

**Supplementary Figure S1.** Neural network configuration.



**Supplementary Figure S2.** ACTINN produce consistent results from run to run. (a) Number of cell types predicted for each cell across 10 runs. (b) Frequency for each cell type in each run.



**Supplementary Figure S3.** ACTINN accurately identifies cell types not in the reference. (a) Cell types identified by unsupervised analysis. (b) Cell types identified by ACTINN. A cell was labelled “uncertain” if its highest probability is smaller than 0.95.



**Supplementary Figure S4.** T cell subtypes predicted by 4 tools. (a) ACTINN. (b) CaSTLe. (c) SingleCellNet. (d) SuperCT. (e) True label inferred by all the predictions and gene expression. (f) Accuracy for the predictions.

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| --- | --- | --- |
| **Cell Type** | **Predicted Type** | **Number** |
| B cell | B cell | 3437 |
| Cardiac Muscle | Cardiac Muscle | 123 |
| Endothelial cell | Endothelial cell | 3858 |
| Epidermis | Epidermis | 2065 |
| Epithelial cell | Epithelial cell | 3421 |
| Erythrocyte | Erythrocyte | 45 |
| Granulocyte | Granulocyte | 744 |
| Hepatocyte | Hepatocyte | 388 |
| Monocyte | Monocyte | 1416 |
| NK cell | NK cell | 215 |
| Stromal cell | Stromal cell | 2803 |
| T cell | T cell | 2143 |
| Cardiac Muscle | Epidermis | 2 |
| Cardiac Muscle | Erythrocyte | 2 |
| Cardiac Muscle | Stromal cell | 1 |
| Endothelial cell | Erythrocyte | 1 |
| Epidermis | Epithelial cell | 1 |
| Epithelial cell | B cell | 1 |
| Erythrocyte | B cell | 2 |
| Erythrocyte | Endothelial cell | 10 |
| Erythrocyte | Epidermis | 2 |
| Erythrocyte | Epithelial cell | 8 |
| Erythrocyte | Monocyte | 3 |
| Erythrocyte | NK cell | 1 |
| Erythrocyte | Stromal cell | 3 |
| Erythrocyte | T cell | 1 |
| Granulocyte | B cell | 1 |
| Granulocyte | Monocyte | 5 |
| Monocyte | B cell | 118 |
| Monocyte | Epithelial cell | 64 |
| Monocyte | Granulocyte | 1 |
| Monocyte | NK cell | 3 |
| NK cell | T cell | 47 |
| Stromal cell | Endothelial cell | 1 |
| Stromal cell | Epithelial cell | 2 |
| Stromal cell | Erythrocyte | 1 |
| T cell | B cell | 4 |
| T cell | NK cell | 3 |

**Supplementary Table S1.** Predicted cell type compared to original cell type when training on the 10X dataset and predicting on the SS2 dataset.

|  |  |  |
| --- | --- | --- |
| **Cell Type** | **Predicted Type** | **Number** |
| B cell | B cell | 8516 |
| Cardiac Muscle | Cardiac Muscle | 60 |
| Endothelial cell | Endothelial cell | 3641 |
| Epidermis | Epidermis | 7492 |
| Epithelial cell | Epithelial cell | 1159 |
| Erythrocyte | Erythrocyte | 130 |
| Granulocyte | Granulocyte | 1096 |
| Hepatocyte | Hepatocyte | 1764 |
| Monocyte | Monocyte | 1244 |
| NK cell | NK cell | 1016 |
| Stromal cell | Stromal cell | 3164 |
| T cell | T cell | 5601 |
| B cell | Monocyte | 3 |
| Endothelial cell | B cell | 1 |
| Endothelial cell | Epithelial cell | 1 |
| Endothelial cell | Stromal cell | 2 |
| Epithelial cell | B cell | 3 |
| Epithelial cell | Epidermis | 150 |
| Epithelial cell | Erythrocyte | 1 |
| Epithelial cell | Monocyte | 3 |
| Erythrocyte | B cell | 5 |
| Erythrocyte | Granulocyte | 15 |
| Erythrocyte | Monocyte | 2 |
| Erythrocyte | T cell | 3 |
| Granulocyte | T cell | 1 |
| Monocyte | Granulocyte | 12 |
| NK cell | B cell | 13 |
| NK cell | Stromal cell | 20 |
| Stromal cell | Endothelial cell | 1 |
| T cell | Monocyte | 1 |
| T cell | NK cell | 46 |

**Supplementary Table S2.** Predicted cell type compared to original cell type when training on the SS2 dataset and predicting on the 10X dataset.