Agonist selectivity of glutamate receptors is specified by two domains structurally related to bacterial amino acid-binding proteins

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By exchanging portions of the AMPA receptor subunit GluR3 and the kainate receptor subunit GluR6, we have identified two discontinuous segments of approximately 150 amino acid residues each that control the agonist pharmacology of these glutamate receptors. The first segment (S1) is adjacent and N-terminal to the putative transmembrane domain 1 (TM1), whereas the second segment (S2) is located between the putative TM3 and TM4. Only the simultaneous exchange of S1 and S2 converts the pharmacological profile of the recipient to that of the donor subunit. The two segments identified in this study share sequence similarities with the ligand-binding site of several bacterial periplasmic amino acid-binding proteins. Based on the X-ray structure of these proteins, we propose a model for the glutamate-binding site of ionotropic glutamate receptors.

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