The Genomic Structure of Conus textile α – Conotoxins

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The marine gastropods known as cone snails (Conus) are highly successful venomous predators (~500 species). The Conus venom (conotoxin or conopeptide) is a group of short, disulfide rich peptides (12 – 39 amino acids in length). Conotoxin genes have been cloned in an effort to understand the origins of toxin diversity. As the genomic structure of the toxins has been elucidated each Conus peptide gene has been found to encode a precursor that typically has an N-terminal signal sequence (~25 amino acids), an intervening ‘pro’ region (~20 - 40 amino acids, depending on the gene superfamily), and at the C-terminal end, the mature toxin in a single copy. Although the signal sequences are highly preserved, the toxin regions are hypermutated, accounting for the astonishingly wide array of conotoxins. In the genomic DNA, the three sections of the prepropeptide that exhibit apparently different mutation rates are separated by introns. The intron sequences are particularly of interest because it has been suggested that exons separated by introns may have the potential to evolve at very different mutation rates.

Previous research conducted in our lab shows that the open reading frames of signal sequences, proregion, and conotoxin sequences of C. textile –conotoxin are coded in two short exons separated by one relatively long intron. This experiment (1999) was conducted by employing the genomic walking method, and the intron sequence was found to be at least 65k base pairs of length. The first exon contained a part of the 5’ UTR sequence, the signal sequence and the first 16 base pairs of the proregion; the second exon had the last 17 base pairs of the "pro" region, the mature toxin sequence, and the 3’ UTR sequence.

The –conotoxin gene from C. textile was analyzed by PCR and gene cloning methods. Primers from the 5’ end were designed by using the C. geographus –conotoxin gene signal sequence, and primers from the other end were synthesized according to the C. geographus –conotoxin 3’-UTR sequence. The initial gel electrophoresis indicated that the PCR amplification resulted in three prominent fragments (the lengths were approximately 1.7 kbp, 3 kbp, and >6 kbp) and the smallest DNA fragment out of the three was cloned and sequenced.

This C. textile –conotoxin sequence structure was found to support the previous