NMR-based structural characterization of the post-synaptic density scaffold protein GKAP

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Scaffold proteins of the post-synaptic density (PSD) have been shown to have a high relevance in different neuronal disorders, as they participate in the regulation and modulation of protein-level processes of learning and memory. Detailed structural description of these proteins might lead to the better understanding of their interactions and mechanism of action, and also their contribution to the associated diseases. GKAP is one of the essential scaffold proteins in the PSD, interacting with the GK domain of PSD-95, the dynein light chain (DLC2) motor protein, and the PDZ domain of Shank. Most of GKAP is predicted to be disordered, and its structure is unknown, except for the GH1 domain on the C terminal. Our aim is to explore the structural ensembles and dynamics that characterize the disordered segments of GKAP: the GK binding region, the dynein binding segment, and the first 300 residues with unknown function or interaction partners. To do so, we are performing protein-protein interaction assays (among others ITC and ECD spectroscopy), and triple resonance 3D NMR measurements on 13C- 15N- labeled protein constructs alone and titrated with their interaction partners. The obtained chemical shifts will serve as input for generating ensemble-based structural models of GKAP, which will contribute to a more detailed description of PSD organization.