Structural description of the multivalent interaction of the post-synaptic scaffold protein GKAP and dynein motor molecule

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GKAP (guanylate-kinase associated protein) is an important scaffold protein in the post-synaptic density, accumulating essential signal transmission proteins like the NMDA receptors-PSD-95-Shank-Homer scaffold complex, but also connecting to the dynein motor via dynein light chain 2 (DLC2, a.k.a. LC8) molecule. It is mostly disordered therefore the structural properties and binding mechanisms can most accurately be described via NMR. We have performed NMR titration measurements and SAXS analysis of the GKAP-DLC2 complex and executed molecular dynamics calculations to describe the multivalent complex structure in atomic detail proposed in the literature. Backbone and sidechain assignments were completed for both GKAP and DLC2 dimer and chemical shift perturbance (CSP) datasets were acquired for both members of the complex. Characterization of the binding kinetics is also performed. Our results indicate that GKAP retains much of its flexibility in the bound state, although the multivalent interactions between the partners might lead to the formation of an elaborate complex structure. This complex of GKAP and DLC2 is reported to go through liquid-liquid phase separation (LLPS) and describing the atomic details of their connection will lead to a better understanding of molecular organization of the post-synaptic density, thus the fundamentals of learning, memory, and synaptic plasticity.