Salmonella cause 1.4 million cases of gastroenteritis and enteric fever per year in the US and lead all other foodborne bacterial pathogens as a cause of death. The most serious Salmonella disease results from extraintestinal infection and bacteremia. The hallmark of these systemic infections is the ability of Salmonella to survive in macrophages, which normally kill bacteria by producing a variety of antimicrobials, including superoxide and other reactive oxygen species. Salmonella resistance to the oxidative burst of phagocytes requires periplasmic Copper/Zinc co-factored superoxide dismutase (SodC), which detoxifies superoxide. I will discuss our structure/function analyses that define the properties of SodC that are critical for protection, as well as our studies to define the bacterial targets of phagocytic superoxide.