National Science Challenges

Centre for High-Value Nutrition

HIGH-VALUE NUTRITION

Ko Ngā Kai Whai Painga

Finding the right bioactives to build a stronger immune system

Olivier Gasser, PhD

27 September 2017

Host Institution

The University of Auckland Te Whare Wānanga o Tāmaki Makaurau New Zealand

University of Otago Te Whare Wānanga o Otāgo New Zealand

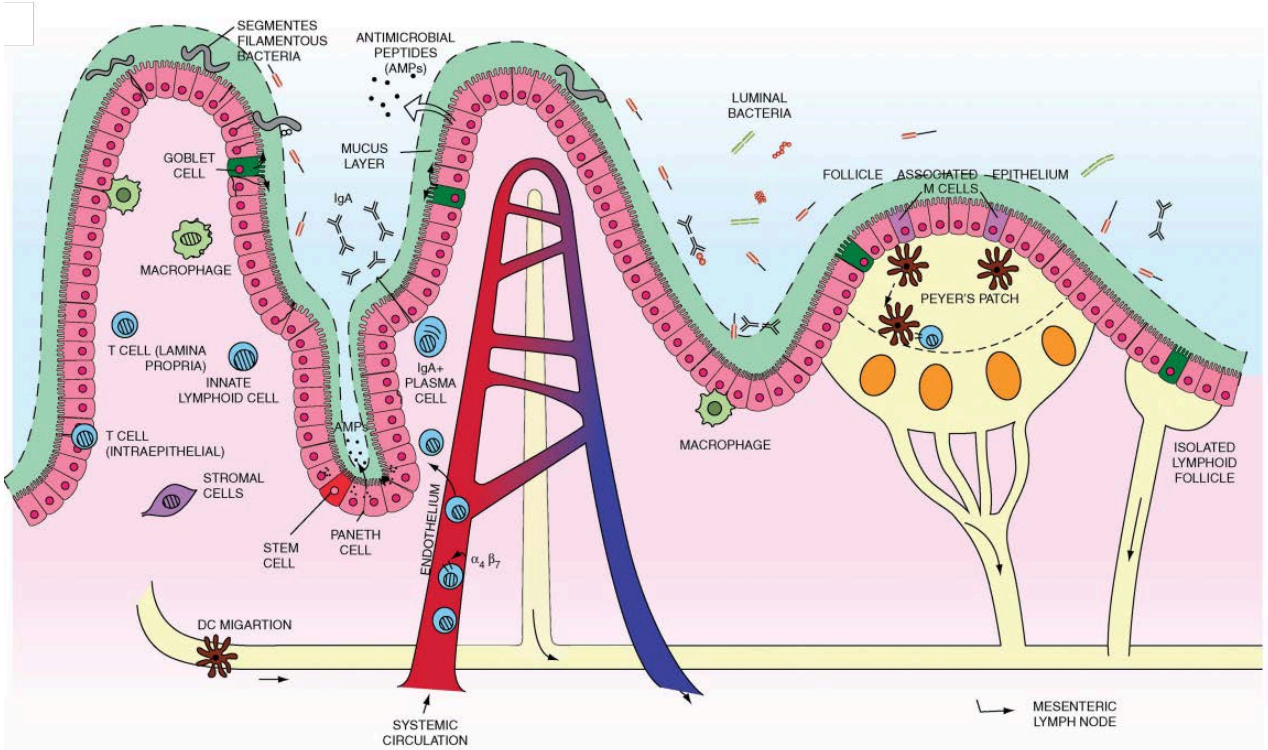
Massey University Te Kunenga ki Pūrehuroa University of New Zealand

agresearch

Plant & Food Research Rangahau Ahumāra Kai

Malaghan Institute of Medical Research

The gut: the largest immune organ



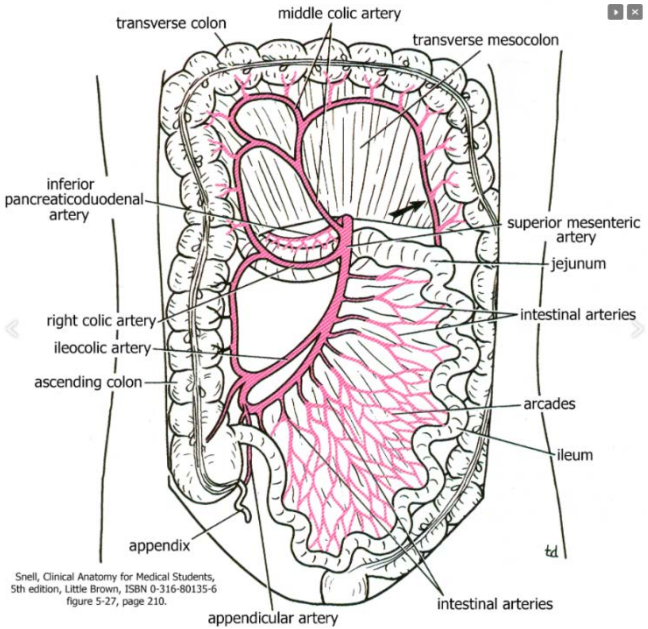
70% of immune system

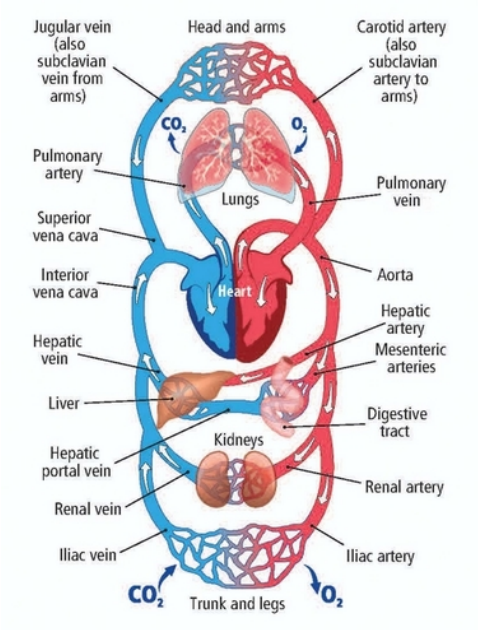
60% of secreted immunoglobulins (grams)

10^6 lymphocytes/g tissue

Cader MZ, *et al*. *Gut* 2013;**62**:1653–1664.

Immune effects beyond the gut

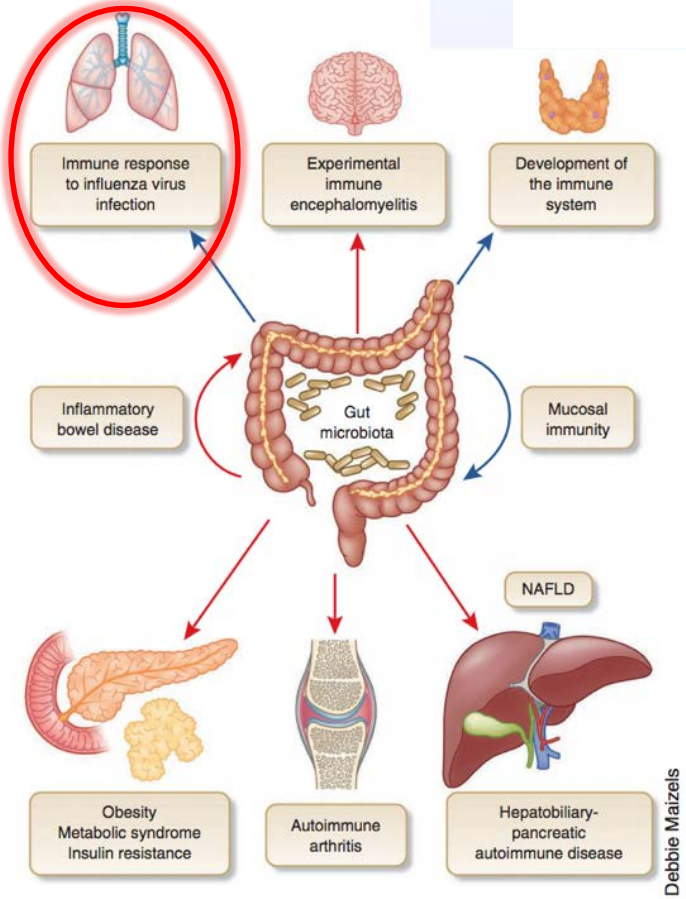




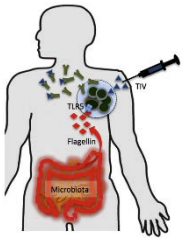
Systemic distribution of:

- **Food metabolites** (sugars, lipids, amino acids, and others)
- **Immune cells**
- **Immune effector molecules**
- **Microbiota-derived metabolites**

Immune effects beyond the gut



How can we identify the right bioactives?



Flu vaccine trial
Observational study
influvac
Inactivated influenza vaccine (surface antigen)

Study completion ✓

Mechanism/biomarker

2016 — 2017 — 2018/19

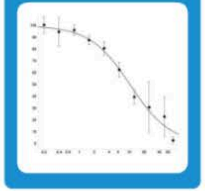
Flu vaccine model
vaccination+challenge

Pollution Allergy
inflammatory diseases

Food selection
dietary interventions

Models established
Foods selected
✓✓✓

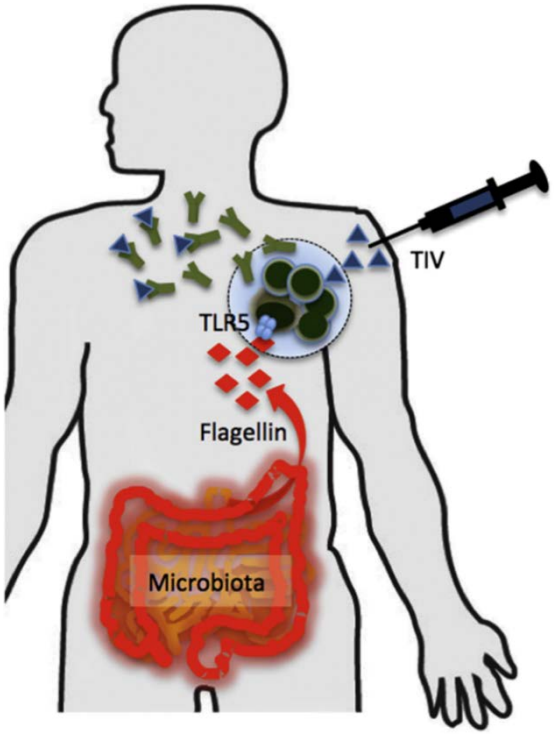
Results



Mechanism (flu)
Biomarker (pollution)
✓✓

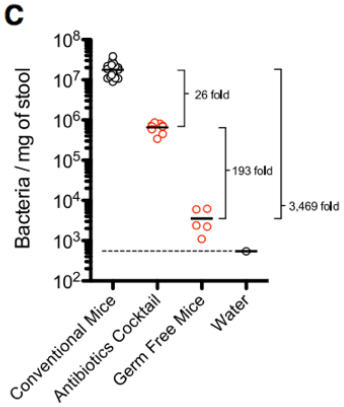
Food(s), mechanism and biomarker(s)

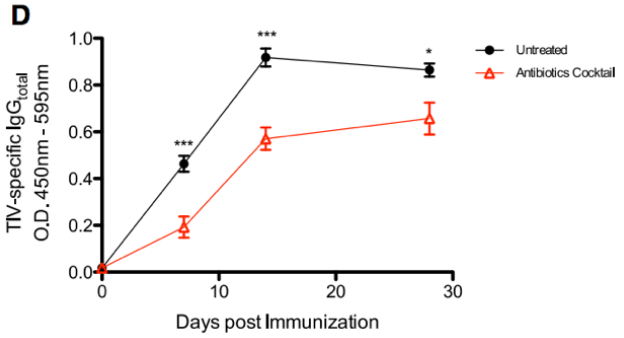
The microbiota: the in-built immune adjuvant



TLR5-Mediated Sensing of Gut Microbiota Is Necessary for Antibody Responses to Seasonal Influenza Vaccination

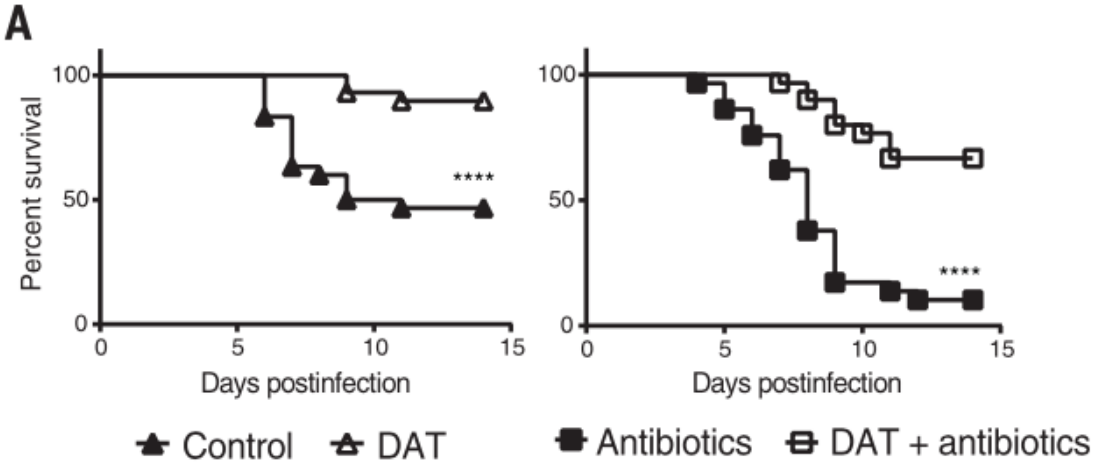
Jason Z. Oh,[1,2] Rajesh Ravindran,[1,2] Benoit Chassaing,[4] Frederic A. Carvalho,[4,5] Mohan S. Maddur,[1,2] Maureen Bower,[6] Paul Hakimpour,[2] Kiran P. Gill,[1,2] Helder I. Nakaya,[3,7] Felix Yarovinsky,[8] R. Balfour Sartor,[6] Andrew T. Gewirtz,[4] and Bali Pulendran[1,2,3,*]





Immunity 41, September 18, 2014 ©2014 Elsevier Inc. 349

The microbiota: the in-built immune adjuvant

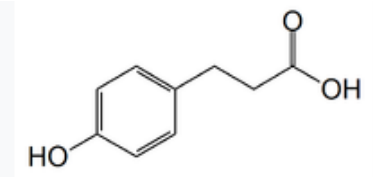


RESEARCH

MICROBIOTA

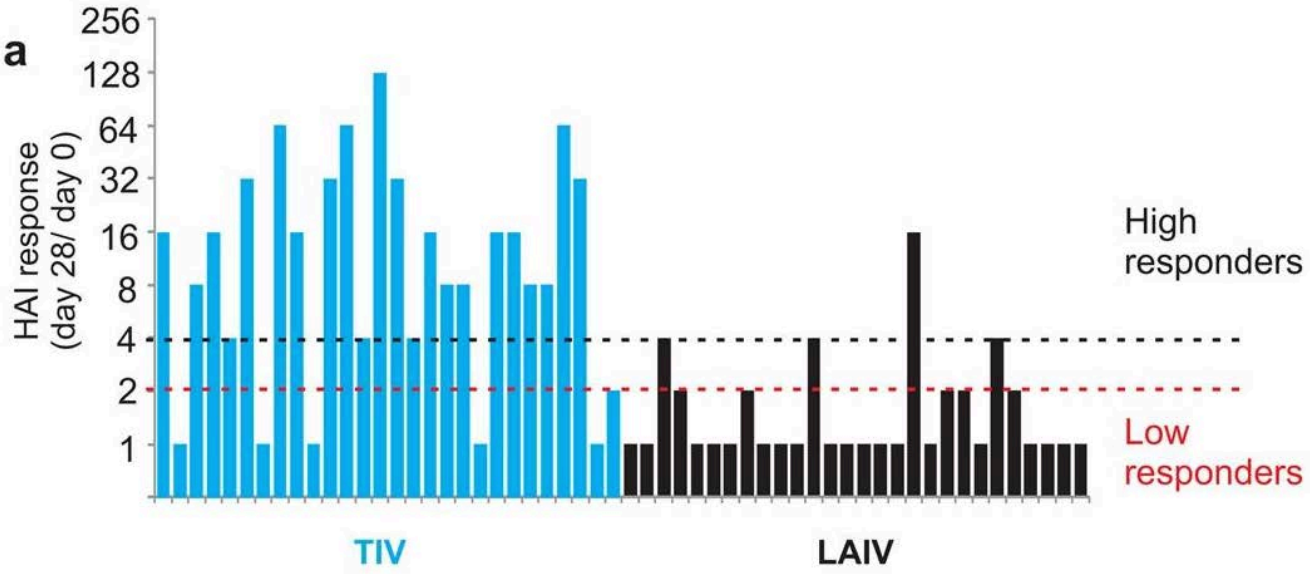
The microbial metabolite desaminotyrosine protects from influenza through type I interferon

Steed *et al.*, *Science* **357**, 498–502 (2017) 4 August 2017



→ type I interferon amplification loop

Is gut microbial composition linked with vaccine efficacy in humans?



Is gut microbial composition linked with vaccine efficacy in humans?

Feasibility study assessing the association between gut microbiota in healthy adults and antibody response to seasonal influenza vaccination

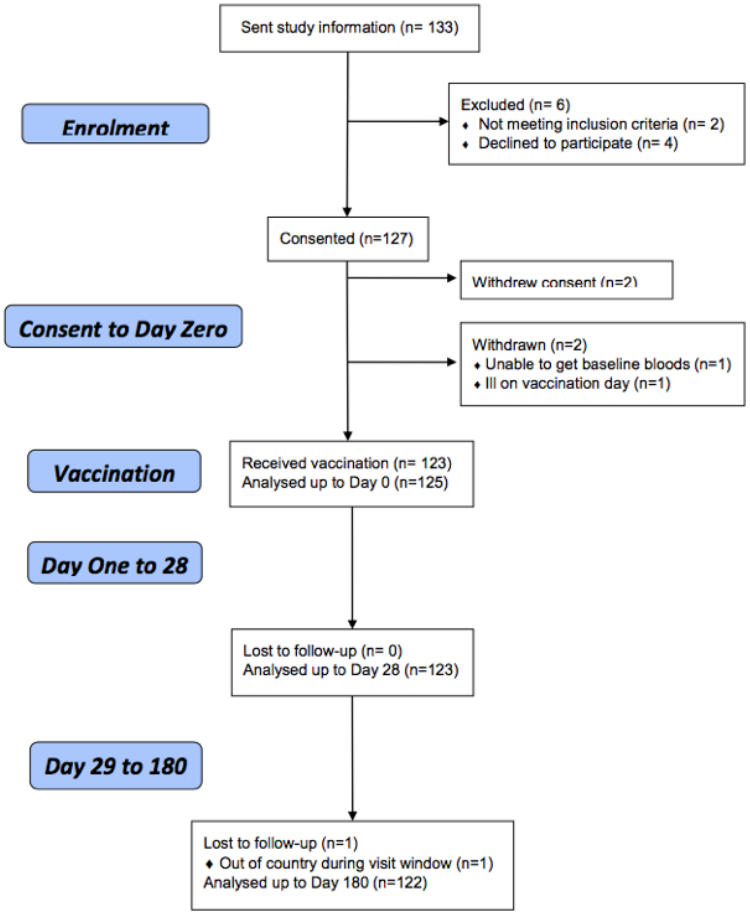
Internal Reference Number / Short title: Gut microbiota and influenza vaccine

Ethics Ref: 15/CEN/207

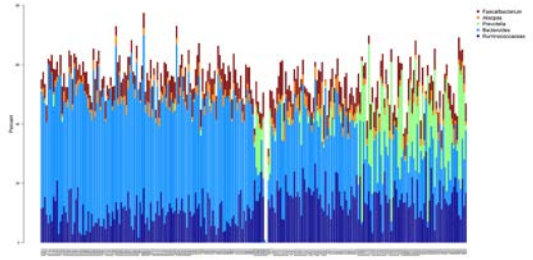
Each 0.5mL of the Influvac® vaccine contains antigens representative of the following type:

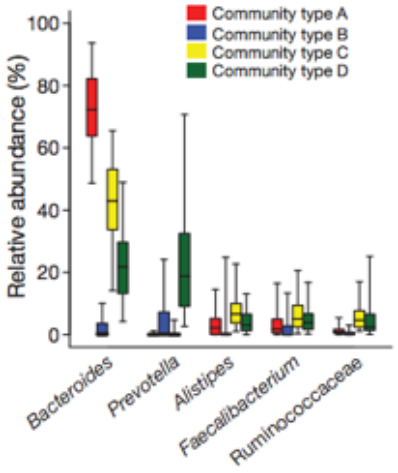
- A/California/7/2009 (H1N1)pdm09-like strain (A/California/7/2009, X-181) 15 µg haemagglutinin/dose
- A/Hong Kong/4801/2014 (H3N2)-like strain (A/New Caledonia/71/2014, X257A) 15 µg haemagglutinin/dose
- B/Brisbane/60/2008-like strain (B/Brisbane/60/2008, wild type) 15 µg haemagglutinin/dose

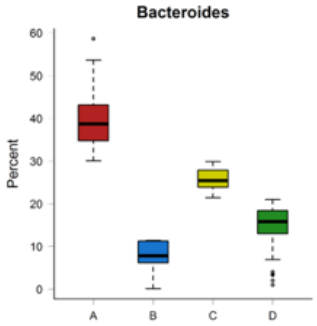
Study protocol

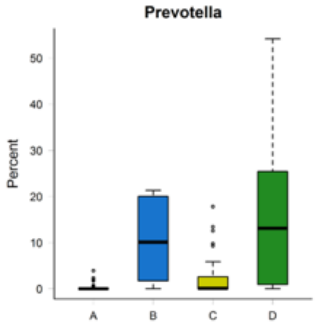


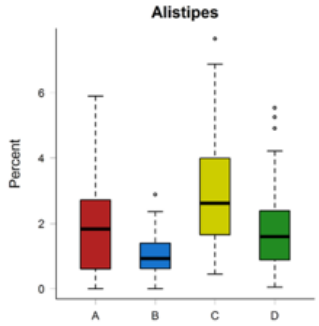
Microbial ‘enterotype’ analysis

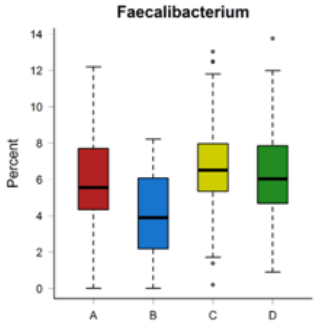


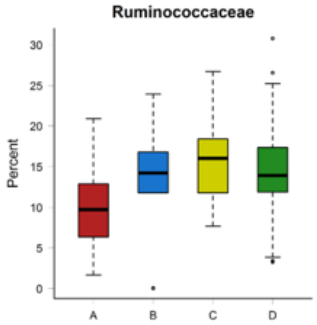


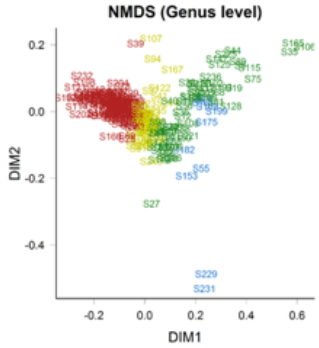












15 MAY 2014 | VOL 509 | NATURE | 357

Stability of enterotypes

	Stool Community Type Day 28 N/123 (%)			
Stool Community Type Day Zero N/123 (%)	**SCT-A 59 (48)**	**SCT-B 6 (4.9)**	**SCT-C 26 (21.1)**	**SCT-D 32 (26.0)**
SCT-A 64 (52)	51	2	10	1
SCT-B 4 (3.3)	1	2	0	1
SCT-C 23 (18.7)	4	0	10	9
SCT-D 32 (26)	3	2	6	21

Abbreviation: SCT, stool community type.

Lack of association between enterotypes and immune outcomes

	Univariate p value	Multivariate p value
HAI titre		
- *H1N1*[c]	0.075	0.099
- *H3N2*[d]	0.60	0.98
- *B*[e]	0.17	0.16
Seroconversion[a]		
- *H1N1*[c]	0.15	0.08
- *H3N2*[d]	0.62	0.79
- *B*[e]	0.57	0.42
- **All strains**	0.87	0.64
Seroprotection[b]		
- *H1N1*[c]	0.43	0.40
- *H3N2*[d]	0.81	0.71
- *B*[e]	0.77	0.59
-All strains	0.62	0.22

Abbreviation: HAI, haemagglutination inhibition

[a] Seroconversion: a ≥4 fold increase in HAI titre if pre vaccination HAI titre was ≥1:10; or a post vaccination HAI titre of 1:40 if pre vaccination HAI titre was <1:10.

[b] Seroprotection: a post vaccination HAI titre of ≥1:40.

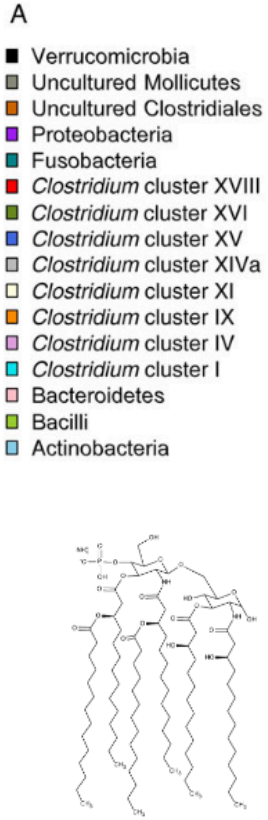
[c] Influenza A (H1N1) A/California/7/2009, X-181

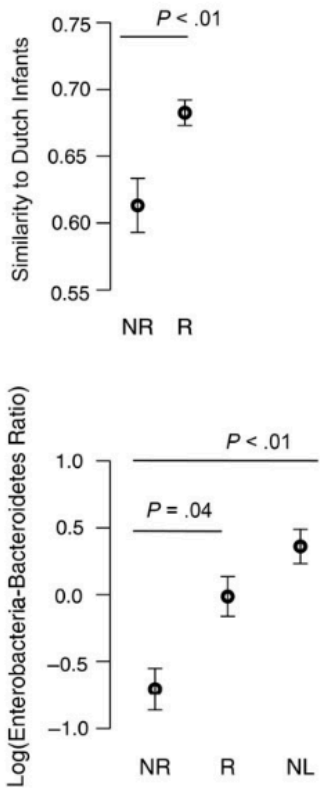
[d] Influenza A (H3N2) A/New Caledonia/71/2014, X257A

[e] Influenza B (B/Brisbane/60/2008, wild type)

No association between enterotypes and vaccine-specific antibody titers.

Lipopolysaccharides and rotavirus vaccination efficacy

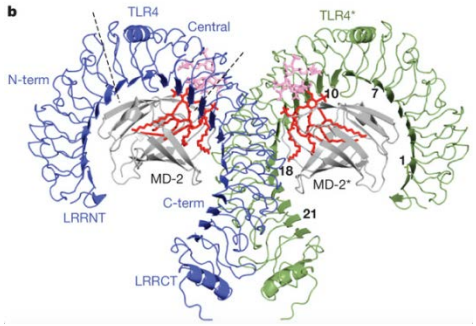




The Journal of Infectious Diseases
MAJOR ARTICLE

Significant Correlation Between the Infant Gut Microbiome and Rotavirus Vaccine Response in Rural Ghana

Vanesse C. Harris,[1,2] George Armah,[3] Susana Fuentes,[3] Katri E. Korpela,[4] Umesh Parashar,[7] John C. Victor,[8] Jacqueline Tate,[7] Carolina de Weerth,[4] Carlo Giaquinto,[9] Willem Joost Wiersinga,[2] Kristen D. C. Lewis,[2,a] and Willem M. de Vos[3,5]



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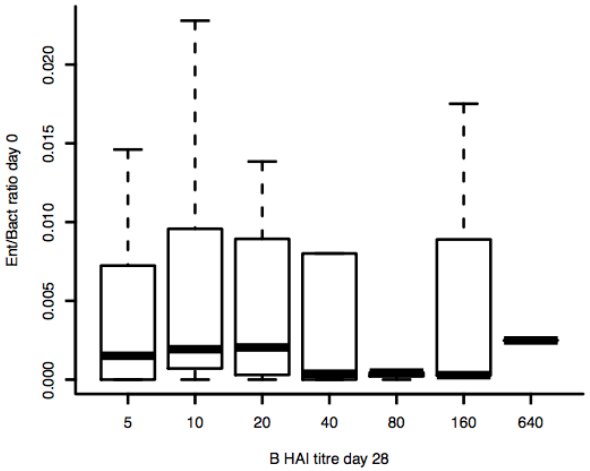
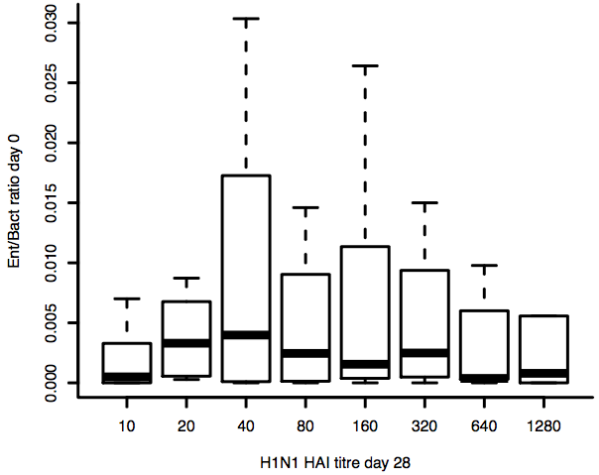
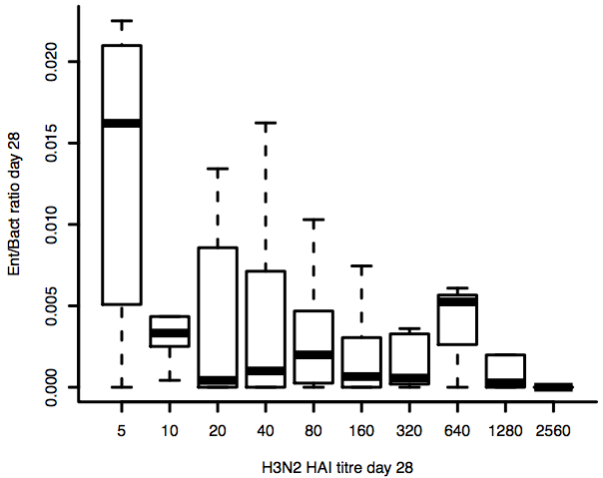
Lipopolysaccharides and influenza vaccination efficacy







Science to date: Can we use food to enhance protection against res

Flu vaccine trial
Observational study
influvac

2016

Study completion ✓

Flu vaccine model
vaccination+challenge

Pollution Allergy
inflammatory diseases

Food selection
dietary interventions

Models established
Foods selected
✓✓✓

Results

Mechanism (flu)
Biomarker (pollution)
✓✓

Food(s), mechanism and biomarker(s)

Successful completion of pilot trial in humans:

- **Bacterial enterotypes do not provide any predictive value for vaccine efficacy.**
- **Canonical analyses revealed different associations between microbial taxa and sub-components of the vaccine.**
- **Transcriptomic and flow cytometric analyses to be incorporated into the analyses.**

Thank you for your attention …