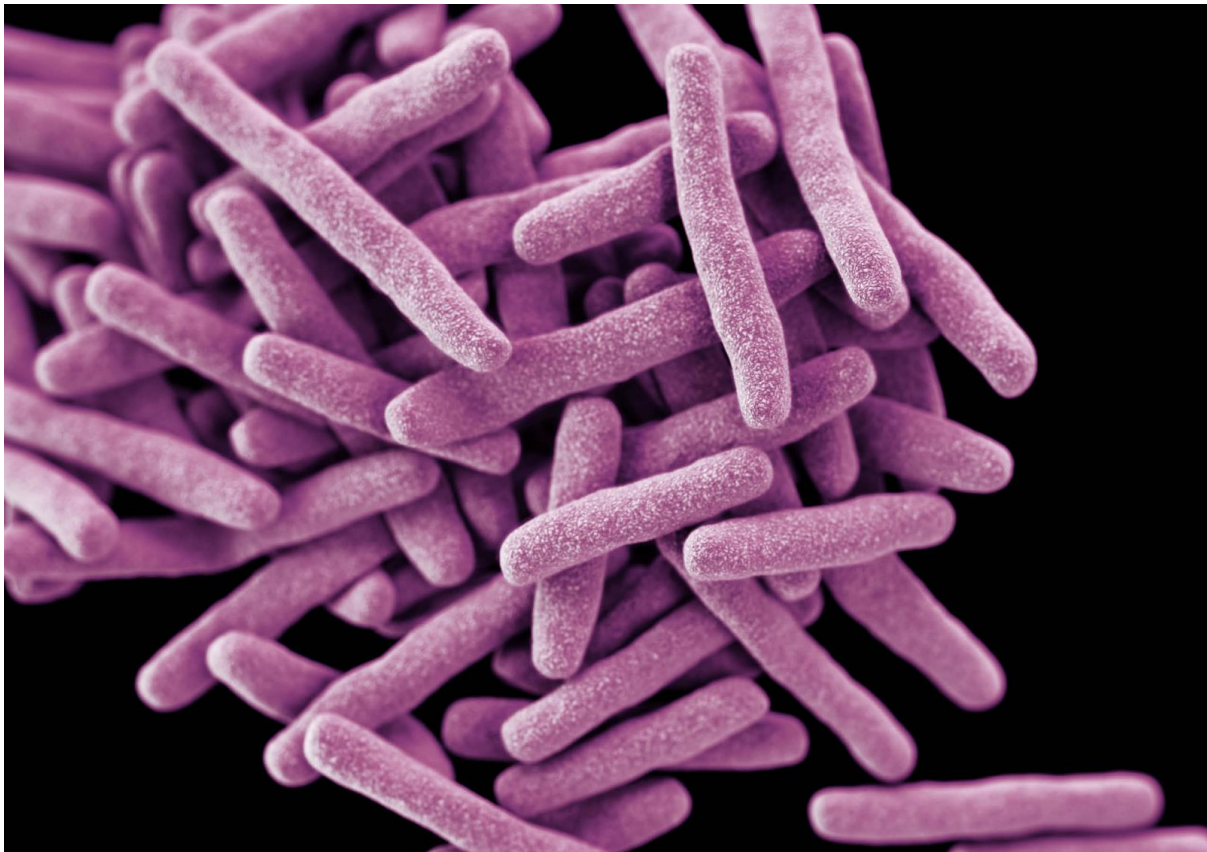


DBT-THSTI study gets new insight towards fighting TB

New Delhi, Jan 07: The worldwide increase in the frequency of multidrug-resistant and extensively drug-resistant cases of tuberculosis is mainly due to therapeutic noncompliance associated with a lengthy treatment regimen. Depending on the drug susceptibility profile, the treatment duration can extend from 6 months to 2 years. This protracted regimen is attributed to a supposedly nonreplicating and metabolically inert subset of the *Mycobacterium tuberculosis* population, called “persisters.” The mechanism underlying stochastic generation and enrichment of persisters is not fully known.



A team of researchers from ITM University, Gwalior, CSIR-IGIB, Singapore Immunology Network, Singapore and DBT -Translational Health Science and Technology Institute (DBT-THSTI), Faridabad worked on this aspect and demonstrated that cholesterol-induced activation of a RNase toxin (VapC12) inhibits translation by targeting proT tRNA in *M. tuberculosis*. This results in cholesterol-specific growth modulation that increases the frequency of generation of the persisters in a heterogeneous *M. tuberculosis* population. Also, a null mutant strain of this toxin (Δ vapC12) demonstrated an enhanced growth phenotype in a guinea pig model of *M. tuberculosis* infection, depicting its role in disease persistence.

These findings will help to identify a novel mechanism of the generation of antibiotic persistence and define targets against the “persister” population. Approaches targeting the

persister population will enhance the rate of clearance of the pathogen, resulting in a significant reduction in the duration of treatment. This will help in significantly reducing the risk associated with the current extended regimen extending from 6 months to 2 years.

This finding is significant since a better understanding of the disease persistence and targeting the M. tuberculosis persister population as a therapeutic strategy will open new paradigms in tuberculosis treatment.

Complete paper is available at: <https://msystems.asm.org/content/5/6/e00855-20>

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