Structure of the nNOS-Syntrophin Complex Reveals Unexpected Modes of PDZ Domain-Mediated Assembly

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The PDZ domain of neuronal nitric oxide synthase (nNOS) can specifically heterodimerize with the PDZ domains of PSD-95 and syntrophin via interactions that do not involve typical COOH-terminal motif recognition. The crystal structure of the nNOS-syntrophin PDZ complex reveals that the domains interact in an unusual linear head-to-tail arrangement. The nNOS PDZ domain has two, opposite interaction surfaces — one face has the canonical peptide binding groove, and the other face has a novel beta-hairpin "finger." This nNOS beta-finger docks in the syntrophin peptide binding groove and mimics a peptide ligand, except that a sharp beta-turn replaces the normally required COOH-terminus. This structure demonstrates that PDZ domains can participate in diverse interactions useful for assembling protein networks: recognition of COOH-terminal motifs, recognition of internal motifs presented within a constrained structure, and formation of head-to-tail oligomers.

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