Citation

Citation (Brief Summary) for the research work submitted for Sun Pharma Science Foundation Science Scholar Awards-2024

Title: *Salmonella* Typhimurium employs spermidine to exert protection against ROS-mediated cytotoxicity and rewires host polyamine metabolism to ameliorate its survival in macrophages

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Summary: A substantial duration of the infection cycle of *Salmonella* involves the macrophages, which present a very hostile environment to the bacteria. However, *Salmonella* is able to survive and proliferate within host macrophages and utilizes it to disseminate to secondary sites of infection. Our study identifies a novel strategy employed by *Salmonella* Typhimurium to counteract oxidative and nitrosative stress within the host macrophages. We demonstrate that spermidine is a critical regulatory molecule in *Salmonella* that regulates multiple antioxidative pathways (*rpoS* mediated *katE*, *soxR* mediated *sodA* and *sodB*, and *emrR* mediated *gshA*) along with a novel antioxidative enzyme (GspSA) in *Salmonella*, to prevent oxidative damage and assist in its virulence in mice. It further rewires host polyamine metabolism using *Salmonella* Pathogenicity Island (SPIs) encoded effectors (SPI-1 and SPI-2 effectors) to prevent nitric oxide production and enhance its survival. To this, we developed an alternative therapeutic strategy. We used an FDA-approved drug, DFMO, which is used in the treatment of human parasite infections and cancer. Our study shows that very low doses (compared to treatment in cancer) of this drug DFMO, can clear *Salmonella* infection in mice. The drug blocks spermidine synthesis in the host (here, mice) and is able to curb pathogen infection, increasing the survival of infected mice.

Citation as PubMed:

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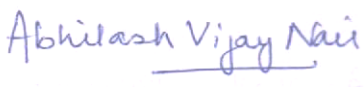

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