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CHUNG LIANG LIM

NMR Metabolic Fingerprinting Revealed Unique NP Metabolomes

The NMR spectrum of a mixture of small molecules is a fingerprint of all of its components. In this study, an NMR fingerprint method was revealed, which takes advantage of the fact that fractions contain simplified NMR profiles, with minimal signal overlap to allow the identification of unique spectral patterns. The approach is exemplified in the identification of a novel natural product, iotrochotazine A (**1**), which is sourced from an Australian marine sponge *Iotrochota* sp. Compound **1** was used as a chemical probe in a phenotypic assay panel based on human olfactory neurosphere-derived cells (hONS) from idiopathic Parkinson's disease patients. At concentration of 1 μm, compound **1** was not cytotoxic but specifically affected the morphology and cellular distribution of lysosomes and early endosomes. Thus, this study has shown the promise of this novel compound as a useful tool in the investigation of molecular mechanisms underlying Parkinson's disease.

紹介論文

Angew. Chem. Int. Ed., **2014**, 53, 6070-6074
NMR Fingerprints of the Drug-like Natural-Product Space Identify Iotrochotazine A: A Chemical Probe to Study Parkinson's Disease
Tanja Grkovic, Rebecca H. Pouwer, Marie-Laure Vial, Luca Gambini, Alba Noel, John N. A. Hopper, Stephen A. Wood, George D. Mellick, and Ronald J. Quinn

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Natural products having gone through million years of evolutionary optimization could be thought as starting points for exploration of target interactions. These natural sources have been and will continue to be a significant source of novel drugs and drug leads. Previously, the authors have reported a strategy for preparing a library of drug-like natural products. Recently, they have generated lead-like enhanced (LLE) extracts and fractions with a method allowing for retention of lead and drug-like components by selection of favourable physicochemical properties. With the main focus on the fraction rather than crude extracts, they were able to identify unique spectral patterns of the small molecules present, leading to the isolation of novel natural products. Iotrochotazine A had specific effects on the early endosome and lysosome markers in a screening test for biological function using a cell model of Parkinson's disease. In this study, the authors have developed a novel method for isolation and identification of novel, drug-like natural products through NMR-guided metabolic fingerprinting. This finding has demonstrated a novel and promising strategy for discovery of new metabolites from natural resources.