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Identification of critical elements determining toxins and insecticide affinity, ligand binding domains and channel properties

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Auteur	Tricoire-Leignel, Hélène [1], Thany, Steeve Hervé [2]
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Résumé en anglais	Insect nicotinic acetylcholine receptors have been objects of attention since the discovery of neonicotinoid insecticides. Mutagenesis studies have revealed that, although the detailed subunit composition of insect nicotinic acetylcholine receptors subtypes eludes us, the framework provided by mutagenesis analysis makes a picture of the subunits involved in the ligand binding and channel properties. In fact, many residues that line the channel or bind to the ligand seemed to be strongly conserved in particular in the N-terminal extracellular region and the second transmembrane domain which constitutes the ion-conducting pathway supporting the flux of ions as well as their discrimination. In fact, the positions are carried by loops B and C, respectively, which contain amino acids directly contributing to the acetylcholine binding site. Mutation ofthese residues accounts for insect resistance to neonicotinoid insecticides such as imidacloprid or a loss ofspecific binding. The discovery of the same mutation at homologous residues in different insect species or its conservation raises the intriguing question of whether a single mutation is essential to generate a resistance phenotype or whether some subunit confer insensitivity to ligand. Consequently, recent finding using information from Torpedo marmorata al subunit and soluble Aplysia californica and Lymnae stagnalis acetylcholine bindingproteins from crystallization suggest that insect nAChR subunits had contributing amino acids in the agonist site structure which participate to affinity and pharmacological properties of these receptors. These new range of data greatly facilitate the understanding of toxin-nAChR interactions and the neonicotinoid binding and selectivity.
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Liens

[1] http://okina.univ-angers.fr/h.tricoire/publications
[2] http://okina.univ-angers.fr/publications?f[author]=11297
[3] http://okina.univ-angers.fr/publications?f[keyword]=8588
[4] http://okina.univ-angers.fr/publications?f[keyword]=964
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