

DBT/ Institute Name: Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram

RGCB's intervention on Drug Resistance in Bacteria: Molecular Mechanisms and Prevention

By Sunderarajan Padmanabhan

New Delhi, February 24: Infectious diseases caused by bacteria continue to be the leading cause of human death and suffering worldwide. The discovery of antibiotics and their application in the treatment had led to a paradigm shift in the fight against infectious diseases. However, in the recent times, the rapid emergence of antibiotic resistance in bacteria has rendered most of the antibiotics ineffective. The overuse of antibiotics and its easy availability over the counter in the local pharmacies is one of the main reasons behind this problem. It is estimated that death by drug-resistant pathogens may surpass the mortality caused by cancer in the near future. There is a need for immediate action.

A two-front strategy is necessary: (i) developing new antibiotics that can act on drug-resistant strains and (ii) understand the molecular mechanisms that govern the emergence of antibiotic resistance.

A major research focus of Dr. Krishna Kurthkoti, DBT Ramalingaswami Faculty Fellow at RGCB is to understand how bacteria develop resistance to antibiotics. The study was conducted using *Mycobacterium smegmatis*. The bacterium is closely related to the causative agent of tuberculosis infection.

It has been well established that antibiotic treatment to bacterial culture kills >99% of bacteria leaving behind a minor population called persisters. It is found that under antibiotic treatment, the mycobacterial persisters develop antibiotic resistance through changes in the genetic material (mutation). These mutations are brought about by activating a bacterial error-prone DNA polymerase. Further analysis revealed that the persister population displayed high levels of reactive oxygen species that have been reported to induce the error-prone polymerase. By eliminating the error-prone polymerase through genetic manipulation, we could drastically reduce the emergence of antibiotic resistance in persisters. Interestingly, homologs of the error-prone systems observed in mycobacteria are present in other bacteria and have been implicated in the development of drug-resistance.

The results of Dr. Kurthkoti's study indicate that inhibition of the error-prone polymerase during antibiotic therapy would significantly reduce the rate of emergence of drug resistance. The findings of the study have been presented in the EMBO TB Conference held at National Institute of Immunology, New Delhi between 11-15th February 2020.

Contact Person Name: Dr. Anish N. P.

Email: anishnp@rgcb.res.in

Phone Number: 0471 2529693