

天然化合物探索に向けたフラクションライブラリーの構築

野川俊彦

微生物や植物などの天然資源から得られる天然化合物群は多様な構造や活性から医薬品開発などに重要な化合物群である。しかし、最近では新規骨格を有する化合物の発見は困難になってきている。また、探索過程での活性評価において、近年のハイスループットスクリーニングへの複雑な混合物である抽出物の適用には多くの問題がある。このような背景から抽出物の粗分画物（フラクション）を用いた化合物探索が一部で試みられている。当研究室でも微生物より有用二次代謝産物を探索するための一つの方法としてフラクションライブラリーを用いている。今回紹介する論文は NCI による大規模フラクションライブラリーの構築とその有用性について検証したものである。

紹介論文

NCI Program for Natural Product Discovery: A Publicly-Accessible Library of Natural Product Fractions for High-Throughput Screening.

Christopher C. Thornburg,¹ and Barry R. O'Keefe*^{2,3} (¹Natural Products Support Group, Leidos Biomedical Research, Inc. Frederic National Laboratory for Cancer Research sponsored by the NCI, ^{2,3}NCI) *ACS chemical biology* **13**, 2484-2497 (2018)

要旨

The US National Cancer Institute's (NCI) Natural Product Repository is one of the world's largest, most diverse collections of natural products containing over 230,000 unique extracts derived from plant, marine, and microbial organisms that have been collected from biodiverse regions throughout the world. Importantly, this national resource is available to the research community for the screening of extracts and the isolation of bioactive natural products. However, despite the success of natural products in drug discovery, compatibility issues that make extracts challenging for liquid handling systems, extended timelines that complicate natural product-based drug discovery efforts and the presence of pan-assay interfering compounds have reduced enthusiasm for the high-throughput screening (HTS) of crude natural product extract libraries in targeted assay systems. To address these limitations, the NCI Program for Natural Product Discovery (NPNPD), a newly launched, national program to advance natural product discovery technologies and facilitate the discovery of structurally defined, validated lead molecules ready for translation will create a prefractionated library from over 125,000 natural product extracts with the aim of producing a publicly-accessible, HTS-amenable library of >1,000,000 fractions. This library, representing perhaps the largest accumulation of natural-product based fractions in the world, will be made available free of charge in 384-well plates for screening against all disease states in an effort to reinvigorate natural product-based drug discovery.