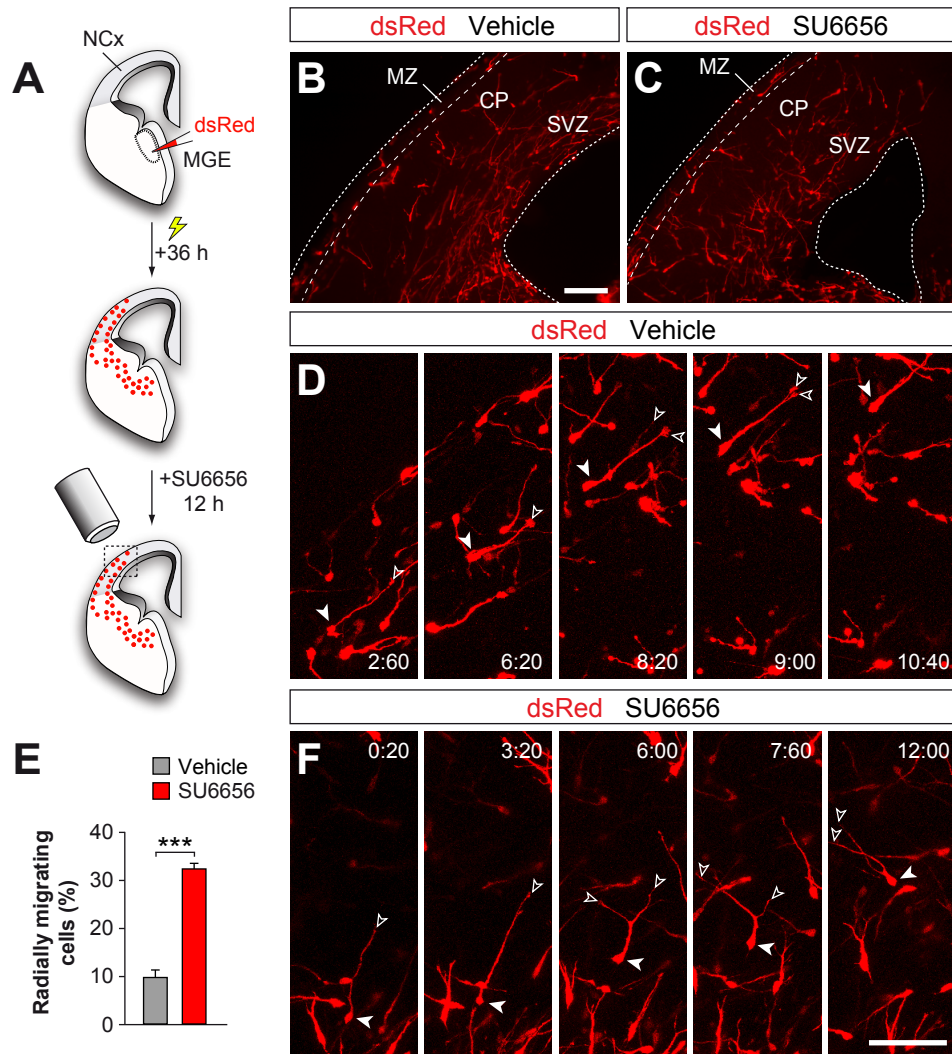


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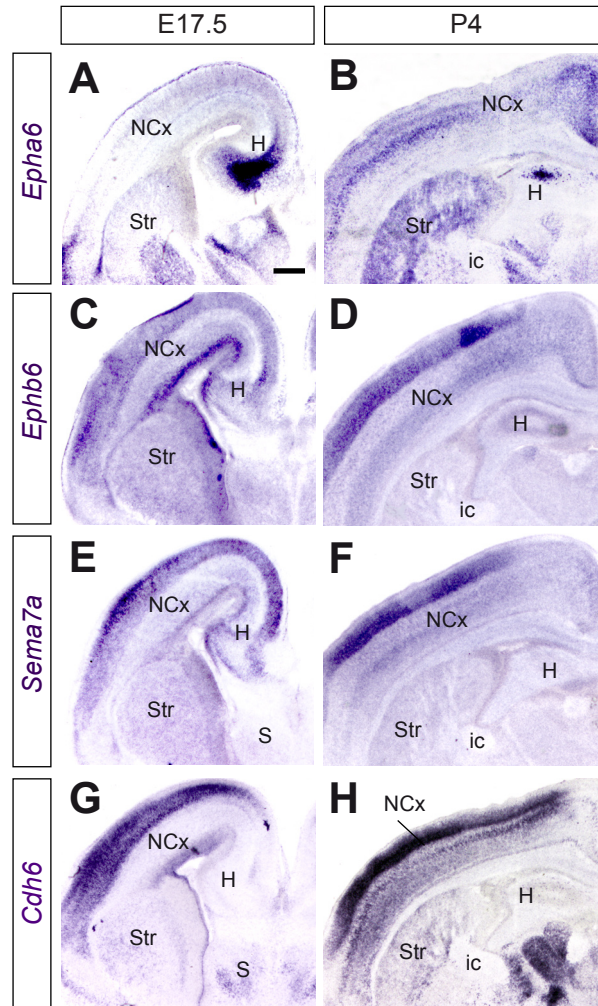
**Supplemental Information**

**Neuregulin 3 Mediates Cortical Plate Invasion  
and Laminar Allocation of GABAergic Interneurons**

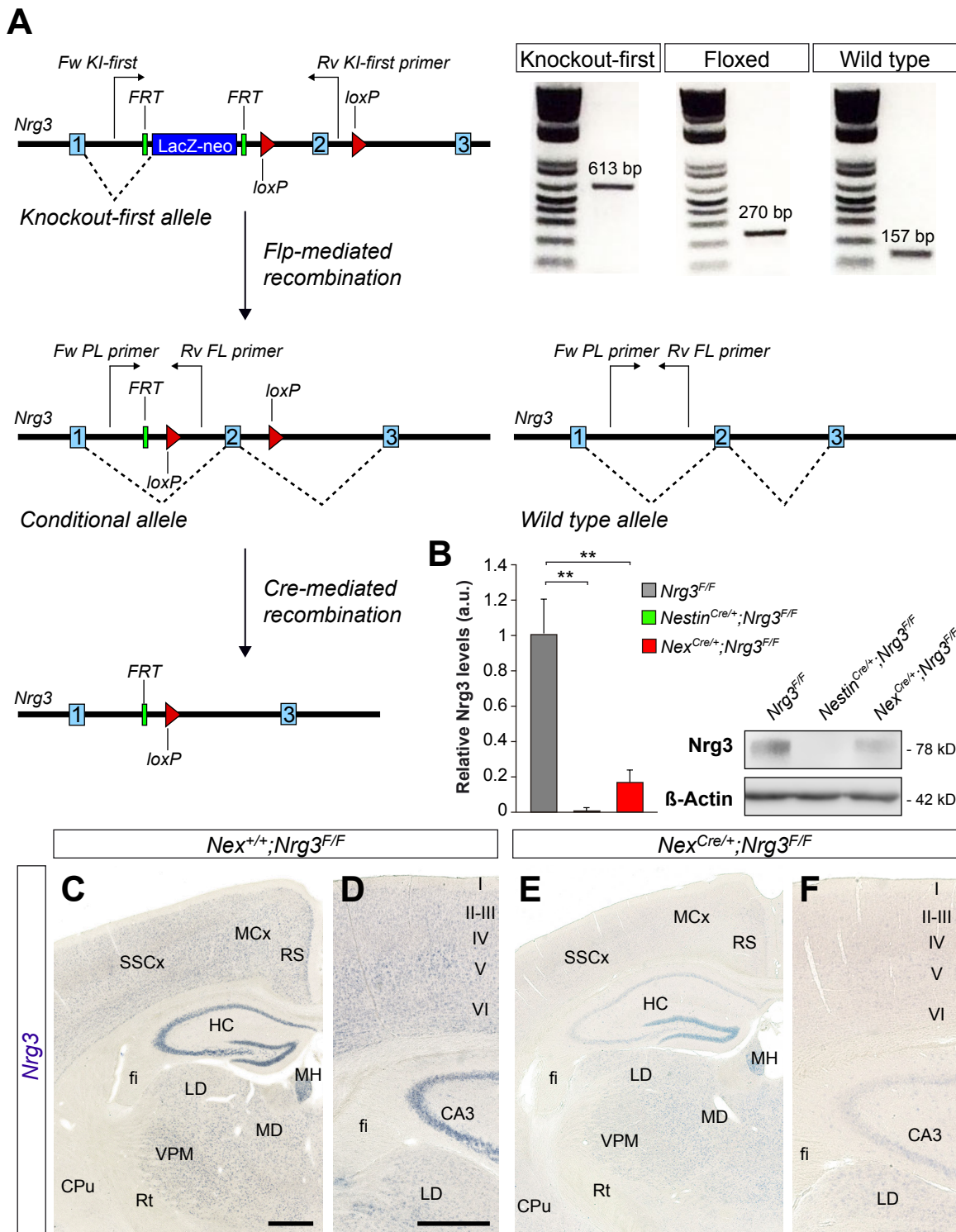
**Giorgia Bartolini, Juan Antonio Sánchez-Alcañiz, Catarina Osório, Manuel Valiente, Cristina García-Frigola, and Oscar Marín**



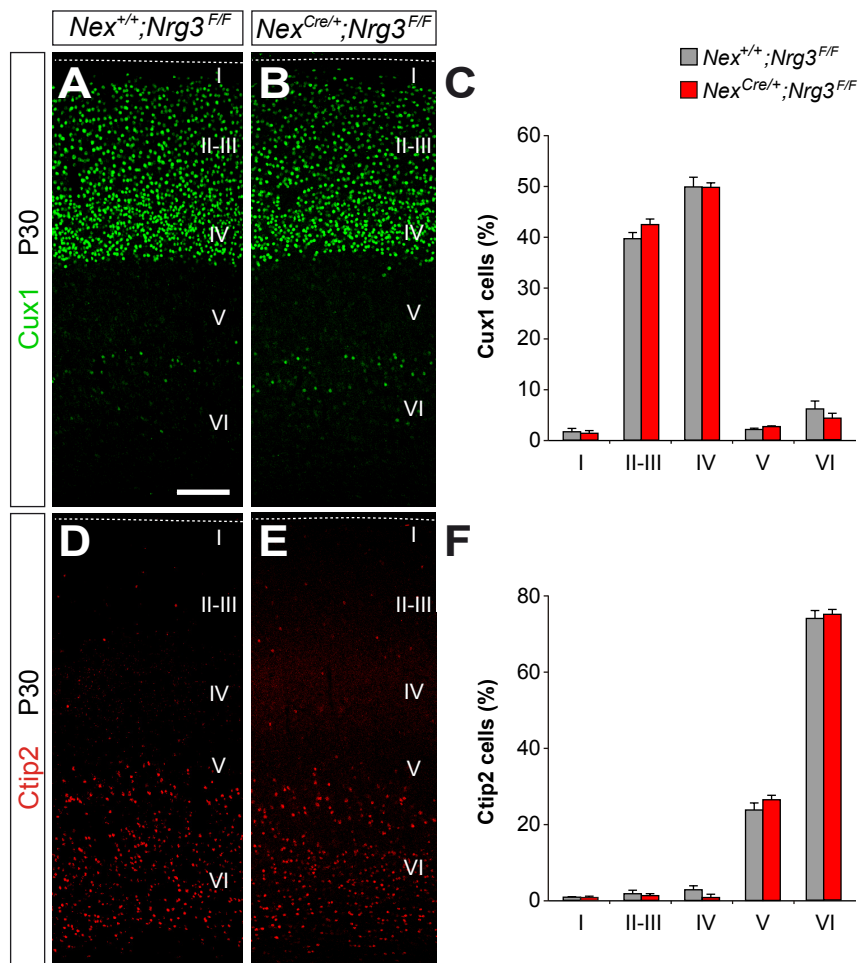
**Figure S1, related to Figure 1.** Loss of chemokine signaling redirects cells towards the cortical plate. **(A)** Schematic of the experimental design. A plasmid encoding *dsRed* was focally electroporated in the MGE of E13.5 acute slices. After 36 h in culture, vehicle or SU6655 was added to the medium, and migrating neurons were analyzed 12 h later. **(B, C)** Distribution of MGE-derived interneurons in the developing pallium after 48 h in culture. **(D, F)** Time-lapse sequence of *dsRed*-electroporated interneurons migrating through the subpallium in a control **(D)** and SU6655-treated **(F)** slice culture. These neurons were recorded for more than 12 hours; only selected frames are displayed. Time is depicted as hours:minutes. White arrowheads mark the soma of interneurons; empty arrowheads indicate leading process branches. **(E)** Quantification of the percentage of radially oriented interneurons in the pallium of control and SU6655-treated slices. Data are represented as mean  $\pm$  SEM;  $n = 240$  cells for each condition from 2 independent experiments.  $t$ -test \*\*\* $p < 0.001$ . Histograms show average  $\pm$  SEM. NCx, neocortex; MGE, medial ganglionic eminence. Scale bars equal 100  $\mu\text{m}$ .



**Figure S2, related to Figure 1.** Differentially expressed genes in pyramidal cells at perinatal stages. Coronal sections through the telencephalon of E17.5 (**A, C, E, G**) and P4 (**B, D, F, H**) mice showing *mRNA* distribution for several candidate genes whose expression is upregulated by late-born pyramidal cells at P4 compared to E17.5. H, Hippocampus; ic, internal capsule; NCx, neocortex; S, septum; Str, striatum; Scale bars equal 250  $\mu\text{m}$ .



**Figure S3, related to Figure 6.** Generation and characterization of *Nrg3* conditional mutant mice. **(A)** Mice carrying a knockout-first allele were bred with pan-Flippase (FLP) mice to generate mice carrying a conditional (floxed) *Nrg3* allele. These mice were subsequently crossed with Cre-expressing mouse strains to generate conditional *Nrg3* mutant mice. The blots show genotyping band sizes for the knockout-first, floxed and wild type *Nrg3* alleles using the primers indicated in the schemas. **(B)** Immunoblots and quantification of Nrg3 protein from cortical homogenates in control (*Nrg3<sup>F/F</sup>*) and two strains of conditional mutant mice (*Nestin<sup>Cre/+</sup>;Nrg3<sup>F/F</sup>* and *Nex<sup>Cre/+</sup>;Nrg3<sup>F/F</sup>*). The existence of a remnant of Nrg3 protein in *Nex<sup>Cre/+</sup>;Nrg3<sup>F/F</sup>* mice suggests that cells other than pyramidal cells express this protein in the cortex. \*\*\* $p < 0.001$ ;  $t$ -test;  $n = 4$ . Histograms show average  $\pm$  SEM. **(C-F)** Expression of *Nrg3* mRNA in the forebrain of control (C, D) and *Nrg3* mutant (E, F) mice at P30. CA3, field CA3; CPu, Caudoputamen; fi, fimbria; HC, hippocampus; LD, laterodorsal thalamic nucleus; MCx, motor cortex; MH, medial habenula; MD, mediodorsal thalamic nucleus; RS, retrosplenial cortex; Rt, reticular nucleus; SSCx, somatosensory cortex; VPM, ventral posteromedial thalamic nucleus; I to VI, cortical layers I to VI, respectively. Scale bars equal 800  $\mu$ m.





**Figure S4, related to Figure 6.** Normal lamination of pyramidal cells in *Nrg3* conditional mutants. **(A, B, D, E)** Distribution of Cux1 **(A, B)** and Ctip2 **(D, E)** expressing neurons in the somatosensory cortex of control **(A, D)** and conditional *Nrg3* **(B, E)** mice at P30. **(C)** Quantification of the distribution of Cux1-expressing cells;  $n = 4$ , Chi-squared test  $p = 1$ . **(F)** Quantification of the distribution of Ctip2-expressing cells;  $n = 4$ , Chi-squared test  $p = 1$ .

**Table S1.** Candidate genes used in the analysis, related to Figure 1

#	Gene Symbol	Locus Link	Assay ID	Public RefSeq
1	Cdh1	mCG20483	Mm00486918_m1	NM_009864.2
2	Cdh2	mCG141325	Mm00483213_m1	NM_007664.4
3	Cdh3	mCG20482	Mm01249209_m1	NM_007665.2
4	Cdh4	mCG116031	Mm00486926_m1	NM_009867.2
5	Cdh5	N.R.	Mm03053719_s1	NM_009868.4
6	Cdhr5	mCG23289	Mm00511182_m1	NM_028069.3
7	Cdh6	mCG8950	Mm00483230_m1	NM_007666.3
8	Cdh7	mCG14554	Mm00556135_m1	NM_172853.2
9	Cdh8	mCG124257	Mm01242096_m1	NM_001039154.1
10	Cdh11	mCG125313	Mm00515462_m1	NM_009866.4
11	Cdh12	mCG19771	Mm01165359_m1	NM_001008420.2
12	Cdh13	mCG141363	Mm00490584_m1	NM_019707.4
13	Cdh15	mCG19581	Mm00483191_m1	NM_007662.2
14	Cdh16	mCG23406	Mm00483196_m1	NM_007663.2
15	Cdh17	mCG5094	Mm00490692_m1	NM_019753.4
16	Cdh20	mCG3576	Mm00457145_m1	NM_011800.4
17	Cdh22	mCG17522	Mm00558118_m1	NM_174988.3
18	Cdh23	mCG1819	Mm00465755_m1	NM_023370.2
19	Cdh24	mCG133655	Mm01313848_g1	NM_199470.2
20	Pcdh1	mCG142244	Mm00547091_s1	NM_029357.3
21	Pcdh7	mCG9825	Mm00479579_m1	NM_018764.2
22	Pcdh8	mCG19385	Mm00480660_m1	NM_001042726.3
23	Pcdh9	N.R.	Mm03038601_m1	NM_001081377.1
24	Pcdh10	mCG7131	Mm00477987_s1	NM_001098171.
25	Pcdh11x	mCG51196	Mm01221603_m1	NM_001081385.1
26	Pcdh12	mCG18330	Mm00450488_m1	NM_017378.2
27	Pcdh15	mCG114141	Mm00480870_m1	NM_001142735.1
28	Pcdh18	mCG7322	Mm00499890_m1	NM_130448.3
29	Pcdh20	mCG17884	Mm00724499_m1	NM_178685.5
30	Epha1	mCG17082	Mm00445804_m1	NM_023580.4
31	Epha2	mCG10037	Mm00438726_m1	NM_010139.2
32	Epha3	mCG127999	Mm00580743_m1	NM_010140.3
33	Epha4	mCG119512	Mm00433056_m1	NM_007936.3
34	Epha5	mCG5337	Mm00433074_m1	NM_007937.3
35	Epha6	mCG127847	Mm00433094_m1	NM_007938.2
36	Epha7	mCG14600	Mm00833876_m1	NM_010141.3
37	Epha8	mCG9328	Mm00433106_m1	NM_007939.2
38	Epha10	mCG17241	Mm00624498_m1	NM_177671.5
39	Ephb1	mCG140739	Mm00557961_m1	NM_173447.3
40	Ephb2	mCG120083	Mm01181015_m1	NM_010142.2
41	Ephb3	mCG129784	Mm00802553_m1	NM_010143.1
42	Ephb4	mCG6855	Mm01201157_m1	NM_001159571.1
43	Ephb6	mCG4984	Mm00432456_m1	NM_001146351.1
44	Efna1	mCG17554	Mm00438660_m1	NM_010107.4
45	Efna2	mCG13393	Mm00433011_m1	NM_007909.3
46	Efna3	mCG17541	Mm01212723_g1	NM_010108.1
47	Efna4	mCG17548	Mm00433013_m1	NM_007910.2
48	Efna5	mCG50503	Mm00438665_m1	NM_010109.3

49	Efnb1	mCG51675	Mm00438666_m1	NM_010110.4
50	Efnb2	mCG17314	Mm00438670_m1	NM_010111.5
51	Efnb3	mCG20906	Mm00433016_m1	NM_007911.5
52	Sema3b	mCG18861	Mm01230580_g1	NM_001042779.1
53	Sema3c	mCG6382	Mm00443121_m1	NM_013657.5
54	Sema3d	mCG115650	Mm00712652_m1	NM_028882.4
55	Sema3e	mCG148351	Mm00809130_s1	NM_011348.2
56	Sema3f	mCG18872	Mm00441325_m1	NM_011349.3
57	Sema4b	mCG19462	Mm00803797_m1	NM_013659.4
58	Sema4d	mCG1273	Mm00443147_m1	NM_013660.3
59	Sema4g	mCG16919	Mm00442518_m1	NM_011976.1
60	Sema5a	mCG141513	Mm00436500_m1	NM_009154.2
61	Sema5b	mCG130168	Mm00443163_m1	NM_013661.2
62	Sema6a	mCG8025	Mm00444441_m1	NM_018744.2
63	Sema6c	mCG13711	Mm00441345_m1	NM_011351.1
64	Sema7a	mCG132078	Mm00441361_m1	NM_011352.2
65	Sema3a	mCG16225	Mm00436469_m1	NM_009152.3
66	Sema4a	mCG8826	Mm00443140_m1	NM_001163490.1
67	Sema4f	mCG126253	Mm00441343_m1	NM_011350.3
68	Sema6b	mCG22980	Mm00443176_m1	NM_001130456.1
69	Sema6d	mCG142100	Mm00553142_m1	N.R.
70	Plxdc2	mCG19758	Mm00470649_m1	NM_026162.5
71	Plxna1	mCG126649	Mm00501110_m1	NM_008881.2
72	Plxna2	mCG116593	Mm00801930_m1	NM_008882.2
73	Plxna3	mCG21221	Mm00501170_m1	NM_008883.2
74	Plxna4	mCG141681	Mm00558881_m1	NM_175750.3
75	Plxnb1	mCG16096	Mm00555359_m1	NM_172775.2
76	Plxnb3	mCG8090	Mm00502216_m1	NM_019587.2
77	Plxnc1	mCG4296	Mm00450687_m1	NM_018797.2
78	Plxnd1	mCG132454	Mm01184367_m1	NM_026376.3
79	Plxnb2	mCG140951	Mm00507118_m1	NM_138749.2
80	Plxdc1	mCG21901	Mm00511436_m1	NM_028199.3
81	Wnt1	mCG18420	Mm00810320_s1	NM_021279.4
82	Wnt2	mCG13463	Mm00470018_m1	NM_023653.5
83	Wnt3	mCG19162	Mm00437336_m1	NM_009521.2
84	Wnt5a	N.R.	Mm03053674_s1	NM_009524.2
85	Wnt5b	mCG131712	Mm00437350_m1	NM_009525.3
86	Nrg3	mCG112807	Mm01209104_m1	NM_001190187.1
87	Nrg1	mCG130630	Mm01212130_m1	NM_178591.2
88	Slc12a5	mCG17512	Mm00803929_m1	NM_020333.2
89	Cxcr7	N.R.	Mm02619632_s1	NM_007722.3
90	Cxcr4	mCG20049	Mm01996749_s1	NM_009911.3
91	Sst	mCG125080	Mm00436671_m1	NM_009215.1
92	Lhx6	mCG22275	Mm00748360_s1	NM_001083126.1
93	Htr3a	mCG3840	Mm00442874_m1	NM_001099644.1
94	Cux1	mCG18016	Mm00501628_m1	NM_009986.3
95	Tbr1	mCG15138	Mm00493433_m1	NM_009322.3

 Negative controls  
 Positive controls

**Table S2.** Differentially expressed genes between E17.5 and P4, related to Figure 1

Genes	FC	Relative to FC=1	SEM	P value
<b>Downregulated P4</b>				
Efnb1	0,131935146	-7,579481492	0,010858182	*** p <0.001
Wnt7b	0,148148267	-6,749994562	0,017206477	*** p <0.001
Epha3	0,219748185	-4,550663295	0,037137542	*** p <0.001
Pcdh18	0,219811865	-4,549344963	0,017100566	*** p <0.001
Wnt7a	0,232457458	-4,3018624	0,016432225	*** p <0.001
Ephb4	0,224967813	-4,445080319	0,022059064	*** p <0.001
Plxna2	0,265450635	-3,767178782	0,032048706	*** p <0.001
Cdh4	0,29277809	-3,415556127	0,021660232	*** p <0.001
Plxnb2	0,296951606	-3,367552082	0,025405263	*** p <0.001
Efnb2	0,299908779	-3,334347213	0,031361909	*** p <0.001
Plxnb1	0,339667339	-2,944056977	0,022038945	*** p <0.001
Plxna4	0,366218157	-2,730612832	0,016955931	*** p <0.001
Efna4	0,395010016	-2,531581376	0,06733275	*** p <0.001
Cdh2	0,428242303	-2,335126616	0,069073452	*** p <0.001
Cdh24	0,466286461	-2,144604408	0,018189949	*** p <0.001
Nrg1	0,56692132	-1,763913199	0,088376771	** p <0.01
Cdh8	0,57582162	-1,736648931	0,064383999	*** p <0.001
Plxna3	0,630977093	-1,584843588	0,080091429	** p <0.01
Epha7	0,6333961	-1,578790902	0,019024541	*** p <0.001
Epha5	0,646999177	-1,545597019	0,074545367	** p <0.01
Plxnc1	0,717391125	-1,393939742	0,021142439	*** p <0.001
Pcdh7	0,729026353	-1,371692526	0,102642193	* p <0.05
Ephb1	0,832465427	-1,201251088	0,038791808	*** p <0.001
Genes	FC	Relative to FC=1	SEM	P value
<b>Upregulated P4</b>				
Efnb3	1,427387934	1,427387934	0,122268558	* p <0.05
Sema6b	1,354327	1,354327	0,109117005	* p <0.05
Sema4a	1,690684	1,690684	0,292424279	* p <0.05
Plxna1	2,027104	2,027104	0,223528133	** p <0.01
Sema4f	2,260192	2,260192	0,228407523	** p <0.01
Efna3	2,185114	2,185114	0,421707061	* p <0.05
Cdh6	2,548228	2,548228	0,074748942	*** p <0.001
Pcdh15	2,592109	2,592109	0,123544917	*** p <0.001
Ephb6	2,957104	2,957104	0,118839367	*** p <0.001
Cdh20	3,301568	3,301568	0,38665171	** p <0.01
Pcdh11x	4,405326	4,405326	0,164233786	*** p <0.001
Nrg3	3,026187	3,026187	0,883286483	** p <0.01
Plxnd1	5,129877	5,129877	0,537959669	*** p <0.001
Pcdh20	5,730245	5,730245	0,24173881	*** p <0.001
Epha6	5,898654	5,898654	0,784251166	*** p <0.001
Plxdc2	7,286740	7,286740	0,91754569	*** p <0.001
Epha8	7,465011	7,465011	0,166917298	*** p <0.001
Efna5	7,852177	7,852177	0,307935615	** p <0.01
Sema7a	8,325405038	8,325405038	1,209628999	** p <0.01

**Table S3.** Summary of data and statistical analyses, related to Figures 1, 3, 4, 5, 6 and 7

FIGURE 1	Measurement	Values	N	Statistical	P value
Fig 1E	Fold change P4/E17.5 (mean ± SEM)	Shown separately in Source data 2	2 independent experiments	Student <i>t</i> -test	Source data 2
FIGURE 3	Measurement	Values	N	Statistical	P value
Fig 3H	Relative migrated distance (mean ± SEM)	Control: 1 ± 0.06; <i>Ig-Nrg1</i> : 1.33 ± 0.08 Control: 1 ± 0.06; <i>Nrg3</i> : 1.13 ± 0.06	Control: 19 explants; <i>Ig-Nrg1</i> : 24 explants Control: 19 explants; <i>Nrg3</i> : 20 explants	One way-ANOVA	p < 0.01 (**) p = 0.157
Fig 3I	Colocalizing area (%) (mean ± SEM)	Control: 2.7 ± 0.6%; <i>CRD-Nrg1</i> : 8.7 ± 1.7% Control: 2.7 ± 0.6%; <i>Nrg3</i> : 6.8 ± 0.9%	Control: 24 explants; <i>CRD-Nrg1</i> : 29 explants Control: 24 explants; <i>Nrg3</i> : 27 explants	One way-ANOVA	p < 0.01 (**) p < 0.01 (**)
Fig 3M	Colocalizing area (%) (mean ± SEM)	<i>ErbB4+/-;HER4heart</i> . Mock: 1.9 ± 0.3%; <i>Nrg3</i> : 7.6 ± 0.8 % <i>ErbB4-/-;HER4heart</i> . Mock: 2.1 ± 0.6%; <i>Nrg3</i> : 2.1 ± 0.5%	<i>ErbB4+/-;HER4heart</i> . Mock: n = 33 explants <i>Nrg3</i> : n = 25 explants <i>ErbB4-/-;HER4heart</i> . Mock: n = 15 explants <i>Nrg3</i> : n = 14 explants	One way-ANOVA	p < 0.001 (***) p = 0.999
FIGURE 4	Measurement	Values	N	Statistical	P value
Fig 4E	Relative migrated distance (mean ± SEM)	Control: 1 ± 0.07; <i>Nrg3</i> : 1.5 ± 0.06 Control: 1 ± 0.07; <i>Nrg3</i> + <i>Cxcl12</i> : 2.1 ± 0.1	Control: n = 18 explants; <i>Nrg3</i> : n = 15 explants Control: n = 18 explants; <i>Nrg3</i> + <i>Cxcl12</i> : n = 27 explants	One way-ANOVA	p < 0.05 (*) p < 0.001 (***)
Fig 4F	Colocalizing area (%) (mean ± SEM)	Control: 2.2 ± 0.7; <i>Nrg3</i> : 7 ± 1.3 Control: 2.2 ± 0.7; <i>Nrg3</i> + <i>Cxcl12</i> : 9.2 ± 1	Control: n = 18 explants; <i>Nrg3</i> : n = 15 explants Control: n = 18 explants; <i>Nrg3</i> + <i>Cxcl12</i> : n = 27 explants	One way-ANOVA	p < 0.05 (*) p < 0.001 (***)
Fig 4I	Cells in red (first) lane (%) (mean ± SEM)	<i>Nrg3/Nrg3</i> : 48.08 ± 1.65%; <i>Nrg3</i> vs GST: 43.41 ± 5.48% <i>Cxcl12/Cxcl12</i> : 50.9 ± 0.54%; <i>Nrg3/Cxcl12</i> : 24.34 ± 2.8%	<i>Nrg3/Nrg3</i> : n = 11; <i>Nrg3/GST</i> : n = 20 <i>Cxcl12/Cxcl12</i> : n = 13; <i>Nrg3/Cxcl12</i> : n = 18	One way-ANOVA	p < 0.001 (***) p < 0.001 (***)
FIGURE 5	Measurement	Values	N	Statistical	P value
Fig 5D	Density of Nkx2.1+ in CP (mean ± SEM)	Control: 3607 ± 166.6 cells/mm2; <i>Nrg3</i> : 4740.3 ± 143.3 cells/mm2	Control: n = 6 embryos; <i>Nrg3</i> : n = 6 embryos	Student <i>t</i> -test	p < 0.001 (***)
FIGURE 6	Measurement	Values	N	Statistical	P value
Fig 6C	<i>ErbB4</i> + cells (%) (mean ± SEM)	Controls: 10.12 ± 0.73 % [I], 13.65 ± 2.04% [II-III], 13.53 ± 1.05% [IV], 24.86 ± 1.14% [V], 37.83 ± 0.78% [VI]; <i>Nrg3</i> mutants: 9.38 ± 0.7% [I], 19.37 ± 0.37% [II-III], 18.65 ± 0.95% [IV], 21.96 ± 0.33% [V], 30.63 ± 1.71% [VI]	n = 4 for each genotype	χ <sup>2</sup>	p < 0.05 (*) for layers II-III, IV, V, VI
Fig 6F	PV+ cells (%) (mean ± SEM)	Controls: 0.32 ± 0.24 % [I], 12.72 ± 0.8% [II-III], 29.41 ± 0.87% [IV], 37.82 ± 0.53% [V], 19.7 ± 0.44% [VI]; <i>Nrg3</i> mutants: 0.31 ± 0.09% [I], 16.36 ± 0.59% [II-III], 30.88 ± 1.23% [IV], 35.74 ± 0.93% [V], 16.69 ± 1.28% [VI]	n = 5 for each genotype	χ <sup>2</sup>	p < 0.05 (*) for layer II-III
Fig 6I	Lhx6+ cells (%) (mean ± SEM)	Controls: 4.93 ± 1.09% [I], 30.17 ± 1.71% [II-III/IV], 41.16 ± 0.99% [V], 23.73 ± 1.29% [VI]; <i>Nrg3</i> mutants: 6.2 ± 1.38% [I], 35.15 ± 1.39% [II-III/IV], 39.61 ± 1% [V], 19.04 ± 1.8% [VI]	n = 5 for each genotype	χ <sup>2</sup>	p < 0.05 (*) for layers II-III and IV
FIGURE 7	Measurement	Values	N	Statistical	P value
Fig 7F	Density of PV+ interneurons (mean ± SEM)	Controls: 8.85 ± 5.50 cells/mm2 [I], 144.29 ± 19.22 cells/mm2 [II-III], 244.44 ± 16.21 cells/mm2 [IV], 274.78 ± 11.69 cells/mm2 [V], 147.37 ± 12.49 cells/mm2 [VI]; <i>ErbB4</i> mutants: 20.32 ± 4.51 cells/mm2 [I], 193.27 ± 7.95 cells/mm2 [II-III], 198.97 ± 10.37 cells/mm2 [IV], 241.67 ± 23.97 cells/mm2 [V], 79.9 ± 10.06 cells/mm2 [VI]	n = 5 for each genotype	χ <sup>2</sup>	p < 0.05 (*) for layers II-III and VI
Fig 7G	PV+/BrdU 12.5 cells (%) (mean ± SEM)	Controls: 4.38 ± 0.09% [II-III], 13.74 ± 3.89% [IV], 43.47 ± 5.18% [V], 38.19 ± 2.44% [VI]; <i>ErbB4</i> mutants: 6.1 ± 2.26% [II-III], 15.17 ± 2.75% [IV], 58.34 ± 3.34% [V], 21.55 ± 1.85% [VI]	n = 5 for each genotype	χ <sup>2</sup>	p < 0.05 (*) for layers V and VI
Fig 7H	PV+/BrdU 15.5 cells (%) (mean ± SEM)	Controls: 53.3 ± 5.86% [II-III], 42.6 ± 3.42% [IV], 4.01 ± 2.76% [V]; <i>ErbB4</i> mutants: 74.35 ± 2.65% [II-III], 17.41 ± 2.28% [IV], 11.13 ± 2.5% [V]	n = 5 for each genotype	χ <sup>2</sup>	p < 0.05 (*) for layers II-III and IV
FIGURE S1	Measurement	Values	N	Statistical	P value
Fig S1E	Radially migrating cells (%) (mean ± SEM)	Vehicle: 10 ± 1.3%; Control: 32 ± 4.1%	2 independent experiments; n = 240 cells	Student <i>t</i> -test	p < 0.001 (***)
FIGURE S3	Measurement	Values	N	Statistical	P value
Fig S3B	Relative <i>Nrg3</i> protein levels (mean ± SEM)	Control: 1 ± 0.21 a.u.; <i>Nestin-Cre</i> : 0.02 ± 0.02 a.u.; <i>Nex-Cre</i> : 0.18 ± 0.07 a.u.	n = 4 for each genotype	One way-ANOVA	p < 0.001 (**)
FIGURE S4	Measurement	Values	N	Statistical	P value
Fig S4C	<i>Cux2</i> + cells (%) (mean ± SEM)	Controls: 1.55 ± 0.64 % [I], 40.12 ± 0.80% [II-III], 50.09 ± 1.65% [IV], 2.28 ± 0.29% [V], 5.97 ± 1.50% [VI]; <i>Nrg3</i> mutants: 1.07 ± 0.14 % [I], 42.32 ± 0.87 % [II-III], 49.50 ± 0.81% [IV], 2.57 ± 0.24% [V], 4.53 ± 0.60% [VI]	n = 4 for each genotype	χ <sup>2</sup>	p = 1
Fig S4F	<i>Ctip2</i> + cells (%) (mean ± SEM)	Controls: 0.01 ± 0.01 % [I], 1.80 ± 0.06% [II-III], 3.28 ± 0.85% [IV], 23.33 ± 1.15% [V], 71.48 ± 1.63% [VI]; <i>Nrg3</i> mutants: 0.10 ± 0.00% [I], 1.15 ± 0.19% [II-III], 1.08 ± 0.07% [IV], 25.33 ± 1.31% [V], 72.33 ± 1.43% [VI]	n = 4 for each genotype	χ <sup>2</sup>	p = 1