Journal Club No.651 February 25, 2014

Construction of a natural product library

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Natural products consisting of unique structures occupy a wider chemical space than synthetic compounds, and this observation holds true for clinical drugs as well. Natural products are biosynthesized by several enzymes, and they preferentially bind to the drug-binding pockets of proteins. Therefore, natural products are considered good sources of lead compounds for drug screening. They constructed a natural product library (CB library) to screen for bioactive agents targeting cancer, microbial diseases, viruses, immune disorders and so on. To construct the CB library, they isolated actinomycetes fromdiverse environmental substrates, including marine sponges, tunicates, lichens,marine sediments and mangrove soils in addition to the conventionally utilized terrestrial soils, and screened their culture extracts. Furthermore, they collected purified compounds from actinomycete cultures that enabled us to perform drug-screening assays at a variety of drug concentrations to minimize false-positive results. The large natural product library constructed consisted of >300 000 samples, including approximately 5500 purified natural compounds.

紹介論文

J. Antibiot. **2012** 65, 443–447

Construction of a natural product library containing secondary metabolites produced by actinomycetes

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To construct a natural product library for drug screening, we isolated secondary metabolites from a wide variety of actinomycetes cultured from marine sponges. The results suggested that marine sponges are a promising source of actinomycetes with the potential to produce new metabolites. Furthermore, we evaluated the chemical space occupied by our natural product library (CB library) by multidimensional principal component analysis and compared it with a commercially available compound library (ZINC library), which was randomly selected from the ZINC library (approximately 30 000 000 compounds). The CB library occupied a wider chemical space than the ZINC library. Bioactive compounds in the CB library possessed a wide chemical space that was not covered by ZINC library. These results indicate that the CB library mainly comprises secondary metabolites from actinomycetes, and it has great potential as a source of compounds for drug screening.

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