

TITLE: CLINICAL *SHIGELLA* STRAINS: INFLAMMATORY PATTERN BY mRNA EXPRESSION IN A MURINE MODEL

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ABSTRACT

Shigellosis is a bacillary dysentery caused by *Shigella*, a gram-negative intracellular human pathogen. The most common experimental model to evaluate immune response against *Shigella* is pulmonary mice infection due easy manipulation and similarity to gut colonization. We performed an epidemiological study with children ranging from 0-10 years with acute diarrhea who attend public hospital during 2007 to 2009. Of all bacteria isolated, *Shigella* was the fifth most common pathogen associated with diarrhea. At this study, we analyzed immune response expression of 4 *Shigella* clinical strains isolated from pediatric shigellosis at murine pulmonary invasion after 24 and 48h infection. In order to select *Shigella* isolates used in this study were performed a PCR with the main virulence genes of *Shigella* and choose 4 strains by its virulence pattern. After pulmonary infection, mRNA expression were analyzed using multiplex quantitative PCR Biomark Platform (Fluidigm) and results were analyzed in statistical software R. As main results, all clinical strains displayed a moderate mRNA expression in 24h infection which was then enhanced at 48h, while M90T standard had opposite regulation with lower mRNA rates in 48h infection, suggesting major differences between well characterized standards and clinical strains. Immune response of #14 strain had its focus at INF- γ while #27 was associated with TNF- α , both related to acute inflammatory response and macrophage activity. Presence of IL-17 higher expression in #27 strain demonstrates a possible association with the induction of Th17 cells. The immunological potential of strain #27 may have relationship with *Shigella* enterotoxins (shET1A, shET1B, and shET2). The immunological potential of strain #27 may have relationship with *Shigella* enterotoxins (shET1A, shET1B, and shET2). Enterotoxins presence was confirmed by PCR and results shows this complete set is absent in all other strains studied. The differences between clinical strains and standards were evident at this study. Clinical strain #27 appears as a great candidate to future studies and may provide new perspectives about differences among invasion and immune response seen in the clinical practice

Keywords: Clinical *Shigella*; mRNA Expression; Murine Model

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