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Creating a novel anti- tubercular drug: A 25 year long sojourn!

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Tuberculosis has been a rampant health threat worldwide and has been the most devastating disease in the under-developed and developing countries. The situation has deteriorated with time due to the emergence of multi- to totally drug resistant strains of *Mycobacterium tuberculosis*. This has reinforced the need to develop novel drugs for curing tuberculosis. The existing drugs that are in use are primarily the semisynthetic derivatives of rifamycin B produced by an actinobacterium, *Amycolatopsis mediterranei*. So far only six, clinically effective semisynthetic derivatives of this compound could be produced. However, further modifications using chemical methods seem difficult. An alternative approach that can be employed is to modify the rifamycin B backbone by using combinatorial biosynthesis, which has been difficult to implement in this case. Through a concerted effort of nearly 25 years we could demonstrate for the first time the production of 24-desmethylrifamycin B, the semisynthetic derivative 24-desmethylrifampicin was found to have a stronger antibacterial activity against MDR strains of *Mycobacterium tuberculosis*. This was achieved by first developing a cloning vector and transformation system for *Amycolatopsis mediterranei* followed by swapping the acyltransferase domain of module six (AT6), that adds propionate to the growing rifmycin chain, with that of module 2 of the rap PKS, that adds acetate to the rapamycin growing chain.

Biography

Rup Lal is a Professor at the Department of Zoology, University of Delhi. He completed his PhD in 1980, from the University of Delhi. He works in the area of microbial diversity and molecular biology. He is the recipient of Alexander von Humboldt Fellowship, DBT Overseas Fellowship and ASM Indo-US Professorship in microbiology. He was a visiting scientist at the Department of Biochemistry, University of Cambridge. He has to his credit more than 150 research publications, attracting over 2712 ISI citations. He has mentored nearly 50 PhD students and more than 100 PG and UG students.

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