IDENTIFICATION OF A PUTATIVE MULTIFUNCTIONAL NONRIBOSOMAL PEPTIDE SYNTHETASE GENE OF Xylaria sp. BCC 1067 WITH UNUSUAL MOTIF OF A CONDENSATION DOMAIN

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Many pharmacologically important peptides are synthesized nonribosomally by multimodular nonribosomal peptide synthetase (NRPSs). These enzyme templates consist of iterated modules that, in their number and organization, determine the primary structure of the corresponding peptide products. These and other multifunctional enzyme complexes, such as polyketide synthases (PKS), are of interest due to their used in unnatural-product or combinatorial biosynthesis. Among the fungi, the genus Xylaria has been reported to produce a large amount of metabolites which have cytotoxic, phytotoxic or antibiotic properties. This report, a gene encoding a putative nonribosomal peptide synthetase of the wood-decayed fungus, Xylaria sp. BCC 1067 has been cloned and partially sequenced. To achieve this, a pair of degenerated oligonucleotide primers, derived from YTSG(ST)TG and NxYGPE core sequences of adenyllylation domain of known NRPS, were used in PCR reaction with genomic DNA from Xylaria sp. BCC 1067. Sequence alignment of PCR product confirmed the putative NRPS gene in Xylaria sp. BCC 1067. This product was used as a probe in the subsequent screening of the genomic λ-FIX II library to identify the remaining part of NRPS gene. Using this method, a 7.8 kb chromosomal DNA fragment bearing a part of the putative NRPS gene was cloned and partial sequenced, revealing two complete internal NRPS modules and a part of the third and fourth modules. In the similarity search, one module reveals a condensation domain that lacks a most highly conserved core sequence (HMMxISDG(WS)S), which are normally found in NRPS of other organisms. The complete sequence of this gene will be used to study the structure and function relationship of this enzyme, with the goal to construct a diverse nonribosomal peptide library in search for novel biologically active compounds.