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Insights into richness of PKS and NRPS gene clusters and genome guided bioprospection for bioactive natural products

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Abstract

Advent of next-generation sequencing and genome-mining tools witnessed a rejuvenation of research on Actinobacteria to meet the growing drug-resistance of pathogenic microbes. Therefore, the Actinobacteria present in underexplored environments are being largely studied in recent days. Intertidal areas, which endure regular periods of immersion and emersion, are important in the coastal or estuarine environment and represent an underexplored biological niche that could be of interest for the discovery. In this study, we have evaluated biosynthetic heterogeneity and richness of intertidal Actinobacteria isolated from Diu Island (India) and demonstrated genome mining in selected potential strain to facilitate the discovery of novel bioactive compounds relevant to antibiotics development. A total of 62 strains affiliated with seven different genera, Streptomyces, Micromonospora, Saccharomonospora, Nocardia, Nocardiopsis, Actinomadura, and Glycomyces were studied. The amplified fragment restriction fingerprinting was done by targeting specific domains of polyketide synthase type II (PKS-II) and non-ribosomal peptide synthetase (NRPS) to reveal the biosynthetic potential and functional heterogeneity of Actinobacteria. The restriction profiles were scored as binary data and visualized in UPGMA dendrograms. Notably, strains affiliated with Streptomyces and Nocardiopsis showed relatively high biosynthetic richness and heterogeneity among the actinobacterial strains. Indeed, those that had a close relation in the 16S rRNA gene-based phylogeny also showed significant heterogeneity, which suggested a quite diverse biosynthetic potential even among closely related isolates. Sequence analysis of randomly selected PKS-II and NRPS fragments revealed their relative similarity to naphthoquinone and anthracycline group compound producing strains. Based on the phylogenetic novelty and biosynthetic richness, three streptomycete strains, JJ36, JJ38, and JJ66 were selected, and their genomes were sequenced using Illumina platform. Resulted draft genome sizes were 6.45, 5.89 and 4.83 Mb, respectively. Genome mining of the assembled draft genomes for secondary metabolite biosynthetic gene clusters relevant to bioactive compounds production was performed using antiSMASH. Interestingly, results revealed the presence of a total 183 secondary metabolite biosynthetic gene clusters including 109 putative gene clusters in the three genomes. This genomic data was further mapped with secondary metabolites profile of particular strains and resulted in the identification of novel compounds affiliated with aromatic ketones.

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