Self-Assembling Molecular Systems Based on Coordination Chemistry

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Education
1980 B.S. Chiba University
1982 M.S. Chiba University
1987 Ph.D. Tokyo Institute of Technology

Professional Employment
1982 Researcher, Sagami Chemical Research Center
1988 Assistant Professor to Associate Professor, Chiba University
1997 Associate Professor, Institute for Molecular Science
1999 Professor, Nagoya University
2002 Professor, The University of Tokyo
2018 Distinguished Professor, Institute for Molecular Science
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Awards
1994 Progress Award in Synthetic Organic Chemistry, Japan
2000 Division Award of Chemical Society of Japan (Organic Chemistry)
2001 Tokyo Techno Forum 21 Gold Medal
2001 Japan IBM Award
2003 Nagoya Silver Medal
2004 Izatt-Christensen Award
2006 G. W. Wheland Award (Chicago University Lectureship Award)
2010 The Reona Esaki Award
2010 The JSCC Award
2011 3M Lectureship Award (University of British Columbia)
2012 Thomson Reuters Research Front Award 2012
2013 The Chemical Society of Japan (CSJ) Award
2013 Arthur C. Cope Scholar Award (ACS National Award)
2013 Merck-Karl Pfister Visiting Professorship (MIT Lectureship Award)
2014 ISNSCE 2014 Nanoprize
2014 Medal with Purple Ribbon
2014 Fred Basolo Medal (Northwestern University)
2018 Wolf Prize in Chemistry
2019 The Imperial Prize and the Japan Academy Prize
2020 The 73rd Chunichi Cultural Award
2020 Clarivate Citation Laureates (Chemistry)
2020 "Major Results" of Nanotechnology Platform, MEXT
2022 Le Grand Prix 2022 de la Fondation de la Maison de la Chimie
2023 Asahi Prize2023
2023 2022 Natta Award (Politecnico di Milano)
2024 Van't Hoff Award

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We are developing new self-assembled molecular systems using coordination chemistry and researching the application of the developed molecular systems. One representative application of the molecular system developed by us is the crystalline sponge (CS) method, which enables the rapid structure elucidation of small molecules. In this method, a porous crystal of a coordination network called CS, which was developed by us and can accommodate various kinds of small molecules, is used. Notably, we can know structures of the small molecules accommodated in the pore of the CS by X-ray crystallography, because the accommodated small molecules periodically aligned in the CS. The CS method has some advantages; i) only nanogram to microgram scale of analytes is required, ii) the absolute stereochemistry can be determined, iii) even oily substances can be analyzed by X-ray crystallography. Because of these fascinating features, the CS method attracts the interests of many people not only in academia but also in industry.

Selected Publications

- Y. Inokuma, S. Yoshioka, J. Ariyoshi, T. Arai, Y. Hitora, K. Takada, S. Matsunaga, K. Rissanen and M. Fujita, "X-Ray Analysis on the Nanogram to Microgram Scale Using Porous Complexes," *Nature* **495**, 461–466 (2013).
- D. Fujita, Y. Ueda, S. Sato, N. Mizuno, T. Kumasaka and M. Fujita, "Self-Assembly of Tetravalent Goldberg Polyhedra from 144 Small Components," *Nature* **540**, 563–566 (2016).

We now apply the CS method in the biological studies, especially studies on the natural product biosynthesis. Scientists in this field often obtain small molecules as products of natural product biosynthetic enzymes. However, it is often difficult to elucidate the complex structures of the enzyme products. We thus consider that the CS method, which enables the rapid structure elucidation of small molecules, is helpful, and can accelerate the studies in this field.

1. Analysis of a Terpene Synthase from a Giant Virus[1–3)]

Giant viruses are unique existence. The size of giant viruses is as large as that of bacteria, whereas normal viruses are much smaller than bacteria. Because of the unique feature of the giant viruses, many researches on the giant viruses have been reported. However, it was unknown whether the giant viruses were producers of natural products or not.

We thus investigated whether the giant viruses have the natural product biosynthetic enzymes, and noticed that a gene coding a protein relatively similar to a terpene synthase exists in the genome of a giant virus Orpheovirus IHUMI-LCC2. The terpene synthase is a kind of natural product biosynthetic enzymes, and responsible for the biosynthesis of the terpenoids, one of the largest groups of the natural products.

We named the terpene synthase from Orpheovirus IHUMI-LCC2 as OILTS (Orpheovirus IHUMI-LCC2 terpene synthase), and analyze it. As a result, we revealed that OILTS can work as the terpene synthase, and found an interesting feature of OILTS (Figure 1). Terpene synthases normally require Mg^{2+} as metal cofactor, and OILTS also requires Mg^{2+} to produce an enzyme product **1**. However, when the metal cofactor was changed to Mn^{2+}, Co^{2+}, or Ni^{2+}, the profile of the enzyme products was changed, and not only **1** but also **2** was produced. In addition, we found that **1** was relatively unstable and easily converted to four degradation products (**3**–**6**) in weakly acidic condition. Notably, the structures of **1**–**6** were successfully analyzed by the CS method.

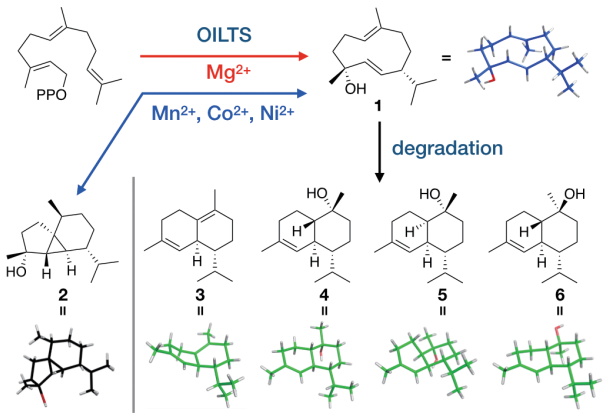

Figure 1. Reactions catalyzed by OILTS, a terpene synthase from a giant virus. Three dimensional structures of **1**–**6** were obtained by the CS method analysis.

We also performed the phylogenetic analysis, comparing terpene synthases from giant viruses and other organisms (Figure 2A). The terpene synthases from giant viruses are revealed to be phylogenetically separated from other terpene synthases. This result suggests the unique evolution of the terpene synthases from the giant viruses.

In addition, we solved the structure of OILTS by protein X-ray crystallography (Figure 2B). Whereas the structure of OILTS was similar to the structures of bacterial terpene synthases, OILTS was a little smaller than other terpene synthases whose structures have been known.

In summary, we reported the first functional analysis of the terpene synthase from the giant virus. We would like to analyze more enzymes from giant viruses in future, to more deeply understand the natural product biosynthesis in the giant viruses. In addition, the CS method could solve the structures of the enzyme products (**1** and **2**) and the degradation products (**3**–**6**) obtained in this study, showing the potential of the CS method to facilitate the studies in the field of natural product chemistry.

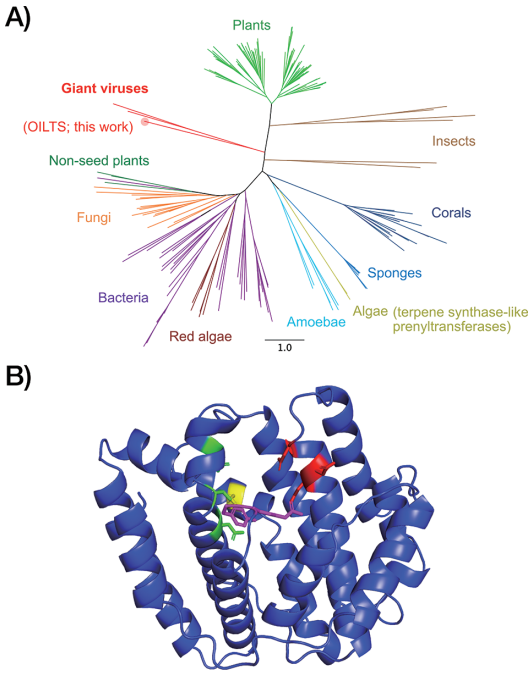

Figure 2. A) Phylogenetic analysis of the terpene synthases from giant viruses and other organisms. The figure is reprinted with permission from ref. 1). Copyright 2023 American Chemical Society. B) Structure of OILTS solved by protein X-ray crystallography.

References

1) Y. Jung, T. Mitsuhashi, S. Sato, M. Senda, T. Senda and M. Fujita, *J. Am. Chem. Soc.* **145**, 25966–25970 (2023).
2) Y. Jung, T. Mitsuhashi, T. Kikuchi and M. Fujita, *Chem. –Eur. J.* **30**, e202304317 (2024).
3) Y. Jung, T. Mitsuhashi, K. Kageyama, T. Kikuchi, S. Sato and M. Fujita, *Chem. –Eur. J.* **39**, e202400512 (2024).