No. 53

Sulfolobus におけるリジン、アルギニン生合成

Lysine and arginine biosynthesis in *Sulfolobus*

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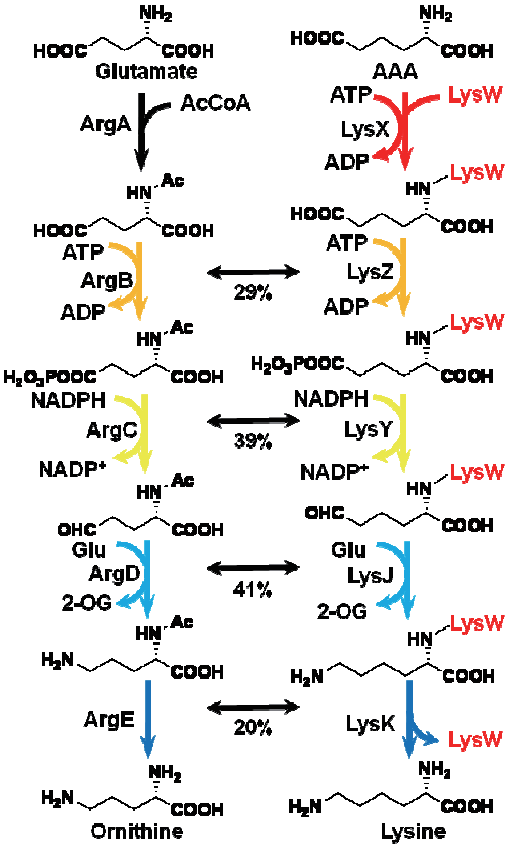
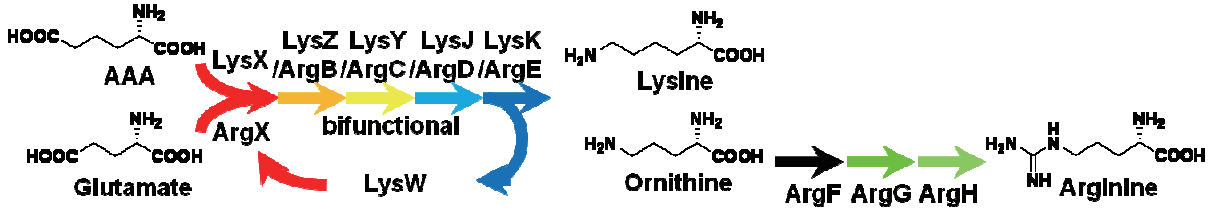
Lysine was believed to be synthesized through the diaminopimelate pathway in bacteria and plants with the only exception in lower eukaryotes that synthesize lysine through α-aminoadipate (AAA). In previous studies we found that the *Thermus thermophilus* synthesizes lysine through AAA but not through saccharopine, which differs from the pathway in lower eukaryotes [1]. The *Thermus* pathway is interesting to discuss about evolution of amino acid biosynthesis because its latter part, from AAA to lysine, is similar to arginine biosynthetic pathway and its former part, from 2-OG to AAA, is similar to a part of leucine biosynthetic pathway and the TCA cycle [2]. On the other hand, LysX, catalyzing the first reaction of the latter part, is not a homolog of ArgA which is the first enzyme of arginine pathway catalyzing the modification of the α-amino group of glutamate by an acetyl group. We found that LysX catalyzes modification of the α-amino group of AAA by LysW, small peptides composed of 54 amino acid residues. In bacteria and archaea possessing *lysX* homologs, LysW is encoded upstream the *lysX,* has highly conserved C-terminal sequence (EDWGE), and has a metal binding motif composed of several Cys residues. In the previous study, we revealed that AAA is attached to the γ-carboxyl group of the C-terminal Glu54 of LysW by LysX reaction. In this system LysW is served as a novel carrier protein [3].



Lysine and arginine biosynthesis in *Thermus*

In *Sulfolobus*, a hyperthermophilic archaeon, there is two *lysX* homologs in their genome, one is in lysine cluster (*lysYZMWXJK*) and the other is in arginine cluster (*argGHcarAB"lysX"*). In addition, *Sulfolobus* has no homolog of *argA* or *argJ* which catalyzes N-modification of Glu by acetylation in arginine biosynthesis, suggesting that the LysX homolog modifies the amino group of glutamate in arginine biosynthesis. Furthermore,

because there is a single copy of *lysW*, *lysJ*, *lysK* ,*lysZ* and *lysY* homolog in *Sulfolobus* genome, it was also suggested that they function in both lysine and arginine biosynthesis.



Predicted lysine and arginine biosynthesis in *Sulfolobus*

To verify this possibility, we analyzed functions of two LysX homologs. Results of *in vitro* activity measurement indicated that the one in lysine cluster (Saci_0754) exhibited activity for AAA and the other in arginine cluster (Saci_1621) did it for Glu only in the presence of LysW (Saci_0753). This results clearly indicated that the LysW homolog functions in both lysine and arginine biosynthesis. Thus we identified *Saci_0754* and *Saci_1621* as *lysX* and *argX,* respectively.

To elucidate interaction between LysW and ArgX, we crystallized LysW-ArgX complex. We have already obtained a data of the complex at 2.2 Å resolution, and are refining the structure. The structure of the complex will be reported in this symposium.

References

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[2] Miyazaki J. *et al.* (2001) *J Bacteriol.* 183, 5067-5073

[3] Horie A. *et al.* (2009) *Nat Chem Biol.* 5, 673-679