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Poster presentation

Computational simulations of interactions of the κ-hefutoxin1 with the voltage-gated potassium ion channels

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κ-Hefutoxin1 adopts a unique three-dimensional fold of two parallel helices linked by two disulfide bridges without any β-sheets[1]. κ-Hefutoxin1 not only blocks the voltage-gated K-channels, Kv1.3 and Kv1.2, but also slows the activation kinetics of Kv1.3 considered solely pore blockers [1]. The recognition of the scorpion toxin κ-Hefutoxin1 by the voltage-gated potassium (Kv1) channels, Kv1.1, Kv1.2, and Kv1.3 was studied by 3D-dock software package. All the 20 available structures of κ-Hefutoxin1 (NMR, MD) were considered during the simulations. The results indicated that the conformation of κ-Hefutoxin1 significantly affected both the recognition and the binding between κ-Hefutoxin1 and the Kv1 channels. Comparing the highest-frequency structures of κ-Hefutoxin1 binding to the Kv1 channels, we found that the Kv1.2 channel, with the highest docking frequencies and the lowest electrostatic interaction energies. From the κ-Hefutoxin1-Kv1.2 binding model, we identified the critical residues for the recognition of these two proteins. κ-Hefutoxin1 is located around the extracellular mouth of the Kv1 channels, making contacts with its helices. Lys 19, Tyr 5, Arg 6, Trp 9 or Arg 10 in the toxin and residues Asp 402, His 404, Thr 407, Gly 401 and Asp 386 in each subunit of the Kv potassium channel are the key residues for the toxin-channel recognition. Moreover, the simulation results demonstrated that the hydrophobic interactions are important in the interaction of negatively charge toxins with potassium channels. Docking results and MD simulations indicated that our three-dimensional model structure of the κ-Hefutoxin1-channel complex is reasonable and can be used as a guide for future biological studies such as the rational design of the blocking agents of the Kv1 channels.

References

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