



Title of Project : Biosynthetic machinery: Deciphering and regulating the system for creating structural diversity of bioactive metabolites

Term of Project : FY2010-2014

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【Purpose of the Research Project】

Recent progress in genomic DNA sequencing technology has provided rapid access to the biosynthetic genes of the bioactive secondary metabolites found in plants and microorganisms. In contrast to conventional organic synthesis, we propose an alternative method for synthesizing bioactive compounds using biosynthetic enzymes.

【Content of the Research Project】

For this purpose, we develop a methodology to rationally decipher the substrate structure and biosynthetic pathway from genomic data based on chemical structures and bioinformatics on natural product biosynthesis. Along with elucidation of individual enzymatic reaction steps, we explore the methodology for reconstitution of the biosynthetic machinery consisting of representative skeletal construction enzymes and widespread modification enzymes using existing and newly developed methods for introducing multiple biosynthetic genes to synthesize bioactive natural products. In addition, we also explore the intriguing diversification of natural

products with regard to molecular evolution by engineering of the biosynthetic machinery.

【Expected Research Achievements】

If we succeed to develop a versatile methodology for reconstruction of artificial biosynthetic gene clusters and for elucidating mechanisms on diversification of the secondary metabolites, this will provide novel way to synthesizing molecule having novel functions. Thus, we can create useful drugs for antibiotic-resistant bacteria, novel antitumor agents, and highly functionalized compounds.

Currently, more than 200,000 metabolites from microorganisms and plants are isolated and characterized. However, actual functions of these metabolites have not been known. When we succeed to correlate the structures and information on the biosynthetic machinery in near future, we can answer the fundamental question why and what purpose nature creates such diverse secondary metabolites with regard to molecular evolution and biological evolution.

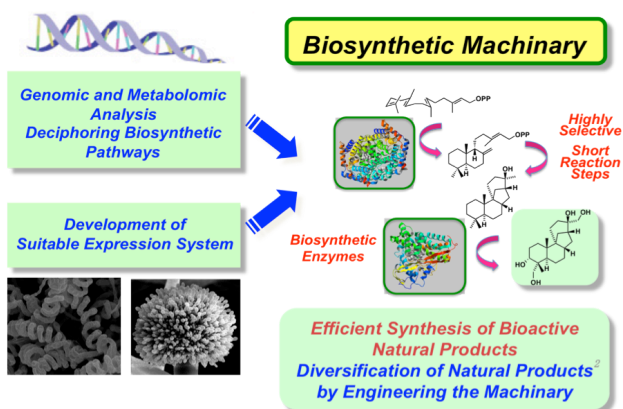


Figure 1 Outline of the Project

【Key Words】

metabolite production
secondary metabolites
antibiotics
antitumor agents
biosynthesis
chemoenzymatic synthesis
bioinformatics
metabolome
genome

【Homepage Address】

<http://kanaya.naist.jp/machinery/index.html>

