Details of the research work duly signed by the applicant, for which the Sun Pharma Science Foundation Research Award is claimed, including references and illustrations (not to exceed 6000 words).

Towards emerging drug resistance in leprosy:

During the years 2015-2019 was devoted to the research on emerging antimicrobial resistance in leprosy. ln the context of the current scenario of elimination of leprosy, the matter of drug resistance in leprosy has become pertinent in view of its public health importance. Drug resistance in leprosy especially to the bactericidal drug, rifampicin, is an issue of major concern. Drug resistance has been reported earlier as well but need arose to look into it in more details about factors responsible for causing drug resistance in leprosy and to identify the way forward towards its better management during the elimination phase of the disease. During this elimination phase it is of utmost importance to diagnose secondary drug resistance and their treatment with alternative regimen as early as possible so that there is no chance of transmission of secondary *M.leprae* drug resistant strain to a naive individual which might emerge as primary drug resistance in leprosy.

It was the first report from my publications which showed the occurrence of both primary and secondary rifampicin resistance and identified a novel mutation at codon 411 of *rpoB* gene **[Clin Microbiol Infect. 2015]** as well as multidrug resistance cases in leprosy **[J Glob Antimicrob Resist. 2018]**. I also confirmed that the reported novel mutation at codon position 442 in rifampicin resistance cases is not conferring resistance in mouse footpad study **[Lepr Rev. 2016]**. I also did in-silico analysis of secondary line drugs in rifampicin resistant cases **[Med Microbiol Immunol. 2015; Int J Mod Eng Res 2016, Helix 2017].**

Government recognition towards awareness of drug resistance and initiation of surveillance network:

My research work, especially on emerging anti-microbial drug resistance in leprosy has been recognized by the Global Leprosy Programme, WHO **[Clin Microbiol Infect 2018]**, Indian Council of Medical Research and later on by the National Leprosy Eradication Programme of Govt. of India. Data generated by my studies played an important role in influencing the Leprosy Division of Ministry of Health, Govt of India to formulate policies pertaining to public health interventions in prevention and spread of leprosy in poor society as well as prevention of drug resistance. My work has already created an awareness for establishment of network for surveillance of detection of drug resistance to anti-leprosy drugs. Government has initiated a mechanism for surveillance of *M. leprae* drug resistance at country level, so that the drug resistance in leprosy should not become an issue in the

future and the patients can be treated more effectively. I was one of the members in the NLEP expert committee on Antimicrobial Resistance in Leprosy. I drafted the SOPs for all the national referral laboratories along with Dr. Utpal Sengupta.

Identification of compensatory mutations:

I studied whole genome sequencing of rifampicin resistant *M.leprae* strains and first identified the presence of compensatory mutations in *rpoC* and *mmpL7* genes, along with *rpoB*, that may additionally be responsible for conferring resistance in those strains. **[Infect Drug Resist. 2018]**.

Diagnosis of drug resistant leprosy in CNS:

I also worked for detection as well as drug susceptibility testing of leprosy bacillus obtained from Brain, that provided a new source for clinicians for diagnosing leprosy involving Central Nervous System. After proper diagnosis and proper treatment, cases showed resolution of brainstem lesions and cord lesions **[Am J Trop Med Hyg. 2019; Am J Trop Med Hyg. 2020 a; Am J Trop Med Hyg. b 2020].**

Study of alternate regimen in rifampicin resistant cases:

As rifampicin is the backbone of MDT treatment for leprosy, it is important to know that if patient is resistant to rifampicin, then which alternative regimen will be effective for him/her. Therefore, I further conducted research on the alternative regimen especially for rifampicin resistant cases **[J Glob Antimicrob Resist 2020].** I have written chapter on Drug resistance in "Ridley Jopling Textbook of Leprosy for Medical students".

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