

References

Adams, D. J., Biggs, P. J., Cox, T., Davies, R., van der Weyden, S., Jonkers, J., Smith, J., Plumb, B., Taylor, R., Nishijima, I., *et al.* (2004). Mutagenic insertion and chromosome engineering resource (MICER). *Nature Genetics* 36, 867-871.

Ahmed, B. Y., Cahkravarthy, S., Eggers, R., Hermens, W. T., Zhang, J. Y., Niclou, S. P., Levelt, C., Sablitzky, F., Anderson, P. N., Lieberman, A. R., and Verhaagen, J. (2004). Efficient delivery of Cre-recombinase to neurons in vivo and stable transduction of neurons using adeno-associated and lentiviral vectors. *BMC Neuroscience* 5, 4.

Aiba, A., Kano, M., Chen, C., Stanton, M. E., Fox, G. D., Herrup, K., Zwingman, T. A., and Tonegawa, S. (1994). Deficient cerebellar long-term depression and impaired motor learning in mGluR1 mutant mice. *Cell* 79.

Akum, B. F., Chen, M., Gunderson, S. I., Riefler, G. M., Scerri-Hansen, M. M., and Firestein, B. L. (2004). Cypin regulates dendrite patterning in hippocampal neurons by promoting microtubule assembly. *Nature Neuroscience* 7, 145-152.

Allen, K. M., Gleeson, J. G., Bagrodia, S., Partington, M., MacMillan, J. C., Cerione, R. A., Mulley, J. C., and Walsh, C. A. (1998). *PAK3* mutation in nonsyndromic X-linked mental retardation. *Nature Genetics* 20, 25-30.

Amir, R. E., Van den Vayver, I. B., Wan, M., Tran, C. Q., Francke, U., and Zoghbi, H. Y. (1999). Rett syndrome is caused by mutations in X-linked MECP2, encoding methyl-CpG-binding protein 2. *Nature Genetics* 23, 185-188.

Angrand, P. O., Daigle, N., van der Hoeven, F., Scholer, H. R., and Stewart, A. F. (1999). Simplified generation of targeting constructs using ET recombination. *Nucleic Acids Research* 27, e16.

Aoki, C., Miko, I., Oviedo, H., Mikeladze-Dvali, T., Alexandre, L., Sweeney, N., and Brecht, D. S. (2001). Electron microscopic immunocytochemical detection of PSD-95, PSD-93, SAP-102 and SAP-97 at postsynaptic, presynaptic and nonsynaptic sites in the adult and neonatal rat visual cortex. *Synapse* 40, 239-257.

Arsenian, S., Ruther, U., and Nordheim, A. (1998). Serum response factor is essential for mesoderm formation during mouse embryogenesis. *EMBO Journal* 17, 6289-6299.

Ashley Jr, C. T., Wilkinson, K. D., Reines, D., and Warren, S. T. (1993). FMR1 protein: conserved RNP family domains and selective RNA binding. *Science* 262, 563-566.

Association, A. P. (2000). *Diagnostic and Statistical Manual of Mental Disorders*, 4-Tr edn (Washington D.C., American Psychiatric Publishing Inc).

Atkins, C. M., Selcher, J. C., Petraitis, J. J., Trzaskos, J. M., and Sweatt, D. (1998). The MAPK cascade is required for mammalian associative learning. *Nature Neuroscience* 1, 602-609.

Austin, C. P. (2004). The knockout mouse project. *Nature Genetics* 36, 921-924.

Bagni, C., and Greenough, T. (2005). From mRNP trafficking to spine dymorphogenesis: the roots of fragile X syndrom. *Nature Reviews Neuroscience* 6, 376-387.

Bancroft, J. D., Stevens, A., and Turner, D. R. (1996). Theory and practice of histological techniques, 4th edn (London, Churchill Livingstone).

Bassand, P., Bernard, A., Rafiki, A., Gayet, D., and Khrestchatisky, M. (1999). Differential interaction of the tSXV motifs of the NR1 and NR2A NMDA receptor subunits with PSD-95 and SAP97. *European Journal of Neuroscience* *11*, 2031-2043.

Bear, M. F., Huber, K. M., and Warren, S. T. (2004). The mGluR theory of fragile X mental retardation. *Trends in Neurosciences* *27*, 370-377.

Becamel, C., Gavarini, S., Chanrion, B., Alonso, G., Galeotti, N., Dumuis, A., Bockaert, J., and Marin, P. (2004). The serotonin 5-HT_{2A} and 5-HT_{2C} receptors interact with specific sets of PDZ proteins. *Journal of Biological Chemistry* *279*, 20257-20266.

Berberich, S., Punnakkal, P., Jensen, V., Pawlak, V., Seeburg, P. H., Hvalby, O., and Kohr, G. (2005). Lack of NMDA receptor subtype selectivity for hippocampal long-term potentiation. *Journal of Neuroscience* *25*, 6907-6910.

Billuart, P., Bienvenu, T., Ronce, N., des Portes, V., Vinet, M. C., Zemni, R., Crollius, H. R., Carrie, A., Fauchereau, F., Cherry, M., *et al.* (1998). Oligophrenin-1 encodes a rhoGAP protein involved in X-linked mental retardation. *Nature* *392*, 923-926.

Birney, E., Andrews, T. D., Bevan, P., Caccamo, M., Chen, Y., Clarke, L., Coates, G., Cuff, J., Curwen, V., Cutts, T., *et al.* (2004). An Overview of Ensembl. *Genome Res* *14*, 925-928.

Bliss, T. V., and Lømo, T. (1973). Long-lasting potentiation of synaptic transmission in the dentate area of the anaesthetized rabbit following stimulation of the perforant path. *Journal of Physiology* 232, 331-356.

Blitzer, R. D., Iyenger, R., and Landau, E. M. (2005). Postsynaptic signaling networks: cellular cogwheels underlying long-term plasticity. *Biological Psychiatry* 57, 113-119.

Blum, S., Moore, A. N., Adams, F., and Dash, P. K. (1999). A mitogen-activated protein kinase cascade in the CA1/CA2 subfield of the dorsal hippocampus is essential for long-term spatial memory. *Journal of Neuroscience* 19, 3535-3544.

Bredt, D. S., and Nicoll, R. A. (2003). AMPA receptor trafficking at excitatory synapses. *Neuron* 40, 361-379.

Brenman, J. E., Christopherson, K. S., Craven, S. E., McGee, A. W., and Bredt, D. S. (1996). Cloning and characterization of postsynaptic density 93, a nitric oxide synthase interacting protein. *J Neurosci* 16, 7407-7415.

Brenman, J. E., Topinka, J. R., Cooper, E. C., McGee, A. W., Rosen, J., Milroy, T., Ralston, H. J., and Bredt, D. S. (1998). Localization of postsynaptic density-93 to dendritic microtubules and interaction with microtubule-associated protein 1A. *Journal of Neuroscience* 18, 8805-8813.

Brocard, J., Warot, X., Wendling, O., Messaddeq, N., Vonesch, J. L., Chambon, P., and Metzger, D. (1997). Spatio-temporally controlled site-specific somatic mutagenesis in the mouse. *Proceedings of the National Academy of Sciences of the United States of America* 94, 14559-14563.

Brown, R. E., Singh, P. B., and Roser, B. (1987). The major histocompatibility complex and the chemosensory recognition of individuality in rats. *Physiology and Behavior* 40, 65-73.

Brown, V., Jin, P., Ceman, S., Darnell, J. C., O'Donnell, W. T., Tenenbaum, S. A., Jin, X., Feng, Y., Wilkinson, K. D., Keene, J. D., *et al.* (2001). Microarray identification of FMRP-associated brain mRNAs and altered mRNA translational profiles in fragile X syndrome. *Cell* 107, 477-487.

Cai, C., Coleman, S. K., Niemi, K., and Keinänen, K. (2002). Selective binding of synapse-associated protein 97 to GluR-A α -amino-5-hydroxy-3-methyl-4-isoxazole propionate receptor subunit is determined by a novel sequence motif. *Journal of Biological Chemistry* 277, 31484-31490.

Capecchi, M. (2005). Gene targeting in mice: functional analysis of the mammalian genome for the twenty-first century. *Nature Reviews Genetics* 6, 507-512.

Carmell, M. A., Zhang, L., Conklin, D. S., Hannon, G. J., and Rosenquist, T. A. (2002). Germline transmission of RNAi in mice. *Nature Structural Biology* 10, 91-92.

Caruana, G., and Bernstein, A. (2001). Craniofacial dysmorphogenesis including cleft palate in mice with an insertional mutation in the *discs large* gene. *Molecular and Cellular Biology* 21, 1475-1483.

Cearley, J. A., and Detloff, P. J. (2001). Efficient repetitive alteration of the mouse Huntington's disease gene by management of background in the tag and exchange gene targeting strategy. *Transgenic Research* 10, 479-488.

Chelly, J., and Mandel, J.-L. (2001). Monogenic causes of X-linked mental retardation. *Nature Reviews Genetics* 2, 669-680.

Chen, C., Kano, M., Abeliovich, A., Chen, L., Bao, S., Kim, J. J., Hashimoto, K., Thompson, R. F., and Tonegawa, S. (1995). Impaired motor coordination correlates with persistent multiple climbing fiber innervation in PKC γ mutant mice. *Cell* 83, 1233-1242.

Chen, C. M., and Behringer, R. R. (2001). CREating breakthroughs. *Nature Biotechnology* 19, 921-922.

Chen, K., and Featherstone, D. E. (2005). Discs-large (DLG) is clustered by presynaptic innervation and regulates postsynaptic glutamate receptor subunit composition in *Drosophila*. *BMC Biology* 3, 1.

Chen, L., Chetkovich, D. M., Petralia, R. S., Sweeney, N. T., Kawasaki, Y., Wenthold, R. J., Brecht, D. S., and Nicoll, R. A. (2000). Stargazin regulates synaptic targeting of AMPA receptors by two distinct mechanisms. *Nature* 408, 936-943.

Chen, L., Yun, S.-W., Seto, J., Lui, W., and Toth, M. (2003). The fragile X mental retardation protein binds and regulates a novel class of mRNAs containing U rich target sequences. *Neuroscience* 120, 1005-1017.

Cho, K. O., Hunt, C. A., and Kennedy, M. B. (1992). The rat brain postsynaptic density fraction contains a homolog of the drosophila discs-large tumor suppressor protein. *Neuron* 9, 929-942.

Collingridge, G. L., Kehl, S. J., and McLennan, H. (1983). The antagonism of amino acid-induced excitations of rat hippocampal CA1 neurones *in vitro*. *Journal of Physiology* 334, 19-31.

Collins, M. O., Yu, L., Coba, M. P., Husi, H., Campuzano, I., Blackstock, W. P., Choudhary, J. S., and Grant, S. G. N. (2005). Proteomic analysis of *in vivo* phosphorylated synaptic proteins. *Journal of Biological Chemistry* 280, 5972-5982.

Comery, T. A., Harris, J. B., Willems, P. J., Oostra, B. A., Irwin, S. A., Weiler, I. J., and Greenough, W. T. (1997). Abnormal dendritic spines in fragile X knockout mice: maturation and pruning deficits. *Proceedings of the National Academy of Sciences of the United States of America* 94, 5401-5404.

Consortium, I. H. G. S. (2001). Initial sequencing and analysis of the human genome. *Nature* 409, 860-921.

Consortium, M. G. S. (2002). Initial sequencing and comparative analysis of the mouse genome. *Nature* 420, 520-562.

Copeland, N. G., Jenkins, N. A., and Court, D. L. (2001). Recombineering: A powerful new tool for mouse functional genomics. *Nature Reviews Genetics* 2, 769-779.

Court, D. L., Swaminathan, S., Yu, D., Wilson, H., Baker, T., Bubunencko, M., Sawitzke, J., and Sharan, S. K. (2003). Mini- λ : a tractable system for chromosome and BAC engineering. *Gene* 315, 63-69.

Crusio, W. E. (2001). Genetic dissection of mouse exploratory behaviour. *Behavioural Brain Research* 125, 127-132.

D'Adamo, P., Welzl, H., Papadimitriou, S., Raffaele di Barletta, M., Tiveron, C., Tatangelo, L., Pozzi, L., Chapman, P. F., Knevett, S. G., Ramsay, M. F., *et al.* (2002). Deletion of the mental retardation gene *Gdil* impairs associative memory and alters social behavior in mice. *Human Molecular Genetics* 11, 2567-2580.

D'Hooge, R., Nagels, G., Franck, F., Bakker, C. E., Reyniers, E., Storm, K., Kooy, R. F., Oostra, B. A., Willems, P. J., and De Deyn, P. P. (1997). Mildly impaired water maze performance in male *Fmr1* knockout mice. *Neuroscience* 76, 367-376.

Davis, S., Vanhoutte, P., Pages, C., Caboche, J., and Laroche, S. (2000). The MAPK/ERK cascade targets both Elk-1 and cAMP response element-binding protein to control long-term potentiation-dependent gene expression in the dentate gyrus *in vivo*. *Journal of Neuroscience* 20, 4563-4572.

de Wit, J., and Verhaagen, J. (2003). Role of semaphorins in the adult nervous system. *Progress in Neurobiology* 71, 249-267.

DeMarco, S. J., and Strehler, E. E. (2001). Plasma membrane Ca^{2+} -ATPase isoforms 2b and 4b interact promiscuously and selectively with members of the membrane-associated guanylate kinase family of PDZ (PSD95/Dlg/ZO-1) domain-containing proteins. *Journal of Biological Chemistry* 276, 21594-21600.

Dickinson, P., Kimber, W. L., Kilanowski, F. M., Webb, S., Stevenson, B. J., Porteous, D. J., and Dorin, J. R. (2000). Enhancing the efficiency of introducing precise mutations into the mouse genome by hit and run gene targeting. *Transgenic Research* 9, 55-66.

Dingledine, R., Borges, K., Bowie, D., and Traynelis, S. F. (1999). The glutamate receptor ion channels. *Pharmacological Reviews* 51, 7-51.

Doetschman, T., Gregg, R. G., Maeda, N., Hooper, M. L., Melton, D. W., Thompson, S., and Smithies, O. (1987). Targeted correction of a mutant HPRT gene in mouse embryonic stem cells. *Nature* 330, 576-578.

Dolzhanskaya, N., Sung, Y. J., Conti, J., Currie, J. R., and Denman, R. B. (2003). The fragile X mental retardation protein interacts with U-rich RNAs in a yeast three-hybrid screen. *Biochemical and Biophysical Research Communications* 205, 434-441.

Dragatsis, I., and Zeitlin, S. (2000). *CaMKII α -cre* transgene expression and recombination patterns in the mouse brain. *Genesis* 26, 133-135.

Dudek, S. M., and Bear, M. F. (1992). Homosynaptic long-term depression in area CA1 of hippocampus and effects of N-methyl-D-aspartate receptor blockade. *Proceedings of the National Academy of Sciences of the United States of America* 89, 4363-4367.

Dymecki, S. M. (2000). Site-specific recombination in cells and mice. In *Gene targeting: a practical approach*, A. L. Joyner, ed. (Oxford, Oxford University Press), pp. 37-96.

El-Husseini, A. E., Craven, S. E., Chetkovich, D. M., Firestein, B. L., Schnell, E., Aoki, C., and Brecht, D. S. (2000a). Dual palmitoylation of PSD-95 mediates its vesiculotubular sorting, postsynaptic targeting and ion channel clustering. *Journal of Cell Biology* 148, 259-271.

El-Husseini, A. E., Topinka, J. R., Lehrer-Graiwer, J. E., Firestein, B. L., Craven, S. E., Aoki, C., and Brecht, D. S. (2000b). Ion channel clustering by membrane-associated guanylate kinases. Differential regulation by N-terminal lipid and metal binding motifs. *Journal of Biological Chemistry* 275, 23904-23910.

Elbashir, S. M., Harborth, J., Lendeckel, W., Yalcin, A., Weber, K., and Tuschl, T. (2001). Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells. *Nature* 411, 494-498.

English, J. D., and Sweatt, D. (1997). A requirement for the mitogen-activated protein kinase cascade in hippocampal long term potentiation. *Journal of Biological Chemistry* 272, 19103-19106.

Erreger, K., Dravid, S. M., Banke, T. G., Wyllie, D. J., and Traynelis, s. F. (2005). Subunit-specific gating controls rat NR1/NR2A and NR1/NR2B NMDA channel kinetics and synaptic signalling profiles. *Journal of Physiology* 563, 345-358.

Farley, F. W., soriano, P., Steffen, L. S., and Dymecki, S. M. (2000). Wide-spread recombinase expression using FLPeR (flipper) mice. *Genesis* 28, 106-110.

Festing, M. F. W., Simpson, E. M., Davisson, M. T., and Mobraaten, L. E. (1999). Revised nomenclature for strain 129 mice. *Mammalian Genome* 10, 836.

Firestein, B., Brenman, J., Aoki, C., Sanchez-Perez, A., El-Husseini, A., and Brecht, D. (1999). Cypin: a cytosolic regulator of PSD-95 postsynaptic targeting. *Neuron* 24, 659-672.

Fishburn, J., Turner, G., Daniel, A., and Brookwell, R. (1983). The diagnosis and frequency of X-linked conditions in a cohort of moderately retarded males with affected brothers. *American Journal of Medical Genetics* 14, 713-724.

Forrest, D., Yuzaki, M., Soares, H. D., Ng, L., Luk, D. C., Sheng, M., Stewart, C. L., Morgan, J. I., Connor, J. A., and Curran, T. (1994). Targeted disruption of NMDA receptor 1 gene abolishes NMDA response and results in neonatal death. *Neuron* 13, 325-338.

Frankland, P. W., and Bontempi, B. (2005). The organization of recent and remote memories. *Nature Reviews Neuroscience* 6, 119-130.

Fujita, A., and Kurachi, Y. (2000). SAP family proteins. *Biochemical & Biophysical Research Communications* 269, 1-6.

Fukaya, M., Ueda, H., Yamauchi, K., Inoue, Y., and Watanabe, M. (1999). Distinct spatiotemporal expression of mRNAs for the PSD-95/SAP90 protein family in the mouse brain. *Neuroscience Research* 33, 111-118.

Fukaya, M., and Watabe, A. M. (2000). Improved immunohistochemical detection of postsynaptically located PSD-95/SAP90 protein family by protease section pretreatment: a study in the adult mouse brain. *Journal of Comparative Neurology* 426, 572-586.

Funke, L., Dakoji, S., and Brecht, D. S. (2005). Membrane-associated guanylate kinases regulate adhesion and plasticity at cell junctions. *Annual Review of Biochemistry* 74, 219-245.

Garcia, E. P., Mehta, S., Blair, L. A. C., Wells, D. G., Shang, J., Fukushima, T., Fallon, J. R., Garner, C. C., and Marshall, J. (1998). SAP90 binds and clusters kainate receptors causing incomplete desensitization. *Neuron* 21, 727-739.

Garcia, R. A. G., Vasudevan, K., and Buonanno, A. (2000). The neuregulin receptor ErbB-4 interacts with PDZ-containing proteins at neuronal synapses. *PNAS* 97, 3596-3601.

Gerlai, R. (1998). A new continuous alternation task in T-maze detects hippocampal dysfunction in mice: a strain comparison and lesion study. *Behavioural Brain Research* 95, 91-101.

Gerlai, R. (2001). Behavioral tests of hippocampal function: simple paradigms, complex problems. *Behavioural Brain Research* 125, 269-277.

Gerlai, R., Fitch, T., Bales, K. R., and Gitter, B. D. (2002). Behavioral impairment of APP^{V717F} mice in fear conditioning: is it only cognition? *Behavioural Brain Research* 136, 503-509.

Ghosh, A., and Greenberg, M. E. (1995). Calcium signaling in neurons: molecular mechanisms and cellular consequences. *Science* 268, 239-247.

Gordon, J. A., and Hen, R. (2004). Genetic approaches to the study of anxiety. *Annual Review of Neuroscience* 27, 193-222.

Gossen, M., and Bujard, H. (1992). Tight control of gene expression in mammalian cells by tetracycline-responsive promoters. *Proceedings of the National Academy of Sciences of the United States of America* 89, 5547-5551.

Grant, S. G. N., and O'Dell, T. J. (2001). Multiprotein complex signaling and the plasticity problem. *Current Opinion in Neurobiology* 11, 363-368.

Gu, Y., McIlwain, K. L., Weeber, e. J., Yamagata, T., Xu, B., Antalffy, B. A., Reyes, C., Yuva-Paylor, L., Armstrong, D., Zoghbi, H., *et al.* (2002). Impaired conditioned fear and enhanced long-term potentiation in *Fmr2* knockout mice. *Journal of Neuroscience* 22, 2753-2763.

Hasty, P., Abuin, A., and Bradley, A. (2000). Gene targeting, principles and practice in mammalian cells. In *Gene targeting: a practical approach*, A. L. Joyner, ed. (Oxford, Oxford University Press), pp. 1-34.

Hebb, D. O. (1949). *The organization of behavior: a neuropsychological theory* (New York, Wiley).

Hebert, A. E., and Dash, P. K. (2002). Extracellular signal-regulated kinase activity in the entorhinal cortex is necessary for long-term spatial memory. *Learning & Memory* 9, 156-166.

Heintz, N. (2001). BAC to the future: The use of BAC transgenic mice for neuroscience research. In *Nature Reviews Neuroscience*, pp. 861-870.

Hinton, V. J., Brown, W. T., Wisniewski, K., and Rudelli, R. D. (1991). Analysis of neocortex in three males with the fragile X syndrome. *American Journal of Medical Genetics* 41, 289-294.

Horio, Y., Hibino, H., Inanobe, A., Yamada, M., Ishii, M., Tada, Y., Satoh, E., Hata, Y., Takai, Y., and Kurachi, Y. (1997). Clustering and enhanced activity of an inwardly rectifying potassium channel, Kir4.1, by an anchoring protein, PSD-95/SAP90. *Journal of Biological Chemistry* 272, 12885-12888.

Huang, Y. Z., Wang, Q., Won, S., Luo, Z. G., Xiong, W. C., and Mei, L. (2002). Compartmentalized NRG signaling and PDZ domain-containing proteins in synapse structure and function. *International Journal of Developmental Neuroscience* 20, 173-185.

Huber, G., and Matus, A. (1984). Differences in the cellular distributions of two microtubule-associated proteins, MAP1 and MAP2, in rat brain. *Journal of Neuroscience* 4, 151-160.

Huber, K. M., Gallagher, S. M., Warren, S. T., and Bear, M. F. (2002). Altered synaptic plasticity in a mouse model of fragile X mental retardation. *Proceedings of the National Academy of Sciences of the United States of America* 99, 7746-7750.

Huettner, J. E. (2003). Kainate receptors and synaptic transmission. *Progress in Neurobiology* 70, 387-407.

Hunt, C. A., Schenker, L. J., and Kennedy, M. B. (1996). PSD-95 is associated with the postsynaptic density and not with the presynaptic membrane at forebrain synapses. *Journal of Neuroscience* 16, 1380-1388.

Husi, H., M.A., W., Choudhary, J. S., Blackstock, W. P., and Grant, S. G. N. (2000). Proteomic analysis of NMDA receptor-adhesion protein signaling complexes. *Nature Neuroscience* 3, 661-669.

Imamura, F., Maeda, S., Doi, T., and Fujiyoshi, Y. (2002). Ligand binding of the second PDZ domain regulates clustering of PSD-95 with the Kv1.4 potassium channel. *Journal of Biological Chemistry* 277, 3640-3646.

Impey, S., Obrietan, K., Wong, S. T., Poser, S., Yano, S., Wayman, G., Deloulme, J. G., Chan, G., and Storm, D. R. (1998). Cross talk between ERK and PKA is required for Ca²⁺ stimulation of CREB-dependent transcription and ERK nuclear translocation. *Neuron* 21, 869-883.

Inagaki, S., Ohoka, Y., Sugimoto, H., Fukioka, S., Amazaki, M., Kurinami, H., Miyazaki, N., Tohyama, M., and Furuyama, T. (2001). Sema4C, a transmembrane semaphorin, interacts with a postsynaptic density protein, PSD-93. *Journal of Biological Chemistry* 276, 9174-9181.

Indra, A. K., Warot, X., Brocard, J., Bornert, J. M., Xiao, J. H., Chambon, P., and Metzger, d. (1999). Temporally-controlled site-specific mutagenesis in the basal layer of the epidermis: comparison of the recombinase activity of the tamoxifen-inducible Cre-ER(T) and Cre-ER(T2) recombinases. *Nucleic Acids Res* 27, 4324-4327.

Jo, D., Nashabi, A., Doxsee, C., Lin, Q., Unutmaz, D., Chen, J., and Ruley, H. E. (2001). Epigenetic regulation of gene structure and function with a cell-permeable Cre recombinase. *Nature Biotechnology* 19, 929-933.

Jun, K., Choi, G., Yang, S.-G., Choi, K. Y., Kim, H., Chang, G. C. K., Storm, D. R., Albert, C., Mayr, G. W., Lee, C.-J., and Shin, H.-S. (1998). Enhanced hippocampal CA1 LTP but normal spatial learning in inositol 1,4,5-trisphosphate 3-kinase(A)-deficient mice. *Learning & Memory* 5, 317-330.

Kalscheuer, V. M., Freude, K., Musante, L., Jensen, L. R., Yntema, H. G., Gecz, J., Sefiani, A., Hoffmann, K., Moser, B., Haas, S., *et al.* (2003). Mutations in the polyglutamine binding protein 1 gene cause X-linked mental retardation. *Nature Genetics* 35, 313-315.

Kandel, E. R., Schwartz, J. H., and Jessell, T. M. (2000). *Principles of neural science*, 4 edn (New York, McGraw-Hill).

Kaufmann, W. E., and Moers, H. W. (2000). Dendritic anomalies in disorders associated with mental retardation. *Cerebral Cortex* 10, 981-991.

Kellendonk, C., Tronche, F., Casanova, E., Anlag, K., Opherk, C., and Schutz, G. (1999). Inducible site-specific recombination in the brain. *Journal of Molecular Biology* 285, 175-182.

Kim, E., Cho, K. O., Rothschild, A., and Sheng, M. (1996). Heteromultimerization and NMDA receptor-clustering activity of chapsyn-110, a member of the PSD-95 family of proteins. *Neuron* 17, 103-113.

Kim, E., Naisbitt, S., Hsueh, Y.-P., Rao, A., Rothschild, A., Craig, A. M., and Sheng, M. (1997). GKAP, a novel synaptic protein that interacts with the guanylate kinase-like domain of the PSD-95/SAP90 family of channel clustering molecules. *Journal of Cell Biology* 136, 669-678.

Kim, J. H., Liao, D., Lau, L. F., and Huganir, R. L. (1998). SynGAP: a synaptic RasGAP that associates with the PSD-95/SAP90 protein family. *Neuron* 20, 683-691.

Kim, M. J., Dunah, A. W., Wang, Y. T., and Sheng, M. (2005). Differential roles of NR2A- and NR2B-containing NMDA receptors in Ras-ERK signaling and AMPA receptor trafficking. *Neuron* 46, 745-760.

Kistner, U., Garner, C. C., and Linial, M. (1995). Nucleotide binding by the synapse associated protein SAP90. *FEBS Letters* 359, 159-163.

Klöcker, N., Bunn, R. C., Schnell, E., Caruana, G., Bernstein, A., Nicoll, R. A., and Brecht, D. S. (2002). Synaptic glutamate receptor clustering in mice lacking the SH3 and GK domains of SAP97. *European Journal of Neuroscience* 16, 1517-1522.

Komiyama, N. H., Watabe, A. M., Carlisle, H. J., Porter, K., Charlesworth, P., Monti, J., Strathdee, D. J. C., O'Carroll, C. M., Martin, S. J., Morris, R. G. M., *et al.* (2002). SynGAP regulates ERK/MAPK signaling, synaptic plasticity and learning in the complex with postsynaptic density 95 and NMDA receptor. *Journal of Neuroscience* 22, 9721-9732.

Koulen, P. (1999). Localization of synapse-associated proteins during postnatal development of the rat retina. *European Journal of Neuroscience* 11, 2007-2018.

Koulen, P., Garner, C. C., and Wassle, H. (1998). Immunocytochemical localization of the synapse-associated protein SAP102 in the rat retina. *Journal of Comparative Neurology* 397, 326-336.

Kutsche, K., Yntema, H., Brandt, A., Jantke, I., Nothwang, H. G., Orth, U., Boavida, M. G., David, D., Chelly, J., Fryns, J.-P., *et al.* (2000). Mutations in *ARHGEF6*, encoding a guanine

nucleotide exchange factor for Rho GTPases, in patients with X-linked mental retardation. *Nature Genetics* 26, 247-250.

Kutsuwada, T., Sakimura, K., Manabe, T., Takayama, C., Katakura, N., Kushiya, E., Natsume, R., Watanabe, M., Inoue, Y., Yagi, T., *et al.* (1996). Impairment of suckling response, trigeminal neuronal pattern formation and hippocampal LTD in NMDA receptor $\epsilon 2$ subunit mutant mice. *Neuron* 16, 333-344.

Kuwahara, H., Araki, N., Makino, K., Masuko, N., Honda, S., Kaibuchi, K., Fukunaga, K., Miyamoto, E., Ogawa, M., and Saya, H. (1999). A novel NE-dlg/SAP102-associated protein, p51-nedasin, related to the amidohydrolase superfamily, interferes with the association between NE-dlg/SAP102 and *N*-methyl-D-aspartate receptor. In *Journal of Biological Chemistry*, pp. 32204-32214.

Kwan, K.-M. (2002). Conditional alleles in mice: practical considerations for tissue-specific knockouts. *Genesis* 32, 49-62.

Lahey, T., Gorczyca, M., Jia, X.-X., and Budnik, V. (1994). The drosophila tumor suppressor gene *dlg* is required for normal synaptic bouton structure. *Neuron* 13, 823-835.

Lallemand, Y., Luria, V., Haffner-Kausz, R., and Lonai, P. (1998). Maternally expressed PGK-Cre transgene as a tool for early and uniform activation of the Cre site-specific recombinase. *Transgenic Research* 7, 105-112.

Lalonde, R., Kim, H. D., and Fukuchi, K. (2004). Exploratory activity, anxiety and motor coordination in bigenic *APP^{swe} + PS1^{E9}* mice. *Neuroscience Letters* 269, 156-161.

Lambert, J.-F., Benoit, B. O., Colvin, G. A., Carlson, J., Delville, Y., and Quesenberry, P. J. (2000). Quick sex determination of mouse fetuses. *Journal of Neuroscience Methods* 95, 127-132.

Larsson, M., Hjalm, G., Sakwe, A. M., Hoglund, A.-S., Larsson, E., Roninson, R. C., Sundberg, C., and Rask, L. (2003). Selective interaction of megalin with postsynaptic density-95 (PSD-95)-like membrane-associated guanylate kinase (MAGUK) proteins. *Biochemical Journal* 373, 381-391.

Lau, L. F., Mammen, A., Ehlers, M. D., Kindler, S., Chung, W. J., Garner, C. C., and Huganir, R. L. (1996). Interaction of the N-methyl-D-aspartate receptor complex with a novel synapse-associated protein, SAP102. *Journal of Biological Chemistry* 271, 21622-21628.

Lebel, R. R., May, M., Pouls, S., Lubs, H. A., Stevenson, R. E., and Schwartz, C. E. (2002). Non-syndromic X-linked mental retardation associated with a missense mutation (P312L) in the FGD1 gene. *Clinical Genetics* 61, 139-140.

Ledermann, B. (2000). Embryonic stem cells and gene targeting. *Experimental Physiology* 85, 603-613.

Lee, E.-C., Yu, D., Martinez, J. L., Tessarollo, L., Swing, D. A., Court, D. L., Jenkins, N. A., and Copeland, N. G. (2001). A highly efficient *Escherichia coli*-based chromosome engineering system adapted for recombinogenic targeting and subcloning of BAC DNA. *Genomics* 73, 56-65.

Leonard, A. S., Davare, M. A., Horne, M. C., Garner, C. C., and Hell, J. W. (1998). SAP97 is associated with the α -amino-3-hydroxy-3-methylisoxazole-4-propionic acid receptor GluR1 subunit. *J Biol Chem* 273, 19518-19524.

Leonoudakis, D., Conti, L. R., Anderson, S., Radeke, C. M., McGuire, L. M. M., Adams, M. E., Froehner, S. C., Yates, J. R., and Vandenberg, C. A. (2004). Protein trafficking and anchoring complexes revealed by proteomic analysis of inward rectifier potassium channel (Kir2.x)-associated proteins. *Journal of Biological Chemistry* 279, 22331-22346.

Levedakou, E. N., Chen, X.-J., Soliven, B., and Popko, B. (2004). Disruption of the mouse *Large* gene in the *enr* and *myd* mutants results in nerve, muscle and neuromuscular junction defects. *Molecular and Cellular Neuroscience* 28, 757-769.

Li, Y., Spangenberg, O., Paarmann, I., Konrad, M., and Lavie, A. (2002). Structural basis for nucleotide-dependent regulation of membrane-associated guanylate kinase-like domains. *Journal of Biological Chemistry* 277, 4159-4165.

Lim, I. A., Hall, D. D., and Hell, J. W. (2002). Selectivity and promiscuity of the first and second PDZ domains of PSD-95 and synapse-associated protein 102. *Journal of Biological Chemistry* 277, 21697-21711.

Lister, R. G. (1987). The use of a plus-maze to measure anxiety in the mouse. *Psychopharmacology* 92, 180-185.

Liu, L., Wong, T. P., Pozza, M. F., Lingenhoehl, K., Wang, Y. X., Sheng, M., Auberson, Y. P., and Wang, Y. T. (2004). Role of NMDA receptor subtypes in governing the direction of hippocampal synaptic plasticity. *Science* 304, 1021-1024.

Liu, P., Jenkins, N. A., and Copeland, N. G. (2003). A highly efficient recombineering-based method for generating conditional knockout mutations. *Genome Res* 13, 476-484.

Lonze, B. E., and Ginty, D. D. (2002). Function and regulation of CREB family transcription factors in the nervous system. *Neuron* 35, 605-623.

Loonstra, A., Mooijs, M., Beverloo, H. B., Al Allak, B., van Drunen, E., Kanaar, R., Berns, A., and Jonkers, J. (2001). Growth inhibition and DNA damage induced by Cre recombinase in mammalian cells. *Proceedings of the National Academy of Sciences of the United States of America* 98, 9209-9214.

Lynch, G. S., Larson, J., Kelso, S., Barrionuevo, G., and Schottler, F. (1983). Intracellular injections of EGTA block induction of hippocampal long-term potentiation. *Nature* 305, 719-721.

Maes, B., Fryns, J.-P., Van Walleggem, M., and Van den Berghe, H. (1994). Cognitive functioning and information processing of adult mentally retarded men with Fragile X syndrome. *American Journal of Medical Genetics* 50, 190-200.

Makino, K., Kuwahara, H., Masuko, N., Nishiyama, Y., Morisaki, T., Sasaki, J., Nakao, M., Kuwano, A., Nakata, M., Ushio, Y., and Saya, H. (1997). Cloning and characterization of NE-dlg: A novel human homolog of the *Drosophila* discs large (dlg) tumor suppressor protein interacts with the APC protein. *Oncogene* 14, 2425-2433.

Malenka, R. C., and Bear, M. F. (2004). LTP and LTD: an embarrassment of riches. *Neuron* 44, 5-21.

Malenka, R. C., Kauer, J. A., Zucker, R. S., and Nicoll, R. A. (1988). Postsynaptic calcium is sufficient for potentiation of hippocampal synaptic transmission. *Science* 242, 81-84.

Massey, P. V., Johnson, B. E., Moulton, P. R., Auberson, Y. P., Brown, M. W., Molnar, E., Collingridge, G. L., and Bashir, Z. I. (2004). Differential roles of NR2A and NR2B-containing NMDA receptors in cortical long-term potentiation and long-term depression. *Journal of Neuroscience* 24, 7821-7828.

Masuko, N., Makino, K., Kuwahara, H., Fukunaga, K., Sudo, T., Araki, N., Yamamoto, H., Yamada, Y., Miyamoto, E., and Saya, H. (1999). Interaction of NE-dlg/SAP102, a neuronal and endocrine tissue-specific membrane-associated guanylate kinase protein, with calmodulin and PSD-95/SAP90. A possible regulatory role in molecular clustering at synaptic sites. *Journal of Biological Chemistry* 274, 5782-5790.

Mayford, M., Wang, J., Kandel, E. R., and O'Dell, T. J. (1995). CaMKII regulates the frequency-response function of hippocampal synapses for the production of both LTD and LTP. *Cell* 81, 891-904.

McGee, A. W., Topinka, J. R., Hashimoto, K., Petralia, R. S., Kakizawa, S., Kauer, F., Aguilera-Moreno, A., Wenthold, R. J., Kano, M., and Brecht, D. S. (2001). PSD-93 knock-out mice reveal that neuronal MAGUKs are not required for development of function of parallel fiber synapses in cerebellum. *Journal of Neuroscience* 21, 3085-3091.

Meng, J., Meng, Y., Hanna, A., Janus, C., and Zhengping, J. (2005). Abnormal long-lasting synaptic plasticity and cognition in mice lacking the mental retardation gene *PAK3*. *Journal of Neuroscience* 25, 6641-6650.

Migaud, M., Charlesworth, P., Dempster, M., Webster, L. C., Watabe, A. M., Makhinson, M., He, Y., Ramsay, M. F., Morris, R. G. M., Morrison, J. H., *et al.* (1998). Enhanced long-term

potentiation and impaired learning in mice with mutant postsynaptic density-95 protein. *Nature* 396, 433-439.

Milner, B., Squire, L. R., and Kandel, E. R. (1998). Cognitive neuroscience and the study of memory. *Neuron* 20, 445-468.

Montgomery, J. M., Zamorano, P. L., and Garner, C. C. (2004). MAGUKs in synapse assembly and function: an emerging view. *Cellular and Molecular Life Sciences* 61, 911-929.

Monyer, H., Burnashev, N., Laurie, D. J., Sakmann, B., and Seeburg, P. H. (1994). Developmental and regional expression in the rat brain and functional properties of four NMDA receptors. *Neuron* 12, 529-540.

Morgan, H. D., Sutherland, H. G. E., Martin, D. I. K., and Whitelaw, E. (1999). Epigenetic inheritance at the agouti locus in the mouse. *Nature Genetics* 23, 314-318.

Morris, R. G. M., Anderson, E., Lynch, G. S., and Baudry, M. (1986). Selective impairment of learning and blockade of long-term potentiation by an *N*-methyl-D-aspartate receptor antagonist, AP5. *Nature* 319.

Morris, R. G. M., Garrud, P., Rawlins, J. N. P., and O'Keefe, J. (1982). Place navigation impaired in rats with hippocampal lesions. *Nature* 297, 681-683.

Muller, B., Kistner, U., Veh, R. W., Cases-Langhoff, C., Becker, B., Gundelfinger, E. D., and Garner, C. C. (1995). Molecular characterization and spatial distribution of SAP97, a novel

presynaptic protein homologous to SAP90 and the *Drosophila* discs-large tumor suppressor protein. *Journal of Neuroscience* 15, 2354-2366.

Muller, B. M., Kistner, U., Kindler, S., Chung, W. J., Kuhlendahl, S., Fenster, S. D., Lau, L. F., Veh, R. W., Huganir, R. L., Gundelfinger, E. D., and Garner, C. C. (1996). SAP102, a novel postsynaptic protein that interacts with NMDA receptor complexes in vivo. *Neuron* 17, 255-265.

Muyrers, J. P., Zhang, Y., and Stewart, A. F. (2001). Techniques: Recombinogenic engineering - new options for cloning and manipulating DNA. *Trends in Biochemical Sciences* 26, 325-331.

Muyrers, J. P., Zhang, Y., Testa, G., and Stewart, A. F. (1999). Rapid modification of bacterial artificial chromosomes by ET-recombination. *Nucleic Acids Research* 27, 1555-1557.

Nagy, A. (2000). Cre recombinase: the universal reagent for genome tailoring. *Genesis* 26, 99-109.

Nagy, A., Gertenstein, M., Vintersten, K., and Behringer, R. (2003). *Manipulating the mouse embryo: a laboratory manual*, 3rd edn (New York, Cold Spring Harbor Press).

Nourry, C., Grant, S. G. N., and Borg, J.-P. (2003). PDZ domain proteins: plug and play! *Science STKE* 179, re7.

Nowak, L., Bregestovski, P., and Ascher, P. (1984). Magnesium gates glutamate-activated channels in mouse central neurones. *Nature* 307, 462-465.

O'Donnell, W. T., and Warren, S. T. (2002). A decade of molecular studies of fragile X syndrome. *Annual Review of Neuroscience* 25, 315-338.

Olsen, O., and Brecht, D. S. (2003). Functional analysis of the nucleotide binding domain of membrane-associated guanylate kinases. *Journal of Biological Chemistry* 278, 6873-6878.

Orford, M., Nefedov, M., Vadolas, J., Zaibak, F., Williamson, R., and Loannou, P. A. (2000). Engineering EGFP reporter constructs into a 200 kb human β -globin BAC clone using *GET recombination*. *Nucleic Acids Res* 28, e84.

Ottersen, O. P., and Landsend, A. S. (1997). Organization of glutamate receptors at the synapse. *European Journal of Neuroscience* 9, 2219-2224.

Paddison, P. J., Caudy, A. A., Bernstein, E., Hannon, G. J., and Conklin, D. S. (2002). Short hairpin RNAs (shRNAs) induce sequence-specific silencing in mammalian cells. *Genes & Development* 16, 948-958.

Paddison, P. J., Silva, J. M., Conklin, D. S., Schlabach, M., Li, M., Aruleba, S., Balija, V., O'Shaughnessy, A., Gnoj, L., Scobie, K., *et al.* (2004). A resource for large-scale RNA-interference-based screens in mammals. *Nature* 428, 427-431.

Parks, C. L., Robinson, P. S., Sibille, E., Shenk, T., and Toth, M. (1998). Increased anxiety of mice lacking the serotonin_{1A} receptor. *Proceedings of the National Academy of Sciences of the United States of America* 95, 10734-10739.

Paxinos, G., and Franklin, K. B. J. (2001). The mouse brain in stereotaxic coordinates, 2nd edn (London, Academic Press).

Pearson, G., Robinson, F., Gibson, T. B., Xu, B.-E., Karandikar, M., Berman, K., and Cobb, M. H. (2001). Mitogen-activated protein (MAP) kinase pathways: regulation and physiological functions. *Endocrine Reviews* 22, 153-183.

Penzes, P., Johnson, R. C., Sattler, R., Zhang, X., Huganir, R. L., Kambampati, V., Mains, R. E., and Eipper, B. A. (2001). The neuronal Rho-GEF kalirin-7 interacts with PDZ domain-containing proteins and regulates dendritic morphogenesis. *Neuron* 29, 229-242.

Petralia, R. S., Sans, N., Wang, Y.-X., and Wenthold, R. J. (2005). Ontogeny of postsynaptic density proteins at glutamatergic synapses. *Molecular and Cellular Neuroscience* 29, 436-452.

Porter, K., Komiyama, N. H., Vitalis, T., Kind, P. C., and Grant, S. G. (2005). Differential expression of two NMDA receptor interacting proteins, PSD-95 and SynGAP, during mouse development. *European Journal of Neuroscience* 21, 351-362.

Purpura, D. P. (1974). Dendritic spine 'dysgenesis' and mental retardation. *Science* 186, 1126-1128.

Rakyan, V. K., Chong, S., Champ, M. E., Cuthbert, P. C., Morgan, H. D., Luu, K. V. K., and Whitelaw, E. (2003). Transgenerational inheritance of epigenetic states at the murine *Axin^{Fu}* allele occurs after maternal and paternal transmission. *Proceedings of the National Academy of Sciences of the United States of America* 100, 2538-2543.

Ramakers, G. J. A. (2002). Rho proteins, mental retardation and the cellular basis of cognition. *Trends in Neurosciences* 25, 191-199.

Ramanan, N., Shen, Y., Sarsfield, S., Lemberger, T., Schutz, G., Linden, D. J., and Ginty, D. D. (2005). SRF mediates activity-induced gene expression and synaptic plasticity but not neuronal viability. *Nature Neuroscience* 8, 759-767.

Ramirez-Solis, R., Davis, A. C., and Bradley, A. (1993). Gene targeting in embryonic stem cells. *Methods in Enzymology* 225, 855-878.

Rasband, M. N., Park, E. W., Zhen, D., Arbuckle, M. I., Poliak, S., Peles, E., Grant, S. G. N., and Trimmer, J. S. (2002). Clustering of neuronal potassium channels is independent of their interaction with PSD-95. *Journal of Cell Biology*.

Renieri, A., Pescucci, C., Longo, I., Ariani, F., Mari, F., and Meloni, I. (2005). Non-syndromic X-linked mental retardation: from a molecular to a clinical point of view. *Journal of Cellular Physiology* 204, 8-20.

Roche, K. W., Ly, C. D., Petralia, R. S., Wang, Y.-X., McGee, A. W., Brecht, D. S., and Wenthold, R. J. (1999). Postsynaptic density-93 interacts with the $\delta 2$ glutamate receptor subunit at parallel fiber synapses. *Journal of Neuroscience* 19, 3926-3934.

Rodgers, R. J., and Johnson, N. J. T. (1995). Factor analysis of spatiotemporal and ethological measures in the murine elevated plus-maze test of anxiety. *Pharmacology Biochemistry and Behaviour* 52, 297-303.

Ropers, H. H., and Hamel, B. C. J. (2005). X-linked mental retardation. *Nature Reviews Genetics* 6, 46-57.

Ross, M. T. (2005). The DNA sequence of the human X chromosome. *Nature* 434, 325-337.

Rozen, S., and Skaletsky, H. (2000). Primer3 on the WWW for general users and for biologist programmers. In *Bioinformatics methods and protocols: methods in molecular biology*, S. Krawetz, and S. Misener, eds. (Totowa, NJ, Humana Press), pp. 365-386.

Sakai, N., Thome, J., Newton, S. S., JChen, J., Kelz, M. B., Steffen, C., Nestler, E. J., and Duman, R. S. (2002). Inducible and brain region-specific CREB transgenic mice. *Molecular Pharmacology* 61, 1453-1464.

Sakimura, K., Kutsuwada, T., Ito, I., Manabe, T., Takayama, C., Kushiya, E., Yagi, T., Aizawa, S., Inoue, Y., Sugiyama, H., and Mishina, M. (1995). Reduced hippocampal LTP and spatial learning in mice lacking NMDA receptor $\epsilon 1$ subunit. *Nature* 373, 151-155.

Sambrook, J., and Russell, D. (2001). *Molecular cloning: a laboratory manual*, 3rd edn (New York, CSHL Press).

Sans, N., Petralia, R. S., Wang, Y. X., Blahos, J., 2nd, Hell, J. W., and Wenthold, R. J. (2000). A developmental change in NMDA receptor-associated proteins at hippocampal synapses. *Journal of Neuroscience* 20, 1260-1271.

Sans, N., Prybylowski, K., Petralia, R. S., Chang, K., Wang, Y.-X., Racca, C., Vicini, S., and Wenthold, R. J. (2003). NMDA receptor trafficking through an interaction between PDZ proteins and the exocyst complex. *Nat Cell Biol* 5, 520-530.

Sans, N., Racca, C., Petralia, R. S., Wang, Y. X., McCallum, J., and Wenthold, R. J. (2001). Synapse-associated protein 97 selectively associates with a subset of AMPA receptors early in their biosynthetic pathway. *Journal of Neuroscience* 21, 7506-7516.

Sattler, R., Xiong, Z., Lu, W.-Y., Hafner, M., MacDonald, J. F., and Tymianski, M. (1999). Specific Coupling of NMDA Receptor Activation to Nitric Oxide Neurotoxicity by PSD-95 Protein. *Science* 284, 1845-1848.

Schmidt, E. E., Taylor, D. S., Prigge, J. R., Barnett, S., and Capecchi, M. R. (2000). Illegitimate Cre-dependent chromosome rearrangements in transgenic mouse spermatids. *Proceedings of the National Academy of Sciences of the United States of America* 97, 13702-13707.

Schwartzberg, P. L., Goff, S. P., and Robertson, E. J. (1989). Germ-line transmission of a c-abl mutation produced by targeted gene disruption in ES cells. *Science* 246, 799-803.

Seabold, G. K., Burette, A., Lim, I. A., Weinberg, R. J., and Hell, J. W. (2003). Interaction of the tyrosine kinase Pyk2 with the *N*-methyl-D aspartate receptor complex via the Src homology 3 domains of PSD-95 and SAP102. *Journal of Biological Chemistry* 278, 15040-15048.

Selcher, J. C., Atkins, C. M., Trzaskos, J. M., Paylor, R., and Sweatt, J. D. (1999). A necessity for MAP kinase activation in mammalian spatial learning. *Learning & Memory* 6.

Selfridge, J., Pow, A. M., McWhir, J., Magin, T. M., and Melton, D. W. (1992). Gene targeting using a mouse HPRT minigene/HPRT-deficient embryonic stem cell system: inactivation of the mouse ERCC-1 gene. *Somatic Cell and Molecular Genetics* 18, 325-336.

Sharma, R. C., and Schimke, R. T. (1996). Preparation of electrocompetent *E.coli* using salt-free growth medium. *Biotechniques* 20, 42-44.

Silva, A. J., Paylor, R., Wehner, J. M., and Tonegawa, S. (1992a). Impaired spatial learning in α -calcium-calmodulin kinase II mutant mice. *Science* 257, 206-211.

Silva, A. J., Stevens, C. F., Tonegawa, S., and Wang, Y. (1992b). Deficient hippocampal long-term potentiation in α -calcium-calmodulin kinase II mutant mice. *Science* 257, 201-206.

Silver, D. P., and Livingston, D. M. (2001). Self-excising retroviral vectors encoding the Cre recombinase overcome Cre-mediated cellular toxicity. *Molecular Cell* 8, 233-243.

Smithies, O., Gregg, R. G., Boggs, S., Koralewski, M. A., and Kucherlapati, R. S. (1985). Insertion of DNA sequences into the human chromosomal β -globin locus by homologous recombination. *Nature* 317, 230-234.

Spowart-Manning, L., and van der Staay, F. J. (2004). The T-maze continuous alternation task for assessing the effects of putative cognition enhancers in the mouse. *Behavioural Brain Research* 151, 37-46.

Sprengel, R., and Single, F. N. (1999). Mice with genetically modified NMDA and AMPA receptors. *Annals of the New York Academy of Sciences* 868, 494-501.

Sprengel, R., Suchanek, B., Amico, C., Brusa, R., Burnashev, N., Rozov, A., Hvalby, O., Jensen, V., Paulsen, O., Andersen, P., *et al.* (1998). Importance of the intracellular domain of NR2 subunits for NMDA receptor function in vivo. *Cell* 92, 279-289.

Stanford, W. L., Cohn, J. B., and Cordes, S. P. (2001). Gene-trap mutagenesis: Past, present and beyond. *Nature Reviews Genetics* 2, 756-768.

Stewart, M., Murphy, C., and Fristrom, J. W. (1972). The recovery and preliminary characterization of X chromosome mutants affecting imaginal discs of *Drosophila melanogaster*. *Developmental Biology* 27, 71-83.

Swaminathan, S., Ellis, H. M., Waters, L. S., Yu, D., Lee, E.-C., Court, D. L., and Sharan, S. K. (2001). Rapid engineering of bacterial artificial chromosomes using oligonucleotides. *Genesis* 29, 14-21.

Sweatt, D. (2004). Mitogen-activated protein kinases in synaptic plasticity and memory. *Current Opinion in Neurobiology* 14, 311-317.

Takeuchi, M., Hata, Y., Hirao, K., Toyoda, A., Irie, M., and Takai, Y. (1997). A family of PSD-95/SAP90-associated proteins localized at postsynaptic density. *Journal of Biological Chemistry* 272, 11943-11951.

Tang, Y.-P., Shimizu, E., Dube, G. R., Rampon, C., Kerchner, G. A., Zhuo, M., Liu, G., and Tsien, J. Z. (1999). Genetic enhancement of learning and memory in mice. *Nature* 401, 63-69.

Tao, Y.-X., Rumbaugh, G., Wang, G.-D., Petralia, R. S., Zhao, C., Kauer, F. W., Tao, F., Zhuo, M., Wenthold, R. J., Raja, S. N., *et al.* (2003). Impaired NMDA receptor-mediated postsynaptic function and blunted NMDA receptor-dependent persistent pain in mice lacking postsynaptic density-93 protein. *Journal of Neuroscience* 23, 6703-6712.

Tarpey, P., Parnau, J., Blow, M., Woffendin, H., Bignell, G., Cox, C., Cox, J., Davies, H., Edkins, S., Holden, S., *et al.* (2004). Mutations in the *DLG3* gene cause non-syndromic X-linked mental retardation. *The American Journal of Human Genetics* 75, 318-324.

Thiels, E., Kanterewicz, B. I., Norman, E. D., Trzaskos, J. M., and Klann, E. (2002). Long-term depression in the adult hippocampus *in vivo* involves activation of extracellular signal-regulated kinase and phosphorylation of Elk-1. *Journal of Neuroscience* 22, 2054-2062.

Thomas, G. M., and Huganir, R. L. (2004). MAPK cascade signalling and synaptic plasticity. *Nature Neuroscience* 5, 173-183.

Thomas, K. R., and Capecchi, M. (1987). Site-directed mutagenesis by gene targeting in mouse embryo-derived stem cells. *Cell* 51, 503-512.

Thompson, S., Clarke, A. R., Pow, A. M., Hooper, M. L., and Melton, D. W. (1989). Germ line transmission and expression of a corrected HPRT gene produced by gene targeting in embryonic stem cells. *Cell* 56, 313-321.

Thyagarajan, B., Guimaraes, M. J., Groth, A. C., and Calos, M. P. (2000). Mammalian genomes contain active recombinase recognition sites. *Gene* 244, 47-54.

Townsend, M., Yoshii, A., Mishina, M., and Constantine-Paton, M. (2003). Developmental loss of miniature N-methyl-D-aspartate receptor currents in NR2A knockout mice. *Proc Natl Acad Sci U S A* *100*, 1340-1345.

Trivier, E., De Cesare, D., Jacquot, S., Pannetier, S., Zackai, E., Young, I., Mandel, J.-L., Sassone-Corsi, P., and Hanauer, A. (1996). Mutations in the kinase Rsk-2 associated with Coffin-Lowry syndrome. *Nature* *384*, 567-570.

Tsien, J. Z., Chen, D. F., Gerber, D., tom, C., Mercer, E. H., Anderson, D. J., Mayford, M., Kandel, E. R., and Tonegawa, S. (1996a). Subregion- and cell type-restricted gene knockout in mouse brain. *Cell* *87*, 1317-1326.

Tsien, J. Z., Huerta, P. T., and Tonegawa, S. (1996b). The essential role of hippocampal CA1 NMDA receptor-dependent synaptic plasticity in spatial memory. *Cell* *87*, 1327-1338.

Valenzuela, D. M. (2003). High-throughput engineering of the mouse genome coupled with high-resolution expression analysis. *Nature Biotechnology* *21*, 652-659.

Van Dam, D., D'Hooge, R., Hauben, E., Reyniers, E., Gantois, I., Bakker, C. E., Oostra, B. A., Kooy, R. F., and De Deyn, P. P. (2000). Spatial learning, contextual fear conditioning and conditioned emotional response in *Fmr1* knockout mice. *Behavioural Brain Research* *117*, 127-136.

van den Bout, C. J., Machon, O., Rosok, O., Backman, M., and Krauss, S. (2002). The mouse enhancer element D6 directs Cre recombinase activity in the neocortex and the hippocampus. *Mechanisms of Development* *110*, 179-182.

van der Weyden, L., Adams, D. J., and Bradley, A. (2002). Tools for targeted manipulation of the mouse genome. *Physiological Genomics* 11, 133-164.

Vazquez, L. E., Chen, H.-J., Sokolova, I., Knuesel, I., and Kennedy, M. B. (2004). SynGAP regulates spine formation. *Journal of Neuroscience* 24, 8862-8872.

Vooijs, M., Jonkers, J., and Berns, A. (2001). A highly efficient ligand-regulated Cre recombinase mouse line shows that *LoxP* recombination is position dependent. *EMBO Reports* 2, 292-297.

Watanabe, M., Fukaya, M., Sakimura, K., Manabe, T., Mishina, M., and Inoue, Y. (1998). Selective scarcity of NMDA receptor channel subunits in the stratum lucidum (mossy fibre-recipient layer) of the mouse hippocampal CA3 subfield. *European Journal of Neuroscience* 10, 478-487.

Watase, K., and Zoghbi, H. (2003). Modelling brain diseases in mice: the challenges of design and analysis. *Nature Reviews Genetics* 4, 296-307.

Weiss, S. M., Lightowler, S., Stanhope, K. J., Kennet, G. A., and Dourish, C. T. (2000). Measurement of anxiety in transgenic mice. *Reviews in the Neurosciences* 11, 59-74.

Wenzel, A., Fritschy, J. M., Mohler, H., and Benke, D. (1997). NMDA receptor heterogeneity during postnatal development of the rat brain: differential expression of the NR2A, NR2B, and NR2C subunit proteins. *J Neurochem* 68, 469-478.

Wenzel, A., Scheurer, L., Kunzi, R., Fritschy, J. M., Mohler, H., and Benke, D. (1995). Distribution of NMDA receptor subunit proteins NR2A, 2B, 2C and 2D in the rat brain. *Neuroreport* 29, 47-48.

Winder, D. G., Martin, K. C., Muzzio, I. A., Rohrer, D., Chruscinski, A., Kobilka, B., and Kandel, E. R. (1999). ERK plays a regulatory role in induction of LTP by theta frequency stimulation and its modulation by β -adrenergic receptors. *Neuron* 24, 715-726.

Wong, W., Newell, E. W., Jugloff, D. G. M., Jones, O. T., and Schlichter, L. C. (2002). Cell surface targeting and clustering interactions between heterologously expressed PSD-95 and the *Shal* voltage-gated potassium channel, Kv4.2. *Journal of Biological Chemistry* 277, 20423-20430.

Woods, D. F., and Bryant, P. J. (1991). The discs-large tumor suppressor gene of drosophila encodes a guanylate kinase homolog localized at septate junctions. *Cell* 66, 451-464.

Wrenn, C. C., Harris, A. P., Saavedra, M. C., and Crawley, J. N. (2003). Social transmission of food preference in mice: methodology and application to galanin-overexpressing transgenic mice. *Behavioral Neuroscience* 117, 21-31.

Yagi, T., Nada, S., Watanabe, N., Tamemoto, H., Kohmura, N., Ikawa, Y., and Aizawa, S. (1993). A novel negative selection for homologous recombinants using diphtheria toxin A fragment gene. *Analytical Biochemistry* 214, 77-86.

Yan, J., Oliveira, G., coutinho, A., Yang, C., Feng, J., Katz, C., Sram, J., Bockholt, A., Jones, I. R., Craddock, N., *et al.* (2004). Analysis of the neuroligin 3 and 4 genes in autism and other neuropsychiatric patients. *Molecular Psychiatry* 10, 329-332.

Yanagawa, Y., Kobayashi, T., Ohnishi, M., Kobayashi, T., Tamura, S., Tsuzuki, T., Sanbo, M., Yagi, T., Tashiro, F., and Miyazaki, J. (1999). Enrichment and efficient screening of ES cells containing a targeted mutation: The use of DT-A gene with the polyadenylation signal as a negative selection marker. *Transgenic Research* 8, 215-221.

Yang, Y., and Sharan, S. K. (2003). A simple two-step, 'hit and fix' method to generate subtle mutations in BACs using short denatured PCR fragments. *Nucleic Acids Res* 31, e80.

Yu, D., Ellis, H. M., Lee, E.-C., Jenkins, N. A., Copeland, N. G., and Court, D. L. (2000). An efficient recombination system for chromosome engineering in *Escherichia coli*. *Proc Natl Acad Sci U S A* 97, 5978-5983.

Yu, Y., and Bradley, A. (2001). Engineering chromosomal rearrangements in mice. *Nature Reviews Genetics* 2, 780-790.

Zamanillo, D., Sprengel, R., Hvalby, O., Jensen, V., Burnashev, N., Rozov, A., Kaiser, K. M. M., Koster, H. J., Borchardt, T., Worley, P., *et al.* (1999). Importance of AMPA receptors for hippocampal synaptic plasticity but not for spatial learning. *Science* 284, 1805-1816.

Zeng, L., Fagotto, f., Zhang, T., Hsu, W., Vasicek, T. J., Perry, W. L., Lee, J. J., Tilghman, S. M., Gumbiner, B. M., and Costantini, F. (1997). The mouse Fused locus encodes Axin, an inhibitor of the Wnt signaling pathway that regulates embryonic axis formation. *Cell* 90, 181-192.

Zhang, P., Li, M. Z., and Elledge, S. J. (2001). Towards genetic genome projects: genomic library screening and gene-targeting vector construction in a single step. *Nature Genetics* 30, 31-39.

Zhang, Y., Buchholz, F., Muyrers, J. P., and Stewart, A. F. (1998). A new logic for DNA engineering using recombination in *Escherichia coli*. *Nature Genetics* 20, 123-128.

Zhang, Y., Muyrers, J. P. P., Testa, G., and Stewart, A. F. (2000). DNA cloning by homologous recombination in *Escherichia coli*. *Nature Biotechnology* 18, 1314-1317.

Zhu, Y., Romero, M. I., Ghosh, P., Ye, Z., Charnay, P., Rushing, E. J., Marth, J. D., and Parada, L. F. (2001a). Ablation of NF1 function in neurons induces abnormal development of cerebral cortex and reactive gliosis in the brain. *Genes & Development* 15, 849-876.

Zhu, Z., Ma, B., Homer, R., Zhen, T., and Elias, J. A. (2001b). Use of the tetracycline-controlled transcriptional silencer (tTS) to eliminate transgene leak in inducible overexpression transgenic mice. *Journal of Biological Chemistry* 276, 25222-25229.