Studies on the interaction of kynurenic acid and glutamate receptor 1 by surface plasmon resonance (SPR) and molecular docking

Imre Dékány[1,4,*], Balázs Roósz[2,*], Zsófia Majláth[3], László Vécsei[3], Edit Csapó[4], Tamás Körtvélyesi[2]

[1] *Department of Medical Chemistry, University of Szeged, Faculty of Medicine, Szeged, H-6720, Hungary*
[2] *Department of Physical Chemistry and Materials Science, University of Szeged, Szeged, H-6720, Hungary*
[3] *Neurology Department, Albert Szent-Györgyi Clinical Center, University of Szeged, Faculty of Medicine, Szeged, H-6720, Hungary*
[4] *Supramolecular and Nanostructured Materials Research Group, Szeged, H-6720, Hungary*
[*] *Corresponding author: i.dekany@chem.u-szeged.hu*

The α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (also known as AMPA receptor) is a non-NMDA-type ionotropic transmembrane receptor. The glutamate molecule is a transmitter in the central nervous system (CNS). AMPARs are found in many parts of the brain and they are the most common receptors in the nervous system. The AMPA GluA2 (GluR2) tetramer was the first and currently the only glutamate receptor which could have been crystallized so far.

AMPARs are composed of four types of subunits, designated as GluR1, GluR2, GluR3, and GluR4, which combine to form tetramers [1]. Kynurenic acid (KYNA) is a product of the metabolism of amino acid *L*-tryptophan. It has been shown that KYNA possesses neuroactivity. It acts as an antiexcitotoxic and anticonvulsant, most likely through acting as an antagonist at excitatory amino acid receptors [2]. Because of this activity, it may influence important neurophysiologic and neuropathologic processes. As a result, kynurenic acid has been considered for use in therapy of certain neurobiological disorders.

In our study the interaction between KYNA and three different (ca. 30 residue) smaller peptides of human glutamate 1 receptor (GLUR1) 201-300 have been investigated by SPR spectroscopy. We studied the adsorption of the above mentioned peptides on gold-coated surface in a concentration range of 10 to 30 μM. The monomolecular layer was formed by bonding of the thiol group of cysteine to gold surface. The adsorption of KYNA on the prepared peptide films was studied in the concentration range of 0.1 – 5.0 mM using 150mM NaCl ionic strength at pH 7.4. The experiments were carried out between $+10^0$C to +40 ^{0}C. The isoster adsorption enthalpy at a given peptide-KYNA stochiometry was calculated by measuring the temperature dependence of the adsorption isotherms. The interactions between KYNA and GLUR1 were mapped by theoretical calculations (docking). The orientation of KYNA and the binding energy were also determined. Initial geometry was optimized by semiempirical quantum chemical method. GLUR1 structure was found in RCSB PDB database (PDB id.: 3SAJ) [3]. Docking calculations are supported to explain the experimental data.

References

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