

SAMPLE ABSTRACT

TITLE An Orphan MbtH-like Protein Interacts with Multiple Nonribosomal Peptide Synthetases in *Myxococcus xanthus* DK1622

AUTHORS Karla Esquilin-Lebron¹, Tye Boynton², Lawrence J. Shimkets², and Michael G. Thomas¹

AFFILIATIONS ¹ Department of Bacteriology, University of Wisconsin-Madison, Madison, Wisconsin, USA, ² Department of Microbiology, University of Georgia-Athens, Athens, Georgia, USA

ABSTRACT TEXT One way bacteria and fungi produce bioactive natural products such as antibiotics and siderophores is through the use of nonribosomal peptide synthetase (NRPS) multimodular assembly lines. Many NRPSs in bacteria require members of the MbtH-like protein (MLP) superfamily for their solubility or function. Although MLPs are known to interact with adenylation domains of NRPSs, the specific role MLPs play in NRPS enzymology has yet to be elucidated. MLPs are nearly always encoded within NRPS-encoding biosynthetic gene clusters (BGCs). In this work, we identified 35 orphan MLPs from a diverse group of bacteria. We define an orphan MLP as being coded by a gene that lies outside an NRPS-encoding BGC or is not directly adjacent to genes predicted to be involved in NRPS-associated biosynthesis. We choose the orphan MLP MXAN_3118 from *Myxococcus xanthus* DK1622 to investigate its role in this bacterium. *M. xanthus* DK1622 genome has fifteen NRPS-encoding BGCs, but only one MLP-coding gene (MXAN_3118). We tested the hypothesis that MXAN_3118 may interact with one or more NRPS. We used comparative genomics to identify two candidate BGCs that may code for MLP-dependent NRPSs. MLP-NRPS interactions were investigated by assessing MLP-dependence of NRPS solubility, whether the MLP and NRPS copurified, and whether protein-protein interactions were detected using an *in vivo* bacterial two-hybrid assay. MXAN_3118 interacted with NRPSs from eight different BGCs. This is the first time an MLP has been identified to naturally interact with multiple NRPS systems in a single organism. The finding of a MLP that functions with multiple NRPS systems suggests that MXAN_3118 may be a universal MLP that can be exploited for the assembly of functional hybrid NRPSs for the structural diversification of NRPS-based natural products.