EC Microbiology Editor's Column - 2017

A Co-Culture of Microbial Endosymbionts Increases the Production of Antimicrobial Polyketide Metabolites

"The co-culture approach is an effective strategy in order to increase the biosynthesis of polyketide antimicrobial metabolites hidden in the microbial endosymbionts"

HC Yashavantha Rao
University of Mysore
India

COLUMN ARTICLE

Microbial endosymbionts as one of the substantial residents in medicinal plant tissues are rarely studied and attracted in recent years since there is an ever increasing need for novel drugs throughout the human history [1]. They strongly establish plant-endophyte and endophyte–endophyte interactions which constitute stress conditions within the host and play a significant role in the biosynthesis of anti-infective drugs [2,3]. Endosymbionts participate in the metabolic pathways of medicinal plants and produce analogous or novel bioactive secondary metabolites and has various applications (Figure 1) [4,5]. Secondary metabolites synthesized by endosymbiotic microbes can provide certain benefits to the host plant, like stimulating growth and enhancing the host's resistance toward biotic and abiotic factors [6].

During its life period, host plants may inhabited by several species of endosymbionts under stress conditions within the restrictive environment. This stress condition can stimulate the production of secondary metabolites that triggers microbial competition and consequently affects both the neighboring microbes and host plants [7]. Since endosymbionts competition in limited space, nutrient supplements serves as a major role that drives the synthesis of antimicrobial metabolites [8].

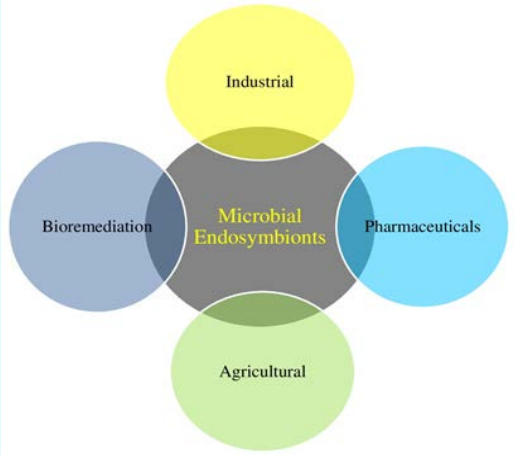

Figure 1: Potential applications of microbial endosymbionts.

Genomic studies have demonstrated that fungi and bacteria harbor a huge number of biosynthetic polyketide synthase (PKS) genes and certain genes are not expressed under laboratory growth conditions [7,9,10]. Hence, biosynthetic gene clusters responsible for the production of metabolites that enhances the competition in natural environments may remain silent under unnatural conditions. One advanced way to overcome this lacuna and mimic natural endosymbionts environment is to grow the PKS gene bearing endosymbionts in mixed cultures where the presence of neighboring endosymbionts may induce the production of polyketide antimicrobial metabolites. This co-culture interaction may induce silent metabolic pathways that might result in the biosynthesis of new antimicro-

Citation: HC Yashavantha Rao. "A Co-Culture of Microbial Endosymbionts Increases the Production of Antimicrobial Polyketide Metabolites". EC Microbiology ECO.01 (2017): 41-42.

bial metabolites, and finally lead to chemical support of the metabolite producing endosymbiont [11]. Co-cultivation based strategy can therefore lead to the increase production of metabolites that are not produced in monoculture, which might be helpful to unmask cryptic and poorly expressed secondary metabolites. Previous studies have revealed that mixing microorganism cultures can stimulate the production of secondary metabolites and increase the biological activities of microbial extracts [12-14]. Polyketides constitute a large family of structurally diverse group of natural secondary metabolites found in fungi, bacteria and plants, which play a significant role in the biodiscovery of anti-infective metabolites from natural resources [7].

Apart from the co-culture interactions, the inducer endosymbiotic strain could also able to induce epigenetic modifications in the producer strain. The interaction of the producer strain with the inducer strain finally enhances the production of antimicrobial metabolites in the producer strain. Taking all the above into account, Co-culture strategy thus simulates the activation of complex regulatory mechanisms, which results in the production of defense molecules and metabolites involved in the symbiotic associations.

BIBLIOGRAPHY

1. Li J., *et al*. "Isolation and characterization of culturable endophytic actinobacteria associated with Artemisia annua L.". *Antonie Van Leeuwenhoek* 101.3 (2012): 515-527.

2. Kusari P., *et al*. "Cross-species biosynthesis of maytansine in Maytenus serrata". *RSC Advances* 6.12 (2016): 10011-10016.

3. Rao HCY and Satish S. "Intra-specific differentiation of fungal endosymbiont Alternaria longissima CLB44 using RNA secondary structure analysis and their anti-infective potential". *The Science of Nature* 103.7-8 (2016): 69.

4. Yu H., *et al*. "Recent developments and future prospects of antimicrobial metabolites produced by endophytes". *Microbiological Research* 165.6 (2010): 437-449.

5. Rao HCY., *et al*. "Chemogenomics driven discovery of endogenous polyketide anti-infective compounds from endosymbiotic Emericella variecolor CLB38 and their RNA secondary structure analysis". *PLoS ONE* 12.2 (2017): e0172848.

6. Padhi S and Tayung K. "Antimicrobial activity and molecular characterization of an endophytic fungus, Quambalaria sp. isolated from Ipomoea carnea". Annals of Microbiology 63.2 (2013): 793-780.

7. Schumann J and Hertweck C. "Advances in cloning, functional analysis and heterologous expression of fungal polyketide synthase genes". *Journal of Biotechnology* 124.4 (2006): 690-703.

8. Oh DC., *et al*. "Libertellenones A-D: induction of cytotoxic diterpenoid biosynthesis by marine microbial competition". *Bioorganic and Medicinal Chemistry* 13.17 (2005): 5267-5273.

9. Hertweck C. "Hidden biosynthetic treasures brought to light". *Nature Chemical Biology* 5.7 (2009): 450-452.

10. Rao HCY., *et al*. "Implication of PKS type I gene and chromatographic strategy for the biodiscovery of antimicrobial polyketide metabolites from endosymbiotic Nocardiopsis prasina CLA68". *The Science of Nature* 103.5-6 (2016): 45.

11. Abdelmohsen UR., *et al*. "Elicitation of secondary metabolism in actinomycetes". *Biotechnology Advances* 33: (2015): 798-811.

12. Degenkolb T., *et al*. "Formation of new lipoaminopeptides, acremostatins A, B and C, by cocultivation of Acremonium sp. Tbp-5 and Mycogone rosea DMS 12973". *Bioscience, Biotechnology and Biochemistry* 66.4 (2002): 883-886.

13. Zhu F and Lin Y. "Marinamide, a novel alkaloid and its methyl ester produced by the application of mixed fermentation technique to two mangrove endophytic fungi from the South China Sea". *Chinese Science Bulletin* 51 (2006): 1426-1430.

14. Zuck KM., *et al*. "Induced production of nformyl alkaloids from Aspergillus fumigatus by co-culture with Streptomyces peucetius". *Journal of Natural Products* 74 (2011): 1653-1657.