

# Analysis

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## 1 摘要

空间转录组分析:

- 鉴定肿瘤细胞
- 肿瘤细胞亚群分析
- 肿瘤细胞和正常细胞之间的差异分析
- 细胞通讯分析
- 肿瘤细胞和正常细胞（巨噬细胞）之间的通讯分析。

## 2 研究设计流程图

## 3 材料和方法

- Seurat
- copyKAT<sup>1</sup>
- monocle3
- cellchat
- clusterProfiler
- ...

## 4 分析结果

- 以 copykat 鉴定了肿瘤细胞，主要为上皮细胞 (epithelial cells, EC) 或基底细胞 (basal cells, BC)。
- 以拟时分析将肿瘤细胞分为三个亚型 (cancer 1, cancer 2, cancer 3)，表现出时间（拟时）递进变化。
- 肿瘤细胞亚型之间的差异分析，肿瘤细胞和正常细胞 (EC, BC) 之间的差异分析，主要聚焦的通路有 ‘Phagosome’、’Antigen processing and presentation’、’Focal adhesion’ 等。
- 细胞通讯分析的整体情况见 Fig. 18。
- 巨噬细胞和肿瘤细胞的通讯，突出表现为 ITGA 受体配体相关通路，共 27 个基因（其中多数为近似的亚型），首要富集于 PI3K-Akt 相关通路，并且和 ‘Focal adhesion’ 等上述分析的结果相一致。

## 5 结论

见 4。

## 6 附：分析流程（癌组织切片）

### 6.1 ST 数据预处理

Figure 1为图 spatial sample QC 概览。选择基因数 2500 - 9000 作为过滤指标。

(对应文件为 Figure+Table/spatial-sample-QC.pdf)

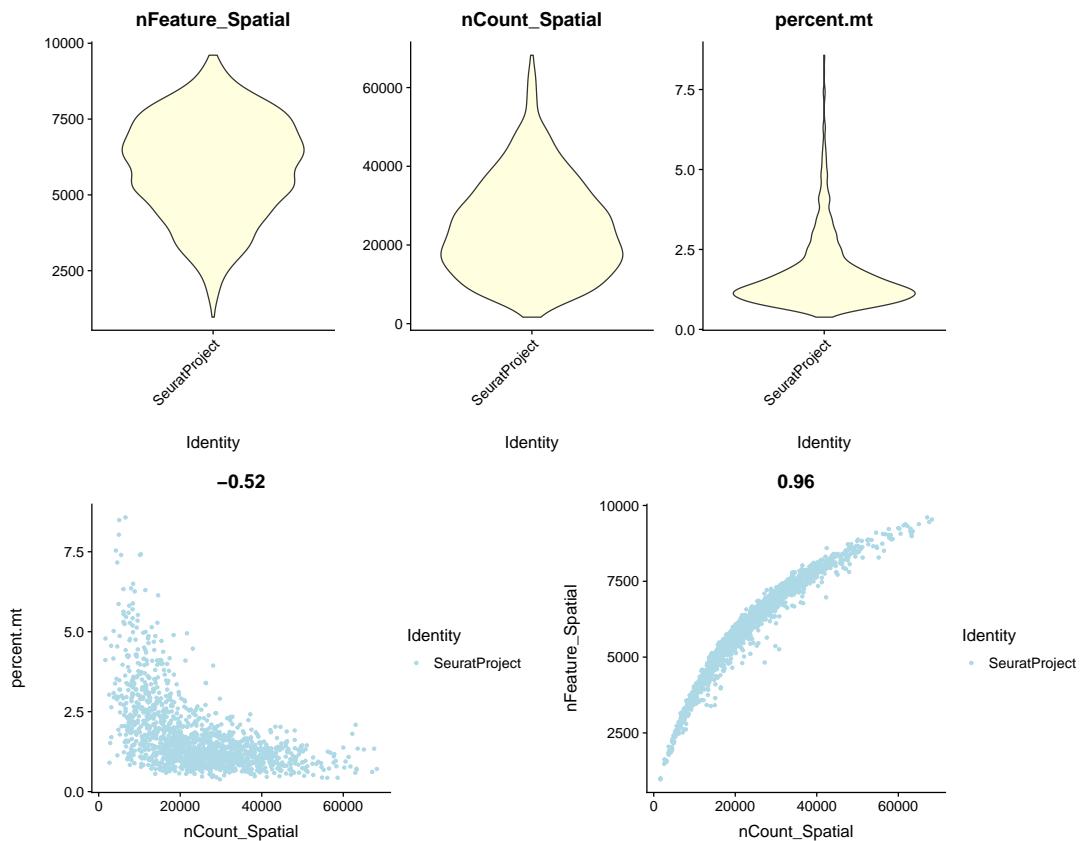


Figure 1: Spatial sample QC

Figure 2为图 PCA ranking 概览。选择主成份 1-15 用于后续聚类。

(对应文件为 Figure+Table/PCA-ranking.pdf)

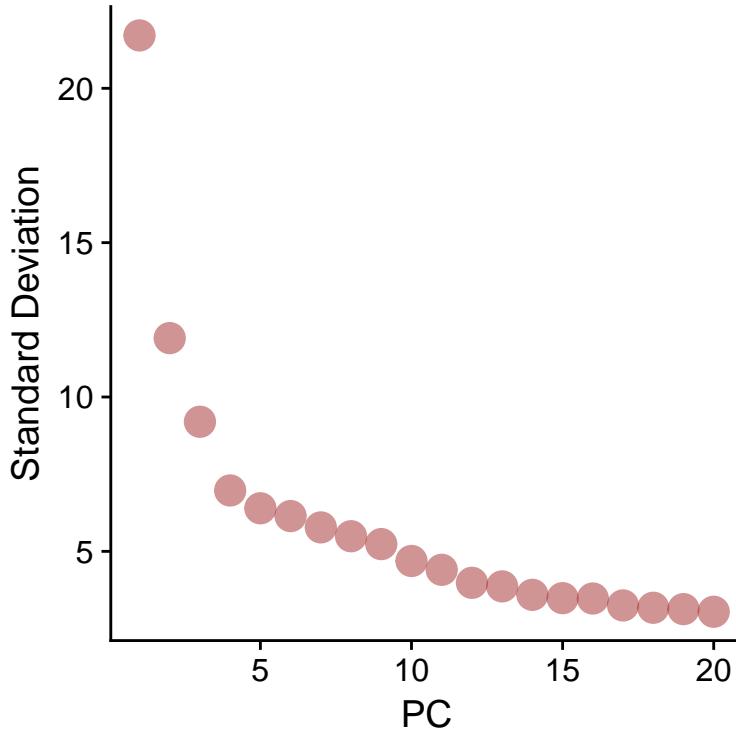


Figure 2: PCA ranking

## 6.2 细胞注释

### 6.2.1 所有细胞类 (Seurat clusters) 的 marker

Table 1为表格 all markers of Seurat clusters 概览。

(对应文件为 [Figure+Table/all-markers-of-Seurat-clusters.csv](#))

注：表格共有 4370 行 8 列，以下预览的表格可能省略部分数据；表格含有 15 个唯一‘cluster’。

Table 1: All markers of Seurat clusters

rownames	p_val	avg_l...	pct.1	pct.2	p_val...	cluster	gene
ISLR	1.244...	2.772...	0.97	0.385	2.437...	0	ISLR
FN1	2.313...	2.726...	1	0.971	4.533...	0	FN1
COMP	4.009...	3.497...	0.827	0.192	7.857...	0	COMP
COL1A1	1.812...	2.682...	1	0.978	3.551...	0	COL1A1
TAGLN	4.759...	2.643...	1	0.877	9.326...	0	TAGLN
BGN	5.201...	2.540...	1	0.76	1.019...	0	BGN
COL1A2	1.085...	2.444...	1	0.988	2.126...	0	COL1A2
AEBP1	3.097...	2.326...	1	0.893	6.069...	0	AEBP1
RARRES2	1.383...	3.100...	1	0.716	2.711...	0	RARRES2

rownames	p_val	avg_l...	pct.1	pct.2	p_val...	cluster	gene
COL5A1	1.498...	2.494...	0.992	0.671	2.937...	0	COL5A1
SPARC	7.275...	2.190...	1	0.951	1.425...	0	SPARC
LUM	1.446...	2.464...	1	0.886	2.834...	0	LUM
MYL9	3.618...	2.054...	1	0.915	7.089...	0	MYL9
NNMT	3.777...	2.486...	1	0.675	7.401...	0	NNMT
POSTN	4.428...	2.680...	1	0.765	8.676...	0	POSTN
...	...	...	...	...	...	...	...

## 6.2.2 SCSA 注释

以肺脏组织的数据集注释。

Figure 3为图 SCSA annotation 概览。

(对应文件为 Figure+Table/SCSA-annotation.pdf)

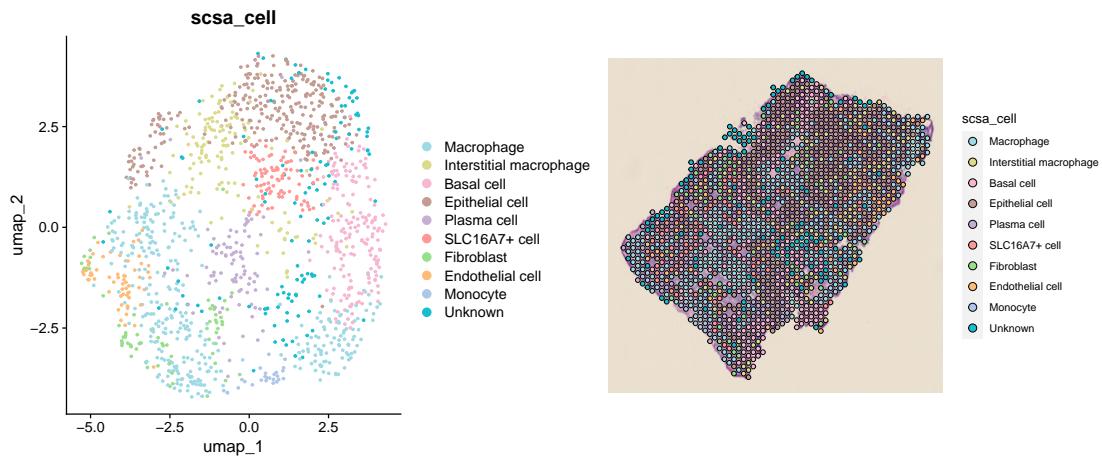


Figure 3: SCSA annotation

## 6.3 依据变异拷贝数鉴定肿瘤细胞

### 6.3.1 copyKAT 解析肿瘤细胞

copyKAT<sup>1</sup>

非整倍体是人类肿瘤细胞中最普遍的特征，约 90% 的肿瘤的基因组是非整倍体，而正常细胞是二倍体<sup>2</sup>

Figure 4为图 copyKAT prediction of aneuploidy 概览。

(对应文件为 Figure+Table/copykat\_heatmap.png)

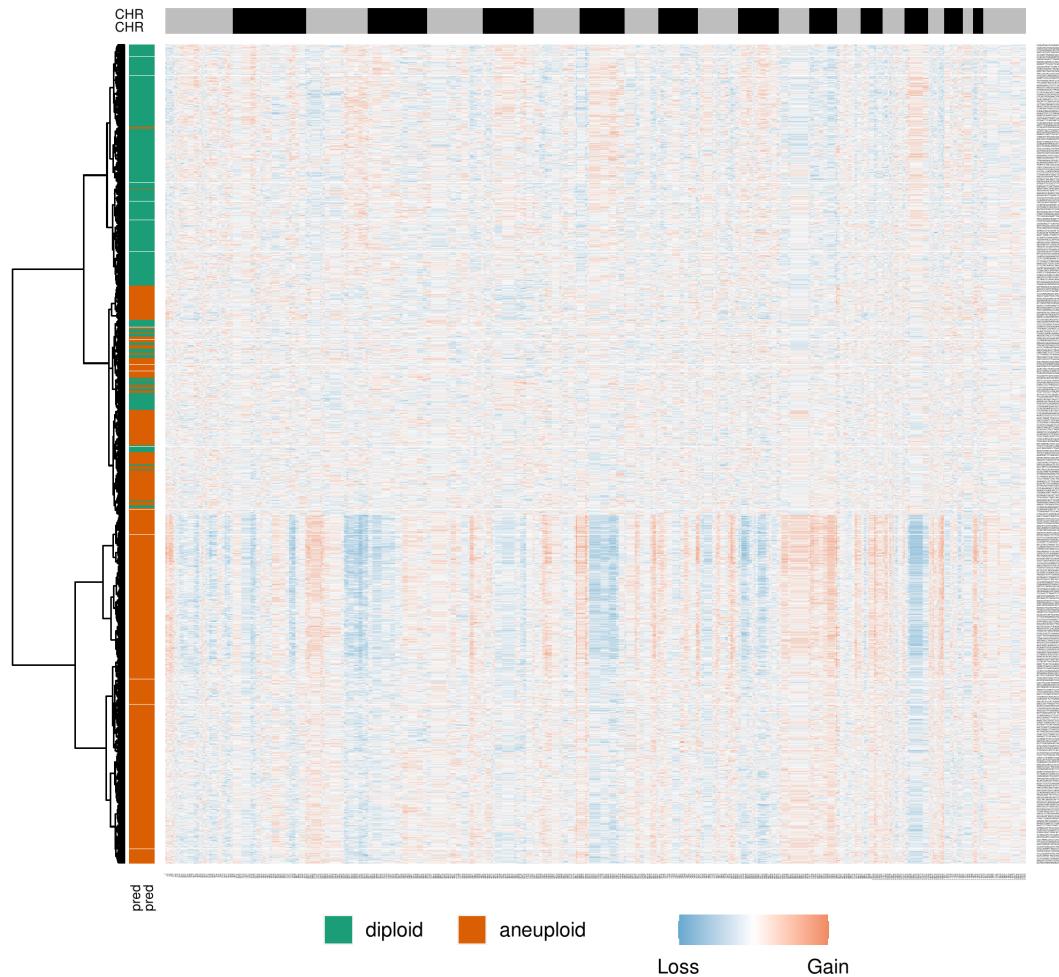


Figure 4: CopyKAT prediction of aneuploidy

Figure 5为图 cell mapped of copyKAT prediction 概览。

(对应文件为 [Figure+Table/cell-mapped-of-copyKAT-prediction.pdf](#))

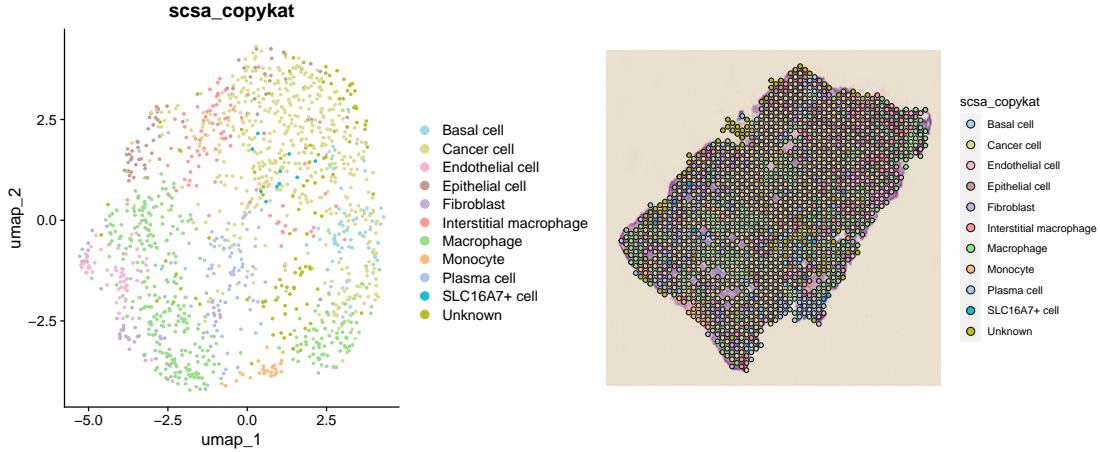


Figure 5: Cell mapped of copyKAT prediction

对比 Fig. 5 和 Fig. 3 可知，癌细胞主要为上皮细胞或基底细胞。

### 6.3.2 肿瘤细胞重聚类

为了区分肿瘤细胞之间的亚型，这里首先将肿瘤细胞重新聚类。

Figure 6为图 re classify of cancer cells 概览。

(对应文件为 Figure+Table/re-classify-of-cancer-cells.pdf)

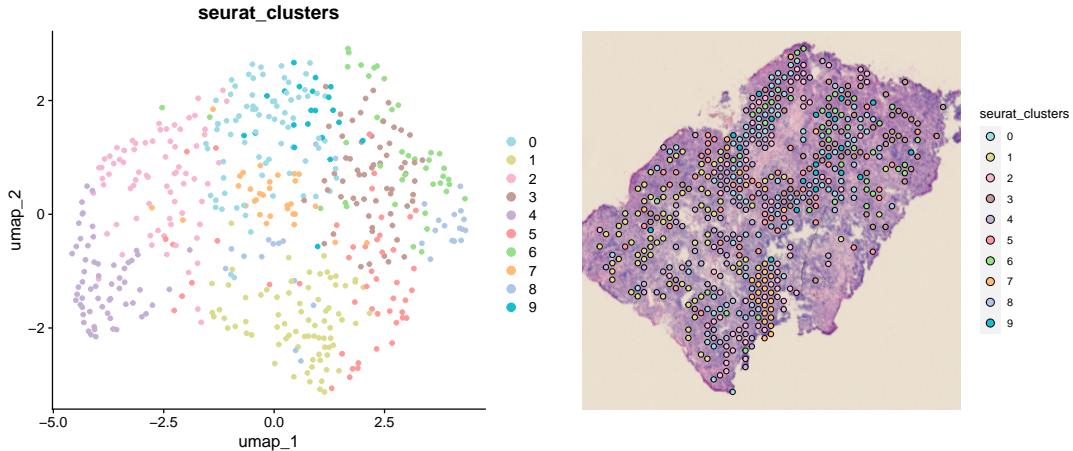


Figure 6: Re classify of cancer cells

## 6.4 拟时分析肿瘤细胞

### 6.4.1 构建拟时轨迹

Figure 7为图 pseudotime visualization of cancer cells 概览。

(对应文件为 Figure+Table/pseudotime-visualization-of-cancer-cells.pdf)

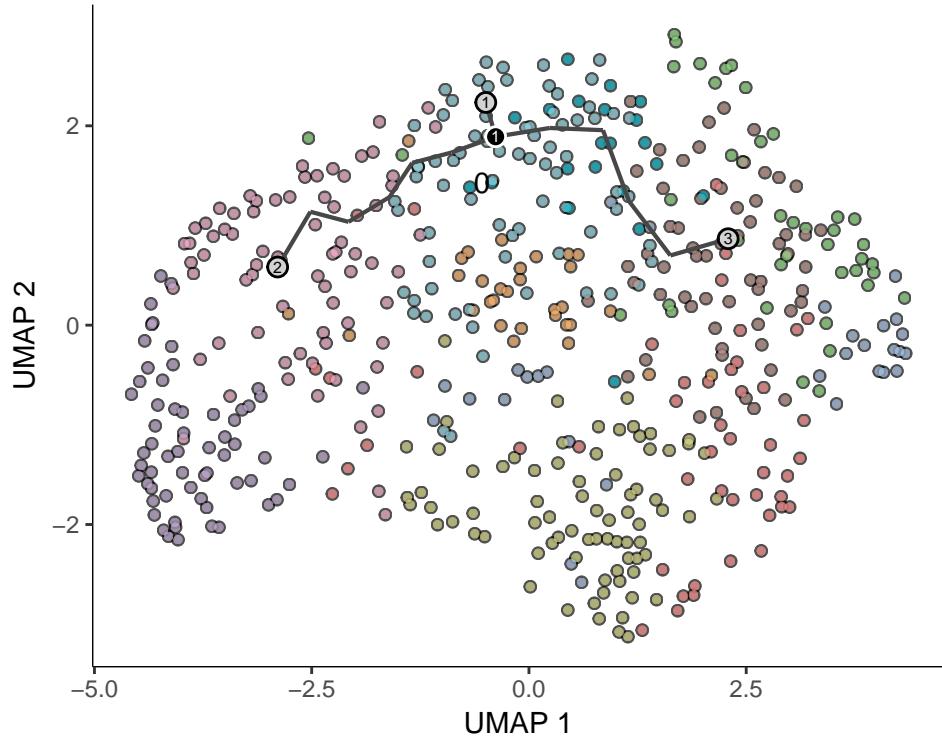


Figure 7: Pseudotime visualization of cancer cells

#### 6.4.2 根据拟时分析区分肿瘤细胞亚类

Figure 8为图 gene module of co expression analysis 概览。

(对应文件为 Figure+Table/gene-module-of-co-expression-analysis.pdf)

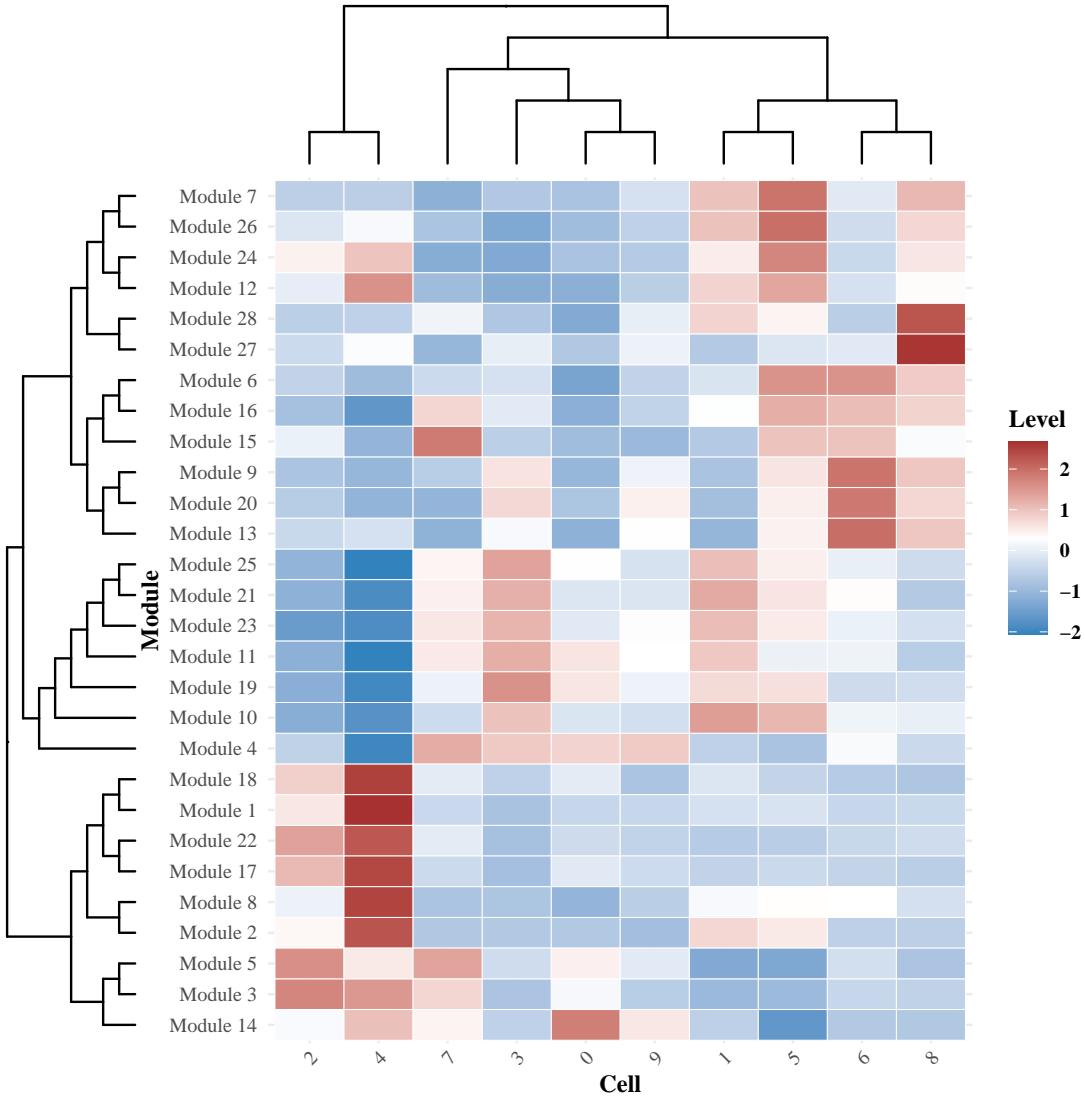


Figure 8: Gene module of co expression analysis

Fig. 8, 根据细胞类的聚类树, 可以将细胞类分为三个大类。

为了选择拟时起点, 这里, 将 Fig. 4 所示的细胞聚类树切分为 15 个大类的细胞, 然后映射到 Fig. 7 对应的聚类图中。可以看到 (Fig. 9), 细胞类类 11 首要分布在左侧区域 (UMAP 图) (1 - 15, 数目越小, 代表越趋近于非整倍体, 即肿瘤细胞), 因此, 左侧区域的细胞更接近于正常细胞。

Figure 9为图 test for selecting pseudotime start point 概览。

(对应文件为 Figure+Table/test-for-selecting-pseudotime-start-point.pdf)

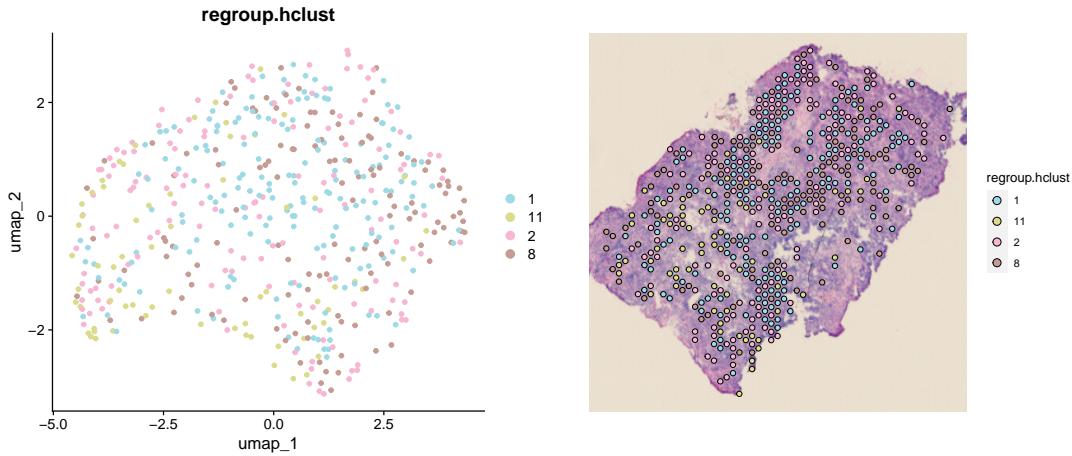


Figure 9: Test for selecting pseudotime start point

因此，选择左侧区域的细胞作为拟时起点。

Figure 10为图 cancer cells subtypes 概览。

(对应文件为 Figure+Table/cancer-cells-subtypes.pdf)

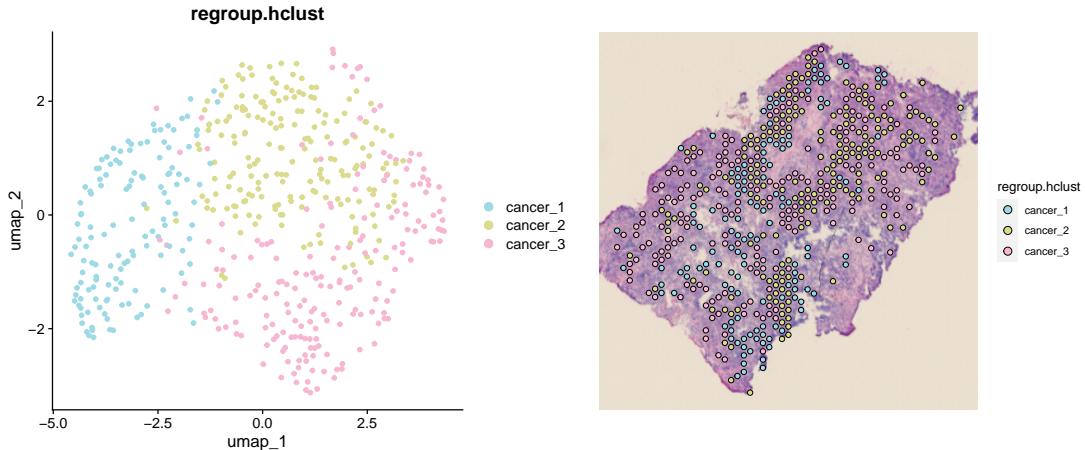


Figure 10: Cancer cells subtypes

#### 6.4.3 肿瘤细胞亚类差异分析和富集分析

以下分析，可关注的通路有：

- Phagosome
- Antigen processing and presentati...
- Focal adhesion
- ...

cancer 1 细胞的 marker 的富集分析有结果，但矫正 p 值均不显著。

Table 2为表格 tables of enrichment of markers of cancer 1 cells 概览。

(对应文件为 Figure+Table/tables-of-enrichment-of-markers-of-cancer-1-cells.csv)

注：表格共有 66 行 9 列，以下预览的表格可能省略部分数据；表格含有 66 个唯一 ‘ID’。

Table 2: Tables of enrichment of markers of cancer 1 cells

ID	Descr...	GeneR...	BgRatio	pvalue	p.adjust	qvalue	geneID	Count
hsa04114	Oocyt...	3/31	131/8622	0.011...	0.379...	0.369...	9133/...	3
hsa04218	Cellu...	3/31	156/8622	0.018...	0.379...	0.369...	9133/...	3
hsa04110	Cell ...	3/31	157/8622	0.018...	0.379...	0.369...	9133/...	3
hsa01524	Plati...	2/31	73/8622	0.028...	0.379...	0.369...	4257/...	2
hsa04115	p53 s...	2/31	74/8622	0.028...	0.379...	0.369...	9133/983	2
hsa04914	Proge...	2/31	102/8622	0.051...	0.552...	0.537...	9133/983	2
hsa00100	Stero...	1/31	20/8622	0.069...	0.552...	0.537...	3930	1
hsa03060	Prote...	1/31	23/8622	0.079...	0.552...	0.537...	6726	1
hsa04514	Cell ...	2/31	158/8622	0.109...	0.552...	0.537...	214/9076	2
hsa04216	Ferro...	1/31	41/8622	0.137...	0.552...	0.537...	7037	1
hsa05014	Amyot...	3/31	364/8622	0.141...	0.552...	0.537...	1345/...	3
hsa02010	ABC t...	1/31	45/8622	0.149...	0.552...	0.537...	154664	1
hsa05130	Patho...	2/31	198/8622	0.158...	0.552...	0.537...	9076/...	2
hsa00270	Cyste...	1/31	52/8622	0.171...	0.552...	0.537...	10768	1
hsa05170	Human...	2/31	212/8622	0.176...	0.552...	0.537...	9133/983	2
...	...	...	...	...	...	...	...	...

Figure 11 为图 enrichment of markers of cancer 2 cells 概览。

(对应文件为 Figure+Table/enrichment-of-markers-of-cancer-2-cells.pdf)

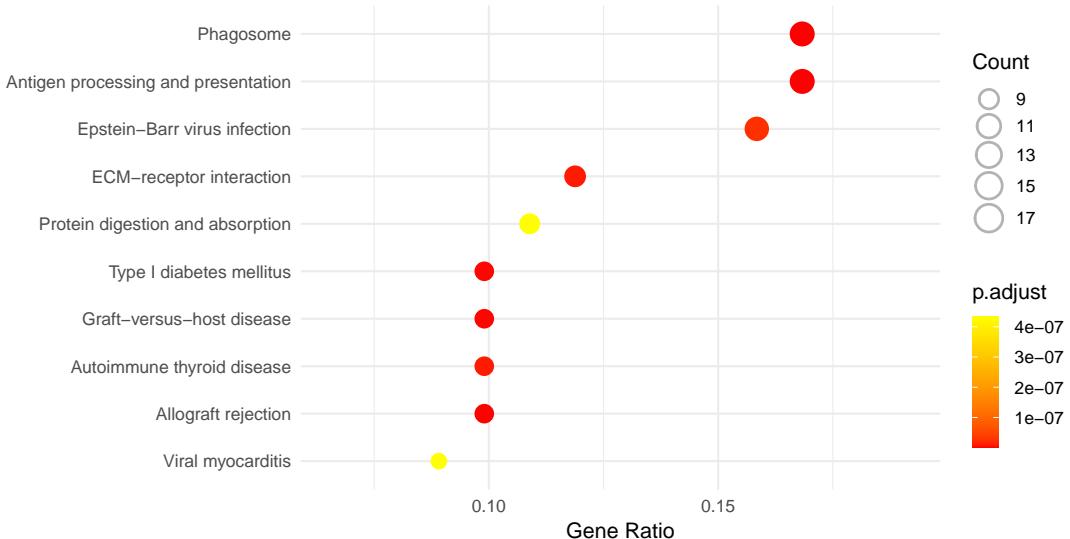


Figure 11: Enrichment of markers of cancer 2 cells

Table 3 为表格 tables of enrichment of markers of cancer 2 cells 概览。

(对应文件为 Figure+Table/tables-of-enrichment-of-markers-of-cancer-2-cells.csv)

注：表格共有 162 行 9 列，以下预览的表格可能省略部分数据；表格含有 162 个唯一 ‘ID’。

Table 3: Tables of enrichment of markers of cancer 2 cells

ID	Descr...	GeneR...	BgRatio	pvalue	p.adjust	qvalue	geneID	Count
hsa04612	Antig...	17/101	78/8622	1.279...	2.072...	1.561...	567/9...	17
hsa04145	Phago...	17/101	152/8622	1.400...	1.134...	8.550...	929/1...	17
hsa05330	Allog...	10/101	38/8622	1.113...	6.013...	4.532...	3002/...	10
hsa05332	Graft...	10/101	42/8622	3.334...	1.350...	1.018...	3002/...	10
hsa04940	Type ...	10/101	43/8622	4.303...	1.394...	1.051...	3002/...	10
hsa04512	ECM-r...	12/101	89/8622	3.862...	9.196...	6.931...	961/1...	12
hsa05320	Autoi...	10/101	53/8622	3.973...	9.196...	6.931...	3002/...	10
hsa05169	Epste...	16/101	202/8622	1.262...	2.556...	1.927...	567/9...	16
hsa05416	Viral...	9/101	60/8622	2.610...	4.340...	3.271...	3105/...	9
hsa04974	Prote...	11/101	103/8622	2.679...	4.340...	3.271...	1306/...	11
hsa05165	Human...	16/101	331/8622	1.273...	1.744...	1.315...	1277/...	16
hsa05310	Asthma	6/101	31/8622	1.292...	1.744...	1.315...	2207/...	6
hsa04640	Hemat...	9/101	99/8622	2.097...	2.455...	1.850...	929/9...	9
hsa04514	Cell ...	11/101	158/8622	2.122...	2.455...	1.850...	914/3...	11
hsa04510	Focal...	12/101	203/8622	3.977...	4.296...	3.238...	1277/...	12
...	...	...	...	...	...	...	...	...

Figure 12 为图 enrichment of markers of cancer 3 cells 概览。

(对应文件为 Figure+Table/enrichment-of-markers-of-cancer-3-cells.pdf)

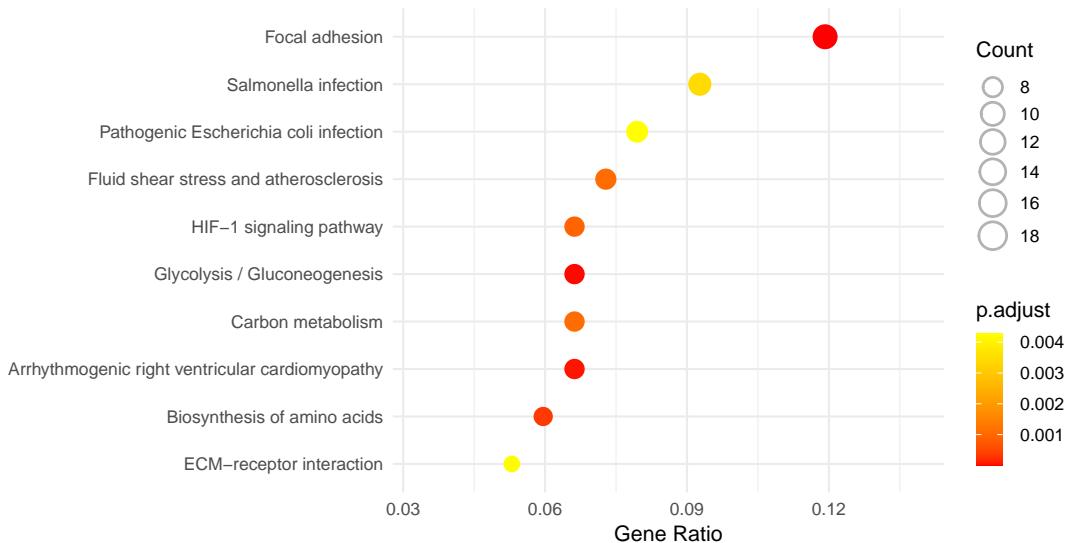


Figure 12: Enrichment of markers of cancer 3 cells

Table 4为表格 tables of enrichment of markers of cancer 3 cells 概览。

(对应文件为 [Figure+Table/tables-of-enrichment-of-markers-of-cancer-3-cells.xlsx](#))

注：表格共有 241 行 9 列，以下预览的表格可能省略部分数据；表格含有 241 个唯一 ‘ID’。

Table 4: Tables of enrichment of markers of cancer 3 cells

ID	Descr...	GeneR...	BgRatio	pvalue	p.adjust	qvalue	geneID	Count
hsa04510	Focal...	18/151	203/8622	1.346...	3.245...	2.707...	71/33...	18
hsa00010	Glyco...	10/151	67/8622	2.124...	2.559...	2.135...	226/2...	10
hsa05412	Arrhy...	10/151	77/8622	8.090...	6.499...	5.422...	71/18...	10
hsa01230	Biosy...	9/151	75/8622	5.726...	0.000...	0.000...	226/4...	9
hsa04066	HIF-1...	10/151	109/8622	1.948...	0.000...	0.000...	226/1...	10
hsa05418	Fluid...	11/151	139/8622	3.015...	0.001...	0.000...	71/44...	11
hsa01200	Carbo...	10/151	115/8622	3.114...	0.001...	0.000...	226/2...	10
hsa05132	Salmo...	14/151	249/8622	0.000...	0.003...	0.002...	10006...	14
hsa04512	ECM-r...	8/151	89/8622	0.000...	0.004...	0.003...	3339/...	8
hsa05130	Patho...	12/151	198/8622	0.000...	0.004...	0.003...	10006...	12
hsa05222	Small...	8/151	92/8622	0.000...	0.004...	0.003...	330/1...	8
hsa04210	Apopt...	9/151	136/8622	0.000...	0.012...	0.010...	71/33...	9
hsa05205	Prote...	11/151	205/8622	0.000...	0.017...	0.014...	71/85...	11
hsa05165	Human...	14/151	331/8622	0.001...	0.033...	0.027...	3133/...	14
hsa05100	Bacte...	6/151	77/8622	0.002...	0.035...	0.029...	71/10...	6
...	...	...	...	...	...	...	...	...

## 6.5 肿瘤细胞来源分析

### 6.5.1 肿瘤与上皮细胞或基底细胞差异分析

接下来的分析回到 Fig. 3 图中，取出上皮细胞或基底细胞对应的细胞类（肿瘤细胞主要分布在这两类细胞中），并且将 Fig. 10 对应的细胞亚型映射。

Figure 13为图 cancer cells in epithelial or basal cells 概览。

(对应文件为 [Figure+Table/cancer-cells-in-epithelial--or-basal-cells.pdf](#))

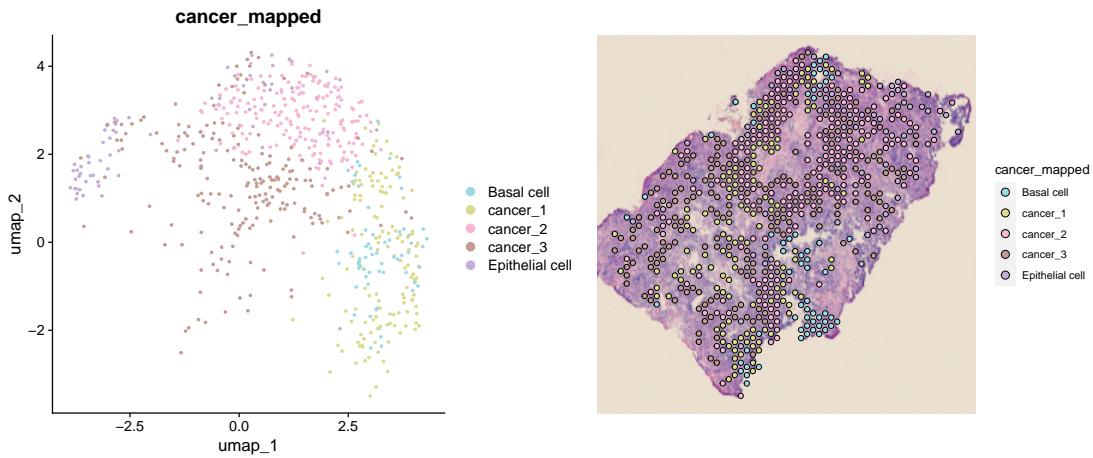


Figure 13: Cancer cells in epithelial or basal cells

### 6.5.2 肿瘤与上皮细胞或基底细胞差异基因的富集分析

以下富集与 6.4.3 相对应，“Phagosome”、“Antigen processing and presentati...” 等为差异基因的主要富集通路。

Figure 14 为图 enrichment of DEGs of Cancer 1 cells vs Basal cells 概览。

(对应文件为 Figure+Table/enrichment-of-DEGs-of-Cancer-1-cells-vs-Basal-cells.pdf)

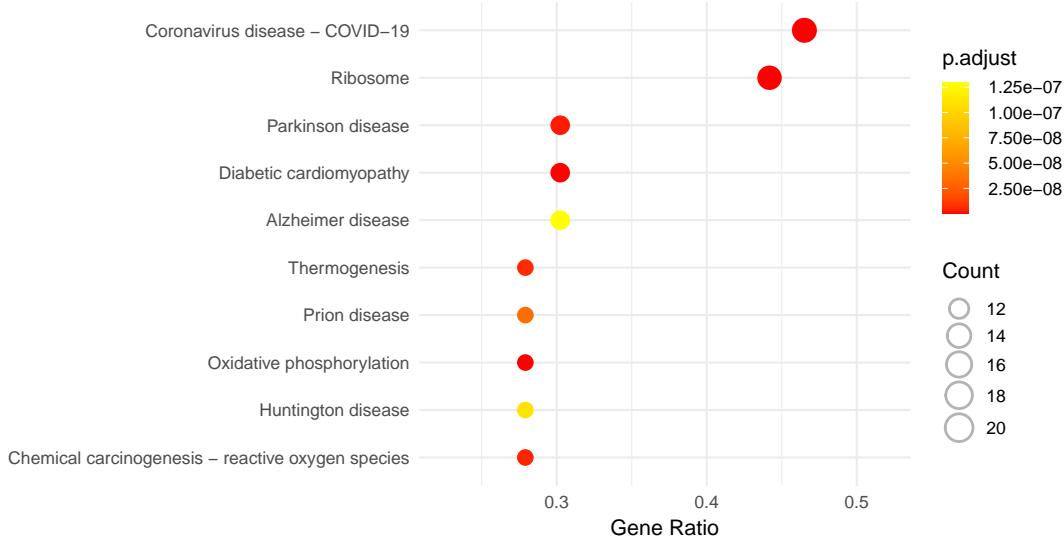


Figure 14: Enrichment of DEGs of Cancer 1 cells vs Basal cells

Figure 15 为图 enrichment of DEGs of Cancer 1 cells vs Epithelial cells 概览。

(对应文件为 Figure+Table/enrichment-of-DEGs-of-Cancer-1-cells-vs-Epithelial-cells.pdf)

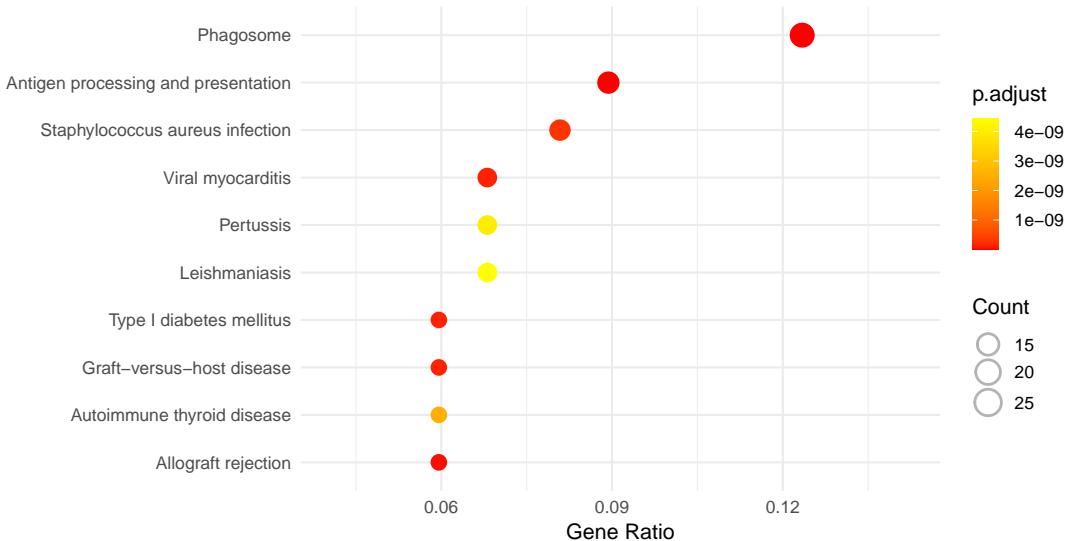


Figure 15: Enrichment of DEGs of Cancer 1 cells vs Epithelial cells

‘All enrichments of DEGs of cancer vs epithelial or basal cells’ 数据已全部提供。

(对应文件为 **all-enrichments-of-DEGs-of-cancer-vs-epithelial-or-basal-cells**)

注：文件夹 all-enrichments-of-DEGs-of-cancer-vs-epithelial-or-basal-cells 共包含 6 个文件。

1. 1\_cancer\_1\_vs\_Basal cell.pdf
2. 2\_cancer\_1\_vs\_Epithelial cell.pdf
3. 3\_cancer\_2\_vs\_Basal cell.pdf
4. 4\_cancer\_2\_vs\_Epithelial cell.pdf
5. 5\_cancer\_3\_vs\_Basal cell.pdf
6. ...

‘Tables of all enrichments of DEGs of cancer vs epithelial or basal cells’ 数据已全部提供。

(对应文件为 **tables-of-all-enrichments-of-DEGs-of-cancer-vs-epithelial-or-basal-cells**)

注：文件夹 tables-of-all-enrichments-of-DEGs-of-cancer-vs-epithelial-or-basal-cells 共包含 6 个文件。

1. 1\_cancer\_1\_vs\_Basal cell.csv
2. 2\_cancer\_1\_vs\_Epithelial cell.csv
3. 3\_cancer\_2\_vs\_Basal cell.csv
4. 4\_cancer\_2\_vs\_Epithelial cell.csv
5. 5\_cancer\_3\_vs\_Basal cell.csv
6. ...

Table 5 为表格 tables of all DEGs of cancer vs epithelial or basal cells 概览。

(对应文件为 **Figure+Table/tables-of-all-DEGs-of-cancer-vs-epithelial-or-basal-cells.csv**)

注：表格共有 1502 行 7 列，以下预览的表格可能省略部分数据；表格含有 6 个唯一‘contrast’。

Table 5: Tables of all DEGs of cancer vs epithelial or basal cells

contrast	p_val	avg_l...	pct.1	pct.2	p_val...	gene
cance...	4.341...	0.369...	1	1	8.506...	RPL9
cance...	1.782...	0.404...	1	1	3.492...	RPL7
cance...	2.722...	-0.97...	1	1	5.335...	MT-ATP6
cance...	5.164...	-1.17...	1	1	1.011...	MT-ND2
cance...	5.763...	-0.84...	1	1	1.129...	MT-CO3
cance...	7.030...	-0.98...	1	1	1.377...	MT-ND1
cance...	7.923...	-0.85...	1	1	1.552...	MT-ND3
cance...	6.299...	-0.71...	1	1	1.234...	MT-CO2
cance...	6.455...	-0.89...	1	1	1.264...	MT-ND4
cance...	1.075...	-0.73...	1	1	2.106...	MT-CO1
cance...	2.747...	-0.42...	1	1	5.383...	HLA-B
cance...	3.005...	0.327...	1	1	5.888...	RPS15A
cance...	5.993...	0.258...	1	1	1.174...	RPL37A
cance...	7.982...	0.289...	1	1	1.564...	RPL17
cance...	2.149...	-0.78...	1	1	4.211...	MT-CYB
...	...	...	...	...	...	...

## 6.6 细胞通讯

以下分析使用的为 Tab. 1 中的基因。

### 6.6.1 所有细胞之间的通讯

将肿瘤细胞亚型映射到 Fig. 3 中，得到 Fig. 16。

Figure 16为图 cancer subtypes in all cells 概览。

(对应文件为 Figure+Table/cancer-subtypes-in-all-cells.pdf)

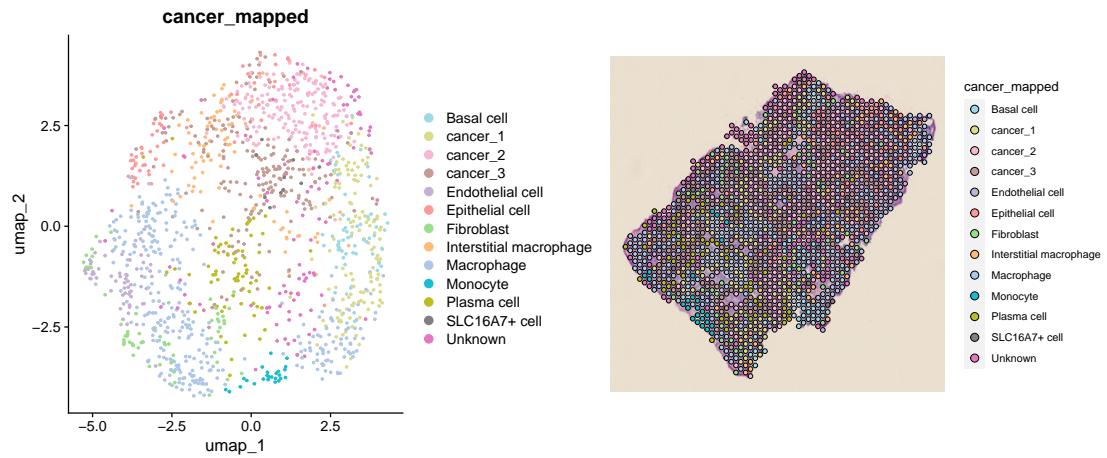


Figure 16: Cancer subtypes in all cells

以 cellchat 计算所有这些细胞之间的通讯关系<sup>3</sup>。

Figure 17为图 overview of cells communication 概览。

(对应文件为 Figure+Table/overview-of-cells-communication.pdf)

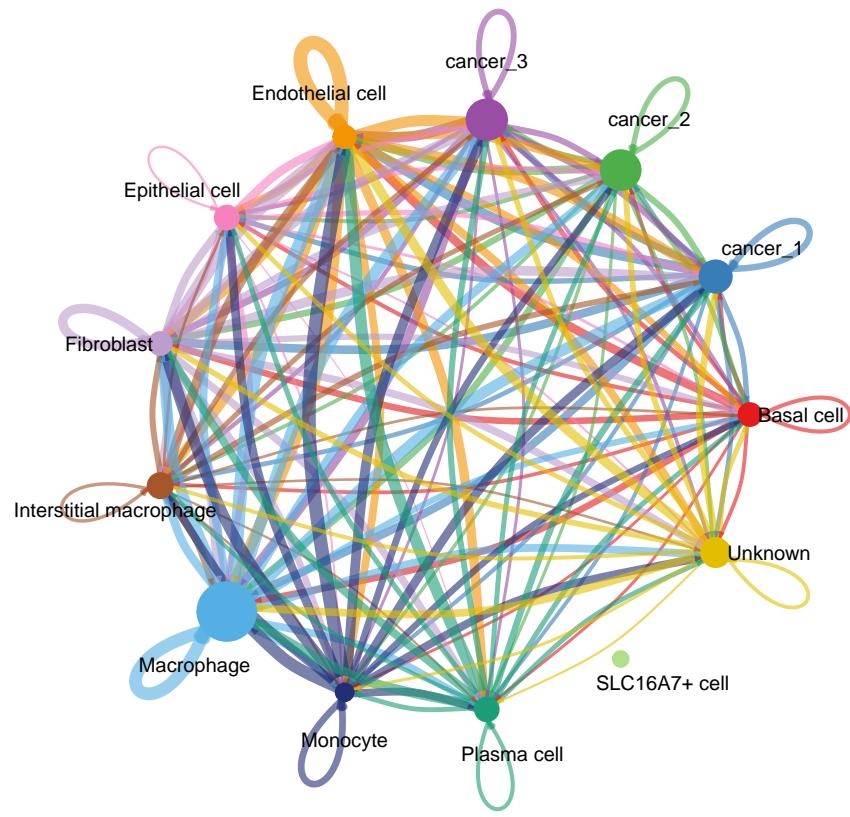


Figure 17: Overview of cells communication

Figure 18为图 all cells communication significance 概览。

(对应文件为 [Figure+Table/all-cells-communication-significance.pdf](#))



Figure 18: All cells communication significance

Figure 19为图 all cells communication roles 概览。

(对应文件为 Figure+Table/all-cells-communication-roles.pdf)

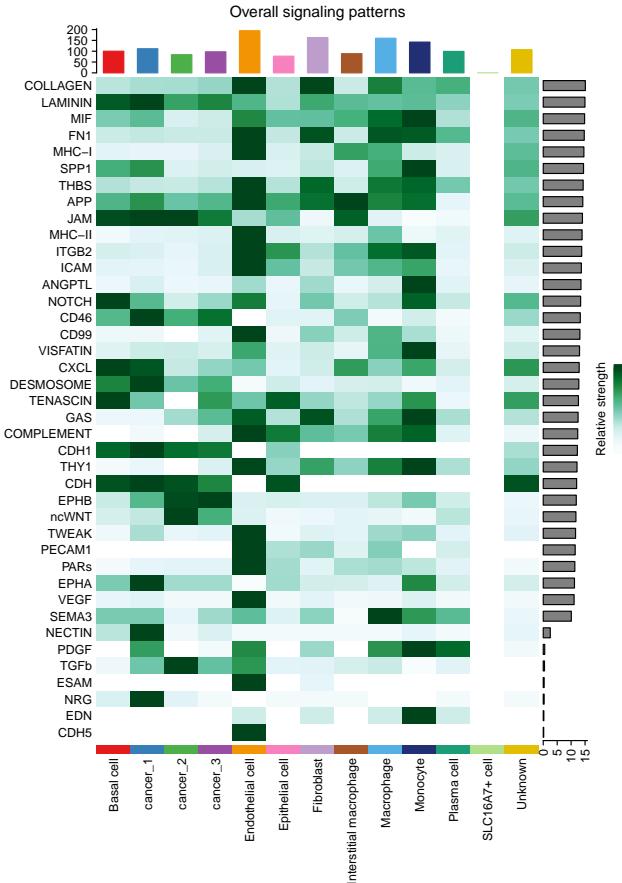


Figure 19: All cells communication roles

### 6.6.2 巨噬细胞和肿瘤细胞之间的互作

以下，我们主要聚焦于巨噬细胞和癌细胞之间的通讯关系。

Table 6为表格 table of communication between macrophage and cancer cells 概览。

(对应文件为 Figure+Table/table-of-communication-between-macrophage-and-cancer-cells.csv)

注：表格共有 409 行 11 列，以下预览的表格可能省略部分数据；表格含有 4 个唯一‘source’。

Table 6: Table of communication between macrophage and cancer cells

source	target	ligand	receptor	prob	pval	inter.....7	inter.....8	pathw...	annot...	evidence
Macro...	cancer_2	TGFB1	ACVR1...	0.000...	0.01	TGFB1...	TGFB1...	TGFB	Secre...	PMID:...
Macro...	cancer_3	TGFB1	ACVR1...	0.000...	0.03	TGFB1...	TGFB1...	TGFB	Secre...	PMID:...
cancer_2	Macro...	TGFB1	ACVR1...	0.001...	0	TGFB1...	TGFB1...	TGFB	Secre...	PMID:...
cancer_3	Macro...	TGFB1	ACVR1...	0.000...	0	TGFB1...	TGFB1...	TGFB	Secre...	PMID:...
Macro...	cancer_1	TGFB1	ACVR1...	0.000...	0.04	TGFB1...	TGFB1...	TGFB	Secre...	PMID:...
Macro...	cancer_2	TGFB1	ACVR1...	0.000...	0	TGFB1...	TGFB1...	TGFB	Secre...	PMID:...

source	target	ligand	receptor	prob	pval	inter.....7	inter.....8	pathw...	annot...	evidence	...
Macro...	cancer_1	WNT5A	FZD10	0.001...	0	WNT5A...	WNT5A...	ncWNT	Secre...	KEGG:...	...
Macro...	cancer_2	WNT5A	FZD10	0.001...	0.02	WNT5A...	WNT5A...	ncWNT	Secre...	KEGG:...	...
Macro...	cancer_3	WNT5A	FZD10	0.001...	0.02	WNT5A...	WNT5A...	ncWNT	Secre...	KEGG:...	...
Macro...	cancer_1	WNT5A	FZD6	0.011...	0.04	WNT5A...	WNT5A...	ncWNT	Secre...	KEGG:...	...
Macro...	cancer_2	WNT5A	FZD6	0.011...	0.04	WNT5A...	WNT5A...	ncWNT	Secre...	KEGG:...	...
Macro...	cancer_2	WNT5A	MCAM	0.001...	0.04	WNT5A...	WNT5A...	ncWNT	Secre...	PMID:...	...
cancer_2	Macro...	WNT5A	MCAM	0.005...	0	WNT5A...	WNT5A...	ncWNT	Secre...	PMID:...	...
cancer_3	Macro...	WNT5A	MCAM	0.004...	0.04	WNT5A...	WNT5A...	ncWNT	Secre...	PMID:...	...
cancer_1	Macro...	PDGFB	PDGFRA	0.000...	0	PDGFB...	PDGFB...	PDGF	Secre...	PMID:...	...
...	...	...	...	...	...	...	...	...	...	...	...

Figure 20为图 visualization of communication between macrophage and cancer cells 概览。

(对应文件为 [Figure+Table/visualization-of-communication-between-macrophage-and-cancer-cells.pdf](#))

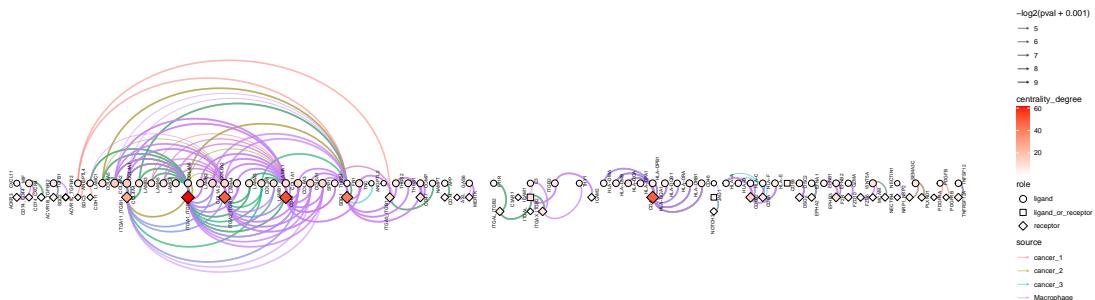


Figure 20: Visualization of communication between macrophage and cancer cells

根据 Fig. 20, 可以关注到互作网络图中中心度 (centrality degree) 较高的 ITGA 相关受体或配体。

### 6.6.3 ITGA 相关配体受体富集分析

根据 Fig. 20, 以下将 ITGA 相关基因做富集分析。

'Enrichment of ITGA related genes' 数据已全部提供。

(对应文件为 [enrichment-of-ITGA-related-genes](#))

注：文件夹 enrichment-of-ITGA-related-genes 共包含 1 个文件。

1. 1\_ids.pdf

Fig. ?? 首要富集到 PI3K-AKT 通路。还可以发现，“Small cell lung cancer” 也是显著富集结果之一。

Table 7为表格 tables of enrichment of ITGA related genes 概览。

(对应文件为 [Figure+Table/tables-of-enrichment-of-ITGA-related-genes.csv](#))

注：表格共有 65 行 9 列，以下预览的表格可能省略部分数据；表格含有 65 个唯一 ‘ID’。

Table 7: Tables of enrichment of ITGA related genes

ID	Descr...	GeneR...	BgRatio	pvalue	p.adjust	qvalue	geneID	Count
hsa04512	ECM-r...	27/36	89/8622	2.645...	1.719...	8.633...	1277/...	27
hsa04510	Focal...	27/36	203/8622	1.474...	4.791...	2.405...	1277/...	27
hsa05165	Human...	27/36	331/8622	1.433...	3.106...	1.559...	1277/...	27
hsa04151	PI3K-...	27/36	359/8622	1.360...	2.211...	1.110...	1277/...	27
hsa05146	Amoeb...	18/36	102/8622	3.269...	4.250...	2.133...	1277/...	18
hsa05222	Small...	17/36	92/8622	4.653...	5.041...	2.530...	1282/...	17
hsa04974	Prote...	11/36	103/8622	1.922...	1.785...	8.962...	1277/...	11
hsa05145	Toxop...	10/36	111/8622	1.592...	1.294...	6.497...	3688/...	10
hsa04933	AGE-R...	9/36	100/8622	1.914...	1.382...	6.942...	1277/...	9
hsa04810	Regul...	9/36	229/8622	2.833...	1.841...	9.245...	2335/...	9
hsa05412	Arrhy...	6/36	77/8622	6.555...	3.873...	1.944...	3672/...	6
hsa04926	Relax...	7/36	129/8622	8.294...	4.492...	2.255...	1277/...	7
hsa05410	Hyper...	6/36	90/8622	1.655...	8.278...	4.156...	3672/...	6
hsa05414	Dilat...	6/36	96/8622	2.421...	1.124...	5.643...	3672/...	6
hsa04670	Leuko...	6/36	115/8622	6.942...	3.008...	1.510...	50848...	6
...	...	...	...	...	...	...	...	...

#### 6.6.4 首要富集的 PI3K 通路

以下结果可以和 6.4.3 和 6.5.2 相对应。

Figure 21 为图 view of enriched genes in PI3K pathway 概览。

(对应文件为 Figure+Table/hsa04151.pathview.png)

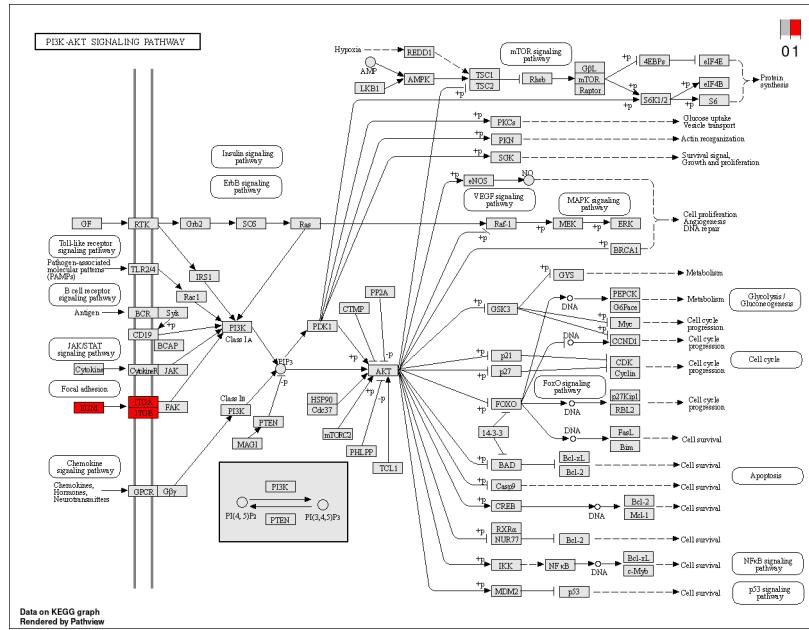


Figure 21: View of enriched genes in PI3K pathway

### 6.6.5 PI3K 通路和 ITGA 相关受体配体的交集

**ITGA\_with\_PI3K :**

COL1A1, COL1A2, COL2A1, COL4A1, COL4A2, COL4A4, COL4A5, COL4A6, COL6A1, COL6A2, COL6A3, FN1, ITGA1, ITGA11, ITGA2, ITGA5, ITGB1, LAMA1, LAMA3, LAMA4, LAMA5, LAMB1, LAMB2, LAMB3, LAMC1, LAMC2, SPP1

### 6.6.6 通讯基因的表达在肿瘤细胞中的拟时变化

以下分析表现了 ITGA 和 PI3K 通路相关的 27 个基因在肿瘤细胞亚型之间的转化（拟时过程）过程中的表达变化。

Figure 22 为图 group 1 communication related genes in pseudotime 概览。

(对应文件为 Figure+Table/group-1-communication-related-genes-in-pseudotime.pdf)

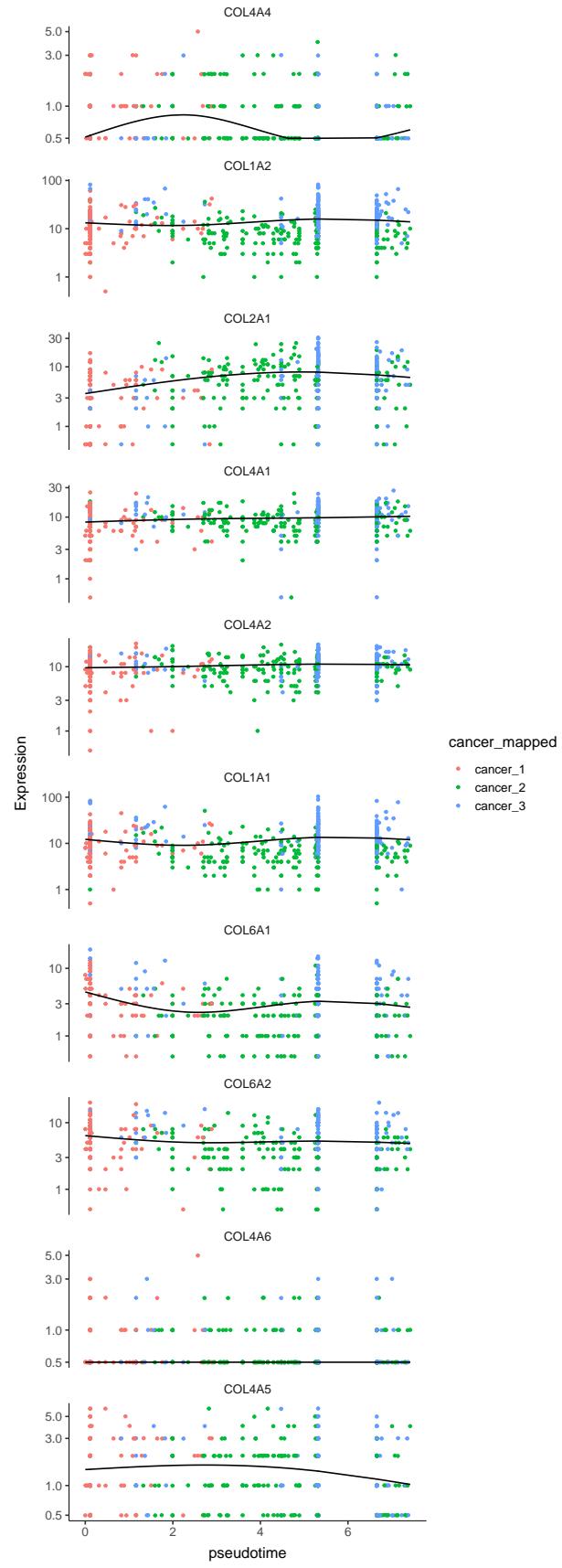


Figure 22: Group 1 communication related genes in pseudotime

Figure 23为图 group 2 communication related genes in pseudotime 概览。

(对应文件为 **Figure+Table/group-2-communication-related-genes-in-pseudotime.pdf**)

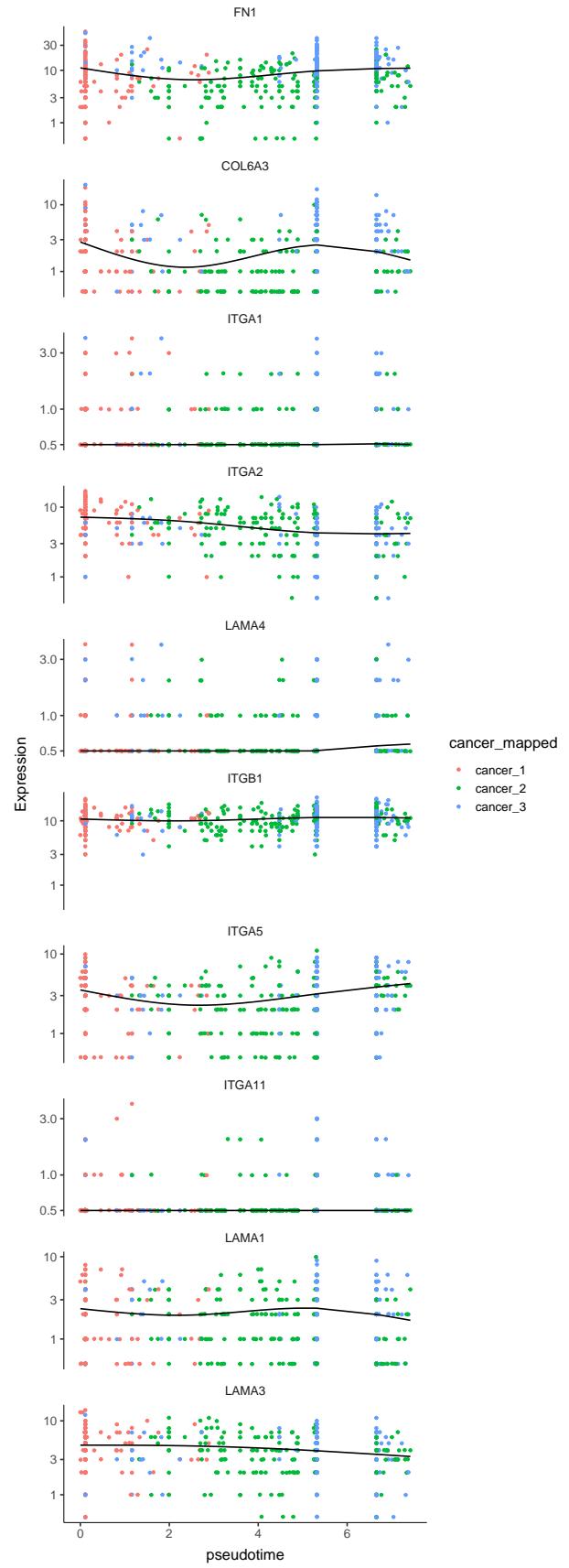


Figure 23: Group 2 communication related genes in pseudotime

Figure 24为图 group 3 communication related genes in pseudotime 概览。

(对应文件为 **Figure+Table/group-3-communication-related-genes-in-pseudotime.pdf**)

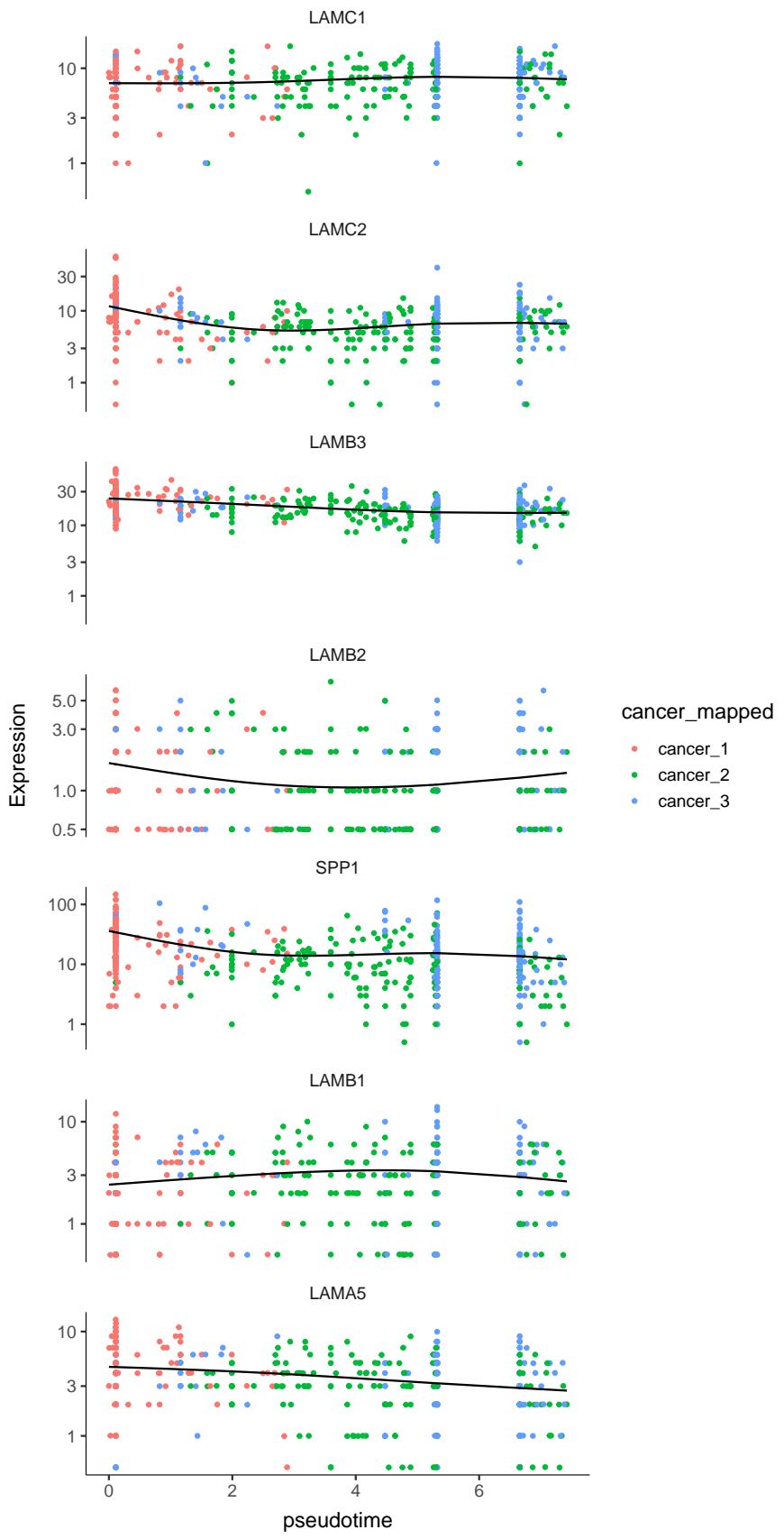


Figure 24: Group 3 communication related genes in pseudotime

## 7 附：分析流程（癌旁组织切片）

### 7.1 Clustering and annotation

Figure 25为图 extra QC 概览。

(对应文件为 Figure+Table/extr-QC.pdf)

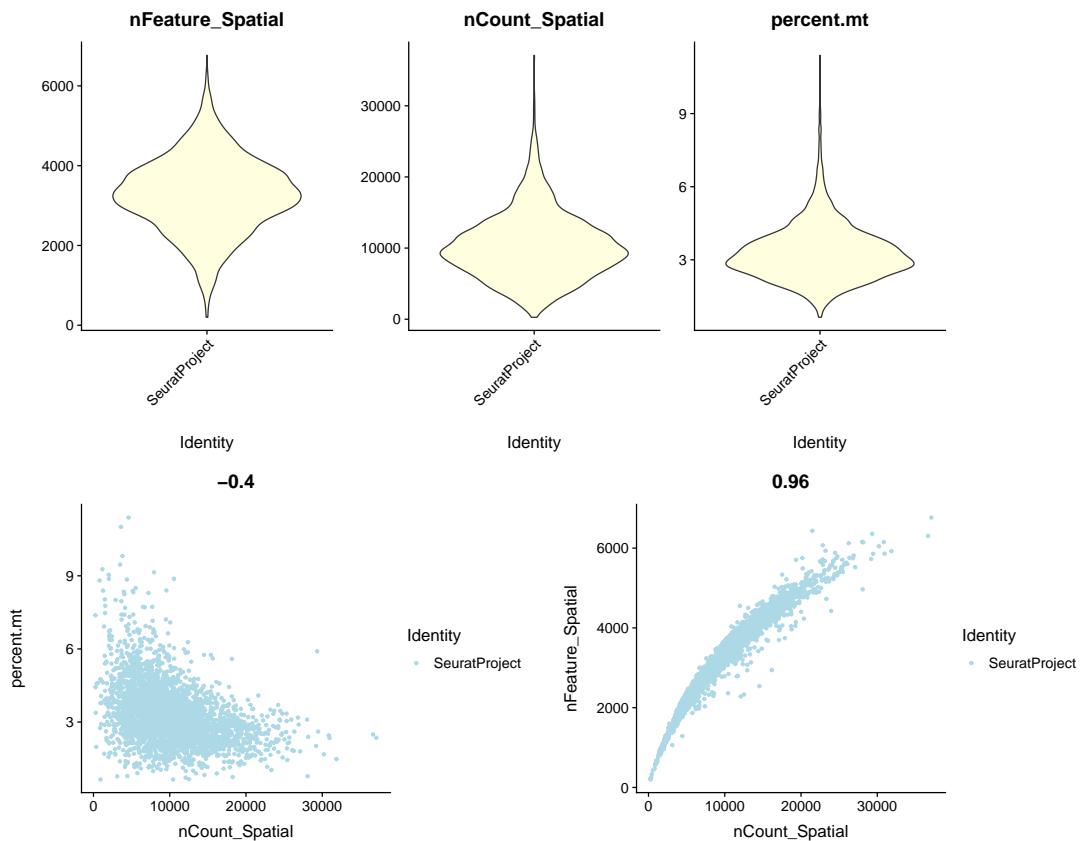


Figure 25: Extra QC

Figure 26为图 extra SCSA annotation 概览。

(对应文件为 Figure+Table/extr-SCSA-annotation.pdf)

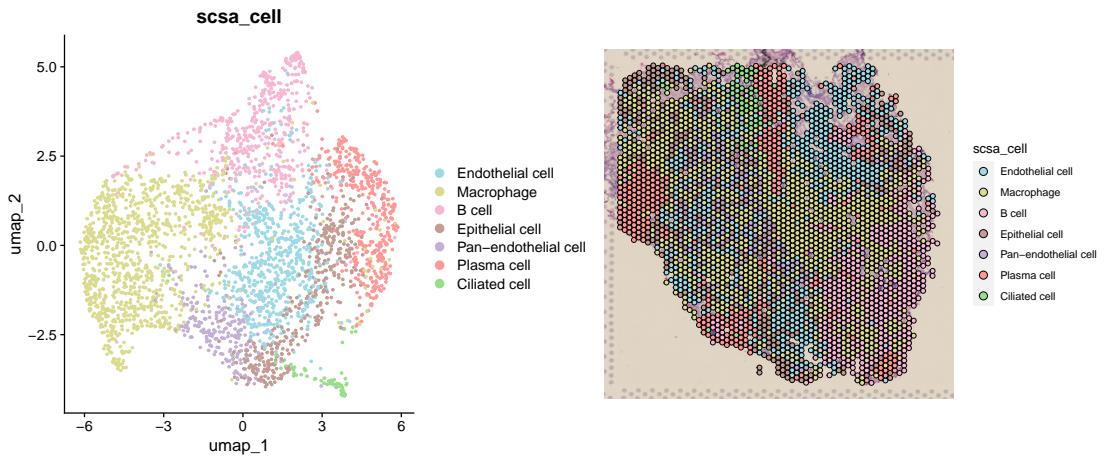


Figure 26: Extra SCSA annotation

## 7.2 Copykat prediction

可以观察到，copyKAT 的细胞类型预测，癌旁组织 Fig. 27 的聚类不及癌组织切片的 Fig. 4 明显。

Figure 27为图 extra copyKAT prediction 概览。

(对应文件为 [Figure+Table/copykat\\_para\\_cancer.png](#))

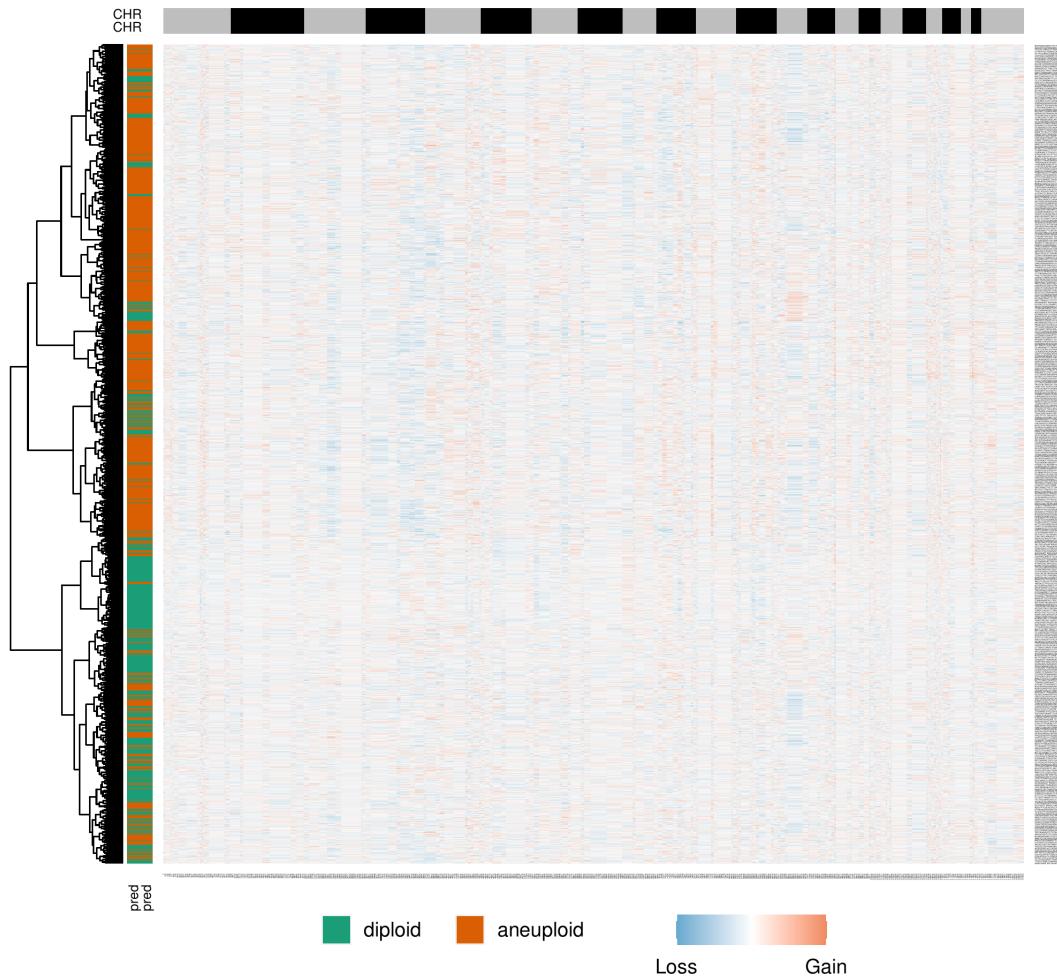


Figure 27: Extra copyKAT prediction

## Reference

1. Gao, R. *et al.* Delineating copy number and clonal substructure in human tumors from single-cell transcriptomes. *Nature Biotechnology* **39**, 599–608 (2021).
2. Gordon, D. J., Resio, B. & Pellman, D. Causes and consequences of aneuploidy in cancer. *Nature Reviews Genetics* **13**, 189–203 (2012).
3. Jin, S. *et al.* Inference and analysis of cell-cell communication using cellchat. *Nature Communications* **12**, (2021).