# MOLECULAR MODELING OF PHONEUTRIA NIGRIVENTER NEUROTOXIN TX2-5, LOOKING FOR STRUCTURE-FUNCTION RELATIONSHIP

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The venom of the aggressive Brazilian solitary 'armed' spider *Phoneutria nigriventer* contains potent neurotoxins. Among them, a family of similar toxins (Tx2 type) cause excitatory symptoms such as salivation, lachrymation, priapism, convulsions, spastic paralysis and death. The toxin Tx2-5 has been sequenced by Cordeiro *et al.* in 1992, together with Tx2-1, Tx2-6 and Tx2-9, and acts on voltage-gated sodium channels. It is a 48 amino acid polypeptide, with 10 cysteine residues. Secondary structure predictions have been performed on the sequence using on-line servers (PHD, PsiPred, nnPredict) and three beta-strands were consensually predicted. The cysteine connectivity pattern has been deduced by sequence alignment with all cysteine-rich short spider toxins whose 3D structures have previously been experimentally determined, and present the so-called Inhibitory-Cysteine-Knot structural motif. Tx2-5 three-dimensional structure was predicted using homology molecular modeling method and Modeller-8v2 package. As all short spider toxins present the same overall fold, and because of their high sequence variability, the templates were chosen according to their cysteine pattern in the spider neurotoxin classification proposed by Kozlov *et al.* in 2005. To understand the mechanisms of action of Tx2-5 on sodium channel and address specific antibodies to inhibit it, we looked for regions of possible interactions with other proteins, using compared structure-function data on sodium channel blocker toxins from scorpions, anemones and cone snails.