Conclusion: High rates of *Mycobacterium tuberculosis* including extensively drug resistant TB were found in children less than one, which indicates the burden of TB infection among woman during childbearing years. INH mono-resistance is of concern as this will not be detected by the current diagnostic algorithm that includes the Xpert MTB/RIF for MTB detection and Rifampicin resistance. Children with INH mono-resistance may benefit from high-dose isoniazid therefore bacteriological confirmation through culture is important in management of childhood TB.

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Mycobacterial lipoprotein mediates mycobacterial survival by inhibiting antimicrobial peptide secretion and blocking phagosomal maturation pathway

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Background: Mycobacterial genome codes for several lipoproteins, and constitute a major component of cell wall. Few of these lipoproteins have been characterized, but function of most of them is yet to be ascertained. Here we establish the role of a previously uncharacterized mycobacterial lipoprotein in intracellular survival through Vitamin D receptor signalling and cathelicidin inhibition.

Methods & Materials: Over-expressing strain of *Mycobacterium smegmatis* was produced by cloning the lipoprotein gene using shuttle vector pSMT3. The cloned strain was checked for its intracellular survival in peritoneal macrophages isolated from mouse and human monocytes cells by Colony Forming Unit (CFU) assay and Flow cytometry analysis with SYTO 9-PI staining. To elucidate role of Vitamin D receptor signalling in bacterial survival, intracellular survival was checked by exogenous addition of active vitamin D3 hormone 1,25-dihydroxyvitamin D3 (1,25D3). Antimicrobial responses to overexpressing strain were evaluated by checking expression of LL-37 and its upstream signalling molecules by Real-Time PCR. Effect on phagosomal maturation was studied by checking for expression of early and phagosomal markers such as EEA1 and Rab7 respectively in presence and absence of VitD3.

Results: *M.smegmatis* over-expressing putative lipoprotein was successfully prepared using pSMT3 shuttle vector. Significantly high CFU counts after 48hrs of infection higher intracellular survival in case of lipoprotein over-expressing strain in both mouse and human macrophages. Decreased PI population among intracellular bacterial as compared to vector control corroborated CFU data. Overexpression of Lipoprotein showed TLR2/4 mediated downregulation of Vitamin D Receptor-related gene Cyp27B1 hydroxylase and consequent suppression of cathelicidin expression in human monocytes. Furthermore inhibition of EEA1 (early endosome) and Rab7 (late endosome) in case of lipoprotein over-expressing strain shows that the gene arrests VitD3-PI,3K mediated phagosomal maturation.

Conclusion: The current study suggests that that putative lipoprotein plays an important role in bacterial survival inside host macrophages. It mediates survival by inhibiting VitD3 mediated anti-microbial response mechanism of host cells. It is hoped that the study provides base for further investigation of mycobacterial virulence and survival.

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Synthesis, ADME and antimycobacterial studies of a novel series of 2-thiazolylimino-5-arylidene-4-thiazolidinone derivatives

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Background: The emergence of multi-drug resistant and extensively drug-resistant cases of tuberculosis has lead to the search for new structural classes of antituberculosis drugs that can be effective against these strains of *Mycobacterium tuberculosis (M. tb)*. There are many reports on antimycobacterial screening of compounds containing the 4-thiazolidinone moiety. The 5-arylidene moiety in the 2-heteroarylimino-5-benzylidene-4-thiazolidinone scaffold plays an important role in antimicrobial activity against Gram-positive and Gram-negative bacteria, yeasts and moulds. We have previously reported the synthesis and antimycobacterial activities of 2-thiazolylimino-5-arylidene-4-thiazolidinone derivatives (AIA 2015, 13, 2, in press). In this study a series of 2-thiazolylimino-5-arylidene-4-thiazolidinones were synthesized and evaluated for their *in vitro* antimycobacterial activity against *M. tb* H37Rv.

Methods & Materials: The 2-thiazolylimino-5-arylidene-4-thiazolidinone derivatives were synthesized as reported earlier, and their structures were confirmed on the basis of spectral data and elemental analysis. Qikprop, the ADME prediction program was used in predicting pharmacokinetic properties of the derivatives, which helped in designing and synthesis of novel and more potent analogs. *In vitro* antimycobacterial activity against drug-sensitive *M. tb* H37Rv strain was evaluated and expressed as % inhibitions. Compounds were tested at 6.25 μg/ml concentration in BACTEC-460 TB radiometric system, and Isoniazid and Rifampicin were taken as reference standards.

Results: The synthesis and antimycobacterial activities (% inhibitions) of 2-thiazolylimino-5-arylidene-4-thiazolidinone derivatives are reported. The chemical modifications not only altered the physicochemical properties but also pharmacological activities. The results revealed that most of the compounds exhibited moderate to excellent *in vitro* activity (88-99.7% inhibition) against *M. tb* H37Rv, and it was considerably affected by various substituents on the aromatic ring. Few active derivatives were demonstrating >99% inhibition of *M. tb* H37Rv at 6.25 μg/mL. The activity was considerably affected by various substituents on the aromatic ring of the 4-thiazolidinone, and compounds with di- and tri- substitutions on the aromatic ring were more active than monosubstituted derivatives.

Conclusion: Several compounds were identified as novel and potential lead for design and synthesis of new antimycobacte-