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Characterization of novel *Bacillus Thuringiensis* strains native to Saudi Arabia with enhanced larvicidaltoxicity against the malaria mosquito *Anopheles Gambiae* S.L

Talat A El-kersh[1], Ashraf M Ahmed[1], Yazeed A Al-sheikh[1], Frédéric Tripet[2], Mohamed S Ibrahim[1] and **Fahd A Al-Mekhlafi[1]**
[1]King Saud University, Saudi Arabia
[2]Keele University, UK

The bacterium *Bacillus thuringiensis*(Bt) is a safe eco-friend entomopathogenicbiocontrol agent widely used to complement chemical control. Hence there is an urgent need for characterizing novel isolates with potent larvicidal activity against mosquito vectors.The present study was initiated to characterize new native *Bt* isolates with mosquitocidal activity from various samples from 16 regions across the Saudi Arabia.Various samples were collected from mosquito breeding sites across different regions in in the country and screened for *Bt* isolation. *Bt* isolates were characterized on the basis of colony morphology, shape of spores and parasporal crystals and through comparisons of biochemical profiles. The larvicidal activity (LC_{50}& LC_{95}) of standardized spore/crystal mixtures of *Bt* isolates were tested against larvae of Anopheles gambiae. At24hour post-treatment and compared with that of the *Bt*.israelensis (*Bti*-H14).A total of 23 (out of 68 native *Bt* isolates) were mosquitocidal. Larvicidal strains were similar in terms of colony morphology, hemolytic and motile. Out of the 23 isolates, 9 showed significantly higher activity (LC_{50} range from 3.90 to 9.5µg/ml) than the *Bti*-H14 (LC_{50} of 13.33 µg/ml) with one strain having as much as 3.4-fold higher activity than the *Bti*-H14. This is the first report of *Bt* strains native to Saudi Arabia with significantly enhanced larvicidal efficacy against the malaria mosquito An. gambiae. These novel *Bt* strains may therefore contribute to novel potent biopesticides and help mitigate the risk of *Bt* resistance emergence in bio-control programs targeting malaria vector populations.

talatkersh@yahoo.com

Novel mechanistic models for target reactions in *Mycobacterium tuberculosis* DNA synthesis pathway

Parag A Deshpande
Indian Institute of Technology, India

Orotidine 5'-monophosphate (OMP) is an important intermediate observed during the *de novo* synthesis pathway of DNA of *Mycobacterium tuberculosis*. It is synthesized by the reaction of α-D-5-phosphoribosyl-1-pyrophosphate (PRPP) and orotate (OA) with the help of Orotatephosphoribosyltransferases (OPRT) and is consumed to yield the nucleotide uridine 5'-monophosphate (UMP) using Orotidine 5'-phosphate decarboxylase (ODCase). These two reactions are popular targets for inhibition to check the growth of *Mycobacterium tuberculosis*. Therefore, a detailed understanding of kinetics and mechanism of these reactions is important as the inhibition of these reactions in organisms like *Mycobacterium tuberculosis* can have implications on development of drugs for cure of tuberculosis.There are several issues concerning the mechanism of the reactions which remain unresolved till date and require attention. Experimental studies have been carried outprobing the mechanism of these reactions. Surprisingly, different studies either report different mechanisms for the reaction which are not in agreement or the mechanisms are suspected tobe organism-dependent thereby making the mechanisms of the reactions doubtful. For every new observation made for these reactions, a series of kinetic studies and tests of different kinetic models are to be done every time. We have developed generic mechanistic models for the activity of OPRT and ODCase for catalyzing the reactions. We propose a detailed reaction pathway for OMP formation and consumption which encompass the features of various key mechanisms. The models were rigorously tested with kinetic data reported in the literature derived from different organisms and our unified mechanisms were able to successfully describe all the test data without any additional assumption. The models will prove to be valuable for assessment of experimental kinetic studies without making any reference to the organism from which the enzymes have been derived.

parag@che.iitkgp.ernet.in