Neurodegenerative diseases such as Alzheimer’s, Huntington’s and Parkinson’s disease as well as different neuropsychiatric disorders, mood disorders, depression, bipolar disease, and schizophrenia are becoming prevalent in aging societies from developing countries. Neurotrophins are a family of growth factors that have been directly implicated in these human pathologies as there is now abundant evidence indicating that alterations on function/expression of one neurotrophin, named BDNF, have been linked to different human neurodegenerative and psychiatric diseases. Neurotrophins are important for cell survival, differentiation, apoptosis, axonal and dendritic growth, and synaptic plasticity in the nervous system. They bind to two different sets of receptors, Trk and p75 neurotrophin receptors, to mediate their functions. Upon activation, Trk neurotrophin receptors function as docking sites for different adaptor proteins triggering different signaling pathways. Understanding the molecular mechanisms by which neurotrophins exert their functions may help to develop efficient treatments for brain diseases. Recently, an ankyrin repeat-rich membrane spanning protein, (ARMS/Kidins220, referred to as ARMS hereafter) has been linked to neurotrophin signaling as ARMS is associated with Trk neurotrophin receptors and is modulated in response to neurotrophins. We have studied the role of ARMS in BDNF-mediated functions. We have observed that ARMS expression is very high during the development (embryonic stages) of the nervous system and declines short after birth. During nervous system development there is a massive dendritic growth and synapse formation in which BDNF participates. Using a mouse model in which ARMS expression was reduced, we have observed that ARMS is important for the proper morphological development of dendritic arbors and spines during an activity- and BDNF-dependent developmental period. In addition, ARMS protein protects two brain cortical areas implicated in neurodegenerative and psychiatric disorders that depend on BDNF. Furthermore, ARMS regulates the trafficking of glutamate channels that are crucial players in the functioning of the synapse. In conclusion, our results suggest that ARMS protein plays a pivotal role on BDNF-dependent functions in the brain that may be relevant on the etiology of different brain diseases. Further studies will be required to address this possibility.