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

Biological Sciences (Agricultural sciences)

Title of Project: Elucidation of mechanisms of biomaterial conversion mediated by amino group-modifying carrier protein and application

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Research Area : Applied Microbiology, Applied Biochemistry
Keyword : Microbial Metabolism, Enzyme Chemistry

【Purpose and Background of the Research】

Carrier proteins bound to carboxyl group are often found in biosynthesis of fatty acids and polyketides for efficient reaction; however, a carrier protein bound to amino group had not been found. We found a novel amino group=bound carrier protein, LysW, in lysine biosynthesis of thermophile. We are also finding the presence of LysW homologs that are involved in the secondary metabolism in *Streptomyces* as well as biosynthesis of amino acid other than lysine. These observations suggest that enzymatic systems using LysW-related carrier proteins play crucial roles in cellular bioconversions.

In this research, using available forefront technologies in structural biology, genetics, natural chemistry, bioinformatics, and so on, we will analyze the primary and secondary metabolisms in which LysW homologs are involved and will try to elucidate recognition of LysW by metabolic enzymes, whole metabolic systems containing LysW homologs, and their regulation. We also try to establish basis for production of useful materials, based on the accumulated information.

【Research Methods】

Most interesting points in this study are how LysW is recognized by enzymes in lysine biosynthesis and how enzymes of lysine and their counterpart of arginine discriminate substrates; however, these remain unsolved. In this research, we will elucidate at molecular and atomic levels how LysW homologs are incorporated into amino acid biosynthetic machineries to contribute to the primary metabolisms, by using techniques including structural biology.

Recently we also find that homologs of LysW and related enzymes are involved in the secondary metabolite biosynthesis in *Streptomyces*. We will analyze the LysW homologs and elucidate what are synthesized by the system. From these studies, we can figure out the biological systems in which amino group-modifying LysW functions. Furthermore, we will try to apply the basic knowledge on recognition mechanisms of LysW homolog and their derivatives at molecular and atomic levels to production of useful materials such as amino acid and secondary metabolites.

【Expected Research Achievements and Scientific Significance】

LysW is unique in that it is served not only as a protecting group, but also as a carrier protein for biosynthetic intermediates. Our research with high originality is expected to produce new basic finding. In addition, because LysW homologs are suggested to be involved in arginine biosynthesis and secondary metabolite production, research on biosynthetic systems containing LysW homologs will be assessed to provide unprecedented biosynthetic system and explore new research area. We had discovered LysW-mediated biosynthesis, and our activity is leading in the field. Promotion of the activity will assure our research of the international initiative. This study will have a ripple effect on both basic science and application, because amino acids and biologically active substance are applicable materials.

【Publications Relevant to the Project】

・T. Okada, T. Tomita, A.P. Wulandari, T. Kuzuyama, and M. Nishiyama. Mechanism of substrate recognition and insight into feedback inhibition of homocitrate synthase from *Thermus thermophilus*. ***J Biol Chem***, **285,** 4195-4205 (2010)

・A. Horie, T. Tomita, A. Saiki, H. Kono, H. Taka, R. Mineki, T. Fujimura, C. Nishiyama, T. Kuzuyama, and M. Nishiyama. Discovery of proteinaceous N-modification in lysine biosynthesis of *Thermus thermophilus*. ***Nat. Chem. Biol.***, **5,** 673-679 (2009)

【Term of Project】 FY2012-2016

【Budget Allocation】 159,700 Thousand Yen

【Homepage Address and Other Contact Information】

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