Mycobacterial Diseases
ISSN: 2161-1068

Short Communication

Functional and structural flexibility of Type III polyketide synthases in mycobacterium marinum

Priti Saxena[1]*, Samir Giri[1], Amreesh Parvez[1], Gorkha Raj Giri1, Shivendra Pratap[2], Monika Kumari[1], Abhiruchi Kant[2], Renu Bisht[1] and Vengadesan Krishnan[2]

1South Asian University, India

2Regional Centre for Biotechnology, India

Abstract

Mycobacterial pathogenesis is hallmarked by lipidic polyketides that decorate cell envelope and mediate infection. However, factors mediating persistence remain largely unknown. Dynamic cell wall remodeling could facilitate different pathogenic phases. Recent studies have implicated type III polyketide synthases (PKSs) in cell wall alterations in several bacteria. Comparative genome analysis revealed several type III pks genes in mycobacteria. Mycobacterium marinum genome harbors four type III pkss that group into three pks genomic clusters. mmar_2470 and mmar_2474 form a cluster with other type I pkss, while mmar_2190 is grouped with genes for several polyketide modifiers. Interestingly, these unique pks genomic clusters are conserved exclusively in pathogenic species. Cell-free reconstitution assays and high-resolution mass spectrometric analyses revealed capability of these proteins to accept various monocarboxyl-CoA substrates and extend with dicarboxyl-CoA extender units to biosynthesize a palette of polyketide metabolites. MMAR_2470 and MMAR_2474 proteins utilized two different extenders to biosynthesize methylated polyketide products while MMAR_2190 produced non-methylated metabolites. Three-dimensional structural analyses for MMAR_2190 revealed a distinct catalytic functioning regulated by rotational flexibility of key active site amino acids. Functional investigations in heterologous mycobacterial strain implicated these proteins to be vital for mycobacterial survival in stationary biofilms. Our study provides new insights on functional importance of type III PKSs conserved in pathogenic mycobacterial species and delineates mechanistically crucial residue positions that can be modulated to generate a repertoire of unusual biologically active type III polyketides.

Biography

Priti Saxena completed PhD in Chemical Biology with Dr. Rajesh Gokhale at NII, Delhi investigating mechanistic and structural aspects of type III polyketide synthases in biosynthesis of novel lipids. She joined IGIB, Delhi with IYBA award from DBT, GoI. Priti entered academia and started her own research group at South Asian University (SAU), Delhi. Her research team attempts to identify bio-functionality of polyketide synthases and modifying enzymes in pathogenesis of Mycobacteria and related Corynebacterineae and dissect molecular intricacies mediating host-pathogen interplay. She is a recipient of SAU Start-up grant and has been awarded CRG grant from SERB, DST, GoI.

Citation: Priti Saxena, Functional and Structural Flexibility of Type III Polyketide Synthases in Mycobacterium marinum, Clinical Microbiology 2021, 12th World Congress on Clinical Microbiology and Infectious Diseases | November 25th, 2021,06