

Optimisation of methods in preparation for a human infection model for Group B Streptococcus (the TIMING study)

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Background and study aims

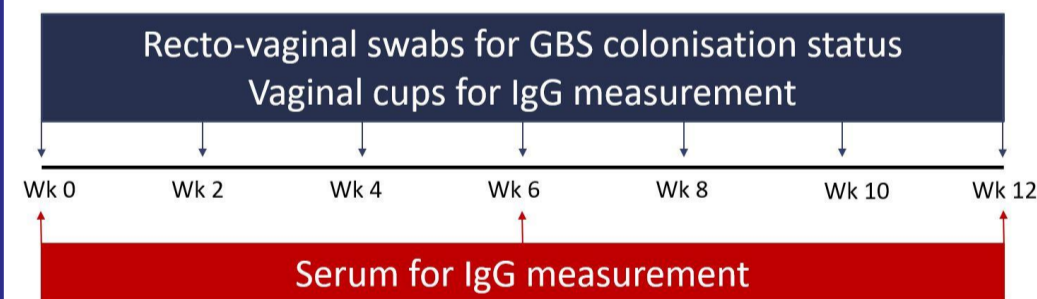
A Controlled Human Infection Model (CHIM) in non pregnant women would be ideal to test the efficacy of a Group B Streptococcus (GBS) vaccine.

TIMING is a feasibility study designed to :

- Develop a method to retrieve vaginal antibodies.
- Optimise a Luminex assay to measure IgG against GBS capsular polysaccharides (CPS).
- Investigate natural colonisation and antibody responses in the vaginal mucosa over time.

Methods

- 70 non-pregnant women were recruited.



- GBS was isolated from recto-vaginal swabs using LIM broth and chromogenic agar, confirmed by MALDI-TOF mass spectrometry. Positive isolates were serotyped by PCR.
- Vaginal secretions were collected from cups by centrifugation. Extraction buffer was added proportionally to the weight of secretions. Antibodies were retrieved in the supernatant after a second centrifugation.
- Serum and vaginal GBS CPS IgG were measured by Luminex. Vaginal total IgG was measured by ELISA.

Results

- Levels of serum specific IgG were higher in colonised individuals than non colonised, but similar in the vagina. The presence of specific antibodies in non colonised individuals show their persistence after pre existing colonisation (Fig.1).
- Levels of serum and vaginal specific IgG were consistent over 3 months (i.e. Fig.2 for Ia CPS IgG in serum) and correlated (Fig.3).

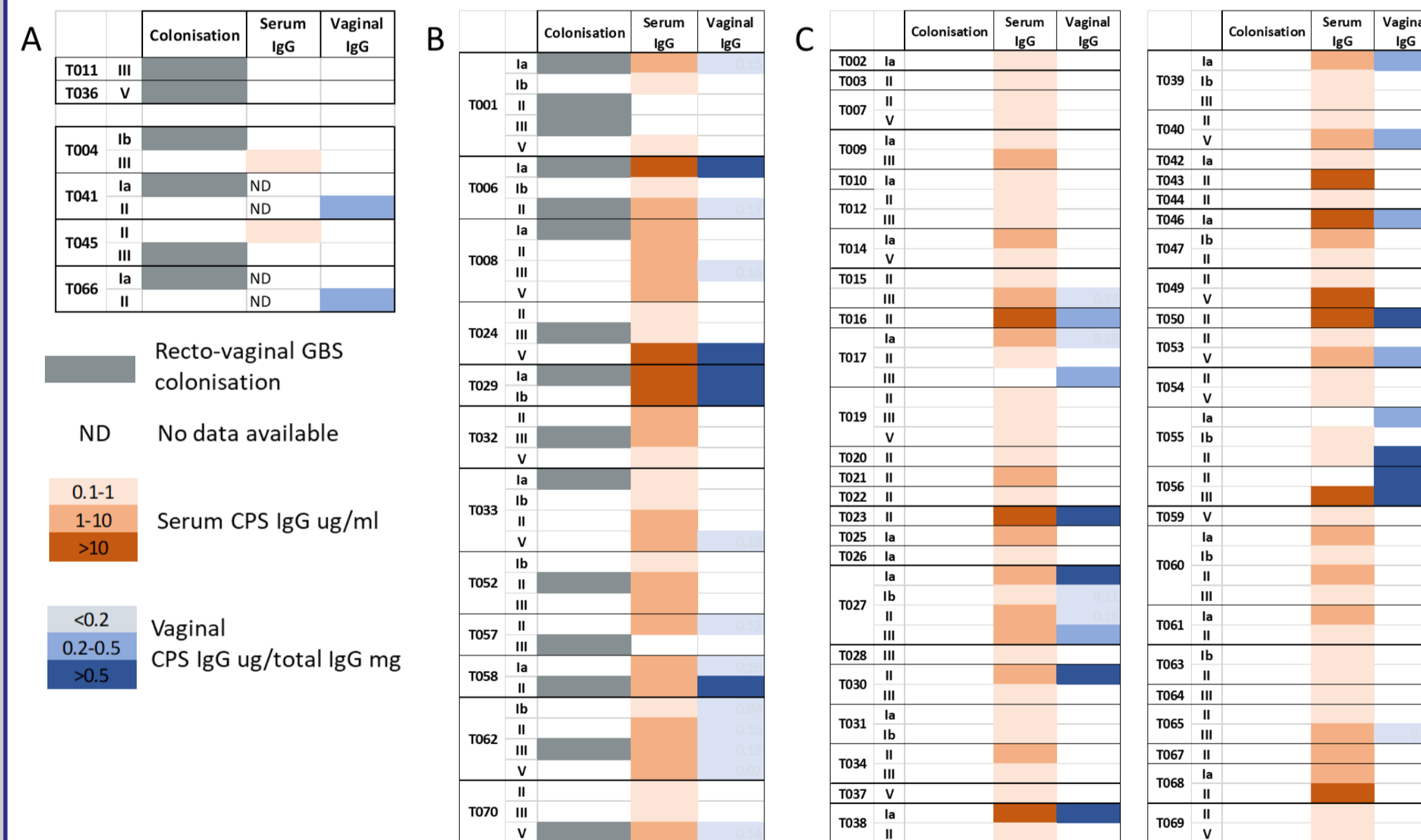


Fig.1: GBS CPS specific IgG present in serum and vagina are not dependent of current colonisation. (A) Heterologous or no antibody in colonised individuals. (B) Homologous antibody levels in colonised individuals. (C) Antibody levels in non-colonised individuals.

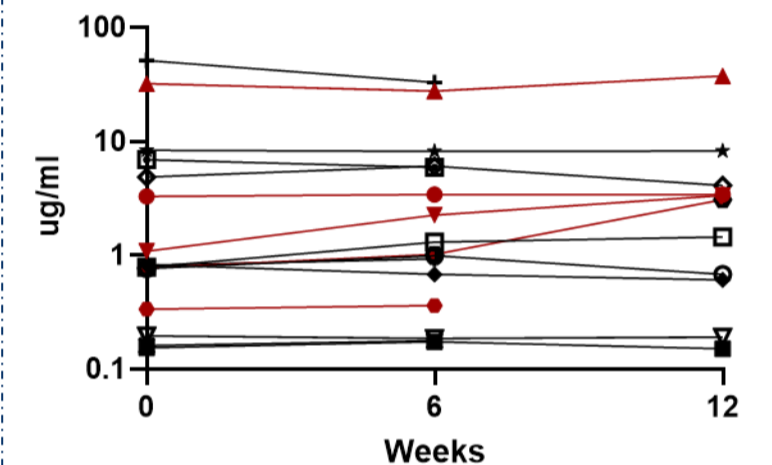


Fig.2: GBS Ia-CPS IgG in serum. In red: individuals colonised by GBS Ia for at least one time point. In black: not colonised by GBS Ia.

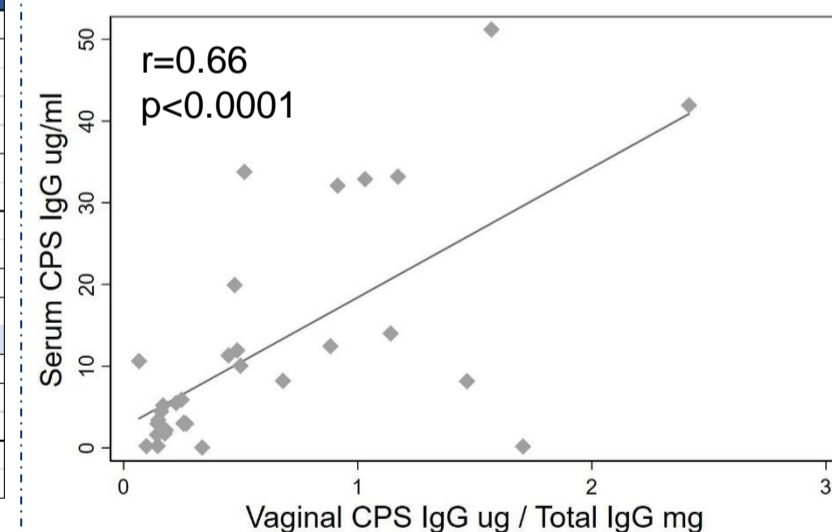


Fig.3: Serum and vaginal GBS CPS specific IgG response correlate.

Conclusion

- A protocol for vaginal antibody elution and a Luminex assay to measure IgG against GBS CPS were successfully developed.
- Specific IgG levels in serum and vagina were persistent and consistent for 3 months. The influence of colonisation will be further investigated.
- Serum and vaginal IgG responses are correlated, suggesting a link between mucosal and systemic IgG responses against GBS.
- A CHIM would enable the study of antibody responses during GBS infection, to investigate the required antibody level to confer protection against infection, and the duration of this protection.