Studies on Environmental Factors Affecting Microbial Functions and their Mode of Action

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The production of secondary metabolites including diverse bioactive compounds from microorganisms is largely affected by environmental factors such as stress and starvation. In the present study, we found that light and microbial metabolites result in the induction of useful microbial functions, and also revealed the molecular mechanism underlying the phenomena induced by these environmental factors.

(i) Molecular mechanism underlying light-inducible carotenoid production in non-phototrophic bacteria [1,2]. We first found that *Streptomyces coelicolor* exhibits light-inducible carotenoid production. Genetic analysis aimed at elucidating the control of light-inducible carotenoid production revealed that a MerR family transcriptional regulator, LitR, adjacently encoding in the carotenoid biosynthesis gene cluster, plays a central role in light-induced transcription. Genomic search showed that a LitR homolog is encoded in the phylogenetically diverged bacteria including not only gram-positive bacteria but also gram-negative bacteria. Our biochemical studies on LitR proteins derived from a gram-negative bacterium, *Thermus thermophilus,* and a gram-positive bacterium, *Bacillus megaterium,* revealed that LitR is a transcriptional regulator with photo-sensory function, based on the evidence that LitR associates with a light-sensing molecule Adenosyl B12 to form a LitR-AdoB12 complex, which exhibits light-sensitive DNA-binding activity and shows light-inducible subunit dissociation. The presence of LitR in bacteria with carotenoid genes indicates that LitR serves as a general photosensitive transcriptional regulator, and non-phototrophic bacteria generally have an ability to sense light and thus produce carotenoids upon exposure to light.

(ii) Chemical factors inducing cryptic antibiotic production based on microbial interaction [3]. We first found a unique biological phenomenon wherein *Streptomyces griseus* remarkably promotes antibiotic production in *Streptomyces tanashiensis*. Further studies identified siderophore desferrioxamine E as the antibiotic inducer in this process. Screening of the bacterial response to desferrioxamine E revealed that this compound remarkably promoted the production of a purple-pigmented antibiotic violacein in *Chromobacterium violaceum*. In another case, a polyether antibiotic promomycin produced by *Streptomyces scabrisporus* strongly induced the production of antibiotics in *Streptomyces griseorubiginosus*. These results indicate that siderophores and antibiotics serve as signaling compounds that induce the production of cryptic secondary metabolites.

References

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