Differential cell-cell communication between SCZ and NTC using cellchat V2

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Method

We are using differential cell-cell communication analysis (implemented via cell chat V2) to investigate some cell-cell communication pattern between neurons and vasculatures implicated in .

Specifically, we have subset the data to spots that are either NeuN+ or claudin+. There exists double positive spots, i.e. spots that are both NeuN+ and Claudin+. These spots are removed from the analysis. Please refer to `EDA.R` for details on what spots being included or not.

> Note: The code generating this report doesn't including running cell chat V2 pipeline. Please refer to `cell_cell_comm_prep.R` to run the cell chat pipeline first.

Boyi's TL;DR

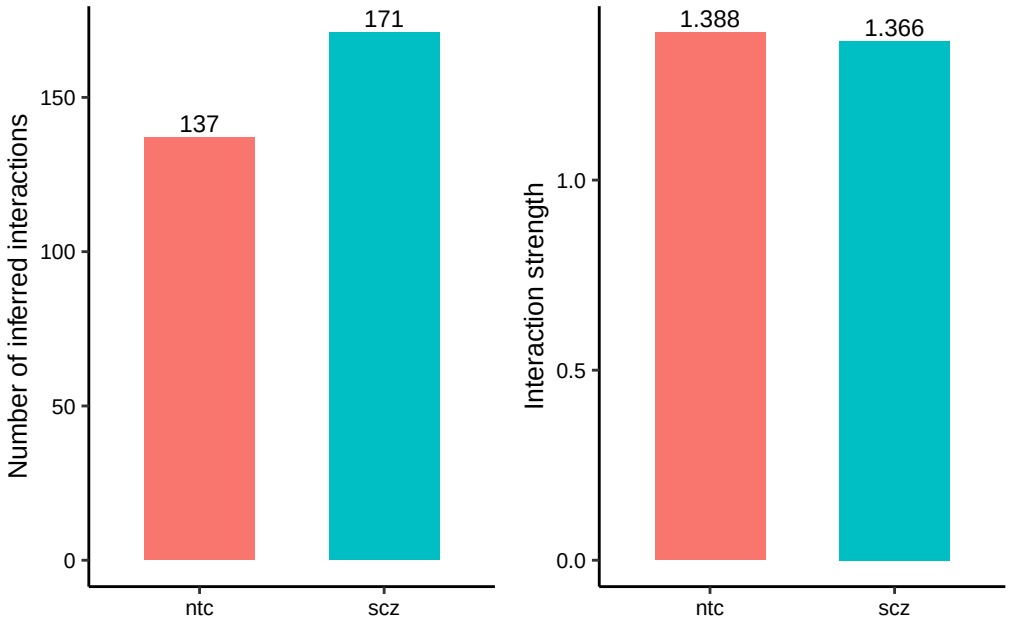
- There are fewer communication pattern among NTC samples compared to SCZ samples
- Most differential communication happens in Neuron-Neuron communication. Specifically, there are more Neuron-Neuron communication among SCZ samples.
- Some important pathways seems to be: `Glutamate` and `PTN` enriched in NTC samples, and `PSAP` and `GABA-A` and `GABA-B` enriched in SCZ samples.

Results

Number of interaction and interaction strength

Overall levelfor SCZ and NTC respectively

- **# of interaction There's fewer neuron-to-vasculature interaction among NTC group compared to SCZ group.**
- The strength between the two groups seems to be equaly strong.



Communication pattern between Neun+ and Claudin+ spots

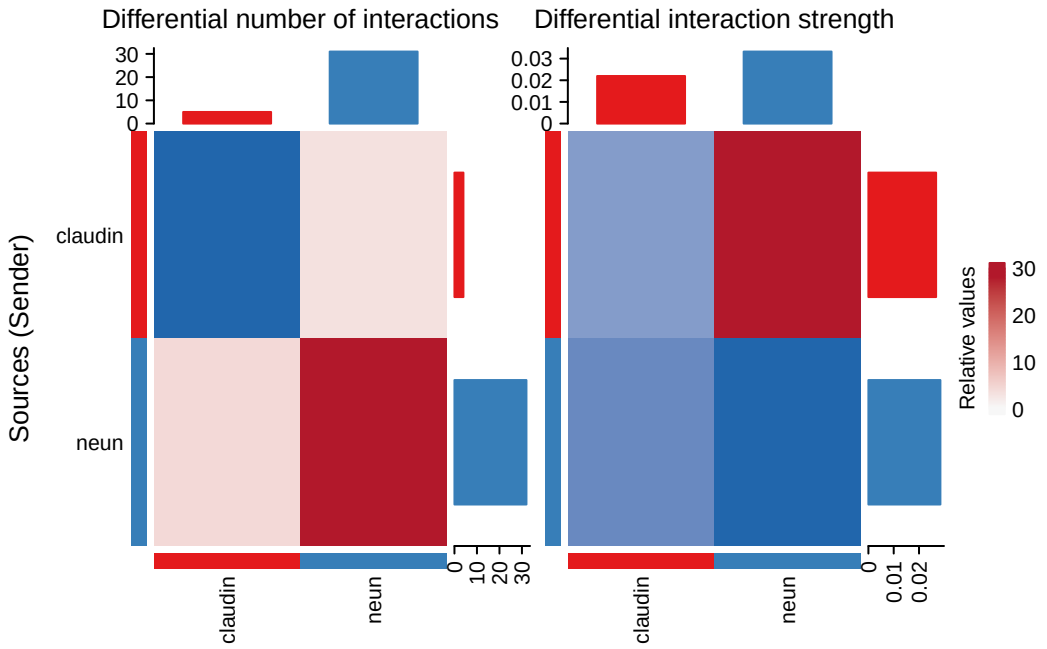
- **Increased (red) signaling in SCZ group, (in reference to NTC group) - many LR pair is enriched in neuron-neuron communication**
- Decreased (blue) signaling in SCZ grup, (in reference to NTC group) - there's limited number of differential communication among claudin-claudin.

  NOTE: The differential number of interactions or interaction strength in the cell-cell communication network between two datasets can be visualized using circle plot, where red (or blue) colored edges represent increased (or decreased) signaling in the second dataset compared to the first one. In our data anlysis, the first data set is **NTC** and the second data set is **SCZ**.

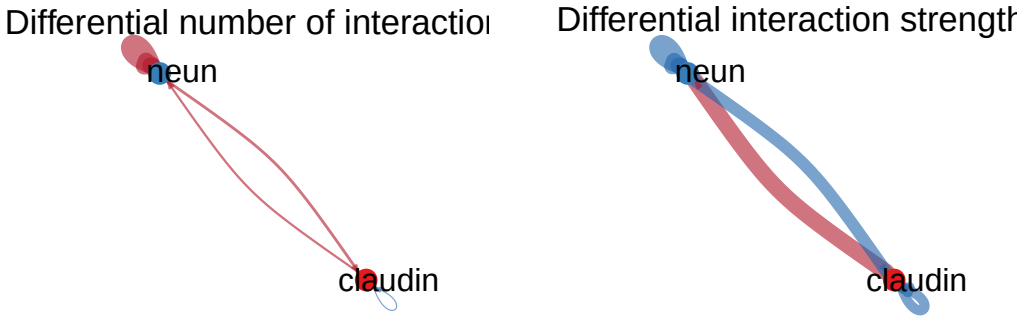
```
Do heatmap based on a merged object
```

```
Do heatmap based on a merged object
```

```
Warning: Heatmap/annotation names are duplicated: Relative values
```



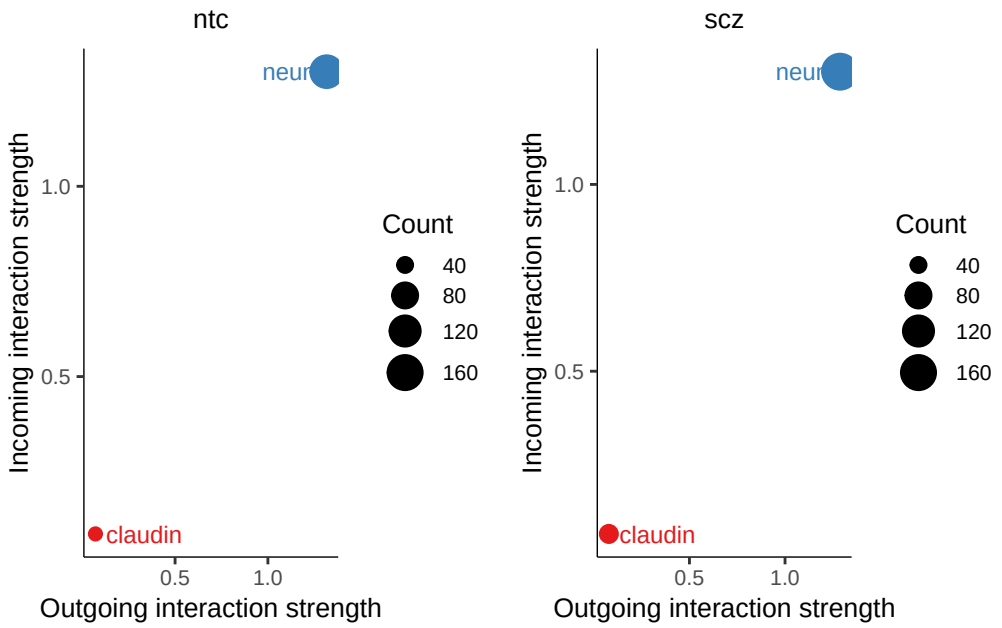
Similarly, we can visualize in a chord diagram.



Compare major sources and targets - Not very informative

This visualization is not that informative.

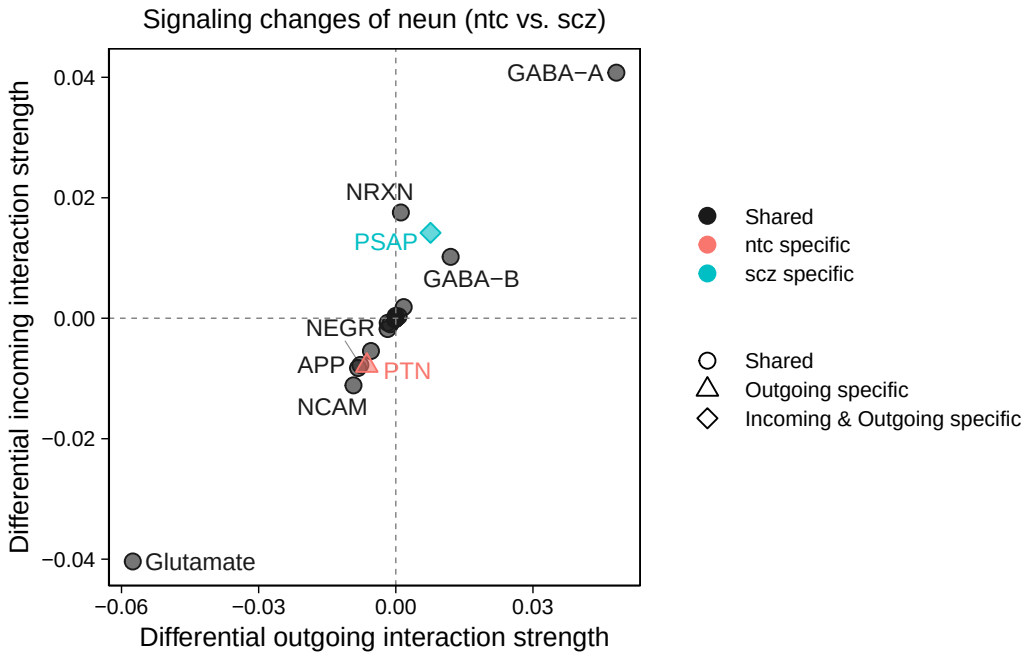
```
Signaling role analysis on the aggregated cell-cell communication network from all signaling
Signaling role analysis on the aggregated cell-cell communication network from all signaling
```



differential signaling Pathway in Neun+ spots

```
Visualizing differential outgoing and incoming signaling changes from ntc to scz
```

```
The following `from` values were not present in `x`: -1
```

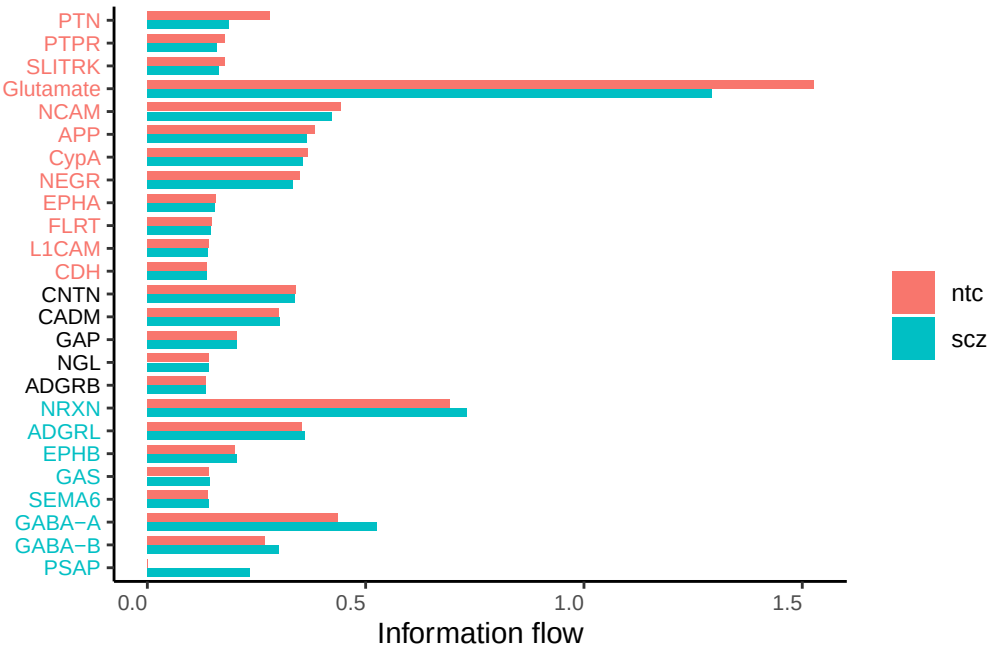


	outgoing	incoming	specificity.out.in	specificity
Glutamate	-5.753654e-02	-4.037887e-02	Shared	Shared
NRXN	1.108326e-03	1.756174e-02	Shared	Shared
NCAM	-9.258032e-03	-1.114233e-02	Shared	Shared
GABA-A	4.824603e-02	4.077083e-02	Shared	Shared
APP	-8.261621e-03	-8.261621e-03	Shared	Shared
CypA	-5.437789e-03	-5.437789e-03	Shared	Shared
ADGRL	1.727520e-03	1.849930e-03	Shared	Shared
NEGR	-7.751347e-03	-7.751347e-03	Shared	Shared
CNTN	-1.790339e-03	-1.790339e-03	Shared	Shared
CADM	-5.399708e-05	3.861607e-04	Shared	Shared
PTN	-6.333790e-03	-7.866632e-03	Outgoing specific	ntc specific
GABA-B	1.199686e-02	1.019160e-02	Shared	Shared
GAP	1.127313e-05	1.127313e-05	Shared	Shared
EPHB	6.244285e-04	3.121617e-04	Shared	Shared
PTPR	-1.767843e-03	-7.574524e-04	Shared	Shared
SLITRK	-1.219425e-03	-1.001534e-03	Shared	Shared
EPHA	-1.519940e-04	-1.733590e-04	Shared	Shared
FLRT	-1.741445e-04	-1.741445e-04	Shared	Shared
GAS	4.300120e-05	6.304955e-05	Shared	Shared
L1CAM	-1.038064e-04	-1.038064e-04	Shared	Shared
NGL	6.831563e-06	6.831563e-06	Shared	Shared
SEMA6	1.026234e-04	1.026234e-04	Shared	Shared

```
CDH       -5.371338e-05 -5.371338e-05                      Shared       Shared
ADGRB     -2.256163e-05 -2.256163e-05                      Shared       Shared
PSAP       7.596743e-03  1.418120e-02 Incoming & Outgoing specific scz specific
            labels
Glutamate Glutamate
NRXN           NRXN
NCAM           NCAM
GABA-A       GABA-A
APP             APP
CypA           CypA
ADGRL         ADGRL
NEGR           NEGR
CNTN           CNTN
CADM           CADM
PTN             PTN
GABA-B       GABA-B
GAP             GAP
EPHB           EPHB
PTPR           PTPR
SLITRK       SLITRK
EPHA           EPHA
FLRT           FLRT
GAS             GAS
L1CAM         L1CAM
NGL             NGL
SEMA6         SEMA6
CDH             CDH
ADGRB         ADGRB
PSAP           PSAP
```

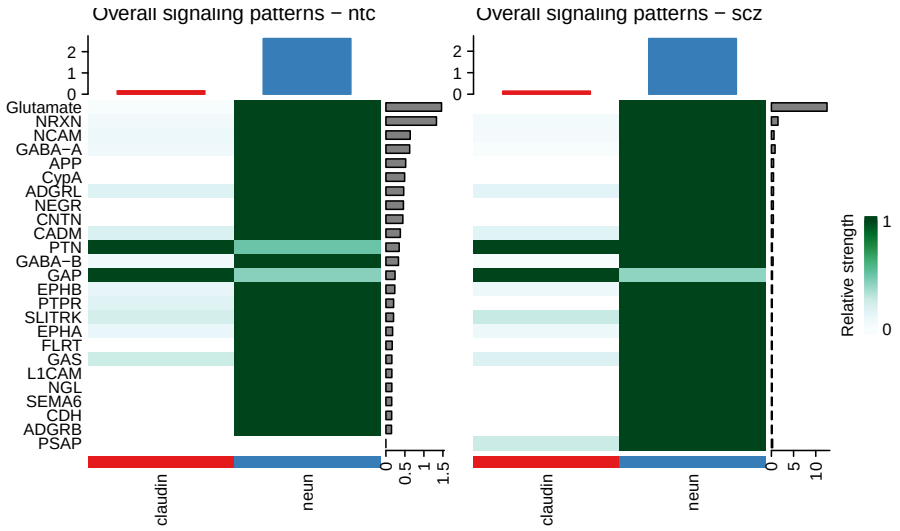
overall information flow of each signaling pathway or ligand-receptor pair

This visualization suggests that there's enriched `PSAP`-realted communication among NeuN+ spots among SCZ samples.

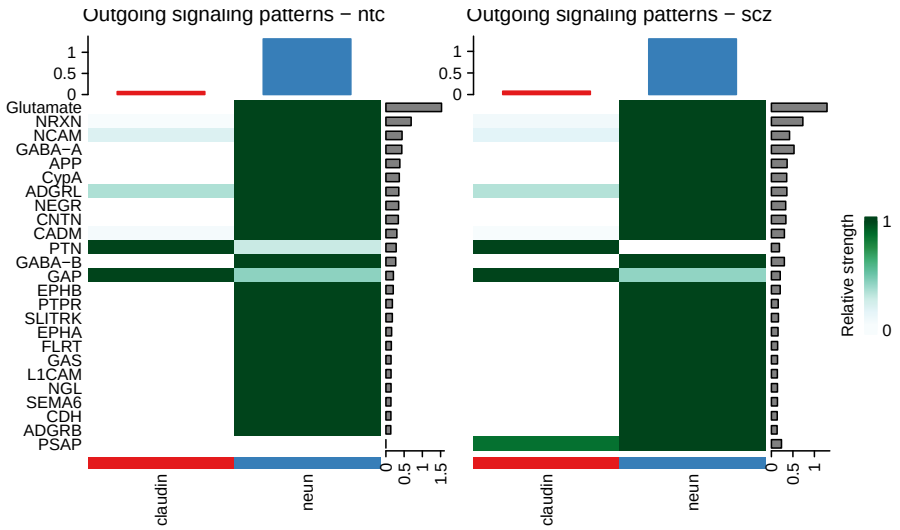


Overall

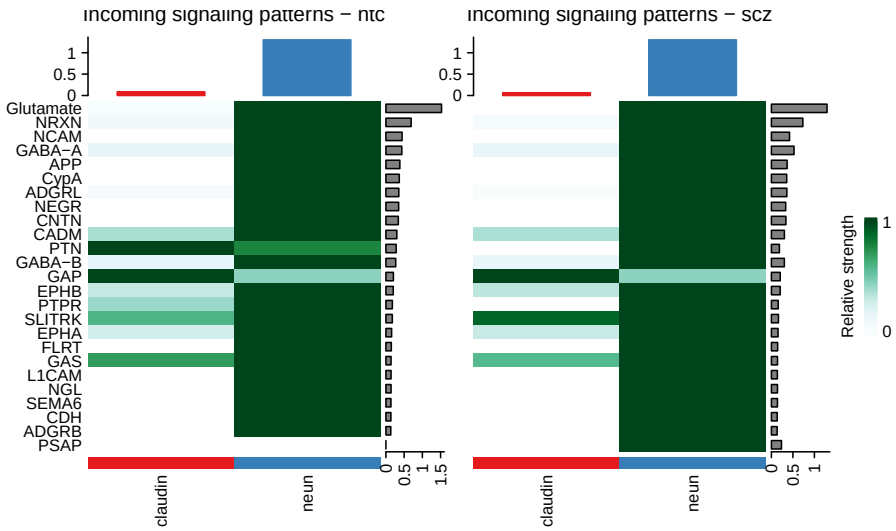
```
Loading required package: grid


========================================
ComplexHeatmap version 2.20.0
Bioconductor page: http://bioconductor.org/packages/ComplexHeatmap/
Github page: https://github.com/jokergoo/ComplexHeatmap
Documentation: http://jokergoo.github.io/ComplexHeatmap-reference

If you use it in published research, please cite either one:
- Gu, Z. Complex Heatmap Visualization. iMeta 2022.
- Gu, Z. Complex heatmaps reveal patterns and correlations in multidimensional
    genomic data. Bioinformatics 2016.


The new InteractiveComplexHeatmap package can directly export static
complex heatmaps into an interactive Shiny app with zero effort. Have a try!

This message can be suppressed by:
  suppressPackageStartupMessages(library(ComplexHeatmap))
========================================
```


Overall signaling patterns − ntc
Overall signaling patterns − scz
Glutamate
NRXN
NCAM
GABA−A
APP
CypA
ADGRL
NEGR
CNTN
CADM
PTN
GABA−B
GAP
EPHB
PTPR
SLITRK
EPHA
FLRT
GAS
L1CAM
NGL
SEMA6
CDH
ADGRB
PSAP
claudin
neun
Relative strength

Outgoing


Outgoing signaling patterns − ntc
Outgoing signaling patterns − scz
Glutamate
NRXN
NCAM
GABA−A
APP
CypA
ADGRL
NEGR
CNTN
CADM
PTN
GABA−B
GAP
EPHB
PTPR
SLITRK
EPHA
FLRT
GAS
L1CAM
NGL
SEMA6
CDH
ADGRB
PSAP
claudin
neun
Relative strength

Incoming

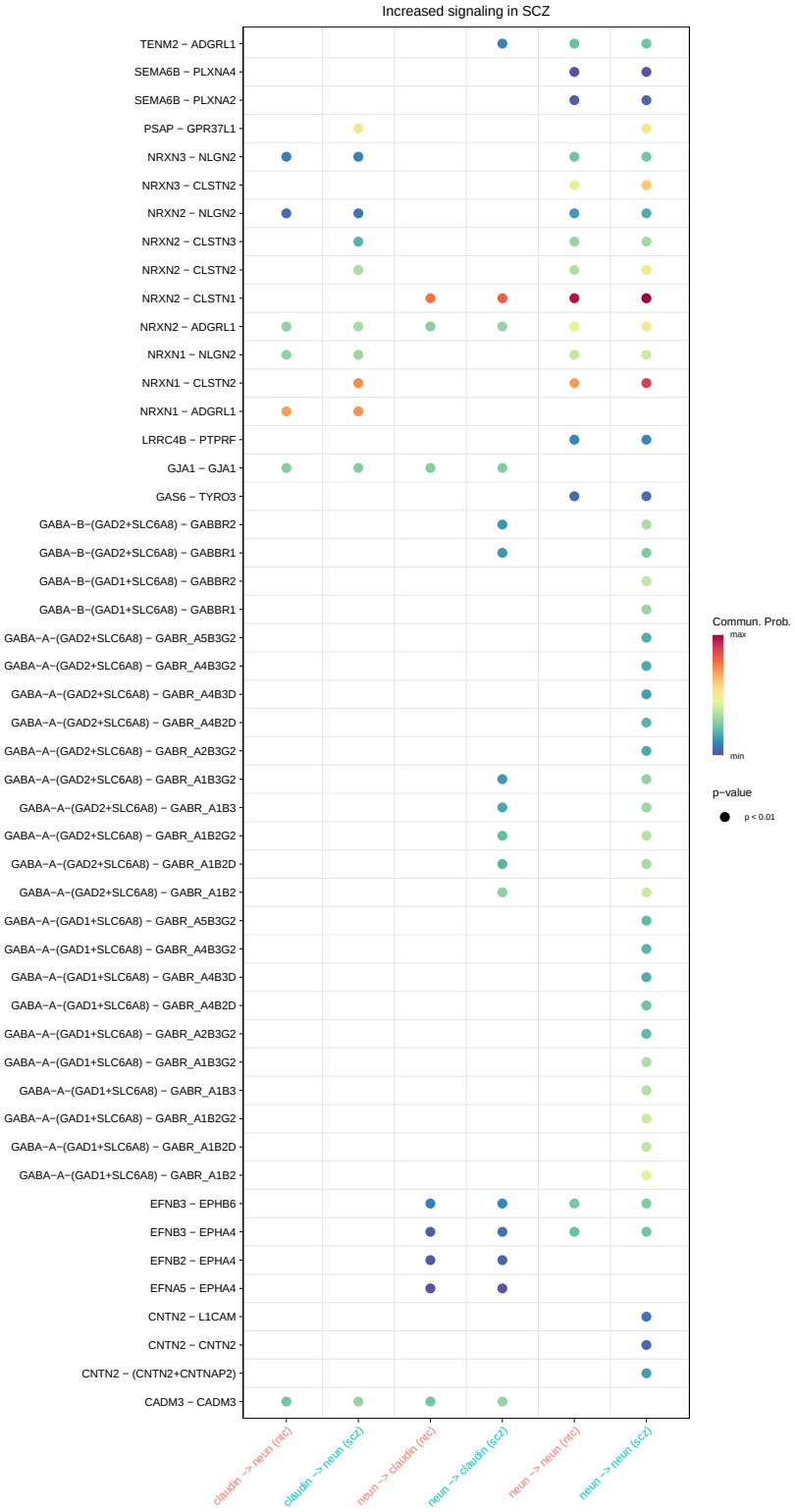


Upregulated and downregulated signaling LR pairs

Overall

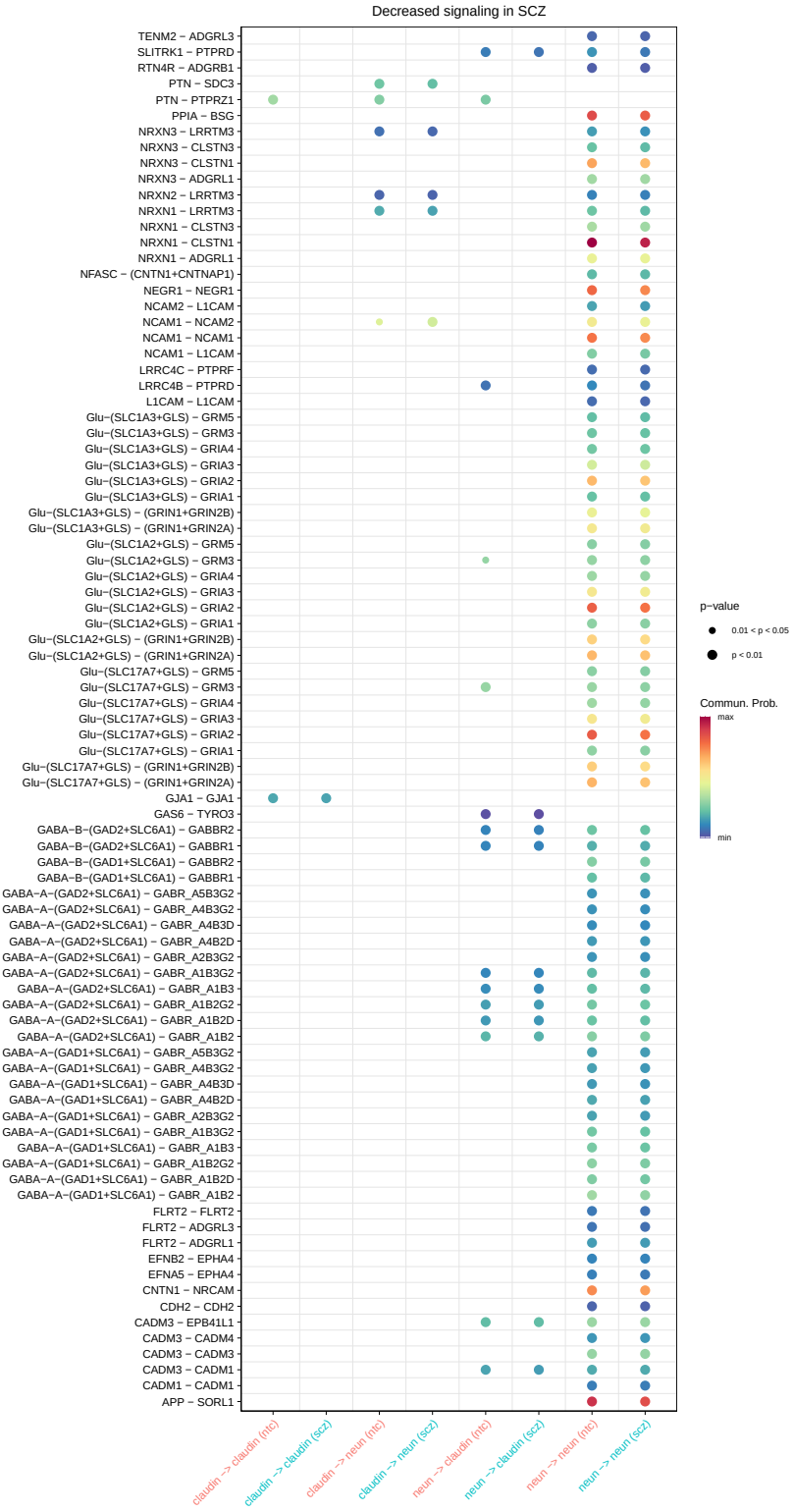
Increased signaling in SCZ

```
Comparing communications on a merged object
```


Increased signaling in SCZ
TENM2 − ADGRL1
SEMA6B − PLXNA4
SEMA6B − PLXNA2
PSAP − GPR37L1
NRXN3 − NLGN2
NRXN3 − CLSTN2
NRXN2 − NLGN2
NRXN2 − CLSTN3
NRXN2 − CLSTN2
NRXN2 − CLSTN1
NRXN2 − ADGRL1
NRXN1 − NLGN2
NRXN1 − CLSTN2
NRXN1 − ADGRL1
LRRC4B − PTPRF
GJA1 − GJA1
GAS6 − TYRO3
GABA−B−(GAD2+SLC6A8) − GABBR2
GABA−B−(GAD2+SLC6A8) − GABBR1
GABA−B−(GAD1+SLC6A8) − GABBR2
GABA−B−(GAD1+SLC6A8) − GABBR1
GABA−A−(GAD2+SLC6A8) − GABR_A5B3G2
GABA−A−(GAD2+SLC6A8) − GABR_A4B3G2
GABA−A−(GAD2+SLC6A8) − GABR_A4B3D
GABA−A−(GAD2+SLC6A8) − GABR_A4B2D
GABA−A−(GAD2+SLC6A8) − GABR_A2B3G2
GABA−A−(GAD2+SLC6A8) − GABR_A1B3G2
GABA−A−(GAD2+SLC6A8) − GABR_A1B3
GABA−A−(GAD2+SLC6A8) − GABR_A1B2G2
GABA−A−(GAD2+SLC6A8) − GABR_A1B2D
GABA−A−(GAD2+SLC6A8) − GABR_A1B2
GABA−A−(GAD1+SLC6A8) − GABR_A5B3G2
GABA−A−(GAD1+SLC6A8) − GABR_A4B3G2
GABA−A−(GAD1+SLC6A8) − GABR_A4B3D
GABA−A−(GAD1+SLC6A8) − GABR_A4B2D
GABA−A−(GAD1+SLC6A8) − GABR_A2B3G2
GABA−A−(GAD1+SLC6A8) − GABR_A1B3G2
GABA−A−(GAD1+SLC6A8) − GABR_A1B3
GABA−A−(GAD1+SLC6A8) − GABR_A1B2G2
GABA−A−(GAD1+SLC6A8) − GABR_A1B2D
GABA−A−(GAD1+SLC6A8) − GABR_A1B2
EFNB3 − EPHB6
EFNB3 − EPHA4
EFNB2 − EPHA4
EFNA5 − EPHA4
CNTN2 − L1CAM
CNTN2 − CNTN2
CNTN2 − (CNTN2+CNTNAP2)
CADM3 − CADM3
claudin −> neun (ntc)
claudin −> neun (scz)
neun −> claudin (ntc)
neun −> claudin (scz)
neun −> neun (ntc)
neun −> neun (scz)
Commun. Prob.
max
min
p−value
p < 0.01

Decreased signaling in SCZ

Comparing communications on a merged object


Decreased signaling in SCZ
TENM2 − ADGRL3
SLITRK1 − PTPRD
RTN4R − ADGRB1
PTN − SDC3
PTN − PTPRZ1
PPIA − BSG
NRXN3 − LRRTM3
NRXN3 − CLSTN3
NRXN3 − CLSTN1
NRXN3 − ADGRL1
NRXN2 − LRRTM3
NRXN1 − LRRTM3
NRXN1 − CLSTN3
NRXN1 − CLSTN1
NRXN1 − ADGRL1
NFASC − (CNTN1+CNTNAP1)
NEGR1 − NEGR1
NCAM2 − L1CAM
NCAM1 − NCAM2
NCAM1 − NCAM1
NCAM1 − L1CAM
LRRC4C − PTPRF
LRRC4B − PTPRD
L1CAM − L1CAM
Glu−(SLC1A3+GLS) − GRM5
Glu−(SLC1A3+GLS) − GRM3
Glu−(SLC1A3+GLS) − GRIA4
Glu−(SLC1A3+GLS) − GRIA3
Glu−(SLC1A3+GLS) − GRIA2
Glu−(SLC1A3+GLS) − GRIA1
Glu−(SLC1A3+GLS) − (GRIN1+GRIN2B)
Glu−(SLC1A3+GLS) − (GRIN1+GRIN2A)
Glu−(SLC1A2+GLS) − GRM5
Glu−(SLC1A2+GLS) − GRM3
Glu−(SLC1A2+GLS) − GRIA4
Glu−(SLC1A2+GLS) − GRIA3
Glu−(SLC1A2+GLS) − GRIA2
Glu−(SLC1A2+GLS) − GRIA1
Glu−(SLC1A2+GLS) − (GRIN1+GRIN2B)
Glu−(SLC1A2+GLS) − (GRIN1+GRIN2A)
Glu−(SLC17A7+GLS) − GRM5
Glu−(SLC17A7+GLS) − GRM3
Glu−(SLC17A7+GLS) − GRIA4
Glu−(SLC17A7+GLS) − GRIA3
Glu−(SLC17A7+GLS) − GRIA2
Glu−(SLC17A7+GLS) − GRIA1
Glu−(SLC17A7+GLS) − (GRIN1+GRIN2B)
Glu−(SLC17A7+GLS) − (GRIN1+GRIN2A)
GJA1 − GJA1
GAS6 − TYRO3
GABA−B−(GAD2+SLC6A1) − GABBR2
GABA−B−(GAD2+SLC6A1) − GABBR1
GABA−B−(GAD1+SLC6A1) − GABBR2
GABA−B−(GAD1+SLC6A1) − GABBR1
GABA−A−(GAD2+SLC6A1) − GABR_A5B3G2
GABA−A−(GAD2+SLC6A1) − GABR_A4B3G2
GABA−A−(GAD2+SLC6A1) − GABR_A4B3D
GABA−A−(GAD2+SLC6A1) − GABR_A4B2D
GABA−A−(GAD2+SLC6A1) − GABR_A2B3G2
GABA−A−(GAD2+SLC6A1) − GABR_A1B3G2
GABA−A−(GAD2+SLC6A1) − GABR_A1B3
GABA−A−(GAD2+SLC6A1) − GABR_A1B2G2
GABA−A−(GAD2+SLC6A1) − GABR_A1B2D
GABA−A−(GAD2+SLC6A1) − GABR_A1B2
GABA−A−(GAD1+SLC6A1) − GABR_A5B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A4B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A4B3D
GABA−A−(GAD1+SLC6A1) − GABR_A4B2D
GABA−A−(GAD1+SLC6A1) − GABR_A2B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A1B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A1B3
GABA−A−(GAD1+SLC6A1) − GABR_A1B2G2
GABA−A−(GAD1+SLC6A1) − GABR_A1B2D
GABA−A−(GAD1+SLC6A1) − GABR_A1B2
FLRT2 − FLRT2
FLRT2 − ADGRL3
FLRT2 − ADGRL1
EFNB2 − EPHA4
EFNA5 − EPHA4
CNTN1 − NRCAM
CDH2 − CDH2
CADM3 − EPB41L1
CADM3 − CADM4
CADM3 − CADM3
CADM3 − CADM1
CADM1 − CADM1
APP − SORL1
claudin −> claudin (ntc)
claudin −> claudin (scz)
claudin −> neun (ntc)
claudin −> neun (scz)
neun −> claudin (ntc)
neun −> claudin (scz)
neun −> neun (ntc)
neun −> neun (scz)
p−value
0.01 < p < 0.05
p < 0.01
Commun. Prob.
max
min

Self-communication among NeuN+

Increased signaling in SCZ

```
Comparing communications on a merged object
```


Increased signaling in SCZ
TENM2 − ADGRL1
SEMA6B − PLXNA4
SEMA6B − PLXNA2
PSAP − GPR37L1
NRXN3 − NLGN2
NRXN3 − CLSTN2
NRXN2 − NLGN2
NRXN2 − CLSTN3
NRXN2 − CLSTN2
NRXN2 − CLSTN1
NRXN2 − ADGRL1
NRXN1 − NLGN2
NRXN1 − CLSTN2
LRRC4B − PTPRF
GAS6 − TYRO3
GABA−B−(GAD2+SLC6A8) − GABBR2
GABA−B−(GAD2+SLC6A8) − GABBR1
GABA−B−(GAD1+SLC6A8) − GABBR2
GABA−B−(GAD1+SLC6A8) − GABBR1
GABA−A−(GAD2+SLC6A8) − GABR_A5B3G2
GABA−A−(GAD2+SLC6A8) − GABR_A4B3G2
GABA−A−(GAD2+SLC6A8) − GABR_A4B3D
GABA−A−(GAD2+SLC6A8) − GABR_A4B2D
GABA−A−(GAD2+SLC6A8) − GABR_A2B3G2
GABA−A−(GAD2+SLC6A8) − GABR_A1B3G2
GABA−A−(GAD2+SLC6A8) − GABR_A1B3
GABA−A−(GAD2+SLC6A8) − GABR_A1B2G2
GABA−A−(GAD2+SLC6A8) − GABR_A1B2D
GABA−A−(GAD2+SLC6A8) − GABR_A1B2
GABA−A−(GAD1+SLC6A8) − GABR_A5B3G2
GABA−A−(GAD1+SLC6A8) − GABR_A4B3G2
GABA−A−(GAD1+SLC6A8) − GABR_A4B3D
GABA−A−(GAD1+SLC6A8) − GABR_A4B2D
GABA−A−(GAD1+SLC6A8) − GABR_A2B3G2
GABA−A−(GAD1+SLC6A8) − GABR_A1B3G2
GABA−A−(GAD1+SLC6A8) − GABR_A1B3
GABA−A−(GAD1+SLC6A8) − GABR_A1B2G2
GABA−A−(GAD1+SLC6A8) − GABR_A1B2D
GABA−A−(GAD1+SLC6A8) − GABR_A1B2
EFNB3 − EPHB6
EFNB3 − EPHA4
CNTN2 − L1CAM
CNTN2 − CNTN2
CNTN2 − (CNTN2+CNTNAP2)
neun −> neun (ntc)
neun −> neun (scz)
Commun. Prob.
max
min
p−value
p < 0.01

Decreased signaling in SCZ

```
Comparing communications on a merged object
```


Decreased signaling in SCZ
TENM2 − ADGRL3
SLITRK1 − PTPRD
RTN4R − ADGRB1
PPIA − BSG
NRXN3 − LRRTM3
NRXN3 − CLSTN3
NRXN3 − CLSTN1
NRXN3 − ADGRL1
NRXN2 − LRRTM3
NRXN1 − LRRTM3
NRXN1 − CLSTN3
NRXN1 − CLSTN1
NRXN1 − ADGRL1
NFASC − (CNTN1+CNTNAP1)
NEGR1 − NEGR1
NCAM2 − L1CAM
NCAM1 − NCAM2
NCAM1 − NCAM1
NCAM1 − L1CAM
LRRC4C − PTPRF
LRRC4B − PTPRD
L1CAM − L1CAM
Glu−(SLC1A3+GLS) − GRM5
Glu−(SLC1A3+GLS) − GRM3
Glu−(SLC1A3+GLS) − GRIA4
Glu−(SLC1A3+GLS) − GRIA3
Glu−(SLC1A3+GLS) − GRIA2
Glu−(SLC1A3+GLS) − GRIA1
Glu−(SLC1A3+GLS) − (GRIN1+GRIN2B)
Glu−(SLC1A3+GLS) − (GRIN1+GRIN2A)
Glu−(SLC1A2+GLS) − GRM5
Glu−(SLC1A2+GLS) − GRM3
Glu−(SLC1A2+GLS) − GRIA4
Glu−(SLC1A2+GLS) − GRIA3
Glu−(SLC1A2+GLS) − GRIA2
Glu−(SLC1A2+GLS) − GRIA1
Glu−(SLC1A2+GLS) − (GRIN1+GRIN2B)
Glu−(SLC1A2+GLS) − (GRIN1+GRIN2A)
Glu−(SLC17A7+GLS) − GRM5
Glu−(SLC17A7+GLS) − GRM3
Glu−(SLC17A7+GLS) − GRIA4
Glu−(SLC17A7+GLS) − GRIA3
Glu−(SLC17A7+GLS) − GRIA2
Glu−(SLC17A7+GLS) − GRIA1
Glu−(SLC17A7+GLS) − (GRIN1+GRIN2B)
Glu−(SLC17A7+GLS) − (GRIN1+GRIN2A)
GABA−B−(GAD2+SLC6A1) − GABBR2
GABA−B−(GAD2+SLC6A1) − GABBR1
GABA−B−(GAD1+SLC6A1) − GABBR2
GABA−B−(GAD1+SLC6A1) − GABBR1
GABA−A−(GAD2+SLC6A1) − GABR_A5B3G2
GABA−A−(GAD2+SLC6A1) − GABR_A4B3G2
GABA−A−(GAD2+SLC6A1) − GABR_A4B3D
GABA−A−(GAD2+SLC6A1) − GABR_A4B2D
GABA−A−(GAD2+SLC6A1) − GABR_A2B3G2
GABA−A−(GAD2+SLC6A1) − GABR_A1B3G2
GABA−A−(GAD2+SLC6A1) − GABR_A1B3
GABA−A−(GAD2+SLC6A1) − GABR_A1B2G2
GABA−A−(GAD2+SLC6A1) − GABR_A1B2D
GABA−A−(GAD2+SLC6A1) − GABR_A1B2
GABA−A−(GAD1+SLC6A1) − GABR_A5B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A4B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A4B3D
GABA−A−(GAD1+SLC6A1) − GABR_A4B2D
GABA−A−(GAD1+SLC6A1) − GABR_A2B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A1B3G2
GABA−A−(GAD1+SLC6A1) − GABR_A1B3
GABA−A−(GAD1+SLC6A1) − GABR_A1B2G2
GABA−A−(GAD1+SLC6A1) − GABR_A1B2D
GABA−A−(GAD1+SLC6A1) − GABR_A1B2
FLRT2 − FLRT2
FLRT2 − ADGRL3
FLRT2 − ADGRL1
EFNB2 − EPHA4
EFNA5 − EPHA4
CNTN1 − NRCAM
CDH2 − CDH2
CADM3 − EPB41L1
CADM3 − CADM4
CADM3 − CADM3
CADM3 − CADM1
CADM1 − CADM1
APP − SORL1
neun −> neun (ntc)
neun −> neun (scz)
p−value
p < 0.01
Commun. Prob.
max
min