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Potential Application of Nitrate reductase as biomarker in identifying novel inhibitors against *M.tuberculosis*

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Mycobacterium tuberculosis, the most important life- threatening bacterial pathogen is responsible for three million deaths annually. Latency in tubercle bacilli has been found as principal cause for long duration of treatment as well as development of resistance. Identification of dormant stage inhibitors could demonstrate desirable effect on eradication of tuberculosis. For past few years, we are involved in developing novel screening tools using respiratory type nitrate reductase (NarGHJI) as biomarker. A significant increase in NarGHJI activity is observed during transition from aerobic to anaerobic dormant stage. We had earlier developed an *in vitro* whole cell based high throughput assay for anti-tubercular screenings. A similar pattern of bacilli dependent conversion of nitrate to nitrite was found to occur during its residence within human Thp1 macrophages. Nitrate reduction by *M. tuberculosis* represents the count of viable bacilli within the host. This screening protocol is also validated on a small set of in-house library. We are able to screen a small in-house library to evaluate these protocols. One of the scaffolds identified from these screens belong to 1,2,4 trozole class of compounds. Altogether, the host cell based assay provides advantage of picking up pro-drug like molecules simultaneously keep apart the false actives which can be easily metabolized. This presentation discusses the developments of whole cell based assays by using nitrate reductase, screenings, identifying novel inhibitors and their target.

Biography

Dhiman Sarkar completed his Ph.D from Jadavpur University and then joined AstraZeneca R & D Bangalore, India. As Research Scientist, he was associated with different projects on anti-tubercular and anti-malarial developments in AstraZeneca (1996 to 2002). He joined National Chemical Laboratory (CSIR-NCL) as senior scientist with the responsibility of developing a screening facility and currently, he is Principal Scientist and Head, Repository of Small Molecules at National Chemical Laboratory, a premier laboratory within CSIR, India. He has published more than 14 papers in peer reviewed journals.