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## References

- Acheson, A., Barker, P. A., Alderson, R. F., Miller, F. D. and Murphy, R. A. (1991) Detection of brain-derived neurotrophic factor-like activity in fibroblasts and Schwann cells: inhibition by antibodies to NGF. *Neuron*, 7(2), 265-275.
- Adachi, N., Kohara, K. and Tsumoto, T. (2005) Difference in trafficking of brain-derived neurotrophic factor between axons and dendrites of cortical neurons, revealed by live-cell imaging. *BMC Neurosci.*, 6(1), 42.
- Alsina, B., Vu, T. and Cohen-Cory, S. (2001) Visualizing synapse formation in arborizing optic axons in vivo: dynamics and modulation by BDNF. *Nat. Neurosci.*, 4(11), 1093-1101.
- Arakawa, T., Haniu, M., Narhi, L. O., Miller, J. A., Talvenheimo, J., Philo, J. S., Chute, H. T., Matheson, C., Carnahan, J., Louis, J. C., Yan, Q., Welcher, A. A. and Rosenfield, R. (1994) Formation of heterodimers from three neurotrophins, nerve growth factor, neurotrophin-3, and brain-derived neurotrophic factor. *J. Biol. Chem.*, 269(45), 27833-27839.
- Armstrong, D. D. (2001) Rett syndrome neuropathology review 2000. *Brain Dev.*, 23, 72-76.
- Audesirk, G., Cabell, L. and Kern, M. (1997) Modulation of neurite branching by protein phosphorylation in cultured rat hippocampal neurons. *Brain Res. Dev. Brain Res.*, 1102(2), 247-260.
- Baker, R. E., Wolters, P. and van Pelt, J. (1997) Chronic blockade of glutamate-mediated bioelectric activity in long-term organotypic neocortical explants differentially effects pyramidal/non-pyramidal dendritic morphology. *Brain Res. Dev. Brain Res.*, 104(1-2), 1-9.
- Baldelli, P., Hernandez-Guijo, J. M., Carabelli, V. and Carbone, E. (2005) Brain-derived neurotrophic factor enhances GABA release probability and nonuniform distribution of N- and P/Q-type channels on release sites of hippocampal inhibitory synapses. *J. Neurosci.*, 25(13), 3358-3368.
- Bampton, E. T., Ma, C. H., Tolkovsky, A. M. and Taylor, J. S. (2005) Osteonectin is a Schwann cell-secreted factor that promotes retinal ganglion cell survival and process outgrowth. *Eur. J. Neurosci.*, 21(10), 2611-2623.
- Barbacid, M., Lamballe, F., Pulido, D., Klein, R. (1991) The trk family of tyrosine protein kinase receptors. *Biochim. Biophys. Acta.*, 1072(2-3), 115-127.
- Bazenet, C. E., Mota, M. A. and Rubin, L. L. (1998) The small GTP-binding protein Cdc42 is required for nerve growth factor withdrawal-induced neuronal death. *Proc. Natl. Acad. Sci. U S A*, 95(7), 3984-3989.
- Benson, D. L. and Tanaka, H. (1998) N-cadherin redistribution during synaptogenesis in hippocampal neurons. *J. Neurosci.*, 18(17), 6892-6904.
- Bentley, C. A. and Lee, K. F. (2000) p75 is important for axon growth and schwann cell migration during development. *J. Neurosci.*, 20(20), 7706-7715.
- Berglund, E. O., Murai, K. K., Fredette, B., Sekerkova, G., Marturano, B., Weber, L., Mugnaini, E. and Ranscht, B. (1999) Ataxia and abnormal cerebellar microorganization in mice with ablated contactin gene expression. *Neuron*, 24(3), 739-750.
- Biffo, S., Offenhauser, N., Carter, B. D. and Barde, Y. A. (1995) Selective binding and internalisation by truncated receptors restrict the availability of BDNF during development. *Development*, 121(8), 2461-2470.
- Brannstorm T. and Kellerth J. O. (1998) Changes in synaptology of adult cat spinal  $\alpha$ -motoneurons after axotomy. *Exp. Brain Res.*, 118(1), 1-13.

- Bothwell, M. (1995) Functional interactions of neurotrophins and neurotrophin receptors. *Annu. Rev. Neurosci.*, 18, 223-253.
- Bräuer, A. U., Savaskan, N. E., Kuhn, H., Prehn, S., Ninnemann, O. and Nitsch, R. (2003) A new phospholipid phosphatase, PRG-1, is involved in axon growth and regenerative sprouting. *Nat. Neurosci.*, 6(6), 572-578.
- Bredt, D. S. and Nicoll, R. A. (2003) AMPA receptor trafficking at excitatory synapses. *Neuron*, 40(2), 361-379.
- Bresler, T., Ramati, Y., Zamorano, P. L., Zhai, R., Garner, C. C. and Ziv, N. E. (2001) The dynamics of SAP90/PSD-95 recruitment to new synaptic junctions. *Mol. Cell. Neurosci.*, 18(2), 149-167.
- Brewer, G. J., Torricelli, J. R., Evege, E. K., Price, P. J. (1993) Optimized survival of hippocampal neurons in B27-supplemented Neurobasal, a new serum-free medium combination. *J. Neurosci. Res.*, 35(5), 567-576.
- Brindley, D. N. (2004) Lipid phosphate phosphatases and related proteins: signaling functions in development, cell division, and cancer. *J. Cell. Biochem.*, 92(5), 900-912.
- Brunig, I., Penschuck, S., Berninger, B., Benson, J. and Fritschy, J. M. (2001) BDNF reduces miniature inhibitory postsynaptic currents by rapid downregulation of GABA(A) receptor surface expression. *Eur. J. Neurosci.*, 13(7), 1320-1328.
- Caceres, A., Banker, G., Steward, O., Binder, L. and Payne, M. (1984) MAP2 is localized to the dendrites of hippocampal neurons which develop in culture. *Brain Res.*, 315(2), 314-318.
- Canals, J. M., Pineda, J. R., Torres-Peraza, J. F., Bosch, M., Martin-Ibanez, R., Munoz, M. T., Mengod, G., Ernfor, P. and Alberch, J. (2004) Brain-derived neurotrophic factor regulates the onset and severity of motor dysfunction associated with enkephalinergic neuronal degeneration in Huntington's disease. *J. Neurosci.*, 24, 7727-7739.
- Canas, N., Pereira, I. T., Ribeiro, J. A., Sebastiao, A. M. (2004) Brain-derived neurotrophic factor facilitates glutamate and inhibits GABA release from hippocampal synaptosomes through different mechanisms. *Brain Res.*, 1016(1), 72-78.
- Cao, X. and Shoichet, M. S. (2001) Defining the concentration gradient of nerve growth factor for guided neurite outgrowth. *Neuroscience*, 103(3), 831-840.
- Cao, X. and Shoichet, M. S. (2003) Investigating the synergistic effect of combined neurotrophic factor concentration gradients to guide axonal growth. *Neuroscience*, 122(2), 381-389.
- Causing, C. G., Gloster, A., Aloyz, R., Bamji, S. X., Chang, E., Fawcett, J., Kuchel, G. and Miller, F. D. (1997) Synaptic innervation density is regulated by neuron-derived BDNF. *Neuron*, 18(2), 257-267.
- Chavis, P. and Westbrook, G. (2001) Integrins mediate functional pre- and postsynaptic maturation at a hippocampal synapse. *Nature*, 411(6835), 317-321.
- Chih, B., Engelman, H. and Scheiffele, P. (2005) Control of excitatory and inhibitory synapse formation by neuroligins. *Science*, 307(5713), 1324-1328.
- Cohen-Cory, S. and Fraser, S. E. (1995) Effects of brain-derived neurotrophic factor on optic axon branching and remodelling in vivo. *Nature*, 378(6553), 192-196.
- Cohen, N. R., Taylor, J. S. H., Scott, L. B., Guillery, R. W., Soriano, P. and Furley, A. J. W. (1997) Errors in corticospinal axon guidance in mice lacking the neural cell adhesion molecule L1. *Curr. Biol.*, 7, 26-33.
- Colman, H., Nabekura, J. and Lichtman, J. W. (1997) Alterations in synaptic strength preceding axon withdrawal. *Science*, 275, 356-361.

- Conner, J. M., Lauterborn, J. C., Yan, Q., Gall, C. M. and Varon, S. (1997) Distribution of brain-derived neurotrophic factor (BDNF) protein and mRNA in the normal adult rat CNS: evidence for anterograde axonal transport. *J. Neurosci.*, 17(7), 2295-2313.
- Connor, B., Young, D., Yan, Q., Faull, R. L., Synek, B. and Dragunow, M. (1997) Brain-derived neurotrophic factor is reduced in Alzheimer's disease. *Brain Res. Mol. Brain Res.*, 49(1-2), 71-81.
- Contos, J. J., Ishii, I. and Chun, J. (2000) Lysophosphatidic acid receptors. *Mol. Pharmacol.*, 58(6), 1188-1196.
- Costa-Mattioli, M., Gobert, D., Harding, H., Herdy, B., Azzi, M., Bruno, M., Bidinosti, M., Ben Mamou, C., Marcinkiewicz, E., Yoshida, M., Imataka, H., Cuello, A. C., Seidah, N., Sossin, W., Lacaille, J. C., Ron, D., Nader, K. and Sonenberg, N. (2005) Translational control of hippocampal synaptic plasticity and memory by the eIF2alpha kinase GCN2. *Nature*, 436(7054), 1166-1173.
- Costanzo, E. M., Barry, J. A. and Ribchester, R. R. (2000) Competition at silent synapses in reinnervated skeletal muscle. *Nat. Neurosci.*, 3, 694-700.
- Croll, S. D., Suri, C., Compton, D. L., Simmons, M. V., Yancopoulos, G. D., Lindsay, R. M., Wiegand, S. J., Rudge, J. S. and Scharfman, H. E. (1999) Brain-derived neurotrophic factor transgenic mice exhibit passive avoidance deficits, increased seizure severity and in vitro hyperexcitability in the hippocampus and entorhinal cortex. *Neuroscience*, 93(4), 1491-1506.
- Dailey, M. E. and Smith, S. J. (1996) The dynamics of dendritic structure in developing hippocampal slices. *Neurosci.*, 16(9), 2983-2994.
- Dalva, M. B., Takasu, M. A., Lin, M. Z., Shamah, S. M., Hu, L., Gale, N. W. and Greenberg, M. E. (2000) EphB receptors interact with NMDA receptors and regulate excitatory synapse formation. *Cell*, 103(6), 945-956.
- Dean, C., Scholl, F. G., Choih, J., DeMaria, S., Berger, J., Isacoff, E. and Scheiffele, P. (2003) Neurexin mediates the assembly of presynaptic terminals. *Nat. Neurosci.*, 6(7), 708-716.
- Demyanenko, G. P., Tsai, A. Y. and Maness, P. F. (1999) Abnormalities in neuronal process extension, hippocampal development, and the ventricular system of L1 knockout mice. *J. Neurosci.*, 19(12), 4907-4920.
- Dijkhuizen, P. A. and Ghosh, A. (2005) BDNF regulates primary dendrite formation in cortical neurons via the PI3-kinase and MAP kinase signaling pathways. *J. Neurobiol.*, 62(2), 278-288.
- Dotti, C. G., Sullivan, C. A., Banker, G. A. (1988) The establishment of polarity by hippocampal neurons in culture. *J. Neurosci.*, 8(4), 1454-1468.
- Du, J. L., Poo, M. M. (2004) Rapid BDNF-induced retrograde synaptic modification in a developing retinotectal system. *Nature*, 429(6994), 878-883.
- Duch, C. and Mentel, T. (2004) Activity affects dendritic shape and synapse elimination during steroid controlled dendritic retraction in *Manduca sexta*. *J. Neurosci.*, 24(44), 9826-9837.
- Elbashir, S. M., Lendeckel, W. and Tuschl, T. (2001) RNA interference is mediated by 21- and 22-nucleotide RNAs. *Genes Dev.*, 15(2), 188-200.
- Elmariah, S. B., Crumling, M. A., Parsons, T. D. and Balice-Gordon, R. J. (2004) Postsynaptic TrkB-mediated signaling modulates excitatory and inhibitory neurotransmitter receptor clustering at hippocampal synapses. *J. Neurosci.*, 24(10), 2380-2393.
- Ernfors, P., Ibanez, C. F., Ebendal, T., Olson, L. and Persson, H. (1990a) Molecular cloning and neurotrophic activities of a protein with structural similarities to nerve growth factor: developmental and topographical expression in the brain. *Proc. Natl. Acad. Sci. U S A*, 87(14), 5454-5458.

- Ernfors, P., Lee, K. F. and Jaenisch, R. (1994) Mice lacking brain-derived neurotrophic factor develop with sensory deficits. *Nature*, 368(6467), 147-150.
- Ernfors, P., Wetmore, C., Olson, L. and Persson, H. (1990b) Identification of cells in rat brain and peripheral tissues expressing mRNA for members of the nerve growth factor family. *Neuron*, 5(4), 511-526.
- Farhadi, H. F., Mowla, S. J., Petrecca, K., Morris, S. J., Seidah, N. G. and Murphy, R. A. (2000) Neurotrophin-3 sorts to the constitutive secretory pathway of hippocampal neurons and is diverted to the regulated secretory pathway by coexpression with brain-derived neurotrophic factor. *J. Neurosci.*, 20(11), 4059-4068.
- Ferrer, I., Goutan, E., Marin, C., Rey, M. J. and Ribalta, T. (2000) Brain-derived neurotrophic factor in Huntington disease. *Brain Res.*, 866(1-2), 257-261.
- Ferrer, I., Marin, C., Rey, M. J., Ribalta, T., Goutan, E., Blanco, R., Tolosa, E. and Marti, E. (1999) BDNF and full-length and truncated TrkB expression in Alzheimer disease. Implications in therapeutic strategies. *J. Neuropathol. Exp. Neurol.*, 58(7), 729-739.
- Fiala, J. C., Feinberg, M., Popov, V., Harris, K. M. (1998) Synaptogenesis via dendritic filopodia in developing hippocampal area CA1. *J. Neurosci.*, 18(21), 8900-8911.
- Figurov, A., Pozzo-Miller, L. D., Olafsson, P., Wang, T. and Lu, B. (1996) Regulation of synaptic responses to high-frequency stimulation and LTP by neurotrophins in the hippocampus. *Nature*, 381(6584), 706-709.
- Fink, C. C., Bayer, K. U., Myers, J. W., Ferrell Jr. J. E., Schulman, H. and Meyer, T. (2003) Selective regulation of neurite extension and synapse formation by the  $\beta$  but not the  $\alpha$  isoform of CaMKII. *Neuron*, 39, 283-297.
- Finkbeiner, S. (2000) Regulation of the brain-derived neurotrophic factor gene. *Cell. Mol. Life Sci.*, 57(3), 394-401.
- Fletcher, T. L., Cameron, P., De Camilli, P. and Banker G. (1991) The distribution of synapsin I and synaptophysin in hippocampal neurons developing in culture. *J. Neurosci.*, 11(6), 1617-1626.
- Fletcher, T. L., De Camilli, P. and Banker, G. (1994) Synaptogenesis in hippocampal cultures: evidence indicating that axons and dendrites become competent to form synapses at different stages of neuronal development. *J. Neurosci.*, 14(11), 6695-6706.
- Fukushima, N., Kimura, Y. and Chun, J. (1998) A single receptor encoded by *vzq-1/lpA1/edg-2* couples to G proteins and mediates multiple cellular responses to lysophosphatidic acid. *Proc. Natl. Acad. Sci. U S A.* 95(11), 6151-6156.
- Fukushima, N., Weiner, J. A., Kaushal, D., Contos, J. J., Rehen, S. K., Kingsbury, M. A., Kim, K. Y. and Chun, J., (2002) Lysophosphatidic acid influences the morphology and motility of young, postmitotic cortical neurons. *Mol. Cell. Neurosci.*, 20(2), 271-282.
- Galuske, R. A., Kim, D. S., Castren, E. and Singer, W. (2000) Differential effects of neurotrophins on ocular dominance plasticity in developing and adult cat visual cortex. *Eur. J. Neurosci.*, 12(9), 3315-3330.
- Gallo, G., Lefcort, F. B. and Letourneau, P. C. (1997) The *trkA* receptor mediates growth cone turning toward a localized source of nerve growth factor. *J. Neurosci.*, 17(14), 5445-5454.
- Gallo, G. and Letourneau, P. C. (1998) Localized sources of neurotrophins initiate axon collateral sprouting. *J. Neurosci.*, 18(14), 5403-5414.
- Gardioli, A., Racca, C. and Triller, A. (1999) Dendritic and postsynaptic protein synthetic machinery. *J. Neurosci.*, 19(1), 168-179.

- Gehlert, D. R., Stephenson, D. T., Schober, D. A. Rash, K. and Clemens, J. A. (1997) Increased expression of peripheral benzodiazepine receptors in the facial nucleus following motor neuron axotomy. *Neurochem. Int.*, 31, 705–713.
- Goodman, L. J., Valverde, J., Lim, F., Geschwind, M. D., Federoff, H. J., Geller, AI. and Hefti, F. (1996) Regulated release and polarized localization of brain-derived neurotrophic factor in hippocampal neurons. *Mol. Cell. Neurosci.*, 7(3), 222-238.
- Gorski, J. A., Zeiler, S. R., Tamowski, S. and Jones, K. R. (2003) Brain-derived neurotrophic factor is required for the maintenance of cortical dendrites. *J. Neurosci.*, 23(17), 6856-6865.
- Goslin, K. and Banker, G. (1990) Rapid changes in the distribution of GAP-43 correlate with the expression of neuronal polarity during normal development and under experimental conditions. *J. Cell Biol.*, 110(4), 1319-1331.
- Goslin, K., Asmussen, H. and Banker, G. (1998) Rat hippocampal neurons in low-density culture. In: Banker G, Goslin K, eds, *Culturing nerve cells*, 2<sup>nd</sup> ed. Cambridge, MA:MIT Press, 339-370
- Goslin, K., Schreyer, D. J., Skene, J. H. and Banker, G. (1990) Changes in the distribution of GAP-43 during the development of neuronal polarity. *J. Neurosci.*, 10(2), 588-602.
- Gotz, R., Raulf, F. and Schartl, M. (1992) Brain-derived neurotrophic factor is more highly conserved in structure and function than nerve growth factor during vertebrate evolution. *J. Neurochem.*, 59(2), 432-442.
- Gould, E., Westlind-Danielsson, A., Frankfurt, M. and McEwen, B. S. (1990) Sex differences and thyroid hormone sensitivity of hippocampal pyramidal cells. *J. Neurosci.*, 10(3), 996-1003.
- Graf, E. R., Zhang, X., Jin, S. X., Linhoff, M. W. and Craig A. M. (2004) Neurexins induce differentiation of GABA and glutamate postsynaptic specializations via neuroligins. *Cell*, 119(7), 1013-1026.
- Grantyn, R., Juttner, R. and Meier, J. (2004) Development and use-dependent modification of synaptic connections in the visual layers of the rodent superior colliculus. In: *The Superior Colliculus*, ed. Hall, W. C. and Moschovakis, A., 173-210. CRC Press, London.
- Grifman, M., Galyam, N., Seidman, S. and Soreq, H. (1998) Functional redundancy of acetylcholinesterase and neuroligin in mammalian neuritogenesis. *Proc. Natl. Acad. Sci. U S A*, 95(23), 13935-13940.
- Groc, L., Petanjek, Z., Gustafsson, B., Ben-Ari, Y., Hanse, E. and Khazipov, R. (2002) In vivo blockade of neural activity alters dendritic development of neonatal CA1 pyramidal cells. *Eur. J. Neurosci.*, 16(10), 1931-1938.
- Gundersen, R. W. and Barrett, J. N. (1979) Neuronal chemotaxis: chick dorsal-root axons turn toward high concentrations of nerve growth factor. *Science*, 206(4422), 1079-1080.
- Guo, X., Rueger, D. and Higgins, D. (1998) Osteogenic protein-1 and related bone morphogenetic proteins regulate dendritic growth and the expression of microtubule-associated protein-2 in rat sympathetic neurons. *Neurosci. Lett.*, 245(3), 131-134.
- Hall, A. C., Lucas, F. R. and Salinas, P. C. (2000) Axonal remodeling and synaptic differentiation in the cerebellum is regulated by WNT-7a signaling. *Cell*, 100(5), 525-535.
- Hallbook, F. (1999) Evolution of the vertebrate neurotrophin and Trk receptor gene families. *Curr. Opin. Neurobiol.*, 9(5), 616-621.

- Han, J., Luby-Phelps, K., Das, B., Shu, X., Xia, Y., Mosteller, R. D., Krishna, U. M., Falck, J. R., White, M. A. and Broek, D. (1998) Role of substrates and products of PI 3-kinase in regulating activation of Rac-related guanosine triphosphatases by Vav. *Science*, 279(5350), 558-560.
- Hamanoue, M., Middleton, G., Wyatt, S., Jaffray, E., Hay, R. T. and Davies, A. M. (1999) Neurotrophins are the most attractive candidates of the molecular factors known to influence dendrite morphogenesis. *Mol. Cell. Neurosci.*, 14(1), 28-40.
- Hashimoto, T., Bergen, S. E; Nguyen, Q. L., Xu, B., Monteggia, L. M, Pierri, J. N, Sun, Z., Sampson, A. R. and Lewis, D. A. (2005) Relationship of brain-derived neurotrophic factor and its receptor TrkB to altered inhibitory prefrontal circuitry in schizophrenia. *J. Neurosci.*, 25(2), 372-383.
- Haubensak, W., Narz, F., Heumann, R. and Lessmann, V. (1998) BDNF-GFP containing secretory granules are localized in the vicinity of synaptic junctions of cultured cortical neurons. *J. Cell Sci.*, 111, 1483-1493.
- Henneberger, C., Grantyn, R. and Rothe, T. (2000) Rapid genotyping of newborn gene mutant mice. *J Neurosci Methods*. 2000 Jul 31;100(1-2):123-6.
- Henneberger, C., Kirischuk, S., Grantyn, R. (2005) Brain-derived neurotrophic factor modulates GABAergic synaptic transmission by enhancing presynaptic glutamic acid decarboxylase 65 levels, promoting asynchronous release and reducing the number of activated postsynaptic receptors. *Neuroscience*, 135(3), 749-763.
- Heymach, J. V. Jr. and Shooter, E. M. (1995) The biosynthesis of neurotrophin heterodimers by transfected mammalian cells. *J. Biol. Chem.*, 270(20), 12297-12304.
- Hofer, M., Pagliusi, S. R., Hohn, A., Leibrock, J. and Barde, Y. A. (1990) Regional distribution of brain-derived neurotrophic factor mRNA in the adult mouse brain. *EMBO J.*, 9(8), 2459-2464.
- Horch, H. W. and Katz, L. C. (2002) BDNF release from single cells elicits local dendritic growth in nearby neurons. *Nat. Neurosci.*, 5 (11), 1177-1184.
- Horch, H. W., Kruttgen, A., Portbury, S. D. and Katz, L. C. (1999) Destabilization of cortical dendrites and spines by BDNF. *Neuron*, 23(2), 353-364.
- Hua, J. Y. and Smith, S. J. (2004) Neural activity and the dynamics of central nervous system development. *Nat. Neurosci.*, 7(4), 327-332.
- Huang, E. J. and Reichardt, L. F. (2001) Neurotrophins: roles in neuronal development and function. *Annu. Rev. Neurosci.*, 24, 677-736.
- Huntley, G. W. and Benson, D. L. (1999) Neural (N)-cadherin at developing thalamocortical synapses provides an adhesion mechanism for the formation of somatotopically organized connections. *J. Comp. Neurol.*, 407(4):453-471.
- Ibanez, C. F. (1998) Emerging themes in structural biology of neurotrophic factors. *Trends Neurosci.*, 21(10), 438-444.
- Inoue, A. and Sanes, J. R. (1997) Lamina-specific connectivity in the brain: regulation by N-cadherin, neurotrophins, and glycoconjugates. *Science*, 276(5317), 1428-1431.
- Ip, N. Y., Ibanez, C. F., Nye, S. H., McClain, J., Jones, P. F., Gies, D. R., Belluscio, L., Le Beau, M. M., Espinosa, R. 3rd. and Squinto, S. P. (1992) Mammalian neurotrophin-4: structure, chromosomal localization, tissue distribution, and receptor specificity. *Proc. Natl. Acad. Sci. U S A*, 89(7), 3060-3064.
- Jahn, R., Schiebler, W., Ouimet, C. and Greengard, P. (1985) A 38,000-dalton membrane protein (p38) present in synaptic vesicles. *Proc. Natl. Acad. Sci. U S A*, 82(12), 4137-4141.

- Jalink, K. and Moolenaar, W. H. (1992) Thrombin receptor activation causes rapid neural cell rounding and neurite retraction independent of classic second messengers. *J. Cell Biol.*, 118(2), 411-419.
- Jalink, K., van Corven, E. J., Hengeveld, T., Morii, N., Narumiya, S., Moolenaar, W. H. (1994) Inhibition of lysophosphatidate- and thrombin-induced neurite retraction and neuronal cell rounding by ADP ribosylation of the small GTP-binding protein Rho. *J. Cell Biol.*, 126(3), 801-810.
- Jamain, S., Quach, H., Betancur, C., Rastam, M., Colineaux, C., Gillberg, I. C., Soderstrom, H., Giros, B., Leboyer, M., Gillberg, C. and Bourgeron, T; Paris Autism Research International Sibpair Study (2003) Mutations of the X-linked genes encoding neuroligins NLGN3 and NLGN4 are associated with autism. *Nat. Genet.*, 34(1):27-29.
- Jones, K. J. , Durica, T. E. and Jacob, S. K. (1997) Gonadal steroid preservation of central synaptic input to hamster facial motoneurons following peripheral axotomy. *J. Neurocytol.*, 26(4), 257-266.
- Jontes, J. D., Buchanan, J. and Smith, S. J. (2000) Growth cone and dendrite dynamics in zebrafish embryos: early events in synaptogenesis imaged in vivo. *Nat. Neurosci.*, 3(3), 231-237.
- Jovanovic, J. N., Thomas, P., Kittler, J. T., Smart, T. G. and Moss, S. J. (2004) Brain-derived neurotrophic factor modulates fast synaptic inhibition by regulating GABA(A) receptor phosphorylation, activity, and cell-surface stability. *J. Neurosci.*, 24(2), 522-530.
- Kalb, R. G. (1994) Regulation of motor neuron dendrite growth by NMDA receptor activation. *Development*, 120(11), 3063-3071.
- Kang, H. and Schuman, E. M. (1995) Long-lasting neurotrophin-induced enhancement of synaptic transmission in the adult hippocampus. *Science*, 267(5204), 1658-1662.
- Kang, H., Schuman, E. M. (1996) A requirement for local protein synthesis in neurotrophin-induced hippocampal synaptic plasticity. *Science*, 273(5280), 1402-1406.
- Kaplan, D. R. and Miller, F. D. (2000) Neurotrophin signal transduction in the nervous system *Curr. Opin. Neurobiol.*, 10(3), 381-391.
- Katz, L. C. and Shatz, C. J. (1996) Synaptic activity and the construction of cortical circuits. *Science*, 274, 1133-1138.
- Kaufmann, W. E. and Moser, H. W. (2000) Dendritic anomalies in disorders associated with mental retardation. *Cereb. Cortex*, 10(10), 981-991.
- Kim, I. J., Drahushuk, K. M., Kim, W. Y., Gonsiorek, E. A., Lein, P., Andres, D. A. and Higgins, D. (2004) Extracellular signal-regulated kinases regulate dendritic growth in rat sympathetic neurons. *J. Neurosci.*, 24(13), 3304-3312.
- Kim, H. G., Wang, T., Olafsson, P. and Lu, B. (1994) Neurotrophin 3 potentiates neuronal activity and inhibits gamma-aminobutyrate synaptic transmission in cortical neurons. *Proc. Natl. Acad. Sci. U S A*, 91(25), 12341-12345.
- Kirschuk, S., Juttner, R. and Grantyn, R. (2005) Time-matched pre- and postsynaptic changes of GABAergic synaptic transmission in the developing mouse superior colliculus. *J. Physiol.*, 563, 795-807.
- Kjoller, L. and Hall, A. (1999) Signaling to Rho GTPases. *Exp. Cell Res.*, 253(1), 166-179.
- Knott, G. W., Quairiaux, C., Genoud, C., Welker, E. (2002) Formation of dendritic spines with GABAergic synapses induced by whisker stimulation in adult mice. *Neuron*, 34(2), 265-273.

- Kolkova, K., Stensman, H., Berezin, V., Bock, E. and Larsson, C. (2005) Distinct roles of PKC isoforms in NCAM-mediated neurite outgrowth. *J. Neurochem.*, 92(4), 886-894.
- Korsching, S. (1993) The neurotrophic factor concept: a reexamination. *J. Neurosci.*, 13(7), 2739-2748.
- Korte, M., Carroll, P., Wolf, E., Brem, G., Thoenen, H. and Bonhoeffer, T. (1995) Hippocampal long-term potentiation is impaired in mice lacking brain-derived neurotrophic factor. *Proc. Natl. Acad. Sci. U S A*, 92(19), 8856-8860.
- Laudenbach, V., Mantz, J., Lagercrantz, H., Desmots, J. M., Evrard, P. and Gressens, P. (2002) Effects of alpha(2)-adrenoceptor agonists on perinatal excitotoxic brain injury: comparison of clonidine and dexmedetomidine. *Anesthesiology*, 96(1), 134-141.
- Lee, R. C., Clandinin, T. R., Lee, C. H., Chen, P. L., Meinertzhagen, I. A. and Zipursky, S. L. (2003) The protocadherin Flamingo is required for axon target selection in the *Drosophila* visual system. *Nat. Neurosci.*, 6(6), 557-563.
- Le Roux, P., Behar, S., Higgins, D. and Charrette, M. (1999) OP-1 enhances dendritic growth from cerebral cortical neurons in vitro. *Exp. Neurol.*, 160(1), 151-163.
- Lessmann, V., Gottmann, K. and Malsangio, M. (2003) Neurotrophin secretion: current facts and future prospects. *Prog. Neurobiol.*, 69, 341-374.
- Levine, J. S., Koh, J. S., Triaca, V. and Lieberthal W. (1997) Lysophosphatidic acid: a novel growth and survival factor for renal proximal tubular cells. *Am. J. Physiol.*, 273, 575-585.
- Levi-Montalcini, R. (1987) The nerve growth factor 35 years later. *Science*, 237, 1154-1162.
- Levi-Montalcini, R. and Hamburger, V. (1951) Selective growth-stimulating effects of mouse sarcoma on the sensory and sympathetic nervous system of the chick embryo. *J. Exp. Zool.* 116, 321-362.
- Lewin, G. R. and Barde, Y. A. (1996) Physiology of the neurotrophins. *Annu. Rev. Neurosci.*, 19, 289-317.
- Li, H., Prince, D. A. (2002) Synaptic activity in chronically injured, epileptogenic sensory-motor neocortex. *J. Neurophysiol.*, 88(1), 2-12.
- Li, Z., Van Aelst, L., Cline, H. T. (2000) Rho GTPases regulate distinct aspects of dendritic arbor growth in *Xenopus* central neurons in vivo. *Nat. Neurosci.*, 3(3), 217-225.
- Lichtman, J. W. and Colman, H. (2000) Synapse elimination and indelible memory. *Neuron*, 25(2), 269-278.
- Lindsell, C. E., Shawber, C. J., Boulter, J. and Weinmaster, G. (1995) Jagged: a mammalian ligand that activates Notch1. *Cell*, 80(6), 909-917.
- Liu, G. (2004) Local structural balance and functional interaction of excitatory and inhibitory synapses in hippocampal dendrites. *Nat. Neurosci.*, 7(4), 373-379.
- Liu, H. S., Jan, M. S., Chou, C. K., Chen, P. H., Ke, N. J. (1999) Is green fluorescent protein toxic to the living cells? *Biochem. Biophys. Res. Commun.*, 260(3), 712-717.
- Llinas, R. R., Ribary, U., Jeanmonod, D., Kronberg, E and Mitra, P. P. (1999) Thalamocortical dysrhythmia: A neurological and neuropsychiatric syndrome characterized by magnetoencephalography, *Proc. Natl. Acad. Sci. USA*, 96, 15222-15227.
- Lohof, A. M., Ip, N. Y. and Poo, M. M. (1993) Potentiation of developing neuromuscular synapses by the neurotrophins NT-3 and BDNF. *Nature*, 363(6427), 350-353.



- Lohmann, C., Finski, A., and Bonhoeffer, T. (2005) Local calcium transients regulate the spontaneous motility of dendritic filopodia. *Nat. Neurosci.*, 8, 305–312.
- Lohmann, C., Myhr, K. L. and Wong, R. O. L. (2002) Transmitter-evoked local calcium release stabilizes developing dendrites. *Nature*, 418, 177-181.
- Lom, B. and Cohen-Cory, S. (1999) Brain-derived neurotrophic factor differentially regulates retinal ganglion cell dendritic and axonal arborization in vivo. *J. Neurosci.*, 19(22), 9928-9938.
- Lu, B. (2003) Pro-region of neurotrophins: role in synaptic modulation. *Neuron*, 39(5), 735-738.
- Luo, L. (2000) Rho GTPases in neuronal morphogenesis. *Nat. Rev. Neurosci.*, 1(3), 173-180.
- Luo, L., Jan, L. Y., Jan, Y. N. (1997) Rho family GTP-binding proteins in growth cone signaling. *Curr. Opin. Neurobiol.*, 7(1), 81-86.
- Lyford, G. L., Yamagata, K., Kaufmann, W. E., Barnes, C. A., Sanders, L. K., Copeland, N. G., Gilbert, D. J., Jenkins, N. A., Lanahan, A. A. and Worley, P. F. (1995) *Arc*, a growth factor and activity-regulated gene, encodes a novel cytoskeleton-associated protein that is enriched in neuronal dendrites. *Neuron*, 14(2), 433-445.
- Maletic-Savatic, M., Malinow, R. and Svoboda, K. (1999) Rapid dendritic morphogenesis in CA1 hippocampal dendrites induced by synaptic activity. *Science*, 283(5409), 1923-1927.
- Manning, T. J. Jr., Rosenfeld, S. S. and Sontheimer, H. (1998) Lysophosphatidic acid stimulates actomyosin contraction in astrocytes. *J. Neurosci. Res.*, 53(3), 343-352.
- Martinez, A., Alcantara, S., Borrell, V., Del Rio, J. A., Blasi, J., Ojal, R., Campos, N., Boronat, A., Barbacid, M., Silos-Santiago, I. and Soriano, E. (1998) *TrkB* and *TrkC* signaling are required for maturation and synaptogenesis of hippocampal connections. *J. Neurosci.*, 18(18), 7336-7350.
- Mathern, G. W., Babb, T. L., Micevych, P. E., Blanco, C. E. and Pretorius, J. K. (1997) Granule cell mRNA levels for BDNF, NGF, and NT-3 correlate with neuron losses or supragranular mossy fiber sprouting in the chronically damaged and epileptic human hippocampus. *Mol. Chem. Neuropathol.*, 30(1-2), 53-76.
- McAllister, A. K., Katz, L. C. and Lo, D. C. (1997) Opposing roles for endogenous BDNF and NT-3 in regulating cortical dendritic growth. *Neuron*, 18(5), 767-778.
- McAllister, A. K., Katz, L. C. and Lo, D. C. (1999) Neurotrophins and synaptic plasticity. *Annu. Rev. Neurosci.*, 22, 295-318.
- McAllister, A. K., Lo, D. C. and Katz, L. C. (1995) Neurotrophins regulate dendritic growth in developing visual cortex. *Neuron*, 15(4), 791-803.
- McAllister, A. K., Katz, L. C. and Lo, D. C. (1996) Neurotrophin regulation of cortical dendritic growth requires activity. *Neuron*, 17(6), 1057-1064.
- Meier, J., Akyeli, J., Kirischuk, S. and Grantyn, R. (2003) GABA(A) receptor activity and PKC control inhibitory synaptogenesis in CNS tissue slices. *Mol. Cell. Neurosci.*, 23(4), 600-613.
- Menei, P., Montero-Menei, C., Whittemore, S. R., Bunge, R. P. and Bunge, M. B. (1998) Schwann cells genetically modified to secrete human BDNF promote enhanced axonal regrowth across transected adult rat spinal cord. *Eur. J. Neurosci.*, 10(2), 607-621.
- Michael, G. J., Averill, S., Nitkunan, A., Rattray, M., Bennett, D. L., Yan, Q. and Priestley, J. V. (1997) Nerve growth factor treatment increases brain-derived neurotrophic factor selectively in *TrkA*-expressing dorsal root ganglion cells and in their central terminations within the spinal cord. *J. Neurosci.*, 17(21), 8476-8490.

- Ming, G., Lohof, A. M., Zheng, J. Q. (1997) Acute morphogenic and chemotropic effects of neurotrophins on cultured embryonic *Xenopus* spinal neurons. *J. Neurosci.*, 17(20), 7860-7871.
- Mitsui, T., Fischer, I., Shumsky, J. S. and Murray, M. (2005) Transplants of fibroblasts expressing BDNF and NT-3 promote recovery of bladder and hindlimb function following spinal contusion injury in rats. *Exp. Neurol.*, 194(2), 410-431.
- Mohrmann, R., Lessmann, V. and Gottmann, K. (2003) Developmental maturation of synaptic vesicle cycling as a distinctive feature of central glutamatergic synapses. *Neuroscience*, 117(1), 7-18.
- Moolenaar, W. H. (1999) Bioactive lysophospholipids and their G protein-coupled receptors. *Exp. Cell Res.*, 253(1), 230-238.
- Moore, H., West, A. R. and Grace, A. A. (1999) The regulation of forebrain dopamine transmission: relevance to the pathophysiology and psychopathology of schizophrenia. *Biol. Psychiatry*, 46(1), 40-55.
- Morales, B., Choi, S. Y., Kirkwood, A. (2002) Dark rearing alters the development of GABAergic transmission in visual cortex. *J. Neurosci.*, 22(18), 8084-8090.
- Moss, S. J. and Smart, T. G. (2001) Constructing inhibitory synapses. *Nat. Rev. Neurosci.*, 2(4), 240-250.
- Mowla, S. J., Farhadi, H. F., Pareek, S., Atwal, J. K., Morris, S. J., Seidah, N. G. and Murphy, R. A. (2001) Biosynthesis and post-translational processing of the precursor to brain-derived neurotrophic factor. *J. Biol. Chem.*, 276(16), 12660-12666.
- Mowla, S. J., Pareek, S., Farhadi, H. F., Petrecca, K., Fawcett, J. P., Seidah, N. G., Morris, S. J., Sossin, W. S. and Murphy, R. A. (1999) Differential sorting of nerve growth factor and brain-derived neurotrophic factor in hippocampal neurons. *J. Neurosci.*, 19(6), 2069-2080.
- Mufson, E. J., Kroin, J. S., Sendera, T. J. and Sobreviela, T. (1999) Distribution and retrograde transport of trophic factors in the central nervous system: functional implications for the treatment of neurodegenerative diseases. *Prog. Neurobiol.*, 57(4), 451-484.
- Murai, K. K., Nguyen, L. N., Irie, F., Yamaguchi, Y. and Pasquale, E. B. (2003) Control of hippocampal dendritic spine morphology through ephrin-A3/EphA4 signaling. *Nat. Neurosci.*, 6(2), 153-160.
- Murer, M. G., Boissiere, F., Yan, Q., Hunot, S., Villares, J., Faucheux, B., Agid, Y., Hirsch, E. and Raisman-Vozari, R. (1999) An immunohistochemical study of the distribution of brain-derived neurotrophic factor in the adult human brain, with particular reference to Alzheimer's disease. *Neuroscience*, 88(4), 1015-1032.
- Nedivi, E., Wu, G. Y., Cline, H. T. (1998) Promotion of dendritic growth by CPG15, an activity-induced signaling molecule. *Science*, 281(5384), 1863-1866.
- Nguyen, T. and Sudhof, T. C. (1997) Binding properties of neuroligin 1 and neuroligin 1beta reveal function as heterophilic cell adhesion molecules. *J. Biol. Chem.*, 272(41), 26032-26039.
- Niblock, M. M., Brunso-Bechtold, J. K., Riddle, D. R. (2000) Insulin-like growth factor I stimulates dendritic growth in primary somatosensory cortex. *J. Neurosci.*, 20(11), 4165-4176.
- Niell, C. M., Meyer, M. P. and Smith, S. J. (2004) In vivo imaging of synapse formation on a growing dendritic arbor. *Nat. Neurosci.*, 7(3), 254-260.
- Neuwald, A. F. (1997) An unexpected structural relationship between integral membrane phosphatases and soluble haloperoxidases. *Protein Sci.*, 6(8), 1764-1767.

- Noguchi, K., Ishii, S. and Shimizu, T. (2003) Identification of p2y9/GPR23 as a novel G protein-coupled receptor for lysophosphatidic acid structurally distant from the Edg family. *J. Biol. Chem.*, 278(28), 25600-25606.
- O'Brien, R. J., Xu, D., Petralia, R. S., Steward, O., Huganir, R. L. and Worley, P. (1999) Synaptic clustering of AMPA receptors by the extracellular immediate-early gene product *Narp*. *Neuron*, 23(2), 309-323.
- O'Leary, D. D. and Wilkinson, D. G. (1999) Eph receptors and ephrins in neural development. *Curr. Opin. Neurobiol.*, 9(1), 65-73.
- Parain, K., Murer, M. G., Yan, Q., Faucheux, B., Agid, Y., Hirsch, E. and Raisman-Vozari, R. (1999) Reduced expression of brain-derived neurotrophic factor protein in Parkinson's disease substantia nigra. *Neuroreport*, 10(3), 557-561.
- Patterson, S. L., Abel, T., Deuel, T. A., Martin, K. C., Rose, J. C., Kandel, E. R. (1996) Recombinant BDNF rescues deficits in basal synaptic transmission and hippocampal LTP in BDNF knockout mice. *Neuron*, 16(6), 1137-1145.
- Pawson, T. and Nash, P. (2000) Protein-protein interactions define specificity in signal transduction. *Genes Dev.*, 14(9), 1027-1047.
- Pflüger, H. J., Hurdelbrink, S., Czjzek, A. and Burrows, M. (1994) Activity-dependent structural dynamics of insect sensory fibers. *J. Neurosci.*, 14(11), 6946-6955.
- Phillips, H. S., Hains, J. M., Armanini, M., Laramée, G. R., Johnson, S. A. and Winslow, J. W. (1991) BDNF mRNA is decreased in the hippocampus of individuals with Alzheimer's disease. *Neuron*, 7(5), 695-702.
- Polleux, F., Morrow, T. and Ghosh, A. (2000) Semaphorin 3A is a chemoattractant for cortical apical dendrites. *Nature*, 404(6778), 567-573.
- Polo-Parada, L., Bose, C. M., Plattner, F. and Landmesser, L. T. (2004) Distinct roles of different neural cell adhesion molecule (NCAM) isoforms in synaptic maturation revealed by analysis of NCAM 180 kDa isoform-deficient mice. *J. Neurosci.*, 24(8), 1852-1864.
- Pozzo-Miller, L. D., Gottschalk, W., Zhang, L., McDermott, K., Du, J., Gopalakrishnan, R., Oho, C., Sheng, Z. H. and Lu, B. (1999) Impairments in high-frequency transmission, synaptic vesicle docking, and synaptic protein distribution in the hippocampus of BDNF knockout mice. *J. Neurosci.*, 19(12), 4972-4983.
- Purves, D. and Hume, R. I. (1981) The relation of postsynaptic geometry to the number of presynaptic axons that innervate autonomic ganglion cells. *J. Neurosci.*, 1(5), 441-452.
- Rao, A. and Craig, A. M. (1997) Activity regulates the synaptic localization of the NMDA receptor in hippocampal neurons. *Neuron*, 19(4), 801-812.
- Raymond, G. V., Bauman, M. L. and Kemper, T. L. (1996) Hippocampus in autism: a Golgi analysis. *Acta Neuropathol. (Berl.)*, 91(1), 117-119.
- Rechsteiner, M. and Rogers, S. W. (1996) PEST sequences and regulation by proteolysis. *Trends Biochem. Sci.*, 21(7), 267-271.
- Redmond, L., Kashani, A.H. and Ghosh A. (2002) Calcium regulation of dendritic growth via CaM Kinase IV and CREB-mediated transcription. *Neuron*, 34, 999-1010.
- Redmond, L., Oh, S. R., Hicks, C., Weinmaster, G. and Ghosh, A. (2000) Nuclear Notch1 signaling and the regulation of dendritic development. *Nat. Neurosci.*, 3(1), 30-40.

- Reszka, A. A., Bulinski, J. C., Krebs, E. G. and Fischer, E. H. (1997) Mitogen-activated protein kinase/extracellular signal-regulated kinase 2 regulates cytoskeletal organization and chemotaxis via catalytic and microtubule-specific interactions. *Mol. Biol. Cell*, 8(7), 1219-1232.
- Ribar, T. J., Rodriguiz, R. M., Khiroug, L., Wetsel, W. C., Augustine, G. J. and Means, A. R. (2000) Cerebellar defects in  $Ca^{2+}$ /calmodulin kinase IV-deficient mice. *J. Neurosci.*, 20(22), RC107.
- Rico, B., Xu, B. and Reichardt, L. F. (2002) TrkB receptor signaling is required for establishment of GABAergic synapses in the cerebellum. *Nat. Neurosci.*, 5(3), 225-233.
- Rittenhouse, C. D., Shouval, H. Z., Paradiso, M. A. and Bear, M. F. (1999) Monocular deprivation induces homosynaptic long-term depression in visual cortex. *Nature*, 397(6717), 347-350.
- Rosier, M. F., Goguel, A. F., Martin, A., Le Paslier, D., Couillin, P., Houlgatte, R., Bernheim, A., Auffray, C. and Devignes, M. D. (1994) A 1.7-Mb YAC contig around the human BDNF gene (11p13): integration of the physical, genetic, and cytogenetic maps in relation to WAGR syndrome. *Genomics*, 24(1), 69-77.
- Rubenstein J. L. and Merzenich, M. M. (2003) Model of autism: increased ratio of excitation/inhibition in key neural systems. *Genes Brain Behav.*, 2, 255-267.
- Ruchhoeft, M. L., Ohnuma, S., McNeill, L., Holt, C. E. and Harris, W. A. (1999) The neuronal architecture of *Xenopus* retinal ganglion cells is sculpted by rho-family GTPases in vivo. *J. Neurosci.*, 19(19), 8454-8463.
- Ruit, K. G., Osborne, P. A., Schmidt, R. E., Johnson, E. M. Jr. and Snider, W. D. (1990) Nerve growth factor regulates sympathetic ganglion cell morphology and survival in the adult mouse. *J. Neurosci.*, 10(7), 2412-2419.
- Saito, S. (1997) Effects of lysophosphatidic acid on primary cultured chick neurons. *Neurosci. Lett.*, 229(2), 73-76.
- Sala, R., Viegi, A., Rossi, F. M., Pizzorusso, T., Bonanno, G., Raiteri M. and Maffei, L. (1998) Nerve-growth factor and brain-derived neurotrophic factor increase neurotransmitters release in rat visual cortex. *Eur. J. Neurosci.*, 10, 2185-2191.
- Salama-Cohen, P., Arevalo, M. A., Meier, J., Grantyn, R. and Rodriguez-Tebar, A. (2005) NGF controls dendrite development in hippocampal neurons by binding to p75NTR and modulating the cellular targets of Notch. *Mol. Biol. Cell*, 16(1), 339-347.
- Sanes, J. R., Lichtman, J. W. (1999) Development of the vertebrate neuromuscular junction. *Annu. Rev. Neurosci.*, 22, 389-442.
- Sara, Y., Biederer, T., Atasoy, D., Chubykin, A., Mozhayeva, M. G., Sudhof, T. C. and Kavalali, E. T. (2005) Selective capability of SynCAM and neuroligin for functional synapse assembly. *J. Neurosci.*, 25(1), 260-270.
- Savaskan, N. E., Brauer, A. U. and Nitsch, R. (2004) Molecular cloning and expression regulation of PRG-3, a new member of the plasticity-related gene family. *Eur. J. Neurosci.*, 19(1), 212-220.
- Scharfman, H. E. (1997) Hyperexcitability in combined entorhinal/hippocampal slices of adult rat after exposure to brain-derived neurotrophic factor. *J. Neurophysiol.*, 78, 1082-1095.
- Scheiffele, P., Fan, J., Choih, J., Fetter, R. and Serafini, T. (2000) Neuroligin expressed in nonneuronal cells triggers presynaptic development in contacting axons. *Cell*, 101(6), 657-669.
- Schikorski, T. and Stevens, C. F. (1997) Quantitative ultrastructural analysis of hippocampal excitatory synapses. *J. Neurosci.*, 17(15), 5858-5867.

- Schneider, R. and Schweiger, M. (1991) A novel modular mosaic of cell adhesion motifs in the extracellular domains of the neurogenic trk and trkB tyrosine kinase receptors. *Oncogene*, 6(10), 1807-1811.
- Seidah, N. G., Benjannet, S., Pareek, S., Chretien, M. and Murphy, R. A. (1996) Cellular processing of the neurotrophin precursors of NT3 and BDNF by the mammalian proprotein convertases. *FEBS Lett.*, 379(3), 247-250.
- Sharp, D. J., Yu, W., Ferhat, L., Kuriyama, R., Rueger, D. C., Baas, P. W. (1997) Identification of a microtubule-associated motor protein essential for dendritic differentiation. *J. Cell Biol.*, 138(4), 833-843.
- Sheng, M. (2001) Molecular organization of the postsynaptic specialization. *Proc. Natl. Acad. Sci. U S A*, 98(13), 7058-7061.
- Sheng, M. and Sala, C. (2001) PDZ domains and the organization of supramolecular complexes. *Annu. Rev. Neurosci.*, 24, 1-29.
- Sin, W. C., Haas, K., Ruthazer, E. S. and Cline, H. A. T. (2002) Dendrite growth increased by visual activity requires NMDA receptor and Rho GTPases. *Nature*, 419(6906), 475-480.
- Smith, M. A., Zhang, L. X., Lyons, W. E., Mamounas, L. A. (1997) Anterograde transport of endogenous brain-derived neurotrophic factor in hippocampal mossy fibers. *Neuroreport*, 8(8), 1829-1834.
- Sobriela, T., Pagcatipunan, M., Kroin, J. S. and Mufson, E. J. (1996) Retrograde transport of brain-derived neurotrophic factor (BDNF) following infusion in neo- and limbic cortex in rat: relationship to BDNF mRNA expressing neurons. *J. Comp. Neurol.*, 375(3), 417-444.
- Song, H. J., Ming, G. L. and Poo, M. M. (1997) cAMP-induced switching in turning direction of nerve growth cones. *Nature*, 388(6639), 275-279
- Steward, O. and Worley, P. (2002) Local synthesis of proteins at synaptic sites on dendrites: role in synaptic plasticity and memory consolidation? *Neurobiol. Learn. Mem.*, 78(3), 508-527.
- Sugimoto, T., Bennett, G. J. and Kajander, K. C. (1990) Transsynaptic degeneration in the superficial dorsal horn after sciatic nerve injury: Effects of a chronic constriction injury, transection, and strychnine. *Pain*, 42(2), 205-213.
- Super, H. and Soriano, E. (1994) The organization of the embryonic and early postnatal murine hippocampus. II. Development of entorhinal, commissural, and septal connections studied with the lipophilic tracer DiI. *J. Comp. Neurol.*, 344(1), 101-120.
- Svensson, M., Tornqvist, E., Aldskogius, H. and Cova, J. L. (1991) Synaptic detachment from hypoglossal neurons after different types of nerve injury in the cat. *J. Hirnforsch.*, 32(5), 547-552.
- Tanaka, T., Saito, H. and Matsuki, N. (1997) Inhibition of GABAA synaptic responses by brain-derived neurotrophic factor (BDNF) in rat hippocampus. *J. Neurosci.*, 17(9):2959-2266.
- Tartaglia, N., Du, J., Tyler, W. J., Neale, E., Pozzo-Miller, L. and Lu, B. (2001) Protein synthesis-dependent and -independent regulation of hippocampal synapses by brain-derived neurotrophic factor. *J. Biol. Chem.*, 276(40), 37585-37593.
- Threadgill, R., Bobb, K. and Ghosh, A. (1997) Regulation of dendritic growth and remodeling by Rho, Rac, and Cdc42. *Neuron*, 19(3), 625-634.
- Tigyi, G. and Miledi, R. (1992) Lysophosphatidates bound to serum albumin activate membrane currents in *Xenopus* oocytes and neurite retraction in PC12 pheochromocytoma cells. *J. Biol. Chem.*, 267(30), 21360-21367.

- Togashi, H., Abe, K., Mizoguchi, A., Takaoka, K., Chisaka, O. and Takeichi, M. (2002) Cadherin regulates dendritic spine morphogenesis. *Neuron*, 35(1), 77-89.
- Tokumura, A., Sinomiya, J., Kishimoto, S., Tanaka, T., Kogure, K., Sugiura, T., Satouchi, K., Waku, K. and Fukuzawa, K. (2002) Human platelets respond differentially to lysophosphatidic acids having a highly unsaturated fatty acyl group and alkyl ether-linked lysophosphatidic acids. *Biochem. J.*, 365, 617-628.
- tom Dieck, S., Sanmarti-Vila, L., Langnaese, K., Richter, K., Kindler, S., Soyke, A., Wex, H., Smalla, K. H., Kampf, U., Franzer, J. T., Stumm, M., Garner, C. C. and Gundelfinger, E. D. (1998) Bassoon, a novel zinc-finger CAG/glutamine-repeat protein selectively localized at the active zone of presynaptic nerve terminals. *J. Cell Biol.*, 142(2), 499-509.
- Tyler WJ, Pozzo-Miller LD (2001) BDNF enhances quantal neurotransmitter release and increases the number of docked vesicles at the active zones of hippocampal excitatory synapses. *J Neurosci* 21:4249-4258
- Umemori, H., Linhoff, M. W., Ornitz, D. M. and Sanes, J. R. (2004) FGF22 and its close relatives are presynaptic organizing molecules in the mammalian brain. *Cell*, 118(2), 257-270.
- Vaillant, A. R., Zanassi, P., Walsh, G. S., Aumont, A., Alonso, A. and Miller, F. D. (2002) Signaling mechanisms underlying reversible, activity-dependent dendrite formation. *Neuron*, 34(6), 985-998.
- Varoqueaux, F., Sigler, A., Rhee, J. S., Brose, N., Enk, C., Reim, K. and Rosenmund, C. (2002) Total arrest of spontaneous and evoked synaptic transmission but normal synaptogenesis in the absence of Munc13-mediated vesicle priming. *Proc. Natl. Acad. Sci. U S A*, 99(13), 9037-9042.
- Vaughn, J. E. (1989) Fine structure of synaptogenesis in the vertebrate central nervous system. *Synapse*, 3(3), 255-285.
- Verhage, M., Maia, A. S., Plomp, J. J., Brussaard, A. B., Heeroma, J. H., Vermeer, H., Toonen, R. F., Hammer, R. E., van den Berg, T. K., Missler, M., Geuze, H. J. and Sudhof, T. C. (2000) Synaptic assembly of the brain in the absence of neurotransmitter secretion. *Science*, 287(5454), 864-869.
- Wahl, S., Barth, H., Ciossek, T., Aktories, K. and Mueller, B. K. (2000) Ephrin-A5 induces collapse of growth cones by activating Rho and Rho kinase. *J. Cell Biol.*, 149(2), 263-270.
- Walsh, M. K. and Lichtman, J. W. (2003) In vivo time-lapse imaging of synaptic takeover associated with naturally occurring synapse elimination. *Neuron*, 37(1), 67-73.
- Wang, T., Xie, K., Lu, B. (1995) Neurotrophins promote maturation of developing neuromuscular synapses. *J. Neurosci.*, 15, 4796-4805.
- Washbourne, P., Bennett, J. E. and McAllister, A. K. (2002) Rapid recruitment of NMDA receptor transport packets to nascent synapses. *Nat. Neurosci.*, 5(8), 751-759.
- Wassef, A., Baker, J. and Kochan, L. D. (2003) GABA and schizophrenia: a review of basic science and clinical studies. *J. Clin. Psychopharmacol.*, 23, 601-640.
- Wayman, G.A., Kaech, S., Grant, W.F., Davare, M., Impey, S., Tokumitsu, H., Nozaki, N., Banker, G. and Soderling, T.R. (2004) Regulation of axonal extension and growth cone motility by calmodulin-dependent protein kinase I. *J. Neurosci.*, 24, 3786-3794.
- Williams, G., Williams, E. J., Maison, P., Pangalos, M. N., Walsh, F. S. and Doherty, P. (2005) Overcoming the inhibitors of myelin with a novel neurotrophin strategy. *J. Biol. Chem.*, 280(7), 5862-5869.
- Woolley, C. S., Gould, E. and McEwen, B. S. (1990) Exposure to excess glucocorticoids alters dendritic morphology of adult hippocampal pyramidal neurons. *Brain Res.*, 531(1-2), 225-231.

- Wu, G. Y. and Cline H.T (1998) Stabilization of dendritic arbor structure in vivo by CaMKII. *Science*, 279, 222–226.
- Wu, G. Y., Deisseroth, K. and Tsien, R. W. (2001) Spaced stimuli stabilize MAPK pathway activation and its effects on dendritic morphology. *Nat. Neurosci.*, 4(2), 151-158.
- Wu, Y. J., Krüttgen, A., Moeller, J. C., Shine, D., Chan, J. R., Shooter, E. M. and Cosgaya, J. M. (2004) Nerve growth factor, brain-derived neurotrophic factor, and neurotrophin-3 are sorted to dense-core vesicles and released via the regulated pathway in primary rat cortical neurons. *J. Neurosci. Res.*, 75, 825-834.
- Yamada, M. K., Nakanishi, K., Ohba, S., Nakamura, T., Ikegaya, Y., Nishiyama, N. and Matsuki, N. (2002) Brain-derived neurotrophic factor promotes the maturation of GABAergic mechanisms in cultured hippocampal neurons. *J. Neurosci.*, 22(17), 7580-7585.
- Yamashita, T., Tucker, K. L. and Barde, Y. A. (1999) Neurotrophin binding to the p75 receptor modulates Rho activity and axonal outgrowth. *Neuron*, 24(3), 585-593.
- Yan, Q., Matheson, C. and Lopez, O. T. (1995) In vivo neurotrophic effects of GDNF on neonatal and adult facial motor neurons. *Nature*, 373(6512), 341-344.
- Yu, X. and Malenka, R. C. (2003)  $\beta$ -catenin is critical for dendritic morphogenesis. *Nat. Neurosci.*, 6, 1169 - 1177.
- Yue, J., Yokoyama, K., Balazs, L., Baker, D. L., Smalley, D., Pilquill, C., Brindley, D. N. and Tigyi, G. (2004) Mice with transgenic overexpression of lipid phosphate phosphatase-1 display multiple organotypic deficits without alteration in circulating lysophosphatidate level. *Cell Signal.*, 16(3), 385-399.
- Zhai, R. G., Vardinon-Friedman, H., Cases-Langhoff, C., Becker, B., Gundelfinger, E. D., Ziv, N. E. and Garner, C. C. (2001) Assembling the presynaptic active zone: a characterization of an active one precursor vesicle. *Neuron*, 29(1), 131-143.
- Zhang, Q. X., Pilquill, C. S., Dewald, J., Berthiaume, L. G., Brindley, D. N. (2000) Identification of structurally important domains of lipid phosphate phosphatase-1: implications for its sites of action. *Biochem. J.*, 345, 181-184.
- Ziv, N. E. and Garner, C. C. (2004) Cellular and molecular mechanisms of presynaptic assembly. *Nat. Rev. Neurosci.*, 5(5), 385-399.
- Ziv, N. E. and Smith, S. J. (1996) Evidence for a role of dendritic filopodia in synaptogenesis and spine formation. *Neuron*, 17(1), 91-102.
- Zoghbi, H. Y. (2003) Postnatal neurodevelopmental disorders: meeting at the synapse? *Science*, 302(5646), 826-830.

## Abbreviations and acronyms

Aa	amino acid
Ab (mAb / pAb)	antibody (monoclonal / polyclonal)
AMPA	$\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
BDNF	brain-derived neurotrophic factor
BSA	bovine serum albumin
cAMP	cyclic adenosine monophosphate
cDNA	complementary DNA
CNS	central nervous system
Cy	cyanine (dyes)
DAPI	4', 6 diamidino-2-phenylindole
DIV	days in vitro
DMSO	dimethyl sulfoxide
DNA	deoxyribonucleic acid
DNQX	6,7-dinitroquinoxaline-2,3-dione
E	embryonic day
EDTA	ethylene diamine tetra acetic acid
EGFP	enhanced green fluorescent protein
EtBr	ethidium bromide
FCS	fetal calf serum
FITC	fluorescein isothiocyanate
GABA	gamma-amino butyric acid
GAPDH	glyceraldehyde-6-phosphate dehydrogenase
GluRs	glutamate receptors
GFP	green fluorescent protein
h	hour (s)
HEPES	N-2-hydroxy-ethylpiperazine-N'-2-ethane sulfonic acid
kD	kilo Dalton
l	liter
IgG	immunoglobulin G
LPA	lysophosphatidic acid
LPP	lipid phosphate phosphatase
M	molar (moles/liter)
MAP kinase	mitogen-associated protein kinase
MAP2	microtubule-associated protein 2
MEM	minimum essential medium



mEPSC/ mIPSC	miniature excitatory/ inhibitory postsynaptic current
min	minute (s)
mg / ml	milligram / milliliter
mRNA	messenger ribonucleic acid
NCAM	neural cell adhesion molecule
NGF	nerve growth factor
NLGN (NL, NLG)	neuroligin
NMDA	N-methyl-D-aspartic acid
ns	not significant
NT	neurotrophin
NT-3 / NT-4	neurotrophic factor-3 / 4
OD	optical density
P	post-natal day
p75 <sup>NTR</sup>	pan neurotrophin receptor
PA	phosphatidic acid
PAF	paraformaldehyde
PBS-CMF	phosphate-buffered saline calcium and magnesium free
PCR	polymerase chain reaction
PI3	phosphatidylinositol 3-kinase
PNS	peripheral nervous system
PO	poly-L-ornithine
PRG / LPR	plasticity-related gene / lipid phosphate phosphatase-related protein
PSD	postsynaptic density
ROI	region of interest
RNA	ribonucleic acid
RT-PCR	reverse transcriptase-polymerase chain reaction
S1P	sphingosine-1-phosphate
siRNA	small interference RNA
S-MCPG	(S)- $\alpha$ -methyl-4-carboxyphenylglycine
Syp I / Syn I	synaptophysin I / synapsin I
t-BDNF	transfected BDNF
TE	tris EDTA
Tris	tris (hydroxymethyl) aminomethane
Trk	tropomyosin related kinase
°C	degree celcius
$\mu$ g / $\mu$ l / $\mu$ m / $\mu$ M	microgram / microliter / micrometer / micromolar
VGAT / VIAAT / VGluT	vesicular GABA / inhibitory amino acid / glutamate transporter

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## **ERKLÄRUNG**

Hiermit versichere ich, dass ich die vorliegende Arbeit selbständig durchgeführt und verfasst habe. Ich habe keine anderen als die angegebenen Hilfsmittel verwendet.

Außerdem versichere ich, dass diese Dissertation an keiner anderen Universität eingereicht wurde, um ein Promotionsverfahren zu eröffnen.

Bhumika Singh

Berlin, November, 2005