S55-4 System enzymology of microbial vitamin B12 metabolism

◯Tetsuo TORAYA[1]

[1]Okayama Univ., Grad. Sch. of Natural Sci. Technol.

Vitamin B12 is produced only by prokaryotes and utilized by animals as an essential micronutrient. Complementation analysis of patients with B12 metabolic abnormality suggested that about 10 gene products are involved in its trafficking and metabolism. Most of them are commonly involved in the bacterial B12 metabolism. Our studies of bacterial B12 enzymes and their activity-maintaining systems will be reported here as models of mammalian B12 enzyme systems. Mammals have adenosylcobalamin (AdoCbl)-dependent methylmalonyl-CoA mutase and methylcobalamin-dependent methionine synthase, in which an adenosyl radical and B12s super-nucleophile are involved, respectively. We have reported the X-ray structures and the action mechanisms of three bacterial B12 enzymes. In general, enzymes utilizing super-active species for catalysis tend to undergo mechanism-based inactivation. We have demonstrated that, in order to overcome this problem, bacteria possess reactivating factors for AdoCbl-dependent enzymes which mediate the release of a damaged cofactor. For methionine synthase, reductive methylation is required for the reactivation of oxidatively inactivated enzyme. Recently, mammalian proteins that play similar roles have been discovered, and their functions investigated. Thus, hints for preventing and treating B12 metabolic abnormality diseases may be obtained from studies of bacterial B12 systems.