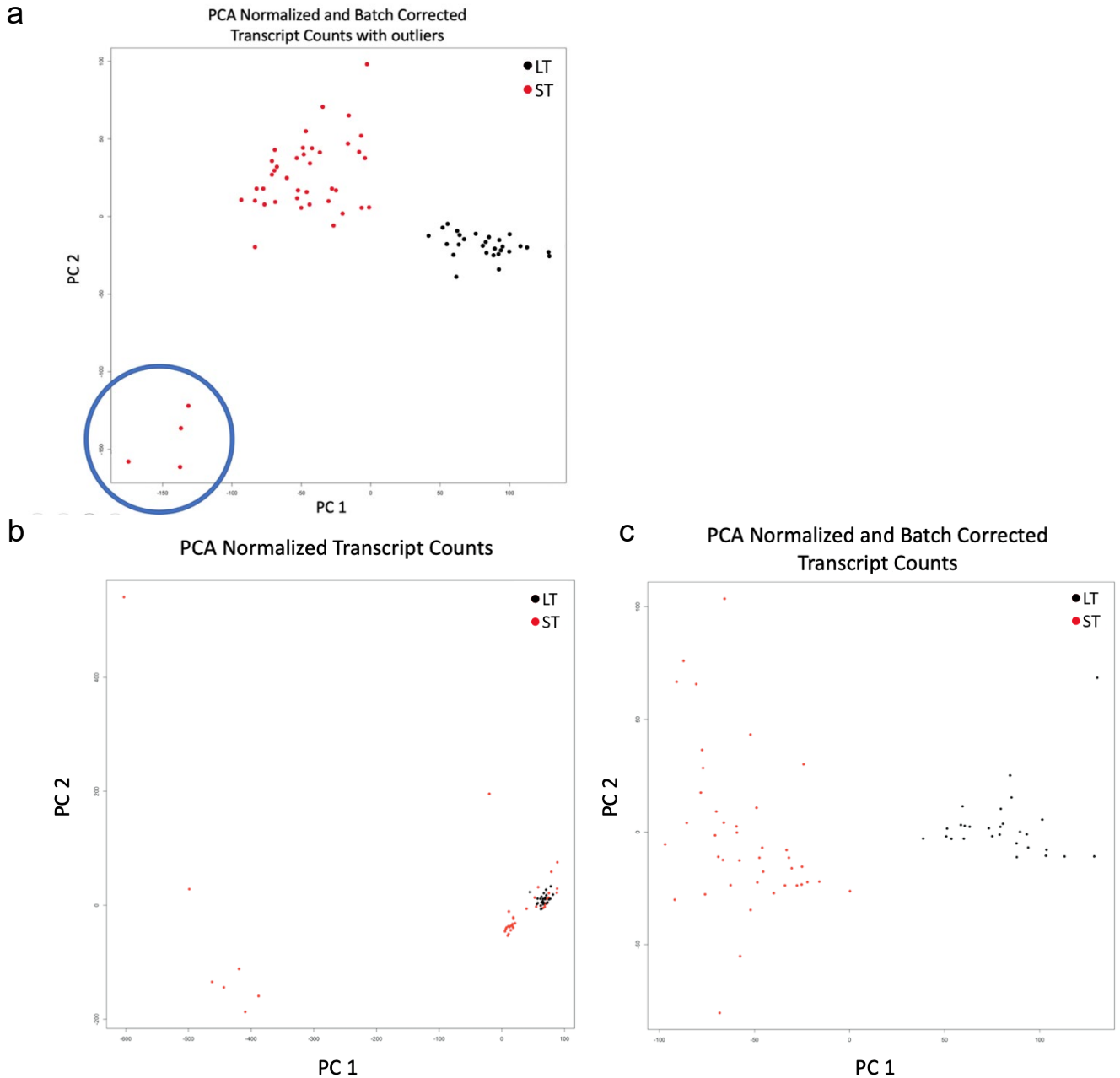
b-c. Box and whisker plots showing the percentage of total mutations for each signature, grouped by the patient’s tumor as a ST or LT survivor (B) or as a primary (P) and metastatic tumor (M) (C). The boxplots define the range of the minimum to the maximum by lines, a box from the first quartile to the third quartile with the median as the center line. Circles outside the range of the data are outliers.



**Supplementary Fig 2 Mutational Spectrum**

a. Stacked bar plot displaying the percent of total mutations that were nucleotide transitions or transversions, according to the key on the right. Each patient is ordered by patient number and their metastatic and primary tumor with ST survivors on the left (001-met – 030-tumor) and LT survivors on the right (031-met – 046-tumor).

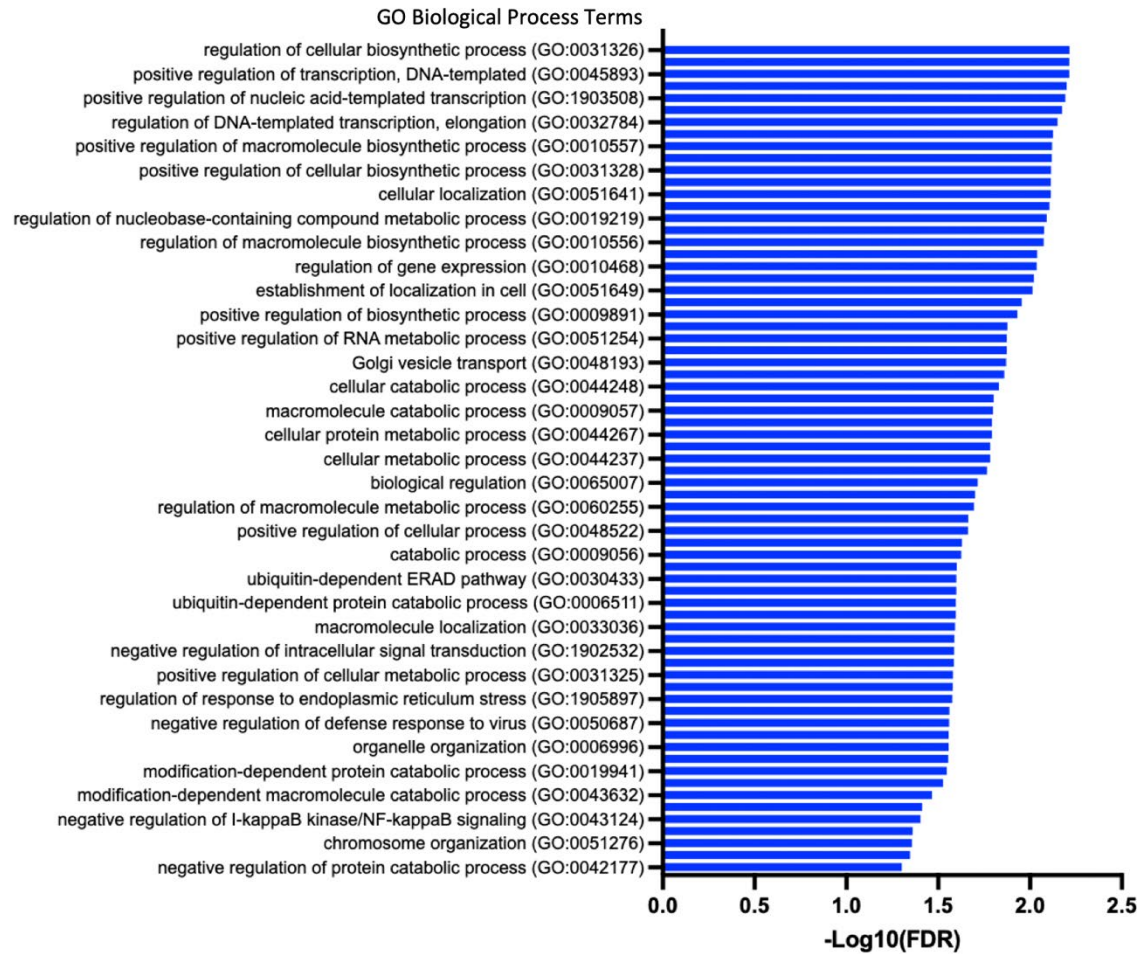
b-c. Box and whisker plots showing the percentage of total mutations for each signature, grouped by the patient’s tumor as a ST or LT survivor (B) or as a primary (P) and metastatic tumor (M) (C). The boxplots define the range of the minimum to the maximum by lines, a box from the first quartile to the third quartile with the median as the center line. Circles outside the range of the data are outliers.



**Supplementary Fig 3** PCA Plots of Log CPM counts in Differential Expression Analysis

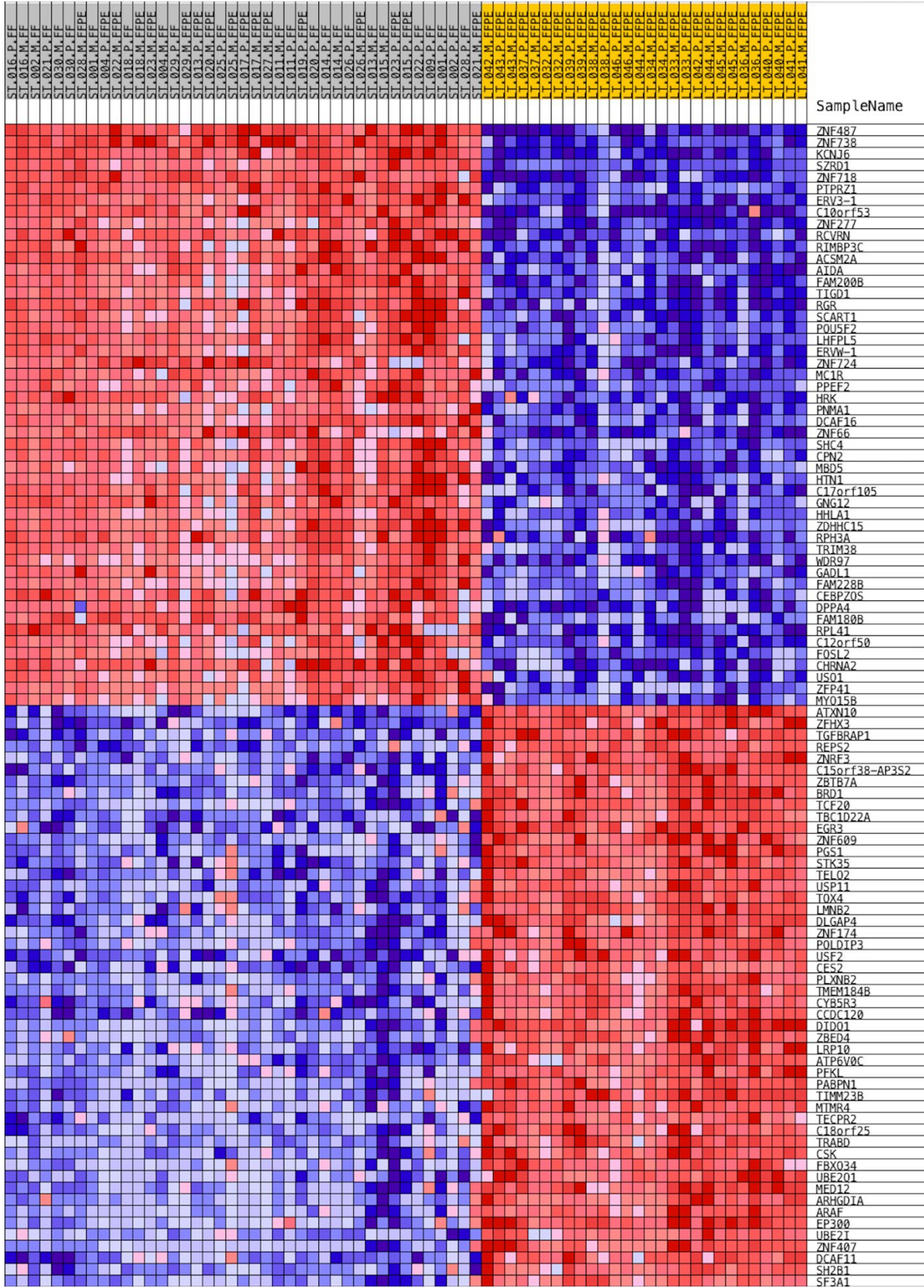
- PCA of cohort samples RNA-sequencing transcript counts with all tumor samples after normalization and batch effect correction with SVA. The 4 samples circled in the plot were removed as outliers.
- PCA of cohort samples RNA-sequencing transcript counts after removal of the 4 outlier samples and normalization.
- PCA of cohort samples RNA-sequencing transcript counts after removal of the 4 outlier samples, normalization, and batch effect correction with SVA.

## Pathway Enrichment for DEGs Unique to Metastatic Tumors



**Supplementary Fig 4** GO Biological Process Pathway Enrichment for Metastatic DEGs Barplot displaying the  $-\text{Log}_{10}(\text{FDR})$  values for each Biological Processes GO term that was statistically overrepresented among the DEGs unique to metastatic tumors





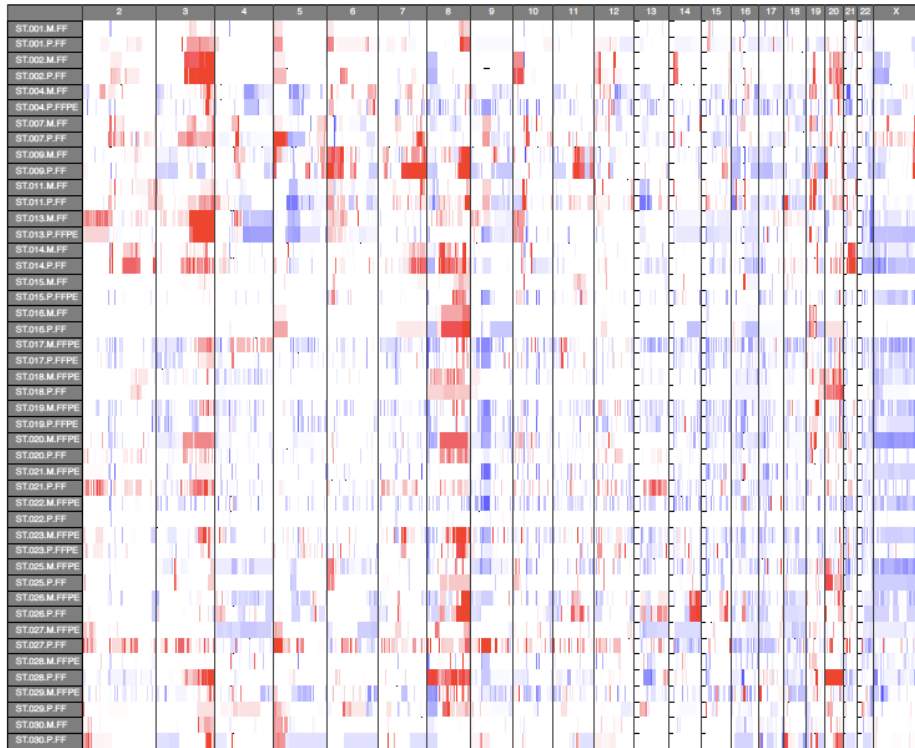


**Supplementary Fig 5** Top upregulated and downregulated DEGs between ST and LT survivors  
Heatmap displaying the top 50 upregulated and top 50 downregulated DEGs between the all ST and LT survivors generated by GSEA.

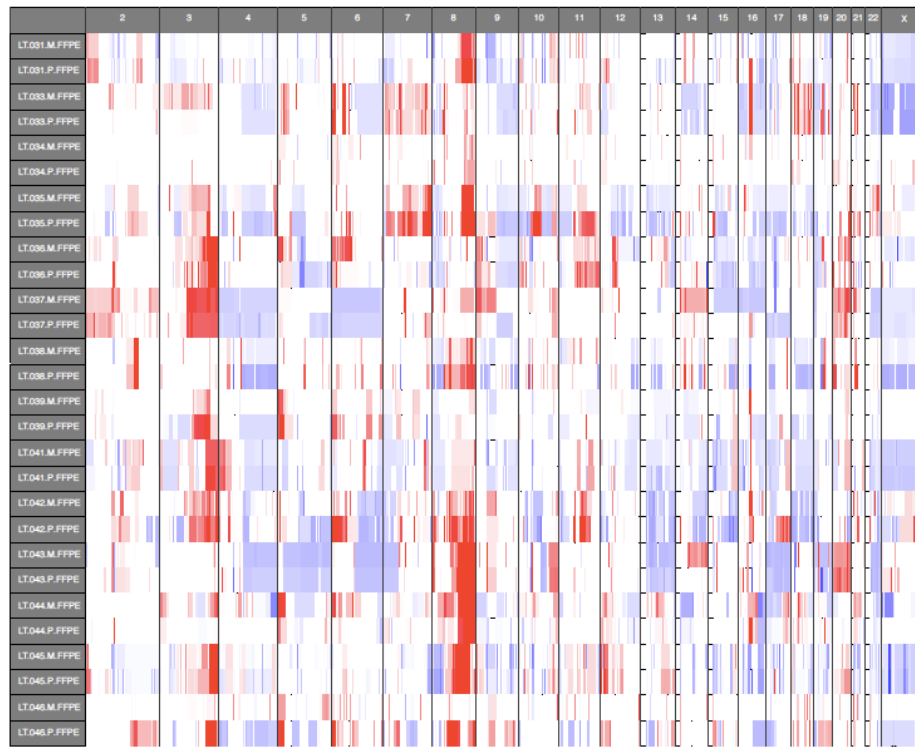
| Category     | Term  | RT | Genes | Count | %   | P-Value | Fold Enrichment | Benjamini | FDR    | Fisher Exact |
|--------------|---|----|-------|-------|-----|---------|-----------------|-----------|--------|--------------|
| KEGG_PATHWAY | <a href="#">Adherens junction</a>                           | RT |       | 6     | 1.9 | 5.2E-3  | 5.3             | 6.2E-1    | 6.2E-1 | 8.9E-4       |
| KEGG_PATHWAY | <a href="#">Protein processing in endoplasmic reticulum</a> | RT |       | 9     | 2.8 | 5.6E-3  | 3.3             | 6.2E-1    | 6.2E-1 | 1.6E-3       |
| KEGG_PATHWAY | <a href="#">SNARE interactions in vesicular transport</a>   | RT |       | 4     | 1.3 | 1.5E-2  | 7.6             | 1.0E0     | 1.0E0  | 1.8E-3       |
| KEGG_PATHWAY | <a href="#">Alcoholic liver disease</a>                     | RT |       | 7     | 2.2 | 2.5E-2  | 3.1             | 1.0E0     | 1.0E0  | 7.4E-3       |
| KEGG_PATHWAY | <a href="#">mTOR signaling pathway</a>                      | RT |       | 7     | 2.2 | 3.7E-2  | 2.8             | 1.0E0     | 1.0E0  | 1.2E-2       |
| KEGG_PATHWAY | <a href="#">mRNA surveillance pathway</a>                   | RT |       | 5     | 1.6 | 6.7E-2  | 3.2             | 1.0E0     | 1.0E0  | 1.9E-2       |
| KEGG_PATHWAY | <a href="#">Phospholipase D signaling pathway</a>           | RT |       | 6     | 1.9 | 8.5E-2  | 2.5             | 1.0E0     | 1.0E0  | 3.1E-2       |
| KEGG_PATHWAY | <a href="#">Insulin resistance</a>                          | RT |       | 5     | 1.6 | 9.1E-2  | 2.9             | 1.0E0     | 1.0E0  | 2.9E-2       |
| KEGG_PATHWAY | <a href="#">MAPK signaling pathway</a>                      | RT |       | 9     | 2.8 | 9.4E-2  | 1.9             | 1.0E0     | 1.0E0  | 4.5E-2       |

**Supplementary Fig 6** Kegg Pathway Enrichment  
KEGG Pathways enriched in DEGs as identified by DAVID

a



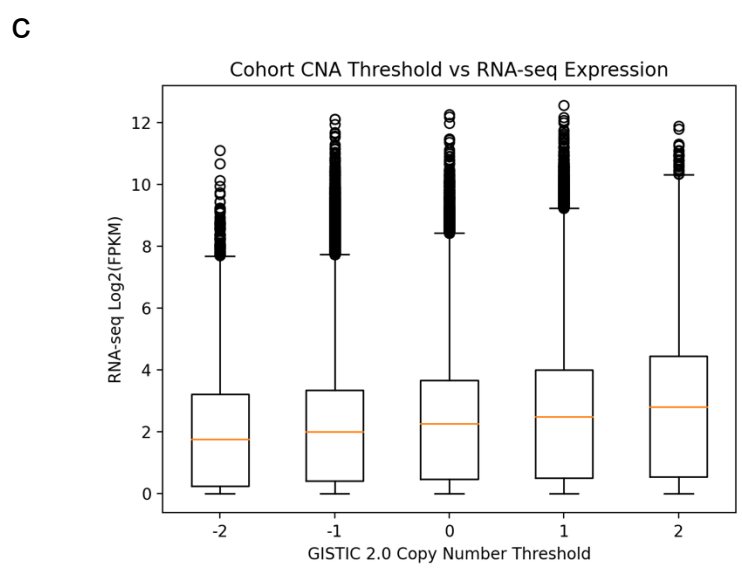
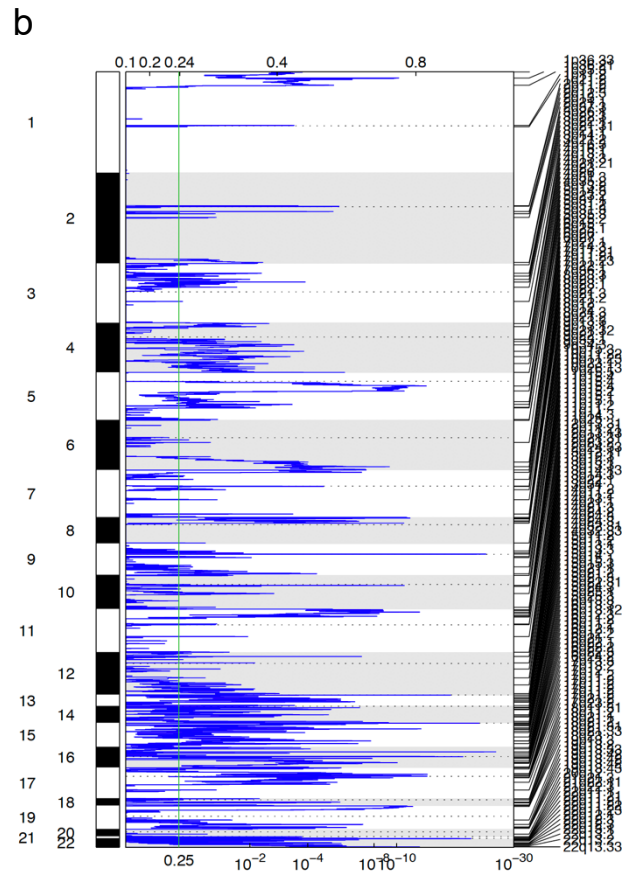
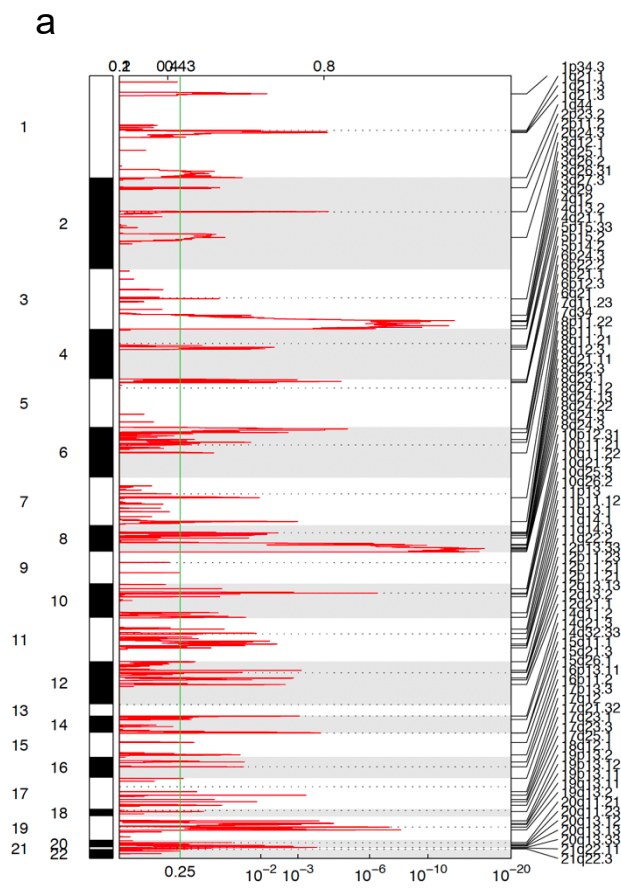
b



0 1 2 3 4  
Copy Number

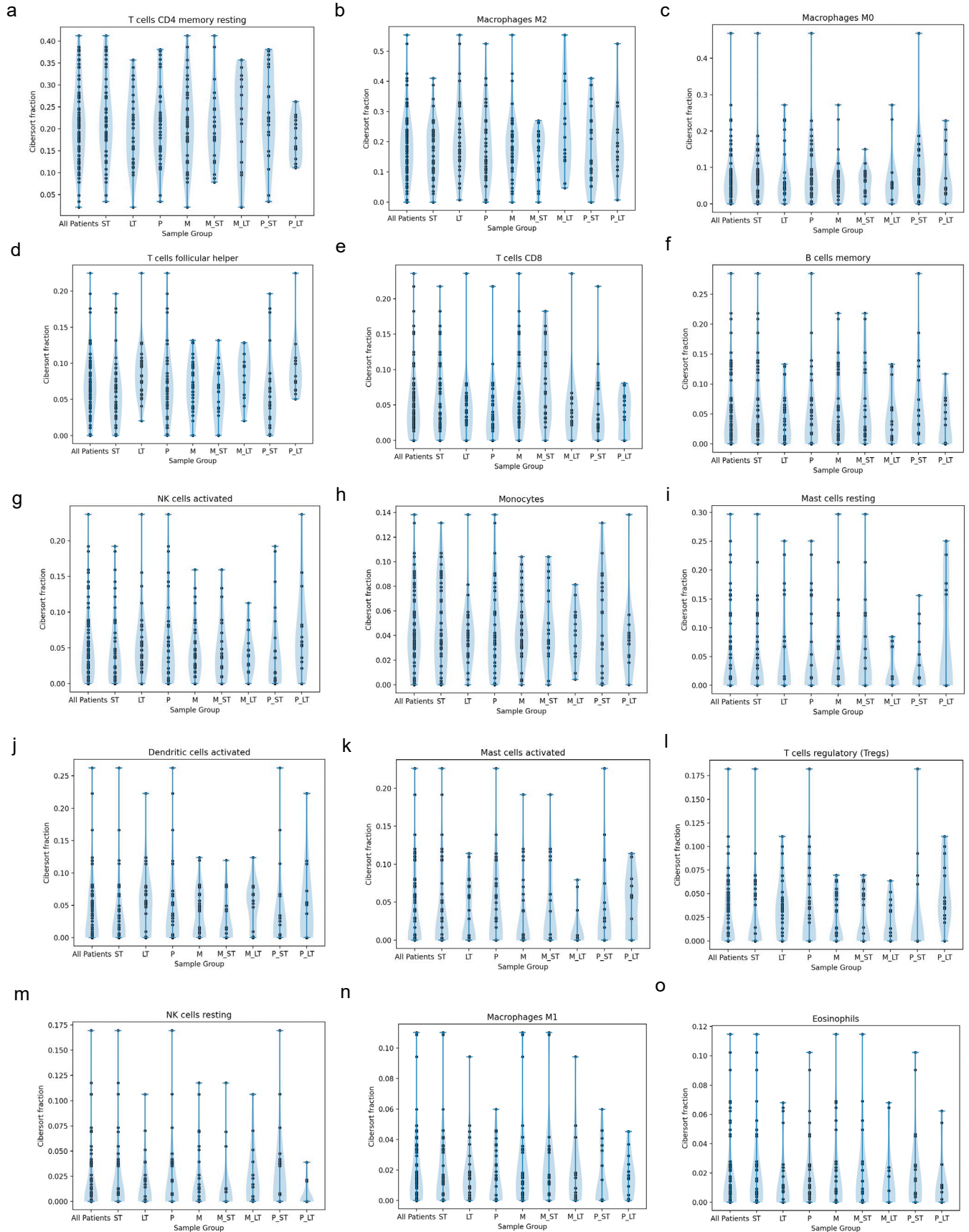
**Supplementary Fig 7** Copy number alterations in tumors of ST and LT survivors

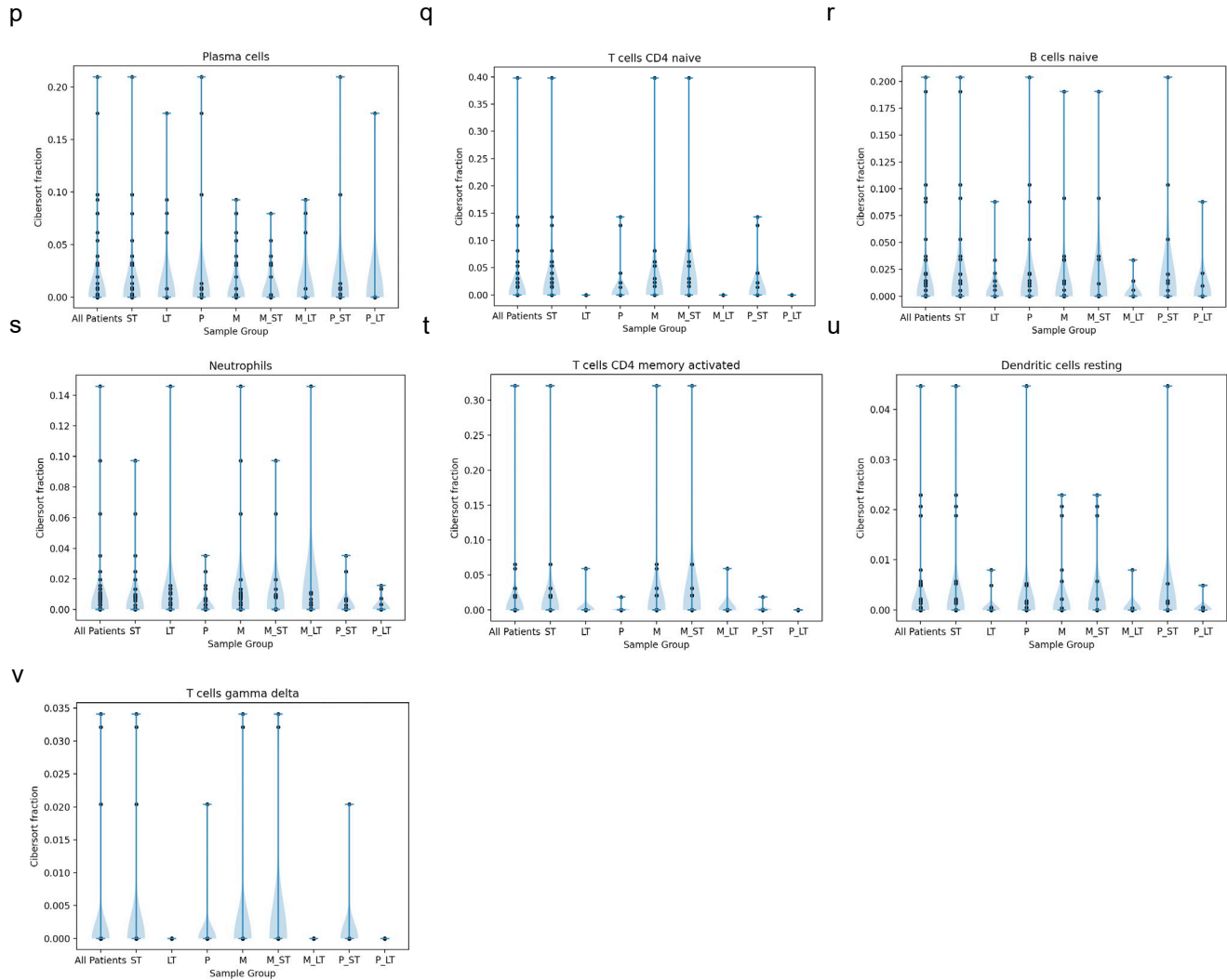
- a. Copy-altered segments in primary and metastatic tumors of ST survivors across the genome. Amplifications are depicted in red while deletions are seen in blue.
- b. Copy-altered segments in primary and metastatic tumors of LT survivors across the genome. Amplifications are depicted in red while deletions are seen in blue.



**Supplementary Fig 8** GISTIC analysis for copy number alterations in tumors of ST and LT survivors

- a. GISTIC Qplot of significantly amplified lesions across genome of all patient tumors (n=74) in cohort with 90% Confidence.
- b. GISTIC Qplot of significantly deleted lesions across genome of all patient tumors (n=74) in cohort with 90% Confidence.
- c. Boxplot of the GISTIC2.0 CNA value for every gene in every patient primary and metastatic sample plotted against their corresponding Log<sub>2</sub>(FPKM) value from RNA-seq. The medians of the FPKM values and the CNA threshold values has a spearmanr correlation value of 0.999 and p-value of  $1.4 \times 10^{-24}$ . (Number of genes in Copy Number Threshold groups from left to right: -2 n= 24316, -1 n= 416616, 0 n=280688, 1 n=346144 , 2 n=51856) The boxplot defines the range of the minimum to the maximum by lines, a box from the first quartile to the third quartile with the median as the center line. Circles outside the range of the data are outliers.





**Supplementary Fig 9** CIBERSORT immune cell fraction violin plots

a-v. Breakdown of the immune cell fractions calculated by CIBERSORT for each of the 22 immune cell signatures broken down by tumor type subgroup (all Patient tumors n= 72, ST survivors n= 44, LT survivors n= 28, Primary tumors n = 36, Metastatic tumors n= 36, ST survivor metastatic tumors n= 22, LT survivor metastatic tumors n=14, ST survivor primary tumors n= 22, and LT survivor metastatic tumors n= 14). The bars of the violin plot represent the range of the data (min and max). The shaded region on either side of the center line display the distribution of the data as a kernel density estimation. In other words, it shows the probability that a data point falls within that value range along the y-axis. Each individual data point is shown by a black dot.