

ISOFORMS, DISTRIBUTION AND ACTIVITIES OF β SPECTRINS AND 4.1 PROTEINS IN BRAIN

ANTHONY J. BAINES, PAOLA A. BIGNONE, NANDINI V. L. HAYES, LISA A. KEATING, GARETH W. PHILLIPS and CATHERINE SCOTT
Department of Biosciences, University of Kent at Canterbury, Canterbury, Kent CT2 7NJ, USA

One aspect of spectrin/4.1/ankyrin function is to act as an „accumulation machine” at the plasma membrane by recruiting selected transmembrane proteins to sites specified by cell adhesion molecules, and stabilizing them by linkage to the internal cytoskeleton [1]. In the nervous system, an important site of intercellular adhesion is the synapse. Spectrin has long been known to be a component of postsynaptic densities (PSDs), and it is established that β II Σ 2 spectrin is in PSDs. More recently we have shown that β II Σ 1, but not β II Σ 2 spectrin, is a PSD component [2]. These observations raise the question of whether the spectrin-binding 4.1 proteins are also PSD components. We find that specific isoforms of each 4.1 protein (4.1R, 4.1B, 4.1N and 4.1G) are enriched in PSDs [3]. An 80 kDa form of 4.1R is enriched in PSDs to an extent comparable with the standard PSD marker PSD-95. 4.1R co-immunoprecipitates with β II Σ 1 spectrin, actin and the characteristic intermediate filament of PSDs, α -internexin (α I). This provides the first description of a mechanism linking α I to the PSD core. PSD spectrin/4.1 proteins bind glutamate receptors: β II Σ 1 spectrin binds NMDA receptors; 4.1 binds AMPA receptors. We hypothesize that the spectrin/4.1 „accumulation machine” bridges glutamate receptors to cytoplasmic α I and actin, thereby promoting their retention at synapses.

REFERENCES

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