Supplemental Figures & Methods

Supplemental Table 1. CellxGene documentation and resource links

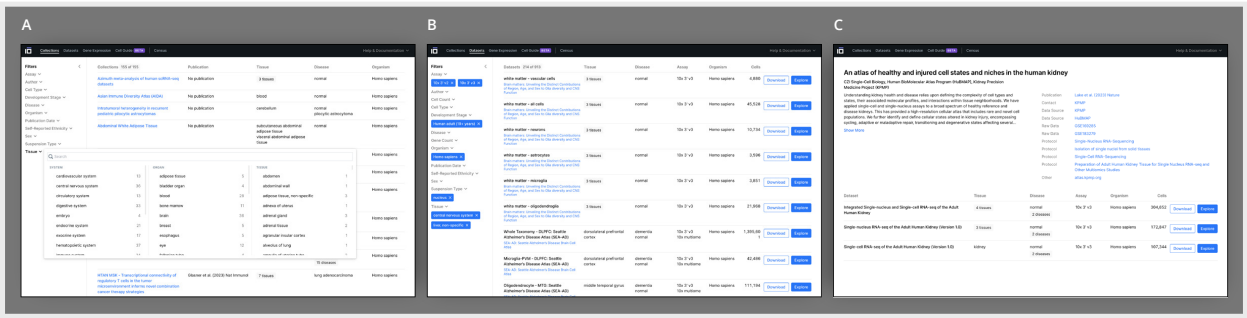
Description	Link
CellxGene Schema	https://github.com/chanzuckerberg/single-cell-curation/tree/main/schema
CellxGene schema changelog	https://github.com/chanzuckerberg/single-cell-curation/blob/main/schema/3.1.0/schema.md#appendix-a-changelog
CellxGene data eligibility criteria and submission process	https://CellxGene.cziscience.com/docs/032__Contribute%20and%20Publish%20Data
Gene Expression data processing & normalization documentation	https://CellxGene.cziscience.com/docs/04__Analyze%20Public%20Data/4_2__Gene%20Expression%20Documentation/4_2_3__Gene%20Expression%20Data%20Processing#data-normalization
Gene Expression source data	https://CellxGene.cziscience.com/docs/04__Analyze%20Public%20Data/4_2__Gene%20Expression%20Documentation/4_2_6__Gene%20Expression%20Source%20Data
TileDB-SOMA	https://github.com/single-cell-data/TileDB-SOMA
Census Python API	https://chanzuckerberg.github.io/CellxGene-census/python-api.html
Census data and schema	https://chanzuckerberg.github.io/CellxGene-census/CellxGene_census_docsite_schema.html#data-included-in-the-census

Supplemental Table 2. Metadata fields and corresponding ontologies

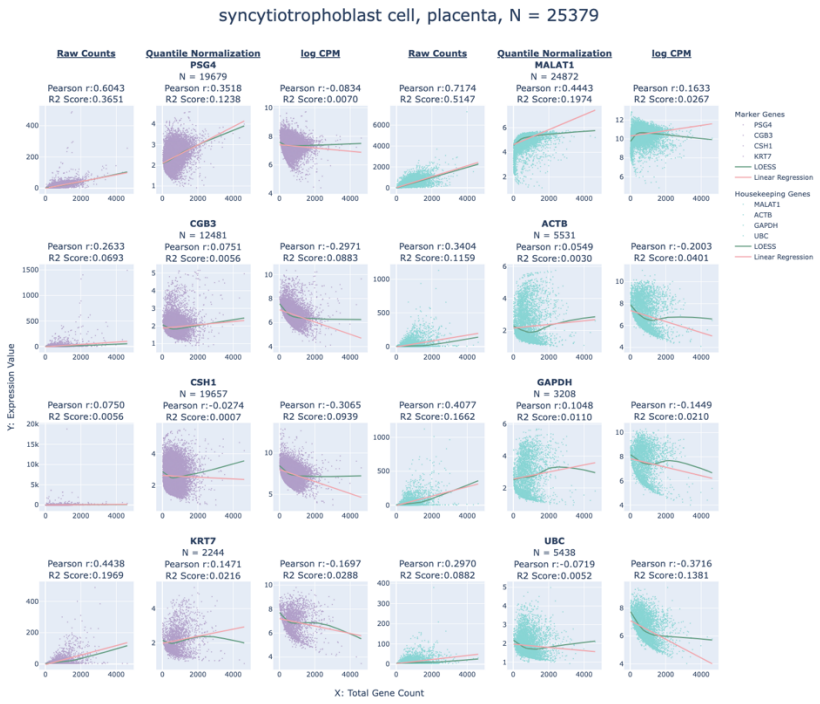
Metadata field	Ontology/Standards	Ontology link
organism (species)	NCBITaxon	http://obofoundry.org/ontology/ncbitaxon.html
development_stage (age)	HsapDv/MmusDv	https://obofoundry.org/ontology/hsapdv.html https://obofoundry.org/ontology/mmusdv.html
is_primary_data	Boolean (true/false)	
gene IDs	Ensembl	https://useast.ensembl.org/Help/View?id=285
sex	PATO	https://obofoundry.org/ontology/pato.html
self_reported_ethnicity	HANCESTRO	https://obofoundry.org/ontology/hancestro.html
disease	MONDO/PATO	https://obofoundry.org/ontology/mondo.html https://obofoundry.org/ontology/pato.html
tissue	UBERON	https://obofoundry.org/ontology/uberon.html
suspension_type	[cell,nucleus]	
assay	EFO [cite]	https://www.ebi.ac.uk/efo/
cell_type	CL [cite]	https://obofoundry.org/ontology/cl.html

Supplemental Table 3. List of Markers and Housekeeping Genes Used for Normalization Analyses

cell_type	tissue	marker genes	housekeeping genes
alveolar type 2 fibroblast cell	lung	LUM, SCARA5, FBLN1, DCN, COL1A2	MALAT1, ACTB, GAPDH, UBC, SDHA
syncytiotrophoblast cell	placenta	KRT7, EGFR, PSG4, CSH1	MALAT1, ACTB, GAPDH, UBC
T cell	kidney	CD3G, CD40LG, CD3D, CD247, CD96	MALAT1, ACTB, GAPDH, UBC, SDHA
plasma cell	lymph node	IRF4, SDC1, PRDM1, CD38	MALAT1, ACTB, GAPDH, UBC
plasma cell	bone marrow	IGHG1, IGHA1, SEC11C, SDC1, DERL3	MALAT1, ACTB, GAPDH, UBC, SDHA

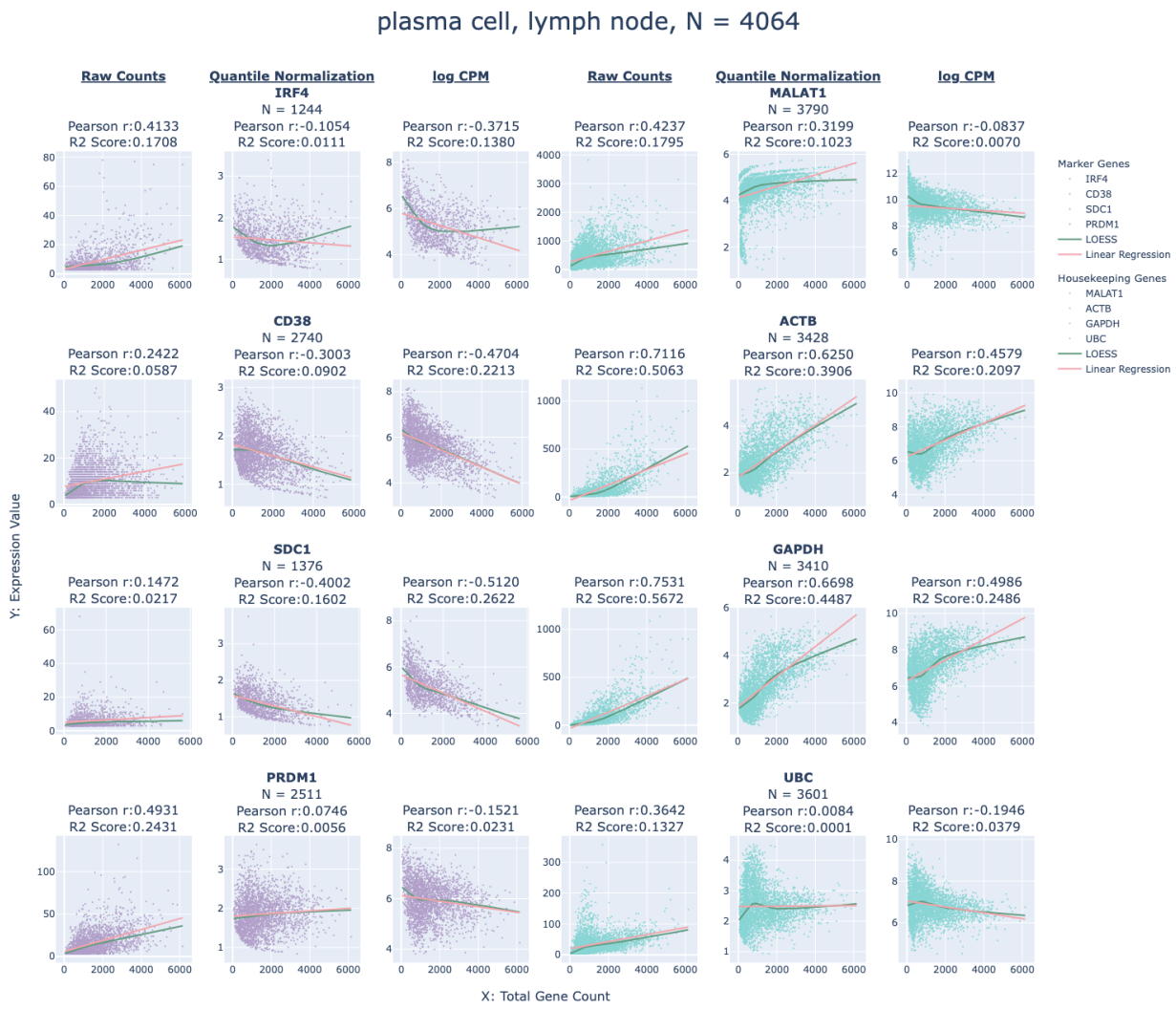


Supplemental Figure 1. (A,B) CellxGene User Interface (UI) allows for researchers to quickly filter and sort through datasets and collections based on collection metadata. (C) Each collection has an associated collections page with details about the author, study, datasets, and other collection metadata. From the collections page, researchers can easily explore any dataset that is part of the collection.

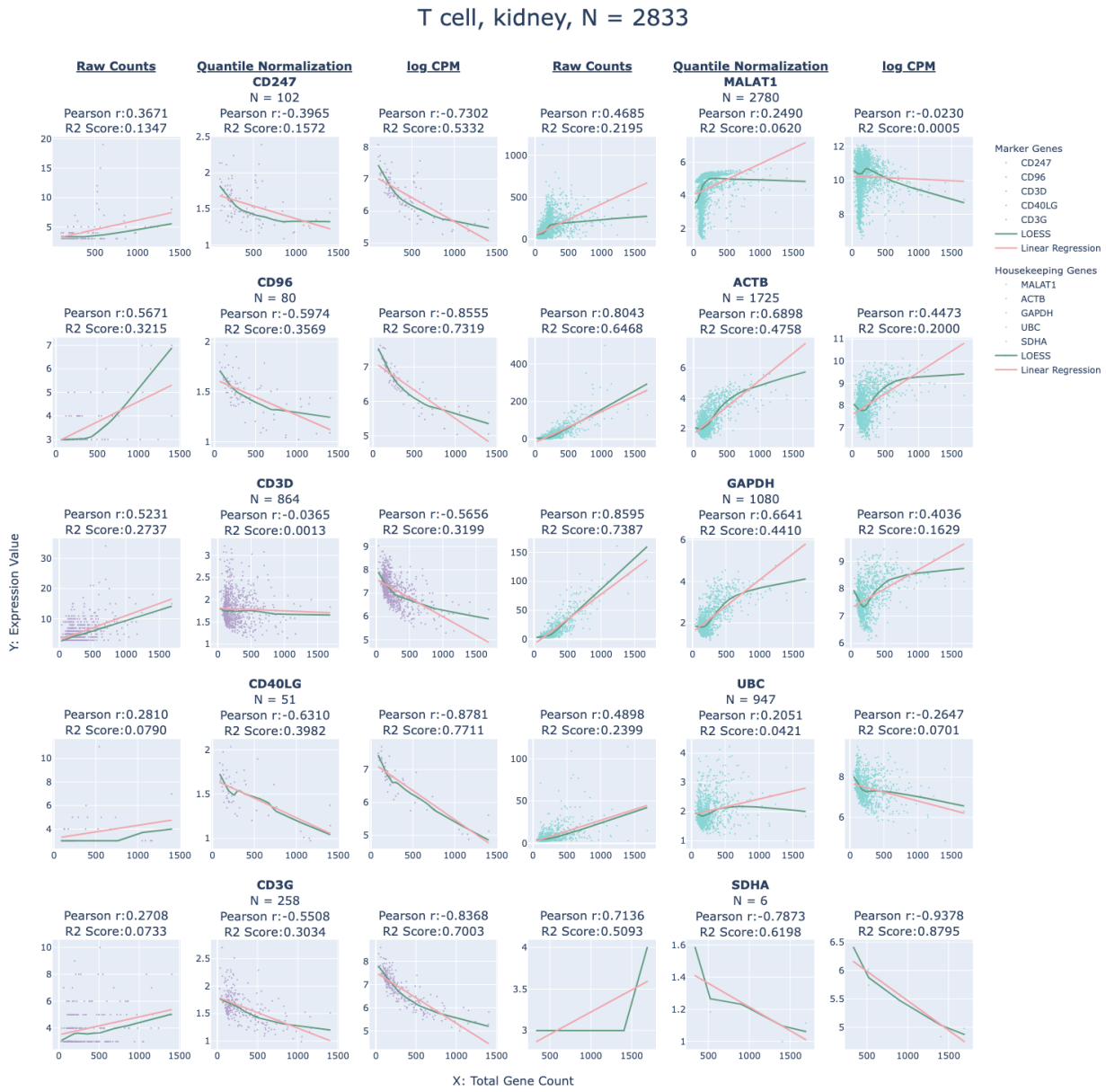


Supplemental Figure 2. **Gene Expression Value as a function of Total Gene Count for raw counts, quantile and log CPM normalizations** for *syncytiotrophoblast cells in placenta* (N = 25379 observations). The X axis represents the total number of genes expressed in a cell, and the Y axis represents the expression values (raw or normalized). N below each gene represents the number of non-zero gene expressions observed for that gene in the cell type. Markers were retrieved from HuBMAP.

Supplemental Figure 3. **Gene Expression Value as a function of Total Gene Count for raw counts, quantile and log transform normalizations** for *alveolar type 2 fibroblast cells in lung* (N = 12218 observations). The X axis represents the total number of genes expressed in a cell, and the Y axis represents the expression values (raw or normalized). N below each gene represents the number of non-zero gene expressions observed for that gene in the cell type. Markers were retrieved from HuBMAP. The scaling factor for the log transform normalization used in this analysis was 1,000,000.



Supplemental Figure 4. Gene Expression Value as a function of Total Gene Count for raw counts, quantile and log CPM normalizations for *plasma cell in lymph node* (N = 4064 observations). The X axis represents the total number of genes expressed in a cell, and the Y axis represents the expression values (raw or normalized). N below each gene represents the number of non-zero gene expressions observed for that gene in the cell type. Markers were retrieved from HuBMAP. The scaling factor for the log transform normalization used in this analysis was 1,000,000.



Supplemental Figure 5. **Gene Expression Value as a function of Total Gene Count for raw counts, quantile and log transform normalizations** for *T cells in the kidney* (N = 2833 observations). The X axis represents the total number of genes expressed in a cell, and the Y axis represents the expression values (raw or normalized). N below each gene represents the number of non-zero gene expressions observed for that gene in the cell type. Markers were retrieved from HuBMAP. The scaling factor for the log transform normalization used in this analysis was 1,000,000.

Supplemental Figure 6. **Gene Expression Value as a function of Total Gene Count for raw counts, quantile and log transform normalizations** for *plasma cell in bone marrow* (N = 1655 observations). The X axis represents the total number of genes expressed in a cell, and the Y axis represents the expression values (raw or normalized). N below each gene represents the number of non-zero gene expressions observed for that gene in the cell type. Markers were retrieved from HuBMAP. The scaling factor for the log transform normalization used in this analysis was 1,000,000.

Supplemental methods

Influence of raw counts distribution on normalized values

We plotted the number of genes expressed per cell against the normalized gene expression values for a number of markers and housekeeping genes for four different cell types in five different tissues: alveolar type 2 fibroblast in lung, syncytiotrophoblast cell in placenta, T cell in kidney, and plasma cell in lymph node and bone marrow. We chose cells for which we could retrieve marker genes from HuBMAP. We used Pearson correlation (from pandas package) to assess the strength of the linear relationship between normalized gene expression and the number of genes expressed in a cell type. We used the R^2 score from a fitted Linear Regression model (from scikit-learn) to assess the contribution of variance explained by the total number of genes expressed in a cell in determining normalized gene expression values. We did this analysis for three different methods: raw counts, quantile normalization and log CPM normalization. The analyses excluded observations where a gene expression value was 0.

For each cell type, we plotted the distributions for a list of markers and housekeeping genes. The full list of markers, obtained from HuBMAP, and housekeeping genes are available in (table S3). We averaged the R^2 scores over marker genes and housekeeping genes across all cell types and reported the aggregated values **(figs. S2-6)**.