Extracting Intercellular Signaling Network of Cancer Tissues using Ligand-Receptor Expression Patterns from Whole-tumor and Single-cell Transcriptomes

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Supplementary

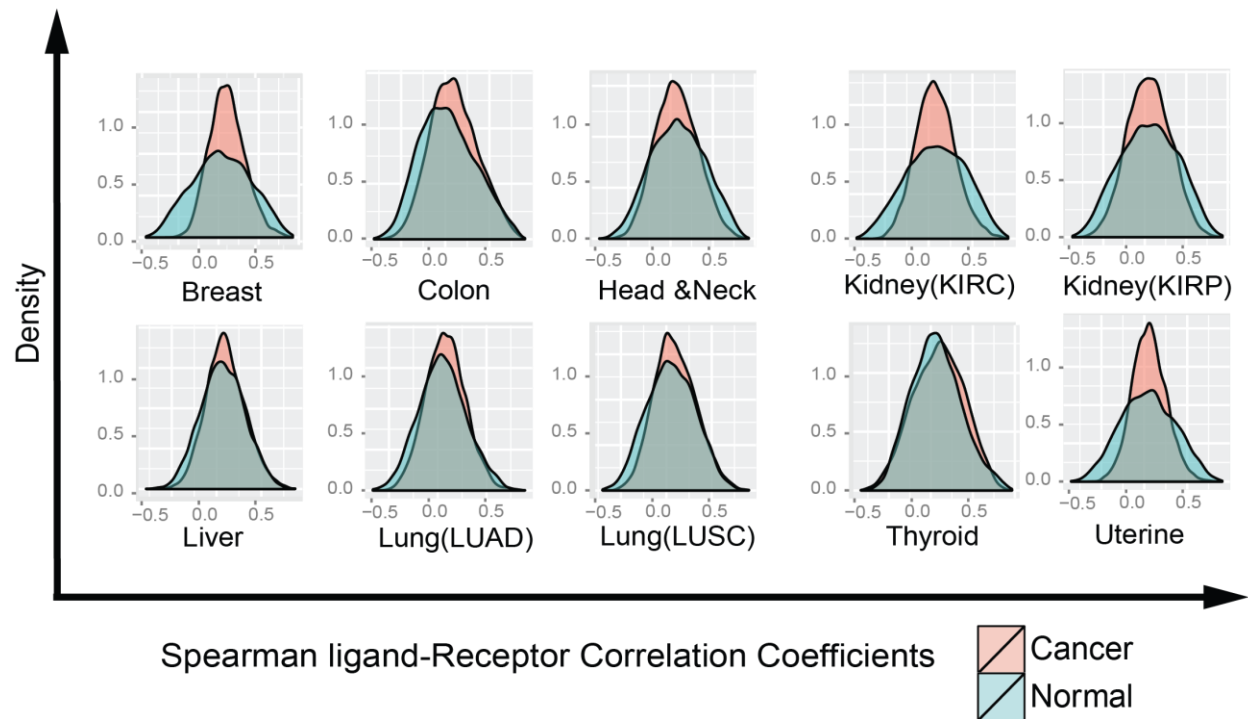Distribution of correlation coefficients of the random ligand-receptor pairs

Figure S1. The distribution of correlation coefficients of the random ligand-receptor pairs for the samples of ten cancer types and their corresponding normal tissues. The random receptor/ ligand pairs were less correlated than the specific pairs at the population level for ten cancer types (see Fig. 4A).

No.	ligand	receptor	Shared cancer types number
1	COL11A1	ITGA2	5
2	COL7A1	ITGA2	5
3	MDK	GPC2	5
4	MMP1	ITGA2	5
5	COL1A1	ITGA11	4
6	COL1A1	ITGA2	4
7	CXCL5	CXCR2P1	4
8	FN1	PLAUR	4
9	JAG2	NOTCH3	4
10	MMP9	EPHB2	4
11	COL1A1	CD44	3
12	COL1A1	TMPRSS6	3
13	COL4A1	ITGA2	3
14	EFNA3	EPHA1	3
15	EFNA4	EPHA1	3

Table S1. The top 15 ligand-receptor pairs both are significantly up-regulated in caner tissues (LIMMA, two folds change, P-value=0.05)

No.	Ligand	Receptor	Ligand Change	Receptor Change	Shared cancer types number
1	CALM1	HMMR	0	1	9
2	SPP1	ITGAV	1	0	9
3	SPP1	ITGB1	1	0	9
4	TNFSF18	TNFRSF18	0	1	9
5	COL11A1	ITGB1	1	0	8
6	CTHRC1	FZD6	1	0	8
7	EFNA3	EPHA5	1	0	8
8	HSPA1A	GRIN2D	0	1	8
9	SPP1	ITGA5	1	0	8
10	ADAM12	ITGB1	1	0	7
11	ASIP	MC1R	0	1	7
12	COL11A1	DDR1	1	0	7
13	COL1A1	ITGAV	1	0	7
14	COL1A1	ITGB1	1	0	7
15	COL5A1	ITGB1	1	0	7

Table S2. The top 15 ligand-receptor pairs in which only one of them is significantly up-regulated in caner tissues (LIMMA, 1 means the gene has two folds up change with P-value =0.05, 0 means the gene unchanged)

No.	ligand	receptor	Shared cancer types
1	ANGPTL1	TEK	8
2	CCL21	CCBP2	7
3	ANGPT1	TEK	6
4	CCL14	CCBP2	6
5	L1CAM	CNTN1	6
6	NCAM1	GFRA1	6
7	ANGPT1	TIE1	5
8	APOD	LEPR	5
9	BST1	CAV1	5
10	CD34	SELP	5
11	CTGF	ERBB4	5
12	DCN	ERBB4	5
13	FGF7	FGFR2	5
14	L1CAM	FGFR2	5
15	LPL	GPIHBP1	5

Table S3. The top 15 ligand-receptor pairs both are significantly down-regulated in caner tissues (LIMMA, two folds change, P-value =0.05)

No.	Ligand	Receptor	Ligand Change	Receptor Change	Shared cancer types number
1	CLCF1	CNTFR	0	-1	9
2	CNTF	LIFR	0	-1	9
3	CORT	SSTR1	0	-1	9
4	CXCL12	CXCR4	-1	0	9
5	NPY	NPY1R	0	-1	9
6	RELN	ITGB1	-1	0	9
7	RSPO3	FZD8	-1	0	9
8	TGFB3	TGFBR3	0	-1	9
10	ANGPT4	TEK	0	-1	8
11	CCL21	CXCR3	-1	0	8
14	CXCL12	CXCR3	-1	0	8
16	GH1	GHR	0	-1	8
17	GH2	GHR	0	-1	8
18	HK1	TACR1	0	-1	8
20	IGF1	IGF1R	-1	0	8
21	LAMA2	ITGB1	-1	0	8
22	NCAM1	PTPRA	-1	0	8
23	PTN	CDH10	-1	0	8
24	UBA52	AGTR1	0	-1	8
27	CALM1	VIPR1	0	-1	7
28	CALM3	PDE1A	0	-1	7
29	CCL14	CCR1	-1	0	7
30	CCL14	CCR3	-1	0	7
31	CCL14	CCR5	-1	0	7
32	CCL25	CCBP2	0	-1	7
33	CCL27	CCBP2	0	-1	7
34	CCL3L3	CCBP2	0	-1	7
35	CCL7	CCBP2	0	-1	7
36	CNTF	IL6ST	0	-1	7

38	COL4A4	ITGAV	-1	0	7
39	COL4A4	ITGB1	-1	0	7
40	COL4A6	CD47	-1	0	7
41	COL4A6	ITGAV	-1	0	7
42	COL4A6	ITGB1	-1	0	7
45	CXCL12	CCR4	-1	0	7

Table S4. The top 45 ligand-receptor pairs in which only one of them is significantly down-regulated in caner tissues (LIMMA, -1 means the gene has two folds down change with P-value =0.05, 0 means the gene unchanged)

No.	Code	Full Name	Distance	P-value
1	BRCA	Breast Carcinoma	0.18	0
2	COAD	Colon adenocarcinoma	0.17	0
3	HNSC	Head & Neck squamous cell carcinoma	0.10	1.24E-08
4	KIRC	Kidney renal clear cell carcinoma	0.14	3.77E-15
5	KIRP	Kidney renal papillary cell carcinoma	0.14	1.72E-14
6	LIHC	Liver hepatocellular carcinoma	0.08	2.65E-05
7	LUAD	Lung adenocarcinoma	0.09	1.94E-06
8	LUSC	Lung squamous cell carcinoma	0.11	2.11E-09
9	THCA	Thyroid carcinoma	0.03	0.24
10	UCEC	Uterine Corpus Endometrial Carcinoma	0.16	0

Table S5. *Kolmogrov-Sminov* test of *Spearman* correlation distribution between normal and caner tissues. The distances and P-values of *Spearman* correlation coefficients distribution between 10 normal and cancer tissues from TCGA were calculated from *Kolmogrov-Sminov* tests. The P-value of 0.01 is set as the cut-off for the significant change of two distributions.

No.	ligand	receptor	Shared cancer types
1	CCL2	CCR5	5
2	C1QA	CR1	4
3	CCL3	CCR5	4
4	ICAM1	ITGAM	4
5	IL15	IL2RB	4
6	PLAU	ITGA5	4
7	VCAM1	ITGB7	4
8	B2M	LILRB1	3
9	CCL2	CCR2	3
10	CCL4	CCR5	3
11	CCL8	CCR5	3
12	CSF1	CSF1R	3
13	CXCL12	CD4	3
14	FN1	ITGAV	3
15	GNAI2	FPR1	3

Table S6. The top 15 ligand-receptor pairs change most from uncorrelated in normal (the Spearman correlations are between -0.25 and 0.25) to correlated (*Spearman* correlations are higher than 0.5) in caner tissues

No.	ligand	receptor	Shared cancer types
1	CGN	TGFBR2	5
2	CHAD	ITGB1	5
3	SEMA6D	TYROBP	5
4	IHH	BOC	4
5	VEGFA	EPHB2	4
6	COL4A1	CD47	3
7	FGF2	FGFR4	3
8	FGF2	SDC1	3
9	GNAI2	IGF1R	3
10	GNAS	ADCY7	3
11	INHA	ACVR1	3
12	LAMA1	NT5E	3
13	PIGF	FLT1	3
14	PSAP	CELSR1	3
15	RTN4	TNFRSF19	3

Table S7. The ligand-receptor pairs change most from negatively correlated in normal (Spearman correlations are lower than -0.5) to uncorrelated (Spearman correlations are between -0.25 and 0.25) in caner tissues

No.	ligand	receptor	Shared cancer types
1	SEMA4G	PLXNB2	5
2	EFNB3	RHBDL2	4
3	FGF2	NRP1	4
4	LIPH	LPAR2	4
5	TGFB3	TGFBR2	4
6	ANGPT1	ITGB1	3
7	APOE	CHRNA4	3
8	BMP6	BMPR2	3
9	CDH1	ERBB3	3
10	CDH1	PTPRF	3
11	COL5A3	SDC3	3
12	EFNA3	EPHA1	3
13	EFNA3	EPHB6	3
14	F8	LRP1	3
15	FGF7	NRP1	3

Table S8. The ligand-receptor pairs change most from positively correlated in normal (Spearman correlations are higher than 0.5) to uncorrelated (Spearman correlations are between -0.25 and 0.25) in caner tissues