**Table 1**

|  |  |  |  |
| --- | --- | --- | --- |
| Individual  Cell Type | Global Group  Index | Global Group Properties | Global Group Name |
| 1 | A | High proportion of cell type specific DE genes; No shared DE genes | High Individual DE |
| 2 | B | Low proportion of cell type specific DE genes; No shared DE genes | Low Individual DE |
| 3 | C | High proportion of cell type specific DE genes; Low proportion of shared DE genes with other cell types in the global group | High Individual DE Low Shared DE |
| 4 | C |
| 5 | C |
| 6 | D | High proportion of cell type specific DE genes; High proportion of shared DE genes with other cell types in the global group | High Individual DE High Shared DE |
| 7 | D |
| 8 | D |
| 9 | E | Low proportion of cell type specific DE genes; High proportion of shared DE genes with other cell types in the global group | Low Individual DE High Shared DE |
| 10 | E |
| 11 | E |
| 12 | F | Low proportion of cell type specific DE genes; Low proportion of shared DE genes with other cell types in the global group | Low Individual DE Low Shared DE |
| 13 | F |
| 14 | F |
| 15 | G | Low proportion of cell type specific DE genes; Low proportion of shared DE genes with other cell types in the global group; High variance of DE genes | Low Individual DE Low Shared DE High Variance DE |
| 16 | G |
| 17 | G |
| 18 | H | High proportion of cell type specific DE genes; Low proportion of shared DE genes with other cell types in the global group; High variance of DE genes | High Individual DE Low Shared DE High Variance DE |
| 19 | H |
| 20 | H |

**Table 2**

|  |  |  |
| --- | --- | --- |
| *Method* | *Global Group Max Violations (%)* | *Global Group Min Violations (%)* |
| SIDEREF | 4.4 | 11.1 |
| PCA (25 Dims.) | 9.6 | 13.8 |
| Euclidean | 19.3 | 30.5 |
| 1 - | Pearson Correlation | | 9.2 | 16.0 |
| 1 - | Spearman Correlation | | 0.1 | 0.6 |
| RAFSIL | 22.1 | 37.8 |
| SIMLR (5 Components) | 40.5 | 31.7 |

**Table 3**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Single Level of Global Groups** | | **Immune Level of Global Groups Included** | |
| ***Method*** | *Global Group Max Violations (%)* | *Global Group Min Violations (%)* | *Global Group Max Violations (%)* | *Global Group Min Violations (%)* |
| SIDEREF | 11.3 | 26.2 | 22.2 | 44.5 |
| PCA (25 Dims.) | 15.2 | 24.2 | 28.8 | 56.1 |
| Euclidean | 41.5 | 84.0 | 51.5 | 83.1 |
| 1 - | Pearson Correlation | | 8.2 | 25.4 | 46.0 | 54.7 |
| 1 - | Spearman Correlation | | 19.2 | 56.1 | 42.5 | 72.0 |
| RAFSIL | 23.0 | 54.9 | 46.0 | 72.9 |
| SIMLR (25 Components) | 26.4 | 33.2 | 35.2 | 47.7 |

**Table 4**

|  |  |  |
| --- | --- | --- |
| *Pathway* | *Cell Type, Organ* | *Gene Set Enrichment p-value* |
| B Cells Top 10 DE Genes | Leukocyte, Bladder | 5.7E-01 |
| Leukocyte, Kidney | 2.5E-07 |
| Leukocyte, Liver | 3.7E-02 |
| Leukocyte, Lung | 1.5E-01 |
| Leukocyte, Thymus | 5.3E-09 |
| B Cells Top 50 DE Genes | Leukocyte, Bladder | 1.2E-05 |
| Leukocyte, Kidney | 9.6E-26 |
| Leukocyte, Liver | 5.2E-05 |
| Leukocyte, Lung | 2.9E-02 |
| Leukocyte, Thymus | 2.1E-36 |
| B Cells Top 100 DE Genes | Leukocyte, Bladder | 1.2E-15 |
| Leukocyte, Kidney | 1.7E-55 |
| Leukocyte, Liver | 1.3E-10 |
| Leukocyte, Lung | 3.9E-04 |
| Leukocyte, Thymus | 1.1E-67 |
| B Cells Top 300 DE Genes | Leukocyte, Bladder | 3.8E-23 |
| Leukocyte, Kidney | 4.0E-42 |
| Leukocyte, Liver | 4.0E-06 |
| Leukocyte, Lung | 2.9E-04 |
| Leukocyte, Thymus | 2.8E-41 |

**Table S1**

|  |  |  |  |
| --- | --- | --- | --- |
| *Cell Type* | *Global Group  Name* | *DE Probability (%)* | *DE Multiplicative Factor Variance* |
| 1 | High Individual DE | 0.04 | 0.84 |
| 2 | Low Individual DE | 0.02 | 0.84 |
| 3 | High Individual DE Low Shared DE | 0.02 | 0.84 |
| 4 | 0.03 | 0.84 |
| 5 | 0.04 | 0.84 |
| 3, 4, 5 | 0.01 | 0.84 |
| 6 | High Individual DE High Shared DE | 0.02 | 0.84 |
| 7 | 0.03 | 0.84 |
| 8 | 0.04 | 0.84 |
| 6, 7, 8 | 0.03 | 0.84 |
| 9 | Low Individual DE High Shared DE | 0.005 | 0.84 |
| 10 | 0.01 | 0.84 |
| 11 | 0.015 | 0.84 |
| 9, 10, 11 | 0.03 | 0.84 |
| 12 | Low Individual DE Low Shared DE | 0.005 | 0.84 |
| 13 | 0.01 | 0.84 |
| 14 | 0.015 | 0.84 |
| 12, 13, 14 | 0.01 | 0.84 |
| 15 | Low Individual DE Low Shared DE High Variance DE | 0.005 | 1.56 |
| 16 | 0.01 | 1.56 |
| 17 | 0.015 | 1.56 |
| 15, 16, 17 | 0.01 | 1.56 |
| 18 | High Individual DE Low Shared DE High Variance DE | 0.02 | 1.56 |
| 19 | 0.03 | 1.56 |
| 20 | 0.04 | 1.56 |
| 18, 19, 20 | 0.01 | 1.56 |

**Table S2**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| *Cell Type* | *Included (Y/N)* | *Global Group 1* | *Global Group 2* | *Exclusion Reason* |
| Natural Killer Cell | Y | NK Cells | Immune Cells |  |
| T Cell | Y | T Cells | Immune Cells |  |
| B Cell | Y | B Cells | Immune Cells |  |
| Early Pro-B Cell | Y | Pro-B Cells | Immune Cells |  |
| Fraction A Pre-Pro B Cell | Y | Pro-B Cells | Immune Cells |  |
| Late Pro-B Cell | Y | Pro-B Cells | Immune Cells |  |
| Endothelial Cell | Y | Endothelial Cells | Endothelial Cells |  |
| Endothelial Cell of Hepatic Sinusoid | Y | Endothelial Cells | Endothelial Cells |  |
| Kidney Capillary Endothelial Cell | Y | Endothelial Cells | Endothelial Cells |  |
| Lung Endothelial Cell | Y | Endothelial Cells | Endothelial Cells |  |
| Basal Cell | Y | Basal Cells | Basal Cells |  |
| Basal Cell of Epidermis | Y | Basal Cells | Basal Cells |  |
| Leukocyte | N |  |  | Broadly Defined |
| Blood Cell | N |  |  | Broadly Defined |
| Myeloid Cell | N |  |  | Broadly Defined |
| Granulocyte | N |  |  | Other Immune Singleton |
| Granulocytopoietic Cell | N |  |  | Other Immune Singleton |
| Basophil | N |  |  | Other Immune Singleton |
| Mast Cell | N |  |  | Other Immune Singleton |
| Monocyte | N |  |  | Other Immune Singleton |
| Classical Monocyte | N |  |  | Other Immune Singleton |
| Non-classical Monocyte | N |  |  | Other Immune Singleton |
| Dendritic Cell | N |  |  | Other Immune Singleton |
| Langerhans Cell | N |  |  | Other Immune Singleton |
| Erythroblast | N |  |  | Other Immune Singleton |
| DN1 Thymic Pro-T Cell | N |  |  | Other Immune Singleton |
| Alveolar Macrophage | N |  |  | Diverse across Tissues |
| Macrophage | N |  |  | Diverse across Tissues |
| Epithelial Cell | Y | None | None |  |
| Duct Epithelial Cell | Y | None | None |  |
| Kidney Collecting Duct Epithelial Cell | Y | None | None |  |
| Luminal Epithelial Cell of Mammary Gland | Y | None | None |  |
| Type II Pneumocyte | Y | None | None |  |
| Kidney Proximal Straight Tubule Epithelial Cell | Y | None | None |  |
| Kidney Loop of Henle Ascending Limb Epithelial Cell | Y | None | None |  |
| Bladder Cell | Y | None | None |  |
| Bladder Urothelial Cell | Y | None | None |  |
| Cardiac Muscle Cell | Y | None | None |  |
| Ciliated Columnar Cell of Tracheobronchial Tree | Y | None | None |  |
| Endocardial Cell | Y | None | None |  |
| Fibroblast | Y | None | None |  |
| Hepatocyte | Y | None | None |  |
| Keratinocyte | Y | None | None |  |
| Kidney Cell | Y | None | None |  |
| Mesangial Cell | Y | None | None |  |
| Neuroendocrine Cell | Y | None | None |  |
| Skeletal Muscle Satellite Cell | Y | None | None |  |
| Stromal Cell | N |  |  | Progenitor |
| Mesenchymal Cell | N |  |  | Progenitor |
| Mesenchymal Stem Cell | N |  |  | Progenitor |
| Immature T Cell | N |  |  | Progenitor |
| Immature B Cell | N |  |  | Progenitor |
| Promonocyte | N |  |  | Progenitor |
| Proerythroblast | N |  |  | Progenitor |
| Hematopoietic Precursor Cell | N |  |  | Progenitor |

**Table S3**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Single Level of Global Groups** | | **Immune Level of Global Groups Included** | |
| ***Method*** | *Global Group Max Violations (%)* | *Global Group Min Violations (%)* | *Global Group Max Violations (%)* | *Global Group Min Violations (%)* |
| SIDEREF | 10.1 | 9.4 | 11.8 | 6.3 |
| PCA (25 Dims.) | 16.7 | 11.5 | 30.3 | 8.9 |
| Euclidean | 47.6 | 81.1 | 53.5 | 79.7 |
| 1 - | Pearson Correlation | | 8.0 | 6.6 | 35.7 | 42.6 |
| 1 - | Spearman Correlation | | 23.7 | 44.7 | 41.0 | 35.8 |
| RAFSIL | 22.7 | 47.5 | 42.3 | 49.2 |
| SIMLR (25 Components) | 34.0 | 20.1 | 46.8 | 30.5 |