**Salmonella Typhimurium Induces Immune Paralysis in Human Peripheral Monocytes**

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LPS tolerance, a well-described phenomenon, is characterized by immune paralysis. Recent studies suggest that this paralysis occurs due to metabolic reprogramming and epigenetic changes in immune cells after an initial stimulus, leading to anergy and an inability to respond to subsequent stimuli. This process is a form of innate immune memory. This study aimed to investigate whether *Salmonella* Typhimurium can induce changes in innate immune cells, specifically exploring its capacity to elicit either trained immunity or tolerance. Using an *in vivo* protocol for trained immunity, human adherent monocytes were isolated from multiple donors and stimulated with live and heat-killed strains of *Salmonella* Typhimurium. Following a wash and a six-day resting period, the monocytes were re-stimulated with LPS and Pam3Cys. Pro-inflammatory cytokines were measured from supernatants at various time points. Additionally, lactate production, a key metabolite in these processes, was assessed. The findings indicate that *Salmonella* Typhimurium induces tolerance in human adherent monocytes, as evidenced by a lack of response to the second stimuli. This non-responsiveness is physiologically significant, as it may prevent tissue damage during sepsis by curbing excessive inflammatory signals. These findings may have significant implications for the management of sepsis and other conditions characterized by dysregulated immune responses.