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Novel high throughput macrophage based screening assay to identify anti-Shigella drugs

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Shigella infections cause more than 200,000 deaths per year, being most of these deaths in children in low income countries. Current treatments of choice for Shigella-caused severe diarrhea and dysenteria include Ciprofloxacin, Azitromycin, Pivmecillinam and Ceftriaxone; however, in the last decade the development and spread of resistance against most antibiotics poses a challenge in controlling shigellosis morbidity and mortality.Shigella is a highly virulent bacterium which colonizes the gastrointestinal epithelium by transferring from the apical to the basolateral site through M cell invasion followed by macrophage phagocitosis. Shigella induces macrophage apoptosis and is released at the basolateral site of the intestinal epithelium where it invades epithelial cells and spreads. Current phenotypic assays available for Shigella include MIC determination in its extracellular context, but a better surrogate of the infection course in order to identify differentiated hits is desirable. Here, we present the standardization and validation of a high throughput screening macrophage based assay using THP-1(human monocytic cell line) in 1536 plate format with a luciferase based readout , which allows rapid screening of large compound collections. This methodology opens new avenues for antimicrobial drug discovery and development of novel medicines to treat shigellosis.

Biography

Working as a GSK scientist for 26 years in different therapeutic areas: Antibacterial, antifungal, Cancer and Malaria, Collaborating with other authors in more than 25 publications in different journals. Currently part of the unit of enteric diseases where as part of its role is the development of new tools for HTS.

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