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Neurotoxins: Enemies and/or friends and why protein engineering?

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A nimal venoms in snakes, spiders, scorpions and other dangerous creatures contain different peptide and protein neurotoxins which on biting cause pain, wounds and often the result is fatal. In this respect the neurotoxins are clearly enemies and the task is to find appropriate antidotes: Most often, it is the production of appropriate antibodies, the process not strictly being in frames of "protein engineering". However, each venom contain tens and hundreds of different neurotoxic peptides/proteins and due to huge number of species differing in the venom composition, in general the venoms are considered as naturally-occurring peptide/ protein libraries of compounds acting mostly on the central nervous system. Thus, it is possible to isolate those which act selectively on a particular enzyme, receptor or ion channel. To-day neurotoxins are invaluable tools in neurobiology and in this respect can be considered as Friends. Protein engineering (in the form of classical chemical modification) is used to identify in those peptides and proteins the functional residues and to prepare labeled derivatives for detecting the desirable receptor targets. Computer modeling of the respective interactions (based on the X-ray or NMR structures of those neurotoxins and their complexes) assists in choosing appropriate modifications in the primary structure and subsequent preparation of the novel peptides and desirable protein mutants by peptide synthesis and heterologous bacterial expression. The described scheme will be illustrated in the lecture by alpha-neurotoxins (proteins) from snake venoms and alpha-conotoxins (peptides) from poisonous *Conus* mollusks, both interacting with different subtypes of nicotinic acetylcholine receptors.

Biography

Victor Tsetlin has received his PhD in 1973, and since 1996 he is working as a Professor and as a corresponding Member of the Russian Academy of Sciences, Head of the Department since 2006. He was a Visiting Scientist at Imperial College, London in 1985 and Visiting Professor at Free University of Berlin in 1993-1995. He was a Member of ESN Council in 1999-2009, Member of the Advisory Board of the *EJB-FEBS* Journal in 2000-2011 and from 2013, Member of the Advisory Board at the *Biochemical Journal*. He is the author of over 250 publications in many journals; among them are *Journal of Neurochemistry*, *Journal of Biological Chemistry*, *Proceedings of National Academy of Sciences*, USA, *Nature Structural and Molecular Biology*, Trends in Pharmacological Science.

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