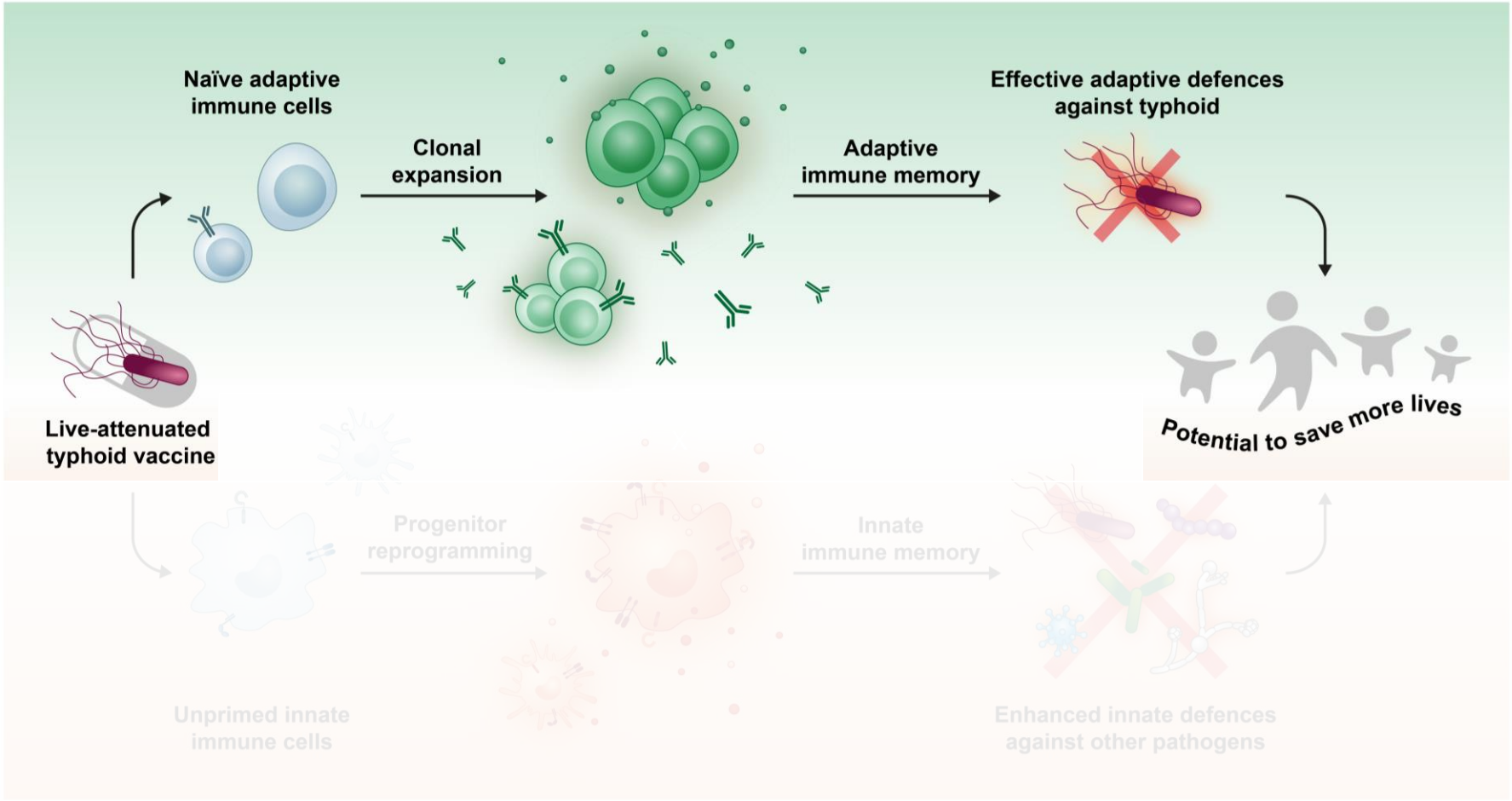
The non-specific immunological impact of human oral vaccination with live-attenuated *Salmonella* Typhi

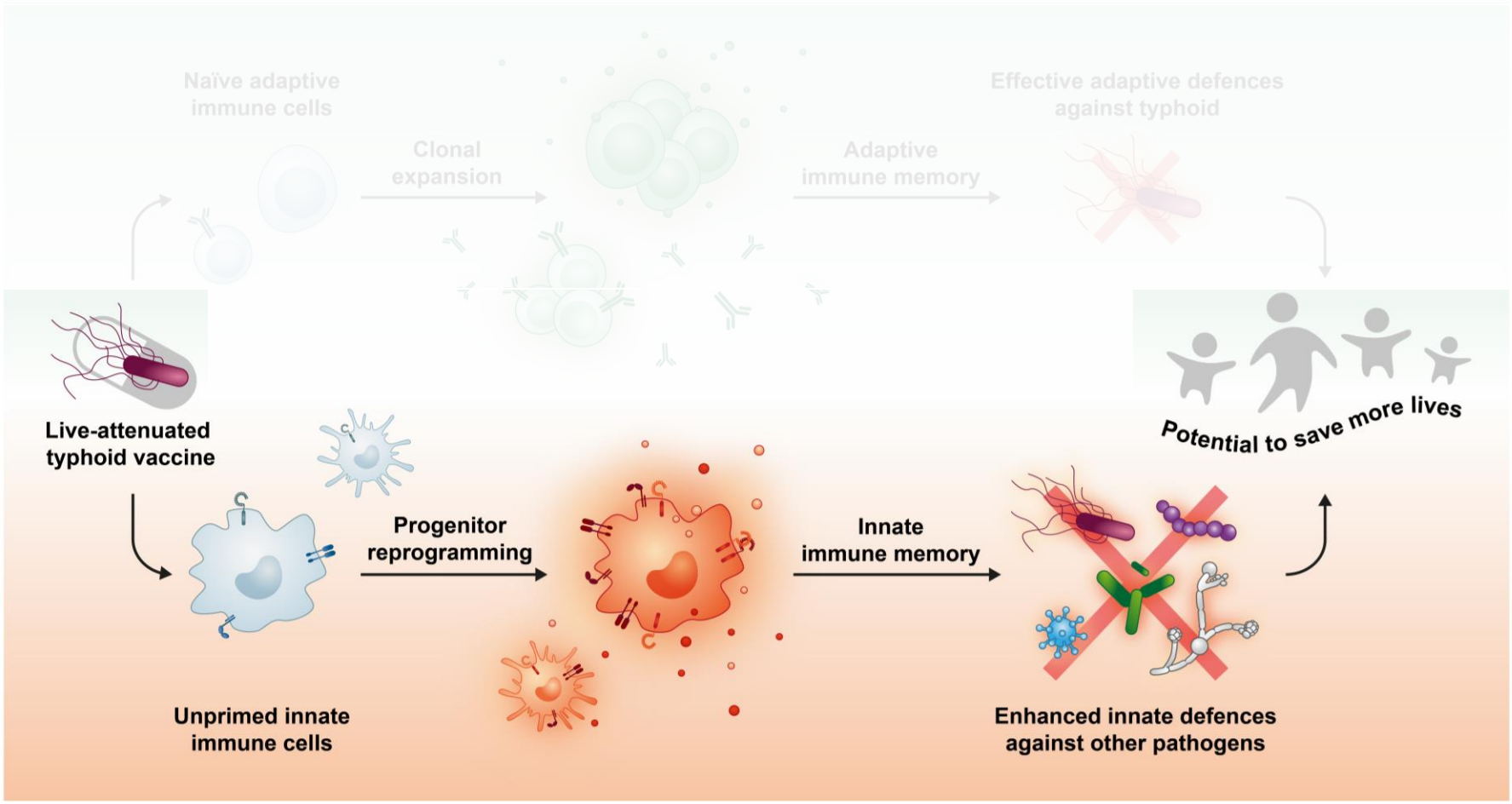
Shaun Pennington

11th international conference on typhoid and other invasive salmonellosis

Live attenuated *Salmonella* and trained immunity



Live attenuated *Salmonella* and trained immunity



Study outline

Day 0
Peripheral Blood

Vaccine

Day 0
Oral Dose 1

Day 2
Oral Dose 2

Day 4
Oral Dose 3

Control

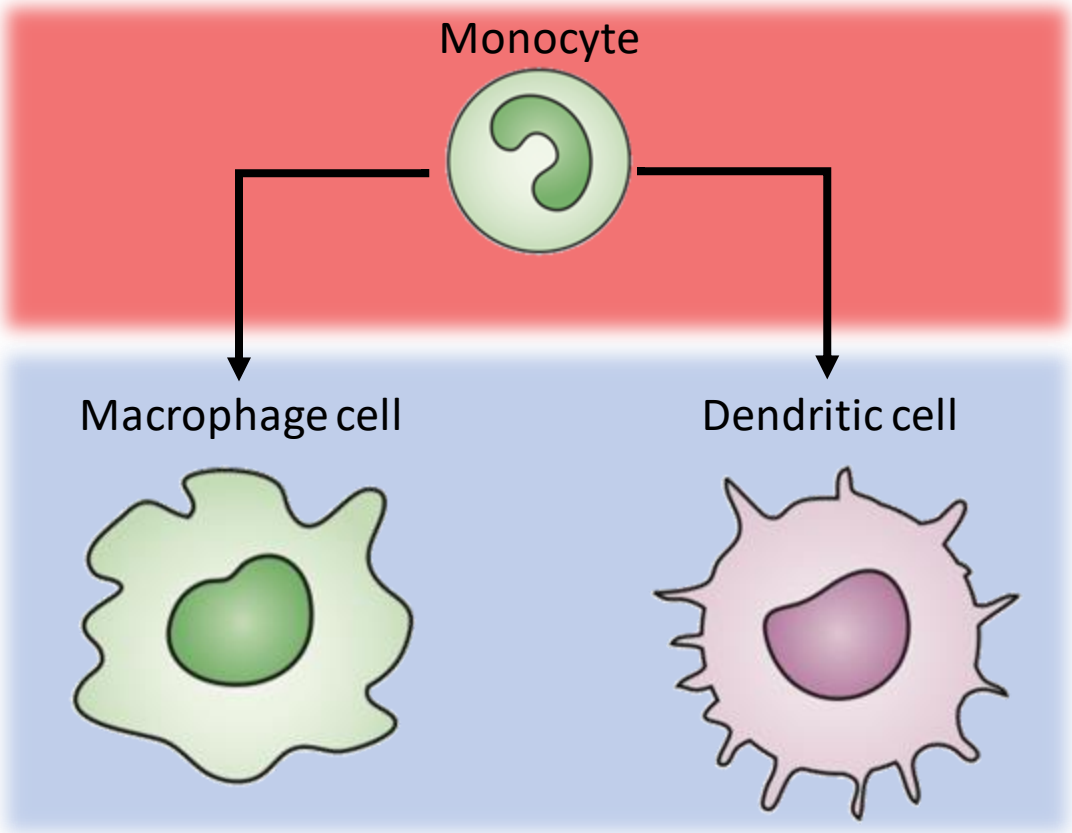
Day 14
Peripheral Blood

Month 3
Peripheral Blood

Month 6
Peripheral Blood

Pennington *et al*., Science Advances (2019)

Changes to monocytes

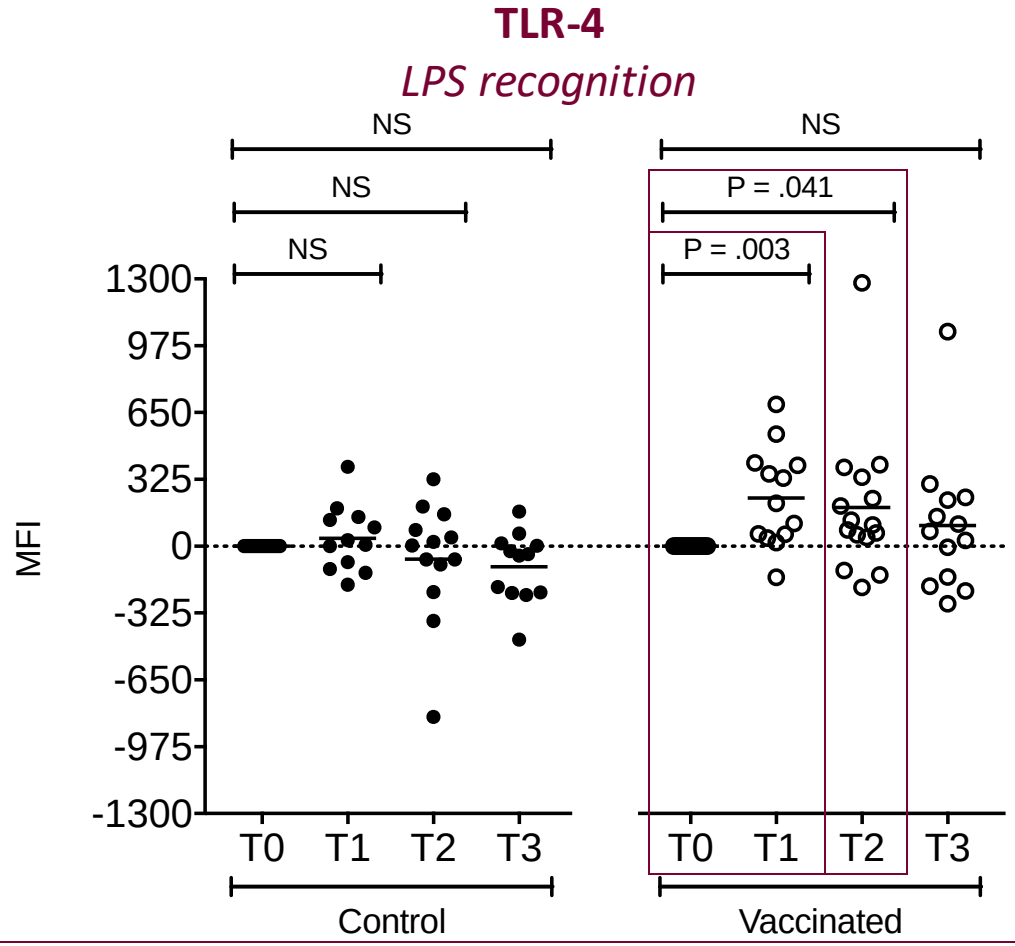


Monocytes with an enhanced capacity to detect, destroy and display pathogens

The nature and longevity of changes consistent with the generation of innate immune memory

Pennington *et al*., Science Advances (2019)

Monocyte phenotype



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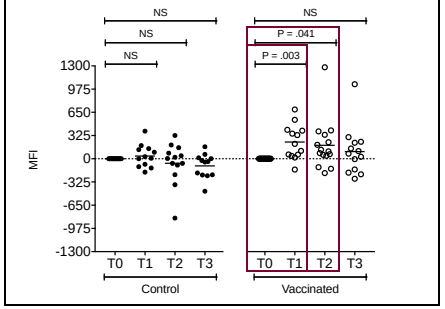
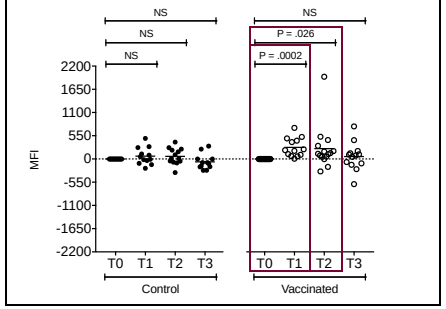
Monocyte phenotype

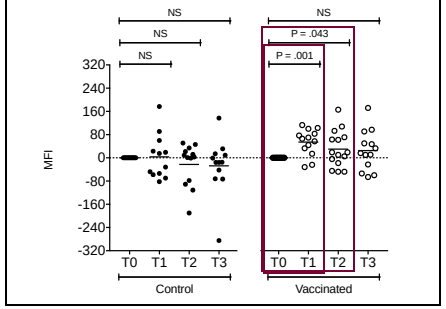
TLR-4
LPS recognition



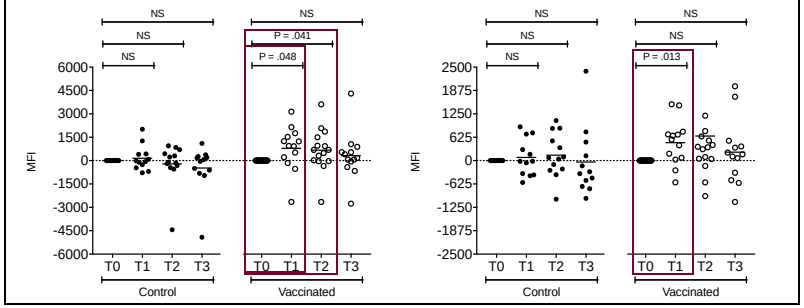
TLR-5
Flagella recognition



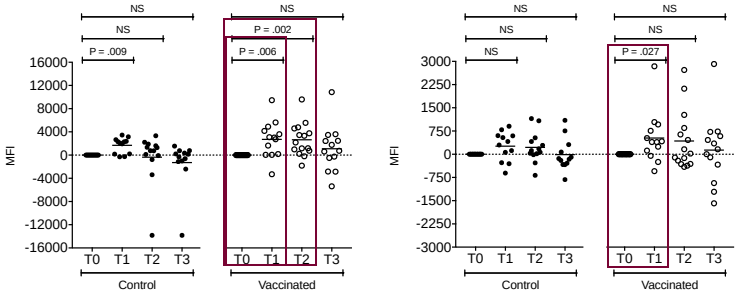
CD303
Antigen capture



CD16 and CD64 (FcR):
Antibody binding



CD11b and CD11c
Complement binding



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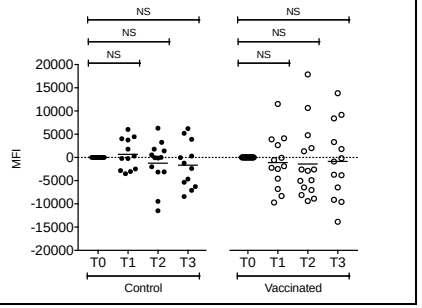
Monocyte phenotype

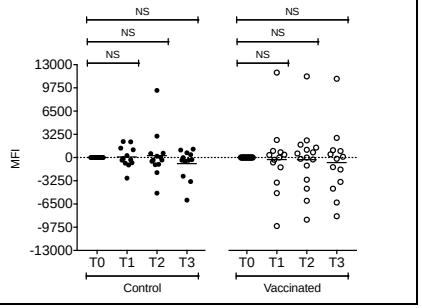
HLA-DR

Antigen presentation



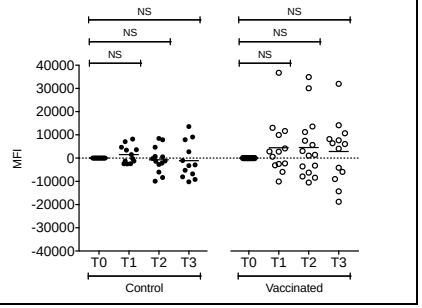
CD206

Glycan recognition



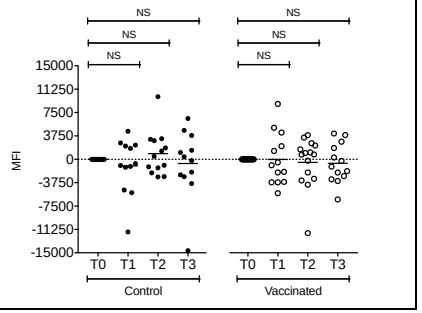
CD18

Cell signalling



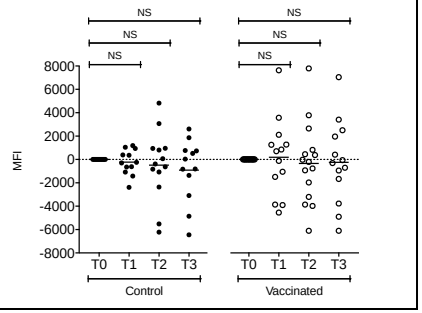
CD14

LPS coreceptor



CD123

Differentiation



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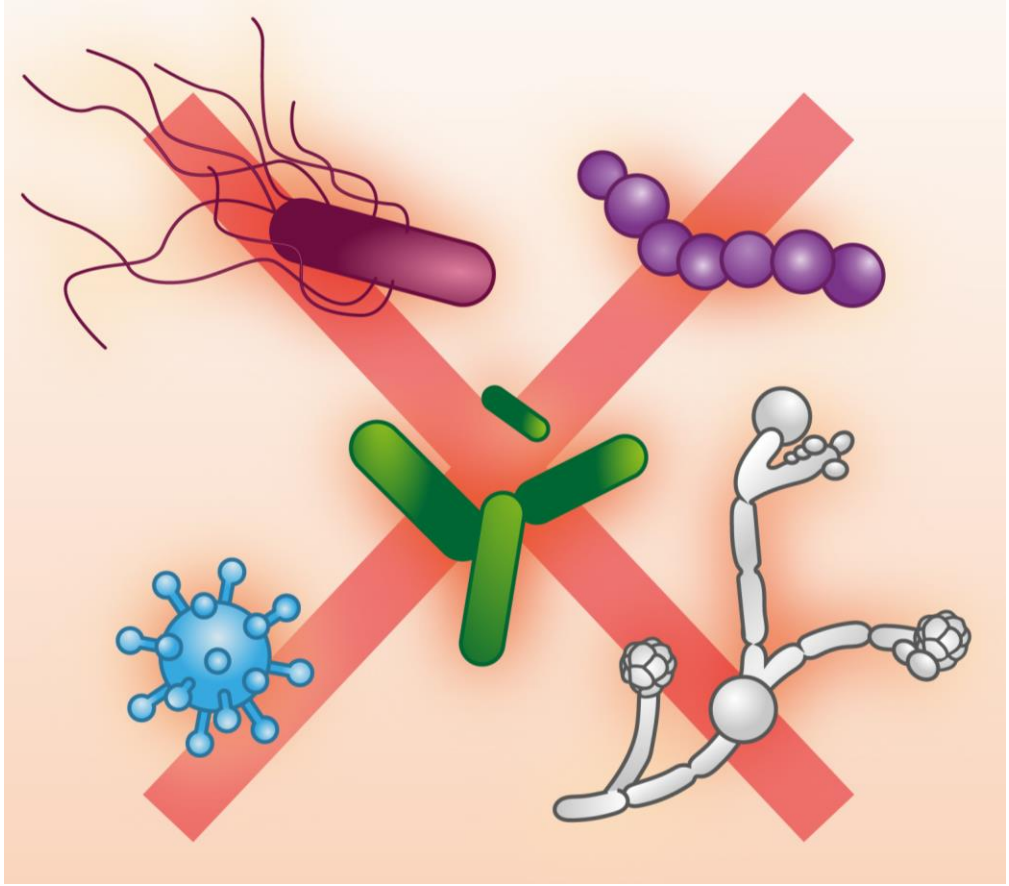
Impact on immunity to other pathogens



Changes in output across multiple cell types in response to stimulation array of different pathogens

Changes indicative of reduced susceptibility to infections caused by unrelated pathogens

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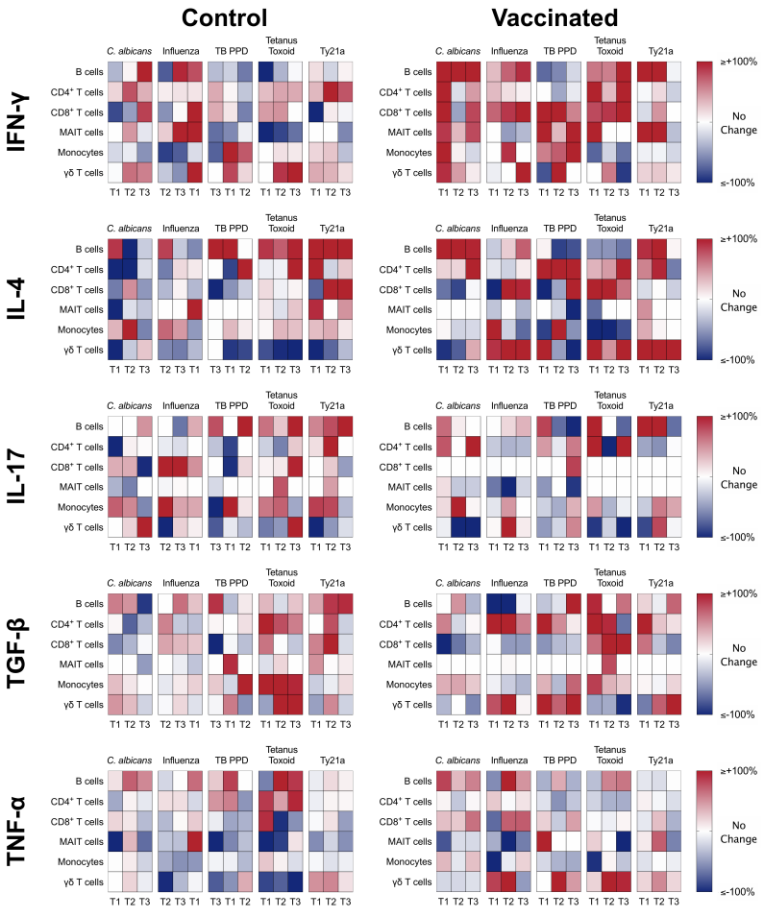
Impact on immunity to other pathogens

- 5 stimuli
- 5 cytokines
- 6 cell types

- More than 21,000 lines of data
- Analysed using linear DAPC
  - Model 1: 92.4%
  - Model 2: 92.4%



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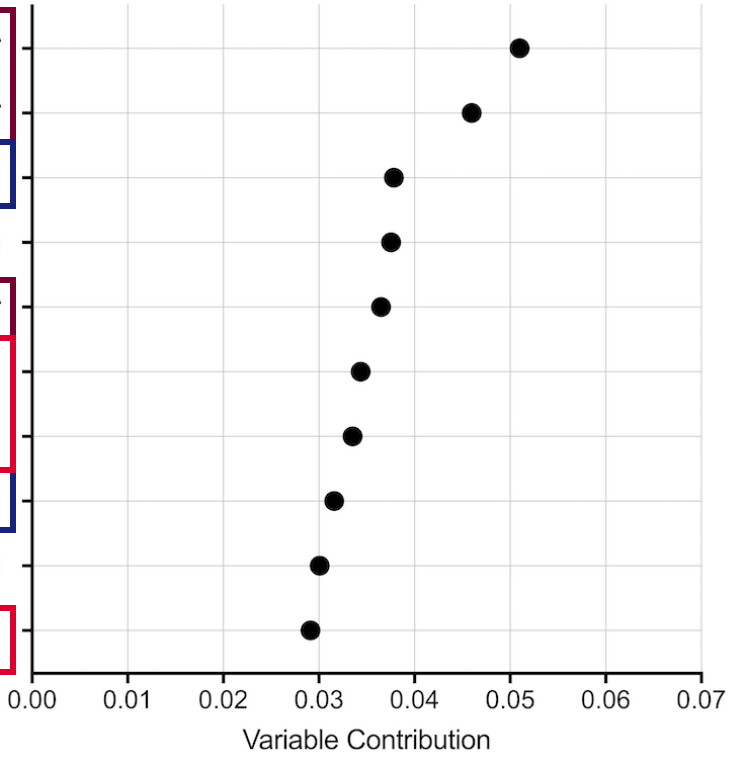
DAPC: largest contributing variables

CELL TYPE	CYTOKINE	SIMULUS
Monocytes	IFN-γ	*C. albicans*
B cells	IL-4	*C. albicans*
B cells	TGF-β	Influenza
$CD4^+$ T cells	IFN-γ	Ty21a
γδ T cells	IL-17	*C. albicans*
B cells	IL-17	Tetanus Toxoid
Monocytes	IL-4	Tetanus Toxoid
Monocytes	TGF-β	Influenza
B cells	TNF-α	TB PPD
γδ T cells	TNF-α	Tetanus Toxoid



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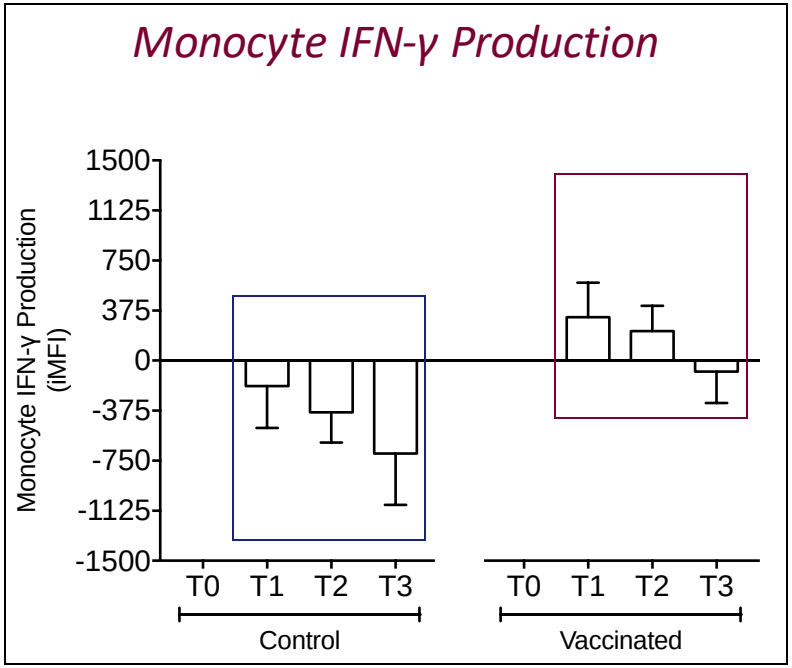
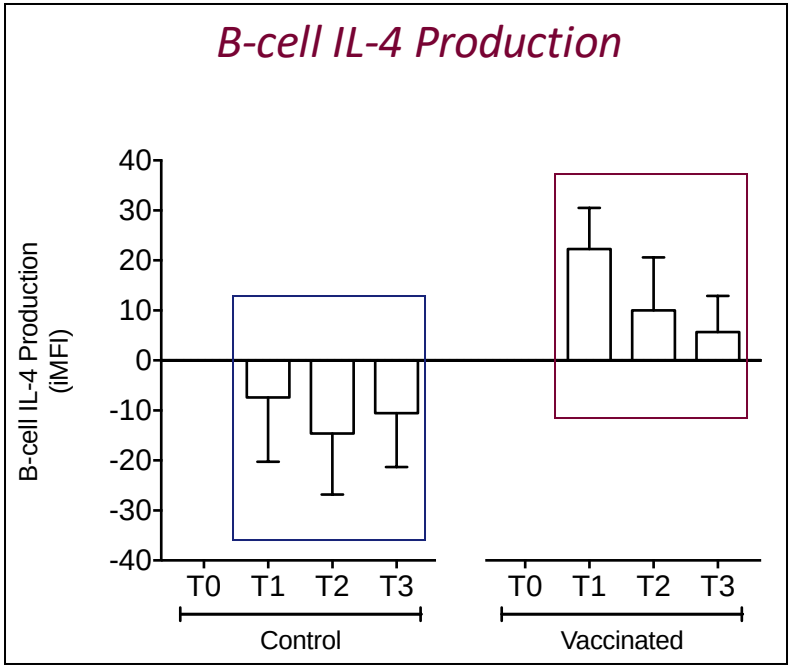
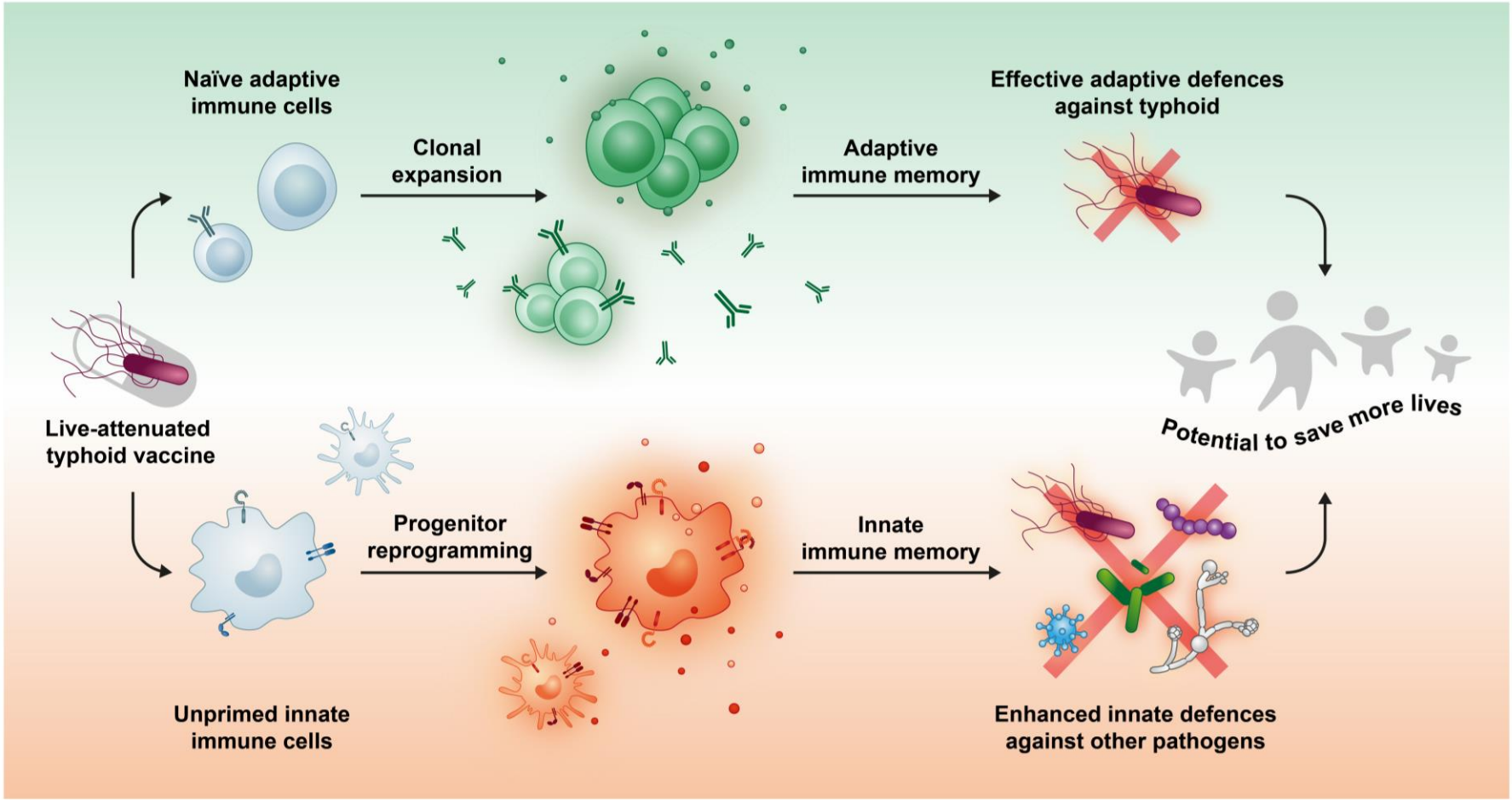
DAPC: largest contributing variables





- IL-4 is essential for the development of protective T_H1 (IFN-γ) responses against *C. albicans*

Implications



Acknowledgements

All our volunteers

The team

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