Dissecting immune responses against iNTS

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Risk factors of iNTS disease in African children

- Infancy
- Malaria
- Malnutrition
- HIV

• Median age 13 months
• 80% of cases were <2 yrs

Nyirenda TS, JID 2014
Morpeth SC, CID 2009
Immunity to *Salmonella* is complex

Hypothetical (Mouse work)

Adapted from Mastroeni P, Curr Mol Med 2002
Antibody mediated serum immunity to NTS in Malawian children

MacLennan CA, JCI 2008
Hypothesis 1

CD4+ T cell immunity to NTS develop in parallel to antibody immunity in the first 2 years of life

Method

• Cross section study
• Healthy children (n=80, age 0-60 months)
• CD4+ T cell ICS; IFN-γ, TNF-α, IL-2
• Serum killing and antibody by ELISA
Early acquisition of STm-specific CD4+ T cells

Nyirenda TS, JID 2014
Delayed acquisition of STm D23580 serum killing

- SBA to STm D23580 mainly correlate with IgG antibodies targeting LPS O 4;5

Nyirenda TS, JID 2014
Sequential acquisition of T cells and antibodies to STm is associated with a decline of iNTS cases

Nyirenda TS, JID 2014
Hypothesis 2

*Salmonella* exposure within the GIT facilitates the acquisition of specific-antibody mediated serum killing

Methods

- Cohort study
- Healthy children (n=60, age 6-18 months)
- Stool culture or PCR for *Salmonella* (1 month interval)
  - PCR targets; FliC (STm) and Fimbriea (STy)
- Serum killing (SBA) (3 months interval)
**Frequency of *Salmonella* exposure events**

Stool samples tested (630)
- 29 *Salmonella* detected (culture or PCR)
- 23 culture positive
- 6 PCR only (208 samples tested)
Incidence of *Salmonella* within the GIT

Kaplan-Meier survival estimate

- 47% (22/47) exposed to *Salmonella* at least once within the GIT (6-18 months)
Salmonella exposure within GIT is associated acquisition of potentially protective SBA

Definition: SBA ≥ -1 log 10 (potentially protective)

Age = 6-18 months (N= 229)

Exposed = 35/42

Non exposed = 108/187

OR 3.65  95% CI (1.54, 8.65)
Summary

- Sequential acquisition of T cells and antibodies to STm is associated with a decline of iNTS cases

- *Salmonella* exposure within GIT is associated acquisition of potentially protective SBA

- Children under-two are more vulnerable to iNTS disease and require vaccine intervention
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