



The early-life gut microbiome and pediatric asthma



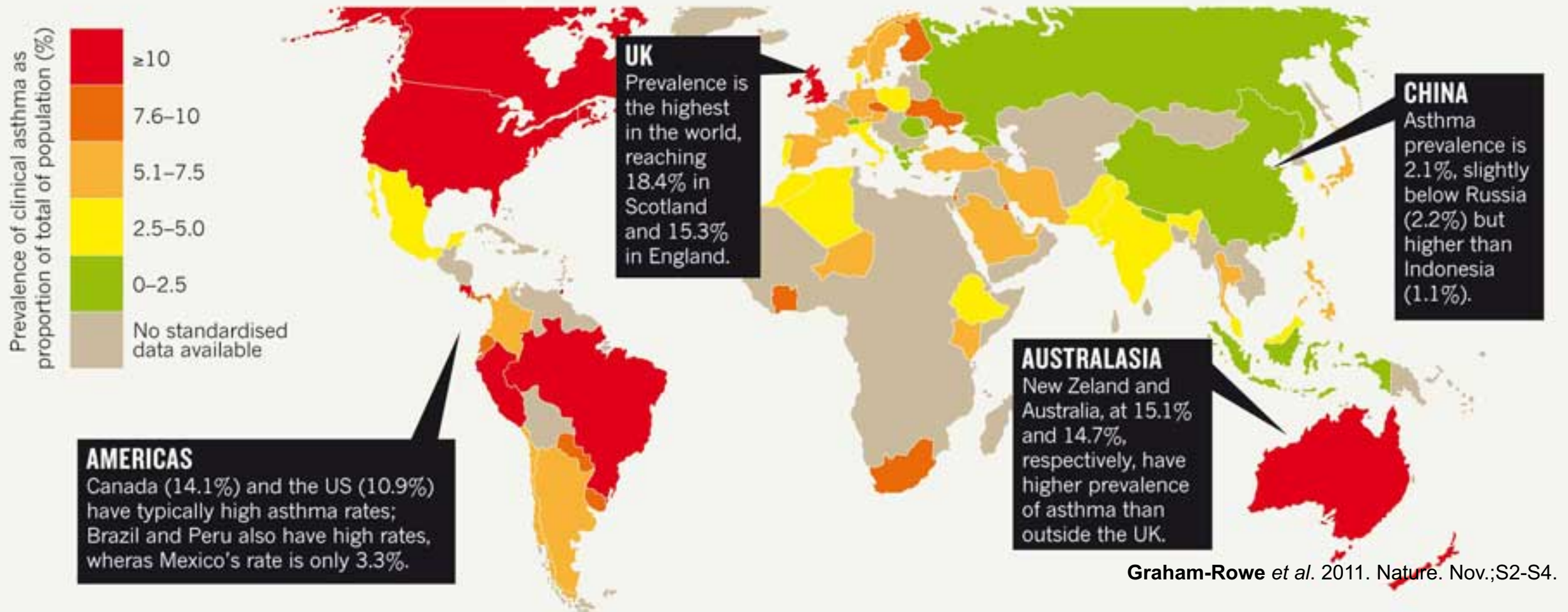
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CALGARY

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Pharmacology and Pediatrics

ASTHMA AROUND THE WORLD

Global studies confirm an association with westernized lifestyles

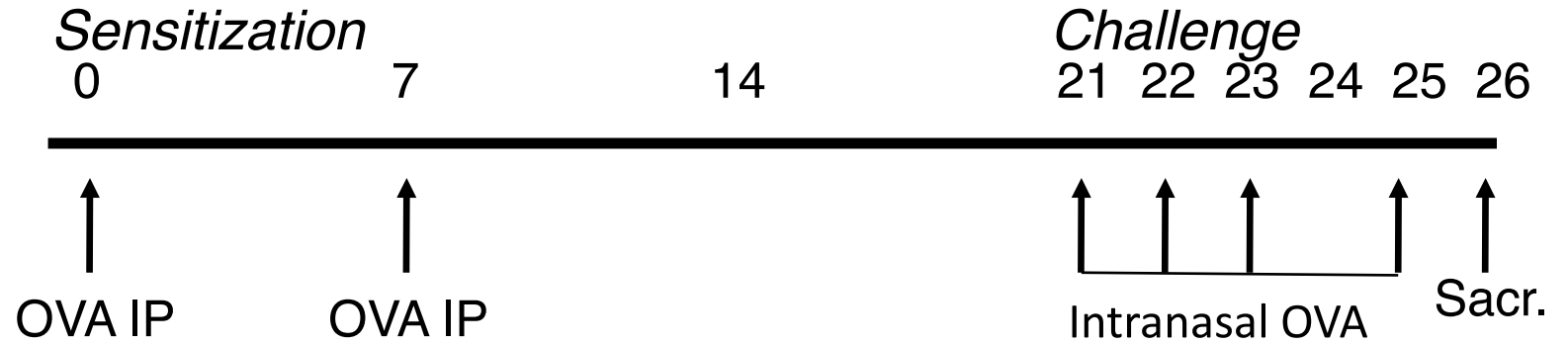


The global distribution is disproportionate.

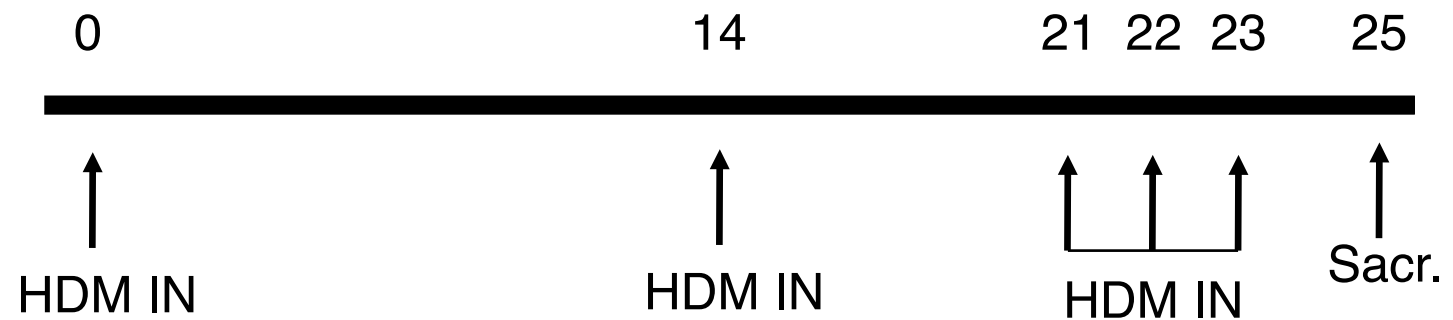
Animal models



Ovalbumin Model of Allergic Asthma



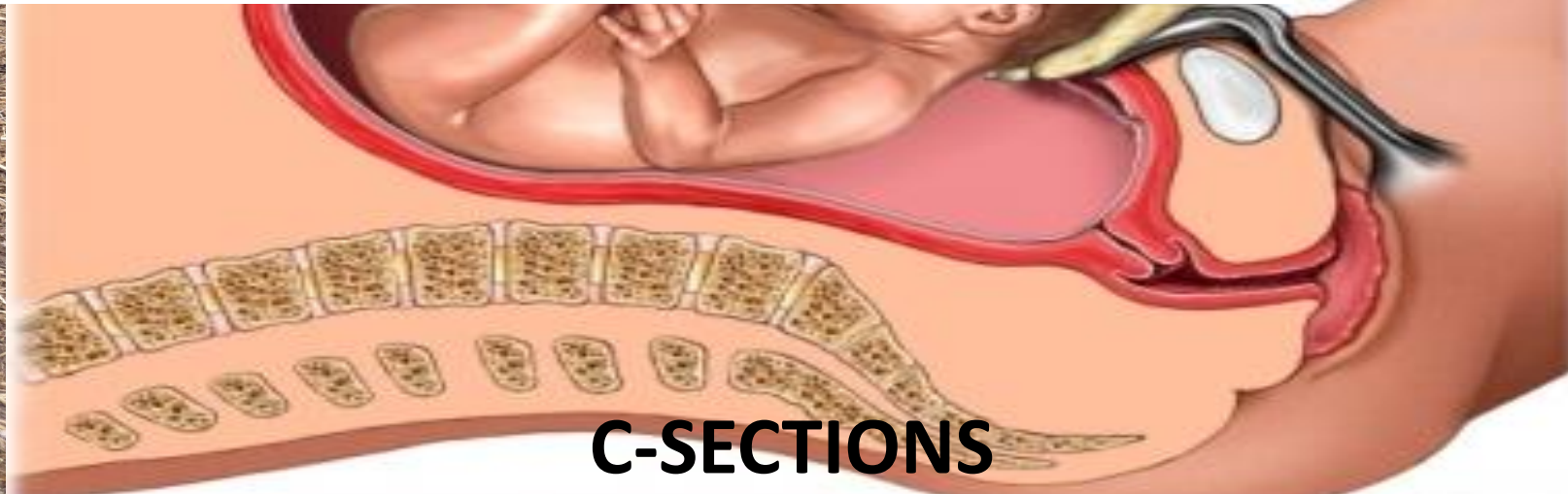
House Dust Mite Model of Allergic Asthma



Epidemiology



FARMS



C-SECTIONS



ANTIBIOTICS



HELMINTHS



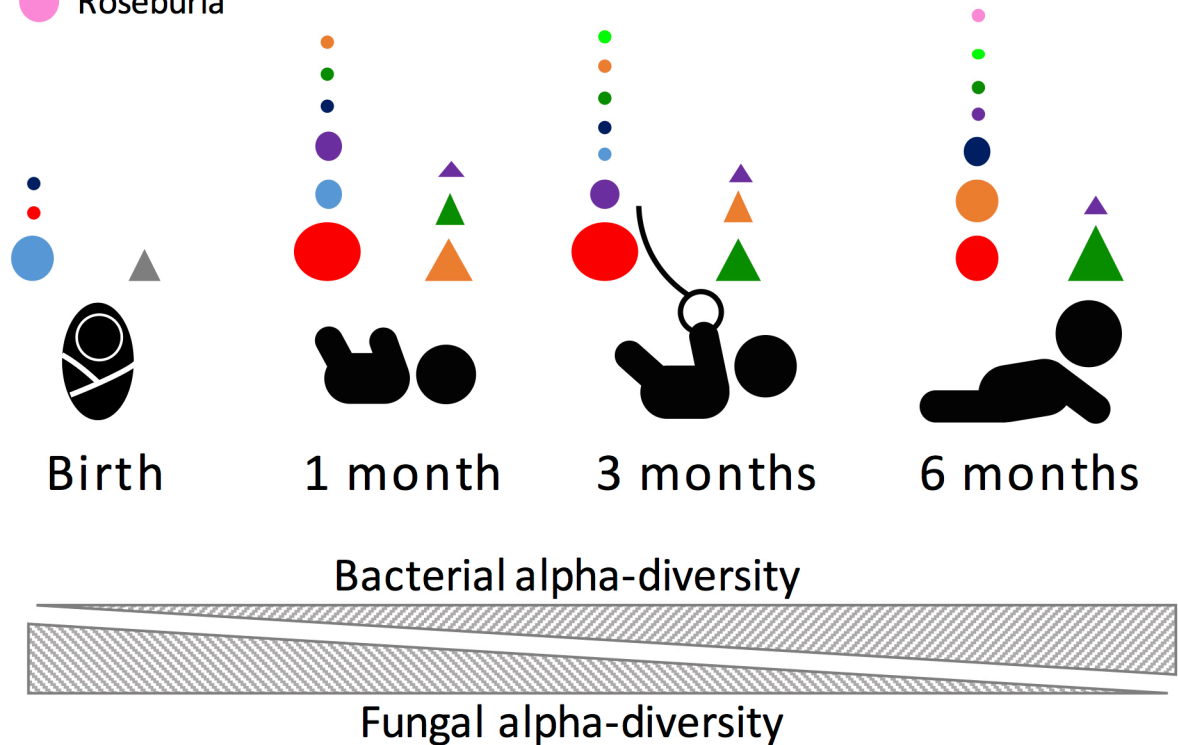
BREASTFEEDING

Bacteria

- Enterobacteriaceae
- Bifidobacterium
- Bacteroides
- Clostridium
- Lactobacillus
- Veillonella
- Lachnospira
- Roseburia

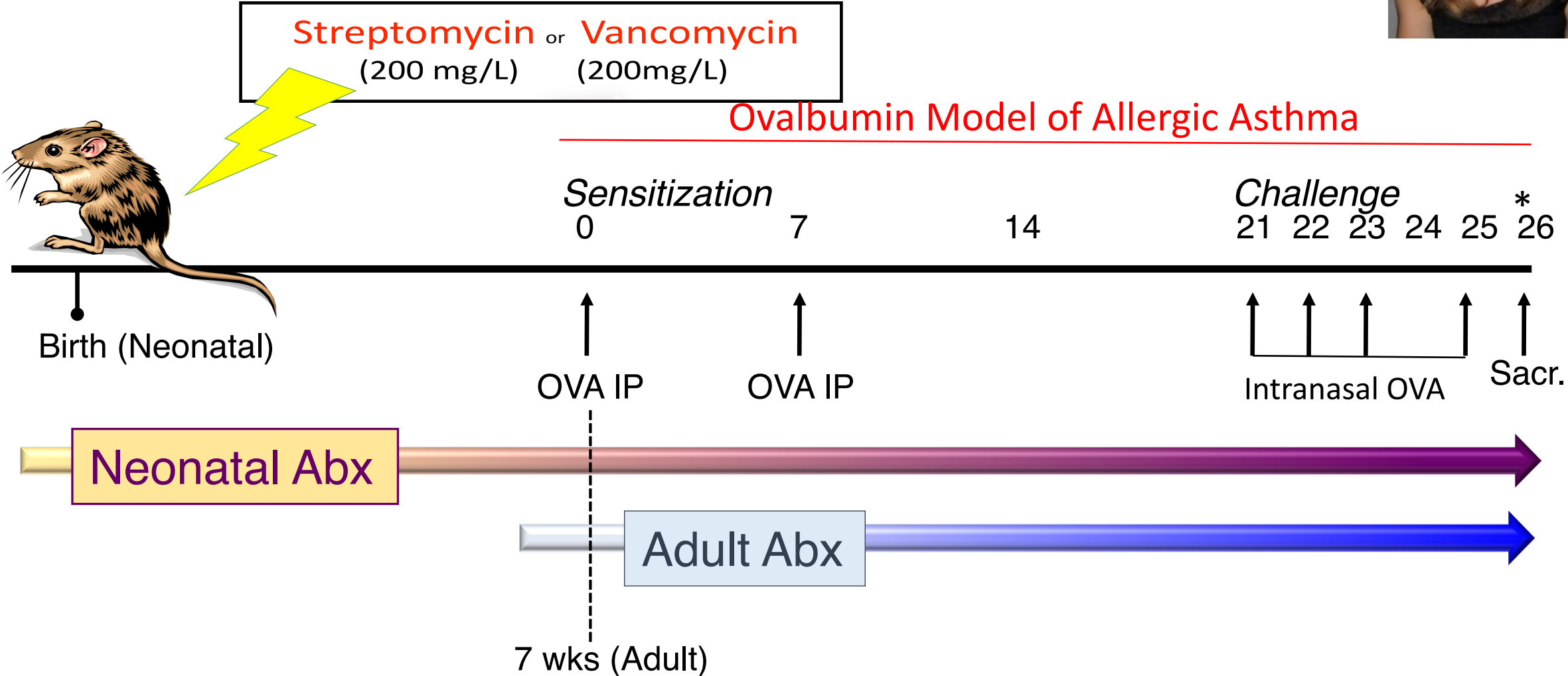
Fungi

- Malassezia
- Rhodotorula
- Candida
- Unknown

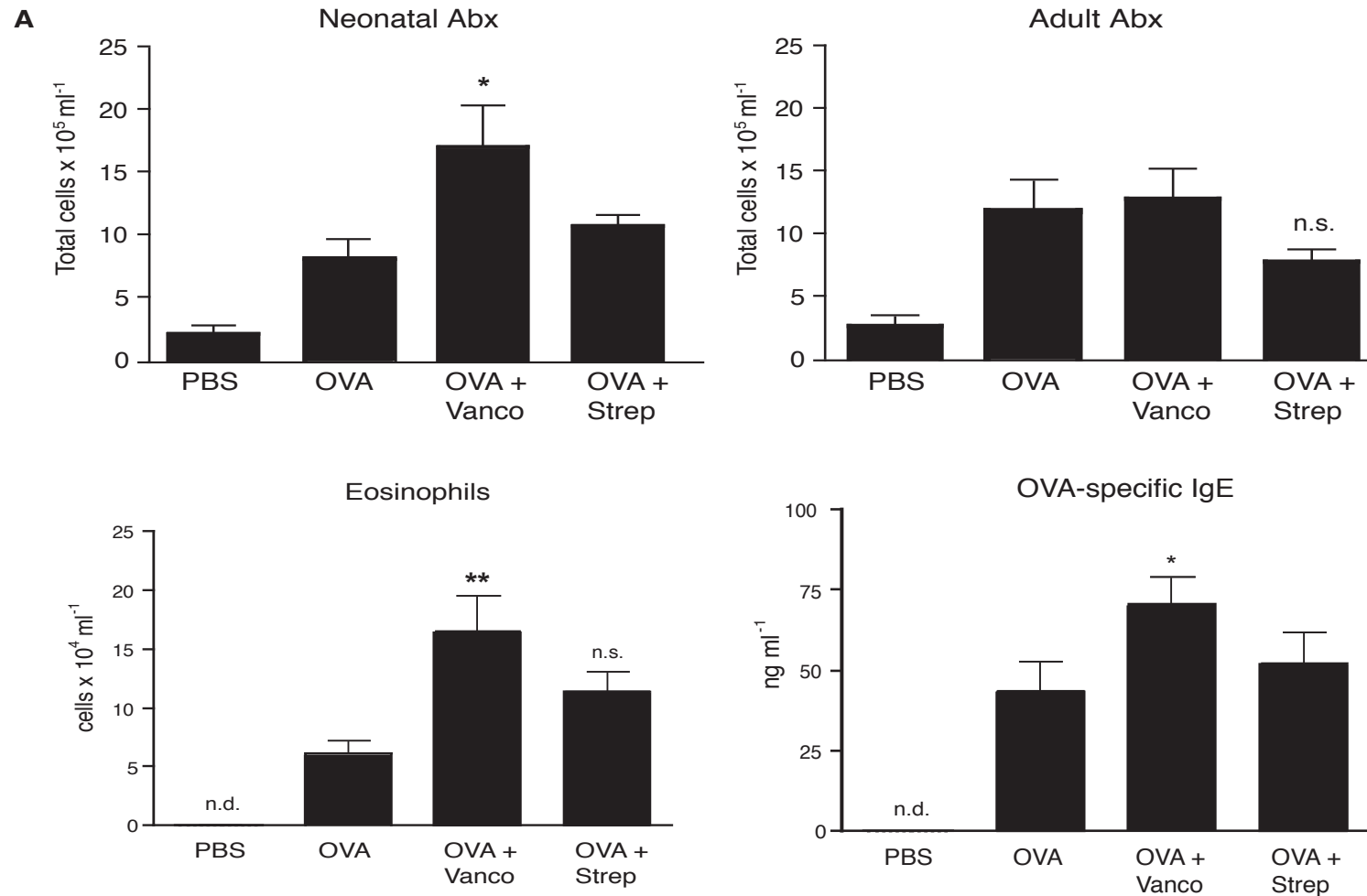


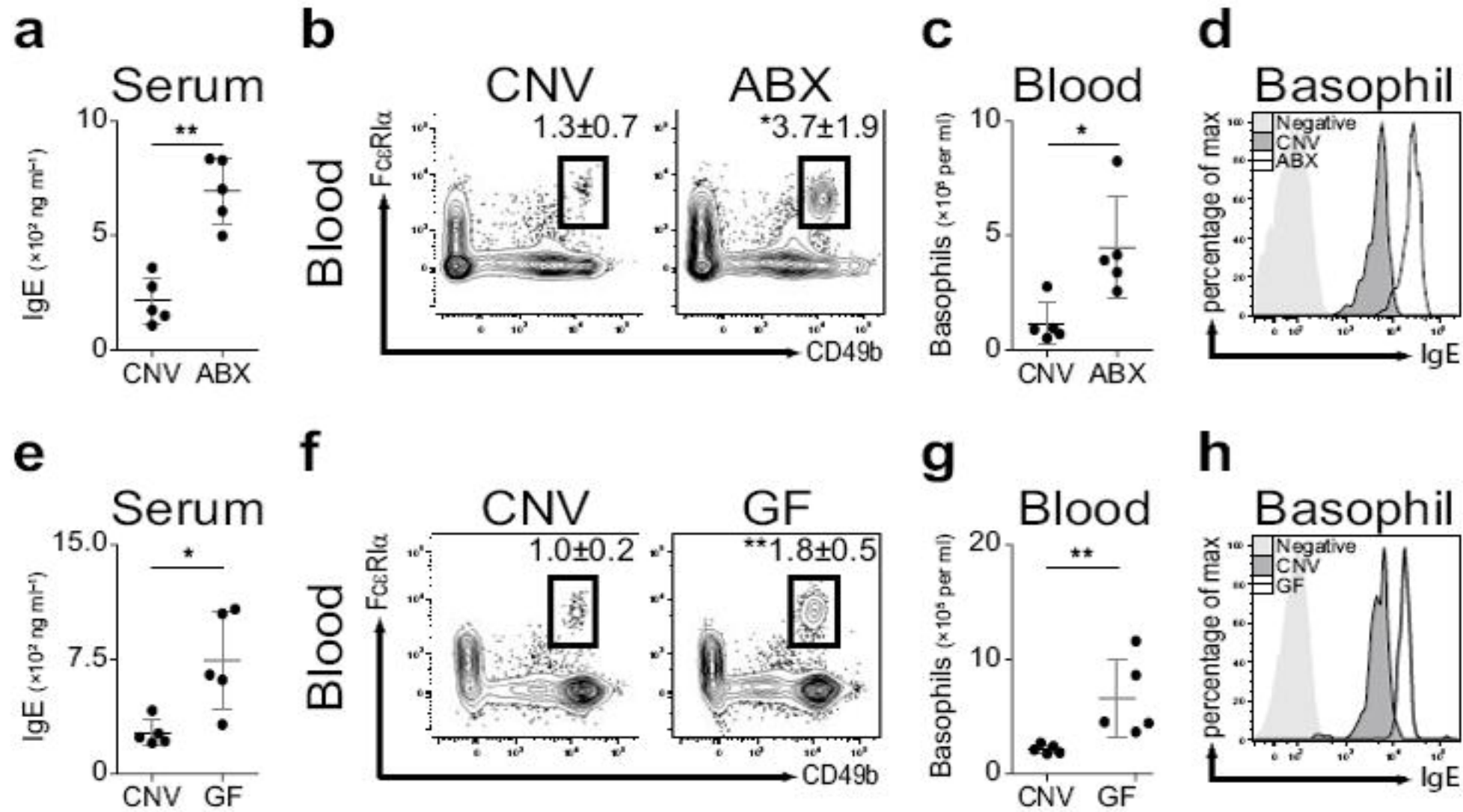
Low resilience during
critical immune
development stage

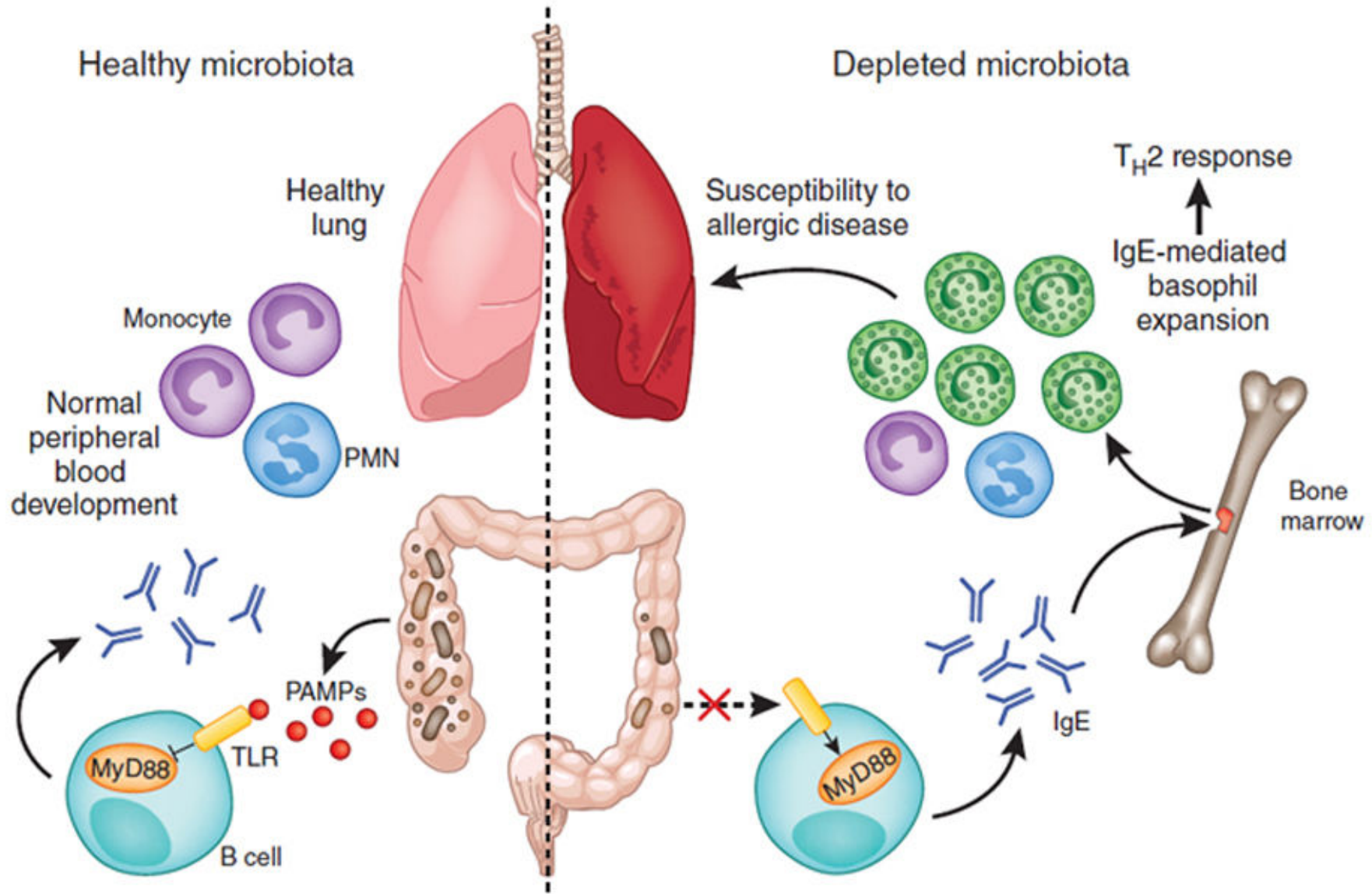
Experimental evidence



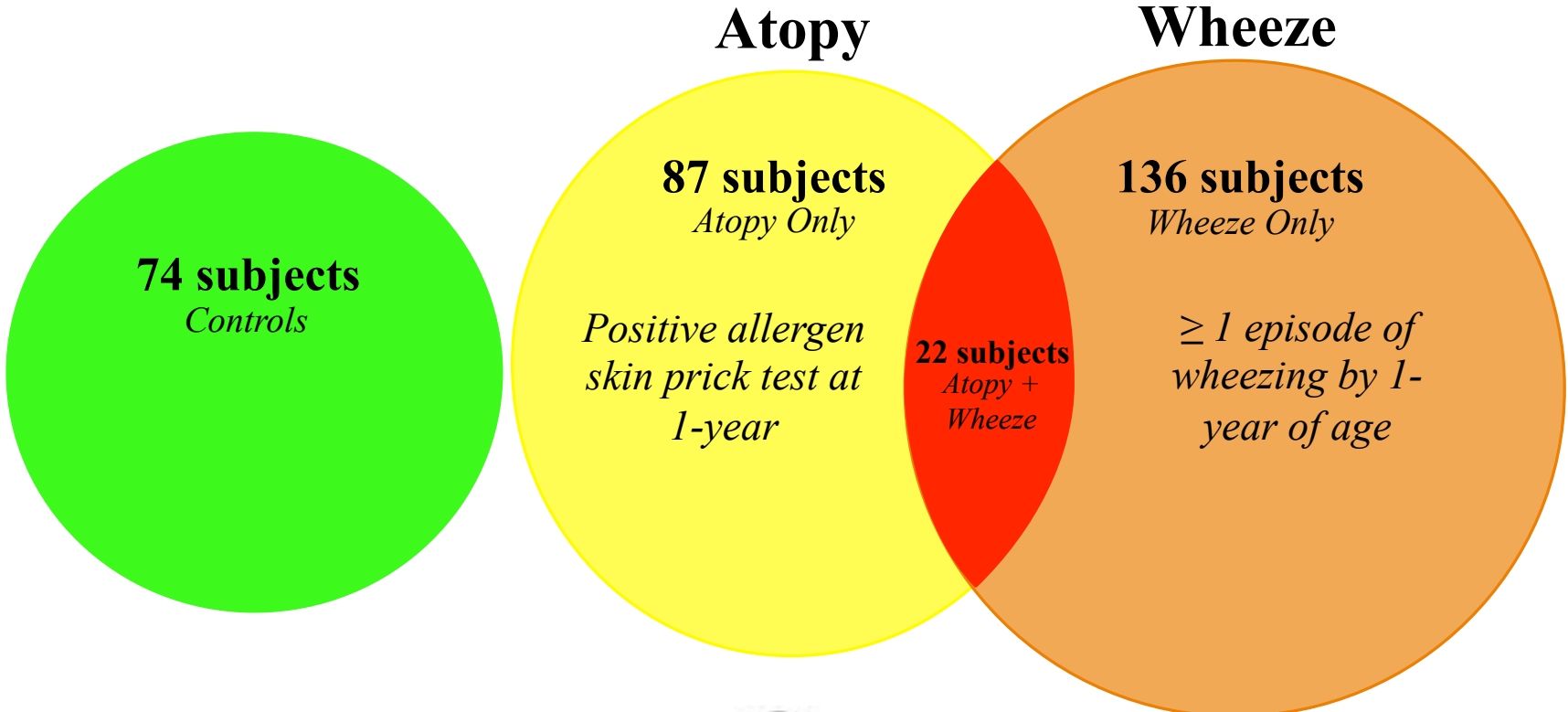
Neonatal antibiotic treatment affects experimental asthma severity



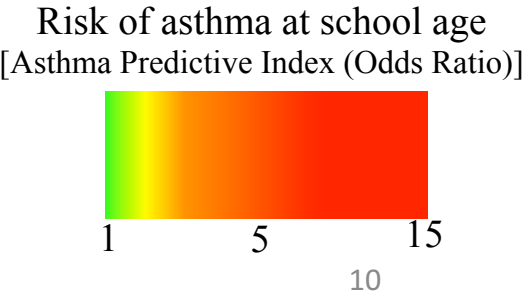




CHILD Study:

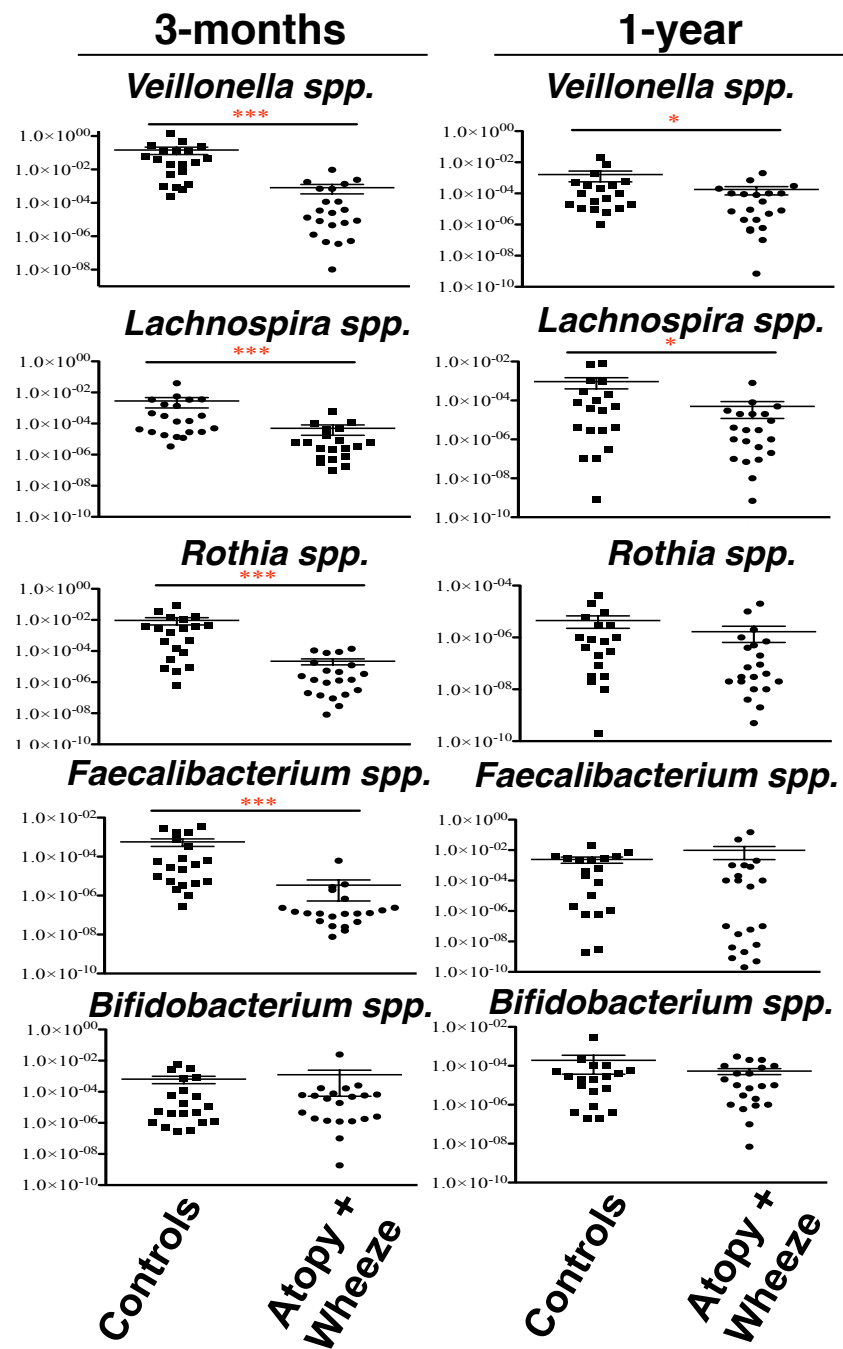


16S rRNA analysis at 3 months and one year of age

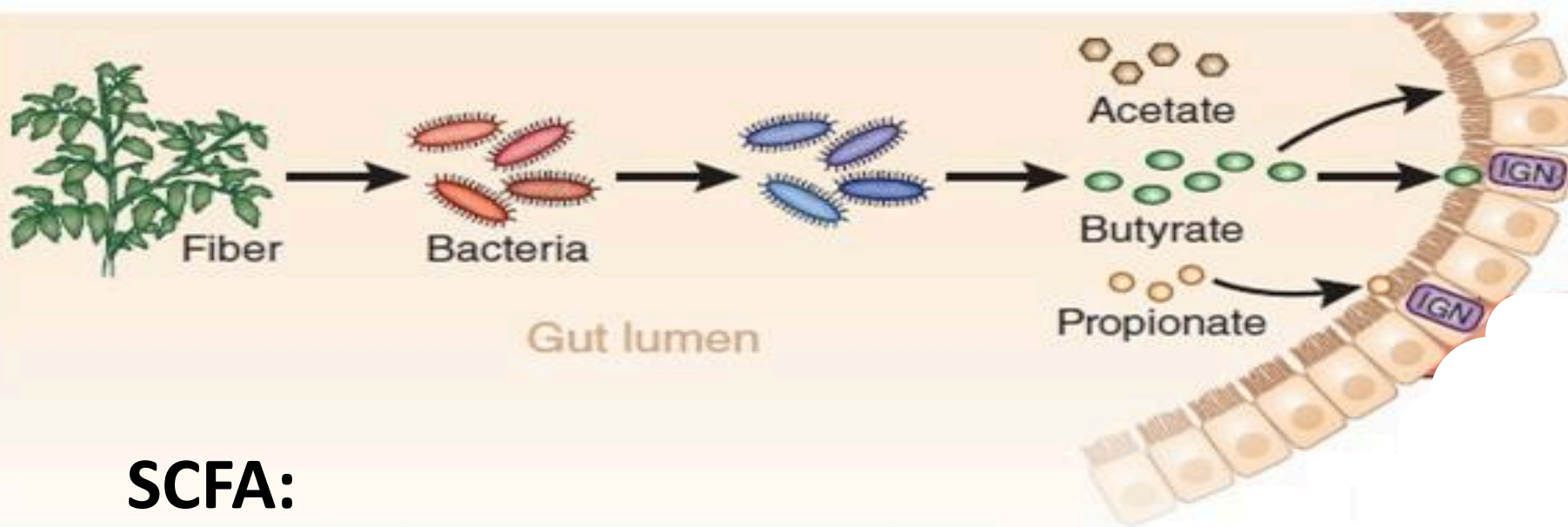


D

Relative Quantification

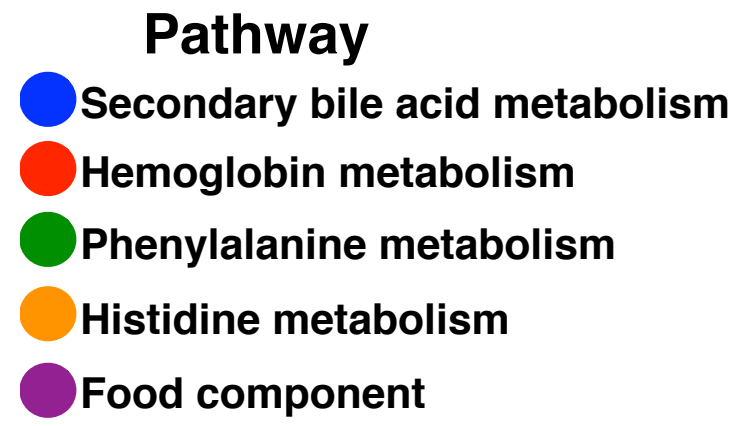
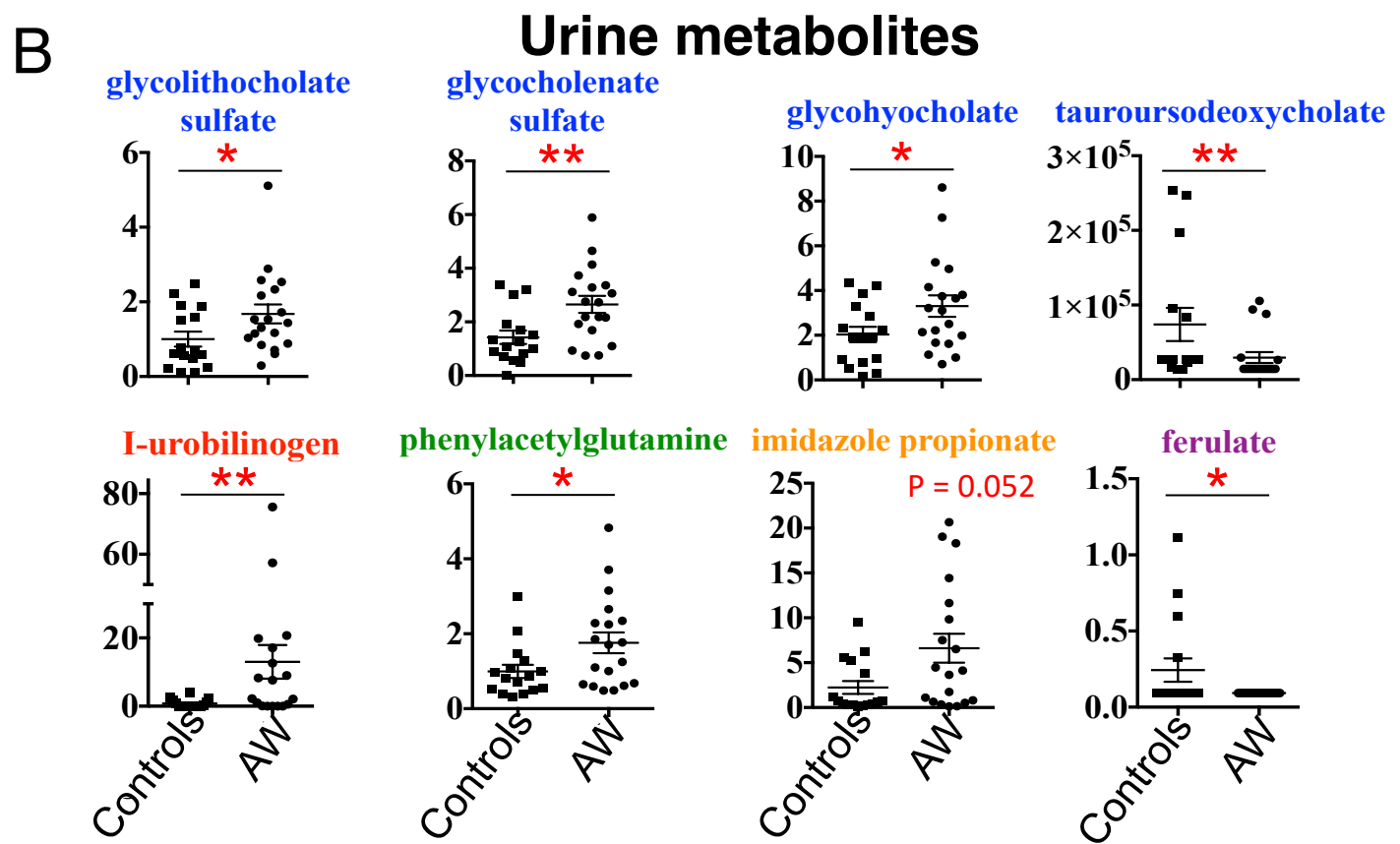
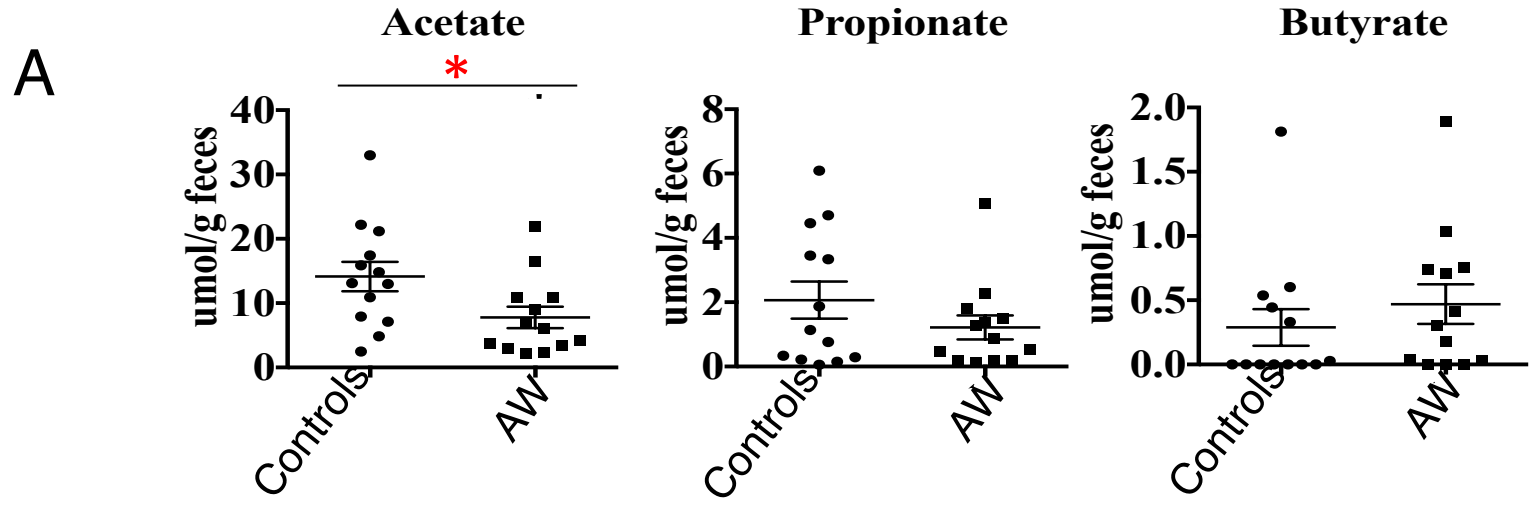


Gut bacterial metabolism: short-chain fatty acids (SCFA)



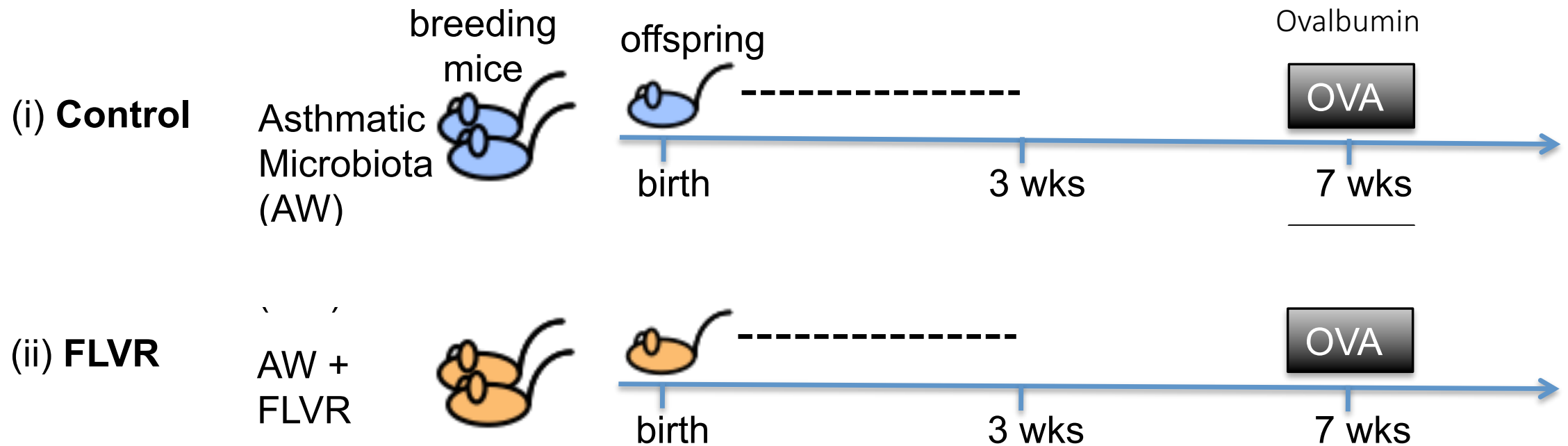
SCFA:

- Used as energy source by intestinal and mucosal immune cells.
- Transported to the liver where they are involved in numerous biochemical pathways of lipid and energy metabolism.
- Involved in immune response regulation.

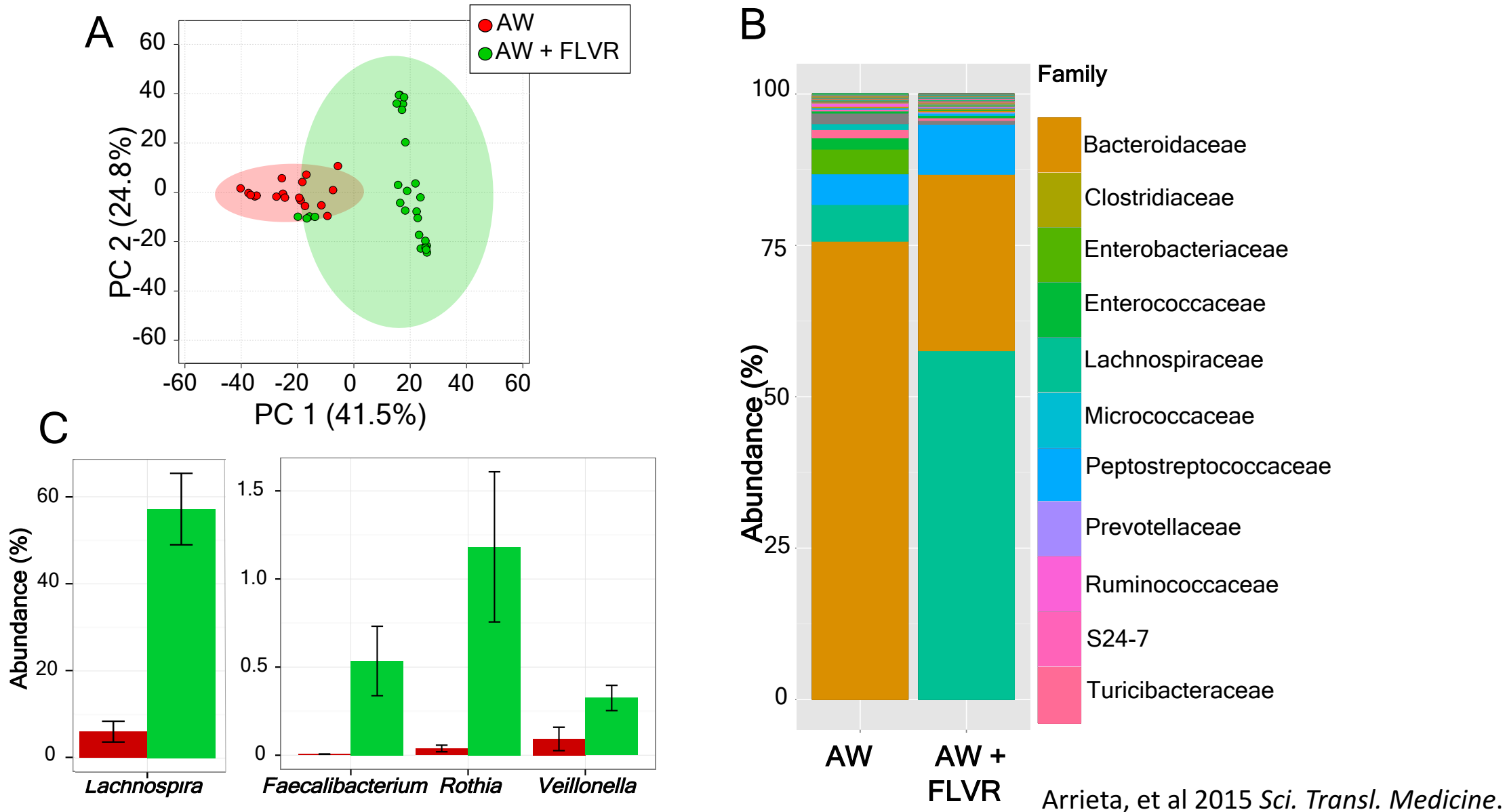


From correlation to causation

Human microbiota transfer (inoculated with feces from AW subject)

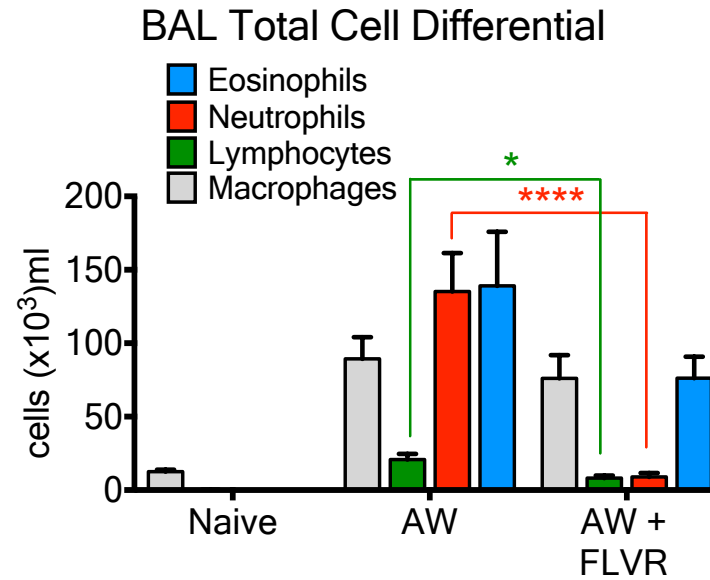
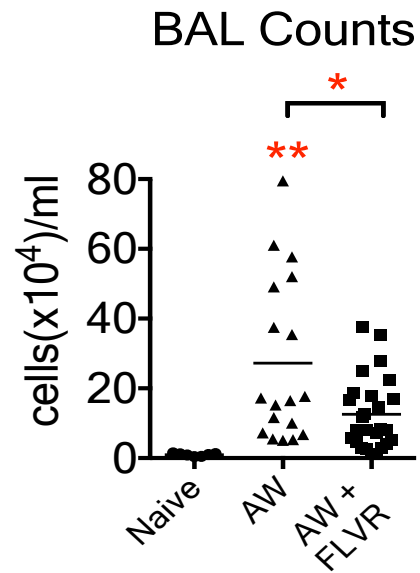


Microbial intestinal colonization in F1 mice

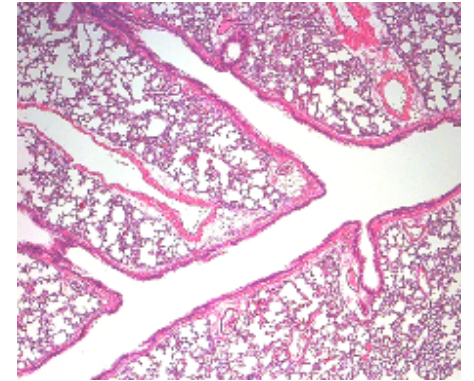


FLVR reduces lung inflammation

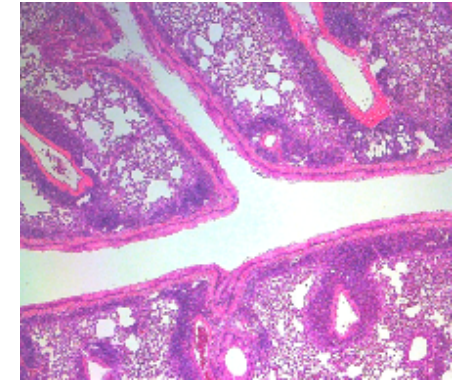
Bronchoalveolar lavage



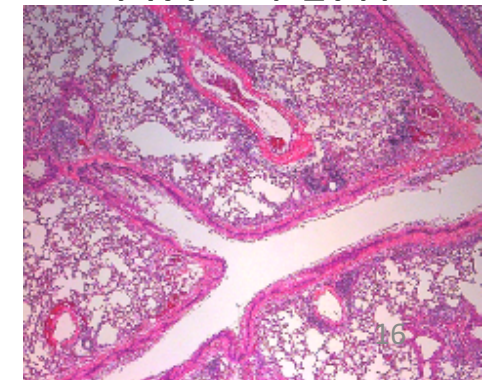
Naive



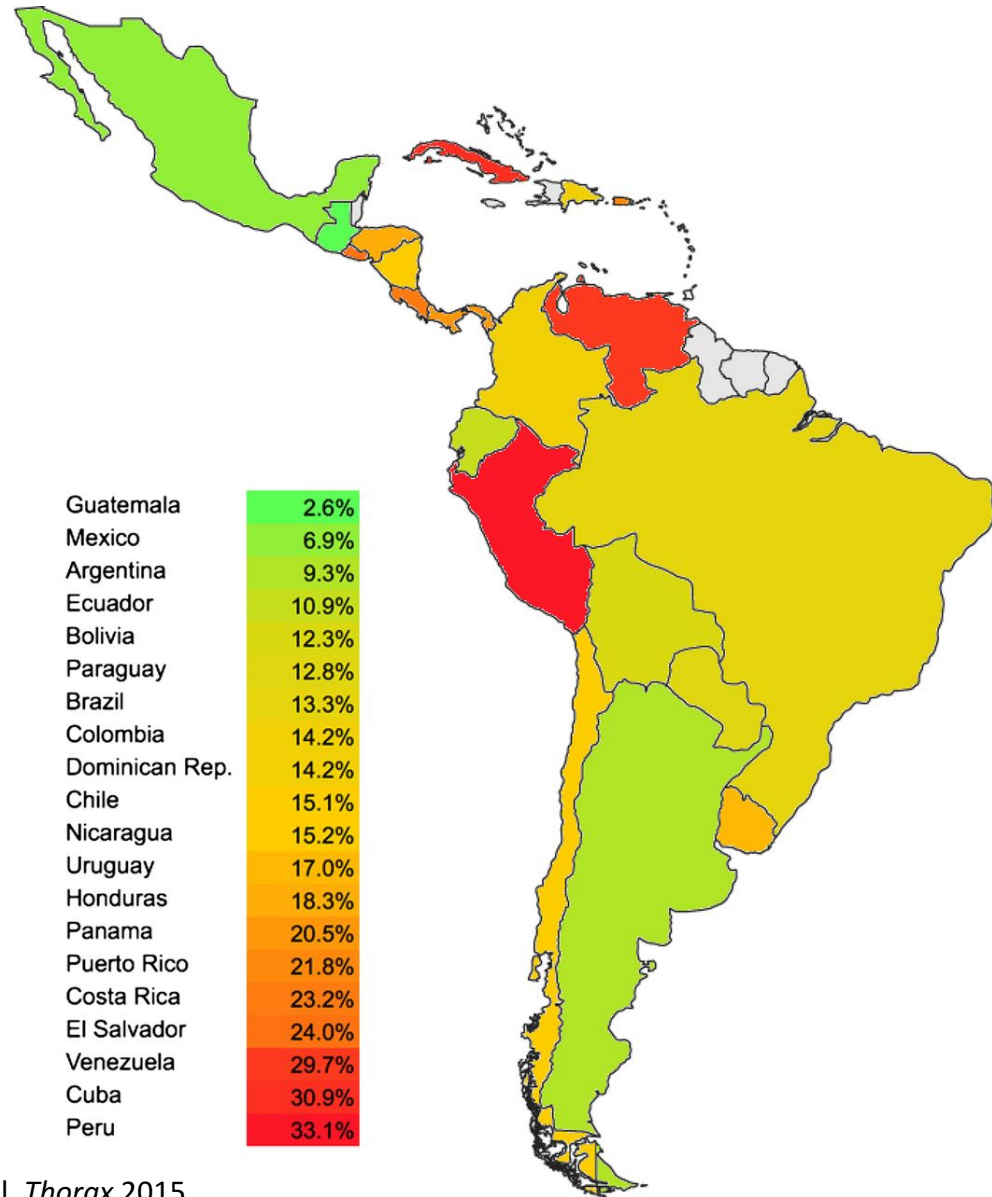
AW



AW + FLVR



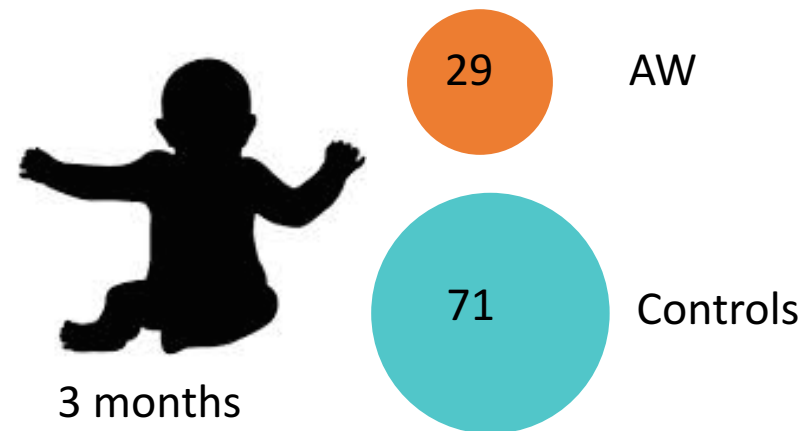
What about asthma elsewhere?



Las Esmeraldas, Ecuador



Prof. Phil Cooper



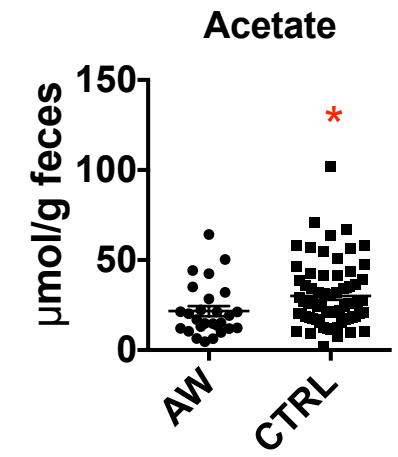
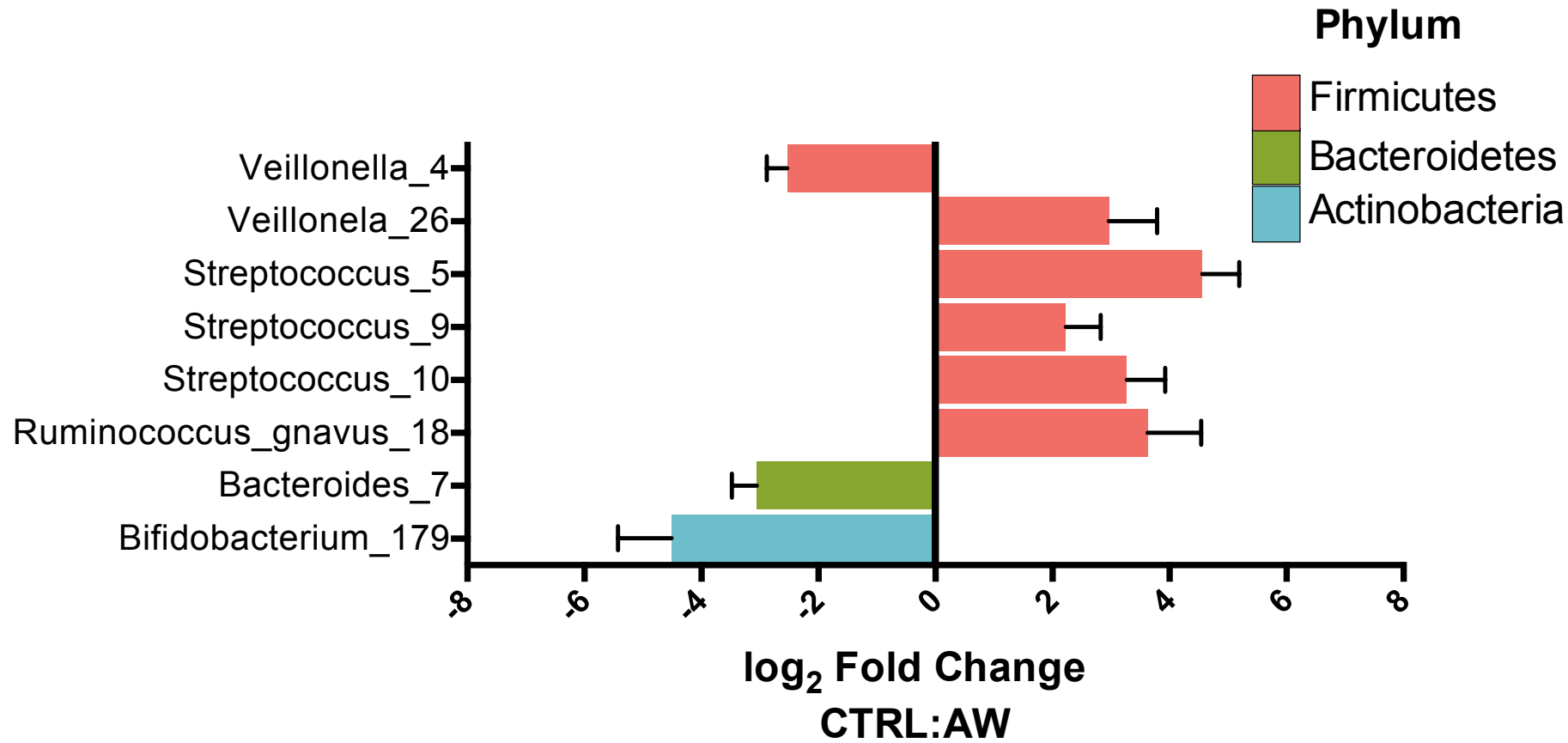
Rural to urban transition



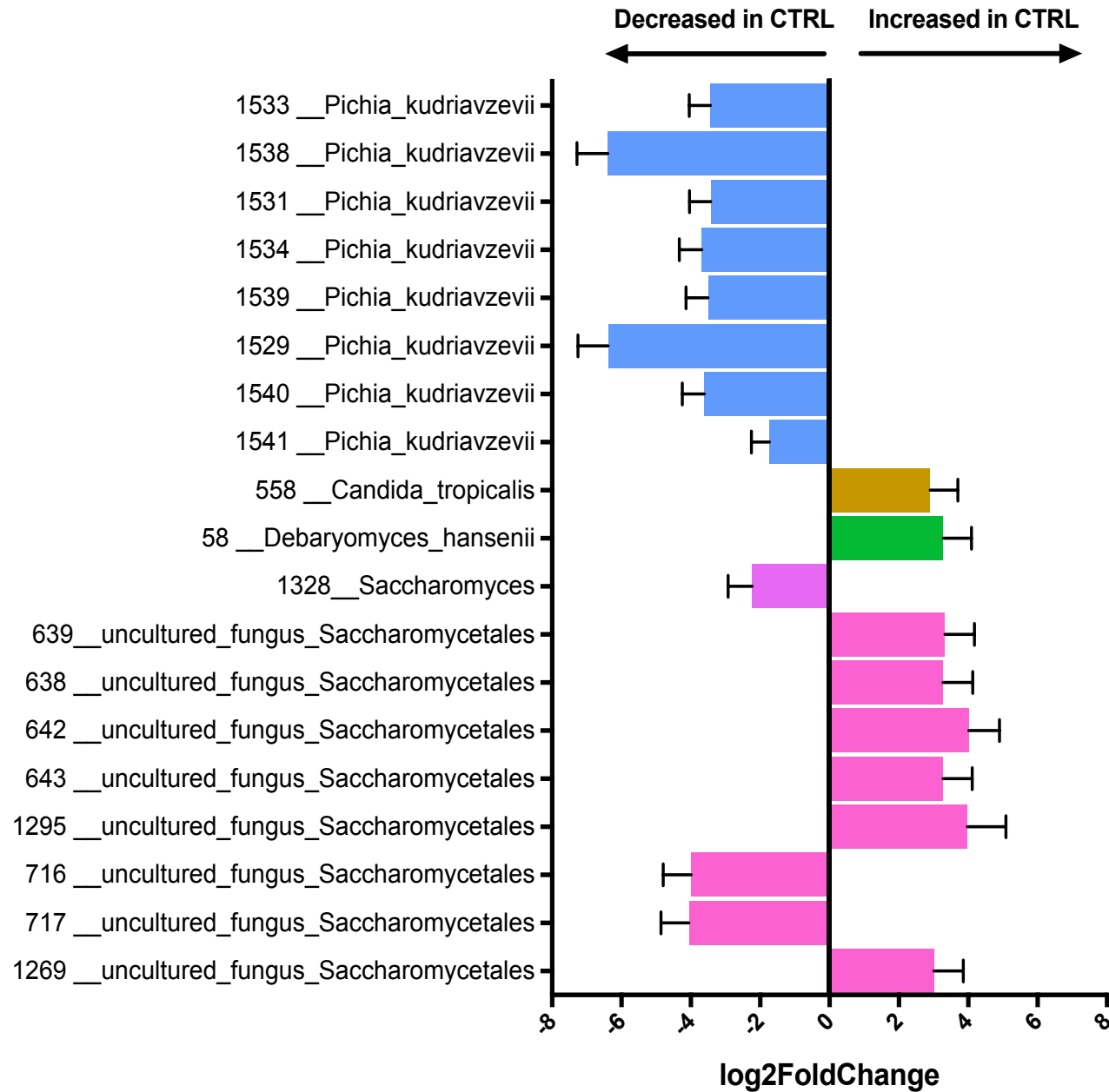
Ecuador cohort: epidemiology

Categorical variable	Odds ratio	P
Maternal antibiotics during pregnancy	2.39	0.02
Vaginal birth	-2.42	0.03
Breastfeeding over 5 months	-0.17	0.02
Child Ascaris infection	3.82	0.05
Child Trichuris infection	-8.18	0.004
Respiratory infections	2.21	0.001
Potable water	2.49	0.02

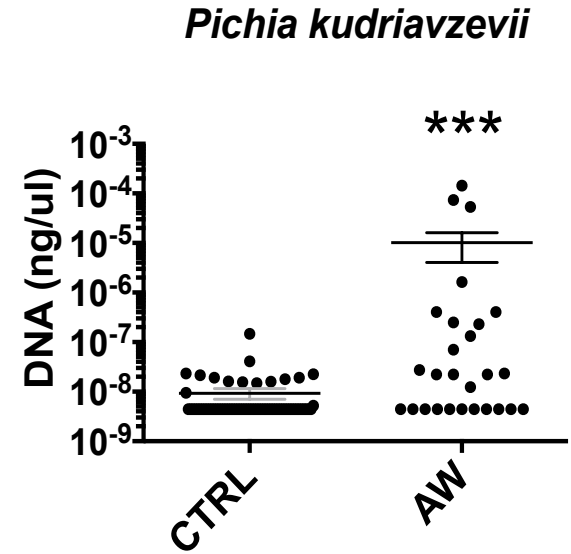
Microbiota in babies at risk of asthma



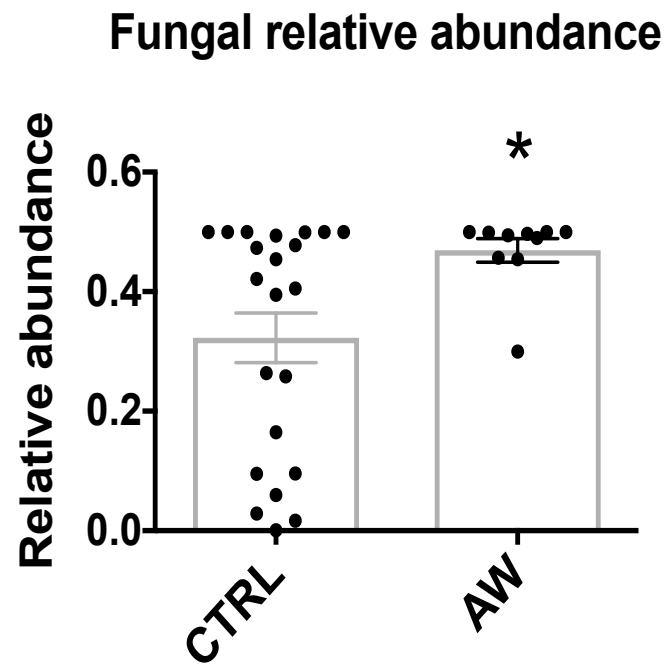
A



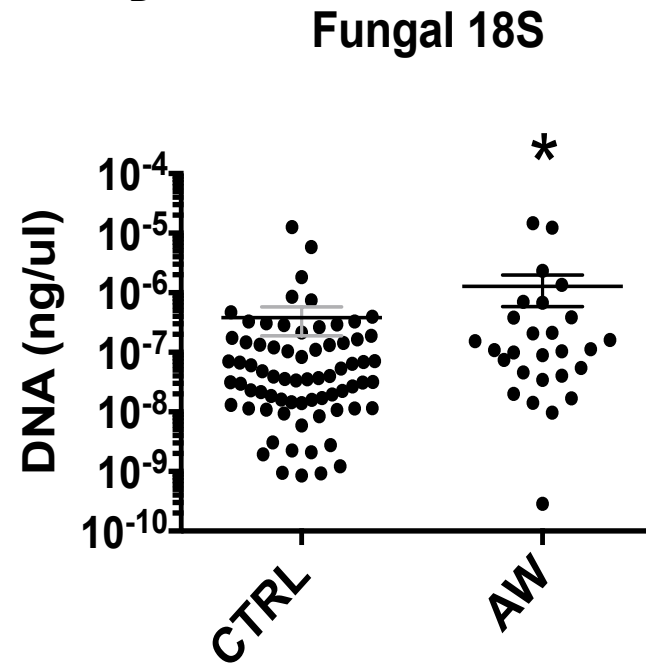
B



A

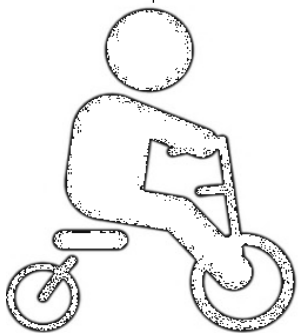
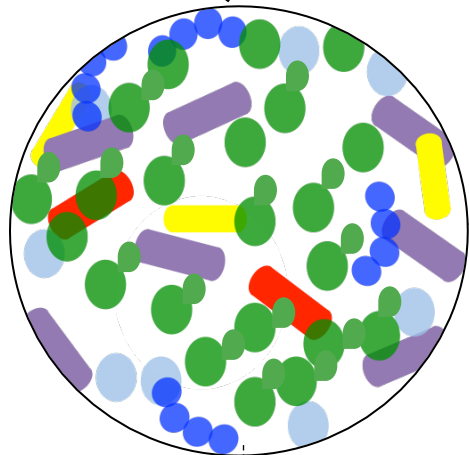
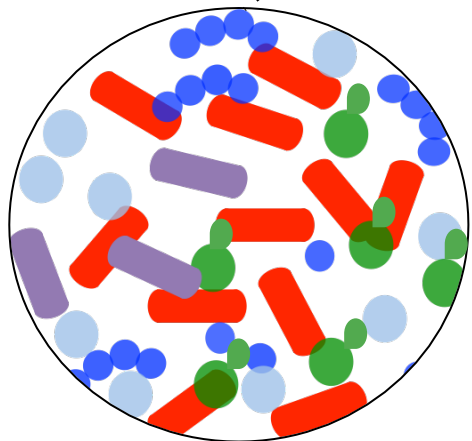


B

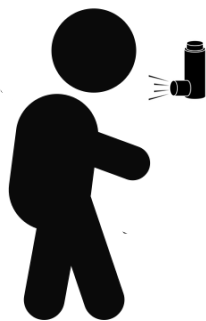




3 months



Healthy



Atopic wheeze



Bacteria

- ↓ *Faecalibacterium* sp.
- ↓ *Lachnospira* sp.
- ↓ *Veillonella* sp.
- ↓ *Rothia* sp.

Bacteria

- ↑ *Streptococcus* sp.
- ↑ *Bacteroides* sp.
- ↓ *Ruminococcus gnavus*
- ↓ *Bifidobacterium* sp.

Fungi

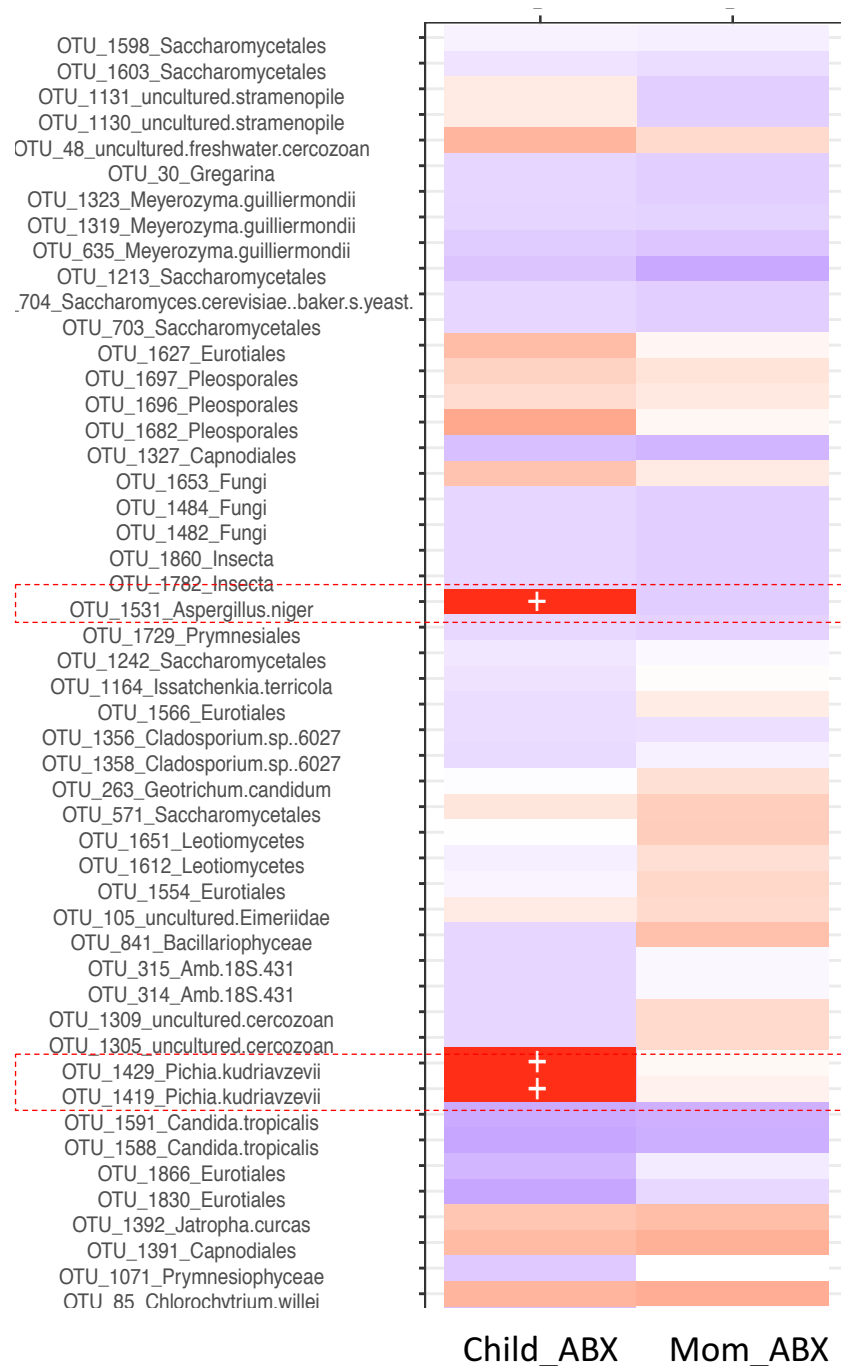
- ↑↑ *Pichia kudriavzevii*
- ↓ Saccharomycetales

Microbial metabolites

- ↓ Acetate

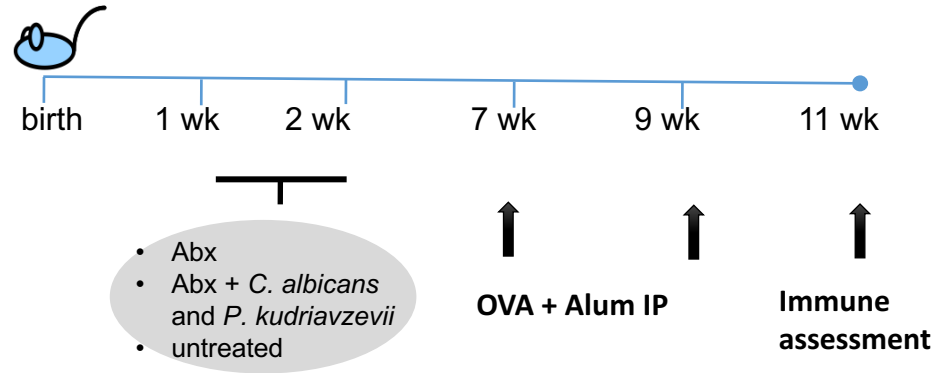
Hypothesis

Antibiotic-driven alterations in the fungal intestinal microbiota affect immune development and asthma.

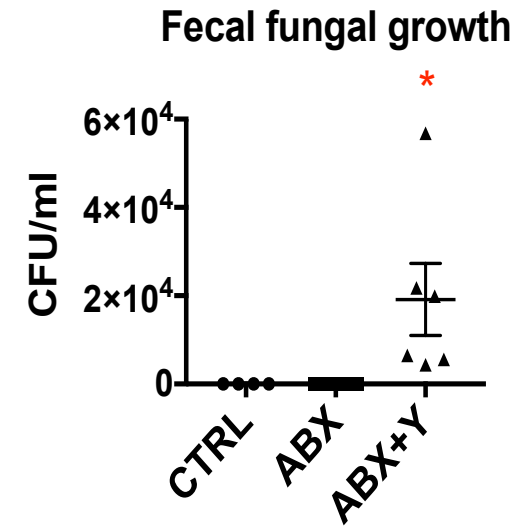


Can fecal fungal overgrowth influence atopy?

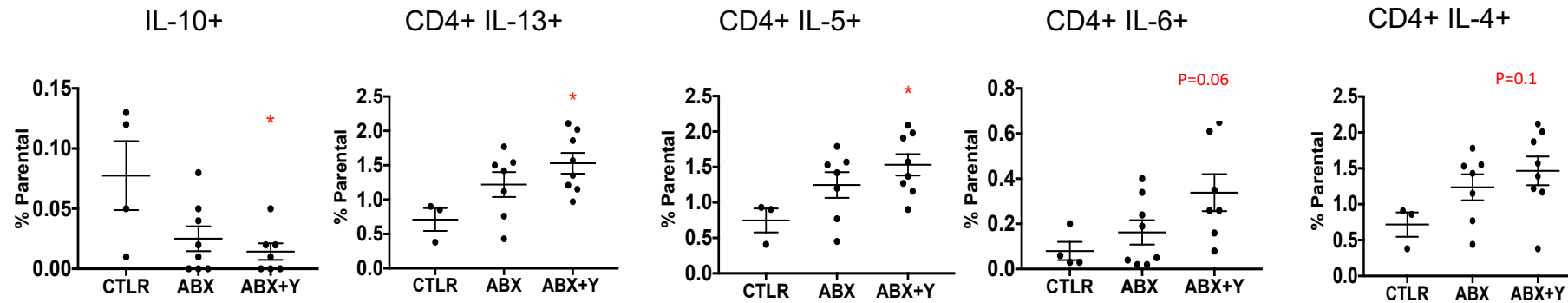
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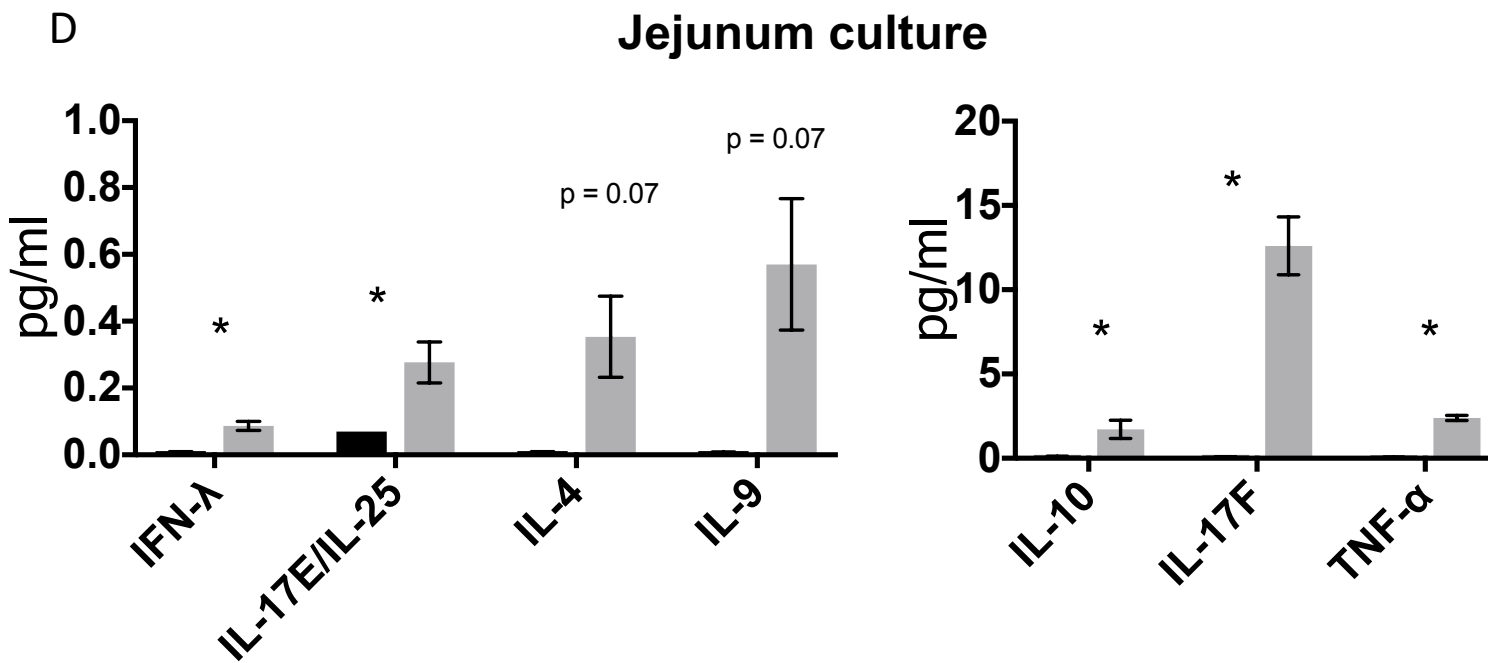
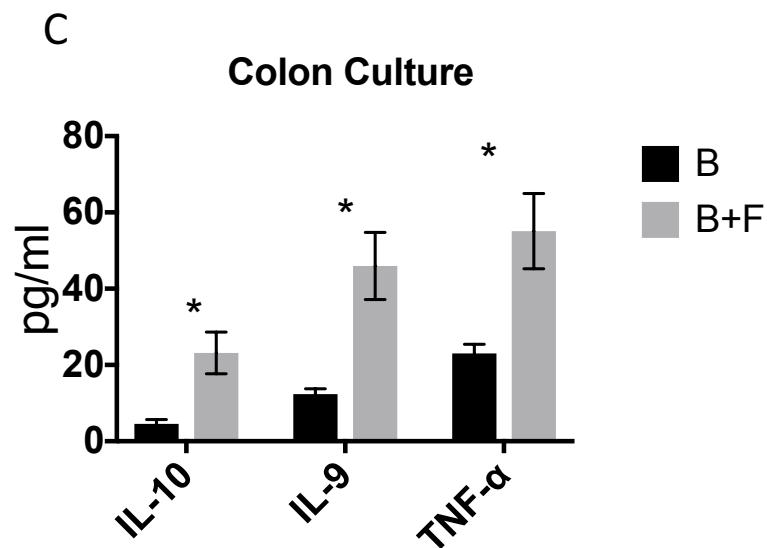
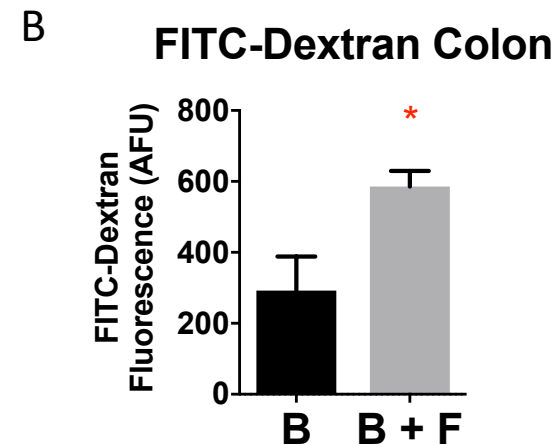
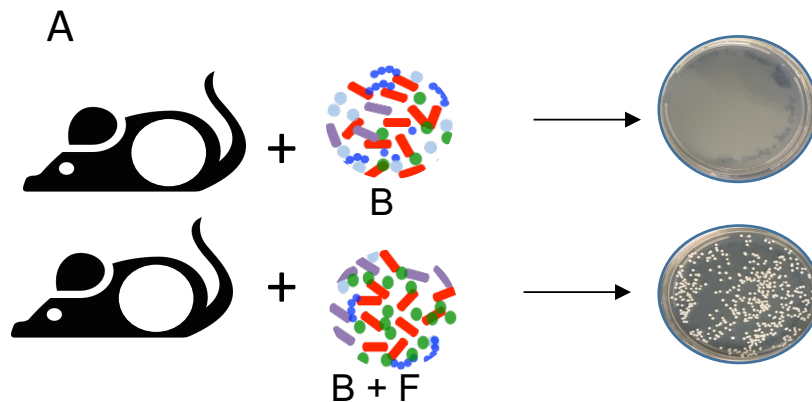
B



C

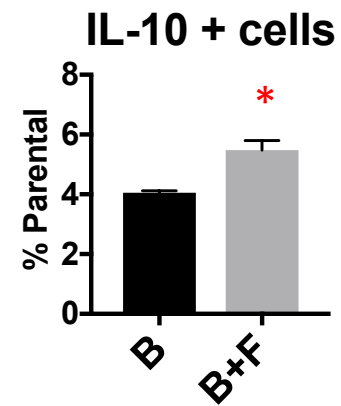
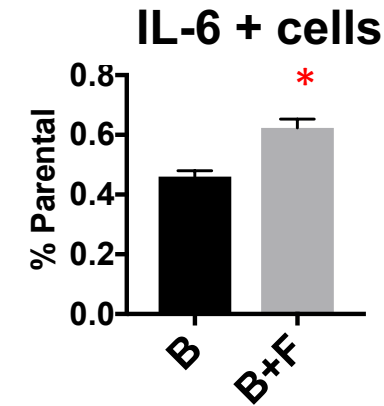
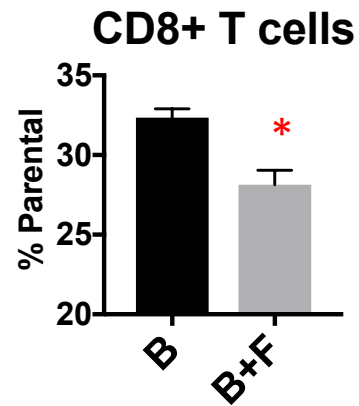
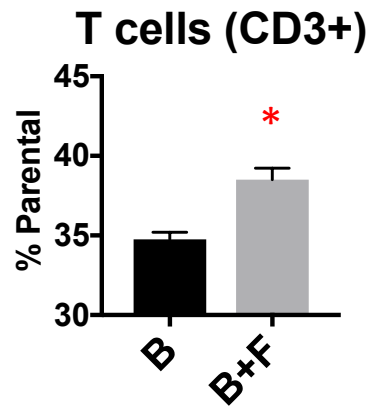
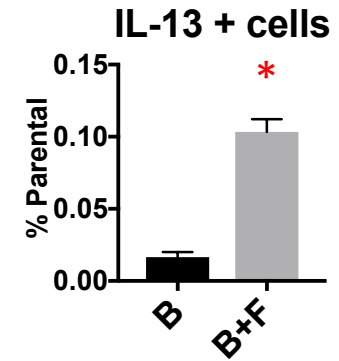
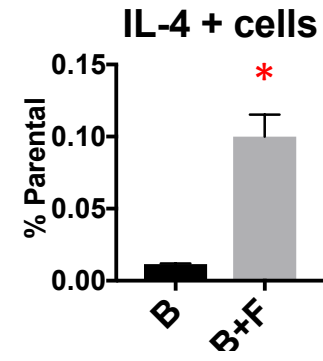
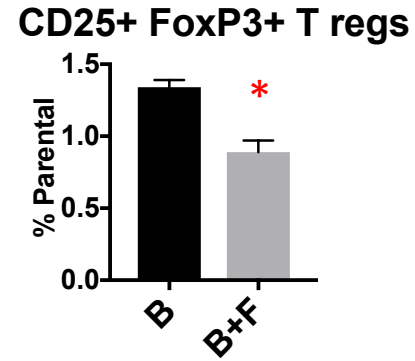
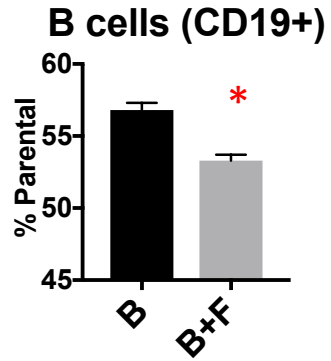


Does fungal gut colonization influence immune development?



Does fungal gut colonization influence immune development?

SPLENOCYTES



Summary

- Changes in the gut microbiome can influence asthma development.
- Early life is the most critical stage for the development of the microbiome.
- The first 100 days of human life represent an early ‘critical window’ in which microbial dysbiosis enhances the risk of asthma and allergic disease.

Summary

- Microbial dysbiosis can change with geographical location.
- Asthma-related microbial dysbiosis is both bacterial and fungal.
- Fungal overgrowth may also explain immune alterations that lead to asthma.
- **Prospective observational microbiome studies are critical to study dysbiotic markers that precede and may be involved in asthma pathogenesis.**



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CHILD Study
HELP CHILDREN
GROW UP HEALTHY



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