

Table S2 Comparison of differentially expressed genes identified from our estimated cell type specific expression profiles and the reference scRNA-seq dataset

| Tissue         | Cell Type                                | Baseline PPV | PPV   | scRNA-seq control cell count | scRNA-seq case cell count | scRNA-seq overall cell count | Pvalue    |
|----------------|------------------------------------------|--------------|-------|------------------------------|---------------------------|------------------------------|-----------|
| Pancreas       | Acinar Cell                              | 0.440        | 0.613 | 25437                        | 6193                      | 31630                        | 8.52E-11  |
|                | Alpha Cell                               | 0.309        | 0.433 | 27877                        | 13541                     | 41418                        | 2.07E-08  |
|                | Beta Cell                                | 0.406        | 0.554 | 21866                        | 6234                      | 28100                        | 3.02E-12  |
|                | Delta Cell                               | 0.329        | 0.476 | 2387                         | 706                       | 3093                         | 4.46E-12  |
|                | Duct Epithelial Cell                     | 0.318        | 0.406 | 6148                         | 3530                      | 9678                         | 2.86E-04  |
|                | Endothelial Cell                         | 0.209        | 0.283 | 2064                         | 893                       | 2957                         | 5.35E-04  |
|                | Epsilon Cell                             | 0.037        | 0.051 | 68                           | 19                        | 87                           | 3.07E-02  |
|                | Leukocyte                                | 0.054        | 0.080 | 493                          | 258                       | 751                          | 8.07E-03  |
|                | Mesenchymal Cell                         | 0.301        | 0.389 | 3881                         | 1887                      | 5768                         | 4.65E-05  |
|                | PP cell                                  | 0.085        | 0.106 | 814                          | 287                       | 1101                         | 3.61E-02  |
| Frontal cortex | Astrocytes                               | 0.057        | 0.140 | 172                          | 459                       | 631                          | 3.25E-02  |
|                | Excitatory neurons                       | 0.309        | 0.344 | 10336                        | 16368                     | 26704                        | 3.35E-01  |
|                | Inhibitory neurons                       | 0.182        | 0.205 | 3582                         | 5893                      | 9475                         | 3.52E-01  |
|                | Microglia/Macrophage                     | 0.024        | 0.069 | 248                          | 428                       | 676                          | 5.78E-02  |
|                | Oligodendrocytes                         | 0.055        | 0.000 | 1887                         | 1574                      | 3461                         | 8.94E-01  |
|                | Oligodendrocyte progenitor cells         | 0.086        | 0.133 | 819                          | 942                       | 1761                         | 1.30E-01  |
| SAT            | Adipocyte                                | 0.563        | 0.888 | 6242                         | 6194                      | 12436                        | 1.96E-70  |
|                | Adipose stem and progenitor cells (ASPC) | 0.482        | 0.840 | 5314                         | 9417                      | 14731                        | 8.93E-75  |
|                | B cell                                   | 0.038        | 0.057 | 55                           | 227                       | 282                          | 4.30E-03  |
|                | Dendritic Cell                           | 0.125        | 0.187 | 156                          | 287                       | 443                          | 1.17E-07  |
|                | Endothelial Cell                         | 0.428        | 0.774 | 2457                         | 4740                      | 7197                         | 2.39E-83  |
|                | Lymphatic endothelial cells (LEC)        | 0.104        | 0.176 | 105                          | 430                       | 535                          | 6.66E-10  |
|                | Macrophage                               | 0.508        | 0.916 | 2857                         | 4409                      | 7266                         | 5.11E-109 |
|                | Mast Cell                                | 0.059        | 0.098 | 183                          | 572                       | 755                          | 1.16E-04  |
|                | Monocyte                                 | 0.063        | 0.096 | 168                          | 629                       | 797                          | 2.16E-04  |
|                | Neutrophil                               | 0.019        | 0.027 | 52                           | 26                        | 78                           | 1.34E-01  |
|                | NK cell                                  | 0.127        | 0.229 | 351                          | 855                       | 1206                         | 1.18E-14  |
|                | Pericyte                                 | 0.103        | 0.191 | 232                          | 300                       | 532                          | 1.48E-13  |
| VAT            | Adipocyte                                | 0.407        | 0.711 | 4425                         | 4943                      | 9368                         | 3.32E-36  |
|                | Adipose stem and progenitor cells (ASPC) | 0.371        | 0.638 | 4553                         | 6914                      | 11467                        | 3.85E-25  |
|                | B cell                                   | 0.014        | 0.044 | 25                           | 42                        | 67                           | 3.49E-06  |
|                | Dendritic Cell                           | 0.047        | 0.042 | 116                          | 300                       | 416                          | 6.94E-01  |
|                | Endometrium                              | 0.040        | 0.054 | 43                           | 262                       | 305                          | 7.61E-02  |
|                | Endothelial Cell                         | 0.278        | 0.548 | 2081                         | 2983                      | 5064                         | 1.61E-31  |
|                | Lymphatic endothelial cells (LEC)        | 0.126        | 0.253 | 577                          | 1077                      | 1654                         | 2.05E-13  |
|                | Macrophage                               | 0.291        | 0.521 | 1597                         | 5731                      | 7328                         | 7.50E-21  |
|                | Mast Cell                                | 0.027        | 0.089 | 81                           | 127                       | 208                          | 1.27E-12  |
|                | Mesothelium                              | 0.441        | 0.780 | 5030                         | 19658                     | 24688                        | 8.76E-43  |
|                | Monocyte                                 | 0.040        | 0.040 | 90                           | 187                       | 277                          | 5.12E-01  |
|                | NK cell                                  | 0.043        | 0.063 | 219                          | 276                       | 495                          | 2.88E-02  |
|                | Pericyte                                 | 0.074        | 0.151 | 686                          | 1835                      | 2521                         | 3.11E-09  |
|                | Smooth muscle cells (SMC)                | 0.056        | 0.076 | 388                          | 692                       | 1080                         | 3.24E-02  |

Note: SAT is the abbreviation for subcutaneous adipose tissue, VAT is the abbreviation for visceral adipose tissue. Baseline PPV indicates the expected overall proportion of genes in our dataset that matches with the differentially expressed (DE) genes in the real scRNA-seq dataset. PPV indicates the proportion of DE genes identified by our method and GWAS-imputed expression data that overlaps with the 'true' set of DE genes from the real scRNA-seq dataset. A significant p-value indicates a higher PPV than expected by chance.