UDC 577.112 DOI: 10.25808/08697698.2018.202.6S.015

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# Oligo-arginine peptides as a new class of ligands of nicotinic acetylcholine receptors

Many peptide ligands of nicotine acetylcholine receptors (nAChRs) contain in their sequences a large number of positively charged amino acid residues. Among the most famous are waglerins and azemiopsin from the snake venoms as well as various alpha-conotoxins from the venom of the marine *Conus* mollusks, such as conotoxins RgIA and GeXIVA which are considered as potential analgesics. The latter contain 4 and 9 arginine residues, respectively. Moreover, our experience with conotoxins has shown that in many cases the introduction of a positive charge into the structure of a naturally-occurring peptide can significantly improve its affinity for distinct nAChR subtype. In particular, the analogue of [D12K]SIA showed 2 orders of magnitude higher efficacy for the muscle-type nAChR compared to the native α-conotoxin SIA [1], and the introduction of Arg9 in the sequence of α-conotoxin PnIA significantly increased affinity for neuronal α7 receptor [2].

For better understanding of the properties of Arg-rich cholinergic peptides, we synthesized a series of oligo-arginines and studied their ability to interact with muscle-type *Torpedo californica* and neuronal alpha7 nAChRs in radiolig and assay, electrophysiology and $Ca^{2+}$-imaging experiments. A direct correlation between the length of oligo-Arg peptide and its cholinergic activity has been identified, the highest measured potency being 69 nM for the 16–membered peptide towards the *T. californica* receptor. Thus, the analysis of Arg-rich cholinergic peptides has promoted the discovery of the oligo-arginines reported here as a novel group of nAChR antagonists, which can be a basis for target work on the designing modified oligo-arginine peptides with increased affinity and selectivity towards distinct nAChRs.

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The work was supported by RFBR grant № 18-04-01366.