INVENTORY:

I-A word file containing:

Figure S1, related to Figure 2, and corresponding legend.

Figure S2, related to Figure 4, and corresponding legend.

Figure S3, related to Figure 5, and corresponding legend.

Figure S4, related to Figure 6, and corresponding legend.

Figure S5, related to Figure 7, and corresponding legend.

Supplemental Table II

Supplemental Table legends

Legends to supplemental movies

Supplemental Experimental Procedures

II-Excel file containing Supplemental Table I

III-Multimedia Files

Video 1, related to Figure 4

Video 2, related to Figure 4

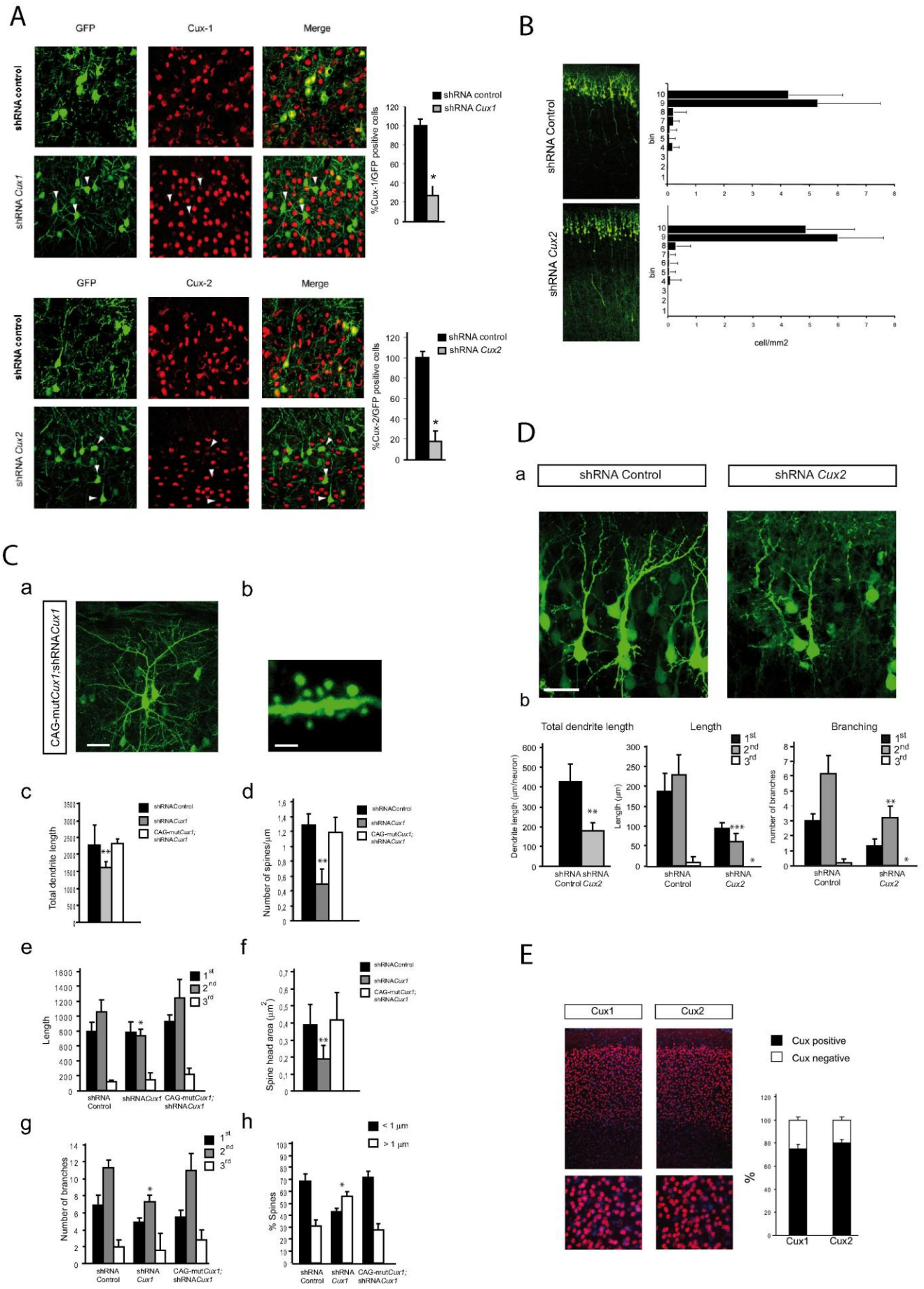
Video 3, related to Figure 4

Video 4, related to Figure 4

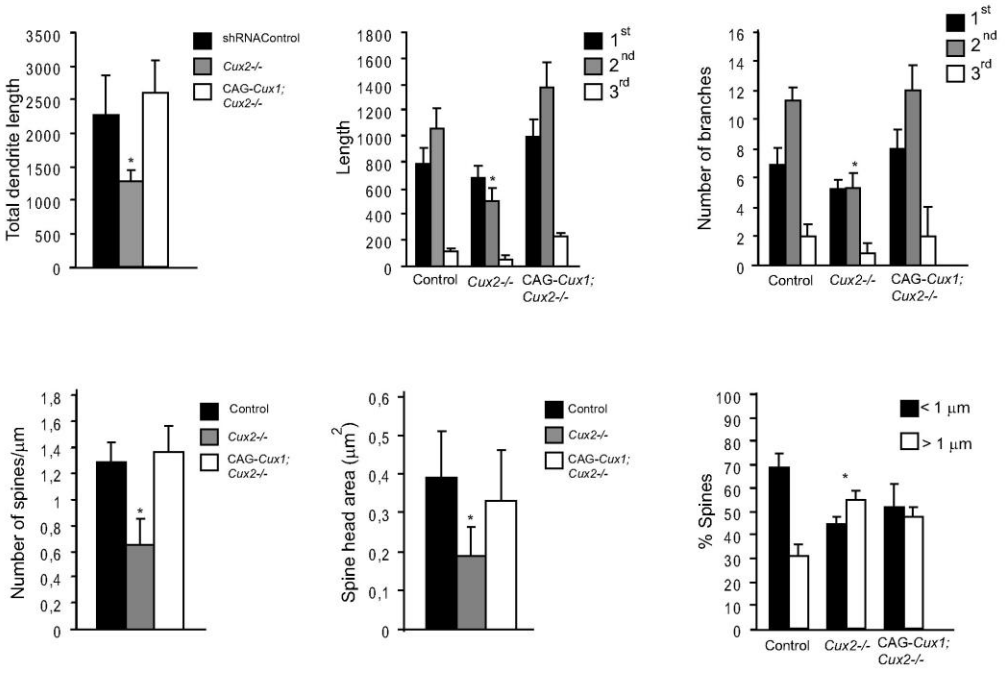
Video 5, related to Figure 6

Video 6, related to Figure 6

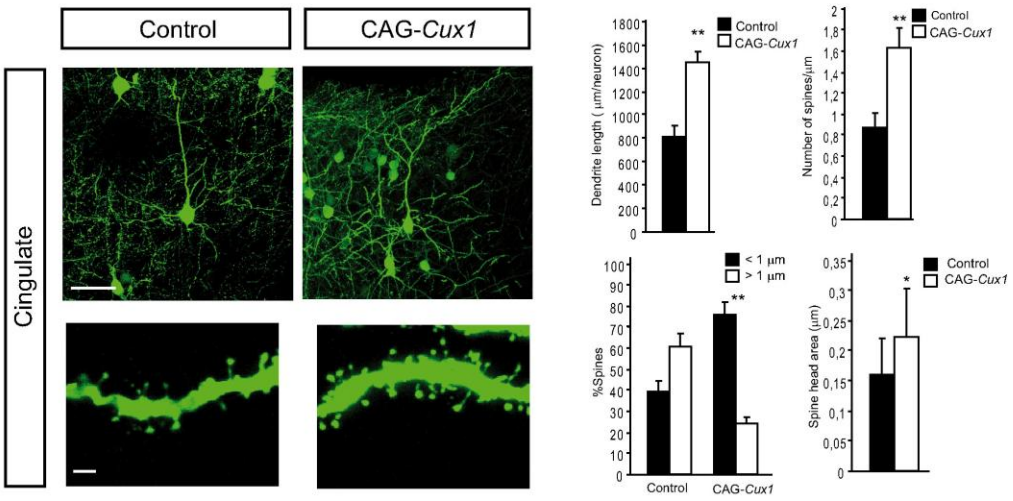
Figure S1, related to Figure 2



F

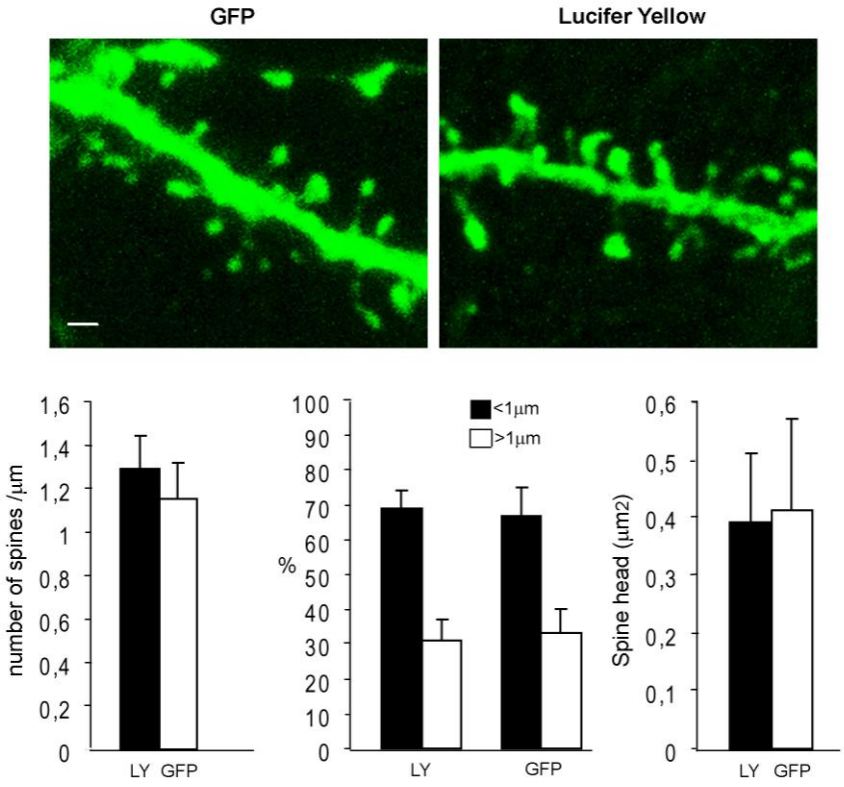

Total dendrite length
shRNAControl
Cux2-/-
CAG-Cux1; Cux2-/-
Length
1st
2nd
3rd
Control
Cux2-/-
CAG-Cux1; Cux2-/-
Number of branches
Number of spines/µm
Spine head area (µm2)
% Spines
< 1 µm
> 1 µm

G


Control
CAG-Cux1
Cingulate
Dendrite length (µm/neuron)
Number of spines/µm
%Spines
Spine head area (µm)
< 1 µm
> 1 µm

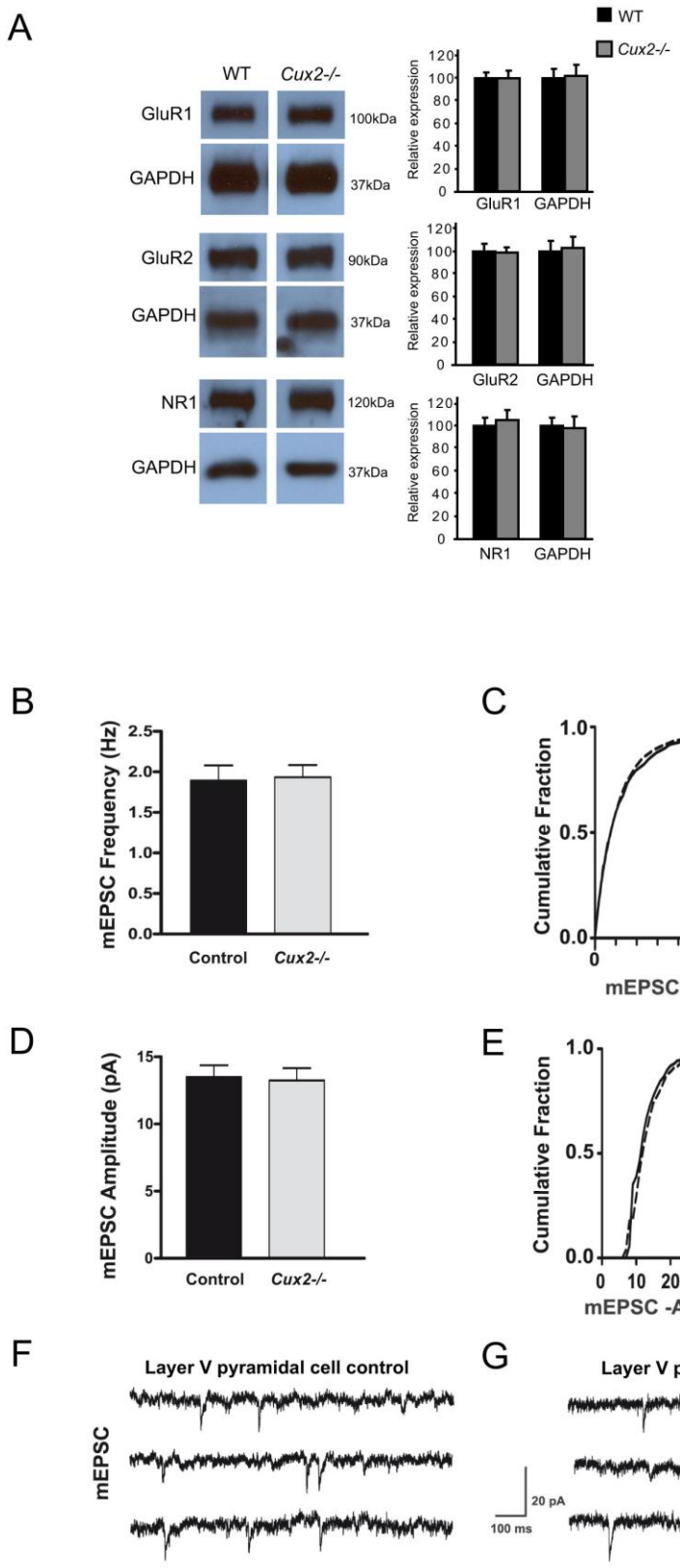
Supplemental Figure 1. **A)** ***In utero electroporation of shRNA lentiviral constructs in E15.5 neuronal precursors efficiently suppresses Cux1 and Cux2 in P21 layer II-III neurons.*** Expression of Cux1 or Cux2 protein (red) in GFP-expressing layer II-III neurons of the P21 cortex electroporated at E15.5. Cux proteins are expressed normally in GFP positive shRNA control targeted neurons but are down-regulated in neurons electroporated with shRNA targeting *Cux1* or *Cux2* (arrowheads). Graphs represent the proportion of GFP positive neurons expressing the indicated Cux protein. * $p<0.001$ compared to control. **B)** ***In utero electroporation of shRNA lentiviral constructs in E15.5 neuronal precursors does not affect the generation or migration of upper layer neurons.*** The percentage of GFP positive neurons in each bin was quantified in P4 sections. Cells were located in the most superficial layers corresponding to their birth date **C)** ***Dendrite branching and spine development is not affected in neurons coelectroporated with a mutated resistant form of Cux1 and shRNAs targeting Cux1.*** Left panels show quantification of dendrite defects **a)** GFP positive neuron coelectroporated with a mutated resistant form of *Cux1* (mut*Cux1*) and shRNAs targeting *Cux1*. **c, e, g)** Quantitative analysis of dendritic arbors in GFP-positive neuron in layers II-III. shRNA control (n= 15), shRNA *Cux1* (n=15) and CAG-mut*Cux1;* shRNA*Cux1* (n=15). * $p<0.01$, and ** $p<0.001$ compared with control. **b)** dendritic spines of neurons coelectroporated with mut*Cux1* and shRNAs targeting *Cux1*. **d, f, h)** Quantitative analysis of dendritic spine defects. $n\geq 15$ dendrite segments and $n\geq 500$ spines for each sample. Equivalent results were obtained for mut*Cux2*. **D)** ***Cux2 controls mechanisms of early dendritic differentiation.*** *In vivo* knock-down of *Cux2* with shRNA lentiviral constructs decreases the number and length of dendrite processes of P4 differentiating layer II-III neurons. **a)** Representative confocal micrographs of a P4 cortex showing GFP-positive layer II-III neurons co-expressing control or shRNA *Cux2*. Bar represents 25 μm. **b)** Quantitative analysis of dendrite morphology defects in *Cux2*-suppressed layer II-III neurons. * $p<0.05$, ** $p<0.01$, and *** $p<0.001$ compared with control. **E)** ***Cux1 and Cux2 protein staining in cortical sections indicates co-expression of both proteins in a subpopulation of cortical neurons***. Quantification of Cux1 or Cux2 positive upper layer neurons in the somatosensory cortex. **F)** ***Over-expression of Cux1 in Cux2-/- upper layer neurons rescues dendritic arborization and spine defects.*** Quantification of dendritic arbors, dendritic spine number and dendritic spine morphology. * $p< 0.001$, compared with control. **G)** ***Dendritic arborization and spine formation in neurons of the cingulate cortex is increase upon Cux1 overexpression.*** Upper panels show representative confocal images of GFP positive neurons and spines of the cingulate cortex electroporated with control plasmids or CAG-*Cux1*. Bar represents 25 μm (upper panels) and 2,5 μm (lower panels). Graphs show quantification of dendritic arbors, dendritic spine number and dendritic spine morphology. * $p<0.005$, ** $p<0.001$, compared with control.

Figure S2 related to Figure 4



Supplemental Figure 2. ***Analysis of GFP label dendritic spines in electroporated upper layer neurons compared to Luciferase Yellow (LY) microinjected cells.*** Representative micrographs showing confocal images of dendritic spines of GFP-positive and Luciferase Yellow (LY) layer II-III neurons in P21 animals. GFP in the P21 cortex was induced by *in utero* electroporation of E15.5 neuronal precursors. Graphs represent the quantitative analysis of dendritic spine numbers, dendritic spine length and morphology. Bar represents 1 μm. No significant differences were found.

Figure S3 related to Figure 5

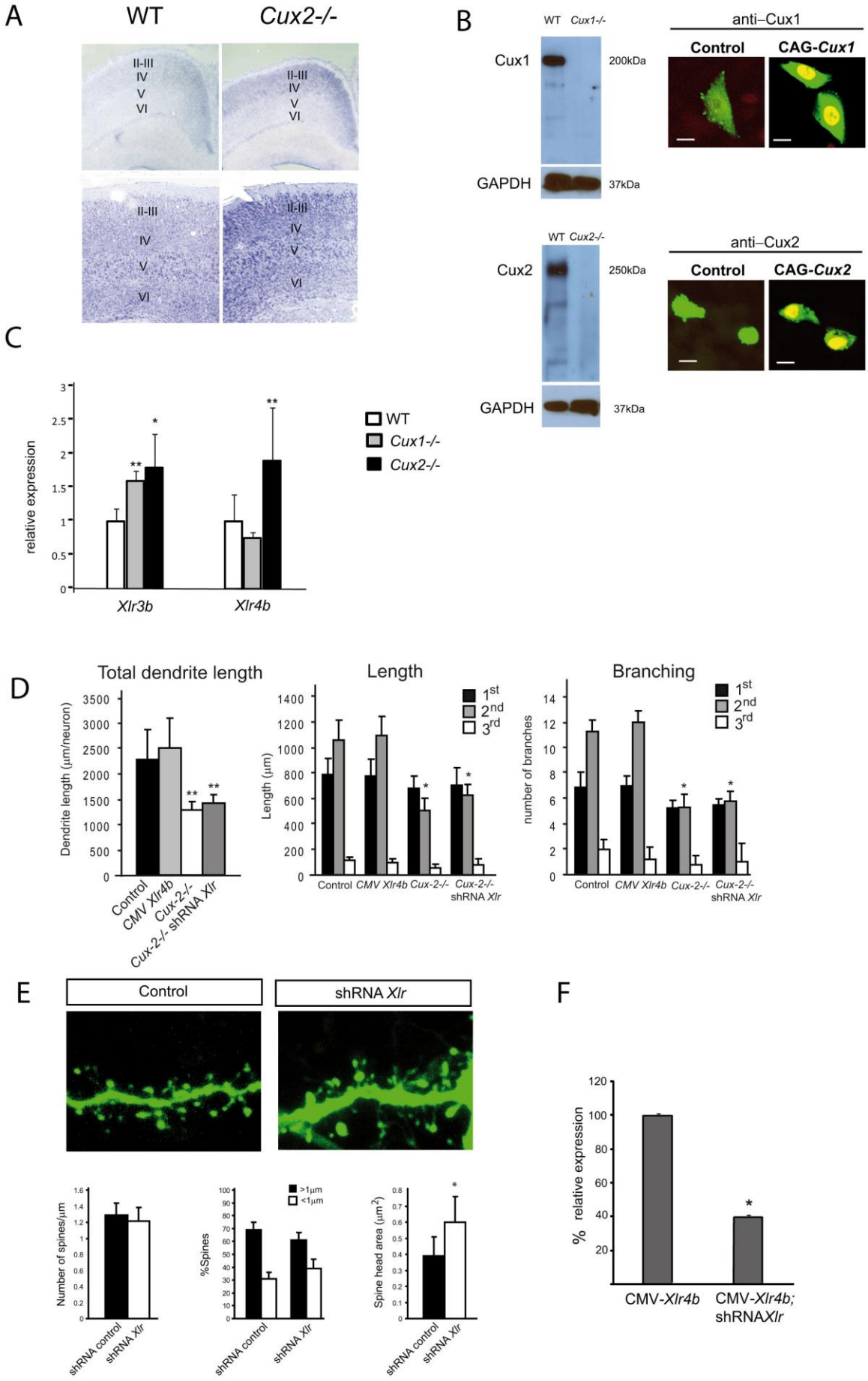


Supplemental Figure 3. A) Western blot analysis of the expression of GluR1, GluR2 and NR1 (NMDAR1) in total cortical lysates. WT (n=3) and *Cux2-/-* (n=3). Graphs show the mean and SD signal quantification of the relative amount of protein in WT and *Cux2-/-* cortices. GAPDH is shown as control. **B-G) mEPSC amplitude and frequency in layer V pyramidal cells**: **B)** Average frequency of mEPSC of layer V pyramidal cells from *Cux2+/-* and *Cux2-/-* mice. Average frequency of mEPSC in layer V pyramidal cells did not differ between *Cux2+/-* and *Cux2-/-* mice ($p > 0.5$, Student's unpaired t test, n = 15 and 15 cells, respectively). **C) Cumulative fraction curves of interevent intervals (IEIs) for mEPSC of layer V pyramidal cells**. Data shows no difference between *Cux2+/-* and *Cux2-/-* mice ($p > 0.5$, K-S test). **D) Average amplitude of mEPSC in layer V pyramidal cells.** No differences were found between *Cux2+/-* and *Cux2-/-* mice ($p > 0.5$, Student's, unpaired t test, n = 15 and 15 cells, respectively). **E) Cumulative fraction curves of amplitude of layer V pyramidal** were similar for both *Cux2+/-* and *Cux2-/-* mice ($p > 0.5$, K-S test). **F, G) Representative traces of mEPSC from layer V pyramidal cells of *Cux2+/-* and *Cux2-/-* mice.** Data in bar graphs depict mean ± SEM; *Cux2+/-*: black bars; *Cux2-/-*: gray bars. IEI: Interevent interval. mEPSC: miniature excitatory postsynaptic currents.

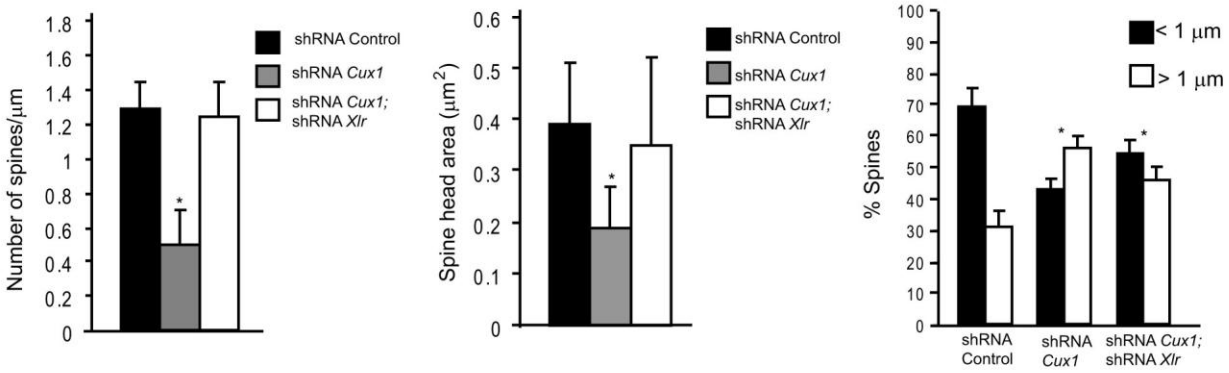
mEPSC frequency and amplitude (mean ± SEM)

Layer V	*Cux2+/-*	*Cux2-/-*
mEPSC frequency	1.90 ± 0.19 (n=15)	1.94 ± 0.15 (n=15)
mEPSC amplitude	13.50 ± 0.87 (n=15)	13.25 ± 0.91 (n=15)

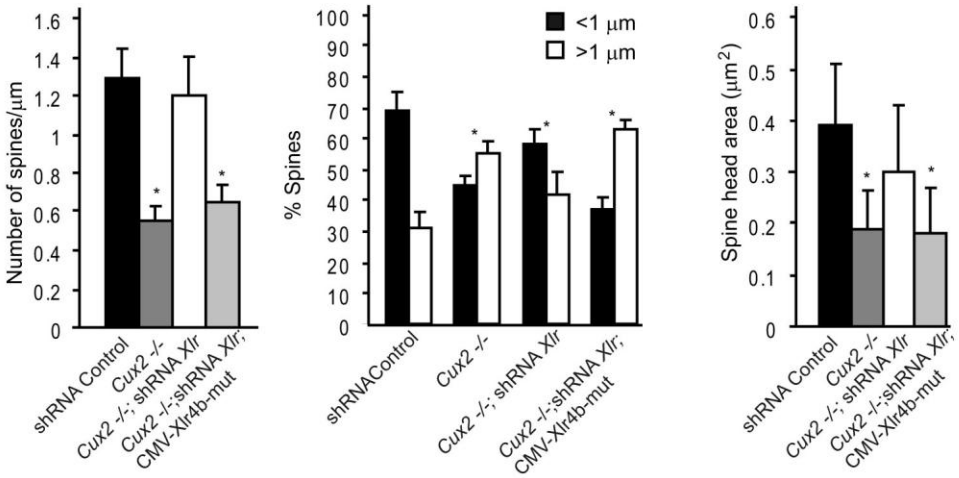
Figure S4 related to Figure 6



G


Number of spines/μm
shRNA Control
shRNA Cux1
shRNA Cux1; shRNA Xlr
Spine head area (μm2)
% Spines
< 1 μm
> 1 μm
shRNA Control
shRNA Cux1
shRNA Cux1; shRNA Xlr

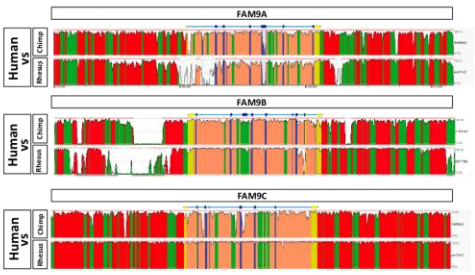
H


Number of spines/μm
shRNA Control
Cux2 -/-
Cux2 -/-; shRNA Xlr
Cux2 -/-;shRNA Xlr; CMV-Xlr4b-mut
% Spines
<1 μm
>1 μm
shRNAControl
Cux2 -/-
Cux2 -/-; shRNA Xlr
Cux2 -/-;shRNA Xlr; CMV-Xlr4b-mut
Spine head area (μm2)
shRNA Control
Cux2 -/-
Cux2 -/-; shRNA Xlr
Cux2 -/-;shRNA Xlr; CMV-Xlr4b-mut

Supplemental Figure 4. A) ***Xlr4 expression in the cortex.*** Expression patterns of *Xlr* genes in different brain regions have been well characterized by RT-PCR (Raefski and O´Neill 2005. Nat Genetics 37:620; Davies et al., 2005. Nat Genetics 37:625). The detailed study of the expression patterns of each *Xlr* gene by *insitu* hybridization is hindered by the high sequence homology of their coding and non coding regions. *In situ* hybridization with a probe for *Xlr4a, b* and *c shows* mRNA expression in P2 (upper panels) and adult (lower panels) WT and *Cux2-/-* cortex. Specific signal was weak in the cortex of WT animals, and background was higher in adult animals. At P2, cingulate cortex, where *Cux1* expression is weaker, gave higher signal than somatosensory areas. In the *Cux2* knock out expression of *Xlr4* mRNAs is increased in the upper layer neurons **B)** ***Characterization of anti-Cux1 and anti-Cux2 antibodies.*** (Left) We confirm that antibodies used for ChIP experiments specifically recognize Cux proteins in lysates from WT cortex but not from *Cux1-/-* or *Cux2-/-* cortex. (Right) Anti-Cux1 and anti-Cux2 antibodies also specifically reacted with Cux1 or Cux2 nuclear protein on COS transfected cells. Bar represents 5μm **C)** ***Cux1 and Cux2 regulate Xlr3b and Xlr4b genes.*** *Xlr3b* and *Xlr4b* expression in WT, *Cux1-/-* and *Cux2-/-* E18 cortex. Expression of *Xlr4b* and *Xlr3b* mRNA is shown in relation to one control sample normalized as 1. Expression of *Xlr* genes is shown as the ratio of the amounts of *Xlr* and *GAPDH* transcripts measured by Q-PCR in total RNA obtained from the cortex of control (*Cux1+/+; Cux2+/+* or *Cux1+/- ;Cux2+/+* or *Cux1+/+ ;Cux2+/-*) (n=5), *Cux1-/-* (n=3) and *Cux2-/-* (n=5) animals.* $p<0.05$ and **$p<0.01$. RT-PCR analysis has shown that dynamic imprinted patterns regulate the developmental expression of *Xlr* genes in different brain regions (Davies et al., 2005; Raefski and O'Neill, 2005). **D)** ***Overexpression or knock down of Xlr genes in WT or Cux2-/- upper layer neurons does not affect dendritic branching***. Dendritic branching and length was evaluated in each condition. CMV empty vector or shRNA *Xlr* alone gave equal results did not affect branching and are represented as control. * $p<0.01$; ** $p<0.001$ compared to control. **E)** ***Knock down of Xlr genes in WT upper layer neurons increases the surface of the dendritic spine head.*** The number, length and the surface area of the head of dendritic spines were measured in the upper layer neurons generated after electroporation of the cortex of E15.5 WT embryos with shRNA lentiviral construct targeting *Xlr* genes. ** $p<0.05$ **F)** ***Efficient known down of Xlr4b using shRNA lentiviral constructs.*** *Xlr4b* expression was measured by Q-PCR in COS1 cells co-transfected with CMV-*Xlr4b* and a combination of three anti-*Xlr* shRNA lentiviral constructs described in Experimental Procedures. * $p<0.05$. **G)** ***Characterization of dendritic spine number and morphology in layer II-III neurons co-electroporated with shRNAs targeting Xlr genes and Cux1***. $n\geq 15$ dendrite segments and $n\geq 500$ spines for each sample.* $p<0.001$ compared to control shRNA. **H)** ***Number and morphology of dendritic spines is not affected in neurons coelectroporated with a mutated resistant form of Xlr4b and shRNAs targeting Xlr.*** The number, length and the surface area of the head of dendritic spines were measured in the upper layer neurons generated after electroporation of the cortex of E15.5. $n\geq 15$ dendrite segments and $n\geq 500$ spines for each sample. * $p<0.001$ compare to shRNA control.

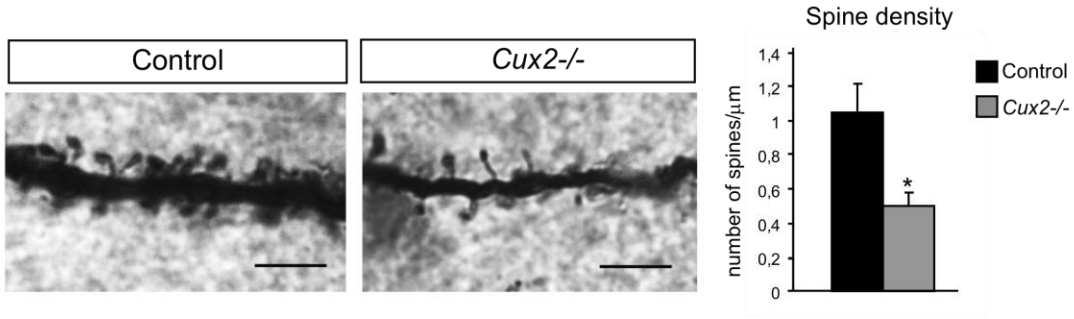
Figure S5 related to Figure 7

A



Gene	CDP BS Position (From ATG)	Genomic Location	ALIGNMENT
hFAM9A	+ 5.975	Intronic	H. Sapiens CCTAGTGTTCCATTATTGGAACG P.Pygmaeus CCTAGTGTTCCATTACTGGAACG M. Mulatta CCTAGTGTTCCATTATTGGAACG
hFAM9A	+ 1.317	Intronic	H. Sapiens ACGCAATTATCTATATAAC P.Pygmaeus ACGCAATTATCTATATAAC M. Mulatta ACGCAATTATCTATATAAC
hFAM9B	+ 15.924	3'Upstream	H. Sapiens -CCCAATAACCTATAG P.Pygmaeus CCCCAATAACCTATAG M. Mulatta -CCCAATAACCTATGT
hFAM9B	+ 14.073	3'Upstream	H. Sapiens CTGAAATGATCAATCATTTATTAGCT P. Throg. CTGAAATGATCAATCATTTATTAGCT P.Pygmaeus CTGAAATGATCAATCATTTATTAGCT M. Mulatta CTGAAATGATCAATCATTTATTAGCT
hFAM9B	+ 7.269	Intronic	H. Sapiens AAACTATAATCAATACATGGAGCTC P. Throg. AAACTATAATCAATACATGGAGCTC P.Pygmaeus AAACTATAATCAATACATGGAGCTC M. Mulatta AAACGATAATCAATACATGGAGCTC
hFAM9B	- 6.447	5'Upstream	H. Sapiens CACAAGTTAATCAATTCTGA P. Throg. CACAAGTTAATCAATTCTGA P.Pygmaeus CACAAGTTAATCAATTCTGA M. Mulatta CACAAGTTAATCAATTCTGA
hFAM9B	- 7.048	5'Upstream	H. Sapiens ACCTTA-TTGATCAGCATAT P. Throg. ACCTTATGTGATCAGCATAT P.Pygmaeus ACCTTA-TTGATCAGCATAT M. Mulatta ACCTTA-TTGATCAGCATAT
hFAM9C	+ 15.771	3'Upstream	H. Sapiens TGACTATAGATTATATTTTA P. Throg. TGACTATAGATTATATTTTA P.Pygmaeus TGACTATAGATTATATTTTA M. Mulatta TGACTATAGATTATATTTTA
hFAM9C	- 5.900	5'Upstream	H. Sapiens TCAGTATGGATTATATTATC P. Throg. TCAGTATGGATTATATTATC P.Pygmaeus TCAGTATGGATTATATTATC M. Mulatta TCAGTATGGATTATATTATC

B



Supplemental Figure 5. A) ***Analysis of Cux1 and Cux2 consensus binding sites in FAM9A, B, C genes.*** The upper panels show the analysis of conserved regions in *FAM9A, B* and *C* genes in primates and humans. The lower table shows conserved Cux binding sites found in primates. **B)** ***Dendritic spines defects in the prefrontal cortex.*** Representative micrographs showing dendritic spines of Golgi-Cox stained neurons in the prefrontal cortex of WT and *Cux2-/-* mice. Bars represent 10 μm. The histogram shows the quantification of spine density (n= 10; * $p < 0.05$).

Table II

GO ID	GO term	GO category	GO term in refseq	GO in dataset	p-value	adj. pvalue
	cholesterol monooxygenase (side-chain-cleaving)					
GO:0008386	activity		1	1	0,0058	0,0112
GO:0042497	triacylated lipoprotein binding		1	1	0,0058	0,0112
GO:0019770	IgG receptor activity		2	1	0,0087	0,0162
GO:0016491	oxidoreductase activity		641	6	0,0109	0,0202
GO:0005132	interferon-alpha/beta receptor binding		3	1	0,0115	0,0207
GO:0003998	acylphosphatase activity		4	1	0,0144	0,0249
GO:0004528	phosphodiesterase I activity		4	1	0,0144	0,0249
GO:0004551	nucleotide diphosphatase activity		4	1	0,0144	0,0249
GO:0016504	protease activator activity		4	1	0,0144	0,0249
GO:0019208	phosphatase regulator activity		4	1	0,0144	0,0249
GO:0004090	carbonyl reductase (NADPH) activity		5	1	0,0173	0,0291
GO:0042809	vitamin D receptor binding	molecular function	5	1	0,0173	0,0291
GO:0019864	IgG binding		6	1	0,0201	0,0332
GO:0004029	aldehyde dehydrogenase (NAD) activity		8	1	0,0258	0,0413
GO:0000146	microfilament motor activity		9	1	0,0286	0,0442
GO:0046966	thyroid hormone receptor binding		9	1	0,0286	0,0442
GO:0005932	basal body		9	2	0,0004	0,0009
GO:0045335	phagocytic vesicle		1	1	0,0058	0,0112
GO:0016459	myosin		43	2	0,0075	0,0144
GO:0009288	flagellum (sensu Bacteria)		2	1	0,0087	0,0162
GO:0042105	alpha-beta T cell receptor complex		4	1	0,0144	0,0249
GO:0005859	muscle myosin		8	1	0,0258	0,0413
GO:0030016	myofibril	cellular component	8	1	0,0258	0,0413
GO:0042101	T cell receptor complex		8	1	0,0258	0,0413
GO:0005786	signal recognition particle (sensu Eukaryota)		10	1	0,0314	0,0484
	positive regulation of tumor necrosis factor-alpha					
GO:0042535	biosynthesis		10	2	0,0005	0,0011
GO:0001747	eye development (sensu Mammalia)		35	2	0,0052	0,0102
GO:0007522	visceral muscle development		1	1	0,0058	0,0112
GO:0042495	detection of triacylated bacterial lipoprotein		1	1	0,0058	0,0112
GO:0043462	regulation of ATPase activity		1	1	0,0058	0,0112
GO:0008152	metabolism		560	6	0,0058	0,0112
GO:0008150	biological_process		1192	9	0,0073	0,014
GO:0001788	antibody-dependent cellular cytotoxicity		2	1	0,0087	0,0162
GO:0001812	positive regulation of type I hypersensitivity		2	1	0,0087	0,0162
GO:0045637	regulation of myeloid cell differentiation		2	1	0,0087	0,0162
GO:0046849	bone remodeling		2	1	0,0087	0,0162
GO:0001805	positive regulation of type III hypersensitivity		3	1	0,0115	0,0207
GO:0001820	serotonin secretion		3	1	0,0115	0,0207
GO:0002027	cardiac chronotropy		3	1	0,0115	0,0207
GO:0007090	regulation of S phase of mitotic cell cycle		3	1	0,0115	0,0207
GO:0030502	negative regulation of bone mineralization		3	1	0,0115	0,0207
	antigen presentation, exogenous antigen via MHC					
GO:0042590	class I		3	1	0,0115	0,0207
GO:0048739	cardiac muscle fiber development		3	1	0,0115	0,0207
GO:0051146	striated muscle cell differentiation		3	1	0,0115	0,0207
GO:0007160	cell-matrix adhesion		59	2	0,0135	0,0242
GO:0001798	positive regulation of type IIa hypersensitivity		4	1	0,0144	0,0249
	SRP-dependent cotranslational protein targeting to					
GO:0006614	membrane		4	1	0,0144	0,0249
GO:0035162	embryonic hemopoiesis		4	1	0,0144	0,0249
	detection of mechanical stimulus during sensory					
GO:0050974	perception		4	1	0,0144	0,0249
GO:0001701	embryonic development (sensu Mammalia)		63	2	0,0153	0,0263
GO:0001539	ciliary or flagellar motility		5	1	0,0173	0,0291
GO:0030239	myofibril assembly	biological process	5	1	0,0173	0,0291
GO:0031032	actomyosin structure organization and biogenesis		5	1	0,0173	0,0291
GO:0051090	regulation of transcription factor activity		5	1	0,0173	0,0291
GO:0006954	inflammatory response		187	3	0,0177	0,0298
GO:0007093	mitotic checkpoint		6	1	0,0201	0,0332
GO:0042116	macrophage activation		6	1	0,0201	0,0332
GO:0042574	retinal metabolism		6	1	0,0201	0,0332
GO:0045410	positive regulation of interleukin-6 biosynthesis		6	1	0,0201	0,0332
GO:0006952	defense response		200	3	0,0211	0,0347
	double-strand break repair via homologous					
GO:0000724	recombination		7	1	0,023	0,0375
GO:0006590	thyroid hormone generation		7	1	0,023	0,0375
GO:0007512	adult heart development		8	1	0,0258	0,0413
GO:0030595	immune cell chemotaxis		8	1	0,0258	0,0413
GO:0001892	embryonic placenta development		9	1	0,0286	0,0442
GO:0002026	cardiac inotropy		9	1	0,0286	0,0442
GO:0006910	phagocytosis, recognition		9	1	0,0286	0,0442
GO:0007250	activation of NF-kappaB-inducing kinase		9	1	0,0286	0,0442
GO:0030279	negative regulation of ossification		9	1	0,0286	0,0442
GO:0030500	regulation of bone mineralization		9	1	0,0286	0,0442
GO:0042088	T-helper 1 type immune response		9	1	0,0286	0,0442
GO:0045214	sarcomere organization		9	1	0,0286	0,0442
GO:0045576	mast cell activation		9	1	0,0286	0,0442

Supplemental Table I and II. Genes differentially expressed in *Cux2-/-* cortex. Table I. Genes differentially expressed in WT cortex versus *Cux2-/-* cortex according to the analysis of gene expression microarrays. For analysis of gene expression, raw data were quantile normalized and expression values (log2 transformed) were obtained for each probe. Next, differential expression was assessed using the linear modelling features of the limma package, a package of Bioconductor: http://www.bioconductor.org/. The M-value (M) is the value of the contrast, the log2-fold change between the two experimental conditions. Column t is the moderated t-statistics. pval is the p value associated of the moderated t-statistic. This value has to be adjusted for multiple testing. adj.pval: is the p value of the moderated t-statistic after some form of adjustment for multiple testing. **Table II**. Gene Ontology (GO) terms of genes differentially expressed in *Cux2-/-* cortex.

Movies legends

Supplemental video 1: 3D reconstruction of dendritic spines in upper layer neurons of WT mice. 3D image reconstruction of GFP positive dendritic spines obtained from serial confocal sections.

Supplemental video 2: 3D reconstruction of dendritic spines in upper layer neurons of *Cux2-/-* mice. 3D reconstruction of GFP positive dendritic spines obtained from using serial confocal sections.

Supplemental video 3: 3D reconstruction of dendritic spines in upper layer neurons after electroporation of shRNA targeting *Cux1*. 3D reconstruction of GFP positive dendritic spines obtained from using serial confocal sections.

Supplemental video 4: 3D reconstruction of dendritic spines in upper layer neurons after electroporation of shRNA targeting *Cux1* in *Cux2-/-* cortex. 3D reconstruction of GFP positive dendritic spines obtained from using serial confocal sections.

Supplemental video 5: 3D reconstruction of dendritic spines in upper layer neurons that over expressed *Xlr4b* in WT mice. 3D reconstruction of GFP positive dendritic spines obtained from using serial confocal sections.

Supplemental video 6: 3D reconstruction of dendritic spines in upper layer neurons after electroporation of shRNA targeting *Xlr* genes in *Cux2-/-* cortex. 3D reconstruction of GFP positive dendritic spines obtained from using serial confocal sections.

Supplemental Experimental Procedures

Electrophysiolgy

*Slice preparation:*Acute brain slices were prepared from *Cux2*+/- and *Cux2*-/- mice (P20) (n=15). Briefly, the mice were decapitated and the brains were rapidly removed in 4°C oxygenated (95% O2-5% CO2) slicing artificial cerebrospinal fluid (sACSF) consisting of (in mM) 220 sucrose, 3 KCl, 1.25 NaH2PO4, 2 MgSO4, 26 NaHCO3, 2 CaCl2, and 10 dextrose (295–305 mosM). Coronal slices (300 μm thick) were cut in 4°C oxygenated slicing medium using a vibroslicer model VT1000S (Leica, Nussloch, Germany). The slices were immediately transferred to a holding chamber, in which they remained submerged in oxygenated normal recording (nACSF) consisting of (in mM) 124 NaCl, 3 KCl, 1.25 NaH2PO4, 1.2 MgSO4, 26 NaHCO3, 2 CaCl2, and 10 dextrose (295–305 mOsm). Slices were heated to 37°C, held at 37°C for 45 min, and then cooled to room temperature. For each experiment, an individual slice was gently transferred to a submersion-type recording chamber, in which it was continuously perfused with oxygenated recording medium at 33–35°C.

Whole cell recording: Whole cell voltage-clamp recordings were obtained from layer II-III pyramidal cell neurons visually identified using an IR-DIC video microscopy system (Nikon, Tokyo, Japan). Patch electrodes (3–7 MΩ) were pulled from 1.5 mm OD borosilicate glass capillary tubing (World Precision Instruments) using a micropipette puller (P-97; Sutter Instruments, Novato, CA), coated with silicone elastomer (Northants, UK), and fire polished. Intracellular patch pipette solution for whole cell voltage-clamp recordings contained (in mM) 135 CsCl2, 10 NaCl, 2 MgCl2, 10 HEPES, 10 EGTA, 2 Na2ATP, 0.2 Na2GTP, and 1.25 QX-314, 0.05% Lucifer yellow CH, adjusted to pH 7.2 with CsOH (285–290 mosM). During the recordings each slice was persused with nACSF containing 1μM bicuculline and 1 μm Tetrodotoxine (TTX) to isolate the miniature EPSC (mEPSC). Cells were held at -70mV and the voltage and current were recorded with a Multiclamp 700B amplifier (Molecular Devices) and monitored with an oscilloscope and with pClamp 10.0 software (Molecular Devices). Whole-cell voltage-clamp data were low-pass filtered at 1 kHz (–3 dB, eight-pole Bessel), digitally sampled at 20 kHz. Whole-cell access resistance was carefully monitored throughout the recording, and cells were rejected if values changed by more than 25% (or exceeded 20 M□); only recordings with stable series resistance of <20 MΩ were used for analysis. Whole-cell currents were analyzed using Mini Analysis 6.0.7 (Synaptosoft, Decatur, GA). Results are presented as mean ± SEM. To compare the results between cells from different animals, we used unpaired Student´s *t*-test, and the cumulative probability curves with Kolmogorov-Smirnov (K.S.) statistical test, with significance level of $p < 0.05$.

Chromatin immunoprecipitation (ChIP):

Primers for putative binding sites of Cux1 and Cux2 on Xlr4b gen (NC_000086 REGION: 70450661..70467792) (-8858-(-8718): F-5'- CAAGACAGATGGGTTTCAAGG -3' and R-5'- CATGCTGGACATTGTTCTGG -3'; -6783-(-6661): F-5'- CAAGGGATGGTTTCTTACCC -3' and R-5'- CCGTAGTTTTCATGGCAATC -3'; -6473-(-6374): F-5'- AGCTACATGTTTCCCGAAGG -3' and R-5'- GCACATTTGGGATGTCTTGC -3'; -1857-(-1761): F-5'- AACATCACTAGGCTCTTTCCAAG -3' and R-5'- ACAGGATGCTCCATTCTACCAC -3'; 726-804: F-5'- TGATCCCTTCCAGTTCGTTC -3' and R-5'- AACAGGCATCAGGTTTCCAC -3'; 2508-2605: F-5'- TTTGTTGTGTGGTGGGGTAG -3' and R-5'- AACTCTGCATGCACTGTGTG -3'; 6037-6131: F-5'- CGCCCTTTGTTTCTTGACTC -3' and R-5'- TGGGCCTTGTCTTACCATTG -3'; 6712-6837 F-5'- TCTTCCTTTTCCCCTTCCTC -3' and R-5'- CTGGAGAAGCATGACTGTATGG3'; 8002-8106: F-5'- AGCTTGCGTCCTGTGATTTC -3' and R-5'- TGACTCATGCCAACAAGTCTG-3'). Q-PCR of serial dilutions of genomic DNA as template was run in parallel to verify linear relationship of Ct versus template and experimental samples.

Primers for putative binding sites of Cux1 and Cux2 on FAM9 genes: FAM9C +15771 GTCGCCACAATCAGGATG; TCAAAAGATCTGCTGGGTGA; FAM9C -5900 GCACAGAGTTGAGGGACCAC; GTGACATCCAGGGCCACTG; FAMA +1317 TGAGGGGTACATGTGCAGGTT; GACACCTGGGCCTACTTGAG; FAMA +5975 TATGGTCTTCCTGCCTTCCA; TGGCTATGTTCTTGAGCGGTA; FAMB +14073 TTGCAACTGCTGGATACCAT; TCATTGCCCTTACCTTACAGC; FAMB +15924 GATGGGTGCACCAAAAATCTC; TTTGGGGTCATTTTTATGTTC; FAMB +7269 ATGTCACTGAAATCTGGCATT; GTTCACTGACAAACCACCACTT; FAMB -6447 CCCACTGCTGCTGTAACAAA; CTGGAAAAGGCAAGGAACTG; FAMB -7048 AGACATCTTTGAGAGGCCATT; GGCTGTCTGGGGAGTCATTA.

The immunoprecipitating antibodies for ChIP assay were: a goat polyclonal anti-Cux1 (CDP, C-20; sc-6327, Santa Cruz Biotechnology). This antibody has been previously characterized and used in previous reports for ChIP experiments (Tiveron et al. 2006. J Neurosci. 26(51): 13273; Brantley et al. 2003. Kidney Int. 63(4): 1240. Khanna-Gupta A, et al. 2003. Blood. 101(9): 3460). We demonstrated that this polyclonal stains nuclear protein specifically on layer II-III and IV of P0 cortex (not shown) and that it specifically recognizes the corresponding 200 kDa band on Western blot analysis performed on protein extracts from WT mice but not *Cux1-/-* animals (Fig S4B). The antibody also specifically react with Cux1 nuclear protein over-expressed in COS cells as assay by immunohistochemistry (Fig S4B) and Western-blot (not shown). The immunoprecipitating antibodies for Cux2 were the serum of a rabbit immunized against the full length Cux2 protein custom generated by Genovac (Freiburg, Germany) by genetic immunization that specifically recognizes nuclear Cux2 protein on COS transfected cells with CAG-Cux2 but not on control cells as assay by immunohistochemistry (Fig S4B) and Western-blot (not shown). It specifically reacts with a 250 kDa

protein band corresponding to Cux2 (Gingras et al., Gene 344, 273) by Westen-blot of lysates of WT cortex but not *Cux2-/-* cortex (Fig S4B).

Hairpin sequences: The hairpin sequences for *Cux2* were CCGGCCGTTTACGTTTATTGTACTCGAGTACAACAATAAACGTAAACGGTTTTTG; CCGGGCTGACTATGAAGAGATTAAACTCGAGTTTAATCTCTTCATAGTCAGCTTTTTG;CCGGCAATCCAGACTGTCCTTCATTCTCGAGAATGAAGGACAGTCTGGATTGTTTTTG; CCGGCCGTTTACGTTTATTGTTGTACTCGAGTACAACAATAAACGTAAACGGTTTTTG The hairpins for Cux1 were CCGGGCAGCTCAAGCACAACATCTCGAGATGTTGTGCTTGATGAGCTGCTTTTTG;CCGGGCCCTCAGCATCCAAGAATTACTCGAGTAATTCTTGGATGCTGAGGGCTTTTTG; CCGGGCCAAGAATAGCACACTCAAACTCGAGAACTTTCCTGTAGAAGCCAGGTTTTTG. The hairpins for Xlr4 and Xlr3 were TGCTGTTGACAGTGAGCGCGGGATCATCAGGGATATTATATAGTGAAGCCACAGATGTATATAATATCCCTGATGATCCCATGCCTACTGCCTCGGA; TGCTGTTGACAGTGAGCGAGGATCATCAGGGATATTATATTAGTGAAGCCACAGATGTAATATAATATCCCTGATGATCCCTGCCTACTGCCTCGGA;TGCTGTTGACAGTGAGCGCGGAATATAGATGTAGACCAAATAGTGAAGCCACAGATGTATTTGGTCTACATCTATATTCCATGCCTACTGCCTCGG.

Phylogenetic analysis: mouse and rat *Xlr4b* and *FAM9* genomic regions were aligned using mVista multiple alignment software. Sequences of Cor1 superfamily members were obtained from treefam (http://www.treefam.org), (acc number:TF328876) and aligned using software Clustalw (NCBI). Binding site search was performed using JASPAR and transfac data bases.

Luciferase reporter assays. Sequence containing *Xlr4b* regulatory regions (see below) corresponding to those identified in the Chip assays were cloned into the pGL4.23 luciferase vector (Promega). The dorsal telencephalon of E12.5 embryos was dissected; cells were dissociated and seeded onto 24 well Poly-Lys coated plates in Neurobasal media supplemented with B27 complement (Invitrogen). Cells were then co-transfected with the corresponding luciferase reporter constructs, CMV-renilla, and CAG-Cux1, CAG-Cux2 or CAG empty vector at a ratio of 10:1:6 using lipofectamine 2000 (Invitrogen). Luciferase and Renilla activity was measure two days after transfection using the Dual-Luciferase Reporter Assay System (Promega) and following the manufacture protocol. Renilla activity was used to normalize transfection. Relative expression of reporter constructs was determined by normalizing the ratio of reporter activity to the control CAG empty vector.

Sequences of the cloned regulatory regions (Cux consensus binding sites in bold).

R1: A region of 1 Kb from -2437 to 1436 of the Xlr4b gen (NC_000086 REGION: 70450661..70467792).

CCAACAACTCACTTAGATGTGACAT**AATTTTGGGATTG**GAACCTTCATTTGGAGACAAGAGGTGTTCAG
TTGGGGCTCTGTCTCAAACATTATTTCATTTAGATTTCCTCCATAGATGTATATATTTTAGGAAGCTTCAA
CTCTATTAGTTCTCCATACTACCCCTCAAATGGCCCTTAATTAGAGTTCTCTCTTCCCACATCCCCTTCTA
CATCCCCTCTCCTACTCCTCCCCACTTGATCCCCTAATTCCAGCCCCTGCATCTATGTATAACTATTAATT
TTATTTTCTTTT**CCTATTGAGATCT**ATCCATACTCCCCAAGTCCCTTACTCTATATGTAAACTCTGTGGTT
CTATGAATTGTGGCTTGGTTGTCATTCATTTAGCAGCTGATATCCACATGTAACTAAATATGTATCATAT
TTGTCTTTCTGGGTCTGGGATACCTCCCACAGGATCACTTTTTT**TTTTTCTAGATCCATCAATTTAC**CTGT
GA**ATTTCATGATTTCATTATT**TAAAGACTGAGT**AATAATCAATTGTATAAAT**GTATCATATTTT**ATTT**
ATCCATTCTTATACTGAGAAACATCACTAGGCTCTTTCCAAGTTTTCACTATTATATAGAGAGCAGCAA
T**AAACATGGATGGGCAATTA**TCTCTGTGGTAGAATGGAGCATCCTGTGGGTATATGCCAAGAAGTGGT
ATAGTTG**GATCTTGAGATAGATTTAT**TCCCAATTCTCTGAGAAACCCTCATATTGGGTTCCAAGGTGGT
TGAACAAGTTTGC**ACTCCCACCATCAATGGAG**GAGTGTTCCATGTGTTCCAGTCTCACCAGCATGAGC
GGTCACTTATGTTTTTGGTCTTAGCCATTCTGATGAGTATAAAATGGAATCTCGGGGTCGTTTTGACTTG
CATTTCCCTGATGGTTAAGGATATTGAACATTTAATCATTTCTCAGCCATTTGAATTTCCTTTAGTGAGAA
TTCTCTGGTTAGATCTGTACCATTGAGT

Mutated R1:

CCAACAACTCACTTAGATGTGACATAACTTCGGTATCGGAACCTTCATTTGGAGACAAGAGGTGTTCAG
TTGGGGCTCTGTCTCAAACATTATTTCATTTAGATTTCCTCCATAGATGTATATATTTTAGGAAGCTTCAA
CTCTATTAGTTCTCCATACTACCCCTCAAATGGCCCTTAATTAGAGTTCTCTCTTCCCACATCCCCTTCTA
CATCCCCTCTCCTACTCCTCCCCACTTGATCCCCTAATTCCAGCCCCTGCATCTATGTATAACTATTAATT
TTATTTTCTTTTCCAATGGATAGGCAGCCAGACCCCCCAAGTCCCTTACTCTATATGTAAACTCTGTGGTT
CTATGAATTGTGGCTTGGTTGTCATTCATTTAGCAGCTGATATCCACATGTAACTAAATATGTATCATAT
TTGTCTTTCTGGGTCTGGGATACCTCCCACAGGATCACTTTTTTTGTTATGAATTCAACAGTTCACCTGTG
AATGTCGTGCTTCCAGTACTTAAAGACTGAGTAAAAAGCAGTTCTACAAATGTATCATATTTTATATAGC
CCTTTTTGTAATGAGAAACATCACTAGGCTCTTTCCAAGTTTTCACTATTATATAGAGAGCAGCAATAAG
CAAGGGTGCGCCATAATCTCTGTGGTAGAATGGAGCATCCTGTGGGTATATGCCAAGAAGTGGTATAGT
TGGAACTCGAAATGGAATTTTTCCCAATTCTCTGAGAAACCCTCATATTGGGTTCCAAGGTGGTTGAACA
AGTTTGCACCCCGACAATAAACGGGGGAGTGTTCCATGTGTTCCAGTCTCACCAGCATGAGCGGTCACT
TATGTTTTTGGTCTTAGCCATTCTGATGAGTATAAAATGGAATCTCGGGGTCGTTTTGACTTGCATTTCCC
TGATGGTTAAGGATATTGAACATTTAATCATTTCTCAGCCATTTGAATTTCCTTTAGTGAGAATTCTCTGG
TTAGATCTGTACCATTGAGT

R2: A region of 2,3 Kb from 5754 to 8254 of the Xlr4b gen (NC_000086 REGION: 70450661..70467792)

CTCTTTCCTTCCATACTGGGGTTCATTGATAGTGTTCATACCTTTAAACGTCTTCTTTCTTTTCTTAGTGTT
ACCATGTCAGGTAAACCTAACTACTAAATGAGCGTCTCCTTTAAGGATTCATTCATGGTTGTGGGTTCCT
TTCAAAGCAGG**AGTTGGTACATTGGTAACA**TTGCCCAAAGTTATACTTACTGTTTTGGGGGAAGTTCTG
ATTTTTATAGCATGGCTTTCTCCCATAATCAGATTTCTTTTGGACAGTG**ACAAATCAATGTAGGAAGT**C
TATACGCCCTTTGTTTCTTGACTCCTTGTGCTTTCTGCATTATTGAACTGTAATTATTCTTTTCCCCTGTGG
ACAATTACAATGGTAAGACAAGGCCCATCAGCATGATGAGGCAAAACTGTAAGTGAAGATAACAGTAT
ATTGAGAATTAGCTACTGTTTTCAATGCATCCTATCCAATTCTTCTCAGCCTCTTTGAACTTGGCCAAGTA
CATTTATATAGTTATTCTGGAATTAATTAACTGTTGTACGCTCAGATTCATTTTCTGGGTTGTTGTTTAAT
GCCTTGTGTTCCTGTTGAATTTCCTTCATCCAGGCTAATTGATATAGGTCCAAACAGCCGCGTGGAAAGA
ATTTATTCCATGTTCTGTAATACTTGGTGTACACTGGGATACATGTATGCAGAGCAGCCAATTTGAAGTG
CTTCTGAGTCGTGGGTATCAGGCTGTAGTCCTTGTGGGGGGAAGCTTTTCAAAATCACACTGCAGGTTTG
AGGTAGCTGTTAGTCTAATCCTCAGTCAGGGCTGCACTTCCTGAGTACTCTCCATTCTCTGTGTATGGTA
ATACTGCAGACTGCTCAGACATCTCCCCCGCCCCTGTCTTCCTCCAACTTTCTGTTCCTCCCTCCTCTTCC
TTTCTCTTCCTTCTCCTCTGTCATCATCTTTAACTTCTTCATATTTTCTTCCTTTTCCCCTTCCTCCCCACAC
CCACTCCAATGTGTACGCATTTCCTATTCTGCCTATAAGATTTTGTTATTATATCCAGATTGCACAGTATA
GCATCACCATACAGTCATGCTTCTCCAGTCTCTTCTTTTGTTTTCCTACCAAAATATTAGTCTTTCTACTG
AGCCATAGGCATTAAGATTCATTTCACTTGCATAGCTCAGCAAGTTGGTCATCAGTTCTAATGCTAAAGT
TTTGGGCTGTTTCTGGTTCTGCATTCACTTAAAGTTATTGAAATATGAAAGAAATAATTAAATAGTTTTA
TCATTTTTCTATACCACATGTCACAAGAGTTTGTTTATAGCAAGTATCTCTCTCTCTGTGGCCCTGGCTAG
CCTGGAGCTCACTATGCAGTGGCTTTACTTGAACTTGCACTGATCCTCCTGCCACTATT**TTGGAGTGATG**
GAATTACAGGTACATTTCACCAAGGTACTCTGCTTAGTGCAACAGGTTTGATGTAGTGTGT**CCTAATCC**

ATTCATTGTTGAACCTTCCGTCATGGTCATAAACATTTCTCATCATGATCACACAAATTTCTGTATCTCC
ATTTGTAGCAATATTGTACTCAGCAATGCAGTTCCATATTTCTGTGGTGGATGCTCTGATTTTCATATAGT
ATACAGTGTACTTTTACTTTAGATTAATTACTGACCATTCCATTTATTGTAATACATACTGATTTTGAACT
GTAACTGTTCACAATTGTGAACCAAGATGGCTTCTAATTAAACATGGCTTTTGGTTTTAGAATCTACAGG
CTATTAAGTGTTGTCGCCGAAAAGCTATTATTGAGGAAGCCAGAAAGCTAATGGACTACTTGGAAAAGA
GAGTTACTGAAGAAACTGTAAGTAGAATATTTTTAAATGGAGTATTAGGATTAATTTGAGCATTAAATTT
CTTTCCTAAAATATATGTCGTATATATACACACAAATATTAATTAGATGTTTAATACCACCAAGGTTCAC
GTAAACAAGCAGGAAGCAAAGGATGGTGTTCAATCATCACTTCTATCCCTGCTAATCTCGTAACACCTG
GAAGAAAGAAGCTCAACCACCATGAAATGACTTCATGATATTTCTAAATCTATGGTGACATGACACTGC
TATTGTAGT**GATTATCAATTCCTTGTTC**ACATCTCTGAGGGGTCAGAAAAACTTTACTGAGAATGTTTT
GTTTGTGGAATTTATCGCACATGTAGTATGGGATCATCAGGGATATTATATATGAGGTCTCGTGTACAGT
TAAAGCTTGCGTCCTGTGATTTCCTGTATGGATACCCTGGGAAATCCTTACTTGGG**AACGTTTGATTTA**
ATAAACATGAAATAGTTTCAGACTTGTTGGCATGAGTCA

Mutated R2:

CTCTTTCCTTCCATACTGGGGTTCATTGATAGTGTTCATACCTTTAAACGTCTTCTTTCTTTTCTTAGTGTT
ACCATGTCAGGTAAACCTAACTACTAAATGAGCGTCTCCTTTAAGGATTCATTCATGGTTGTGGGTTCCT
TTCAAAGCAGGAGGTGATAAATGGGCAAAATTGCCCAAAGTTATACTTACTGTTTTGGGGGAAGTTCTG
ATTTTTATAGCATGGCTTTCTCCCATAATCAGATTTCTTTTGGACAGTGACTAAGCAGTGCAGCAAGTGG
AGGTGGTCGGTGTTTCTTGACTCCTTGTGCTTTCTGCATTATTGAACTGTAATTATTCTTTTCCCCTGTGG
ACAATTACAATGGTAAGACAAGGCCCATCAGCATGATGAGGCAAAACTGTAAGTGAAGATAACAGTAT
ATTGAGAATTAGCTACTGTTTTCAATGCATCCTATCGAGTTCTTCTCAGCCTCTTTGAACTTGGCCAAGTA
CATTTATATAGTTATTCTGGAATTAATTAACTGTTGTACGCTCAGATTCATTTTCTGGGTTGTTGTTTAAT
GCCTTGTGTTCCTGTTGAATTTCCTTCATCCAGGCTAATTGATATAGGTCCAAACAGCCGCGTGGAAAGA
ATTTATTCCATGTTCTGTAATACTTGGTGTACACTGGGATACATGTATGCAGAGCAGCGAGTTTGAAGTG
CTTCTGAGTCGTGGGTATCAGGCTGTAGTCCTTGTGGGGGGAAGCTTTTCAAAATCACACTGCAGGTTTG
AGGTAGCTGTTAGTCTAATCCTCAGTCAGGGCTGCACTTCCTGAGTACTCTCCATTCTCTGTGTATGGTA
ATACTGCAGACTGCTCAGACATCTCCCCCGCCCCTGTCTTCCTCCAACTTTCTGTTCCTCCCTCCTCTTCC
TTTCTCTTCCTTCTCCTCTGTCATCATCTTTAACTTCTTCATATTTTCTTCCTTTTCCCCTTCCTCCCCACAC
CCACTCGAGTGTGTACGCATTTCCTATTCTGCCTATAAGATTTTGTTATTATATCCAGATTGCACAGTATA
GCATCACCATACAGTCATGCTTCTCCAGTCTCTTCTTTTGTTTTCCTACCAAAATATTAGTCTTTCTACTG
AGCCATAGGCATTAAGATTCATTTCACTTGCATAGCTCAGCAAGTTGGTCATCAGTTCTAATGCTAAAGT
TTTGGGCTGTTTCTGGTTCTGCATTCACTTAAAGTTATTGAAATATGAAAGAAATAATTAAATAGTTTTA
TCATTTTTCTATACCACATGTCACAAGAGTTTGTTTATAGCAAGTATCTCTCTCTCTGTGGCCCTGGCTAG
CCTGGAGCTCACTATGCAGTGGCTTTACTTGAACTTGCACTGATCCTCCTGCCACTATTTTCGAATGCTG
AAAGTATAGGTACATTTCACCAAGGTACTCTGCTTAGTGCAACAGGTTTGATGTAGTGTGTCCAAAGCC
GTTTATAGTAGAACCTTCCGTCATGGTCATAAACATTTCTCATCATGATCACACAAATTTCTGTATCTCC
ATTTGTAGCAATATTGTACTCAGCAATGCAGTTCCATATTTCTGTGGTGGATGCTCTGATTTTCATATAGT
ATACAGTGTACTTTTACTTTAGATTAATTACTGACCATTCCATTTATTGTAATACATACTGATTTTGAACT
GTAACTGTTCACAATTGTGAACCAAGATGGCTTCTAATTAAACATGGCTTTTGGTTTTAGAATCTACAGG
CTATTAAGTGTTGTCGCCGAAAAGCTATTATTGAGGAAGCCAGAAAGCTAATGGACTACTTGGAAAAGA
GAGTTACTGAAGAAACTGTAAGTAGAATATTTTTAAATGGAGTATTAGGATTAATTTGAGCATTAAATTT
CTTTCCTAAAATATATGTCGTATATATACACACAAATATTAATTAGATGTTTAATACCACCAAGGTTCAC
GTAAACAAGCAGGAAGCAAAGGATGGTGTTCAATCATCACTTCTATCCCTGCTAATCTCGTAACACCTG
GAAGAAAGAAGCTCAACCACCATGAAATGACTTCATGATATTTCTAAATCTATGGTGACATGACACTGC
TATTGTAGTGAGTAGCATTTGCTGGTGCACATCTCTGAGGGGTCAGAAAAACTTTACTGAGAATGTTTTG
TTTGTGGAATTTATCGCACATGTAGTATGGGATCATCAGGGATATTATATATGAGGTCTCGTGTACAGTT
AAAGCTTGCGTCCTGTGATTTCCTGTATGGATACCCTGGGAAATCCTTACTTGGGAATGTGTGGTTAAAG
AAGCATGAAATAGTTTCAGACTTGTTGGCATGAGTCA

In Situ Hybridization: A probe containing nucleotides 397-892 of *Xlr4b* sequence (NCBI GeneBank acc: NM 021365) was amplified using 5´GGAAGA GAA AGT ATG GGG TGA3' and 5'GGA TCC TAA TAC GAC TCA CTA TAG GGA G TGA AGT CAT TTC ATG GTG GTTG3' and that recognizes *Xlr4b, 4a, 4c*

and *4E* was used and in situ hybridization was performed as described (Nieto et al., 2004. *J Comp Neurol* 479, 168).

shRNA resistant forms: shRNA resistant forms were generated introducing silent mutations in the coding regions targeted by the *shRNAs*. Sequence for mutated *Xlr4b(mXlr4b)*:ATGGCCAGCAAGATCAAAGGCAGGCCCCCTAAGCAGCCAAAAGTGACCCCCGCTCTGCC
TTCCAACGACTCTCAGCAGCTCCACGAGAATAACCCAGGAAATAACCTGGCACTCGAAACATGCGGGG
AGTCTTCCAGTAGCCACGGAACTGGCGGACCCAAGCCTGGGCCATCTAAAAAGACCCTGAATGAAAGA
AAACGGAAGTACGGTGTCAGTGTGAACAAAACAGTCCAGAATATTGAGTGGAACGTGGATCACTTCCTC
AAGGTCCAGCATGAACGCCGACAGGAGCTGTATAAAGACTACTCACACCAGTTCCTGACCCTCGTGATG
ATGTGGAATATCGAcGTCGAtCAGATTAAGAAACAGGCCGGGAAGCTCAGCGATATCCTGGACGAACAG
CAGAAACTCTTCCAGCAGTTTCAGTCCATTCATATGCAGAAGATCGAGGAGTTCAAGGAGCTGTGCGAT
AGGCACCTCAAGAACCTGCAGGCCATCAAGTGCTGTAGACGGAAGGCAATCATTGAAGAGGCCCGCAA
GCTCATGGACTATCTGGAAAAGAGAGTGACCGAGGAGACAGTCCATGTGAATAAGCAGGAGGCTAAGG
ATGGAGTGCAGTCTAGTCTGCTGTCTCTGCTGATCAGCTGAACCCAGCTTTCTTGTACAAAGTGGTCCCC
GAATTC; mutated *Cux1(mCux1)*:
ATGGCCGCTAACGTGGGCTCCATGTTCCAGTACTGGAAGAGGTTTGACCTGCAGCAGCTGCAGAGAGAG
CTGGATGCTACAGCCACTGTGCTGGCCAATAGACAGGACGAGAGCGAACAGTCCAGGAAGAGACTGAT
CGAGCAGTCCCGGGAATTCAAGAAAAACACACCTGAAGACCTGCGCAAACAGGTGGCCCCACTGCTGA
AGTCTTTCCAGGGCGAGATTGATGCTCTGTCTAAAAGGAGTAAGGAGGCCGAAGCCGCTTTTCTGACCG
TGTATAAGAGACTGATCGACGTGCCAGATCCTGTGCCAGCCCTGGACGTGGGACAGCAGCTGGAGATTA
AGGTGCAGAGGCTGCACGATATCGAGACCGAAAATCAGAAACTGAGAGAGACACTGGAGGAATACAAC
AAGGAGTTTGCCGAAGTGAAGAACCAGGAAGTGACAATTAAGGCTCTGAAAGAGAAGATCCGGGAGTA
TGAACAGACTCTGAAGTCCCAGGCCGAGACCATCGCTCTGGAGAAAGAACAGAAGCTGCAGAACGACT
TCGCCGAGAAAGAACGCAAGCTGCAGGAAACCCAGATGAGCACCACATCCAAACTGGAGGAAGCCGAG
CACAAGCTGCAGACTCTGCAGACCGCTCTGGAGAAGACCCGGACAGAACTGTTTGACCTGAAAACAAA
GTACGATGAGGAAACTACCGCTAAGGCCGACGAGATCGAAATGATTATGACTGATCTGGAGAGGGCTA
ATCAGAGGGCTGAAGTGGCTCAGAGGGAGGCTGAAACCCTGAGGGAGCAGCTGAGCTCCGCTAACCAT
TCTCTGCAGCTGGCCAGTCAGATTCAGAAGGCTCCTGACGTGGAGCAGGCCATCGAAGTGCTGACCCGG
TCTAGTCTGGAGGTGGAACTGGCCGCTAAGGAGCGCGAAATTGCCCAGCTGGTGGAGGATGTGCAGAG
GCTGCAGGCCAGCCTGACCAAGCTGAGAGAAAATTCTGCTAGTCAGATCTCTCAGCTGGAGCAGCAGCT
GAACGCGAAAAACAGTACTCTGAAGCAGCTGGAGGAAAAACTGAAGGGACAGGCTGACTACGAGGAA
GTGAAGAAAGAGCTGAACACTCTGAAGTCTATGGAGTTCGCCCCTAGTGAAGGAGCTGGGACTCAGGA
TAGCACCAAGCCACTGGAGGTGCTGCTGCTGGAGAAGAACCGGTCTCTGCAGAGTGAGAATGCCACCCT
GCGCATTAGCAACTCCGACCTGTCCGGCCCCTATAGCACAAATTCCATCAGCTCCCCAAGCCCTCTGCAG
CAGTCCCCTGATGTGAACGGAATGGCCCCATCTCCCAGTCAGAGCGAGTCCGCTGGGTCTATTAGTGAA
GGCGAGGAAATTGACACAGCCGAGATCGCTCGGCAGGTGAAAGAACAACTAATTAAACATAATATTGG
ACAGCGCATCTTCGGGCATTACGTGCTGGGCCTGTCCCAGGGAAGCGTGTCCGAGATCCTGGCCAGGCC
TAAACCATGGAATAAGCTGACCGTGAGAGGCAAGGAACCATTCCACAAAATGAAGCAGTTTCTGTCTGA
CGAGCAGAACATTCTGGCCCTGCGGAGTATCCAGGGCCGGCAGAGGGAGAACCCAGGACAGAGCCTGA
ATCGCCTGTTTCAGGAAGTGCCTAAGAGGAGAAACGGGTCCGAGGGCAATATTACAACTAGGATCAGA
GCTTCTGAGACAGGAAGTGATGAAGCCATCAAAAGCATTCTGGAGCAGGCTAAGAGGGAACTGCAGGT
GCAGAAAACTGCCGAGCCCGTGCAGACATCTAGTACTAGCTCCTCTGGGAACAGCGACGATGCTATCAG
ATCCATTCTGCAGCAGGCTAGGAGGGAGATGGAAGCTCAGCAGGCCGCTCTGGACCCTGCCCTGAAGCC
AGCTCCTCTGTCCCAGCCAGATCTGACCATTCTGACACCCAAGCATCTGTCTGCCAGTCCTATGTCTACT
GTGAGTACCTACCCCCCTCTGGCTATCTCTCTGAAGAAAACCCCTGCCGCTCCAGAAACTTCTACCGCCG
CTCTGCCAAGTGCTCCTGCCCTGAAGAAAGAGGCCCAGGACGTGCCCACACTGGATCCACCAGGATCTG
CTGACGCTGCTCAGGGCGTGCTGAGGCCTATGAAGAGCGAGCTGGTGCGCGGCTCCACTTGGAAAGATC
CATGGTGGAGCCCAATCCAGCCCGAGAGGAGAAATCTGACTAGTAGCGAGGAAACCAAGGCCGACGAG
ACCACAGCTTCTGGCAAAGAAAGGGCTGGATCCTCTCAGCCTAGGGCTGAGCGCAGCCAGCTGCAGGG
ACCAAGCGCCTCCGCCGAGTACTGGAAGGAATGGCCAAGCGCCGAATCCCCCTATTCTCAGAGTAGCGA
GCTGAGCCTGACAGGCGCTTCTAGGAGTGAGACTCCTCAGAACTCCCCACTGCCCTCCTCTCCTATTGTG
CCAATGGCCAAACCCGCTAAGCCTAGCGTGCCTCCACTCACACCAGAGCAGTATGAAGTGTACATGTAT
CAGGAGGTGGACACAATCGAACTGACTAGGCAGGTGAAAGAAAAGCTGGCCAAGAATGGAATTTGCCA
GAGAATCTTCGGGGAGAAAGTGCTGGGACTCTCTCAGGGAAGCGTGTCCGATATGCTGTCTAGGCCTAA
ACCATGGAGTAAGCTGACCCAGAAAGGGAGGGAACCCTTCATCAGAATGCAGCTGTGGCTGAACGGAG

AGCTGGGACAGGGAGTGCTGCCAGTGCAGGGACAGCAGCAGGGACCCGTGCTGCACAGTGTGGCTAGC
CTGCAGGACCCACTGCAGCAGGGATGCGTGAGTAGCGAGTCCACACCCAAGACTTCTGCCAGTTGTAGC
CCCGCTCCTGAGTCTCCCATGTCCTCTAGTGAGTCCGTGAAGTCTCTGACTGAGCTGGTGCAGCAGCCAT
GTCCCGCCATCGAGACCAGCAAAGAAGGCAAGCCACCTGAGCCATCCGACCCACCAGCTTCCGATTCTC
AGCCTACTACCCCTCTGCCACTGAGTGGACACAGCGCtCTGTCtATTCAGGAGCTGGTGGCTATGAGCCCC
GAGCTGGACACCTACGGGATCACAAAAAGGGTGAAGGAAGTGCTGACCGATAACAATCTGGGGCAGAG
ACTGTTCGGCGAGACAATCCTGGGCCTGACTCAAGGAAGTGTGAGCGATCTGCTGGCCAGGCCCAAGCC
TTGGCATAAACTGTCCCTGAAGGGCCGGGAGCCATTTGTGCGCATGCAGCTCTGGCTCAACGACCCCAA
CAATGTGGAAAAACTGATGGATATGAAGAGAATGGAGAAGAAAGCCTACATGAAGCGGCGCCACAGCT
CCGTGTCCGACTCTCAGCCTTGCGAGCCTCCAAGCGTGGGGATTGATTATAGCCAGGGAGCTTCCCCAC
AGCCACAGCATCAGCTGAAGAAACCTCGGGTGGTGCTGGCTCCAGAGGAAAAAGAGGCCCTGAAGCGC
GCTTACCAGCAGAAACCTTATCCAAGCCCCAAGACCATCGAGGAACTGGCCACACAGCTGAATCTGAAG
ACATCTACTGTGATTAACTGGTTCCACAATTATCGGAGCCGCATCAGGAGAGAGCTGTTTATCGAGGAA
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