



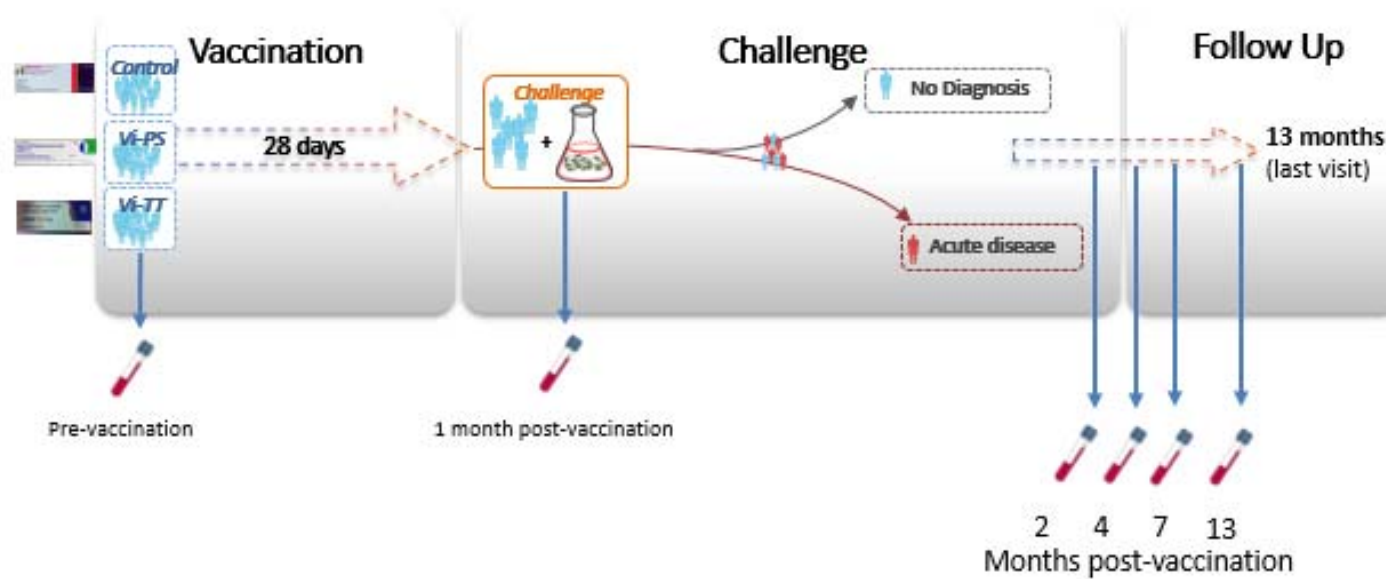
Anti-Vi IgG and IgA Persistence following Immunisation with Vi Conjugate and Polysaccharide Vaccines

Lizzy Jones

27th March 2019

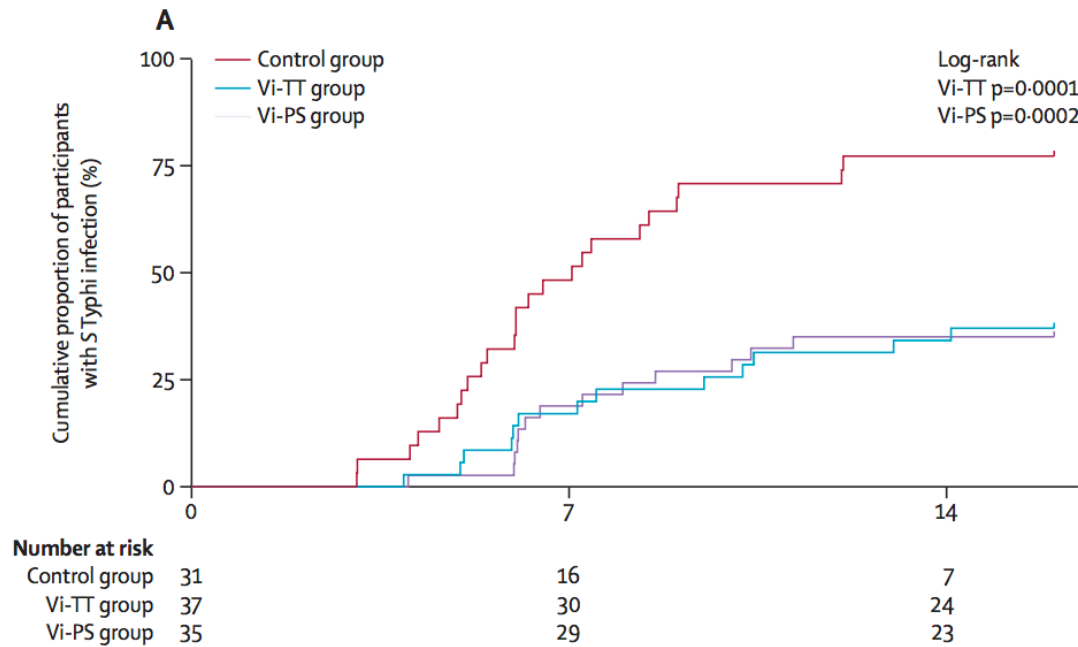
Vaccines Against *Salmonella* Typhi

Oxford typhoid fever
Controlled Human Infection Model (CHIM)



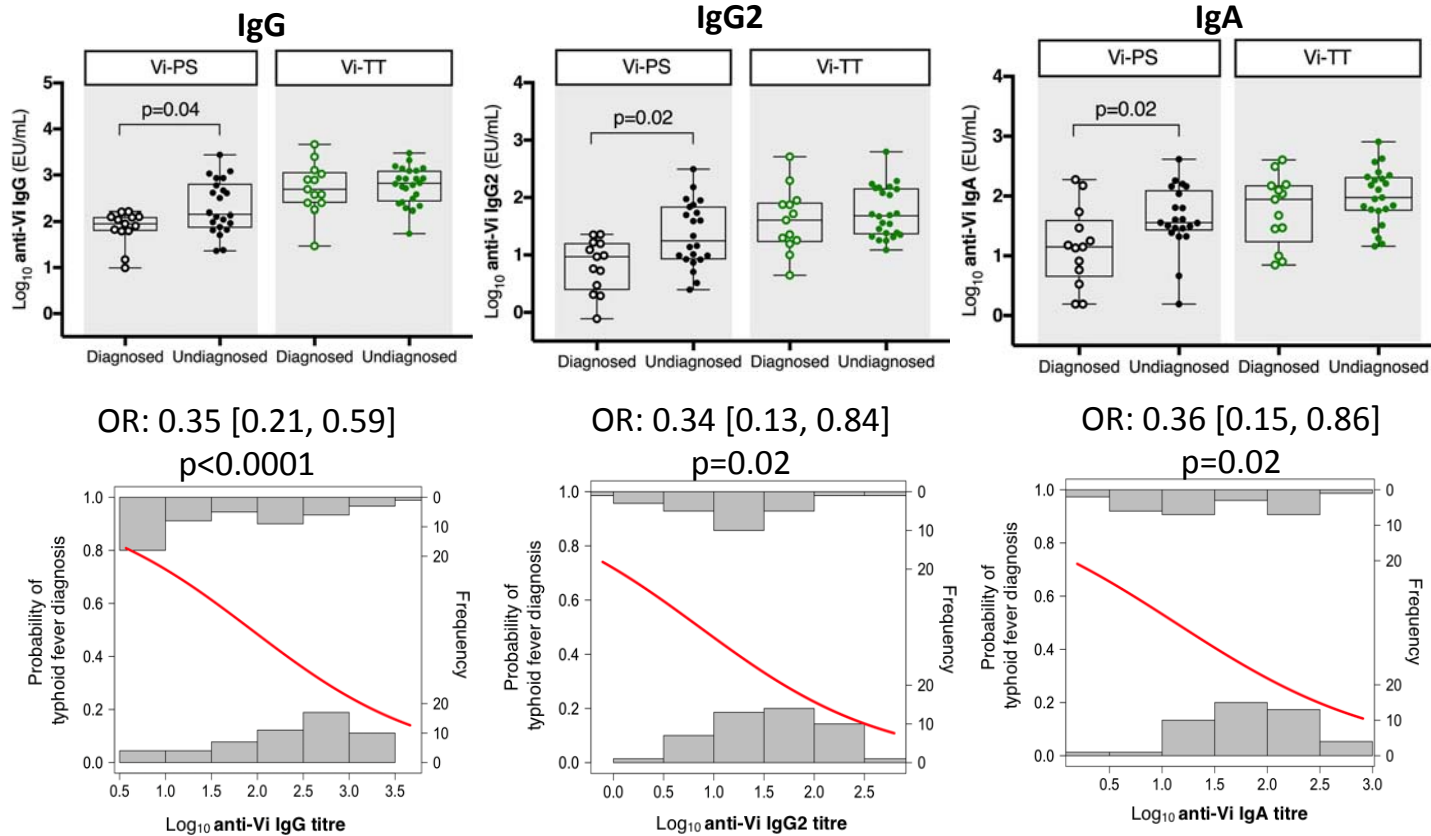
Typhoid Diagnosis defined as fever $\geq 38^{\circ}\text{C}$ for >12 hours or positive blood culture

Vi-vaccination reduces Typhoid Fever cases by >50%



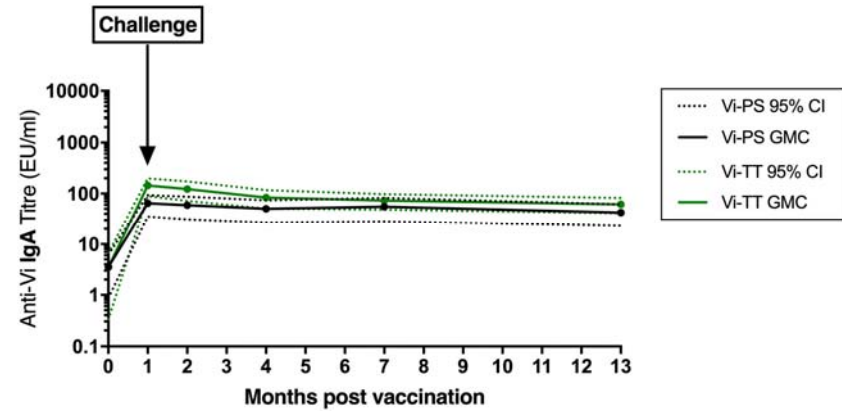
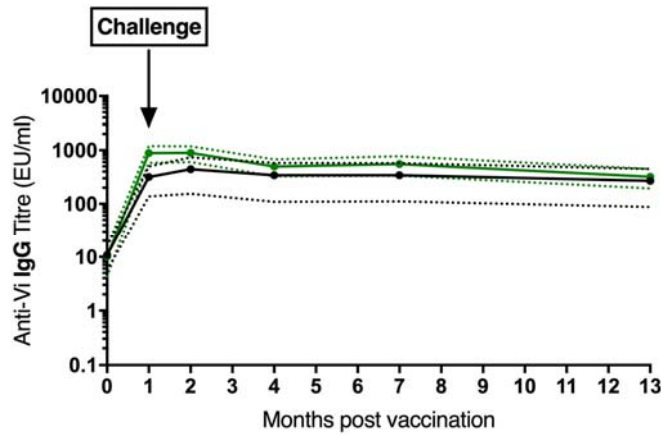
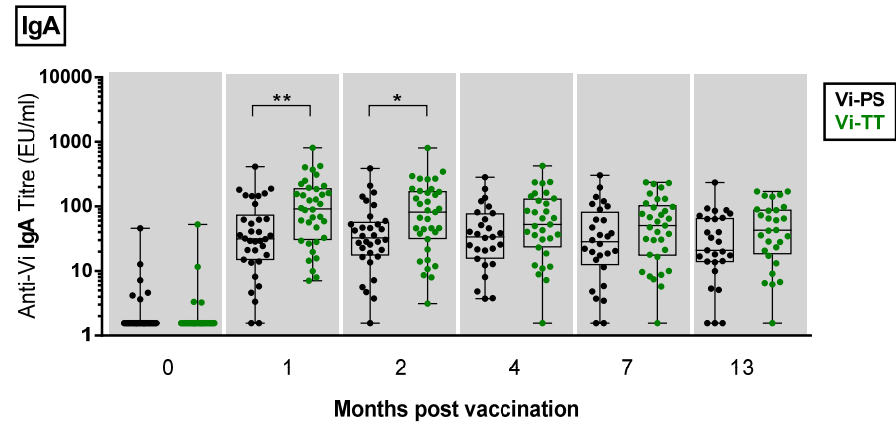
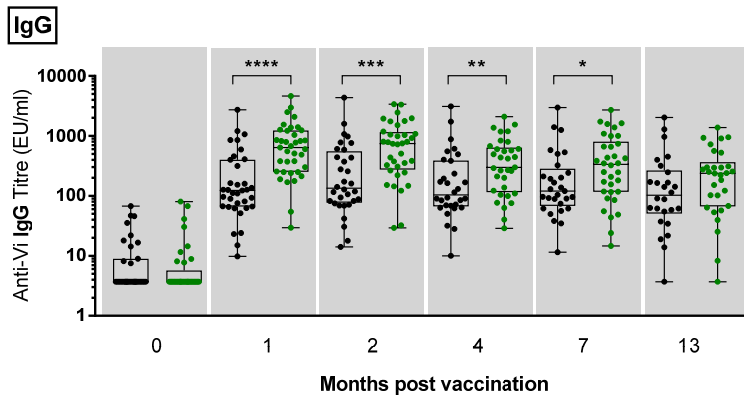
Jin et al., Lancet (2017)

Higher anti-Vi IgG, IgG2 and IgA titres are associated with a decreased risk of typhoid fever diagnosis

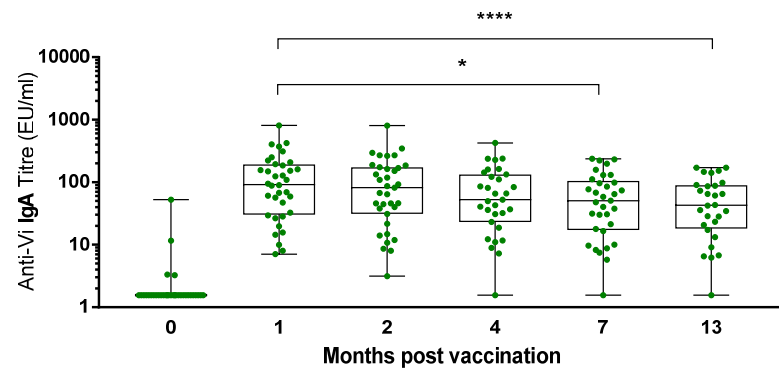
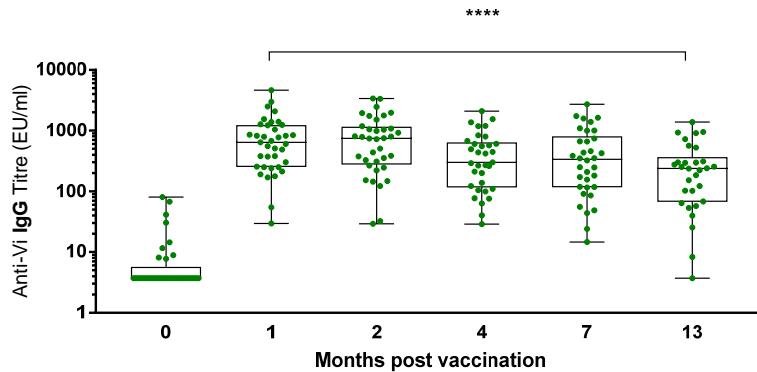
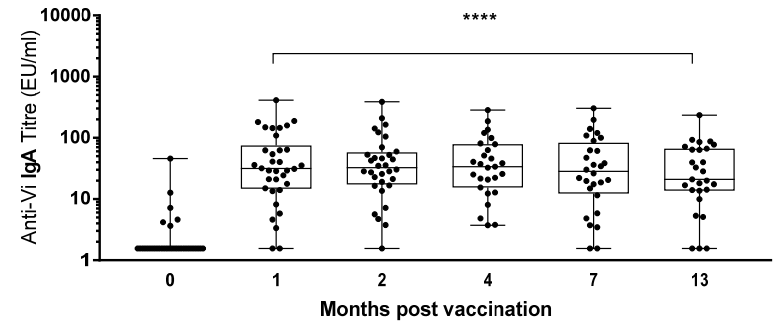
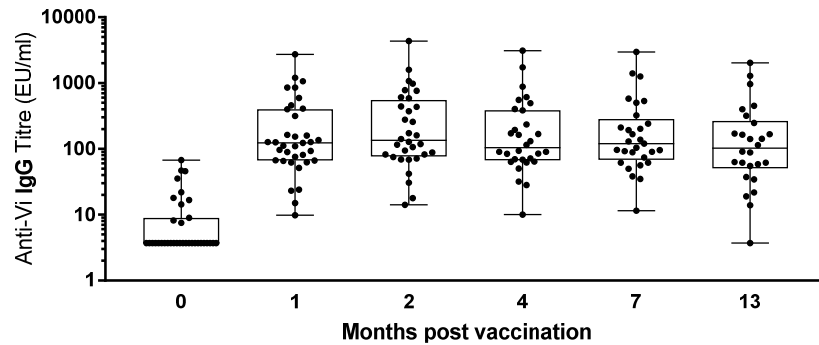


Slide courtesy of Celina Jin

High anti-Vi IgG and IgA titres persist 13 months post Vi-vaccination (no significant difference between Vi-TT and Vi-PS)



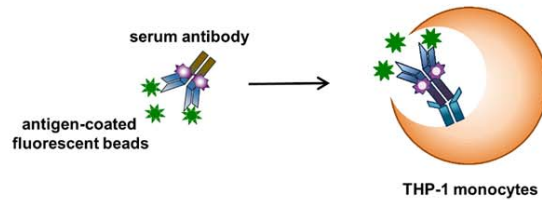
High anti-Vi IgG and IgA titres persist 13 months post Vi-vaccination



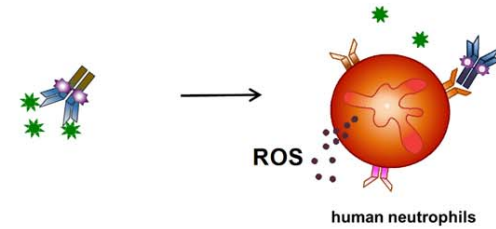
Vi-PS
Vi-TT

Persistence of antibody effector functions in response to Vi vaccination

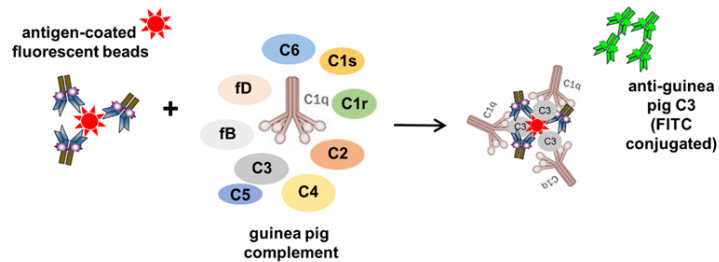
Antibody-dependent cellular phagocytosis



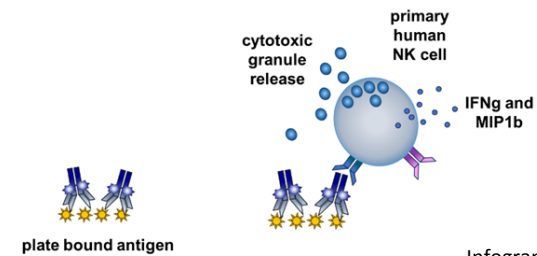
Antibody-dependent neutrophil phagocytosis



Antibody-dependent complement deposition



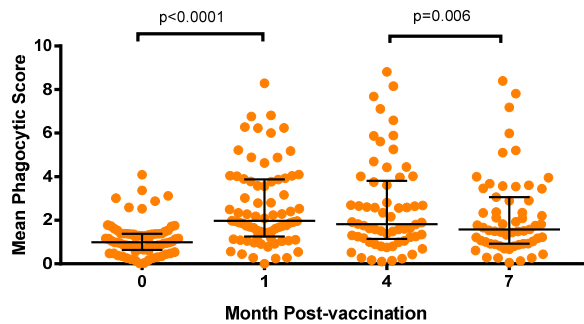
Antibody-dependent NK cell activation



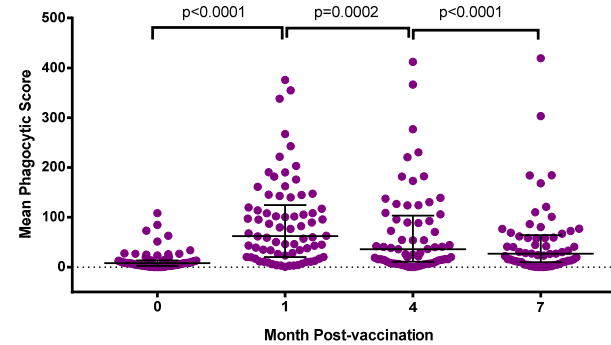
Infographic courtesy of Bonnie Gunn, Ragon Institute.

Long lasting functional antibodies produced in response to Vi vaccination

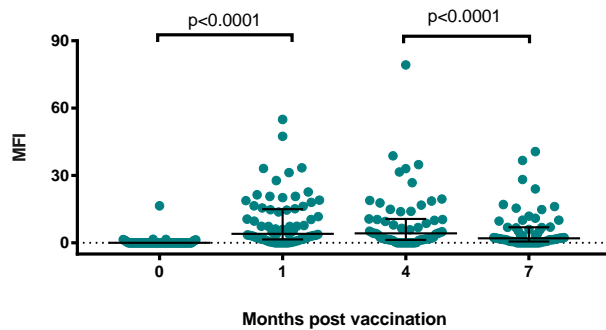
Antibody dependent Cellular Phagocytosis



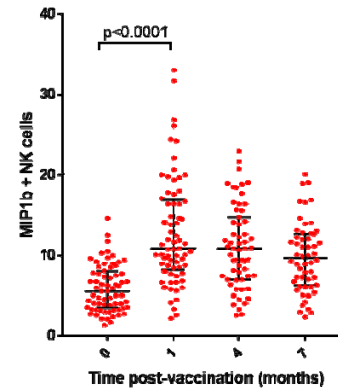
Antibody Dependent Neutrophil Phagocytosis



Antibody Dependent Complement Deposition



Antibody Dependent NK cell Degranulation



Same pattern of NK cell activation when assessing IFN γ and CD107a release

Graphs courtesy of Celina Jin and Jenny Hill



Acknowledgements



Volunteers

OVG Typhoid Study Team

BILL & MELINDA
GATES foundation



Ragon Institute
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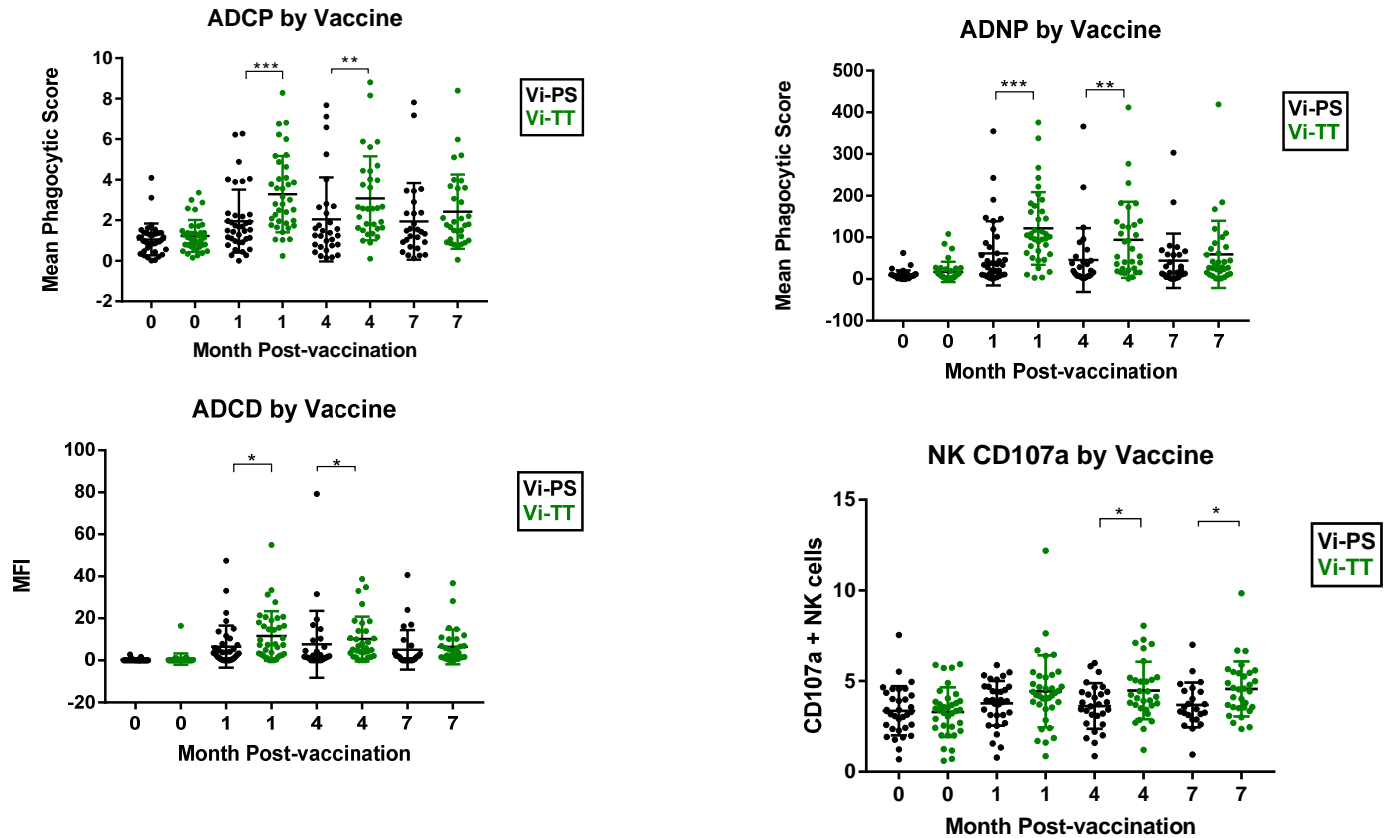


BILL & MELINDA
GATES foundation



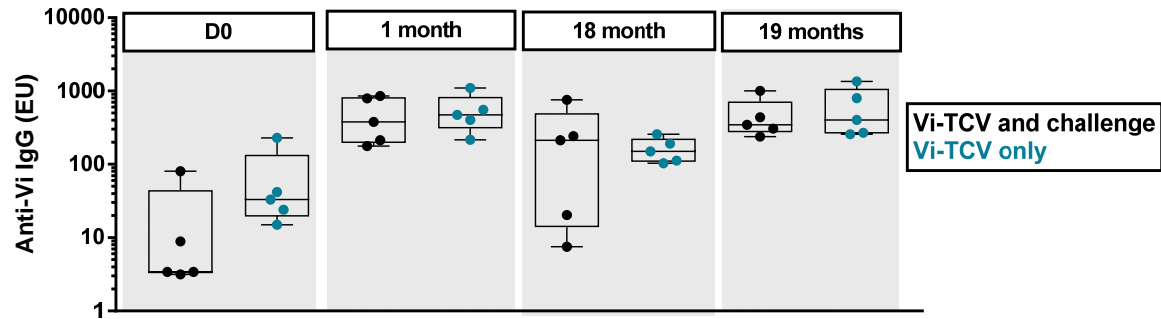
NHS
National Institute for
Health Research

Vaccination with Vi-TT induces higher levels of functional antibody

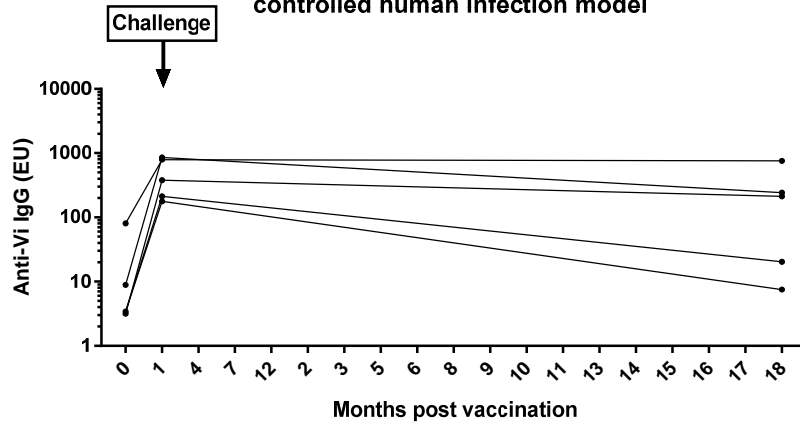


Exposure to *S. Typhi* 1 month after does result in a boost in Vi antibody titres

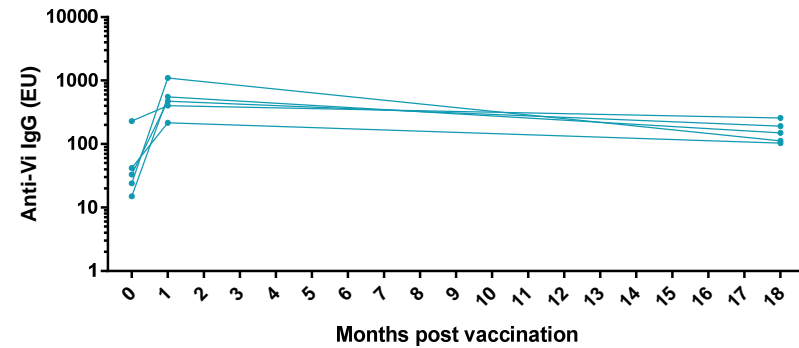
Comparison of antibody persistence in vaccinated and exposed individuals



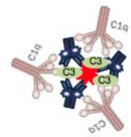
Anti-Vi IgG responses to Vi-TCV in a controlled human infection model



Anti-Vi IgG responses to Vi-TCV in a controlled human infection model



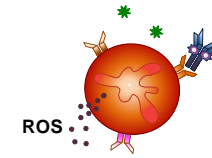
One month post-vaccination, Fc-mediated functional responses are significantly higher in Vi-TT than Vi-PS vaccinees



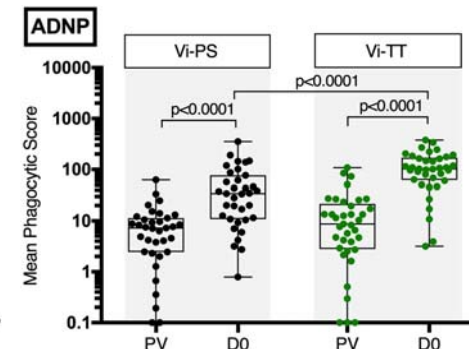
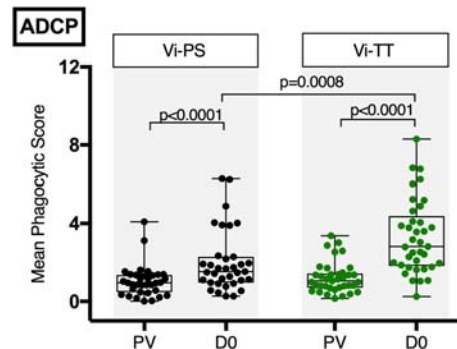
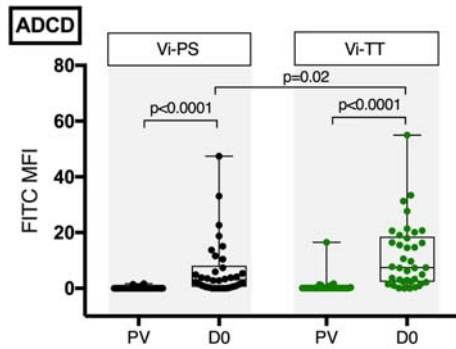
Antibody-dependent Complement deposition



Antibody-dependent Cellular (macrophage) phagocytosis

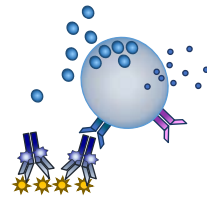


Antibody-dependent Neutrophil phagocytosis

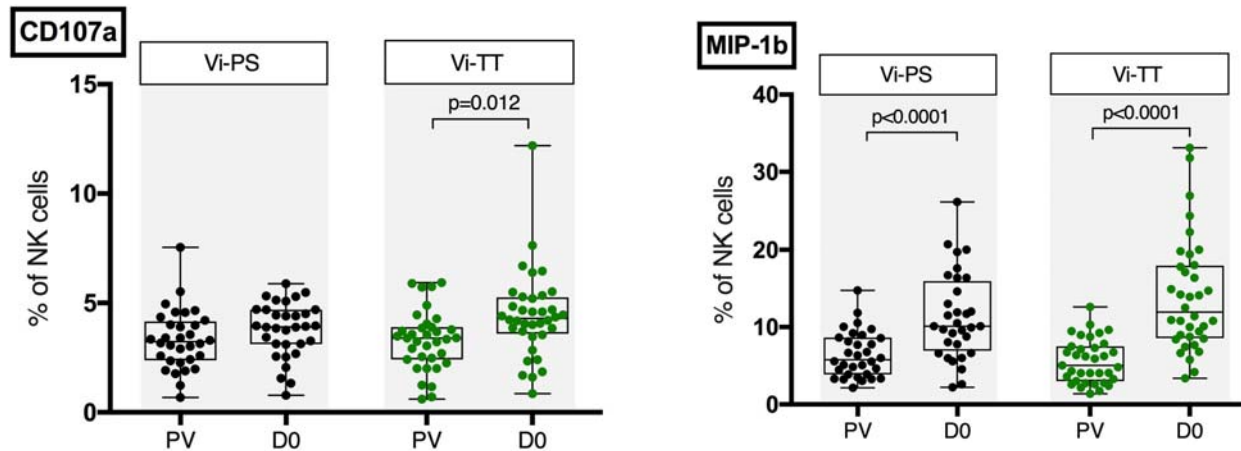


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Vi-TT vaccination increases NK cell degranulation one month post-vaccination in comparison with Vi-PS



Antibody-dependent
NK cell degranulation – CD107a
Chemokine release – MIP-1b
Cytokine release - IFN γ



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