



## In silico prediction of substrate specificity of adenylation domains of NRPSs genes of some cyanobacteria strains as a mining tool for natural bioactive compounds

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**Abstract:** Cyanobacteria have the ability to produce a wide variety of natural bioactive compounds. Horizontal gene transfer is thought to play a role in the sporadic distribution of bioactive compounds producers among cyanobacteria. The most prevalent cyanobacterial natural products are produced in combinatorial pathways like mixed PKS/NRPS systems. Nonribosomal peptide synthetases (NRPSs), synthesize a diverse array of bioactive small peptides, many of which are used in medicine. Therefore, there is considerable interest in predicting NRPS substrate specificity in order to identification the natural bioactive products. To investigation the relationship between natural product genes and the role of horizontal gene transfer in the evolutionary history, we amplified and sequenced the NRPS genes. Moreover, we used some *bioinformatics software* tools, in order to prediction of peptide compound and an amino acid activated by a specific unknown NRPS A module by some cyanobacteria strains isolated from different Climatic/Geographic Regions and Habitats. *Fischerella* sp. Sara 1 KY618863, *Nostoc* sp. BN KY303912 and three *Nostoc* sp. isolated from agricultural areas, salt water and dry limestones, respectively, were analysed using a combination of the genome mining softwares, AntiSMASH, and NaPDoS. Moreover, Adenylation domain substrate specificity predictions for NRPS enzymes, the signature sequence and the name of the compound, were made using NRPSpreditor2. The results of bioinformatics analysis showed that, Microcistin synthetase B as natural compound, D A W F L G N V as signature sequences and McyB-M1-Leu as predicted amino acid were detected from *Fischerella* sp. Sara 1 KY618863, *Nostoc* sp. BN KY303912. However, NRPS gene fragments could not be amplified from three *Nostoc* sp. isolated from dry limestones. The negative PCR results from the initial NRPS PCRs were confirmed through subsequent annealing-temperature gradient NRPS PCRs. This result suggests that the ability of lateral gene transfer to produce the natural bioactive compound has been lost during evolutionary history in these strains. The data presented here highlight the need for future studies to define the linkages between Horizontal gene transfer in maintenance of NRPS genes among cyanobacteria distributed in different Climatic/Geographic Regions and Habitats.

**Keywords:** Prediction of substrate; Adenylation domains; NRPSs genes, Natural bioactive compounds; Horizontal gene transfer

### References

- [1] Calteau, A., Fewer, D. P., Latifi, A., Coursin, T., Laurent, T., Jokela, J., Gugger, M. (2014). Phylum-wide comparative genomics unravel the diversity of secondary metabolism in Cyanobacteria. *BMC genomics*, 15(1), 977.
- [2] Lee, T. V., Johnson, R. D., Arcus, V. L., & Lott, J. S. (2015). Prediction of the substrate for nonribosomal peptide synthetase (NRPS) adenylation domains by virtual screening. *Proteins: Structure, Function, and Bioinformatics*, 83(11), 2052-2066.
- [3] Rantala, A., Fewer, D. P., Hisbergues, M., Rouhiainen, L., Vaitomaa, J., Börner, T., & Sivonen, K. (2004). Phylogenetic evidence for the early evolution of microcystin synthesis. *Proceedings of the National Academy of Sciences of the United States of America*, 101(2), 568-573.