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In my school days, I was fascinated by medicinal natural products such as morphine and penicillin, and ever since I joined the research group of Profs. Ushio Sankawa and Yutaka Ebizuka of the University of Tokyo 35 years ago, I've been working on biosynthetic studies on natural products. Why do organisms produce such diverse secondary metabolites? How does nature create such complex and unique molecules? My dream was to solve the mystery of these biosynthetic machineries and exploit it for further production of pharmaceutically important molecules.

Recent advances in synthetic biology are quite remarkable. When I was a student, I worked on tracer experiments using isotopically labeled precursors to elucidate the biosynthetic pathway, and then purification and characterization of the biosynthetic enzymes catalyzing each chemical reaction. Therefore, until we finally reached the blueprint of the genes encoding the compounds, there was a further considerably long way to go. In contrast, nowadays, genome sequences of many organisms are readily available in the data base, and it became routine to obtain whole draft genome sequence of organisms of your interest. Together with the development of bioinformatics, genome mining has now become directly linked to the search for novel molecules. Further, by engineering the biosynthetic machineries, we can now even design and create artificial biosynthetic pathways.

Nature produces complex secondary metabolites through surprisingly simple and efficient way. First, constructs basic core skeletons from a limited number of simple building blocks derived from primary metabolism, which is followed by various modification reactions. On the other hand, enzymes involved in the biosynthesis often exhibit remarkably broad substrate tolerance and catalytic potential, which is one of the major factors for generating molecular diversity of natural products. Therefore, I believe that research on the biosynthetic enzymes will contribute to future drug discovery, and have been working on the development of a rational methodology, for example, for creation of supranatural type novel molecules by expanding catalytic repertoires of the enzymes. In this presentation, I will introduce our next-generation natural products chemistry research, which aims rational design of biosynthetic machineries.