

The resilient synapse: insights from genetic interference of synaptic cell adhesion molecules

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Published online: 1 September 2006
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The online version of the original article can be found at: <http://dx.doi.org/10.1007/s00441-006-0267-4>.

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Table 1 was rendered incorrectly: the phenotype details and reference for neuroligin mistakenly appeared on the line for β -neurexins. The corrected table is reproduced in full here.

Table 1 Phenotype of genetic lack-of-function models of important SCAMs (SCAMs synaptic cell adhesion molecules. CNS central nervous system, PNS peripheral nervous system, NMJ neuromuscular junction, PSD95 postsynaptic density protein 95, LTP long-term potentiation, HSPG heparan sulphate proteoglycans, AChR acetylcholine receptor, NMDAR N-methyl-D-aspartate receptor, TGF- β transforming growth factor β , GABA γ -aminobutyric acid). All phenotypes refer to cited mouse models except when explicitly stated otherwise

SCAM	Genetic model	Phenotype, main findings	Reference
NCAM	Knockout of all NCAM isoforms	CNS: smaller olfactory bulb, fasciculation and pathfinding defects, impaired synaptic plasticity PNS: smaller NMJs, immature vesicle-recycling mechanism, periodic transmission failures	Cremer et al. 1998, 1997, 1994; Polo-Parada et al. 2001; Rafuse et al. 2000
	NCAM 180 knockout	CNS: disorganization of the olfactory bulb PNS: periodic transmission failures at the NMJ	Polo-Parada et al. 2004; Tomasiewicz et al. 1993
	Conditional hippocampus-specific knockout of all NCAM isoforms	Impaired synaptic plasticity in CA1 neurons	Bukalo et al. 2004
L1 adhesion molecule	L1 knockout	Poor survival, axon guidance defects in the corticospinal tract, ventricle dilatation, cerebellar vermis hypoplasia, altered dendritic morphology and orientation, reduced GABAergic transmission, decreased density of symmetric synapses in the hippocampus, abnormalities of spatial learning and exploratory behavior	Cohen et al. 1998; Dahme et al. 1997; Demyanenko et al. 2001, 1999; Fransen et al. 1998; Saghatelian et al. 2004
	Conditional hippocampus-specific L1 knockout	Increase in basal excitatory transmission	Law et al. 2003
SynCAM	SynCAM 1 knockout	Male infertility due to defects in spermatogenesis; no major defects in the nervous system	Fujita et al. 2006; van der Weyden et al. 2006
Sidekick	Not available as yet		
SYG	syg-1 knockout (<i>Caenorhabditis elegans</i>)	Synaptic vesicles form ectopic clusters and fail to accumulate at normal synaptic sites	Shen and Bargmann 2003
	syg-2 knockout (<i>C. elegans</i>)	Ectopic synapses, lack of synapses at normal locations,	Shen et al. 2004
Nectin	Nectin-1 and nectin-3 knockouts	Mutants viable, fertile except for male nectin-3 knockouts, microphthalmia, impaired mossy fibre tract in stratum lucidum, reduced number of puncta adherentia junctions at mossy fiber synapses on CA3 pyramidal cells, normal basic neurotransmission, normal LTP	Honda et al. 2006
	Nectin-2 knockout	Disturbed nuclear and cytoskeletal morphology and mitochondrial localization in spermatozoa	Bouchard et al. 2000
Neurexin	α -neurexins: knockouts for all three genes	Perinatal lethality of double and triple mutants, largely reduced evoked and spontaneous neurotransmission, lower density of type 2 synapses PNS: impaired synaptic homeostasis at NMJs	Kattenstroth et al. 2004; Missler et al. 2003; Sons et al. 2006
	β -neurexins: not available as yet		
Neuroigin	Neuroigin 1 knockout	No obvious phenotype	Song et al. 1999
	Neuroigin 2–4 knockouts: not available yet		
Cadherin	N-cadherin knockout	Embryonically lethal, irregular somites, undulating neural tube, severe cardiac defects	Radice et al. 1997
	Dominant-negative N-cadherin mutant	Increased spine length, filopodia-like spine morphology, reduced spine head	Togashi et al. 2002
	E-cadherin knockout	Embryonically lethal, trophoectodermal epithelium fails to form, polarization of morula disturbed	Larue et al. 1994; Riethmacher et al. 1995
	Protocadherin- γ knockout	Neonatally lethal, apoptotic degeneration of spinal interneurons	Wang et al. 2002
	Protocadherin- γ knockout with rescue of apoptotic cells	Reduced current amplitudes, number of synaptic puncta reduced	Weiner et al. 2005
Catenin	β -catenin knockout and β -catenin Δ PDZ mutant	Reduction of the reserve pool of vesicles, reduced response to prolonged repetitive stimulation	Bamji et al. 2003
	δ -catenin knockout	Reduced levels of PSD95 and N-cadherin, deficits	Israely et al. 2004

Table 1 (continued)

SCAM	Genetic model	Phenotype, main findings	Reference
	α N-catenin knockout	in spatial learning and fear conditioning Early postnatal death, impaired development of the cerebellum and hippocampus	Togashi et al. 2002
Laminin	Laminin β 2 knockout	Perinatal lethality, massive proteinuria, lack of active zones and junctional folds at the NMJ, Schwann cell invasion into the synaptic cleft, decrease in neurotransmitter release, increased synaptic depression	Knight et al. 2003; Noakes et al. 1995
	α 2 ^{dy/dy} mutant with a deletion in α 2 chain	Decreased number and size of junctional folds at the NMJ, normal neurotransmission	Banker et al. 1979; Carbonetto 1977
	Laminin α 4 knockout	Misalignment of active zones and junctional folds at the NMJ	Patton et al. 2001
HSPG	Laminin α 5 knockout	Embryonic lethality, multiple developmental defects	Miner et al. 1998
	Syndecan3-knockout	Enhanced LTP in area CA1	Kaksonen et al. 2002
	Glypican 3 knockout	Developmental overgrowth, early lethality, cystic and dysplastic kidneys, skeletal defects	Cano-Gauci et al. 1999
	Perlecan knockout	Lack of collagen-tailed acetylcholinesterase at the NMJ, early postnatal death	Arikawa-Hirasawa et al. 2002a
	Agrin knockout	Postsynaptic AChR aggregates are reduced in number, size, and density at the NMJ	Gautam et al. 1996
Wnt	wnt-7a knockout	Transiently reduced accumulation of synapsin1 at prospective synaptic sites of glomerular rosettes	Lucas and Salinas 1997
Ephrin receptor	EphB1/EphB2/EphB3 triple knockout	Viable and fertile, abnormal spine morphology	Henkemeyer et al. 2003
	EphB2 knockout	Reduced LTP at hippocampal CA1 and dentate gyrus synapses, 40% reduction of NMDAR levels because of redistribution, synaptic depression extinguished	Grunwald et al. 2001; Henderson et al. 2001
	Eph5A dominant-negative mutant	Mistargeted hippocampal axons, disrupted hippocamposeptal topography	Yue et al. 2002
Ephrin ligand	Ephrin B3 Δ C' signalling domain / β -galactosidase knockin	Impaired mossy fiber LTP	Armstrong et al. 2006
TGF- β	TGF- β knockout	Neuronal degeneration, increased sensitivity to excitotoxicity, microgliosis	Brionne et al. 2003
Semaphorin	Sema3A knockout	Bone and heart defects, reduced neuropil in the brain, abnormal orientation of apical dendrites in cortical neurons, defects of fasciculation and axon guidance	Behar et al. 1996; Taniguchi et al. 2003, 1997
	Sema3B knockout	Defasciculation of the anterior commissure	Falk et al. 2005
	Sema3C knockout	Perinatal lethality, cardiovascular defects	Feiner et al. 2001
	Sema3F conventional and neuron-specific knockouts	Defects of fasciculation and axon guidance in the limbic system, olfactory sensory neurons and some cranial motor nerves, episodes of epileptic activity	Cloutier et al. 2004; Sahay et al. 2005, 2003
	Sema6A knockout	Misrouting of certain thalamocortical projections	Leighton et al. 2001
	Sema7A knockout	Impaired growth of the lateral olfactory tract	Pasterkamp et al. 2003