Int J Clin Exp Med 2016;9(11):20754-20760
www.ijcem.com /ISSN:1940-5901/IJCEM0035727

Review Article

The effect of drebrin on plasticity of dendritic spines and synapses in neurons

Guiming Sha, Lina Ma, Yun Li

Department of Geriatrics, Xuan Wu Hospital, Capital Medical University, Beijing 100053, China

Received July 13, 2016; Accepted September 2, 2016; Epub November 15, 2016; Published November 30, 2016

Abstract: Development regulation brain protein (drebrin) is a kind of actin binding proteins which are associated with brain development. Drebrin is located in the dendritic spines in neurons, and plays an important role in dendritic spine morphology and synaptic plasticity. The morphology and function of dendritic spines are responsible for the conditions of synapse development and are involved in the mechanisms of learning and memory functions. The decline in the level of drebrin results in the abnormal dendritic spine morphology and synaptic plasticity, which cognitive impairment as clinical manifestations. Therefore, it is of great importance to assess the effect of drebrin on plasticity of dendritic spines in neurons and to examine its regulation mechanisms, which will provide a new target in the treatment of cognitive impairment and related diseases. In this paper, we present a review on research progress about the effect of drebrin on the plasticity of dendritic spines in neurons.

Keywords: Drebrin, dendritic spine, synaptic plasticity, cognitive impairment, neuron

Introduction

Development regulation brain protein (drebrin), a regulatory protein associated with brain development, plays a critical role in regulating the morphological plasticity of dendritic spines. The morphology and function of dendritic spines are responsible for the conditions of synapse development and are involved in the mechanisms of learning and memory functions. Drebrin fulfills its regulatory role in the morphological occurrence and synaptic plasticity of neurons by adjusting the aggregation of the cytoskeletal protein F-actin. A significant decrease in drebrin expression has been observed in the upper region of the temporal lobe among patients with Alzheimer's disease (AD) and mild cognitive impairment [1]. Therefore, it is of great importance to assess the effect of drebrin on plasticity of dendritic spines in neurons and to examine its regulation mechanisms, which will provide a new target in the treatment of cognitive impairment and related diseases. In this paper, we present a review on research progress about the effect of drebrin on the plasticity of dendritic spines in neurons.

Sources and distribution of drebrin

Drebrin, a type of actin-binding protein (ABP), is related to neuronal growth and regulation of brain development [2]. Shirao et al. first discovered drebrin in the chick embryo in 1986 [3]. Drebrin has a molecular weight of 70 kD, and mammalian drebrin can be divided into four subtypes: drebrin E1, drebrin E2, drebrin A, and s-drebrin A. These four subtypes are common in that they are all derived from the same gene, which expresses different subtypes of drebrin probably by alternative splicing of varying mRNAs at the late stage [4, 5]. Drebrin A is expressed in non-nervous tissue, while the other three subtypes are only expressed in nervous tissue.

There are two isoforms of drebrin: embryonic type (drebrin E) and adult type (drebrin A). The embryonic type can be further subdivided into drebrin E1 and E2. Moreover, a small, truncated drebrin A has been isolated from mouse brain at the mRNA level, called s-drebrin A. Therefore, mammalian drebrin includes four subtypes in total. Drebrin E is present in brain neurons during brain development and is also expressed

outside the brain. In the early stage of brain development, drebrin E is dominantly expressed as a common isomer [6]. During brain development, drebrin E expression decreases, while drebrin A expression gradually increases. During late-stage brain development, drebrin A holds a distinct dominance in the adult brain. Drebrin A is a neuron-specific subtype primarily distributed in dendritic spines of mature neurons, and occasionally present in the cell bodies and dendrites. Therefore, only drebrin A is present in the mature brain tissue to promote the formation of dendritic spines and influence plasticity [7-9].

Drebrin and dendritic spines/synapses

Neuronal synapses have two basic elements: the postsynaptic structure consists mostly of dendritic spines, and the presynaptic structure consists of axon terminals. Dendritic spines, which are abundant subcellular structures with dynamic changes in the actin cytoskeleton, exist in the postsynaptic region of most excitatory neurons in the adult brain. Morphologically, dendritic spines are tiny dendritic projections on neuronal dendrites [10, 11]. Drebrin A is mainly concentrated in the dendritic spines of excitatory synapses. Dendritic spines are the major component maintaining the basic morphology and function of synapses, and their main structures include the actin cytoskeleton, postsynaptic density (PSD), and neurotransmitter receptor. Abnormalities in dendritic spines affect the overall structure and function of synapses. The formation of dendritic spines depends on expression and content of dendritic spine protein (drebrin), which is related to the morphology of dendritic spines. Drebrin regulates the formation and plasticity of dendritic spines by binding to or disassociating from F-actin [7].

Cognitive impairment in early AD is associated with synaptic degeneration [12]. Drebrin A aggregates have been observed in new axon-dendrite connections in the dendritic membrane area. This finding suggests that drebrin A expression occurs during the initial stage of synapse formation; inhibition of drebrin A expression through antisense oligonucleotides can lead to cognitive deficits [13, 14]. Moreover, significant decreases in the size, number, and density of dendritic spines have been found in the brain of AD patients and animal models, wherein drebrin expression was also markedly reduced [15, 16].

Role of drebrin

Drebrin, together with F-actin, has a critical role in the morphological changes of dendritic spines in neurons [17]. Drebrin can also promote the formation and influence plasticity of dendritic spines, facilitate migration and promote neuronal repair, and regulate intracellular signal transduction.

Promotion of dendritic spine formation

Under physiological conditions, drebrin regulates the developmental formation of dendritic spines, which ensure the development of presynaptic components and thereby maintain normal physiological functions of the nervous system. Numerous neurological diseases associated with cognitive decline present with an abnormal dendritic spine morphology and a decreased number of dendritic spines in hippocampal neurons [18-20]. Drebrin affects the morphology and structure of dendritic spines and further causes synaptic changes. Drebrin plays a role in regulating the structure of the actin cytoskeleton, as well as in maintaining and regulating the morphology and plasticity of dendritic spines. Therefore, any degree of decline in drebrin levels will lead directly to morphological abnormalities of dendritic spines, such as collapse and shrinkage. Morphological changes in dendritic spines correlate with synaptic function, thus resulting in synaptic dysfunction and cognitive impairment [21].

The drebrin-actin complex, comprised drebrin A and actin, is responsible for the conversion from filopodia to dendritic spines and plays a critical role in regulating dendritic spine morphology [22]. Blocking the formation of the drebrin-actin complex prevents postsynaptic aggregation of post synaptic density-95 (PSD-95) and leads to synaptic dysfunction. Drebrin is mainly expressed in dendritic spines of neurons and adjusts dendritic spine morphology by binding to or disassociating from fibrous actin. Inhibition of drebrin A expression in developing neurons affects the cluster formation of F-actin and PSD-95 and reduces filopodia density, thereby inhibiting spine formation [13].

Abnormal changes in dendritic spines were found to be associated with abnormal drebrin expression in *in vitro* cell culture. Overexpression of drebrin A in mature neuronal cells leads to longer dendritic spines, with a wide and large shape [24]. At 21 days in primary neuronal culture of drebrin A expression in dendritic spines mainly presents as blotchy aggregation. Conversely, if drebrin A expression is inhibited, the density of dendritic spines decreases correspondingly [23]. Therefore, overly high or low levels of drebrin protein expression affect the morphology and number of dendritic spines [24]. Overexpression of drebrin A can cause extension of dendritic spines, while inhibition of drebrin A reduces the density of dendritic spines, thus forming finer mature spines [23].

Animal experiments have revealed a decline in drebrin expression level at the early onset of AD, which is accompanied by morphological changes in dendritic spines. Quantitative immunoelectron microscopy of APP/PS1 knockin AD model mice revealed significantly decreased drebrin-immunoreactive dendritic spines in the cerebral cortex, as well as deformed and disordered dendrites in hippocampal neurons and a reduced density of dendritic spines in the hippocampus [9, 15, 16]. These observations indicate that decreased drebrin expression leads to dendritic spine transformation and cognitive deficits.

Regulation of dendritic spine plasticity

In the central nervous system, the hippocampus is involved in learning and memory functions. Synaptic plasticity forms a neurobiological basis for learning and memory, and changes can result in learning and memory impairment [25, 26]. Decreased drebrin expression could be responsible for the loss of dendritic spine plasticity. A significant reduction in drebrin expression has been observed in postmortem brain tissue of clinical AD patients; drebrin expression was not only reduced in the hippocampus, but also markedly decreased in the entire cerebral cortex of AD patients [27].

Drebrin in neural spines not only regulates the morphological changes of neural spines and synaptic plasticity, but it is also required for growth of neuronal axons. In healthy individuals, drebrin levels gradually decline with age [28]. Dendritic spines are the structural basis for signaling transmission of mature synapses and plasticity. The ability to alter spine shape or length, or the stability of synaptic connections, provides powerful mechanisms for excitatory synaptic plasticity of the cerebral cortex and marginal region (e.g., hippocampus and amygdala) [29]. In the cerebral cortex, approximately 75% of neurons have a high density of dendrites, and the majority of them are excitatory neurons [30]. Moreover, most cortical excitatory synapses have connections with dendritic spines of other excitatory neurons [31]. Excitatory synaptic plasticity involves more advanced brain functions, such as learning, memory, or cognition, and is believed to alter based on the shape and density of dendritic spines [30, 31]. In APPsw mice, activation of cysteine protease and cleavage of actin in the brain leads to a considerable loss of drebrin and cytoskeletal collapse, thereby affecting spine synapse plasticity. A behavioral study of drebrin A knockout rats found that a reduction of drebrin induces defects in cognitive function other than spatial memory, likely due to hypofunction of synaptic spines [17].

Promotion of neuronal migration

The formation of a functional nervous system requires migration of neurons to the correct site in the developing brain. At the embryonic stage, most neurons are immature. Around the newborn stage, the number of neurons tends to stabilize and a relatively complete neural network is formed. Changes in the cytoskeleton structure form a kinetic and morphological foundation for cell differentiation and migration, synapse formation, and neuronal network establishment. It is unknown how environmental factors are coupled to a specific cytoskeleton to generate and guide the dominant process. Drebrin acts as an actin-binding protein and causes protrusions in various cell types, thus playing a critical role in regulating neuronal morphology. Using motor neurons as a migration model, results showed that drebrin plays a vital role in generating and guiding the dominant processes. Without drebrin, the dominant process is not formed and neuronal cells do not migrate, although axonal growth is not seriously affected [32-36].

Drebrin is essential in two phases of neuronal migration: one is the generation of the dominant process and onset of cell migration; the

other is correct orientation and navigation process, namely, the track of cell bodies. The ability of neurons to maintain function in the cells is essential to generating and maintaining the proper connections [37, 38]. However, drebrin has also been shown to induce direct migration that is unrelated to axonal guidance in separate motor neurons [32]. Recently, the genomic and chromosomal localization of drebrin 1 (Dbn1), a mouse drebrin gene, have been reported, and preliminary research shows that Dbn1 may regulate the formation of dendritic spines and migration of neurons [39].

Promotion of neuronal repair

Animal studies have examined drebrin changes in rat spinal motor neurons using immunohistochemical methods after unilateral sciatic nerve transection. Immunohistochemical results showed that after 3 days, drebrin is considerably decreased in motor neurons on the injured side, and laser confocal microscopy of motor neurons revealed a significant increase of drebrin in the cell membrane region. At 10 days, drebrin expression on the injured side dropped to a level with no significant difference from the non-injured side. These observations suggest that drebrin plays a critical role in synaptic repair after axotomy of motor neurons [40]. PSD includes receptors, signal transduction proteins, and cytoskeletal proteins [41]. The positioning of drebrin, CaMKII, and α-actin-2 relies on F-actin. Although N-methyl-D-aspartic acid receptor (NMDA) receptors and PSD-95 are independent, their mRNA signals are attenuated after axotomy [42].

Regulatory mechanisms of drebrin

Currently, the molecular mechanisms of drebrin and related signal transduction pathways are still being explored and remain unclear. The following points are summarized in accordance with the literature.

AMPA and NMDA receptor modulation

Drebrin aggregation has been shown to be related to the stability regulated by a-amino-3-hydroxy-5-methyl-4-isoxa-zolep-propionate (AMPA) receptors and the mobility regulated by NMDA receptors. On the one hand, AMPA receptor activation maintains the increase of stable drebrin within drebrin spines; on the other hand, NMDA receptor activation leads to decreased mobility of drebrin [43]. The actin cytoskeleton, which is the major cytoskeletal component in dendritic spines, regulates NMDA receptors in a calcium-dependent manner. Drebrin is a major actin-binding protein capable of inhibiting the actin-binding activity of fascin and α-actinin. Moreover, drebrin can induce tropomyosin to separate from actin fibers [44]. When subjected to external stimuli, drebrin disappears from dendritic spines and reappears in dendritic axons and cell bodies. This process results in shape changes in dendritic spines andis thus closely associated with synaptic plasticity and intracellular signal transduction.

Interaction between myosin and actin

Drebrin A connects with actin filaments through one drebrin molecule and 5-6 actin molecules. Drebrin A reduces the Mg-ATPase activity of myosin V, and *in vitro* motion analysis has revealed that drebrin A is responsible for the connection of F-actin to a glass surface coated with myosin V. However, once it is connected to the surface, drebrin A will not affect the sliding rate of F-actin. This finding indicates that drebrin A reduces the interaction between actin and myosin V in neurons, which probably affects spine kinetics, vesicle trafficking, and other activities driven by myosin V [45]. Drebrin E and F-actin are co-localized in the cell body of developing neurons, especially in the base area of filopodia [46]. Inhibition of drebrin A by antisense RNA promotes PSD protein aggregation [47]. Additionally, inhibition of drebrin A expression by antisense RNA results in increased activity and anger-like behavior in mice, suggesting that drebrin A impacts spine activity [14].

Intracytoplasmic signal molecule regulation

Drebrin is an upstream regulator for a variety of ABPs. In addition to directly binding to F-actin, drebrin competes with other ABPs for F-actin and modulates the interaction of F-actin and ABPs. Cofilin and drebrin competitively bind to actin and thereby regulate the morphology and plasticity changes of dendritic spines. Phosphorylation of the PAK signaling pathway mediates activity of cofilin and actin [49]. The main component of senile plaque, Aβ, has neurotoxic effects. Research has shown that Aβ42 oligomer-induced reduction of drebrin expres-

sion is regulated and affected by PAK overexpression [50]. In addition to PAK, drebrin is regulated by a variety of molecules. For example, drebrin is directly decomposed by caspase-6. TNF-α has been observed in AD patients, while IL-1b expression results in decreased drebrin by activating pro-apoptotic factors and caspase-3 [3].

Moreover, drebrin has been found to be regulated by Ras, a downstream regulatory site in calcium-dependent signaling pathways [51]. Curcumin can reduce Sim2 expression, leading to increased neuronal expression of drebrin in a high blood sugar environment [8]. Thus, drebrin can bind to and interact with a variety of signal transduction proteins and play a role in the maintenance of neural activity.

Conclusion

In summary, drebrin is an actin-binding protein located in the dendritic spines of neurons, which, together with actin filaments, regulate the morphological changes of dendritic spines and synaptic plasticity. Decreased drebrin expression can result in abnormal dendritic spine morphology and synaptic function, further leading to cognitive impairment and related diseases. Therefore, the study of drebrin A is of great importance to further our understanding of the brain's advanced learning and memory functions, the pathogenesis of cognitive impairment-related diseases, and the development of clinical treatment strategies.

Acknowledgements

This work was supported by the following grants: Capital Medical University Project of Basic and Clinical Research Collaboration (16JL14) and the Ministry of Education in China Project of Humanities and Social Sciences (16YJAZH034).

Disclosure of conflict of interest

None.

Address correspondence to: Drs. Lina Ma and Yun Li, Department of Geriatrics, Xuan Wu Hospital, Capital Medical University, #45 Changchun Street, Xicheng District, Beijing 100053, China. Tel: 86-010-83198492; Fax: 86-010-83198492; E-mail: malina0883@126.com (LNM); Tel: 86-010-83198707; Fax: 86-010-83198707; E-mail: liyunxw@163.com (YL)

References

[1] Mufson EJ, Binder L, Counts SE, DeKosky ST, de Toledo-Morrell L, Ginsberg SD, Ikonomovic MD, Perez SE, Scheff SW. Mild cognitive impairment: pathology and mechanisms. Acta Neuropathol 2012; 123: 13-30.

[2] Shirao T, Obata K. Immunochemical homology of 3 developmentally regulated brain proteins and their developmental change in neuronal distribution. Brain Res 1986; 394: 233-44.

[3] Rao JS, Kellom M, Kim HW, Rapoport SI, Reese EA. Neuroinflammation and synaptic loss. Neurochem Res 2012; 37: 903-910.

[4] Jin M, Tanaka S, Sekino Y, Ren Y, Yamazaki H, Kawai-Hirai R, Kojima N, Shirao T. A novel brain specific mouse drebrincDNA cloning, chromosomal mapping, genomic structure, expression, and functional characterization. Genomics 2002; 79: 686-692.

[5] Terakawa Y, Agnihotri S, Golbourn B, Nadi M, Sabha N, Smith CA, Croul SE, Rutka JT. The role of drebrin in glioma migration and invasion. Exp Cell Res 2013; 319: 517-528.

[6] Sekino Y, Tanaka S, Hanamura K, Yamazaki H, Sasagawa Y, Xue Y, Hayashi K, Shirao T. Activation of N-methyl-D-aspartate receptor induces a shift of drebrin distribution: disappearance from dendritic spines and appearance in dendritic shafts. Mol Cell Neurosci 2006; 31: 493-504.

[7] Aoki C, Sekino Y, Hanamura K, Fujisawa S, Mahadomrongkul V, Ren Y, Shirao T. Drebrin A is a postsynaptic protein that localizes in vivo to the submembranous surface of dendritic sites forming excitatory synapses. J Comp Neurol 2005; 483: 383-402.

[8] Wang X, Song Y, Chen L, Zhuang G, Zhang J, Li M, Meng XF. Contribution of single-minded 2 to hyperglycaemia-induced neurotoxicity. Neurotoxicology 2013; 35: 106-112.

[9] Mahadomrongkul V, Huerta PT, Shirao T, Aoki C. Stability of the distribution of spines containing drebrin A in the sensory cortex layer I of mice expressing mutated APP and PS1 genes. Brain Res 2005; 1064: 66-74.

[10] Lin YC, Yeckel MF, Koleske AJ. Abl2/Arg controls dendritic spine and dendrite arbor stability via distinct cytoskeletal control pathways. J Neurosci 2013; 33: 1846-1857.

[11] Carlisle HJ, Kennedy MB. Spine architecture and synaptic plasticity. Trends Neurosci 2005; 28: 182-187.

[12] Coleman P, Federoff H, Kurlan R. A focus on the synapse for neuroprotection in Alzheimer

disease and other dementias. Neurology 2004; 63: 1155-1162.
[13] Tojima T, Takahashi M, Ito E. Dual regulation of LIM kinase 1 expression by cyclic AMP and calcium determines cofilin phosphorylation states during neuritogenesis in NG108-15 cells. Brain Res 2003; 985: 43-55.
[14] Kobayashi R, Sekino Y, Shirao T, Tanaka S, Ogura T, Inada K, Saji M. Antisense knockdown of drebrin A, a dendritic spine protein, causes stronger preference, impaired pre-pulse inhibition, and an increased sensitivity to psychostimulant. Neurosci Res 2004; 49: 205-217.
[15] Junm Y, Lu G, Jianfeng Y, et al. Age-related changes of the expression of P21-activted kinase in hippocampus an APP/PS 1 transgenic mice model of Alzheimer's disease. Chinese Journal of Neuroanatomy 2008; 24: 1-7.
[16] Jacobsen DJ, Wu CC, Redwine JM, Comery TA, Arias R, Bowlby M, Martone R, Morrison JH, Pangalos MN, Reinhart PH, Bloom FE. Early-onset behavioral and synaptic deficits in a mouse model of Alzheimer's disease. Proc Natl Acad Sci U S A 2006; 103: 5161-5166.
[17] Sekino Y, Kojima N, Shirao T. Role of actin cytoskeleton in dendritic spine morphogenesis. Neurochem Int 2007; 51: 92-104.
[18] Pitt J, Thorner M, Brautigan D, Larner J, Klein WL. Protection against the synaptic targeting and toxicity of Alzheimer's-associated Aβ oligomers by insulin mimetic chiroinositols. FASEB J 2013; 27: 199-207.
[19] Zhao L, Ma QL, Calon F, Harris-White ME, Yang F, Lim GP, Morihara T, Ubeda OJ, Ambegaokar S, Hansen JE, Weisbart RH, Teter B, Frautschy SA, Cole GM. Role ofp2 1-activated kinase pathway defects in the cognitive deficits of Alzheimer disease. Nat Neurosci 2006; 9: 234-242.
[20] Lacor PN, Buniel MC, Furlow PW, Clemente AS, Velasco PT, Wood M, Viola KL, Klein WL. Abeta oligomer-induced aberrations in synapse composition, shape, and density provide a molecular basis for loss of connectivity in Alzheimer's disease. J Neurosci 2007; 27: 796-807.
[21] Zhou Q, Homma KJ, Poo MM. Shrinkage of dendritic spines associated with long term depression of hippocampal synapses. Neuron 2004; 44: 749-757.
[22] Park H, Yamada K, Kojo A, Sato S, Onozuka M, Yamamoto T. Drebrin (developmentally regulated brain protein) is associated with axo-somatic synapses and neuronal gap junctions in rat mesencephalic trigeminal nucleus. Neurosci Lett 2009; 461: 95-99.
[23] Takahashi H, Mizui T, Shirao T. Down-regulation of drebrin A expression suppresses synaptic targeting of NMDA receptors in developing hippocampal neurones. J Neurochem 2006; 97: 110-115.
[24] Mizui T, Takahashi H, Sekino Y, Shirao T. Overexpression of drebrin A in immature neurons induces the accumulation of F-actin and PSD-95 into dendritic filopodia, and the formation of large abnormal protrusions. Mol Cell Neurosci 2005; 30: 149-157.
[25] Volk LJ, Bachman JL, Johnson R, Yu Y, Huganir RL. PKM-ζ is not required for hippocampal synaptic plasticity, learning and memory. Nature 2013; 493: 420-423.
[26] Volianskis A, Bannister N, Collett VJ, Irvine MW, Monaghan DT, Fitzjohn SM, Jensen MS, Jane DE, Collingridge GL. Different NMDA receptor subtypes mediate induction of long-term potentiation and two forms of short-term potentiation at CA1 synapses in rat hippocampus in vitro. J Physiol 2013; 591: 955-972.
[27] Shim KS, Lubec G. Drebrin, a dendritic spine protein, is manifold decreased in brains of patients with Alzheimer's disease and Down syndrome. Neurosci Lett 2002; 324: 209-212.
[28] Sbai O, Khrestchatisky M, Esclapez M, Ferhat L. Drebrin A expression is altered after pilocarpine-induced seizures: Time course of changes is consistent for a role in the integrity and stability of dendritic spines of hippocampal granule cells. Hippocampus 2012; 22: 477-493.
[29] Shirao T, Sekino Y. Clustering and anchoring mechanisms of molecular constituents of postsynaptic scaffolds in dendritic spines. Neurosci Res 2001; 40: 1-7.
[30] Keller A. Use-dependent inhibition of dendritic spines. Trends Neurosci 2002; 25: 541-544.
[31] Marrs GS, Steven HG, Dailey ME. Rapid formation and remodeling of postsynaptic dendrites in developing dendrites. Nat Neurosci 2001; 4: 1006-1013.
[32] Dun XP, Bandeira de Lima T, Allen J, Geraldo S, Gordon-Weeks P, Chilton JK. Drebrin controls neuronal migration through the formation and alignment of the leading process. Mol Cell Neurosci 2012; 49: 341-350.
[33] Cubedo N, Cerdan E, Sapede D, Rossel M. CXCR4 and CXCR7 cooperate during tangential migration of facial motoneurons. Mol Cell Neurosci 2009; 40: 474-484.
[34] Marcos S, Backer S, Causeret F, Tessier-Lavigne M, Bloch-Gallego E. Differential roles of Netrin-1 and its receptor DCC in inferior olivary neuron migration. Mol Cell Neurosci 2009; 41: 429-439.
[35] Zhu Y, Matsumoto T, Mikami S, Nagasawa T, Murakami F. SDF1/CXCR4 signalling regulates two distinct processes of precerebellar neuronal migration and its depletion leads to abnor-

mal pontine nuclei formation. Development 2009; 136: 1919-1928.
[36] Renaud J, Kerjan G, Sumita I, Zagar Y, Georget V, Kim D, Fouquet C, Suda K, Sanbo M, Suto F, Ackerman SL, Mitchell KJ, Fujisawa H, Chédotal A. Plexin-A2 and its ligand, Sema6A, control nucleus-centrosome coupling in migrating granule cells. Nat Neurosci 2008; 11: 440-449.
[37] Allen J, Chilton JK. The specific targeting of guidance receptors within neurons: who directs the directors? Dev Biol 2009; 327: 4-11.
[38] Bence R, Richard JW. Microdomains in forebrain spines: an ultrastructural perspective. Mol Neurobiol 2013; 47: 77-89.
[39] Peitsch WK, Hofmann I, Bulkescher J, Hergt M, Spring H, Bleyl U, Goerdt S, Franke WW. Drebrin, an actin binding, cell type characteristic protein: induction and localization in epithelial skin tumors and cultured keratinocytes. J Invest Dermatol 2005; 125: 761-774.
[40] Kobayashi S, Shirao T, Sasaki T. Drebrin expression is increased in spinal motoneurons of rats after axotomy. Neurosci Lett 2001; 311: 165-168.
[41] Trinidad JC, Thalhammer A, Burlingame AL, Schoepfer R. Activity-dependent protein dynamics define interconnected cores of coregulated postsynaptic proteins. Mol Cell Proteomics 2013; 12: 29-41.
[42] Che YH, Tamatani M, Tohyama M. Changes in mRNA for post-synaptic density-95 (PSD-95) and carboxyterminal PDZ ligand of neuronal nitric oxide synthase following facial nerve transection. Mol Brain Res 2000; 76: 325-335.
[43] Takahashi H, Yamazaki H, Hanamura K, Sekino Y, Shirao T. Activity of the AMPA receptor regulates Drebrin stabilization in dendritic spine morphogenesis. J Cell Sci 2009; 122: 1211-1219.
[44] Kojima N, Shirao T. Synaptic dysfunction and disruption of postsynaptic drebrin-actin complex: a study of neurological disorders accompanied by cognitive deficits. Neurosci Res 2007; 58: 1-5.
[45] Ishikawa R, Katoh K, Takahashi A, Xie C, Oseki K, Watanabe M, Igarashi M, Nakamura A, Kohama K. Drebrin attenuates the interaction between actin and myosin-V. Biochem Biophys Res Commun 2007; 359: 398-401.
[46] Sasaki Y, Hayashi K, Shirao T, Ishikawa R, Kohama K. Inhibition by drebrin of the actin-bundling activity of brain fascin, a protein localized in filopodia of growth cones. J Neurochem 1996; 66: 980-988.
[47] Takahashi H, Sekino Y, Tanaka S, Mizui T, Kishi S, Shirao T. Drebrin-dependent actin clustering in dendritic filopodia governs synaptic targeting of postsynaptic density-95 and dendritic spine morphogenesis. J Neurosci 2003; 23: 6586-6595.
[48] Calon F, Lim GP, Yang F, Morihara T, Teter B, Ubeda O, Rostaing P, Triller A, Salem N Jr, Ashe KH, Frautschy SA, Cole GM. Docosahexaenoic acid protects from dendritic pathology in an Alzheimer's disease mouse model. Neuron 2004; 43: 633-645.
[49] Yang N, Higuchi O, Ohashi K, Nagata K, Wada A, Kangawa K, Nishida E, Mizuno K. Cofilin phosphorylation by LIM-kinase 1 and its role in Rac-mediated actin reorganization. Nature 1998; 393: 809-812.
[50] Arber S, Barbayannis FA, Hanser H, Schneider C, Stanyon CA, Bernard O, Caroni P. Regulation of actin dynamics through phosphorylation of cofilin by LIM-kinase. Nature 1998; 393: 805-809.
[51] Biou V, Brinkhaus H, Malenka RC, Matus A. Interactions between drebrin and Ras regulate dendritic spine plasticity. Eur J Neurosci 2008; 27: 2847-2859.