Additional File 1: Table S1 Key Resource Table.

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Antibodies		
Ankyrin G Monoclonal Antibody (4G3F8)	Invitrogen	Cat #33-8800
Anti-bIII tubulin	Abcam	Cat #ab195879
Anti-bIII tubulin	Abcam	Cat # Ab18207
Anti-pfyn	Cell Signaling	Cat #2101S
Anti-β-Actin−Peroxidase antibody, Mouse monoclonal	Sigma-Aldrich	Cat #A3854, RRID: AB_262011
CD68 Monoclonal antibody	Proteintech	Cat #66231-2-Ig, RRID: AB_2881622
CD86 Polyclonal antibody	Proteintech	Cat #13395-1-AP, RRID: AB_2074882
CDK5 Antibody	Cell Signaling	Cat #2506, RRID: AB_2078855
Fyn Antibody	Cell Signaling	Cat #4023, RRID: AB_10698604
IBA1 Monoclonal antibody	Proteintech	Cat #66827-1-Ig, RRID: AB_2882170
iNOS Polyclonal antibody	Proteintech	Cat #18985-1-AP, RRID: AB_2782960
MAP2 Polyclonal Antibody	Invitrogen	Cat #PA5-17646, RRID: AB_11006358
Phospho-CDK5 (Tyr15) Antibody	Cell Signaling	Cat #94254
Plexin A2 (D42B5) Rabbit mAb	Cell Signaling	Cat #5658, RRID: AB_10691688
Recombinant Anti-Neuropilin 1 antibody [EPR3113]	Abcam	Cat #ab81321, RRID: AB_1640739
SEMA3A Polyclonal Antibody	Invitrogen	Cat #PA5-67972, RRID: AB_2691930
TMEM119 Monoclonal antibody	Proteintech	Cat #66948-1-Ig, RRID: AB_2882272
TNF Alpha Polyclonal antibody	Proteintech	Cat #17590-1-AP, RRID: AB_2271853
Goat anti-Mouse IgG (H+L) Highly Cross-Adsorbed Secondary Antibody, Alexa Fluor 488	Invitrogen	Cat #A-11029, RRID: AB_2534088
Goat anti-Rabbit IgG (H+L) Cross-Adsorbed ReadyProbes™ Secondary Antibody, Alexa Fluor 594	Invitrogen	Cat #R37117, RRID: AB_2556545
mouse anti-rabbit IgG-HRP	Santa Cruz	Cat #sc-2357, RRID: AB_628497
m-IgGκ BP-HRP	Santa Cruz	Cat #sc-516102, RRID: AB_2687626
Chemicals, peptides, and recombinant proteins		
10x Tris/Glycine Buffer	Bio-Rad Laboratoires	Cat #1610734
10x Tris/Glycine/SDS Buffer	Bio-Rad Laboratoires	Cat #1610732
4x Laemmli Sample Buffer	Bio-Rad Laboratoires	Cat #1610747
B-27™ Plus Neuronal Culture System	ThermoFisher Scientific	Cat #A3653401
Bio-Rad Protein Assay Dye Reagent Concentrate, 450 ml	Bio-Rad Laboratoires	Cat #5000006
Bovine Serum Albumin (BSA)	Sigma-Aldrich	Cat #A3294
Clarity Western ECL Substrate, 500 ml	Bio-Rad Laboratoires	Cat #170-5061
Complete™, Mini Protease Inhibitor Cocktail	Sigma-Aldrich	Cat #11836153001
DPBS, calcium, magnesium	ThermoFisher Scientific	Cat #14040133
Essential 8™ Medium	ThermoFisher Scientific	Cat #A1517001
Fetal Bovine Serum, heat inactivated, qualified, One Shot™, Brazil	ThermoFisher Scientific	Cat #10108165
Geltrex™ hESC-Qualified, Ready-To-Use, Reduced Growth Factor Basement Membrane Matrix	ThermoFisher Scientific	Cat #A1569601
Geneticin™ Selective Antibiotic (G418 Sulfate) (50 mg/mL	ThermoFisher Scientific	Cat #10131035
Image-iT™ Fixative Solution (4% formaldehyde, methanol-free)	Invitrogen	Cat #FB002
L-Glutamine (200 mM)	ThermoFisher Scientific	Cat #25030024
Lipofectamine Messenger Max mRNA Transfection Reagent	Invitrogen	Cat #LMRNA015

Lipofectamine™ 2000 Transfection Reagent	Invitrogen	Cat #11668019
Mounting Medium with DAPI - Aqueous, Fluoroshield	Abcam	Cat #AB104139
Opti-MEM™ I Reduced Serum Medium	ThermoFisher Scientific	Cat #31985062
Penicillin-Streptomycin (10,000 U/mL)	ThermoFisher Scientific	Cat #15140122
Ripa Buffer	ThermoFisher Scientific	Cat #89900
Spectra™ Multicolor Broad Range Protein Ladder	ThermoFisher Scientific	Cat #26634
Tris Buffered Saline 10x	Bio-Rad Laboratoires	Cat #706435
Triton X-100 Detergent	Bio-Rad Laboratoires	Cat #1610407
Trypsin-EDTA (0.05%), phenol red	Sigma-Aldrich	Cat #T3924
Critical commercial assays		
Semaphorin 3A ELISA kit	Cusabio	Cat #CSB-E15913h
Experimental models: Cell lines		
Human iPSC-Derived Neural Stem Cells (Female)	Axol Bioscience	Cat #Ax0016
Human iPSC-Derived Neural Stem Cells (Male)	Axol Bioscience	Cat #Ax0015
Human Microglia Primary Cell Culture - Frozen Vial	Celprogen	Cat #37089-01
Oligonucleotides		
Neuropilin-1 siRNA	Ambion	Cat #AM16708 ID:107267
PlexinA2 siRNA	Ambion	Cat #4392420 ID: S10700
Sema-3A siRNA	Ambion	Cat #4392420 ID: S20284
Silencer GAPDH siRNA Positive Control	Ambion	Cat #AM4624
Silencer Negative Control #1 siRNA	Ambion	Cat #AM4611
Recombinant DNA		
Semaphorin 3A (SEMA3A) (NM_006080) Human Tagged ORF Clone	Origene	Cat #RG213681
pCMV6-AC-GFP Mammalian Expression Vector	Origene	Cat #PS100010
Software and algorithms		
FIJI	Schindelin et al., 2012	https://fiji.sc/; RRID: SCR_002285
Image Lab	Bio-Rad Laboratoires	https://www.bio-rad.com/it-it/product/image-lab-software?ID=KRE6P5E8Z
ImageJ	Schneider et al., 2012	https://imagej.nih.gov/ij/; RRID:SCR_003070
Synapse and Neurite Detector (SynD)	Schmitz, Hjorth, et al 2011	https://www.johanneshjorth.se/files/SynD/
Prism 9	GraphPad	https://www.graphpad.com/scientificsoftware/prism/; RRID:SCR_002798
Zen Black	Zeiss	RRID:SCR_018163
Zen Blue	Zeiss	RRID:SCR_013672
Other		
12 mm Coverslips	Epredia	Cat #CB00120RA120MZN0
Epredia™ SuperFrost Plus™ Adhesion slides	ThermoFisher Scientific	Cat #J1800AMNZ
4–15% Mini-PROTEAN® TGX Stain-Free™ Protein Gels, 10 well, 30 µl	Bio-Rad Laboratoires	Cat #4561084
Thick Blot Filter Paper, Precut, 7.5 x 10 cm	Bio-Rad Laboratoires	Cat #1703932
Low Fluorescence Western Membrane (PVDF)	Abcam	Cat #ab133411

Additional File 1: Table S2 Dendritic branching analysis of Figure 1E. Data are the mean ± SEM of three independent experiments in triplicate. Two-way ANOVA followed by Tukey's test for multiple comparisons. *P < 0.05; **P < 0,01; ****P < 0,0001 vs Ctrland #P<0.05 vs Sema 3A + siNpn 1.

µm	Ctrl vs. Sema 3A	Ctrl vs. Sema 3A + siNpn 1	Ctrl vs. siNpn 1	Sema 3A vs. Sema 3A + siNpn 1	Sema 3A vs. siNpn 1	Sema 3A + siNpn 1 vs. siNpn 1
0	ns (0,9857)	ns (0,9725)	ns (0,9466)	ns (0,9972)	ns (0,9943)	ns (>0,9999)
1	ns (0,7254)	ns (0,5604)	ns (0,6032)	ns (0,9338)	ns (0,9868)	ns (0,9899)
2	ns (0,8136)	ns (0,4248)	ns (0,0903)	ns (0,7917)	ns (0,3792)	ns (0,9899)
3	** (0,0034)	ns (0,9725)	ns (0,9991)	* (0,0237)	** (0,0077)	ns (0,9899)
4	**** (<0,0001)	ns (>0,9999)	ns (0,9763)	**** (<0,0001)	**** (<0,0001)	ns (0,9899)
5	* (0,0148)	ns (0,4248)	ns (0,4304)	** (0,0017)	*** (0,0002)	ns (0,9899)
6	* (0,0121)	ns (0,6976)	ns (0,5154)	** (0,0068)	*** (0,0002)	ns (>0,9999)
7	** (0,0013)	ns (0,9148)	ns (0,8427)	** (0,0068)	*** (0,0002)	ns (>0,9999)
8	** (0,0089)	ns (0,9725)	ns (0,9466)	* (0,0415)	** (0,0043)	ns (>0,9999)
9	** (0,0081)	ns (0,9964)	ns (0,9927)	ns (0,0697)	* (0,0102)	ns (>0,9999)
10	**** (<0,0001)	ns (0,9964)	ns (0,6897)	** (0,0034)	**** (<0,0001)	ns (0,9274)
11	**** (<0,0001)	ns (>0,9999)	ns (0,9763)	** (0,0063)	**** (<0,0001)	ns (0,9899)
12	** (0,0012)	ns (0,8532)	ns (0,7458)	** (0,0027)	**** (<0,0001)	ns (>0,9999)
13	**** (<0,0001)	ns (0,9725)	ns (0,9927)	** (0,0029)	**** (<0,0001)	ns (0,9274)
14	** (0,0053)	ns (0,9148)	ns (0,9763)	ns (0,3504)	** (0,0043)	ns (0,793)
15	** (0,0013)	ns (0,9148)	ns (0,9763)	ns (0,2053)	** (0,0012)	ns (0,793)
16	****(<0,0001)	ns (0,9148)	ns (0,9763)	** (0,0013)	**** (<0,0001)	ns (0,793)
17	** (0,0013)	ns (0,9964)	ns (0,9019)	* (0,0247)	*** (0,0004)	ns (0,9899)
18	* (0,0116)	ns (0,9148)	ns (0,9763)	* (0,0247)	** (0,0087)	ns (0,9899)

19	** (0,0019)	ns (0,9148)	ns (0,9763)	** (0,0085)	** (0,0017)	ns (0,9899)
20	ns (0,1133)	ns (0,9964)	ns (0,5154)	ns (0,2819)	ns (0,9353)	ns (0,6081)
21	ns (0,3564)	ns (0,9725)	ns (0,9991)	ns (0,3875)	ns (0,3792)	ns (0,9899)
22	ns 0,9502	ns (0,9964)	ns (0,9991)	ns (0,9338)	ns (0,9868)	ns (0,9899)
23	ns 0,1054	ns (>0,9999)	ns (0,9763)	ns (0,3875)	ns (0,3792)	ns (0,9899)
24	ns 0,8296	ns (>0,9999)	ns (0,9763)	ns (0,9338)	ns (0,9868)	ns (0,9899)
25	ns 0,9416	ns (>0,9999)	ns (0,9763)	ns (0,9789)	ns (0,9998)	ns (0,9899)
26	ns (0,9944)	ns (0,9964)	ns (0,9991)	ns (0,9789)	ns (0,9998)	ns (0,9899)
27	ns (0,9416)	ns (>0,9999)	ns (>0,9999)	ns (0,9789)	ns (0,9579)	ns (>0,9999)
28	ns (0,9920)	ns (>0,9999)	ns (>0,9999)	ns (0,9972)	ns (0,9943)	ns (>0,9999)
29	ns (0,6676)	ns (>0,9999)	ns (>0,9999)	ns (0,8579)	ns (0,7435)	ns (>0,9999)
30	ns (0,4485)	ns (0,9725)	ns (0,9466)	ns (0,9338)	ns (0,8734)	ns (>0,9999)
31	ns (>0,9999)	ns (0,9964)	ns (0,9927)	ns (0,9972)	ns (0,9943)	ns (>0,9999)
32	ns (0,1816)	ns 0,9964)	ns (0,9927)	ns (0,6341)	ns (0,4285)	ns (>0,9999)
33	ns (0,0980)	ns (0,9964)	ns (0,9927)	ns (0,5078)	ns (0,2894)	ns (>0,9999)
34	ns (0,0980)	ns (0,9964)	ns (0,9927)	ns (0,5078)	ns (0,2894)	ns (>0,9999)
35	ns (0,3224)	ns (>0,9999)	ns (0,9763)	ns (0,6341)	ns (0,2134)	ns (0,9899)
36	ns (0,6872)	ns (0,9964)	ns (0,9019)	ns (0,7548)	ns (0,3327)	ns (0,9899)
37	ns (0,5473)	ns (0,9148)	ns (0,6032)	ns (0,3875)	ns (0,0700)	ns (0,9899)
38	ns (0,2318)	ns (0,9148)	ns (0,6032)	ns (0,1956)	* (0,0172)	ns (0,9899)
39	ns (0,2318)	ns (0,9148)	ns (0,6032)	ns (0,1956)	* (0,0172)	ns (0,9899)
40	ns (0,3741)	ns (0,9148)	ns (0,6032)	ns (0,2819)	* (0,0360)	ns (0,9899)
41	ns (0,3922)	ns (0,4248)	ns (0,4304)	# (0,0415)	* (0,0172)	ns (0,9899)
42	ns (0,1216)	ns (0,6976)	ns (0,9466)	# (0,0415)	ns (0,0565)	ns (0,9274)
43	ns (0,5876)	ns (0,3039)	ns (0,2799)	# (0,0415)	* (0,0172)	ns (0,9899)
44	ns (0,7799)	ns (0,2053)	ns (0,3511)	# (0,0415)	ns (0,0565)	ns (0,9274)
45	ns (0,5876)	ns (0,3039)	ns (0,2799)	# (0,0415)	* (0,0172)	ns (0,9899)
46	ns (0,3922)	ns (0,4248)	ns (0,4304)	# (0,0415)	* (0,0172)	ns (0,9899)

47	ns (0,3922)	ns (0,4248)	ns (0,4304)	# (0,0415)	* (0,0172)	ns (0,9899)
48	ns (0,7799)	ns (0,2053)	ns (0,1662)	# (0,0415)	* (0,0172)	ns (0,9899)
49	ns (0,7799)	ns (0,2053)	ns (0,3511)	# (0,0415)	ns (0,0565)	ns (0,9274)
50	ns (0,7799)	ns (0,2053)	ns (0,3511)	# (0,0415)	ns (0,0565)	ns (0,9274)