Posters

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Human Lactoferrin and the Siderophore Aerobactin Independently Impact Intestinal Invasion by Neonatal Escherichia coli Bacteremia Isolates

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Human Lactoferrin and the Siderophore Aerobactin Independently Impact Intestinal Invasion by Neonatal *Escherichia coli* Bacteremia Isolates

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Background

E. coli is a major cause of neonatal sepsis

After ingestion, *E. coli* translocates the neonatal gut causing bacteremia

E. coli virulence depends on iron acquisition mechanisms, including siderophore systems

Lactoferrin (LF) protects against neonatal sepsis through immunomodulatory and antimicrobial effects which include iron chelation

It is not known whether siderophores in neonatal *E. coli* strains have an impact on LF's effects on bacterial invasion and survival in intestinal epithelium.

Objective

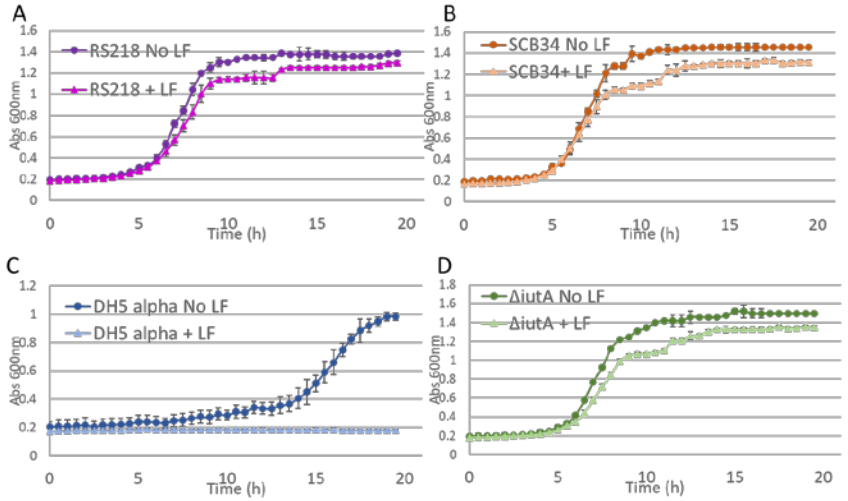
To investigate the effects of human LF and the siderophore aerobactin on intestinal invasion and survival of septicemia-producing neonatal *E. coli*.

Methods

- Neonatal *E. coli* septicemia isolates RS218 and SCB34, and the nonpathogenic laboratory strain DH5α were first compared in their ability to grow in liquid media with 1 mg/mL human lactoferrin (LF) by measuring optical density over 20 h at 37°C.
- A deletion mutant in SCB34 lacking the aerobactin siderophore receptor gene *iutA* (*ΔiutA*) was also tested.
- Invasion of T84 intestinal epithelial cells was compared between SCB34 and *ΔiutA* using a modified gentamicin protection assay
- Invasion was assessed in the presence of 1 mg/mL LF at the time of infection, and after overnight incubation of T84 cells with 1 mg/mL LF.

Results

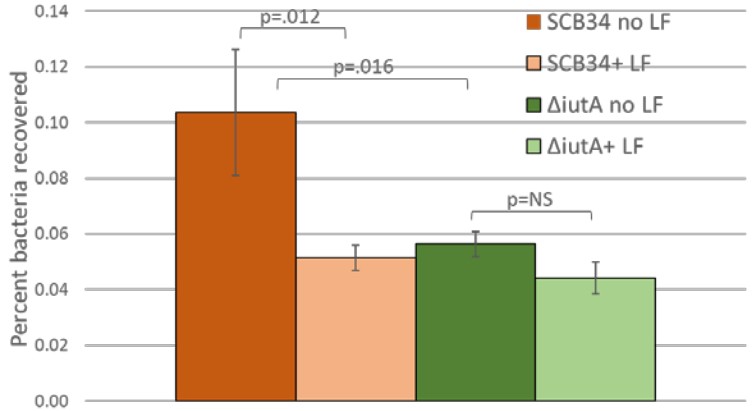
Lactoferrin Impairs the Growth of Neonatal *E. coli* Bacteremia Isolates



Automated optical density growth curves show decreased growth in the presence of lactoferrin (LF) for the neonatal *E. coli* bacteremia isolates RS218 (A), and SCB34 (B) and its corresponding *iutA* deletion mutant, *ΔiutA* (D). This effect was greater for the nonpathogenic DH5α strain (C). Two-tailed T-test P value <.001 for mid-logarithmic and stationary phases comparisons, A-D.

Results

Lactoferrin Decreases Intestinal Invasion of Neonatal *E. coli* Bacteremia Isolate SCB34



- LF pretreatment of T84 intestinal cells prior to infection significantly reduced the recovery of live bacteria from within intestinal cells.
- Addition of LF at the time of infection did not affect invasion and recovery of live bacteria, confirming that *E. coli* does not undergo substantial growth prior to invasion in this model (not shown).
- Invasion by *ΔiutA* in LF-untreated T84 cells was significantly reduced compared to WT SCB34 and decreased further in the presence of LF, although the difference was not statistically significant.

Conclusions and Future Studies

- LF significantly impairs growth of neonatal *E. coli* clinical isolates but does not completely abolish it.
- LF also decreases neonatal *E. coli* intestinal epithelial invasion.
- The effect of LF in decreasing intestinal invasion was independent of the function of the siderophore aerobactin, which by itself is necessary for invasion.
- The iron-dependent mechanisms determining host-*E. coli* interactions are potential therapeutic targets against neonatal sepsis.