Neisseria lactamica induces anti-*Neisseria meningitidis* B-cell responses

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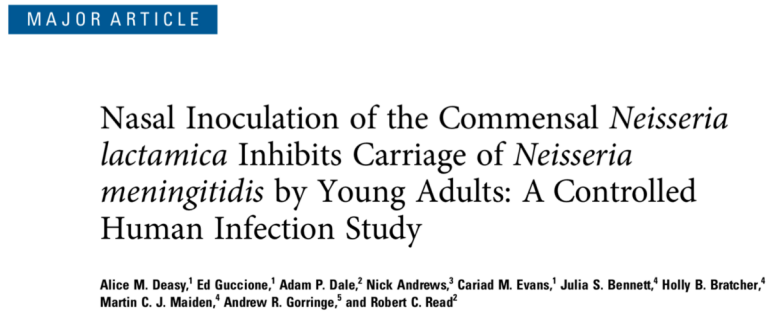
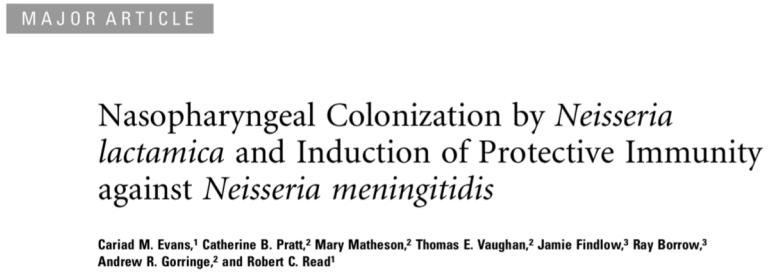
Background:

- There is an inverse relationship between pharyngeal colonisation with *Neisseria lactamica* (Nlac) and *Neisseria meningitidis* (Nmen).
- Controlled human infection with Nlac displaces Nmen and prevents new Nmen colonisation events.
- The mechanism underlying this phenomenon is not yet elucidated. If it was understood, it could be exploited to develop novel strategies to prevent Nmen colonisation +/- disease.
- Nlac colonisation does not induce anti-Nmen serum bactericidal activity (SBA).
- We propose that the induction of cross-reactive adaptive cellular or humoral responses, independent of SBA, may be responsible for observed effect.


MAJOR ARTICLE

Nasal Inoculation of the Commensal *Neisseria lactamica* Inhibits Carriage of *Neisseria meningitidis* by Young Adults: A Controlled Human Infection Study

Alice M. Deasy,[1] Ed Guccione,[1] Adam P. Dale,[2] Nick Andrews,[3] Cariad M. Evans,[1] Julia S. Bennett,[4] Holly B. Bratcher,[4] Martin C. J. Maiden,[4] Andrew R. Gorringe,[5] and Robert C. Read[2]


MAJOR ARTICLE

Nasopharyngeal Colonization by *Neisseria lactamica* and Induction of Protective Immunity against *Neisseria meningitidis*

Cariad M. Evans,[1] Catherine B. Pratt,[2] Mary Matheson,[2] Thomas E. Vaughan,[2] Jamie Findlow,[3] Ray Borrow,[3] Andrew R. Gorringe,[2] and Robert C. Read[1]

Aims:

- To assess whether Nlac colonisation induces anti-Nmen B cell responses.
- To assess whether B cell response frequencies were associated with Nlac colonisation density.

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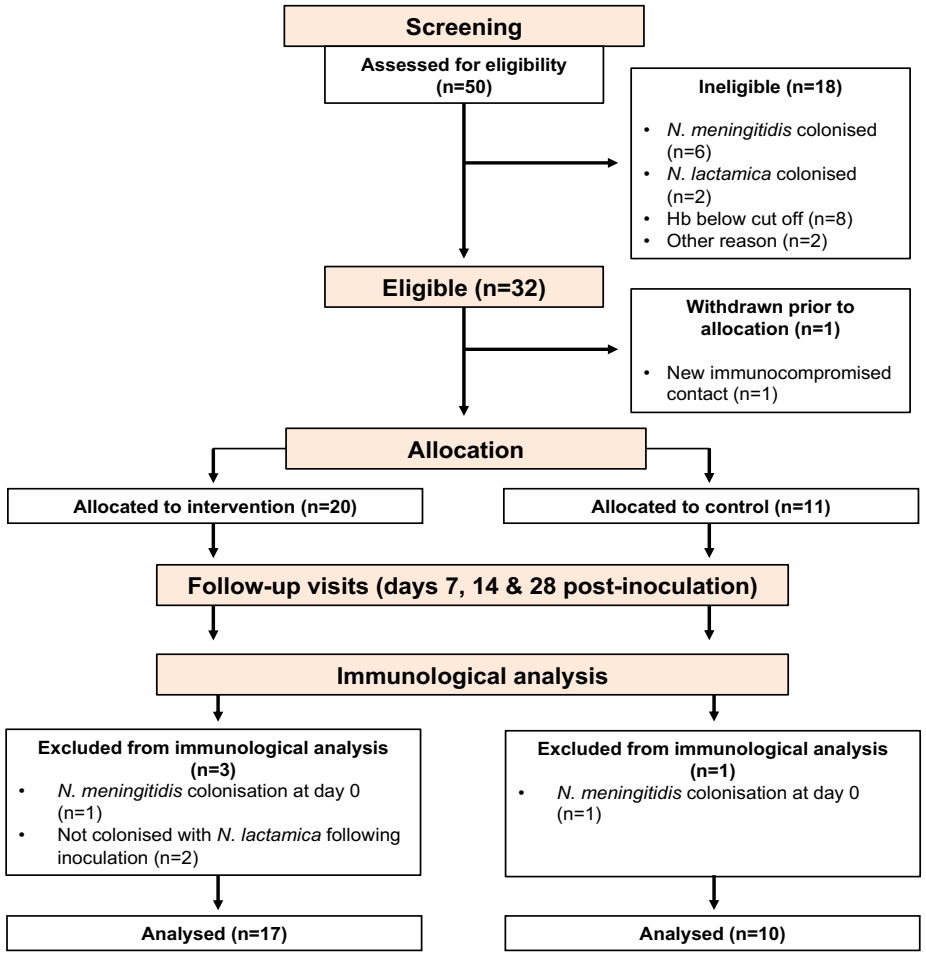
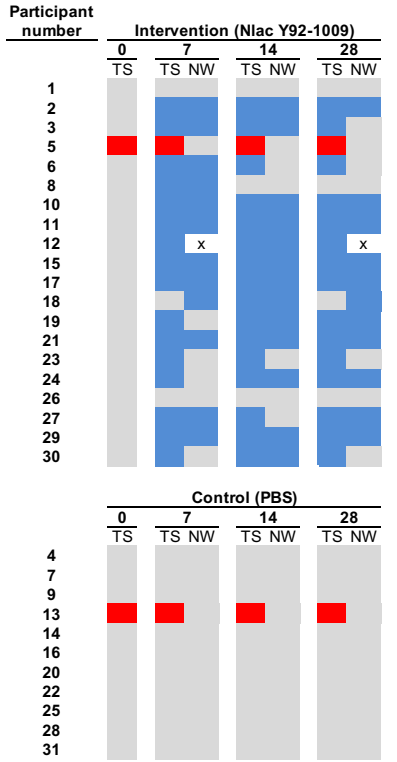
Study design:

- Healthy adults randomised 2:1 to received intra-nasal inoculation with intervention (Nlac, 10^5 CFU) or control (PBS).
- Nlac/Nmen colonisation status assessed at 0, 7, 14 and 28 days (culture of oropharyngeal swab and nasal wash).
- Blood taken at all time points to assess cellular responses.

Study flow diagram:



Nlac/Nmen colonisation:



Key:

Nlac colonised (blue)
Nmen colonised (red)
TS (oropharyngeal swab)
NW (nasal wash)

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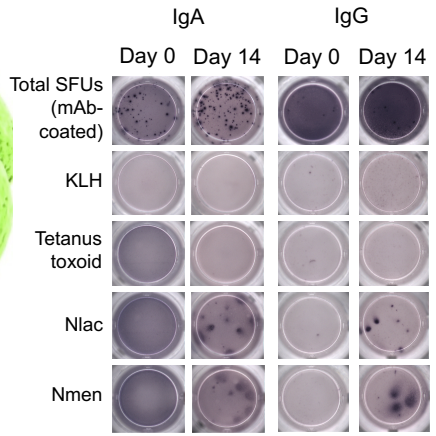
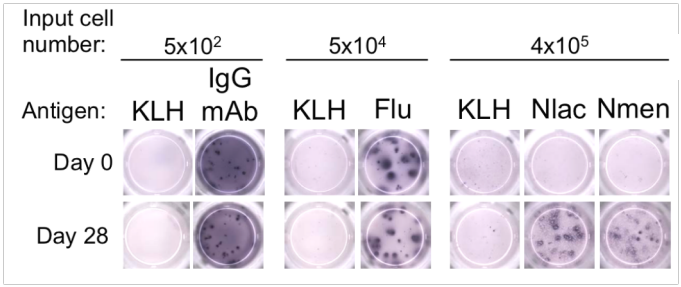
Colonisation with Nlac induces anti-Nmen B_{PLAS} & B_{MEM} responses

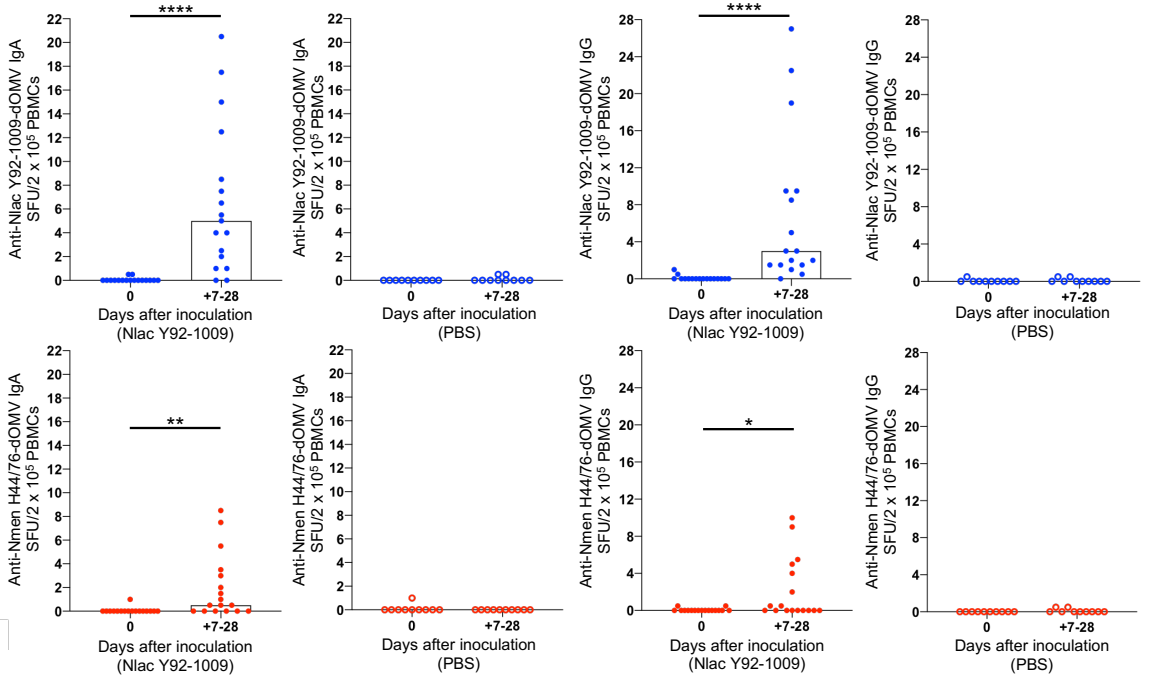
IgA/IgG B_{PLAS} ELISpot



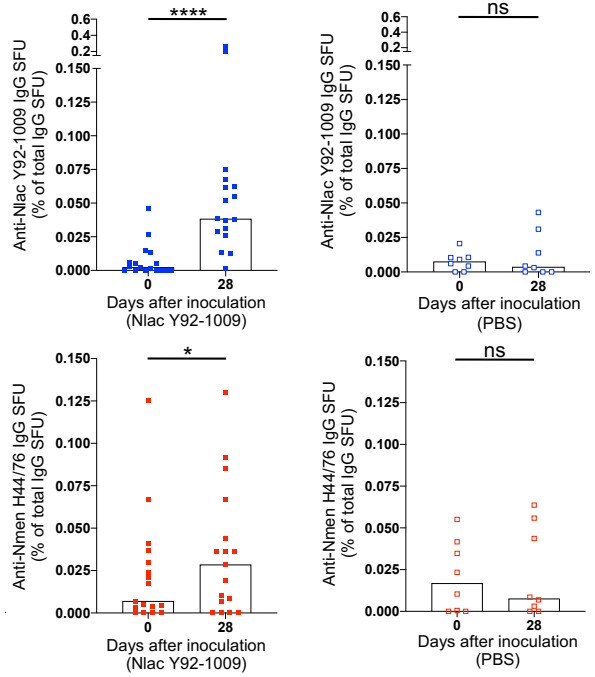
IgG B_{MEM} ELISpot



Collated B_{PLAS} data



Collated B_{MEM} data



* $P < 0.05$, ** $P \leq 0.01$, **** $P \leq 0.0001$ (Wilcoxon matched pairs signed rank test)

Key:

- Keyhole limpet haemocyanin (KLH)
- Nlac (Y92-1009) dOMV (Nlac)
- Nmen (H44/76) dOMV (Nmen)
- Influenza haemagglutinin (H1N1) (Flu)

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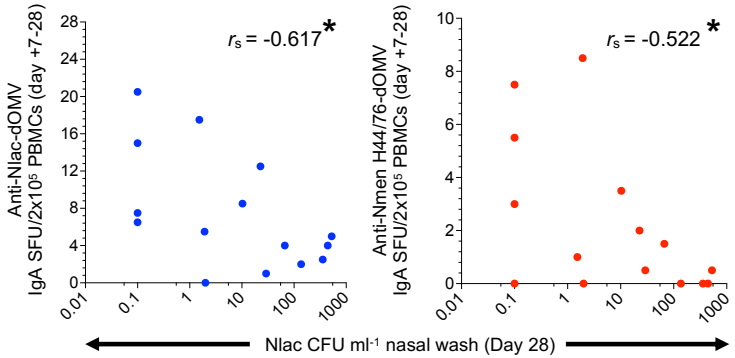
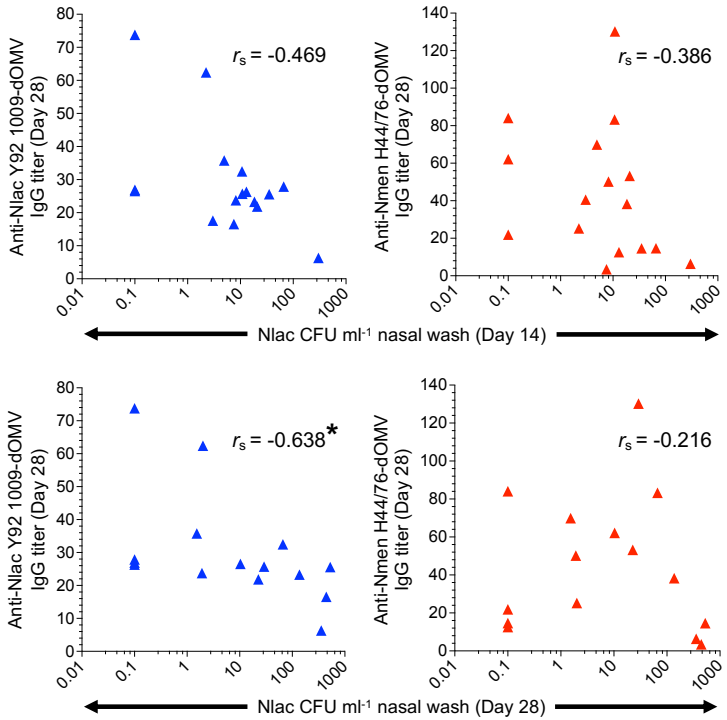
Nlac-specific B_{PLAS} responses and IgG titers are associated with Nlac colonisation density

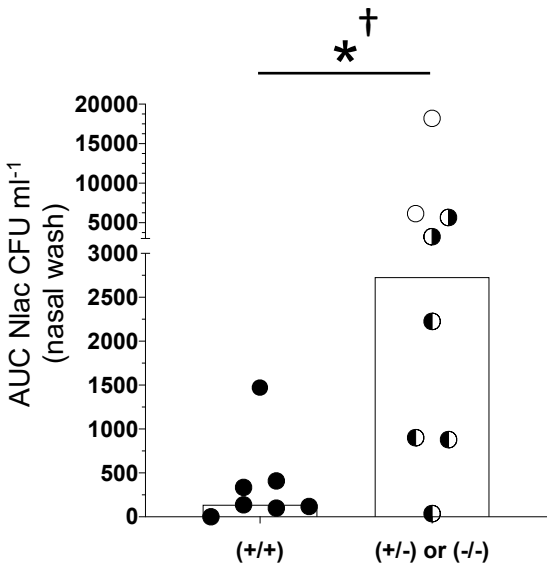
Nlac colonisation density *vs.* **IgA B_{PLAS}** responses



Nlac colonisation density *vs.* day-28 **IgG** responses (plasma)



Nlac colonisation density *vs.* baseline **Nlac/Nmen IgG B_{MEM}** responses



† Mann-Whitney (*P <0.05)

Correlations assessed with Spearman's Rho (r_s) (* $P < 0.05$)

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Conclusions

- Colonisation with Nlac induced B_{PLAS} and B_{MEM} responses specific to Nlac and Nmen, suggesting that the previously observed protective effect of Nlac on Nmen may have an immunological basis.
- Nlac colonisation density negatively correlated with anti-Nlac IgG titers and anti-Nlac IgA-secreting B_{PLAS} frequencies suggesting that the magnitude of these responses may play a role in controlling Nlac colonisation density.
- We predict that protection against Nmen colonisation may only occur in those where Nlac colonisation results in the formation of anti-Nmen B cell and antibody responses.

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