

MEETING ABSTRACTS

DESIGN OF A COMBINED APTAMER FOR PARAOXON AND ACETYLCHOLINESTERASE BY IN SILICO APPROACH

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Poisoning by organophosphates (OPs) takes one of the leading places in the total number of exotoxicoses. Detoxication of OPs at the first stage of poisoning could be achieved with the help of aptamers, which are able to bind poisons in the bloodstream [1]. The effectiveness of the aptamers for OPs could be strengthened by their possibility to bind non-covalently with the peripheral anionic site (PAS) of acetylcholinesterase (AChE) defending the active site gorge from OPs molecules. In the present work, we have applied for the first time the *in silico* design of a combined aptamer for paraoxon and PAS of AChE. Based on the published sequence of an aptamer binding organophosphorus pesticides [2], its three-dimensional model was constructed. The most probable binding site for paraoxon was determined by molecular docking and molecular dynamics (MD) methods. Then the nucleotides of the binding site were mutated consequently and the values of free binding energy were calculated using MD trajectories and MM-PBSA approach [3]. On the basis of the energy values, the sequences that bind paraoxon most efficiently have been selected. Molecular docking of sixteen possible nucleotide pairs into PAS of AChE was performed and the pairs that bind with PAS most efficiently have been selected. The 5'-end of the aptamers for paraoxon was modified based on the results of molecular docking. The calculations have shown that the final aptamers interact with paraoxon and PAS of AChE more efficiently than AChE interacts with paraoxon.

Keywords: acetylcholinesterase; aptamer; molecular modeling; paraoxon

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References

1. Ku, T.H., Zhang, T., Luo, H., Yen, T.M., Chen, P.W., Han, Y., Lo, Y.H., 2015. Nucleic acid aptamers: an emerging tool for biotechnology and biomedical sensing. *Sensors (Basel)*. 15, 16281-16313.
2. Wang, L., Liu, X., Zhang, Q., Zhang, C., Liu, Y., Tu, K., Tu, J., 2012. Selection of DNA aptamers that bind to four organophosphorus pesticides. *Biotechnol. Lett.* 34, 869-874.
3. Kumari, R., Kumar, R., Open Source Drug Discovery Consortium, Lynn, A., 2014. g_mmpbsa - a GROMACS tool for high-throughput MM-PBSA calculations. *J. Chem. Inf. Model.* 54, 1951-1962.