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海綿メタゲノムライブラリー由来の新規化合物探索

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[Objective] Marine sponges have been prolific sources of novel and structurally diverse natural products. Recent evidences implicated that marine sponges harbor large numbers of diverse symbiotic bacteria, which are likely the true producers of numerous sponge-derived natural products. Therefore, the bacteria associated with marine sponges would constitute important sources of biologically active compounds. However, since cultivable bacteria represent a very small portion of the total sponge-associated bacteria, the vast majority of them remain uncultured under conventional culture conditions. Metagenomic approaches based on direct construction of DNA library from environmental samples have been proven to be powerful tools for exploiting the new bioactive metabolites from the uncultivable bacteria. Thus, we undertook the project to search for novel metabolites from the Japanese marine sponge *Discodermia calyx* metagenomic library expressed in *Escherichia coli*.

[Methods] The *D. calyx* metagenomic library (~40 kbp insert DNA, 2.5×10^5 cfu) was constructed according to the CopyControl Fosmid Library Production Kit. We searched for the positive clone based on function-based screening. Active compounds were separated and purified by Diaion HP20 resin, RP-18, Sephadex LH-20 and ODS-HPLC. Their structures were elucidated by comprehensive spectroscopic analysis.

[Results] Two positive clones were discovered from the metagenomic library. Six porphyrins including two novel derivatives were isolated and identified.

[Discussion] Two active clones were detected and clone specific metabolites induced by each clone were obtained. These results implied that the metagenomic fosmid library derived from marine sponges might be promising source for further mining new antibacterial compounds, gene and enzymes.