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Inactivation of DNA repair genes leads to activation of vitamin B_1 biosynthesis in *Thermus thermophilus* HB8

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Oxidative stress generates harmful reactive oxygen species (ROS) that attack biomolecules including DNA. In living cells, there are several mechanisms for detoxifying ROS or repairing oxidatively-damaged DNA. However, the relationship between these two mechanisms had not been well understood.

In this study, transcriptomic analyses clarified that, in *Thermus thermophilus* HB8, disruption of DNA repair genes *mutS*, *mutL*, and *mutS2* induces the biosynthesis pathway for vitamin B_1 (thiamine), which can serve as an ROS scavenger. In addition, disruption of *mutS*, *mutL*, or *mutS2* resulted in an increased rate of oxidative stress-induced mutagenesis. Co-immunoprecipitation and pull-down experiments revealed the interactions of MutS2 with MutS and MutL, indicating that these proteins cooperatively participate in the repair of oxidatively damaged DNA. Based on these results, it is suggested that bacterial cells sense the accumulation of oxidative DNA damage or absence of DNA repair activity, and signal the information to the transcriptional regulation machinery for an ROS-detoxifying system (Figure 1). Although such a concept has not been previously proposed, it has been reported that, in mammals, the vitamin B_1 transporter gene is under control of a tumor-suppressing transcriptional factor, p53. There may be an analogy in the DNA-damage-dependent control of intracellular vitamin B_1 level between bacteria and mammals.

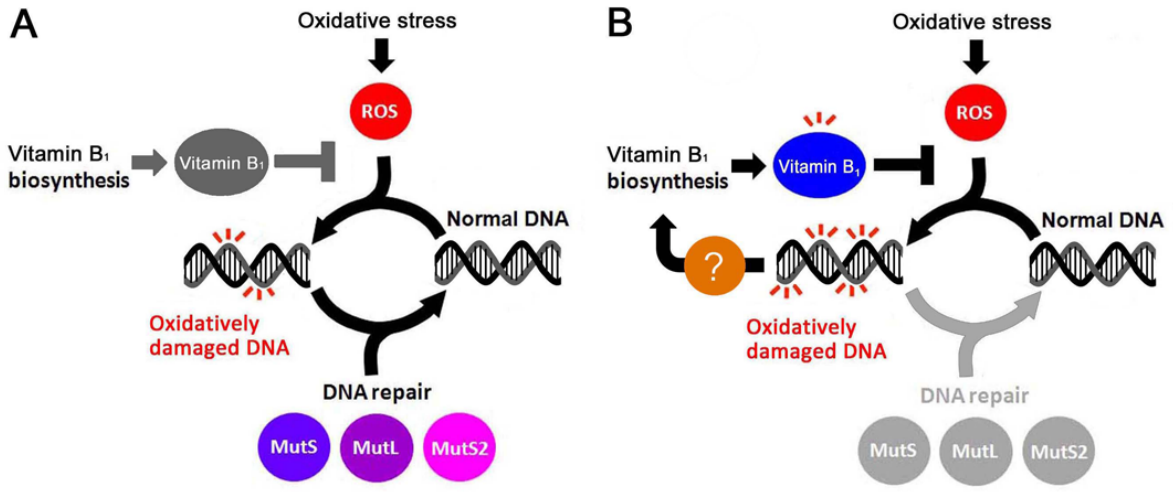

Figure 1: Inactivation of DNA repair genes leads to the induction of vitamin B_1 biosynthesis. Extracellular oxidative stress and intracellular redox metabolism generate ROS, which can attack DNA to yield oxidatively damaged DNA. (A) In the wild-type strain, oxidatively damaged DNA is repaired by DNA repair enzymes including MutS, MutL, and MutS2. (B) In the Δ*mutS*, Δ*mutL*, and Δ*mutS2* strains, the genes for vitamin B_1 biosynthesis are activated to prevent the accumulation of oxidative damage in DNA via an unknown mechanism.