

There is a pressing unmet need for new antibiotics, particularly for Gram-negative bacterial pathogens. To identify probes of the host-pathogen interface that may have antibiotic potential, we developed a quantitative, high throughput, phenotypic screen for small molecules that prevent the growth of *Salmonella enterica* in macrophages, a kind of white blood cell that kills non-pathogenic bacteria. We screened the 14,400 compounds of the Maybridge HitFinder Library, a collection of compounds with drug-like properties. This approach identified 70 compounds that reduce bacterial load but were not previously known to have antibacterial activity. We verified 60 of the hits in a secondary screen that quantifies bacterial colony forming units by plating lysed macrophages. Only three of these hits inhibited bacterial growth in standard microbiological media, indicating the remainder function specifically in the context of an infected macrophage. I will describe the screening platform and present the results of our recent studies characterizing top hits.