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Countering bacterial antibiotic resistance

Uropathogenic Escherichia coli (UPEC) causes urinary tract infections, e.g., cystitis, which are treated by gentamicin. The protein ss, encoded by the rpoS gene, controls E. coli general resistance. We discovered that rpoS deletion renders UPEC more sensitive to Gm and other bactericidal antibiotics, and proteomic analysis suggested a weakened antioxidant defense as the reason. Reactive oxygen species (ROS) detectors (psfiA gene reporter and appropriate chemicals) indicated greater ROS generation by Gm in the mutant. Gm treatment along with an antioxidant, or under anaerobic conditions (that prevent ROS formation), decreased drug lethality. Treating UPEC infection of mice bladder corroborated these findings in vivo. Thus, oxidative stress produced by insufficient quenching of metabolic ROS accounted for greater sensitivity of the mutant. E. coli strains missing antioxidant proteins also generated greater ROS and were also more sensitive to Gm. These lacked the ROS quencher proteins, (e.g., SodA/SodB; KatE/SodA), or the pentose phosphate pathway proteins, which provide NADPH (e.g., Zwf/Gnd; TalA) required by the quenchers. Use of a microfluidic device indicated that the results applied to a single cell level. Gm is known to kill a cteria by inhibiting protein synthesis, but UPEC has developed resistance to this mode of killing. Therefore, these findings provide a timely means of restoring Gm effectiveness by curbing antioxidant proteins. Using bioinformatic approaches, we have identified several small molecules that inhibit these proteins and can enhance Gm effectiveness. In space flights, astronauts often suffer from cystitis. Bacterial gene regulation can differ in normal vs. microgravity (MG) experienced during space flights. However, the "EcAMSat" Stanford/NASA mission showed that ss-controls Gm resistance also in MG. EcAMSat employed a free- flying "nanosatellite" equipped with a highly sophisticated microfluidic system for autonomous determination of UPEC sensitivity to Gm and its telemetric transmission in real time during space flight to Earth. Bacterial multidrug resistance (MDR), such as the one regulated by the emrRAB operon and the EmrR protein is a major public health problem. Its activation is due to alteration in the EmrR protein structure, which too can be prevented by small molecules and bioinformatic approaches that we have pursued.

Biography:

Dr. AC Martin is a professor of Microbiology and Immunology from Stanford University School of Medicine. He was born in USA and completed his PhD in the year 1969 in the field of microbiology from University of California, Los Angeles. Professor Martin is having a teaching knowledge of around 55 years. He is an active member for many microbiological and immunological societies and association. Professor Martin received the Fulbright Scholar award in the year 1964-1971. He is the author for 142 publications along with few patents. He has been a part of many scientific conferences during his teaching and educational career. He had received the funding from reputed organization for his research work. His current research interest includes immunology, Microbiology, Cancer, Genetics studies etc. Currently Professor Martin is working on Exosome (EV) project and also on the Extension of the ongoing antibiotic work.

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