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ANALYTICAL CHEMISTRY IN RESEARCH ON NICOTINIC RECEPTOR INTERACTIONS WITH NEUROTOXIC PEPTIDES AND PROTEINS

Authors work is in the field of neurobiology and neurochemistry, close to the analytical chemistry, the topic of this conference. Their main targets are nicotinic acetylcholine receptors (nAChR). Invaluable instruments for nAChR research are snake venom, α-neurotoxins and in proteomic studies of venoms they recently found a new variant (αδ-bungarotoxin) of classical α-bungarotoxin which inhibits muscle-type and neuronal α7 nAChRs, but more reversibly. Another result of proteomics was covalently bound dimeric α-cobratoxin. Computer modelling, peptide synthesis, analytical chemistry and mass-spectrometry's allowed as to obtain α-conotoxin PnIA analogues which for the neuronal α7 nAChR had a 50-fold higher affinity than PnIA itself. Neurotoxic peptides and proteins interacting with nAChRs provide information about their binding sites necessary for drug design against neurodegenerative diseases, pain and inflammatory processes. For understanding physiological processes and drug design, of great importance are human proteins having the same three-finger folding as snake venom α-neurotoxins. Some of them, like Lynx1 and SLURP-1, are localized in the brain and in the immune system close to nAChRs and modulate their assembly and functioning. An illustration of matching the analytical chemistry with other modern approaches is our recent work with Australian researchers who prepared SLURP-1 (81 amino-acid residues, 5 disulfides) by total chemical synthesis. It had the same NMR structure as recombinant SLURP-1 (having an extra N-terminal Met residue), but by combination of radioligand analysis, calcium imaging and electrophysiology they demonstrated that this difference resulted in the selectivity shift from α7 to α9/α10 nAChR.

References

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BIOGRAPHY

Tsetlin V did his Ph D Degree in Chemistry (1973) at the Shemyakin-Ovchinnikov Institute; Head of the Department for molecular neuroimmune signaling; Professor (1996); Corresponding Member of the Russian Academy of Sciences (2006). He was honored with Russian State Prize in Science and Technology (1985) and the Humboldt Prize (1992). He is an Invited Scientist at Imperial College, London (1983-1984), Institute of Protein Research, Osaka (1992-1993), Free University of Berlin (1993-1994). He is the author of over 250 papers, including those in *PNAS, Neuron, Nature Str. Mol. Biol.,* Member of the *FEBS J* Advisory Board (2000-2011), *Biochem. J.* (2013 - present). His Citation Index is 4280 and Hirsh index 34.

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