Engineering of Natural Products Biosynthesis

Ikuro Abe (Sch. Pharm. Sci., Univ. Shizuoka, and PRESTO, JST)

The main focus of my research has been to understand the mechanism of the biosynthesis of a wide variety of naturally occurring substances. A multidisciplinary approach involving synthesis, enzymology, molecular biology, and structural biology has been employed to address fundamental problems at the interface of chemistry and biology. Manipulation of key enzymes involved in the biosynthesis of the basic scaffolds of pharmaceutically important secondary metabolites (e.g. polyketides and isoprenoids) thus leads to production of biologically active, supra-natural products with remarkable structural diversity. In this lecture, I will briefly overview the recent progress of our research on structure-function analysis of squalene cyclizing enzymes and plant type III polyketide synthases, which includes (1) structure-based rational design of "supra-natural" enzymes with altered substrate and product specificities, and (2) exploration of catalytic potential of the enzymes by using synthetic substrate analogs.