

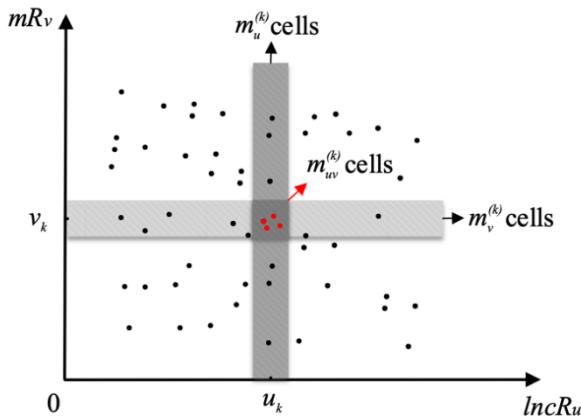
Supplementary Materials for
**Inferring cell-specific lncRNA regulation with
single-cell RNA-sequencing data in the
developing human neocortex**

Meng Huang¹, Jiangtao Ma², Changzhou Long¹, Xiucai Ye^{1,3,*}, Tetsuya
Sakurai^{1,3}

¹Department of Computer Science, University of Tsukuba, Tsukuba, 3058577, Japan,

²Department of Automation, Xiamen University, Xiamen, 361005, China, ³Center for Artificial
Intelligence Research, University of Tsukuba, Tsukuba, 3058577, Japan

*Corresponding author: Xiucai Ye. Fax: 029-853-5449; E-mail: yexiucai@cs.tsukuba.ac.jp



Statistic of $lncR_u$ and mR_v in cell k :

$$\rho_{uv}^{(k)} = \frac{m_{uv}^{(k)}}{m} - \frac{m_u^{(k)}}{m} \cdot \frac{m_v^{(k)}}{m}$$

Figure S1. Statistic model of regulation between $lncR_u$ and mR_v in cell k . u_k and v_k represent expression values of $lncR_u$ and mR_v in cell k , respectively. The neighbourhoods of u_k and v_k are denoted by the medium and light grey boxes, respectively. The neighbourhood of (u_k, v_k) is represented by the dark grey box (the intersection between the light and medium grey boxes). $m_v^{(k)}$, $m_u^{(k)}$, and $m_{uv}^{(k)}$ denote the number of points in the light, medium and dark grey boxes, respectively.

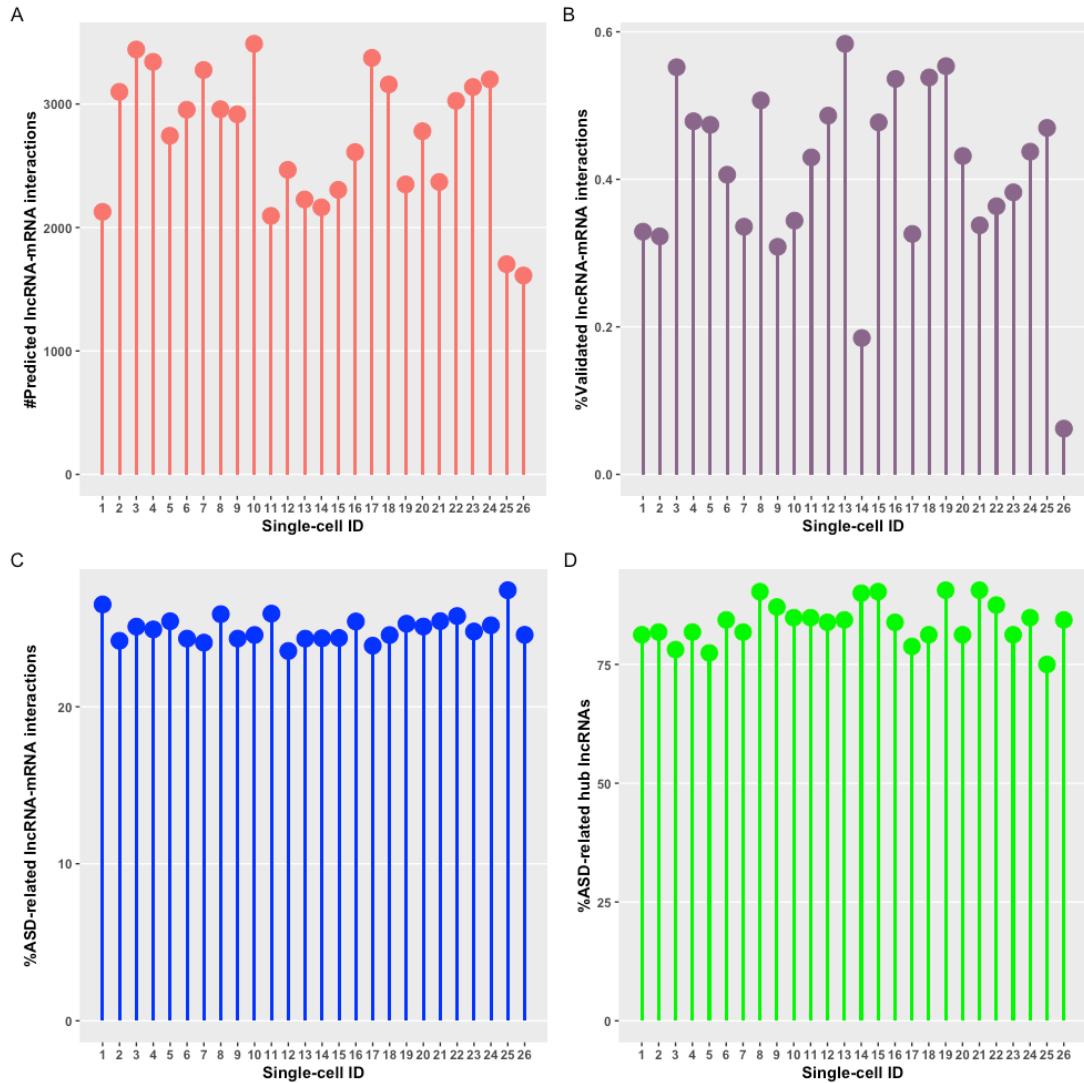


Figure S2. Cell-specific lncRNA-mRNA interactions and hub lncRNAs in GW19.5 development stage of human neocortex. (A) Number of predicted lncRNA-mRNA interactions. (B) Percentage of validated lncRNA-mRNA interactions. (C) Percentage of ASD-related lncRNA-mRNA interactions. (D) Percentage of ASD-related hub lncRNAs.

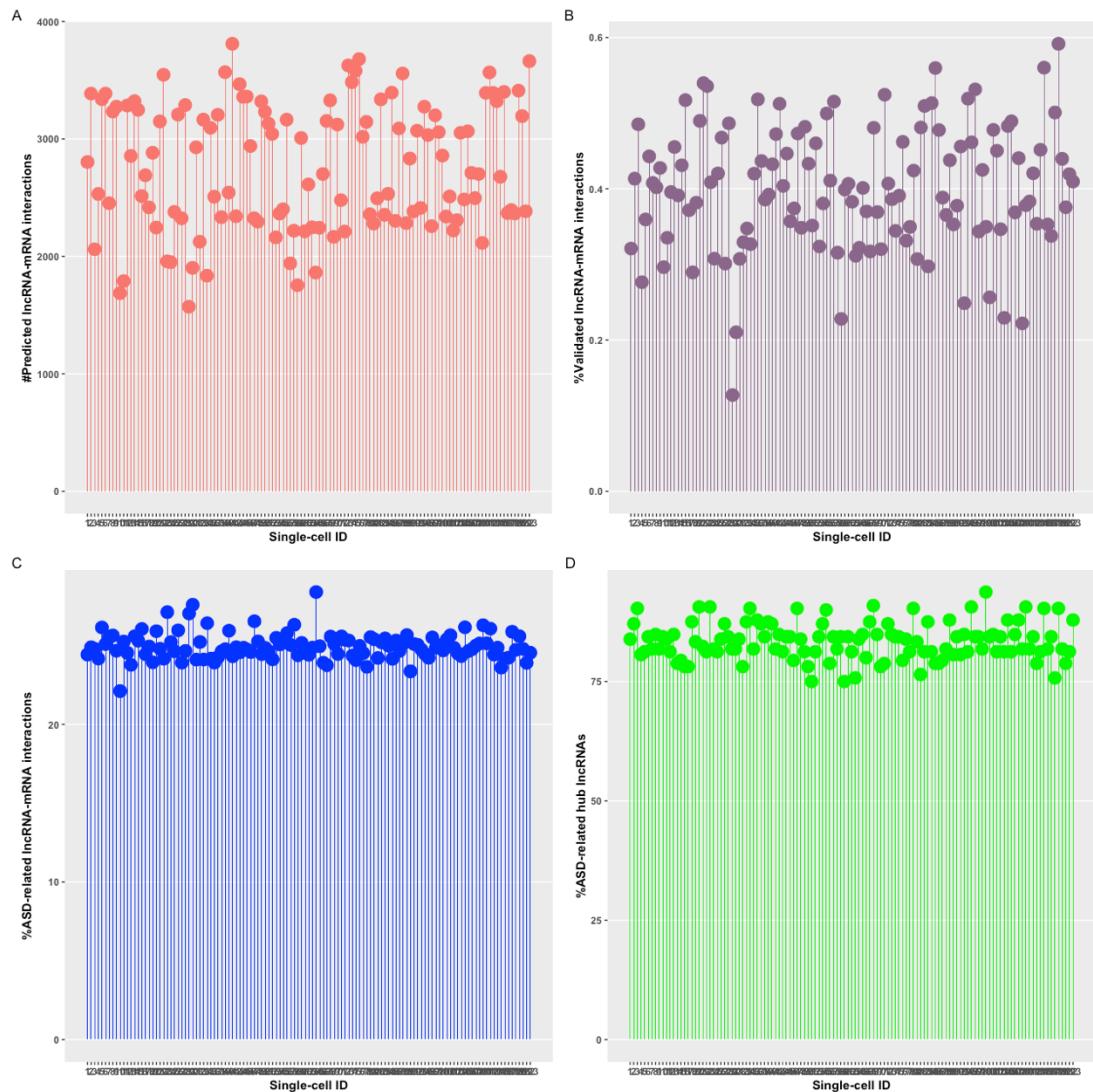


Figure S3. Cell-specific lncRNA-mRNA interactions and hub lncRNAs in GW20.5 development stage of human neocortex. (A) Number of predicted lncRNA-mRNA interactions. (B) Percentage of validated lncRNA-mRNA interactions. (C) Percentage of ASD-related lncRNA-mRNA interactions. (D) Percentage of ASD-related hub lncRNAs.

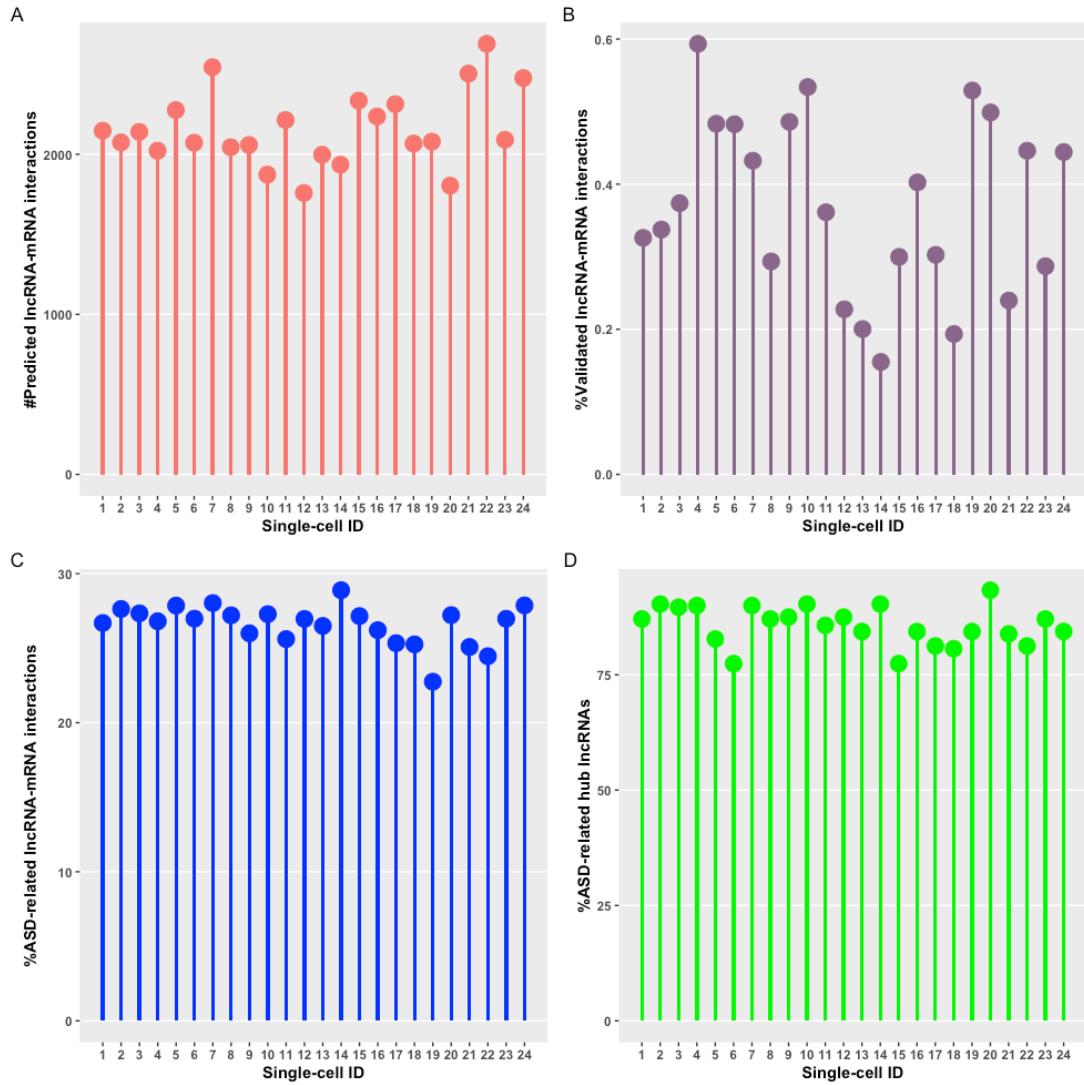


Figure S4. Cell-specific lncRNA-mRNA interactions and hub lncRNAs in GW21 development stage of human neocortex. (A) Number of predicted lncRNA-mRNA interactions. (B) Percentage of validated lncRNA-mRNA interactions. (C) Percentage of ASD-related lncRNA-mRNA interactions. (D) Percentage of ASD-related hub lncRNAs.

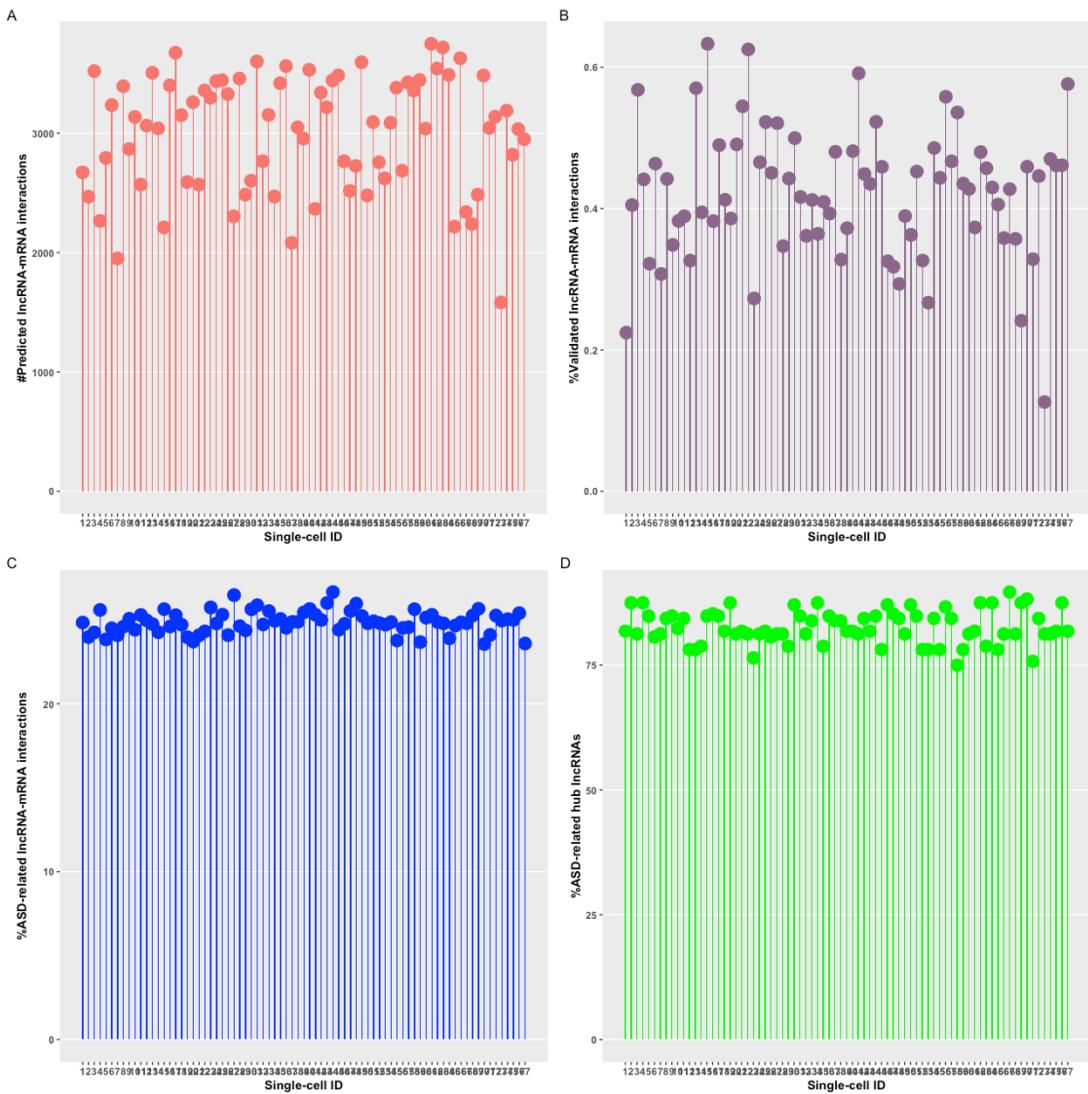


Figure S5. Cell-specific lncRNA-mRNA interactions and hub lncRNAs in GW23.5 development stage of human neocortex. (A) Number of predicted lncRNA-mRNA interactions. (B) Percentage of validated lncRNA-mRNA interactions. (C) Percentage of ASD-related lncRNA-mRNA interactions. (D) Percentage of ASD-related hub lncRNAs.

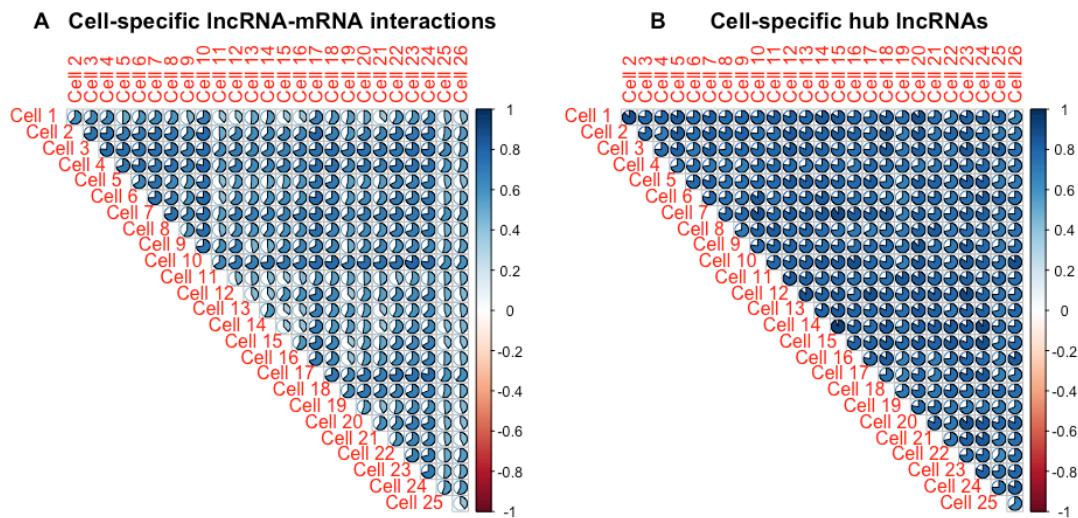


Figure S6. Single-cell similarity plot with 26 cells in GW19.5 development stage of human neocortex. (A) Similarity plot in terms of cell-specific lncRNA-mRNA interactions. (B) Similarity plot in terms of cell-specific hub lncRNAs. Colored areas indicate higher similarity between single cells.

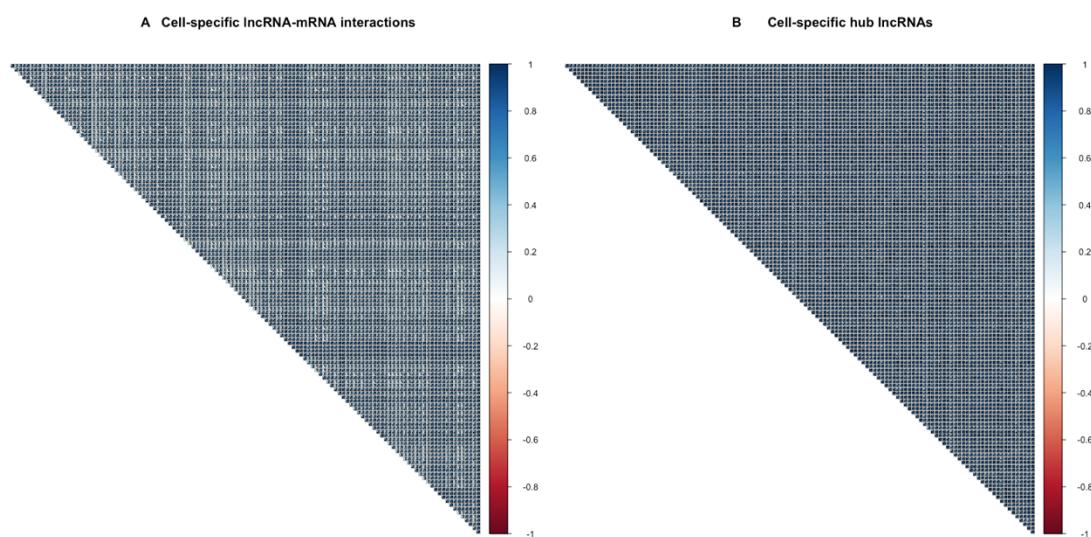


Figure S7. Single-cell similarity plot with 123 cells in GW20.5 development stage of human neocortex. (A) Similarity plot in terms of cell-specific lncRNA-mRNA interactions. (B) Similarity plot in terms of cell-specific hub lncRNAs. Colored areas indicate higher similarity between single cells.

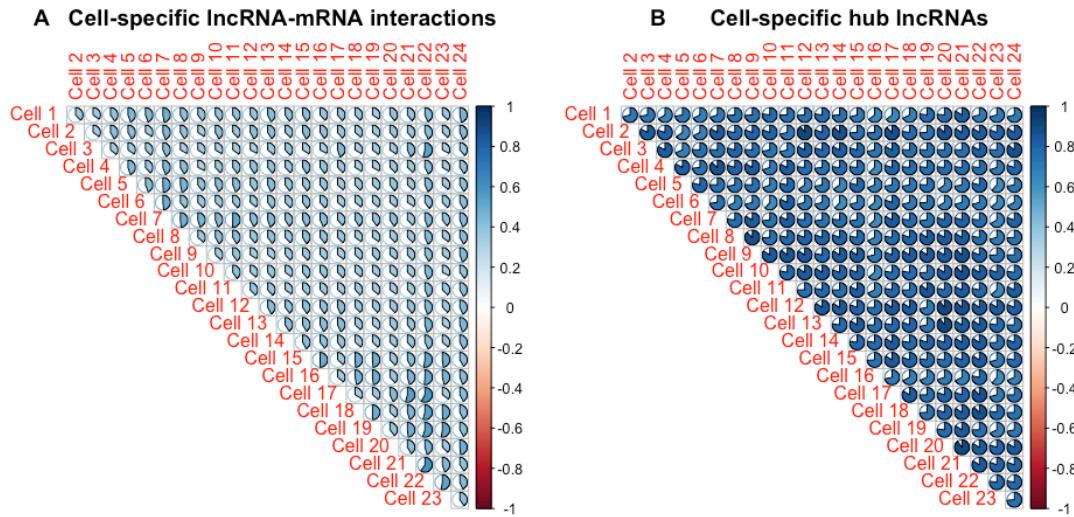


Figure S8. Single-cell similarity plot with 24 cells in GW21 development stage of human neocortex. (A) Similarity plot in terms of cell-specific lncRNA-mRNA interactions. (B) Similarity plot in terms of cell-specific hub lncRNAs. Colored areas indicate higher similarity between single cells.

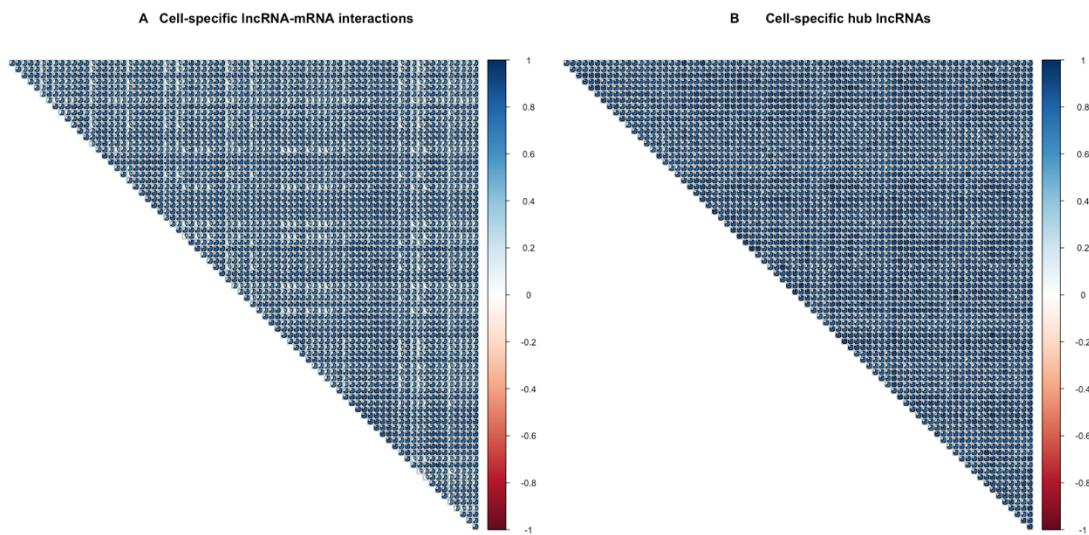


Figure S9. Single-cell similarity plot with 77 cells in GW23.5 development stage of human neocortex. (A) Similarity plot in terms of cell-specific lncRNA-mRNA interactions. (B) Similarity plot in terms of cell-specific hub lncRNAs. Colored areas indicate higher similarity between single cells.

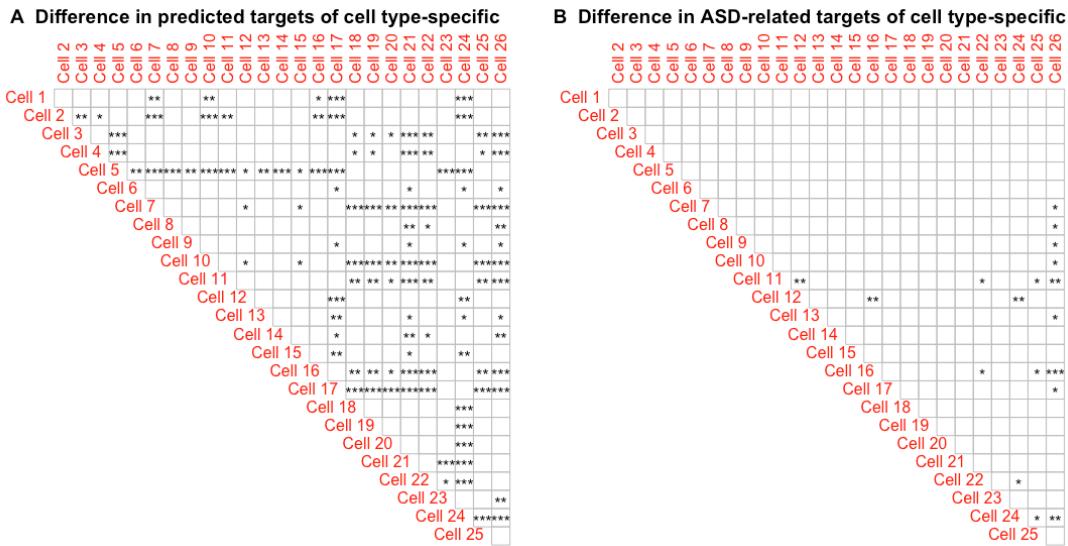


Figure S10. The cell type-specific lncRNA regulation between any pair of cells in GW19.5 development stage. (A) Difference in predicted targets of cell type-specific lncRNA. (B) Difference in ASD-related targets of cell type-specific lncRNA. Empty square shapes denote p values > 0.05 , * denotes p value < 0.05 , ** denotes p value < 0.01 and *** denotes p value < 0.001 .

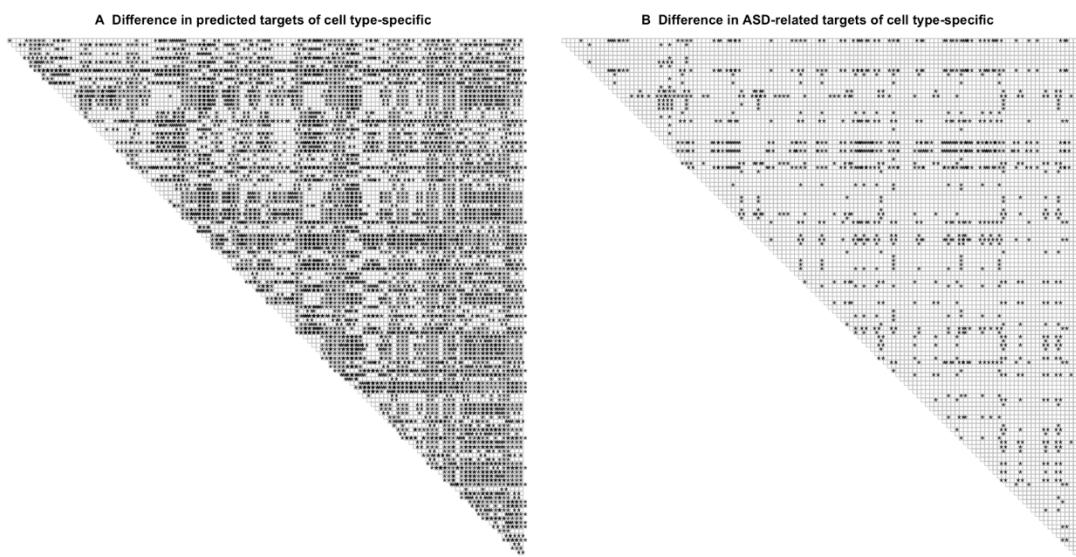


Figure S11. The cell type-specific lncRNA regulation between any pair of cells in GW20.5 development stage. (A) Difference in predicted targets of cell type-specific lncRNA. (B) Difference in ASD-related targets of cell type-specific lncRNA. Empty square shapes denote p values > 0.05 , * denotes p value < 0.05 , ** denotes p value < 0.01 and *** denotes p value < 0.001 .

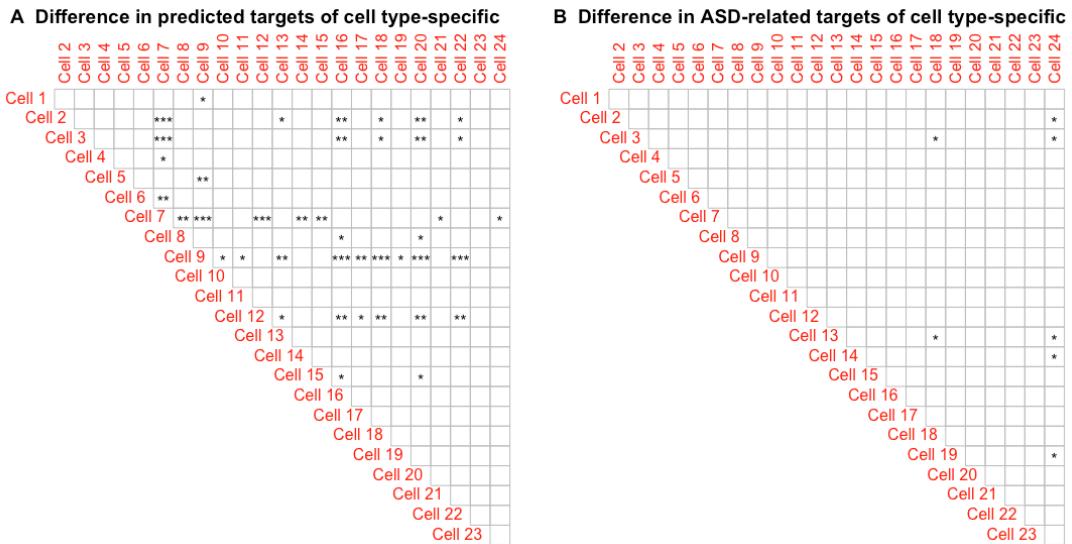


Figure S12. The cell type-specific lncRNA regulation between any pair of cells in GW21 development stage. (A) Difference in predicted targets of cell type-specific lncRNA. (B) Difference in ASD-related targets of cell type-specific lncRNA. Empty square shapes denote p values > 0.05 , * denotes p value < 0.05 , ** denotes p value < 0.01 and *** denotes p value < 0.001

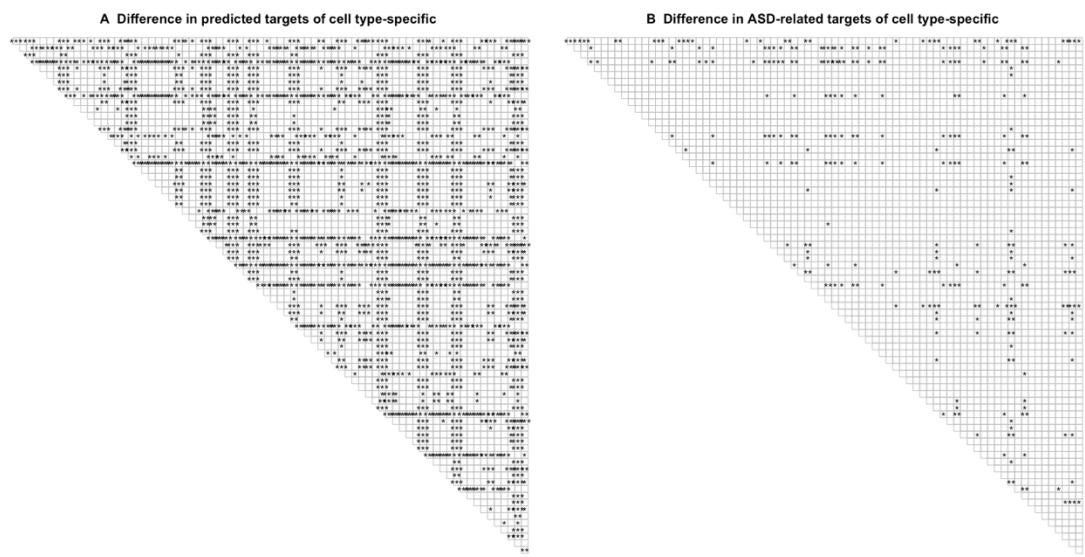


Figure S13. The cell type-specific lncRNA regulation between any pair of cells in GW23.5 development stage. (A) Difference in predicted targets of cell type-specific lncRNA. (B) Difference in ASD-related targets of cell type-specific lncRNA. Empty square shapes denote p values > 0.05 , * denotes p value < 0.05 , ** denotes p value < 0.01 and *** denotes p value < 0.001

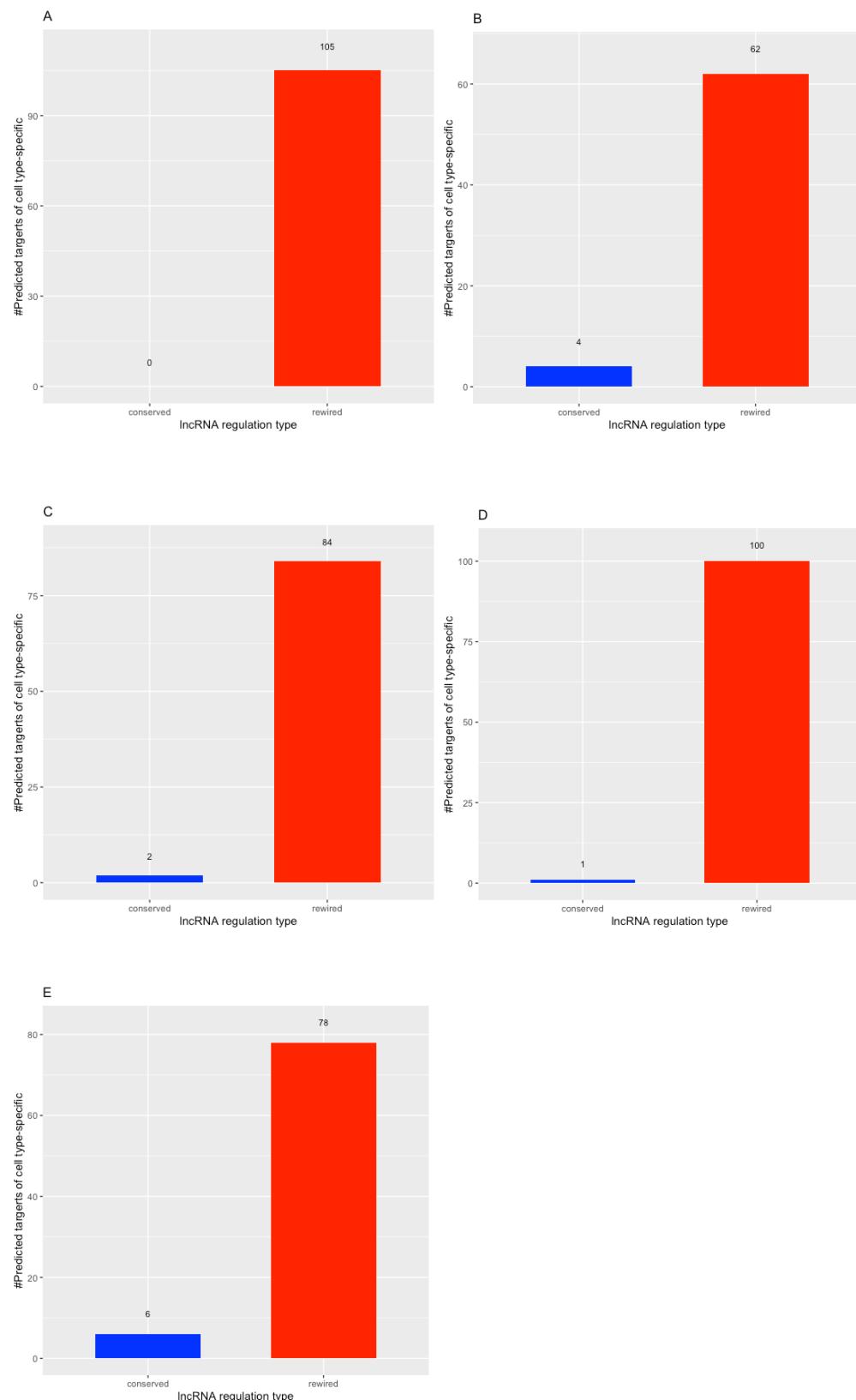


Figure S14. Number of conserved and rewired targets of cell type-specific regulation in different development stages of human neocortex. (A) GW16. (B) GW19.5. (C) GW20.5. (D) GW21. (E) GW23.5.

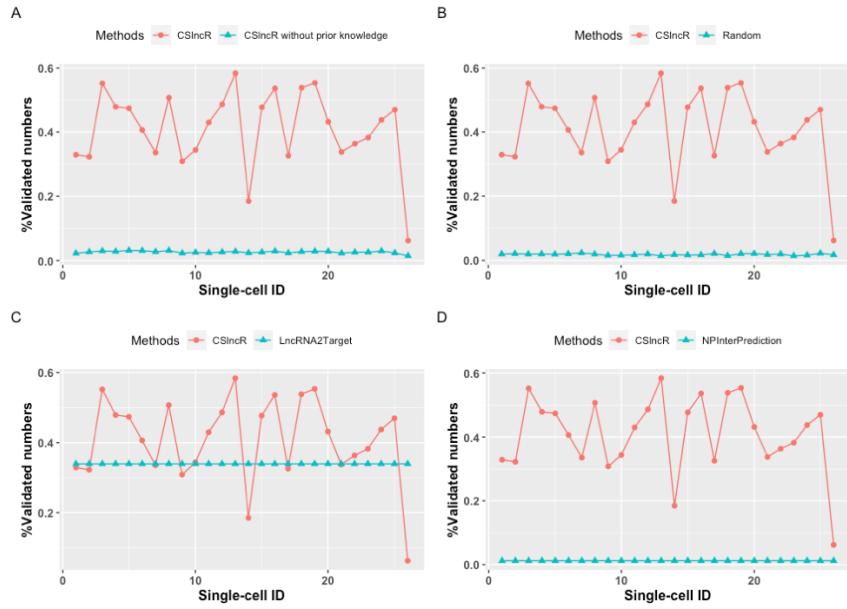


Figure S15. Comparison in terms of the percentage of validated lncRNA-mRNA interactions in GW19.5 development stage. (A) Comparison results between CSIncR (with prior knowledges) and CSIncR without prior knowledges. (B) Comparison results between CSIncR and Random method. (C) Comparison results between CSIncR and LncRNA2Target. (D) Comparison results between CSIncR and NPInterPrediction.

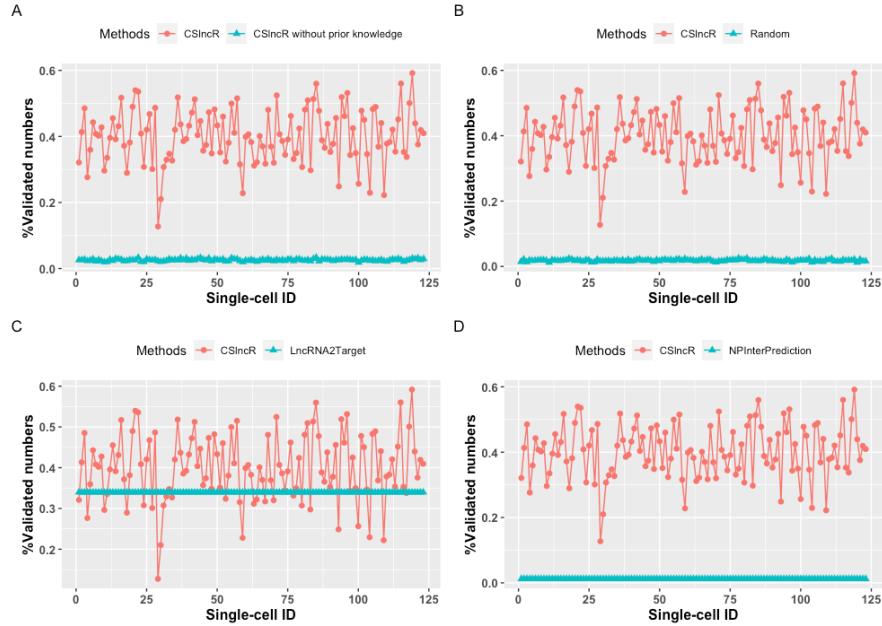


Figure S16. Comparison in terms of the percentage of validated lncRNA-mRNA interactions in GW20.5 development stage. (A) Comparison results between CSIncR (with prior knowledges) and CSIncR without prior knowledges. (B) Comparison results between CSIncR and Random method. (C) Comparison results between CSIncR and LncRNA2Target. (D) Comparison results between CSIncR and NPInterPrediction.

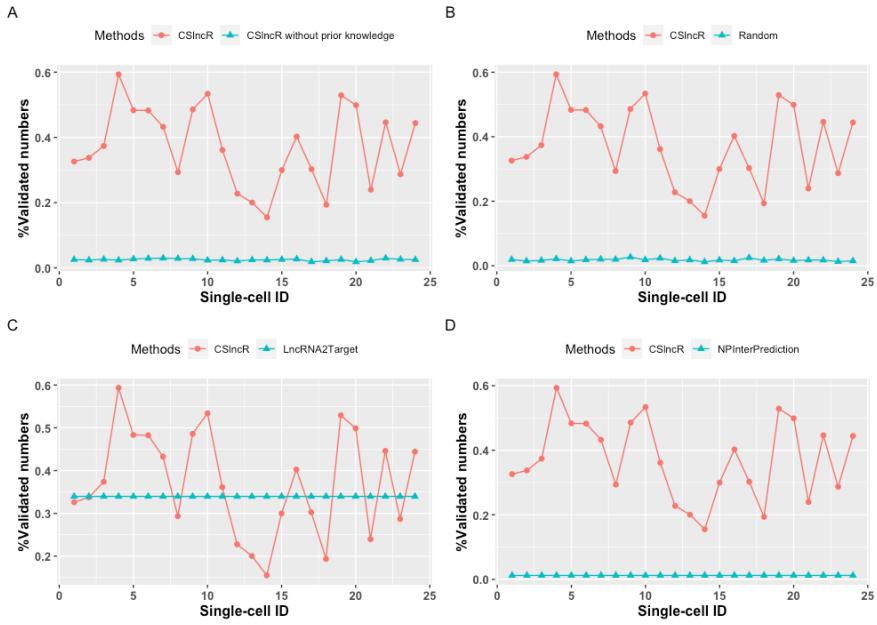


Figure S17. Comparison in terms of the percentage of validated lncRNA-mRNA interactions in GW21 development stage. (A) Comparison results between CSIncR (with prior knowledges) and CSIncR without prior knowledges. (B) Comparison results between CSIncR and Random method. (C) Comparison results between CSIncR and LncRNA2Target. (D) Comparison results between CSIncR and NPInterPrediction.

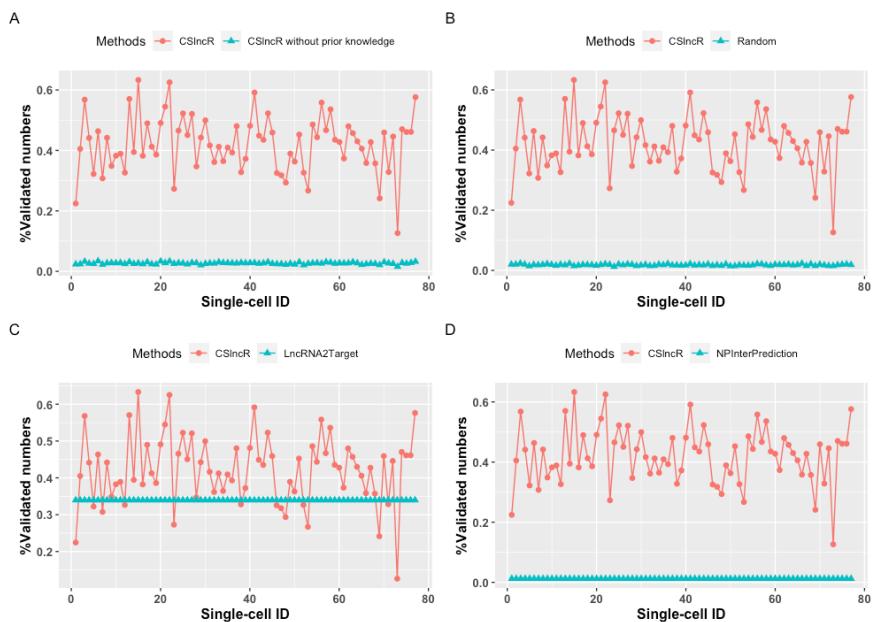


Figure S18. Comparison in terms of the percentage of validated lncRNA-mRNA interactions in GW23.5 development stage. (A) Comparison results between CSIncR (with prior knowledges) and CSIncR without prior knowledges. (B) Comparison results between CSIncR and Random method. (C) Comparison results between CSIncR and LncRNA2Target. (D) Comparison results between CSIncR and NPInterPrediction.

Table S1. Enrichment analysis of the rewired lncRNA-mRNA regulatory networks associated with cell type-specific in GW16, GW19.5, GW20.5, GW21, and GW23.5 development stages of human neocortex.

Stages	#GO	#KEGG	#Reactome	#Hallmark	#Cell marker	Enriched in ASD or not?
GW16	132	2	25	1	0	No
GW19.5	103	3	18	1	8	Yes
GW20.5	91	5	31	1	0	No
GW21	130	3	16	3	0	Yes
GW23.5	96	3	26	1	1	No

Table S2. Hub cells from each cell-cell crosstalk network in GW16 development stage of human neocortex. The cell-cell crosstalk networks are generated in terms of network similarity and hub lncRNA similarity.

Terms	Hub cells	Degree
Network similarity	GW16_8	25
	GW16_2	23
	GW16_26	23
	GW16_10	22
	GW16_7	20
	GW16_23	19
Hub lncRNA similarity	GW16_8	22
	GW16_3	21
	GW16_13	18
	GW16_6	18
	GW16_11	17
	GW16_25	17

Table S3. Hub cells from each cell-cell crosstalk network in GW19.5 development stage of human neocortex. The cell-cell crosstalk networks are generated in terms of network similarity and hub lncRNA similarity.

Terms	Hub cells	Degree
Network similarity	S44.A6	24
	S44.C9	23
	S44.B7	22
	S44.F6	22
	S44.A8	21
Hub lncRNA similarity	S44.D5	17
	S44.D9	17
	S44.E10	17
	S44.G5	17
	S44.G9	17
	S44.B7	16

Table S4. Hub cells from each cell-cell crosstalk network in GW20.5 development stage of human neocortex. The cell-cell crosstalk networks are generated in terms of network similarity and hub lncRNA similarity.

Terms	Hub cells	Degree
Network similarity	A1_N708_S502	120
	A2_N702_S504	118
	A2_N712_S508	117
	A2_N702_S507	116
	A2_N702_S508	114
	A1_N707_S506	113
	A2_N705_S507	113
	A2_N710_S506	113
	A2_N702_S506	111
	A1_N704_S504	109
	A1_N701_S503	108
	A2_N710_S507	108
	A2_N711_S508	108
	A1_N709_S501	107
	A1_N709_S503	107
	A2_N711_S502	107
	A2_N710_S503	106
	A1_N701_S508	105
	A2_N710_S508	102
	A2_N705_S502	100
	A2_N706_S508	98
	A1_N703_S502	96
	A2_N701_S503	96
	A2_N704_S503	95
	A2_N705_S505	94
Hub lncRNA similarity	A1_N712_S504	108
	A1_N704_S503	106
	A1_N704_S506	103
	A2_N702_S501	101
	A2_N708_S502	101
	A1_N701_S508	100
	A1_N703_S504	96
	A2_N706_S507	95
	A1_N702_S503	94
	A2_N709_S503	93
	A1_N708_S502	91
	A1_N709_S508	91
	A1_N701_S506	90
	A2_N702_S507	90
	A2_N706_S503	90
	A2_N706_S508	90
	A2_N710_S506	90
	A1_N702_S501	89
	A1_N709_S506	89
	A1_N702_S506	87
	A1_N712_S502	85
	A1_N705_S505	84
	A2_N710_S508	84

A2_N710_S507	82
A1_N701_S505	80

Table S5. Hub cells from each cell-cell crosstalk network in GW21 development stage of human neocortex. The cell-cell crosstalk networks are generated in terms of network similarity and hub lncRNA similarity.

Terms	Hub cells	Degree
Network similarity	GW21_6	23
	GW21_8	22
	GW21p3_15	20
	GW21p3_8	17
	GW21p3_13	15
Hub lncRNA similarity	GW21_5	18
	GW21p3_2	16
	GW21_6	16
	GW21p3_4	15
	GW21p3_5	15

Table S6. Hub cells from each cell-cell crosstalk network in GW23.5 development stage of human neocortex. The cell-cell crosstalk networks are generated in terms of network similarity and hub lncRNA similarity.

Terms	Hub cells	Degree
Network similarity	S46.F8	74
	S46.C8	72
	S46.G1	72
	S46.B3	69
	S46.G4	69
	S46.E4	68
	S46.A11	67
	S46.D6	67
	S46.D2	65
	S46.E11	63
	S46.F9	63
	S46.G9	63
	S46.B10	61
	S46.F4	61
	S46.G11	61
Hub lncRNA similarity	S46.C8	59
	S46.F12	59
	S46.C7	58
	S46.D7	54
	S46.E11	54
	S46.F2	54
	S46.H3	53
	S46.A2	52
	S46.A4	52
	S46.C10	51
	S46.E12	51
	S46.H10	51
	S46.A5	50
	S46.A11	49

Table S7. The identified cell-cell crosstalk modules in GW16 development stage of human neocortex. The cell-cell crosstalk networks are generated in terms of network similarity and hub lncRNA similarity.

Terms	Module ID	GW16_ID
Network similarity	1	1, 2, 3, 4, 5, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26
Hub lncRNA similarity	1	1, 2, 3, 4, 5, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26

Table S8. The identified cell-cell crosstalk modules in GW19.5 development stage of human neocortex. The cell-cell crosstalk networks are generated in terms of network similarity and hub lncRNA similarity.

Terms	Module ID	S44.ID
Network similarity	1	A10, A11, A6, A8, A9, B6, B7, B8, B9, C9, D10, D5, D8, D9, E10, F10, F6, F9, G10, G5, G7, G8, G9, H5, H6
Hub lncRNA similarity	1	A10, A11, A6, A8, A9, B6, B7, B8, B9, C9, D10, D5, D8, D9, E10, F10, F6, F9, G10, G5, G7, G8, G9, H5, H6, H9

Table S9. The identified cell-cell crosstalk modules in GW20.5 development stage of human neocortex. The cell-cell crosstalk networks are generated in terms of network similarity and hub lncRNA similarity.

Terms	Module ID	ID
Network similarity	1	A1_N701_S501, A1_N701_S503, A1_N701_S505, A1_N701_S506, A1_N701_S507, A1_N701_S508, A1_N702_S501, A1_N702_S503, A1_N702_S504, A1_N702_S505, A1_N702_S506, A1_N702_S507, A1_N702_S508, A1_N703_S502, A1_N703_S503, A1_N703_S504, A1_N703_S505, A1_N703_S506, A1_N704_S501, A1_N704_S502, A1_N704_S503, A1_N704_S504, A1_N704_S506, A1_N704_S507, A1_N705_S502, A1_N705_S503, A1_N705_S505, A1_N705_S506, A1_N705_S507, A1_N706_S502, A1_N706_S503, A1_N706_S504, A1_N706_S505, A1_N706_S506, A1_N706_S507, A1_N707_S503, A1_N707_S505, A1_N707_S506, A1_N707_S507, A1_N708_S502, A1_N708_S508, A1_N709_S501, A1_N709_S502, A1_N709_S503, A1_N709_S506, A1_N709_S508, A1_N710_S501, A1_N710_S502, A1_N710_S504, A1_N710_S505, A1_N710_S508, A1_N711_S503, A1_N711_S504, A1_N711_S505, A1_N711_S507, A1_N711_S508, A1_N712_S501, A1_N712_S502, A1_N712_S503, A1_N712_S504, A1_N712_S505, A1_N712_S507, A1_N712_S508, A2_N701_S501, A2_N701_S502, A2_N701_S503, A2_N701_S506, A2_N701_S507, A2_N701_S508, A2_N702_S501, A2_N702_S504, A2_N702_S506, A2_N702_S507, A2_N702_S508, A2_N703_S501, A2_N703_S503, A2_N703_S506, A2_N703_S508, A2_N704_S501, A2_N704_S503, A2_N704_S506, A2_N704_S508, A2_N705_S502, A2_N705_S504, A2_N705_S505, A2_N705_S507, A2_N706_S501, A2_N706_S503, A2_N706_S504, A2_N706_S506, A2_N706_S507, A2_N706_S508, A2_N707_S501, A2_N707_S504, A2_N707_S505, A2_N707_S507,

Hub lncRNA 1 similarity	A2_N707_S508, A2_N708_S502, A2_N708_S503, A2_N708_S506, A2_N708_S508, A2_N709_S503, A2_N709_S505, A2_N709_S506, A2_N709_S507, A2_N709_S508, A2_N710_S501, A2_N710_S502, A2_N710_S503, A2_N710_S506, A2_N711_S501, A2_N711_S502, A2_N711_S504, A2_N711_S505, A2_N711_S507, A2_N711_S508, A2_N712_S502, A2_N712_S507, A2_N712_S508 A1_N701_S501, A1_N701_S503, A1_N701_S505, A1_N701_S506, A1_N701_S507, A1_N701_S508, A1_N702_S501, A1_N702_S503, A1_N702_S504, A1_N702_S505, A1_N702_S506, A1_N702_S507, A1_N702_S508, A1_N703_S502, A1_N703_S503, A1_N703_S504, A1_N703_S505, A1_N703_S506, A1_N704_S501, A1_N704_S502, A1_N704_S503, A1_N704_S504, A1_N704_S505, A1_N704_S506, A1_N704_S507, A1_N705_S502, A1_N705_S503, A1_N705_S504, A1_N705_S505, A1_N705_S507, A1_N706_S502, A1_N706_S503, A1_N706_S504, A1_N706_S505, A1_N706_S506, A1_N706_S507, A1_N707_S503, A1_N707_S505, A1_N707_S506, A1_N707_S507, A1_N708_S502, A1_N708_S503, A1_N708_S504, A1_N708_S505, A1_N708_S506, A1_N708_S507, A1_N709_S501, A1_N709_S502, A1_N709_S503, A1_N709_S504, A1_N709_S505, A1_N709_S506, A1_N709_S507, A1_N710_S501, A1_N710_S502, A1_N710_S503, A1_N710_S504, A1_N710_S505, A1_N710_S506, A1_N711_S503, A1_N711_S504, A1_N711_S505, A1_N711_S507, A1_N712_S501, A1_N712_S502, A1_N712_S503, A1_N712_S504, A1_N712_S505, A1_N712_S506, A1_N712_S507, A1_N712_S508, A2_N701_S501, A2_N701_S502, A2_N701_S503, A2_N701_S506, A2_N701_S507, A2_N701_S508, A2_N702_S501, A2_N702_S504, A2_N702_S506, A2_N702_S507, A2_N702_S508, A2_N703_S503, A2_N703_S506, A2_N703_S508, A2_N704_S501, A2_N704_S503, A2_N704_S506, A2_N705_S502, A2_N705_S504, A2_N705_S505, A2_N705_S506, A2_N706_S501, A2_N706_S503, A2_N706_S504, A2_N706_S505, A2_N706_S507, A2_N707_S501, A2_N707_S504, A2_N707_S505, A2_N707_S506, A2_N708_S502, A2_N708_S503, A2_N708_S504, A2_N708_S505, A2_N708_S506, A2_N709_S501, A2_N709_S502, A2_N709_S503, A2_N709_S504, A2_N709_S505, A2_N709_S506, A2_N709_S507, A2_N710_S502, A2_N710_S503, A2_N710_S504, A2_N710_S505, A2_N710_S506, A2_N710_S507, A2_N711_S501, A2_N711_S502, A2_N711_S503, A2_N711_S504, A2_N711_S505, A2_N711_S506, A2_N711_S507, A2_N711_S508, A2_N712_S502, A2_N712_S503, A2_N712_S504, A2_N712_S505, A2_N712_S506, A2_N712_S507, A2_N712_S508
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Table S10. The identified cell-cell crosstalk modules in GW21 development stage of human neocortex. The cell-cell crosstalk networks are generated in terms of network similarity and hub lncRNA similarity.

Terms	Module ID	GW21ID
Network similarity	1	p3_1, p3_10, p3_11, p3_12, p3_13, p3_14, p3_15, p3_16, p3_2, p3_3, p3_4, p3_5, p3_6, p3_7, p3_8, p3_9, _1, _2, _3, _4, _5, _6, _7, _8
Hub lncRNA similarity	1	p3_1, p3_10, p3_11, p3_12, p3_13, p3_14, p3_15, p3_16, p3_2, p3_3, p3_4, p3_5, p3_6, p3_7, p3_8, p3_9, _1, _2, _3, _4, _5, _6, _7, _8

Table S11. The identified cell-cell crosstalk modules in GW23.5 development stage of human neocortex. The cell-cell crosstalk networks are generated in terms of network similarity and hub lncRNA similarity.

Terms	Module ID	S46.ID
Network similarity	1	A1, A10, A11, A12, A2, A4, A5, A6, A7, A8, A9, B1, B10, B11, B12, B2, B3, B4, B5, B7, B8, B9, C10, C11, C12, C3, C4, C5, C6, C7, C8, C9, D1, D10, D12, D2, D4, D5, D6, D7, D8, D9, E1, E11, E12, E2, E3, E4, E7, E8, F1, F10, F11, F12, F2, F4, F5, F6, F7, F8, F9, G1, G11, G2, G4, G5, G6, G7, G9, H10, H2, H5, H7, H8, H9
Hub lncRNA similarity	1	A1, A10, A11, A12, A2, A4, A5, A6, A7, A8, A9, B1, B10, B11, B12, B2, B3, B4, B5, B7, B8, B9, C10, C11, C12, C3, C4, C5, C6, C7, C8, C9, D1, D10, D12, D2, D3, D4, D5, D6, D7, D8, D9, E1, E11, E12, E2, E3, E4, E7, E8, F1, F10, F11, F12, F2, F4, F5, F6, F7, F8, F9, G1, G11, G2, G4, G5, G6, G7, G9, H10, H2, H3, H5, H7, H8, H9