

**【Grant-in-Aid for Scientific Research (S)】**  
**Science and Engineering (Engineering)**



**Title of Project : Development of platform for ultra high-throughput screening of novel bioactive compound producers**

Haruko Takeyama  
(Waseda University, Faculty of Science and Engineering, Professor)

Research Project Number : 17H06158 Researcher Number : 60262234

Research Area : Biofunction, Bioprocess

Keyword : Raman spectrometry, Database, Bioactive compound, Single-cell analysis, Microbe

**【Purpose and Background of the Research】**

The studies for screening of lead compounds (bioactive compounds) from microbes have a long history. So far, over 20000 kinds of bioactive compounds have been discovered from environmental microbes. If we can identify the potential producers and obtain the biosynthetic gene clusters for the production of bioactive compounds, we can achieve to acquiring the lead compounds and apply them for production of new drugs. To achieve this, we need a new platform for ultra-high-throughput screening of bioactive compound producers from various microbes and obtaining biosynthetic gene sequences from uncultivable strains.

**【Research Methods】**

In this study, we aimed to construct the Raman spectrum database of microbial secondary metabolite from libraries of microbes isolated from soil and the ocean. The Raman spectroscopy can reveal the molecular structure of target molecule non-invasively, so that cells producing metabolites can be identified at the single-cell level. Furthermore, in order to screen bioactive compound producers from environmental microbes, we will acquire Raman spectrum of single cells based on microfluidic platform. For uncultivable microbes, we will also obtain genome information from single cells. For this purpose, we will improve high throughput cell-handling technology using microfluidic device and informatics analysis method for analyze their genomic features. We will proceed with the functional analysis of the obtained novel bioactive compound gene clusters and establish this technique as world leading reading technology in the field of drug discovery lead compound screening (Fig. 1).

**【Expected Research Achievements and Scientific Significance】**

The *in vivo* Raman signal database which constructed in this research is expected to be useful tool in various research fields including

drug discovery and industrial production of biochemical compounds. In addition, the single-cell genomics platform will make effective use of unused resources such as uncultivable microbes. This ultra-high-throughput screening platform would be a fundamental technology indispensable for exploring lead compounds in future drug discovery research and its applications.

**【Publications Relevant to the Project】**

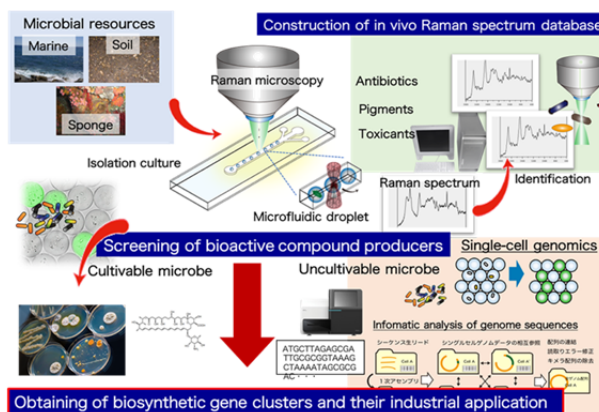


Fig. 1 Platform for screening of bioactive compound producers

- Miyaoka R, et al. 2014. In situ detection of antibiotics Amphotericin B produced in *Streptomyces nodosus* using Raman microspectroscopy. *Marine Drugs*. 12(5), 2827-2839
- Wilson MC, et al. 2014. An environmental bacterial taxon with a large and distinct metabolic repertoire. *Nature* 12959. 506(7486):58-62

**【Term of Project】** FY2017-2021

**【Budget Allocation】** 157,700 Thousand Yen

**【Homepage Address and Other Contact Information】**

<http://www.f.waseda.jp/haruko-takeyama/>  
haruko-takeyama@waseda.jp