

Examples to demonstrate the generality of sclBD

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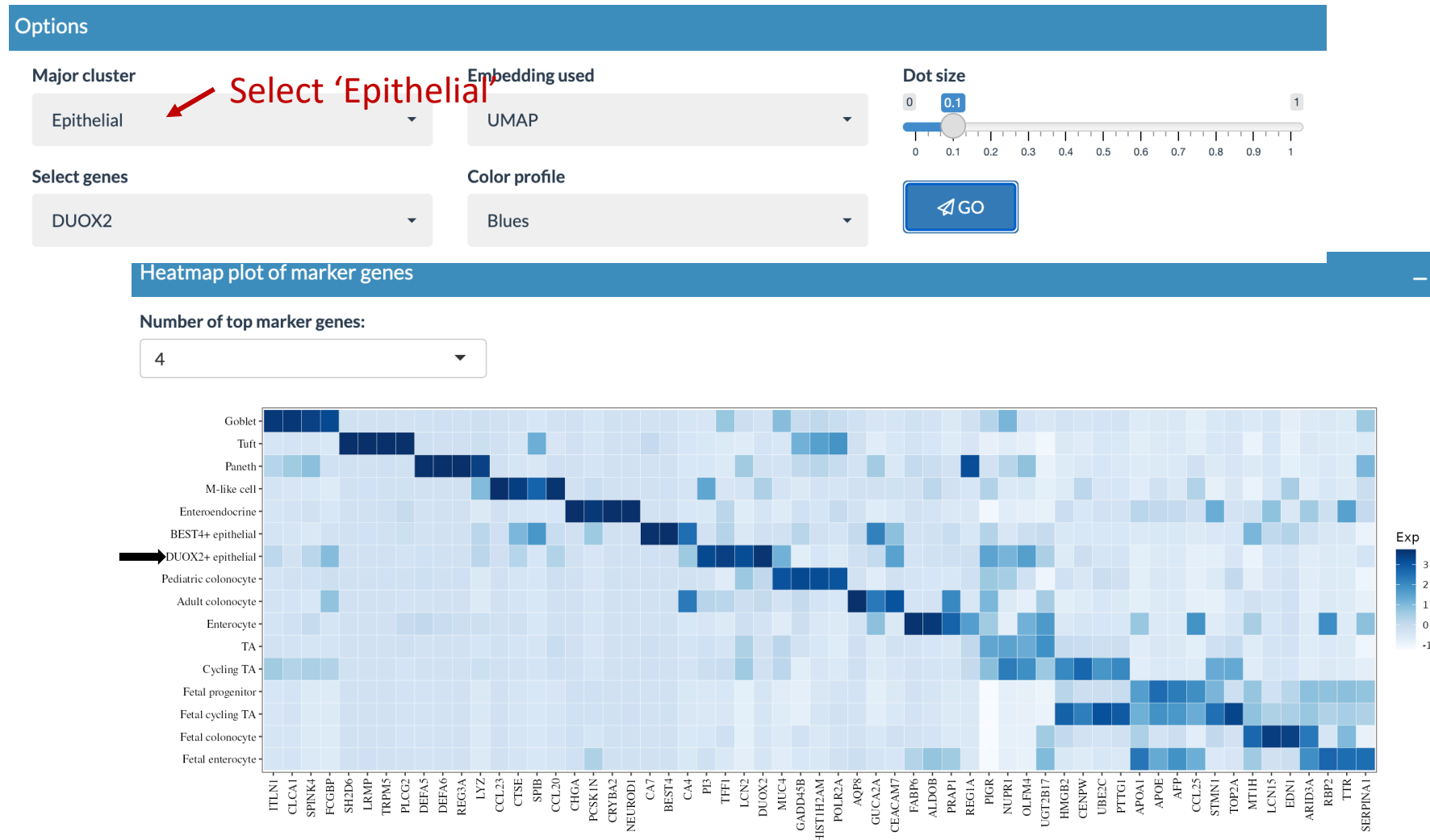
Thursday, December 15, 2022

Outlines

- **Explore the transcriptome features of DUOX2+ epithelial cells and compare the gene expression between health and disease**
- Explore the gene regulatory networks of DUOX2+ epithelial cells and compare the activity regulon between health and disease

First step: Select epithelial cells in the 'Gene Expression Profile' tab

Turn to the Exploration Panel, click the Gene Expression Profile



Second step: Explore differentially expressed genes (DEGs) in 'Marker genes of each cell subtype' table

Marker genes of each cell subtype						
Show 10 entries		Search: <input type="text"/>				
gene	cluster	p_val_adj	p_val	avg_log2FC	pct.1	pct.2
All	DUOX2+	All	All	All	All	All
PI3	DUOX2+ epithelial	0.0000	0.0000	1.6788	0.8970	0.1360
TFF1	DUOX2+ epithelial	0.0000	0.0000	1.4515	0.7980	0.1770
LCN2	DUOX2+ epithelial	0.0000	0.0000	1.3643	0.9560	0.2830
DUOX2	DUOX2+ epithelial	0.0000	0.0000	1.2653	0.6710	0.0330
CEACAM6	DUOX2+ epithelial	0.0000	0.0000	1.2393	0.7810	0.1250
S100P	DUOX2+ epithelial	0.0000	0.0000	1.2128	0.8630	0.2540
DUOXA2	DUOX2+ epithelial	0.0000	0.0000	1.2077	0.5790	0.0220
PLA2G2A	DUOX2+ epithelial	0.0000	0.0000	1.1573	0.9050	0.3470
CEACAM5	DUOX2+ epithelial	0.0000	0.0000	1.1511	0.9560	0.3520
REG4	DUOX2+ epithelial	0.0000	0.0000	1.0428	0.5660	0.1740
Showing 1 to 10 of 462 entries (filtered from 8,152 total entries)				Previous	1	2
					3	4
					5	...
					47	Next

Differentially expressed genes of DUOX2+ epithelial cells in the epithelial compartment sorted by log2 fold change of average gene expression levels.

Third step: Explore DEGs of DUOX2+ epithelial cells or any gene of interest in epithelial compartment

Options

Major cluster: **Select 'Epithelial'**
Epithelial

Select genes: **Select of gene of interest**
DUOX2

Embedding used: UMAP

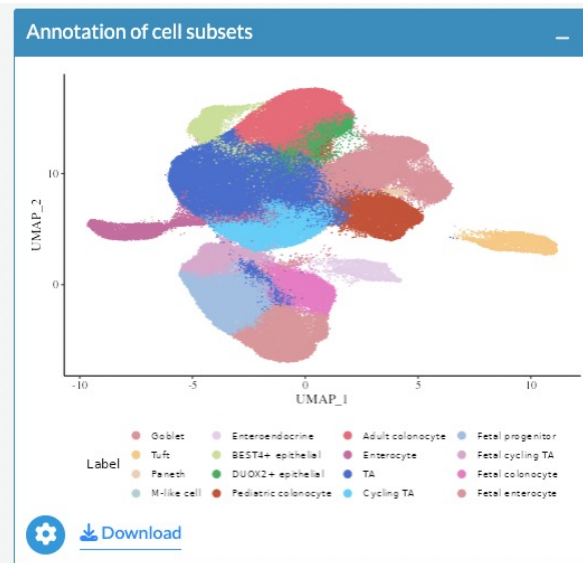
Color profile: RdPu

Dot size: 0.1

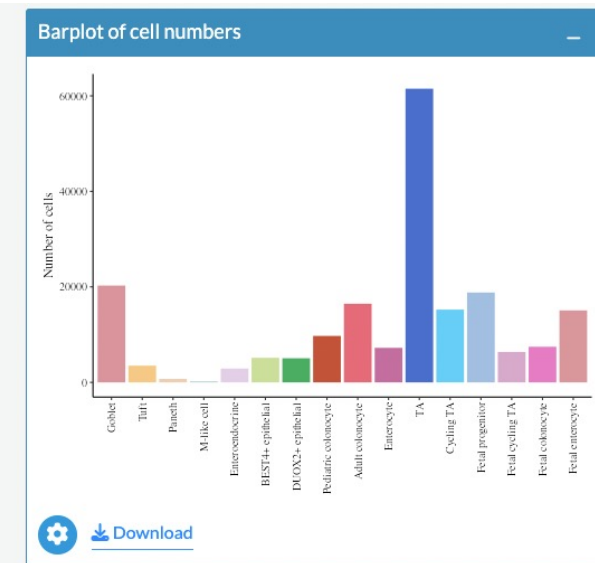
GO



The expression of *DUOX2* in epithelial cells



The cell subtypes in the epithelial compartment



Number of cells of each cell subset in the epithelial compartment

Third step: Explore DEGs of DUOX2+ epithelial cells or any gene of interest in in epithelial compartment



Violin plot of the average expression levels of the selected genes in each cell subtype in the epithelial compartment.

Bubble plot showing the gene expression of selected genes in each cell subtype in the epithelial compartment.

Forth step: Compare gene expression of HLA-II molecules across cell subtypes in epithelial cells

Turn to the Exploration Panel, click the Gene Expression Profile

Select dataset

Select genes: HLA-DRA, HLA-DRB1 Select gene of interest

Major cluster: Epithelial Select 'Epithelial'

Tissue: blood, largeInt, lymphNode, s

Development stage: adult, fetal, pediatric

Study: B. Huang et al., Cell, 2019, B.

Color profile: Reds

Embedding used: UMAP

Minor cluster: Cycling GC B, Cycling plasma

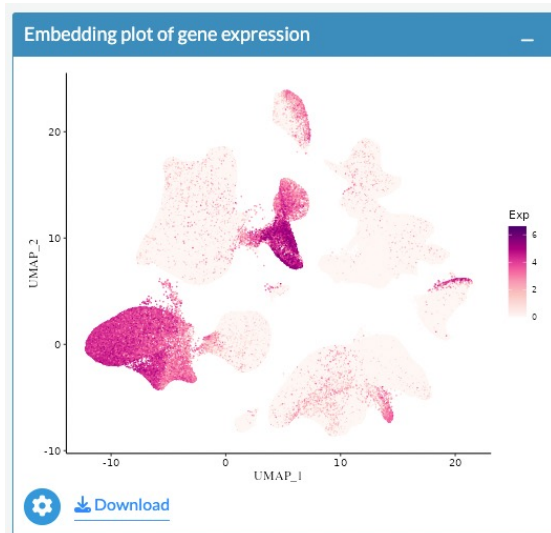
Location: blood, appendix, cecum, color

Disease state: CD_PBM, CD_inflamed, CD

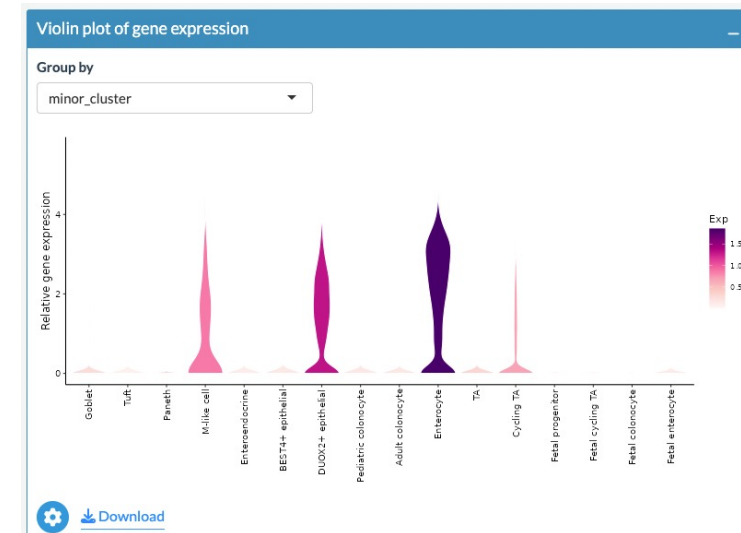
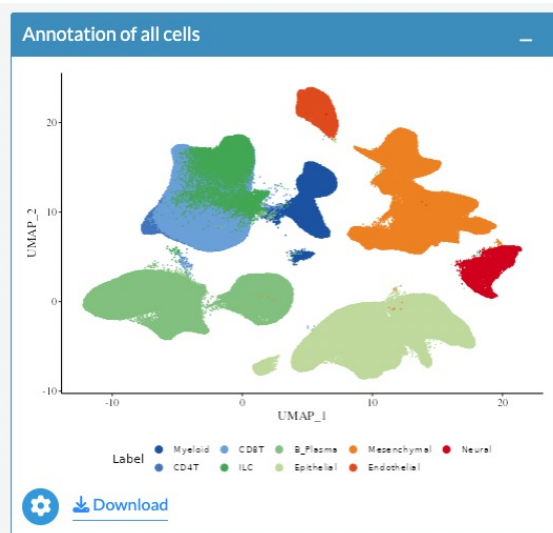
Sample: GSM3433578, GSM3433579

Dot size: 0.1

GO



Expression of HLA-II molecules in all major clusters in scIBD.



Expression of HLA-II molecules across cell subtypes in the epithelial compartment.

Fifth step: Compare gene expression of HLA-II molecules in DUOX2+ epithelial cells between health and disease

Turn to the Exploration Panel, click the Gene Expression Profile

Select dataset

Select genes: HLA-DRA, HLA-DRB1 (Select gene of interest)

Major cluster: Epithelial

Tissue: blood, largeInt, lymphNode, s

Development stage: adult (Select stage of interest)

Study: B. Huang et al., Cell, 2019, B.

Color profile: Reds

Embedding used: UMAP

Minor cluster: DUOX2+ epithelial (Select 'DUOX2+ epithelial')

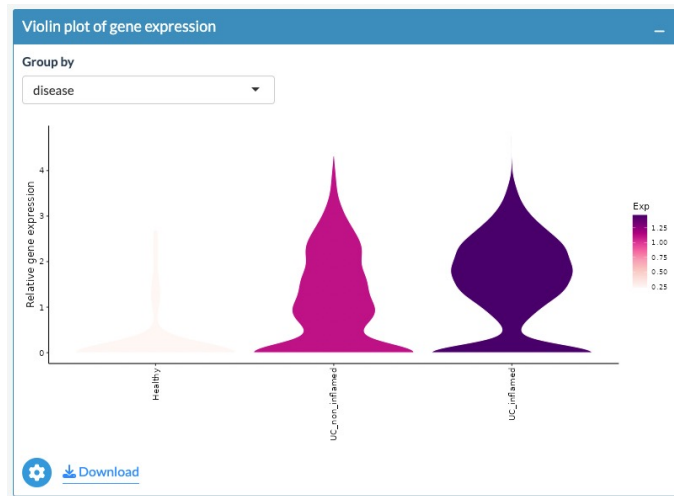
Location: blood, appendix, cecum, color

Disease state: Healthy, UC_inflamed, UC_nc (Select disease statuses to compare)

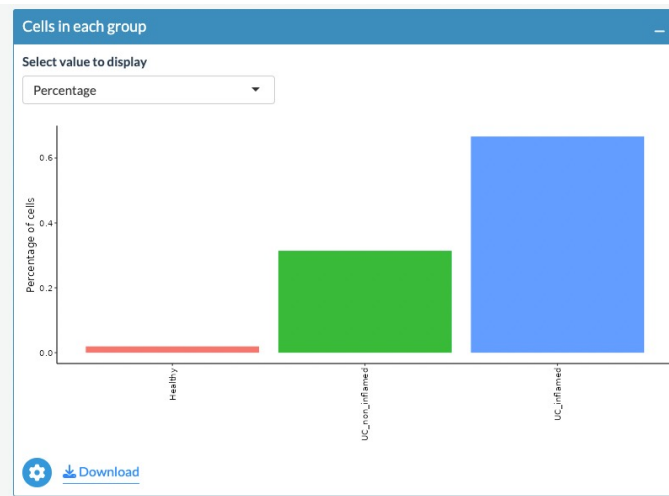
Sample: GSM3433578, GSM3433579

Dot size: 0.1

GO



Compare gene expression of MHL-molecules in DUOX2+ epithelial cells in healthy, UC non-inflamed and UC inflamed tissues.



Number of cells in each group.

Sixth step: Compare gene expression of HLA-II molecules in enterocytes between health and disease

Turn to the Exploration Panel, click the Gene Expression Profile

Select dataset

Select genes: HLA-DRA, HLA-DRB1 (Select gene of interest)

Major cluster: Epithelial

Tissue: blood, largeInt, lymphNode, s

Development stage: adult (Select stage of interest)

Embedding used: UMAP

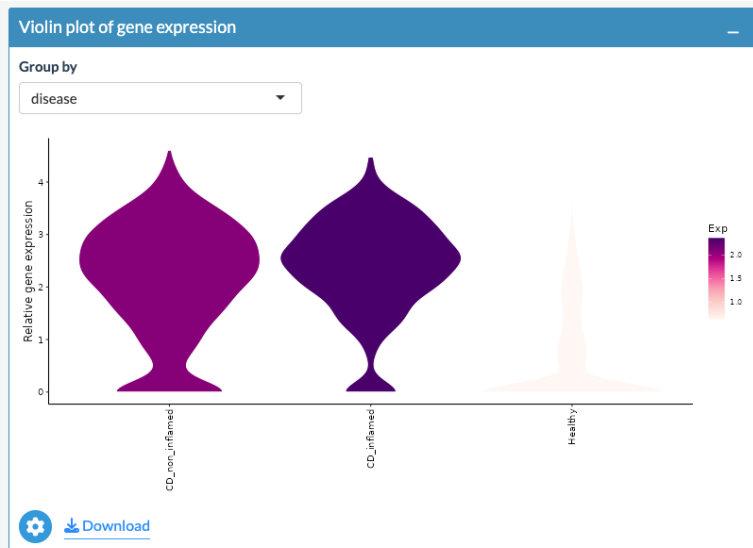
Minor cluster: Enterocyte (Select 'Enterocyte')

Location: blood, appendix, cecum, color

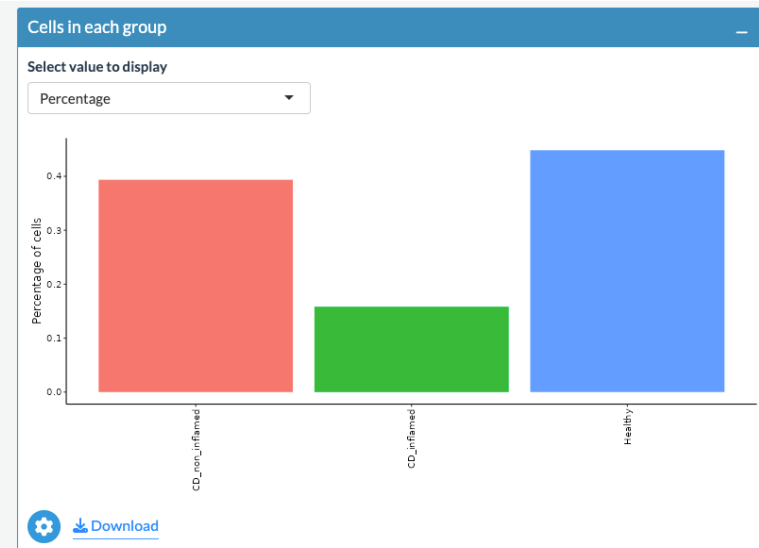
Disease state: CD_inflamed, CD_non_inflam (Select disease statuses to compare)

Sample: GSM3433578, GSM3433579

GO



Compare gene expression of MHLI-molecules in enterocytes in healthy, UC non-inflamed, and UC inflamed tissues.



Number of cells in each group.

More: Explore the preference of development stages of cell subtypes

Turn to the Exploration Panel, click the Gene Expression Profile

Select dataset

Select genes: HLA-DRA, HLA-DRB1

Major cluster: Epithelial (Select major cluster of interest)

Development stage: adult, fetal, pediatric

Study: B. Huang et al., Cell, 2019, B. I

Color profile: Reds

Embedding used: UMAP

Minor cluster: Cycling GC B, Cycling plasma

Location: blood, appendix, cecum, colon

Disease state: CD_PBMC, CD_inflamed, CD

Sample: GSM3433578, GSM3433579

Dot size: 0.1

GO



Cell compositions of cell subtypes in epithelial compartment.

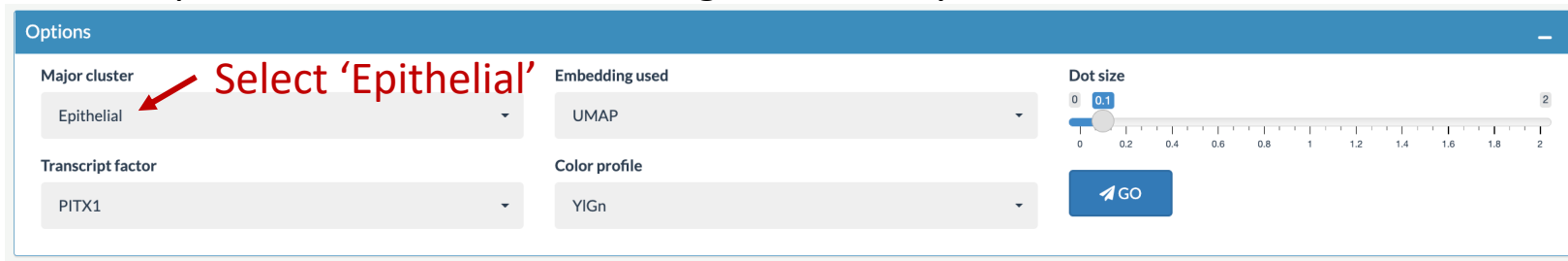
DUOX2+ epithelial cells were only presented in samples from the pediatric and adult stages, not from the fetal stage in sclBD.

Outlines

- Explore the transcriptome features of DUOX2+ epithelial cells and compare the gene expression between health and disease
- **Explore the gene regulatory networks of DUOX2+ epithelial cells and compare the activity regulon between health and disease**

First step: Explore regulons in epithelial compartment

Turn to the Exploration Panel, click the Regulon Activity Profile



Options

Major cluster: Epithelial (Select 'Epithelial')

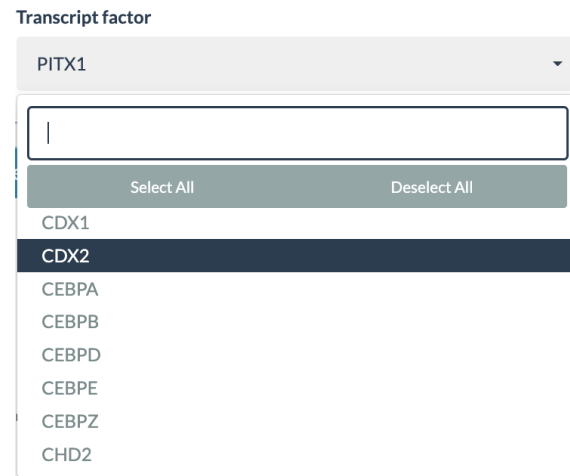
Embedding used: UMAP

Transcript factor: PITX1

Color profile: YIGn

Dot size: 0.1

GO



Transcript factor

PITX1

Select All Deselect All

- CDX1
- CDX2
- CEBPA
- CEBPB
- CEBPD
- CEBPE
- CEBPZ
- CHD2

All regulons in epithelial cells are listed in the drop-down box. Users can select any regulon of interest or go to the '**Regulon specificity scores (RSS) in each cell type**' table to browser cell type specific regulons.

Second step: Explore cell type-specific regulons in DUOX2+ epithelial cells

Turn to the Exploration Panel, click the Regulon Activity Profile

Options

Major cluster

Select 'Epithelial'

Epithelial

Transcript factor

PITX1

Embedding used

UMAP

Color profile

YIGn

Dot size

00.12

00.20.40.60.811.21.41.61.81.82

GO

Regulon specificity scores (RSS) in each cell type

Show10entries

Search:

	Goblet	Tuft	Paneth	M-like cell	Enteroendocrine	BEST4+ epithelial	DUOX2+ epithelial	Pediatric colonocyte	Adult colonocyte	Enterocyte	TA	Cycling TA	Fetal progenitor	Fetal cycling TA	Fetal colonocyte	Fetal enterocyte
PITX1	0.15	0.01	0.00	0.00	0.03	0.05	0.11	0.02	0.11	0.05	0.22	0.11	0.10	0.04	0.04	0.04
GRHL3	0.06	0.05	0.01	0.01	0.01	0.04	0.09	0.09	0.13	0.02	0.08	0.02	0.02	0.01	0.02	0.03
RFX5	0.11	0.02	0.01	0.01	0.02	0.04	0.09	0.09	0.05	0.14	0.25	0.13	0.05	0.01	0.01	0.05
NFE2L3	0.12	0.01	0.01	0.01	0.01	0.04	0.08	0.06	0.05	0.09	0.31	0.16	0.02	0.01	0.02	0.02
ETS1	0.14	0.06	0.01	0.01	0.03	0.06	0.08	0.11	0.18	0.06	0.25	0.06	0.06	0.02	0.04	0.11
CD59	0.14	0.02	0.01	0.00	0.02	0.06	0.08	0.07	0.19	0.06	0.30	0.11	0.07	0.03	0.05	0.08
NFE2L1	0.12	0.04	0.01	0.00	0.01	0.05	0.07	0.10	0.20	0.11	0.21	0.05	0.06	0.01	0.03	0.10
POU2F1	0.07	0.11	0.01	0.01	0.03	0.03	0.07	0.11	0.05	0.02	0.21	0.06	0.04	0.05	0.01	0.04
SP2	0.13	0.07	0.01	0.01	0.03	0.05	0.07	0.11	0.15	0.05	0.28	0.09	0.07	0.03	0.05	0.06
TBX10	0.23	0.02	0.01	0.00	0.02	0.05	0.07	0.03	0.09	0.03	0.26	0.11	0.12	0.05	0.06	0.05

Showing 1 to 10 of 419 entries

Previous

1

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Next

Third step: Explore DUOX2+ epithelial-specific regulons or any regulon of interest in epithelial compartment

Turn to the Exploration Panel, click the Regulon Activity Profile

Options

Major cluster: Epithelial Select 'Epithelial'

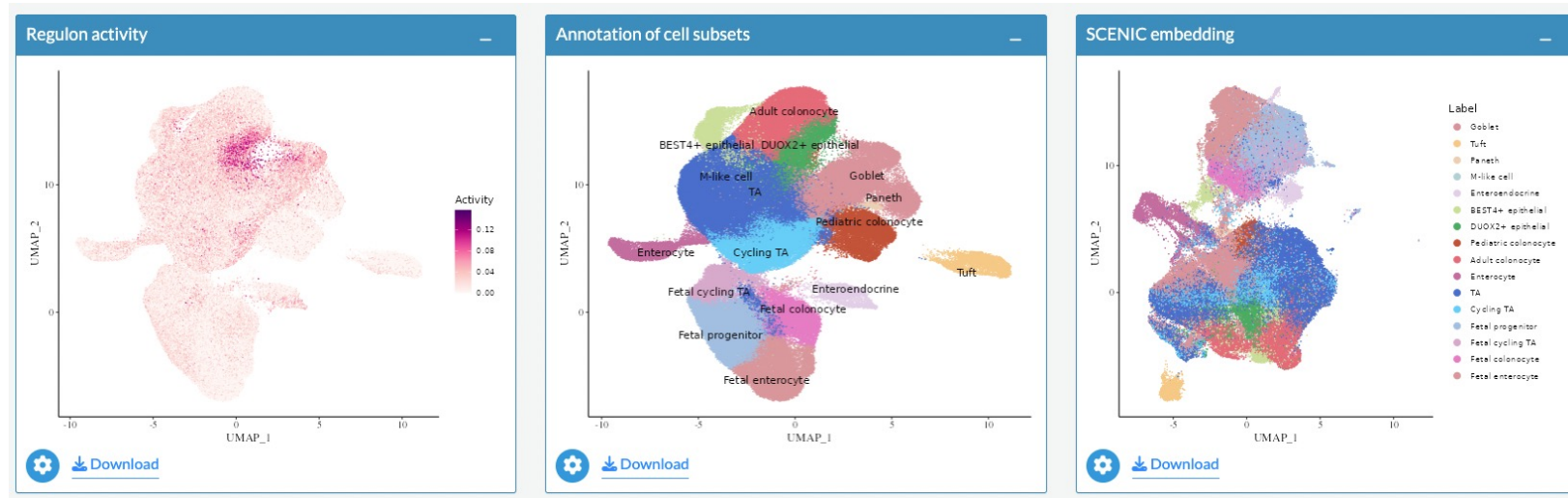
Transcript factor: PITX1 Select 'PITX1'

Embedding used: UMAP

Color profile: YIGn

Dot size: 0.1

GO



Regulon activities of PITX1 regulon in epithelial cells

UMAP plot of cells based on gene expression

UMAP plot of cells based on regulon activity

Third step: Explore DUOX2+ epithelial-specific regulons or any regulon of interest in epithelial compartment

Turn to the Exploration Panel, click the Regulon Activity Profile

Options

Major cluster

Epithelial

Select 'Epithelial'

Transcript factor

PITX1

Select 'PITX1'

Embedding used

UMAP

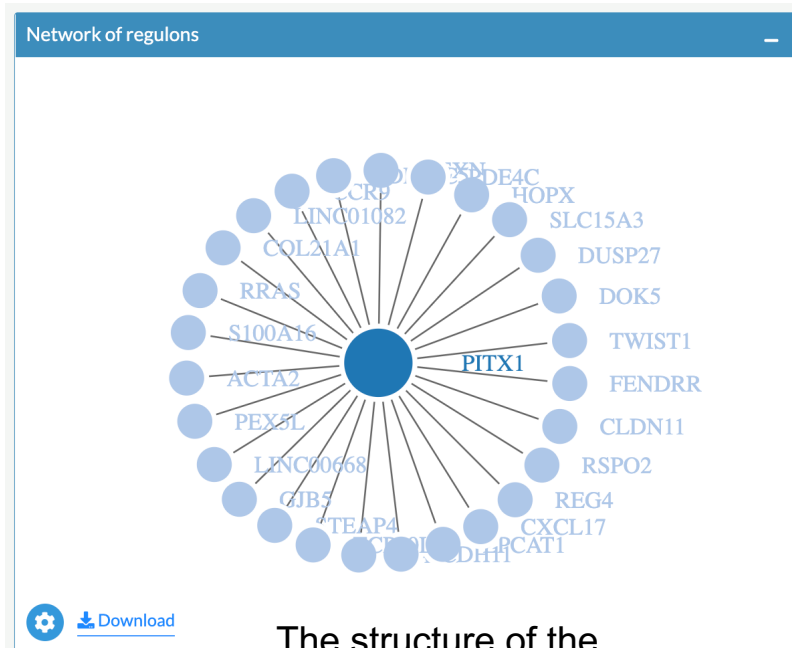
Color profile

YlGn

Dot size

00.12

GO



The structure of the selected regulon

Network of regulons					
Show	10	entries	Search: <input type="text"/>		
TF	target	correlation	p-value	expression	
<div>All</div>	<div>All</div>	<div>All</div>	<div>All</div>	<div>All</div>	
1	PITX1	GJB5	0.5475	1.309e-41	0.4736
2	PITX1	NEXN	0.6513	3.255e-51	0.3902
3	PITX1	REG4	0.4214	4.383e-241	2.0126
4	PITX1	S100A16	0.3375	3.159e-213	1.4061
5	PITX1	DUSP27	0.2504	9.293e-03	0.5555
6	PITX1	CAPG	0.4879	0e+00	0.8748
7	PITX1	CCR9	0.8368	7.946e-06	0.3486
8	PITX1	CLDN11	0.7383	3.729e-11	0.4597
9	PITX1	PEX5L	0.7857	2.433e-05	0.4453
10	PITX1	HOPX	0.6306	1.429e-22	0.7406
Showing 1 to 10 of 28 entries			Previous	1	2 3 Next

Correlation of TF and its target genes.

Forth step: Explore differentially activated regulons between health and disease in epithelial cells

Turn to the Exploration Panel, click the Regulon Activity Comparison

Select dataset

Major cluster

Epithelial

Minor cluster

Adult colonocyte, BEST4+ ep

Location

blood, appendix, cecum, color

Disease state

CD_PBMC, CD_inflamed, CD

Sample

GSM3433578, GSM3433579

Submit

GO

Transcript factor

PITX1

Tissue

blood, largeInt, lymphNode, s

Development stage

adult, fetal, pediatric

Study

B. Huang et al., Cell, 2019, B.

Color profile

Reds

Compare regulons between healthy and UC

Show10entries

Search:

gene	UC_inflamed	Healthy	FoldChange	p.value	p.adjust
All	All	All	All	All	All
RFX5	0.042718	0.016440	2.449472	0.000000	0.000000
NFE2L3	0.073421	0.032640	2.182573	0.000000	0.000000
ZBTB40	0.013699	0.005331	2.163928	0.000000	0.000000
EGR4	0.010417	0.005158	1.691655	0.000000	0.000000
ZNF436	0.007414	0.003458	1.663145	0.000000	0.000000
PITX1	0.027530	0.016265	1.594513	0.000000	0.000000
RUNX3	0.006697	0.003253	1.574623	0.000000	0.000000
KDM4A	0.005257	0.002432	1.531633	0.000000	0.000000
HOXD13	0.099801	0.064639	1.520456	0.000000	0.000000
TBX10	0.086436	0.056469	1.504046	0.000000	0.000000

Showing 1 to 10 of 419 entries

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The result of the differential analysis of the regulons in epithelial cells was shown in the 'Compare regulons between healthy and UC' tab

Fifth step: Compare regulon activities between health and disease in epithelial cells

Turn to the Exploration Panel, click the Regulon Activity Comparison

Select dataset

Major cluster: Epithelial *Select 'Epithelial'*

Minor cluster: Adult colonocyte, BEST4+ ep

Location: blood, appendix, cecum, colon

Disease state: CD_PBM, CD_inflamed, CD

Sample: GSM3433578, GSM3433579

Submit: GO

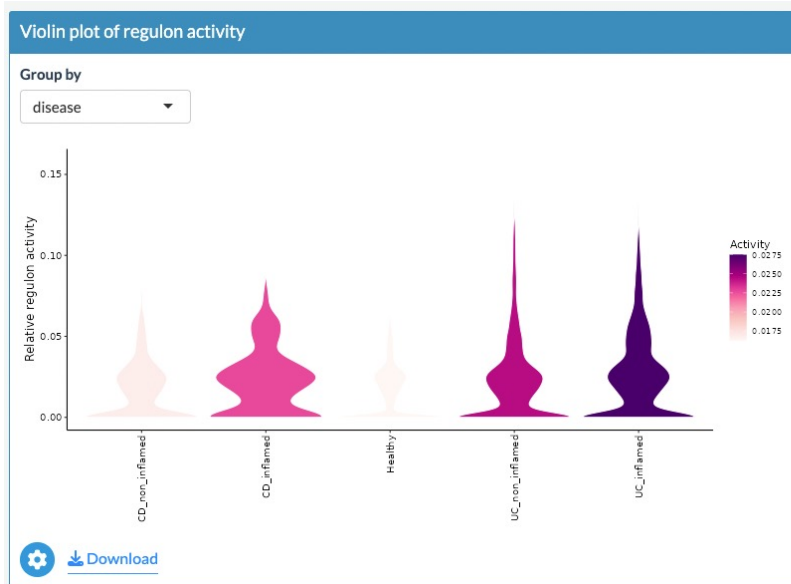
Transcript factor: PITX1 *Select regulon of interest*

Tissue: blood, largeInt, lymphNode, s

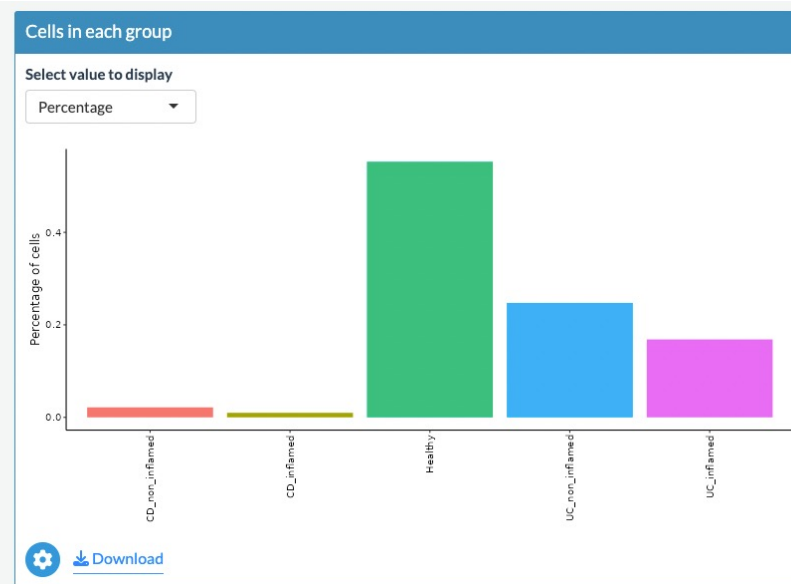
Development stage: adult *Select stage of interest*

Study: B. Huang et al., Cell, 2019, B. i

Reds



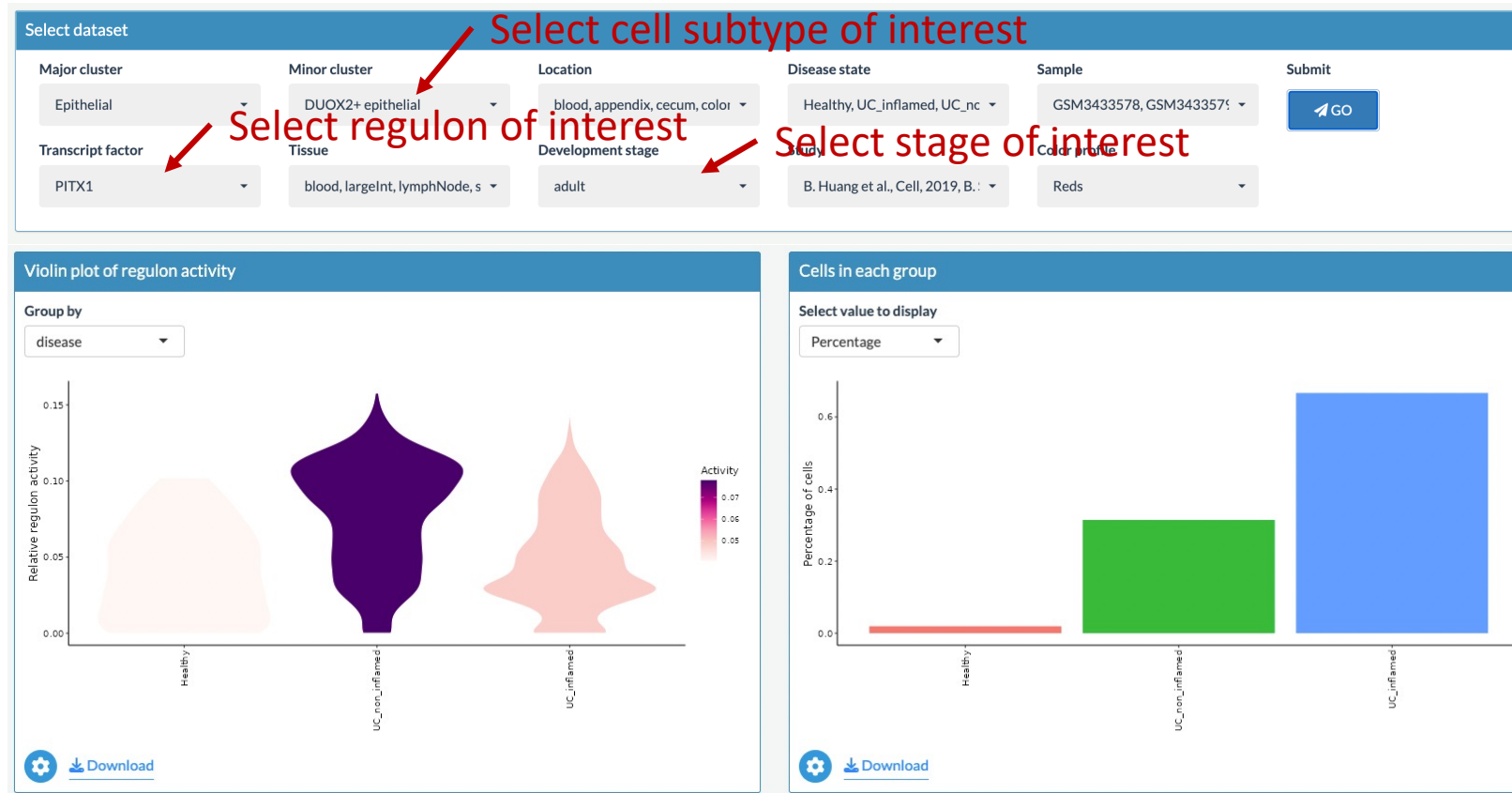
Compare the activity of PITX1 regulon in epithelial cells across different disease statuses.



Number of cells in each group.

Sixth step: Compare regulon activities between health and disease in DUOX2+ epithelial cells

Turn to the Exploration Panel, click the Regulon Activity Comparison



Compare the activity of PITX1 regulon in DUOX2+ epithelial cells across different disease statuses.

Number of cells in each group.

Thanks!