

【Grant-in-Aid for Scientific Research (S)】

Biological Sciences (Agricultural Sciences)



Title of Project : Studies on mechanisms of biosynthesis of biomolecules via amino-group carrier protein and expansion of structural diversity of secondary metabolites

Makoto Nishiyama

(The University of Tokyo, Biotechnology Research Center, Professor)

Research Project Number : 17H06168 Researcher Number : 00208240

Research Area : Applied Microbiology, Applied Biochemistry

Keyword : Microbial Metabolism, Enzyme Chemistry

【Purpose and Background of the Research】

Carrier proteins that bind a carboxyl group of a substrate are known in biosynthesis of fatty acids and polyketides. We found a novel-type carrier protein, amino-group carrier protein (AmCP), which binds the amino group of a substrate, in lysine and arginine biosynthesis of thermophiles. We also showed involvement of AmCP in secondary metabolisms of *Streptomyces*. These observations suggest that metabolic system using AmCP plays crucial roles in cellular processes.

In this study, we will determine the crystal structures of lysine/arginine biosynthetic enzymes, and analyze secondary metabolite biosynthesis using AmCP in *Streptomyces*. Through a series of the studies, mechanisms to create structural diversities of chemical compounds, which will expand chemical library, will be elucidated.

【Research Methods】

We will analyze functions of AmCP-mediated systems in lysine/arginine biosynthesis and secondary metabolisms at molecular and atomic levels. Structural biology is mainly conducted for enzymes for lysine and arginine biosynthesis from thermophiles, which will reveal mechanisms by which enzymes had acquired high substrate specificity. Especially, enzyme-AmCP complexes

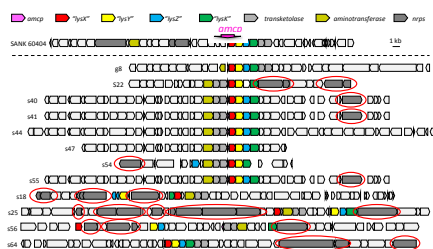


Fig. 1. *amcp*-containing clusters for secondary metabolite biosynthesis. Red ovals show *nps* genes.

are main targets of this analysis. Because most reactions in secondary metabolisms are unknown, we will analyze and unveil them by forefront

technologies. This analysis will be conducted especially for enzymes that are involved in novel reactions and/or novel chemical architecture formation

【Expected Research Achievements and Scientific Significance】

We discovered that AmCP is utilized in both primary and secondary metabolisms. These discoveries with high originality are highly evaluated in the related fields. This study analyzes enzymes that use AmCP globally at atomic levels, and determines chemical structures of their products. Our study that may discover unprecedented chemistry generated by unknown enzymes is highly creative and pioneering, leading to generation of new research fields, and therefore will contribute to keeping our international initiative in the fields. We will analyze biosynthesis of useful biomolecules, and, therefore, will provide valuable information as applied science.

【Publications Relevant to the Project】

T. Ouchi, T. Tomita, A. Horie, A. Yoshida, T. Kuzuyama, M. Nishiyama et al. (2013) Lysine and arginine biosyntheses mediated by a common carrier protein in *Sulfolobus*. *Nat Chem Biol*, **9**, 277-283.

F. Hasebe, K. Matsuda, T. Shiraishi, T. Tomita, T. Kuzuyama, M. Nishiyama et al. (2016) Amino group carrier protein-mediated secondary metabolite biosynthesis in *Streptomyces*. *Nat Chem Biol*, **12**, 967-972.

【Term of Project】 FY2017-2021

【Budget Allocation】 160,700 Thousand Yen

【Homepage Address and Other Contact Information】

<http://park.itc.u-tokyo.ac.jp/biotec-res-ctr/saibo/ukinou/>