Dereplication of antitumor compounds produced by marine microorganisms in a drug discovery process

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ABSTRACT

Motivation:

Despite the fact that the oceans cover more than 70% of the Earth's surface and that the marine environment contains unlimited biodiversity, including many unique microorganisms, marine-derived microbial natural products remain largely unexplored. Taking advantage of this gap the biopharmaceutical company, Pharmamar, has developed an anticancer drug discovery platform with the objective of identifing novel compounds that are synthesized by marine macro and microorganisms. In this way Pharmamar finds new drug options that open the door to innovative ways to tackle cancer.

The early detection of known bioactive compounds, which can be labourious, appears to be a critical step in the process. However, advances in the development of new chemical analysis techniques, coupled with database evaluations, can serve as tools for rapid detection of known compounds requiring only small quantities of sample and/or minimal efforts in sample preparation.

Methods:

In our study, we started with 39 samples from marine depths collected by the Geological and Mining Institute expedition. After the microbiological isolation, the finger printing´s rep-PCR and the RNA16s taxonomic identification at the species level of each strain, a total of 1962 different strains were isolated. Subsequently, we proceeded with the Screening Fermentation and the cytotoxic evaluation in order to identify and keep those strains that exhibited antitumor activity and to discard those lacking in activity.

Only 14 strains were selected from the total of those which demonstrated cytotoxic activity (approximately 20%). Later, these strains were evaluated in vitro and analysed by Retest-HPLC/MS, which enables the revalidation of the cytotoxic activity and guarantees that the activity is not due to any chemical compound contained in the database elaborated by PharmaMar.

Results and conclusions:

Two different groups of strains are determined by the results obtained in this study. Firstly, we find the strains which produce secondary metabolites with antitumor activity, but they are already contained in the database. Secondly, we find those bioactive-producing strains. Only three strains of the total analysed were suitable for being considered as new candidates for the next step in the process.

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