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The voltage-dependent sodium channel : A well-known molecular target of saxitoxins (cyanotoxins), ciguatoxins and brevetoxins (phycotoxins)

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Résumé

Because of its highly selectivity to Na ions, and activation and inactivation gating properties, the voltage-dependent sodium channel plays a fundamental role in generating and conducting action potentials. The channel alpha-subunit is a transmembrane protein composed of 4 domains (DI-DIV), each of them consisting in 6 segments (S1-S6). The segment S4 is responsible for the channel activation and the P loop, connecting S5 and S6, is involved in the channel selectivity. Receptor-sites for toxins have been identified on this alpha-subunit. Indeed, aquatic neurotoxins interacting specifically with this channel are widely distributed among the various organisms responsible for intoxications or envenomations. In particular, saxitoxins, gonyautoxins and derivatives, a family of divalent and tricyclic cations produced by some dinoflagellates and cyanobacteria and responsible for Paralytic Shellfish Poisoning, interact with the receptor-site 1 of sodium channels, leading to pore blockade and thus to current and action potential inhibition. This is exemplified by an electrophysiological study of oyster cerebro-visceral nerve sensitivity to saxitoxin which decreases during recent exposure of bivalve mollusks to contaminated dinoflagellates in natural and, in a more subtle way, experimental environments, providing better understanding of the mechanisms associated with the contamination of bivalve mollusks and, therefore, of the means of detecting and counterbalancing this contamination (1). Ciguatoxins and brevetoxins, two families of cyclic polyethers produced by some dinoflagellates and responsible for Ciguatera Fish Poisoning and Neurologic Shellfish Poisoning, respectively, interact with the receptor-site 5 of sodium channels, leading to partly blockade of inactivation and thus to spontaneous and/or repetitive action potentials. Consequently, toxin-induced cell swelling occurs. This is exemplified by electrophysiological and confocal-imaging studies of toxin effects on vertebrate myelinated nerve fibers (2,3). (1) Boullot *et al.*, *Mar. Drugs*, 2021, 19(7):380. (2) Mattei *et al.*, *J. Neurosci. Res.*, 1999, 55(6):666-673. (3) Mattei *et al.*, *Neuropharmacology*, 2014, 85:417-426.

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