Microbiome Ireland

Interfacing Food & Medicine

The Microbiome in Allergy and Asthma

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Agriculture and Food Development Authority

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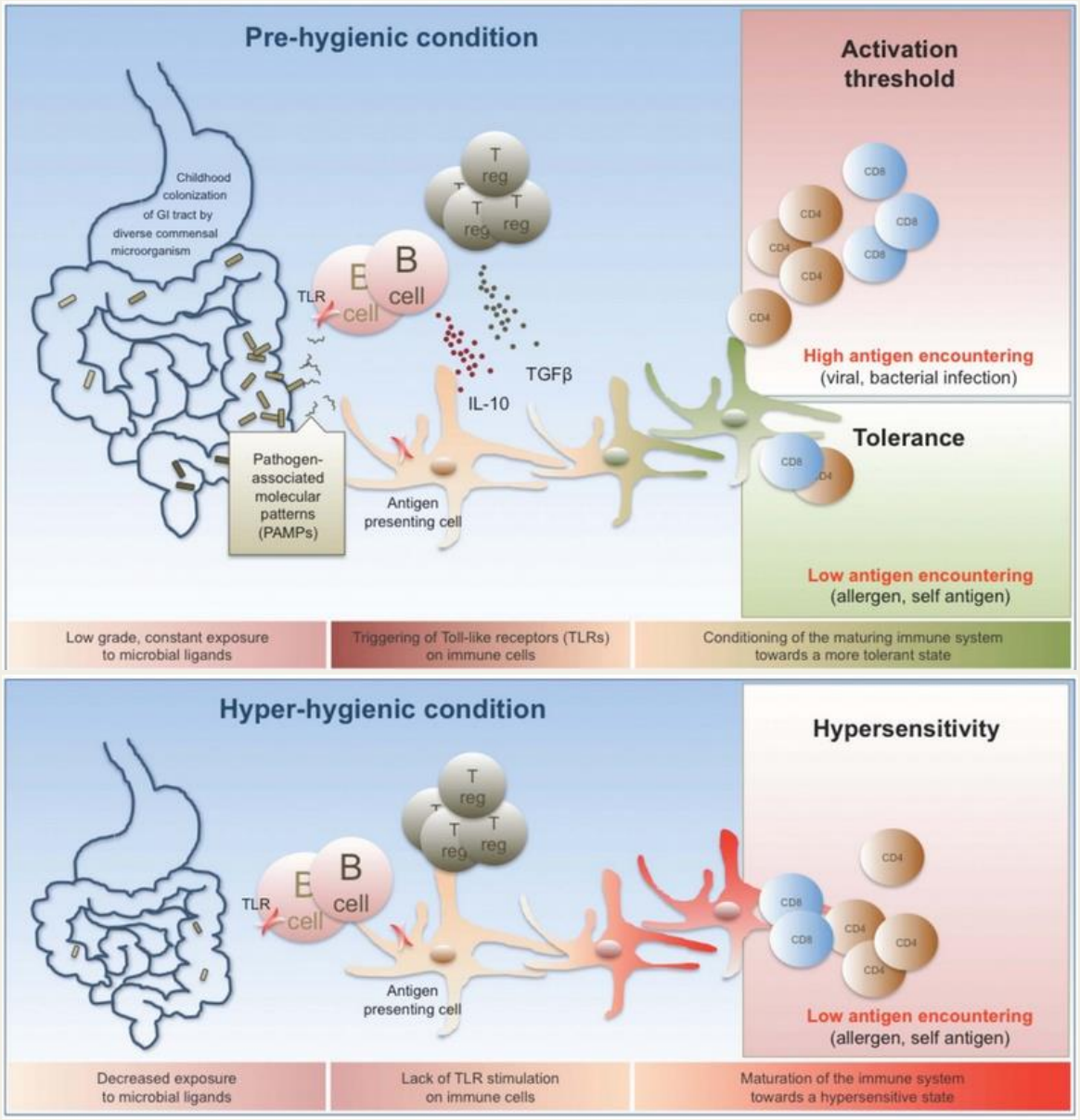
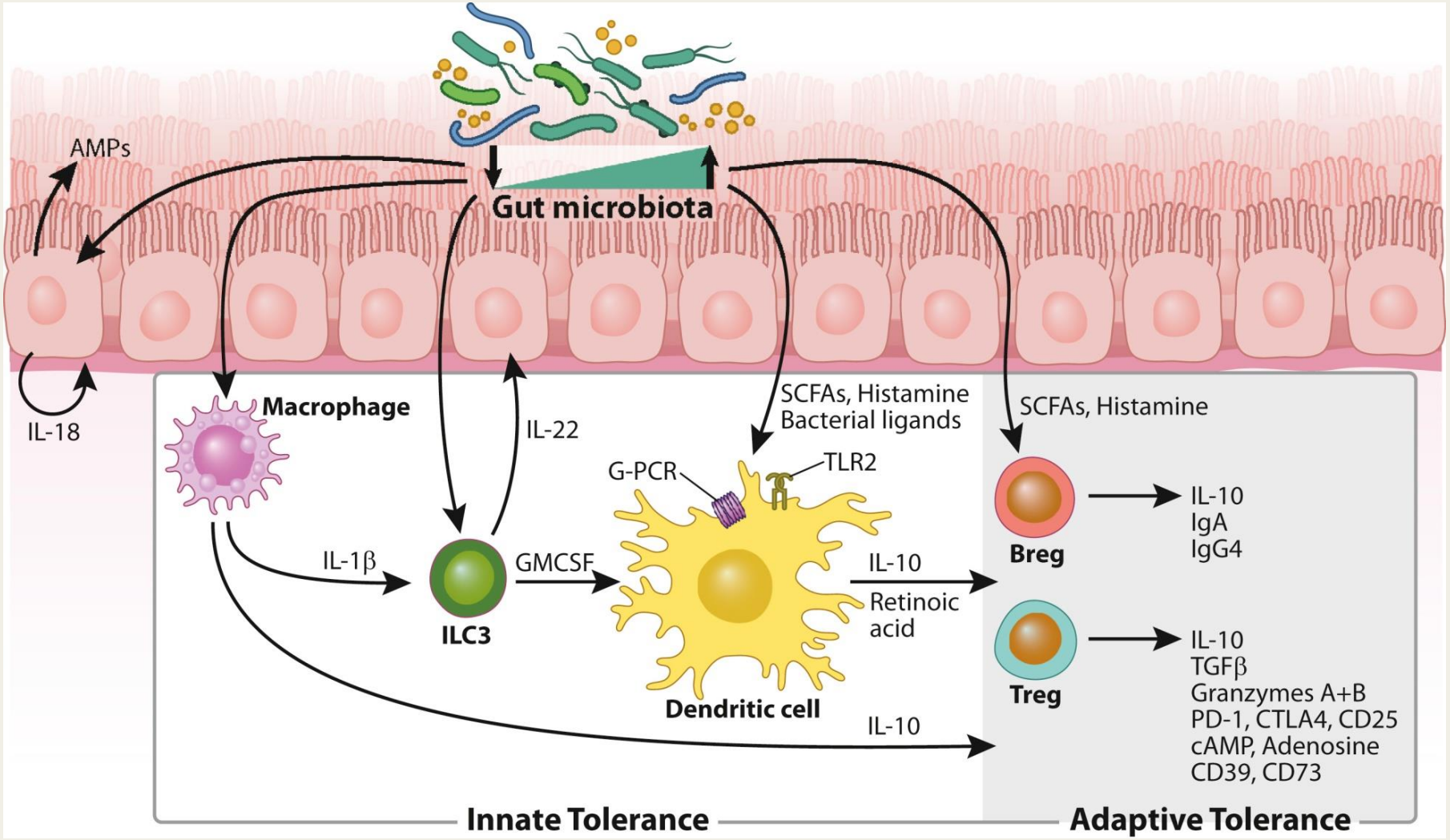
Bacterial Stimulation of Immune Tolerance



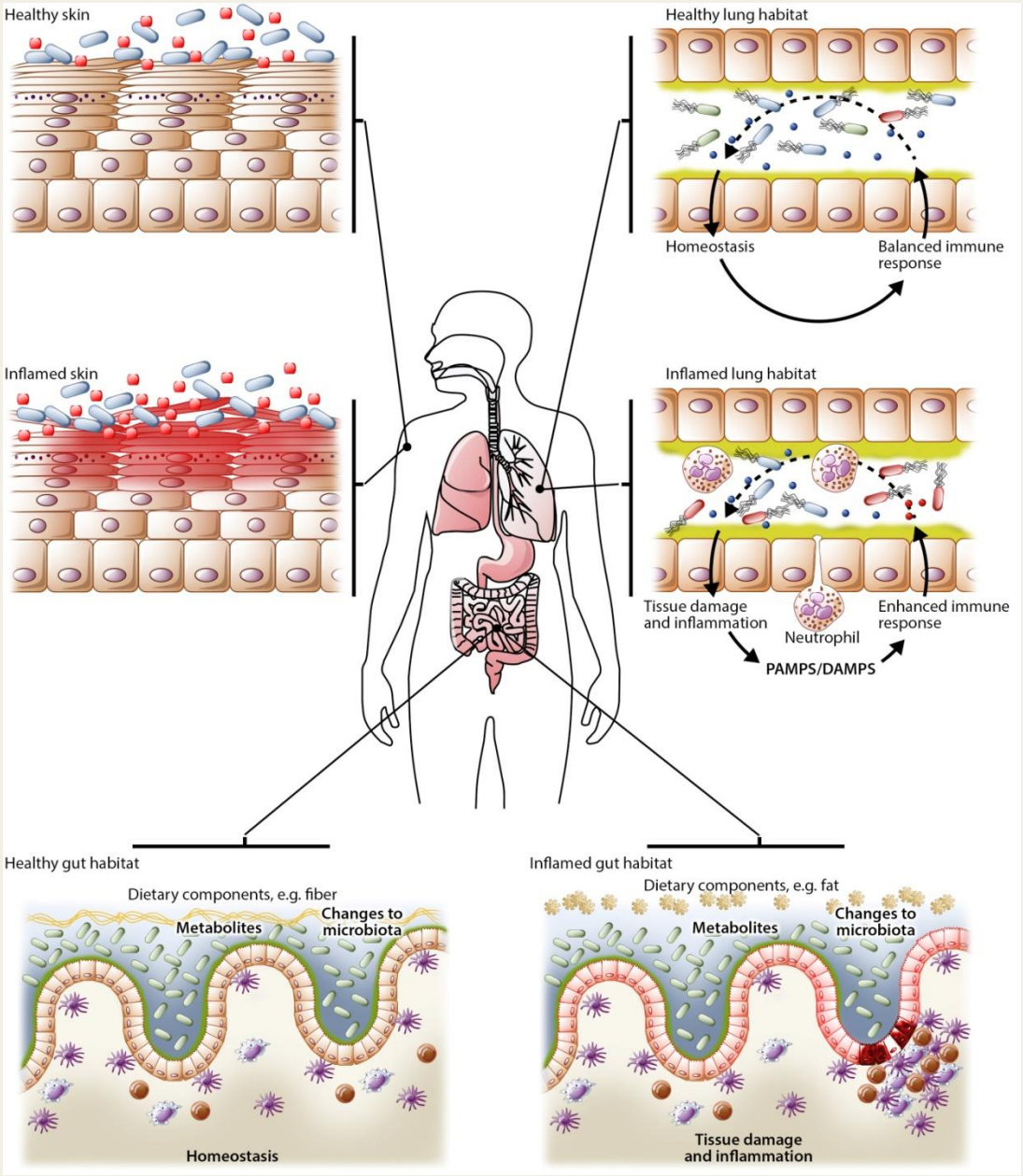
Ngoi et al., Discov Med 2011

Multiple Microbiota Interactions with the Mucosal Immune System



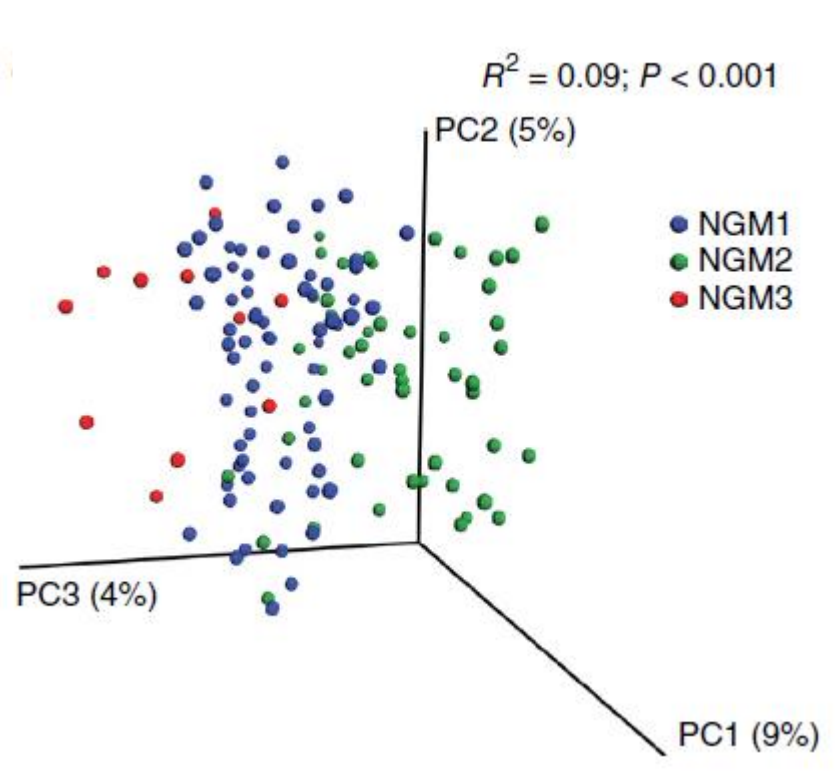
Sampson et al., JACI 2018

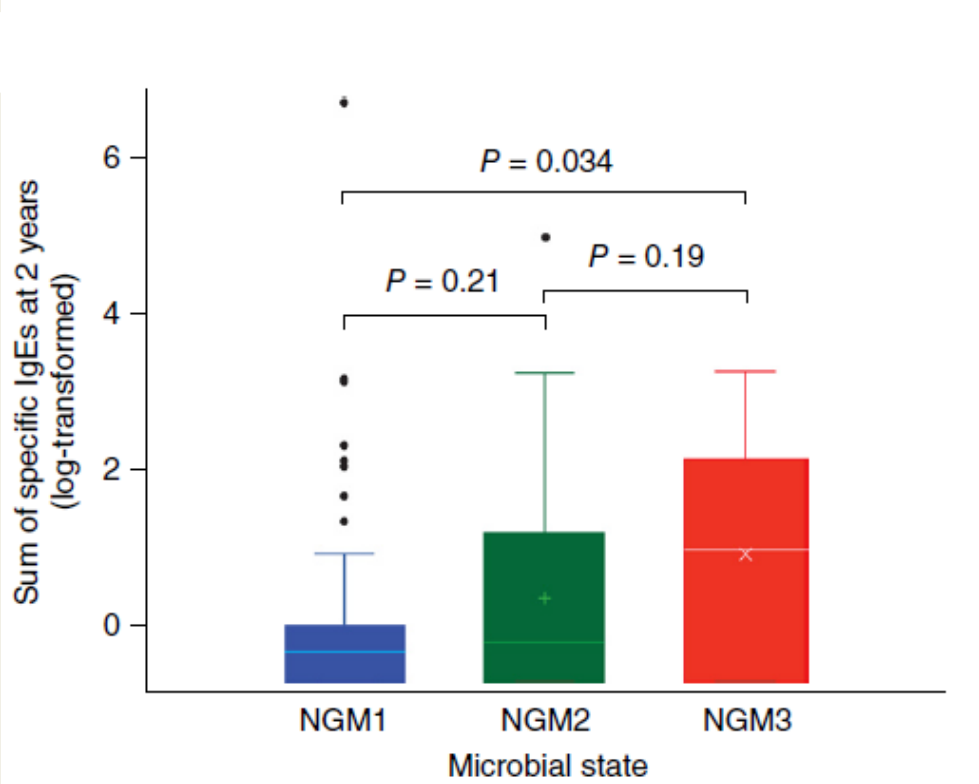
Microbial Dysbiosis



Huang et al., JACI 2017

Early Life Microbial Dysbiosis Asociated with Atopy Risk

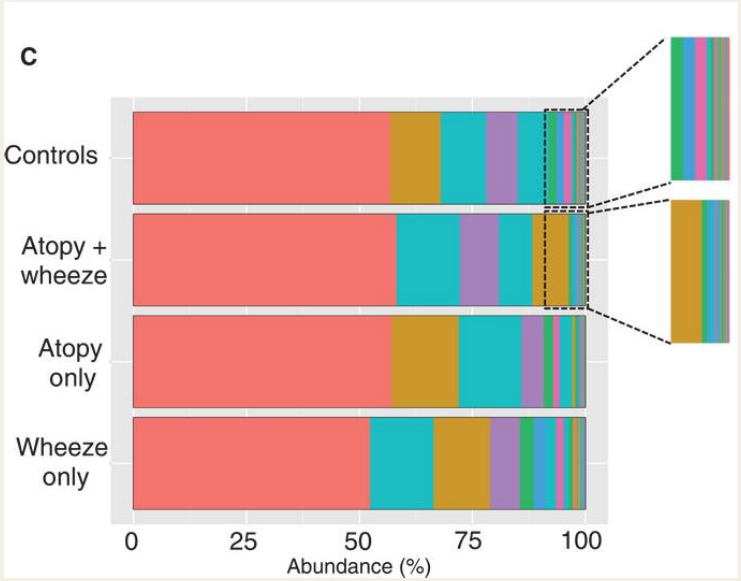


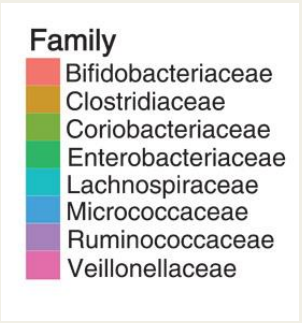


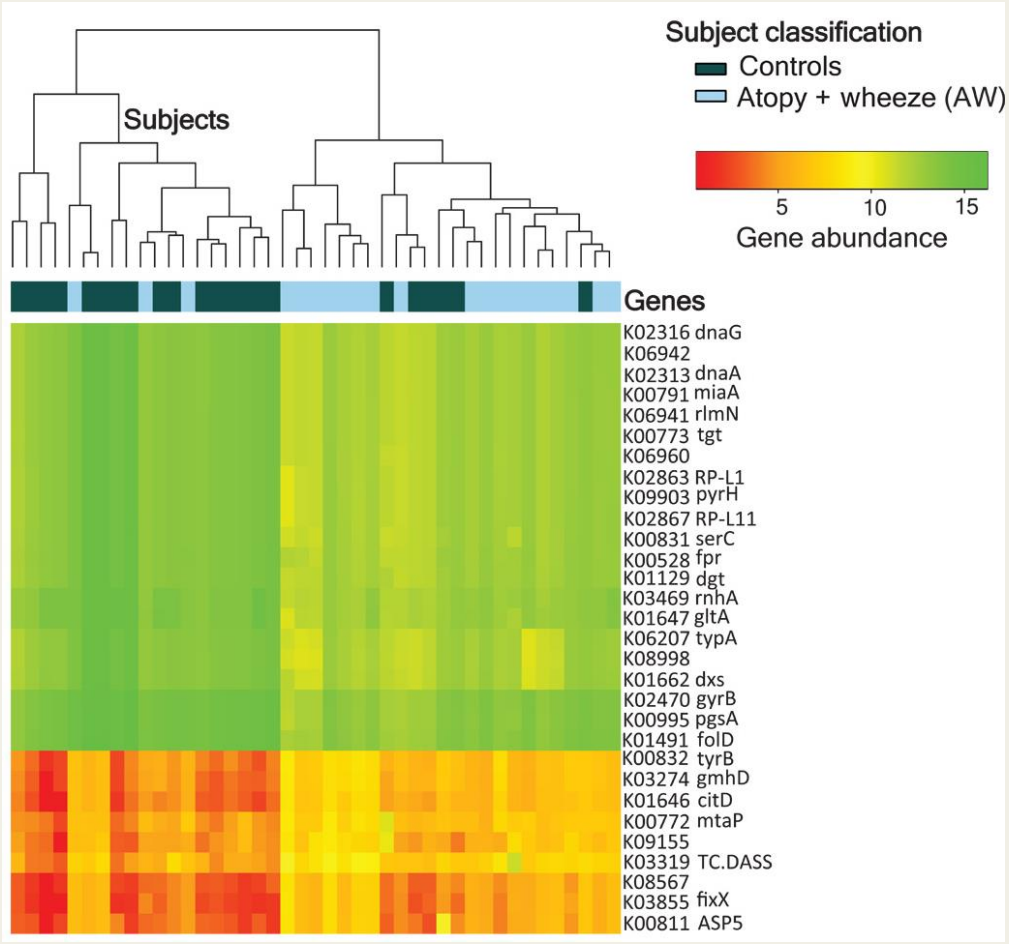
NGM3 has lower relative abundance of Bifidobacteria, Akkermansia and Faecalibacterium

Fujimura et al., Nature Medicine 2016

Early Life Microbial Dysbiosis Asociated with Atopy & Wheeze

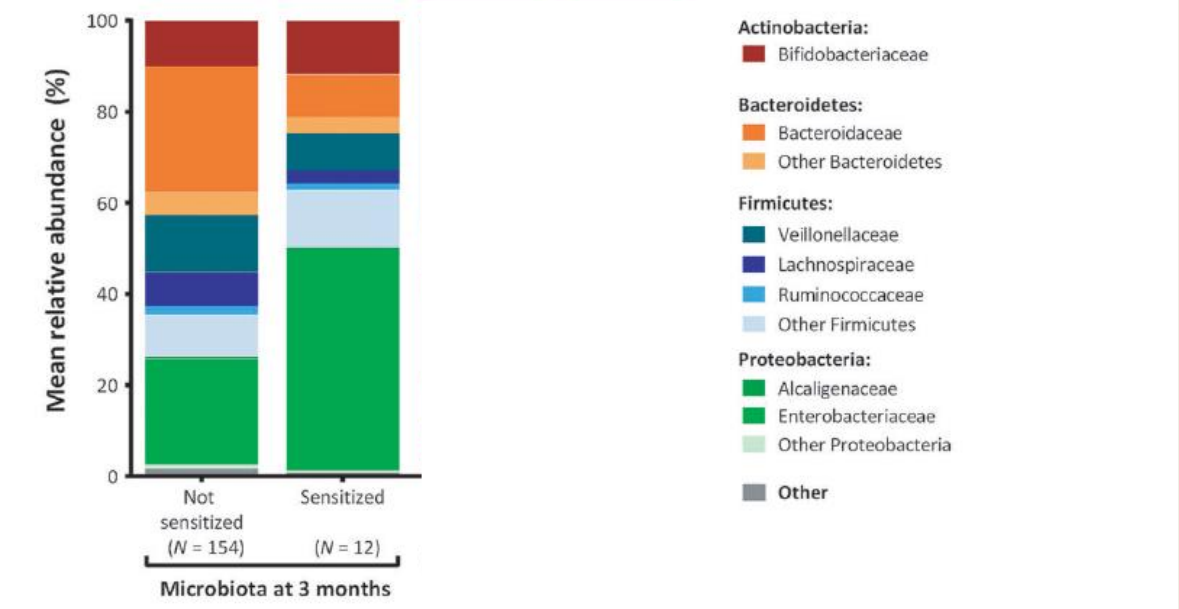


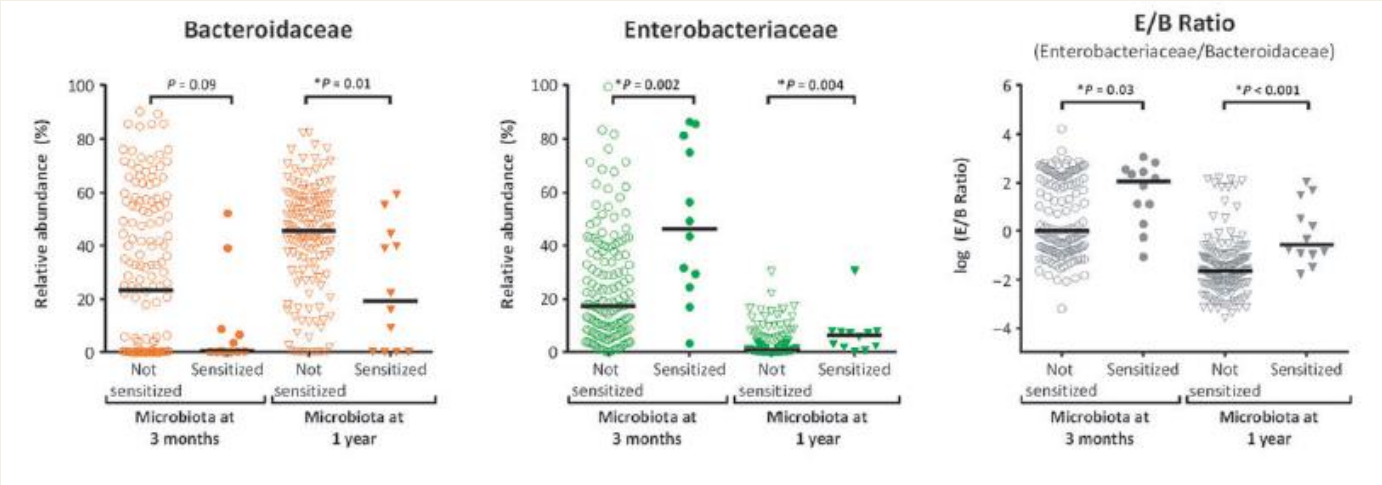




Arrieta et al., Sci Transl Med 2015

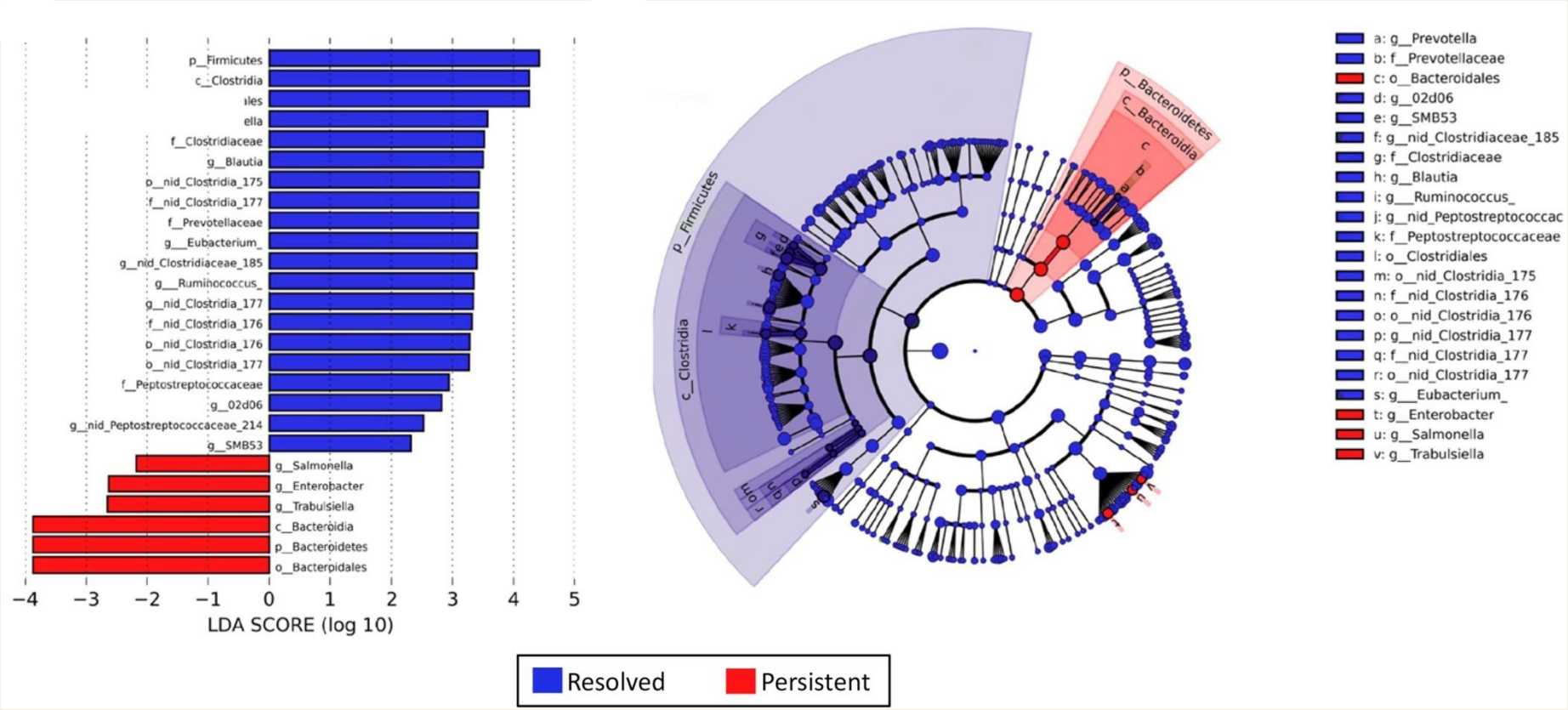
Microbiota Dysbiosis and Food Allergen Sensitization





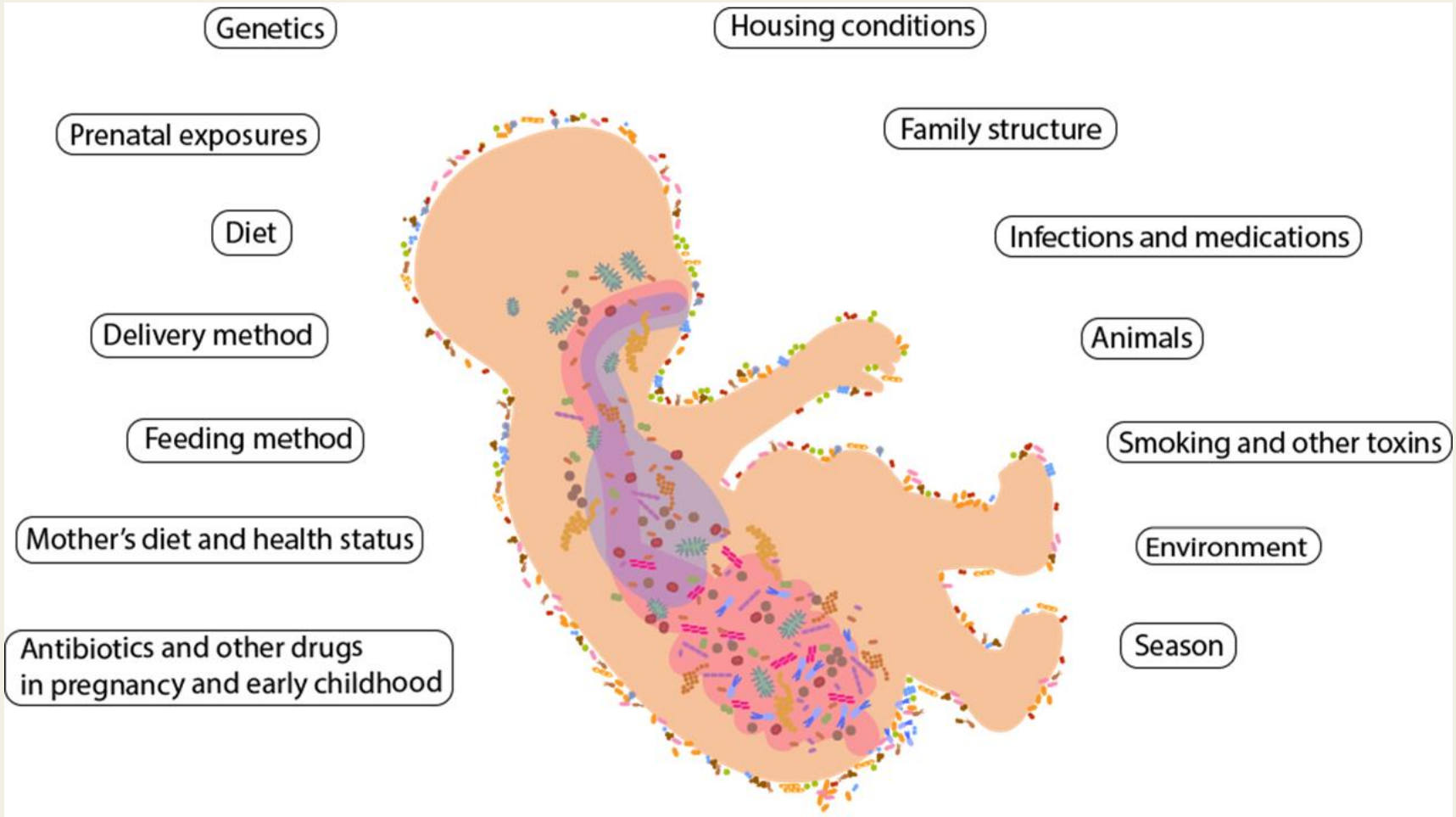
Azad et al., CEA 2015

Microbiome Composition Associates with Milk Allergy Resolution



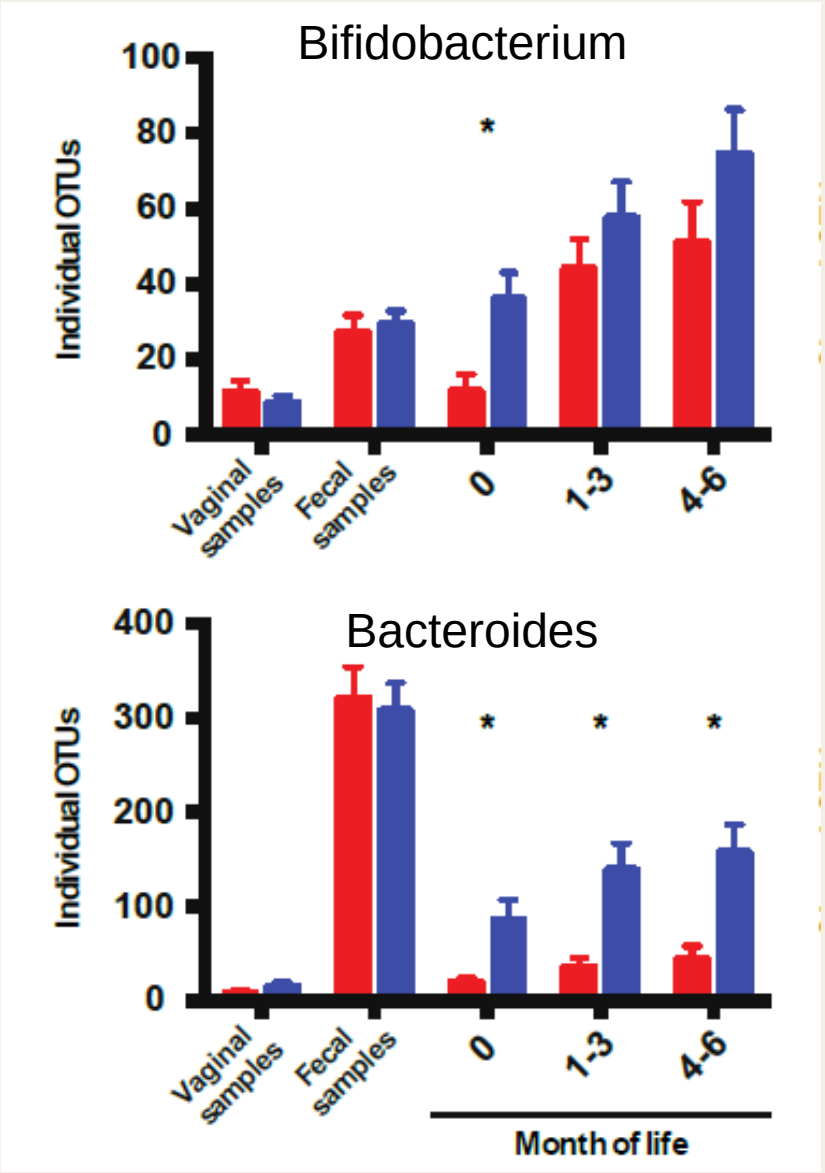
Bunyavanich et al, JACI 2016

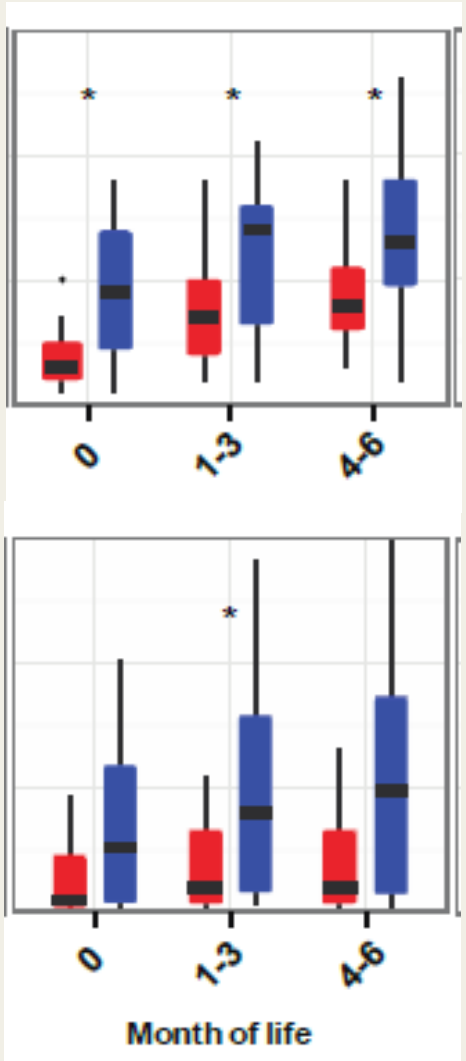
What Influences Microbiome Development?



Lunjani et al, Allergy 2018

Delivery Mode Influences the Gut Microbiota



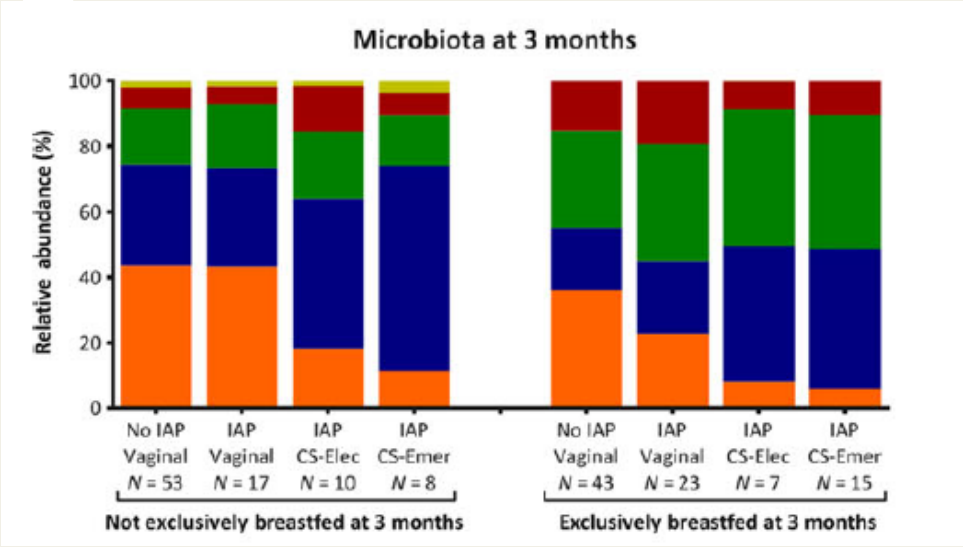


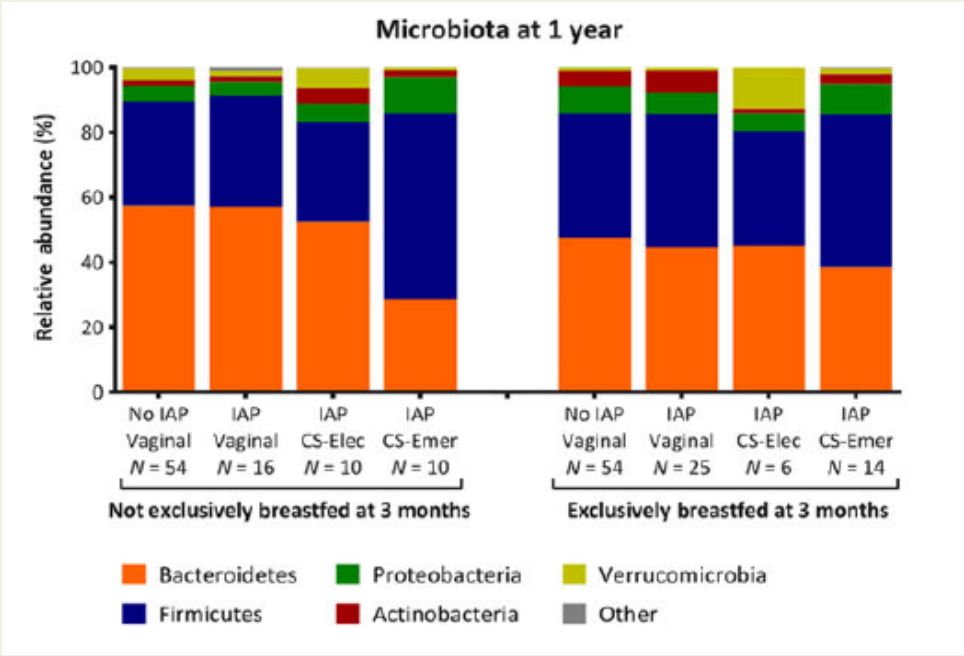
Bokulich et al,
Science Translational Medicine 2016

Antibiotic Use Delays Microbiome Maturation

Bokulich et al,
Science Translational Medicine 2016

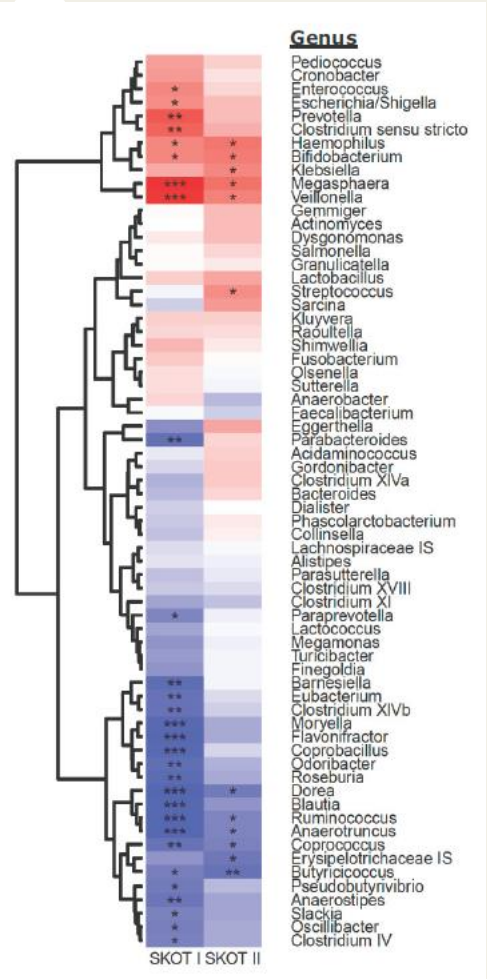
Interaction between Antibiotics and Delivery Mode





Azad, et al., BLOG 2016

Breast-feeding Influences the Gut Microbiota



Firmicutes	9 months	18 months	36 months
Firmicutes (F1b)	0,566	0,182	0,4265
Lactobacillus spp. (F2)	0,0001***	0,1736	0,4136
L. acidophilus (F4)	0,6249	0,172	0,9128
C. butyricum (F5)	0,8274	0,0561	0,6691
C. leptum group (F6)	0,0267*	0,4015	0,5951
C. coccoides group (F7)	0,0021**	0,0097**	0,8153
E. hallii (F8)	0,0193*	0,4321	0,6329
Roseburia spp. (F9)	0,0316*	0,4482	0,6901
Enterococcus spp. (F10)	0,0731	0,0379*	0,5529
Bacteroidetes			
Bacteroidetes (B1)	0,016*	0,243	0,2087
Bacteroides/Prevotella groups (B2)	0,0177*	0,0128*	0,1326
Bacteroides spp. (B3)	0,126	0,3384	0,0709
B. fragilis group (B4)	0,0004***	0,0984	0,8973
B. vulgatus (B5)	0,0345*	0,0115*	0,1967
B. thetaiotaomicron (B6)	0,0016**	0,017*	0,3561
B. eggerthii (B7)	0,1241	0,9103	0,8546
B. distasonis (B8)	0,2906	0,1402	0,8114
Prevotella spp. (B9)	0,3372	0,1112	0,076
Alistipes spp. (B10)	0,1745	0,2494	0,3157
Bifidobacteria			
Bifidobacterium spp. (A1b)	0,0002***	0,51	0,5306
B. bifidum (A2)	0,6315	0,4082	0,8208
B. adolescentis (A3)	0,8294	0,9744	0,946
B. catenulatum (A4)	0,4334	0,4076	0,7047
B. longum (A5)	0,0477*	0,8546	0,2187
B. breve (A6)	0,7623	0,467	0,6985
Other bacteria			
Enterobacteriaceae (P1)	0,6179	0,6436	0,0523
E. coli (P2)	0,6053	0,555	0,1425
Desulfovibrio spp. (P3)	0,0449*	0,1072	0,9721
A. muciniphila (V1)	0,0451*	0,0863	0,811
M.smithii (E1)	0,0753	0,3251	0,6047

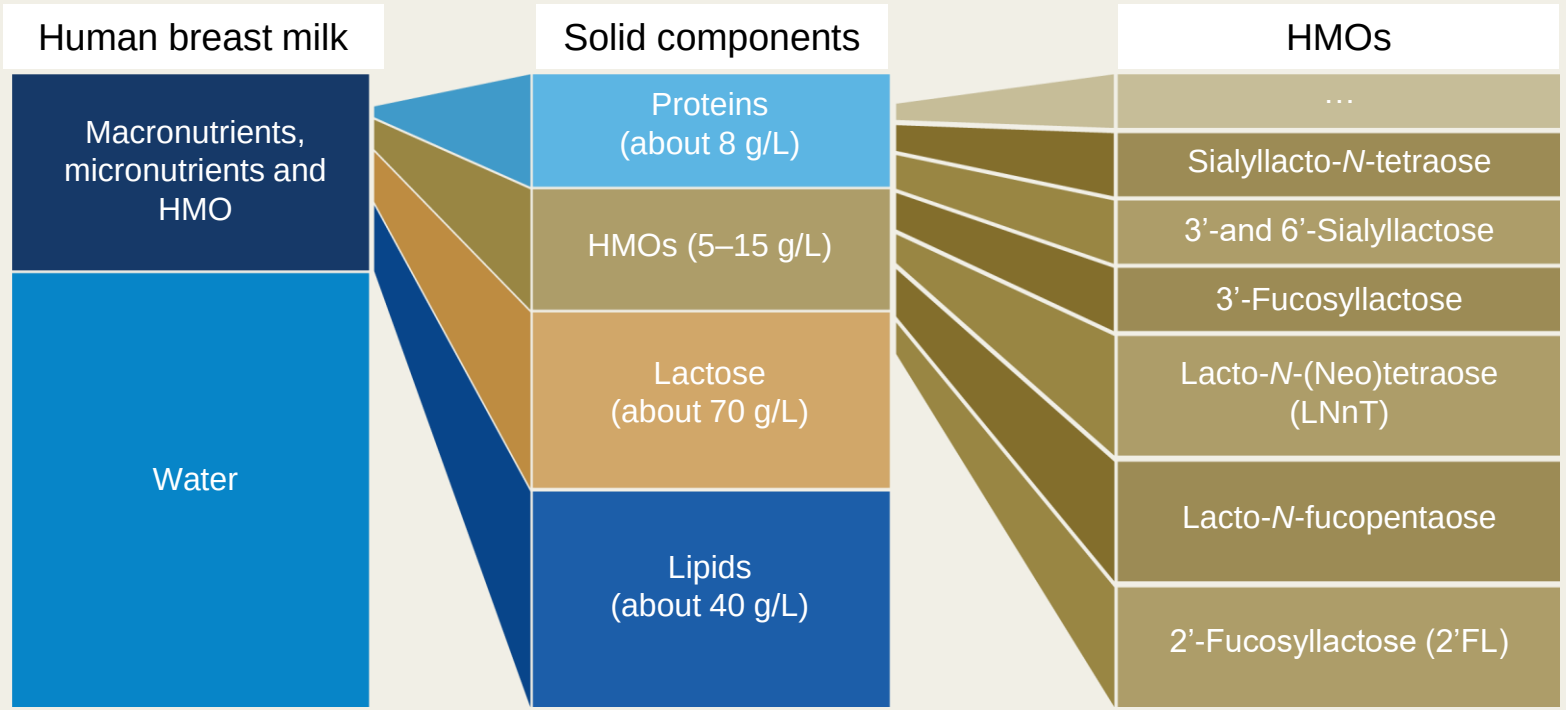
Increased in breastfed at 9 months

Decreased in breastfed at 9 months

*p<0.05; **p<0.01**; ***p<0.001

Laursen et al, mSphere 2015
Bergstrom et al, AEM 2014

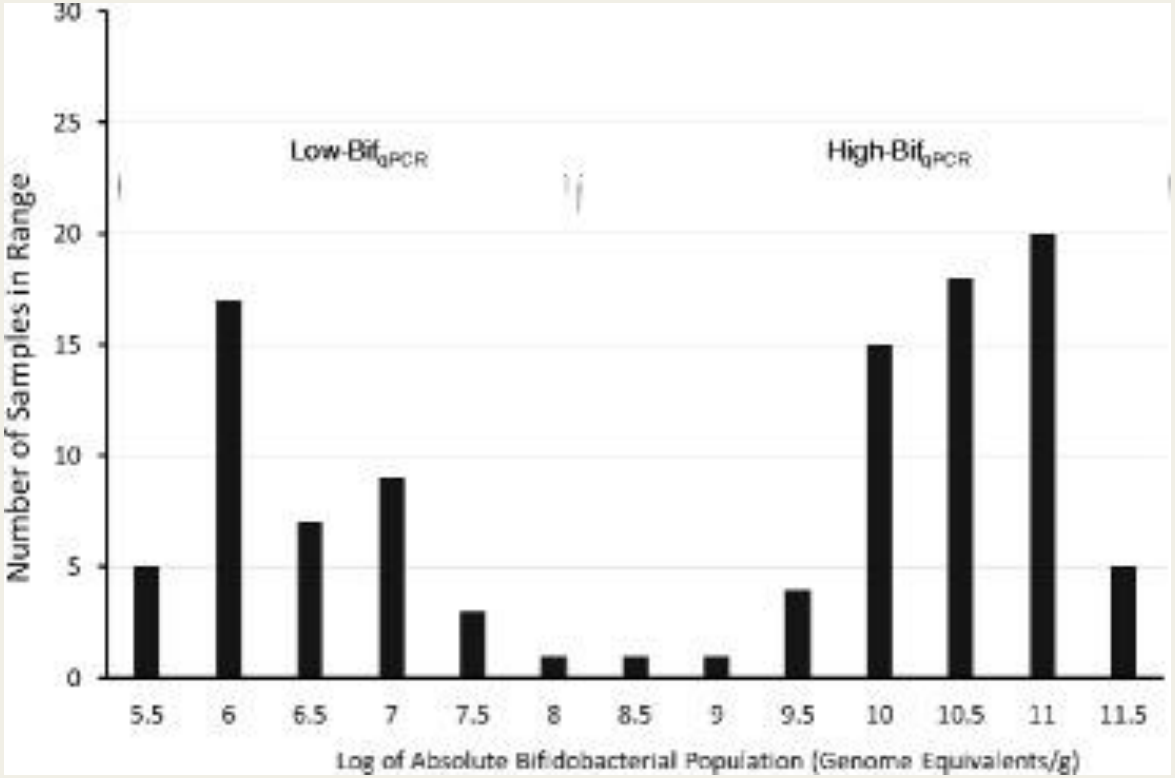
How Does Breast-feeding Influence the Gut Microbiota?



Human milk oligosaccharides (HMOs)
Third most abundant component of human breast milk
Over 150 different HMOs identified

HMO composition is influenced by genetic fucosyltransferase-2 secretor status, lactation stage, gestational age, maternal health, ethnicity, geographic location and breastfeeding exclusivity

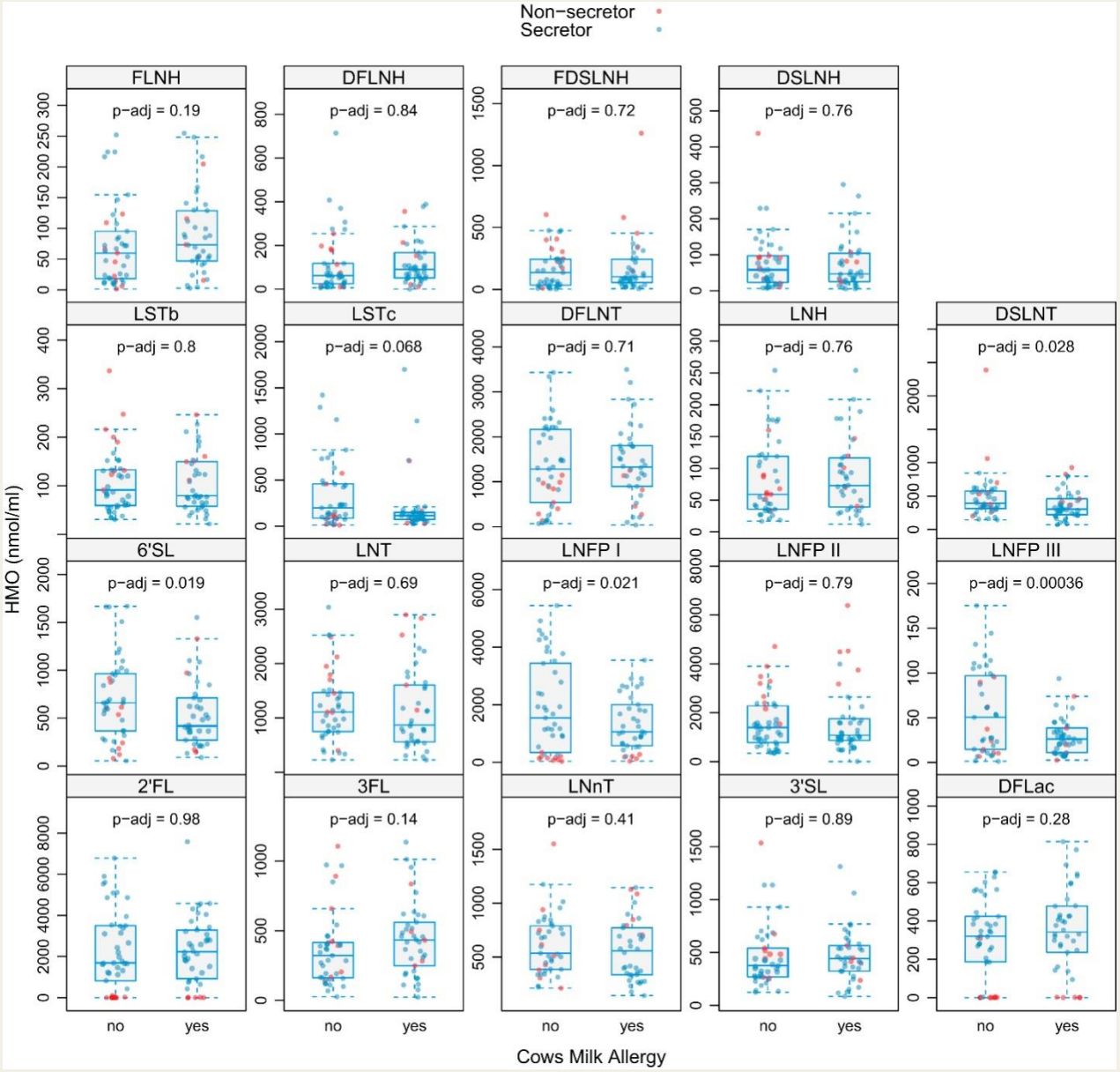
Maternal fucosyltransferase 2 (FUT 2) status affects the gut bifidobacterial communities of breastfed infants



Human milk oligosaccarides containing α1,2-fucosyl linkages

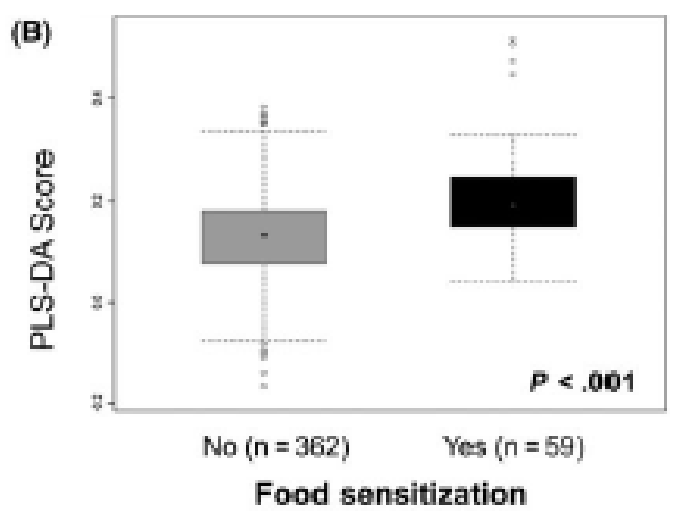
Lewis et al., Microbiome 2015

HMOs and Cow's Milk Allergy



Seppo et al, JACI 2017

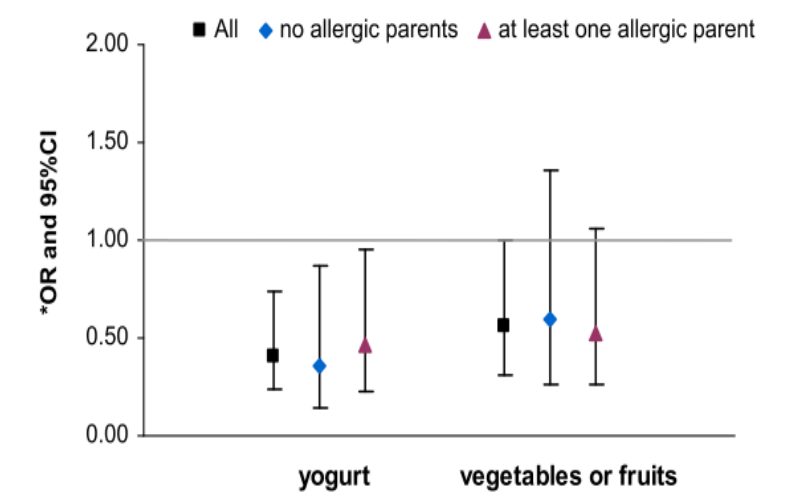
HMOs and Food Sensitisation



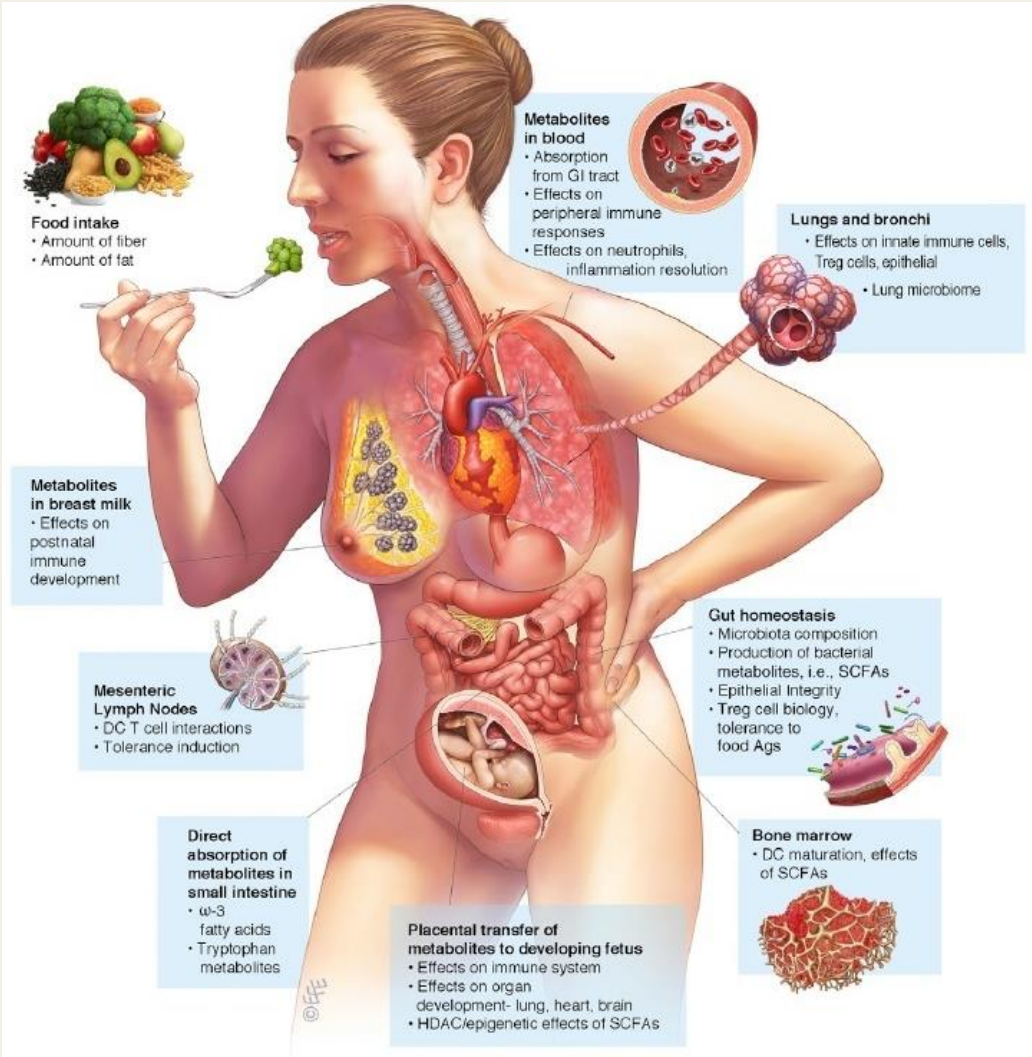
HMO	Higher (+) or Lower (–) in milk consumed by healthy infants	PLS-DA Scaled Importance Score	Rank
FDSLNH	+	100	1
LNH	–	78	2
LNFPII	+	73	3
LNnT	+	73	4
LNT	–	67	5
LNFPI	+	67	6
LSTc	+	63	7
FLNH	+	60	8
2'FL	–	60	9
DSLNH	–	57	10

Miliku et al, Allergy 2018

Diet-Bacterial Interactions - Metabolites

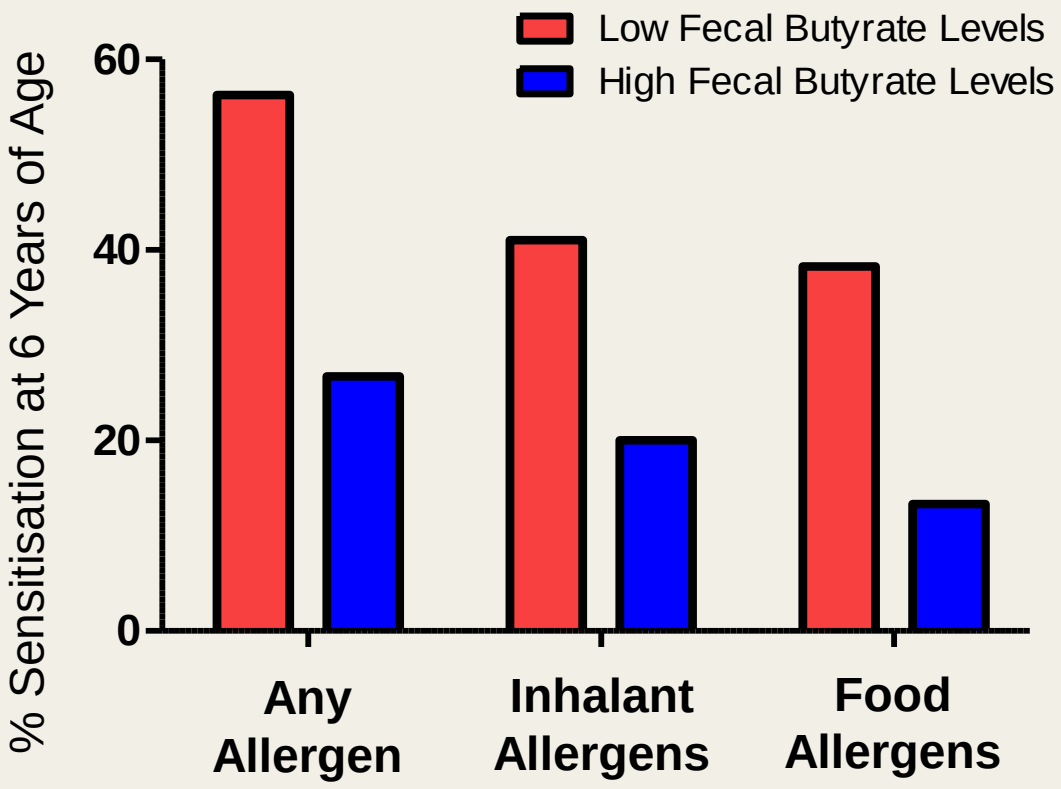


Roduit et al.,
J Allergy Clin Immunol 2012



Thorburn, Macia & Mackay
Immunity 2014

SCFA Levels in Fecal Samples of 1 Year Old Children



PASTURE/EFRAIM birth cohort (n=301)

Roduit & Frei et al., Allergy 2018

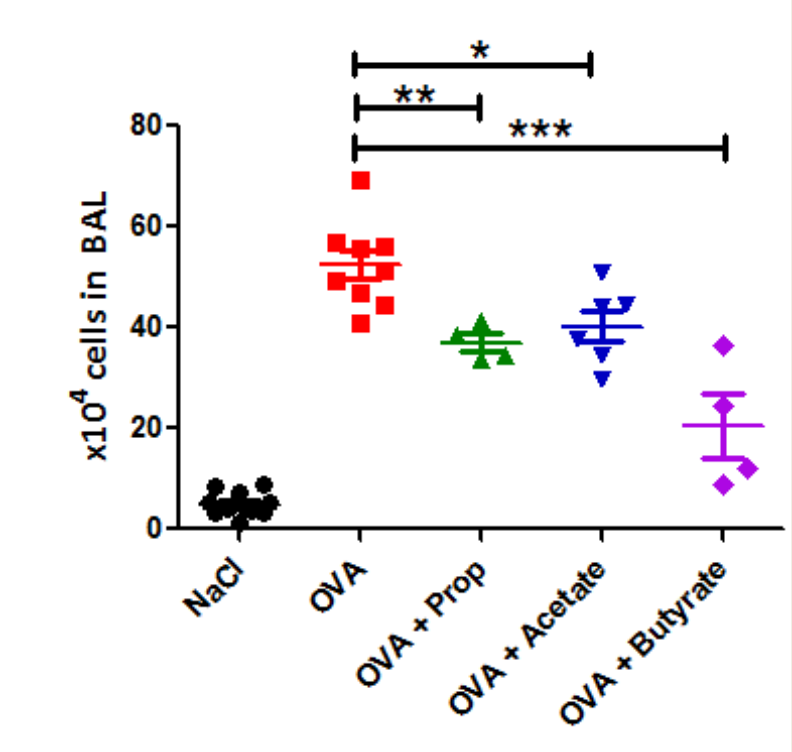
SCFA Levels in Fecal Samples of 1 Year Old Children

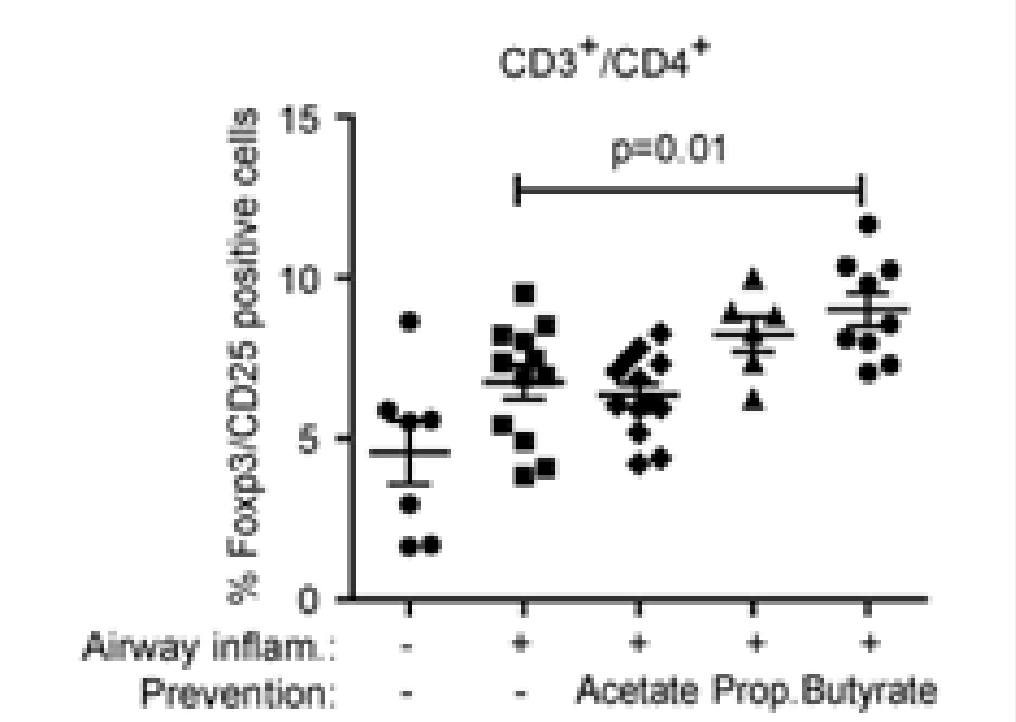
	Butyrate <95P (<26.9 µmol/g)	Butyrate ≥95P (≥26.9 µmol/g)	Propionate <95P (<32.9 µmol/g)	Propionate ≥95P (≥32.9 µmol/g)	Acetate <95P (<114.7µmol/g)	Acetate ≥95P (≥114.7 µmol/g)
	%	%	%	%	%	%
Asthma up to 6 yrs	12.2	6.7 ↓	12.2	6.7 ↓	11.8	14.3
Allergic rhinitis up to 6 yrs	9.7	0.0 ↓	9.0	13.3	9.0	13.3
Food allergy up to 6 yrs	11.6	6.7 ↓	10.9	20.0	11.6	6.7 ↓
Atopic dermatitis up to 6 yrs	47.5	31.3 ↓	46.7	46.7	46.7	46.7
Inhalant sensitization at 6yrs	41.0	20.0 ↓	41.4	13.3 ↓	39.9	40.0
Food sensitization at 6yrs	38.3	13.3 ↓	37.9	20.0 ↓	38.7	6.7 ↓
Any sensitization at 6yrs	56.3	26.7 ↓	56.7	20.0 ↓	55.6	40.0

PASTURE/EFRAIM birth cohort (n=301)

Roduit & Frei et al., Allergy 2018

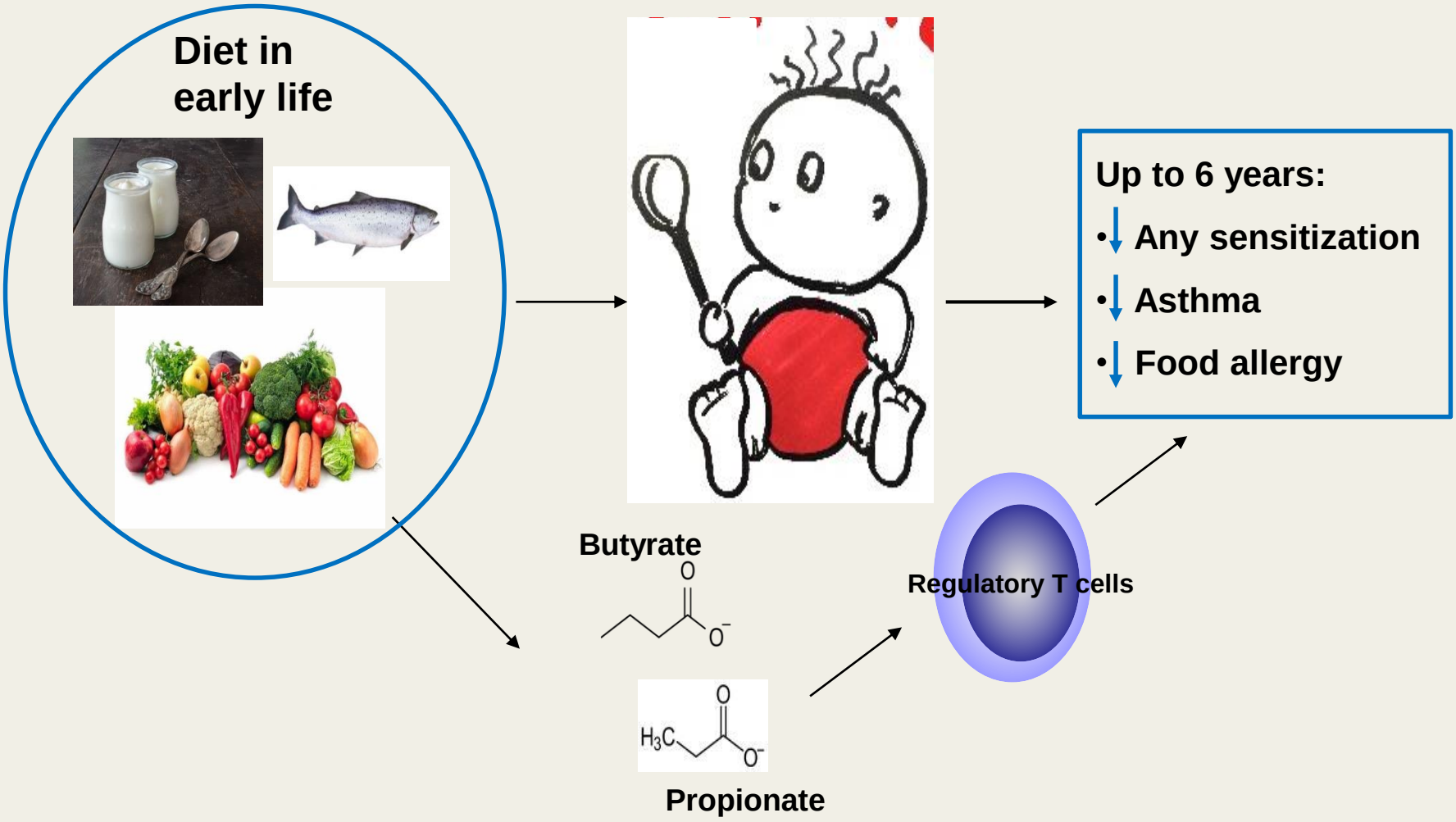
SCFAs and Respiratory Allergy in Murine Models





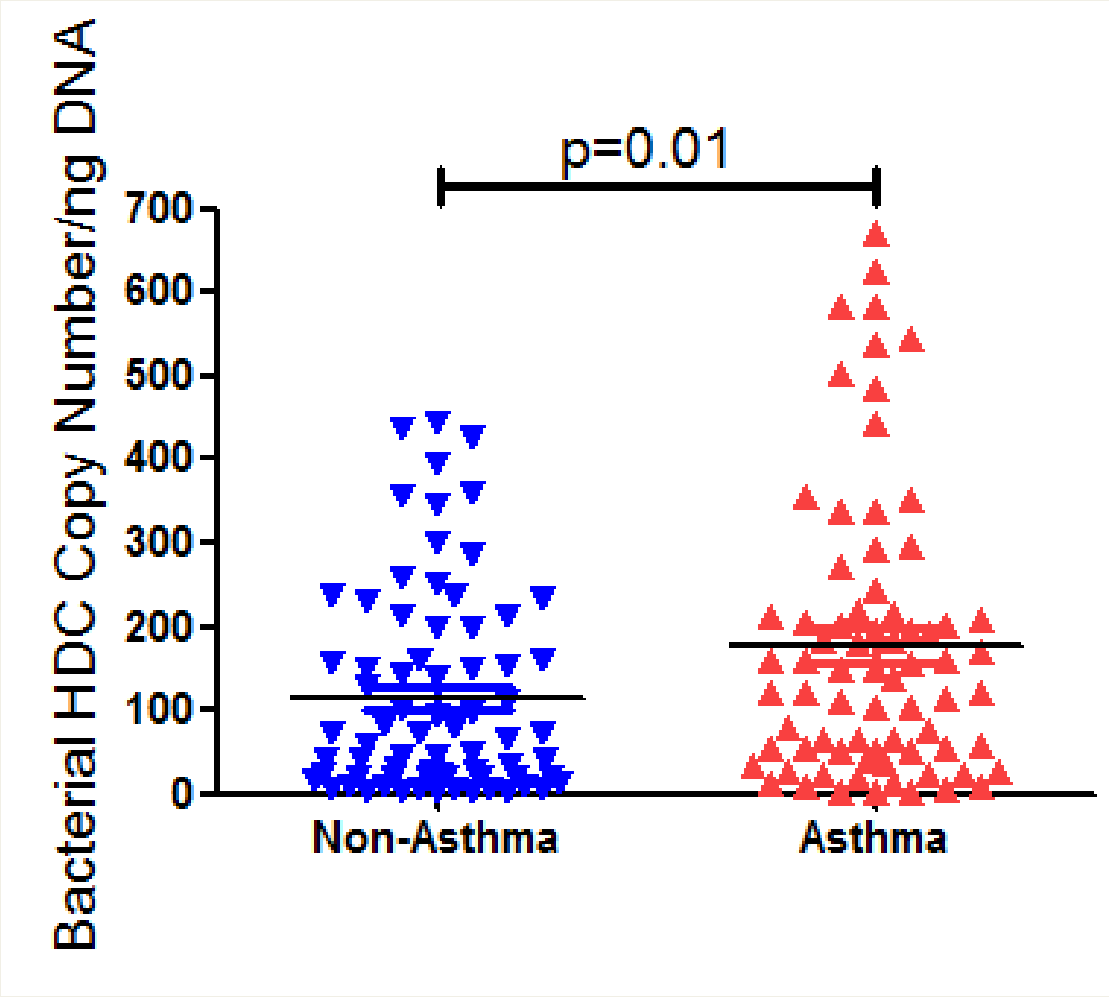
Roduit & Frei et al., Allergy 2018

SCFAs Reduce Allergic Sensitization



Roduit et al., Allergy 2018

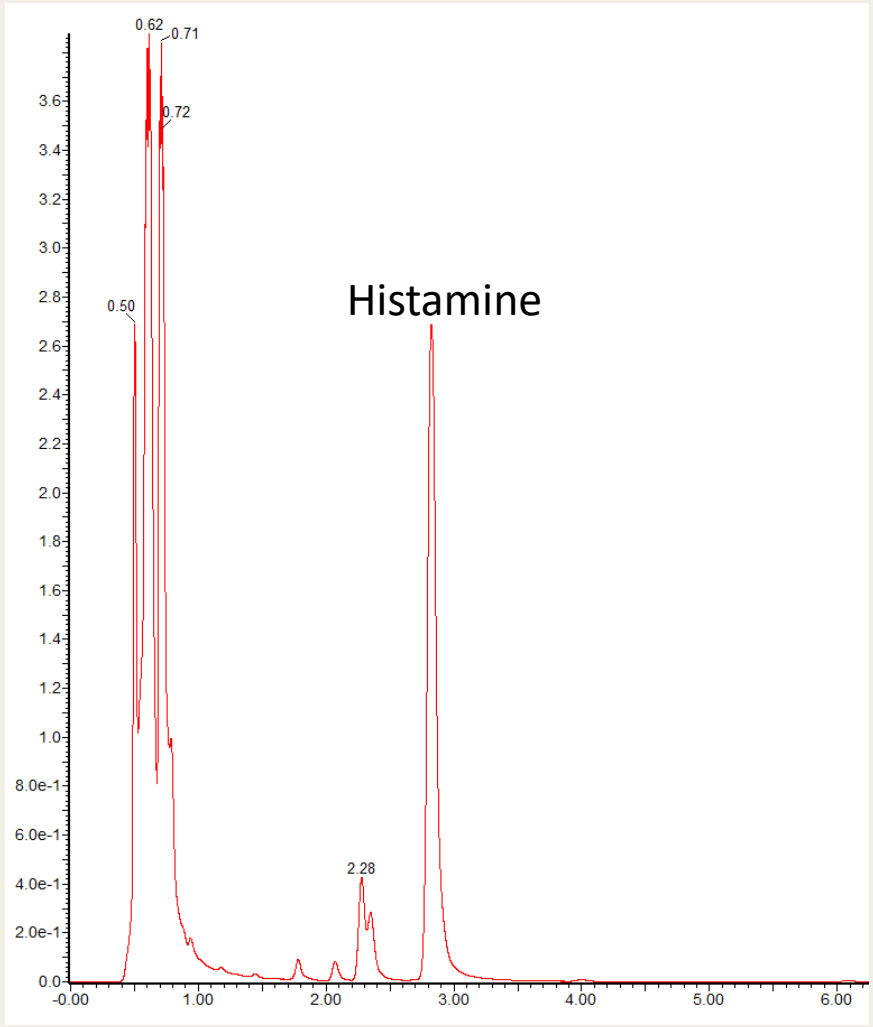
Histamine Secreting Bacteria

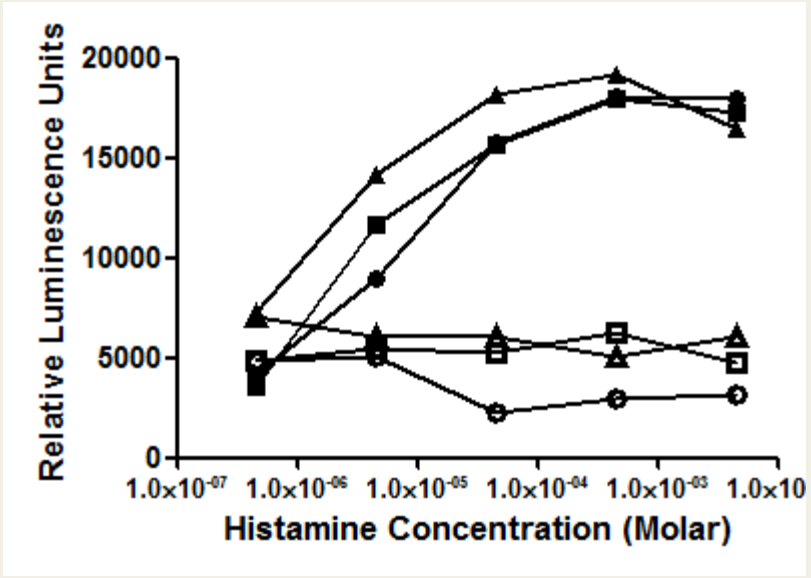


The number of histamine secreting bacteria is increased in asthma patients

Barcik et al., JACI 2016

Histamine Secreted from Bacteria is Immunologically Active

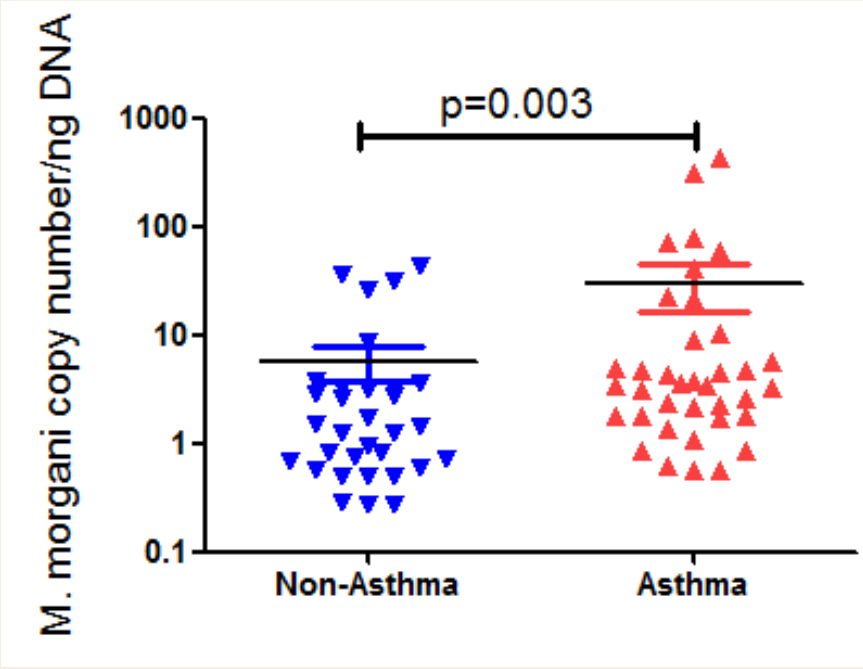


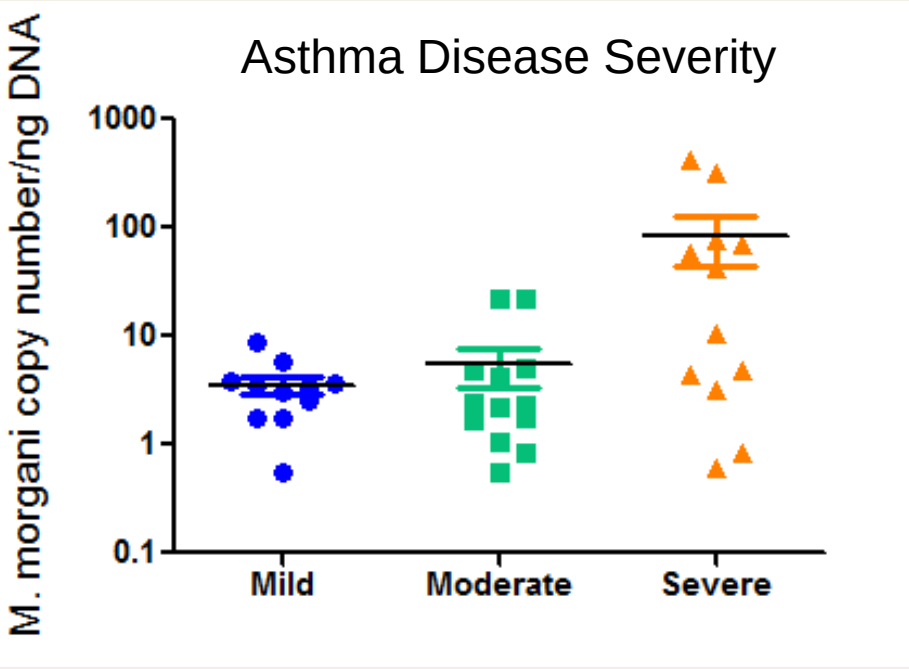


- Histamine
- Histamine & Antagonist
- Supernatant 1
- Supernatant 1 & Antagonist
- Supernatant 2
- Supernatant 2 & Antagonist

Barcik et al., JACI 2016

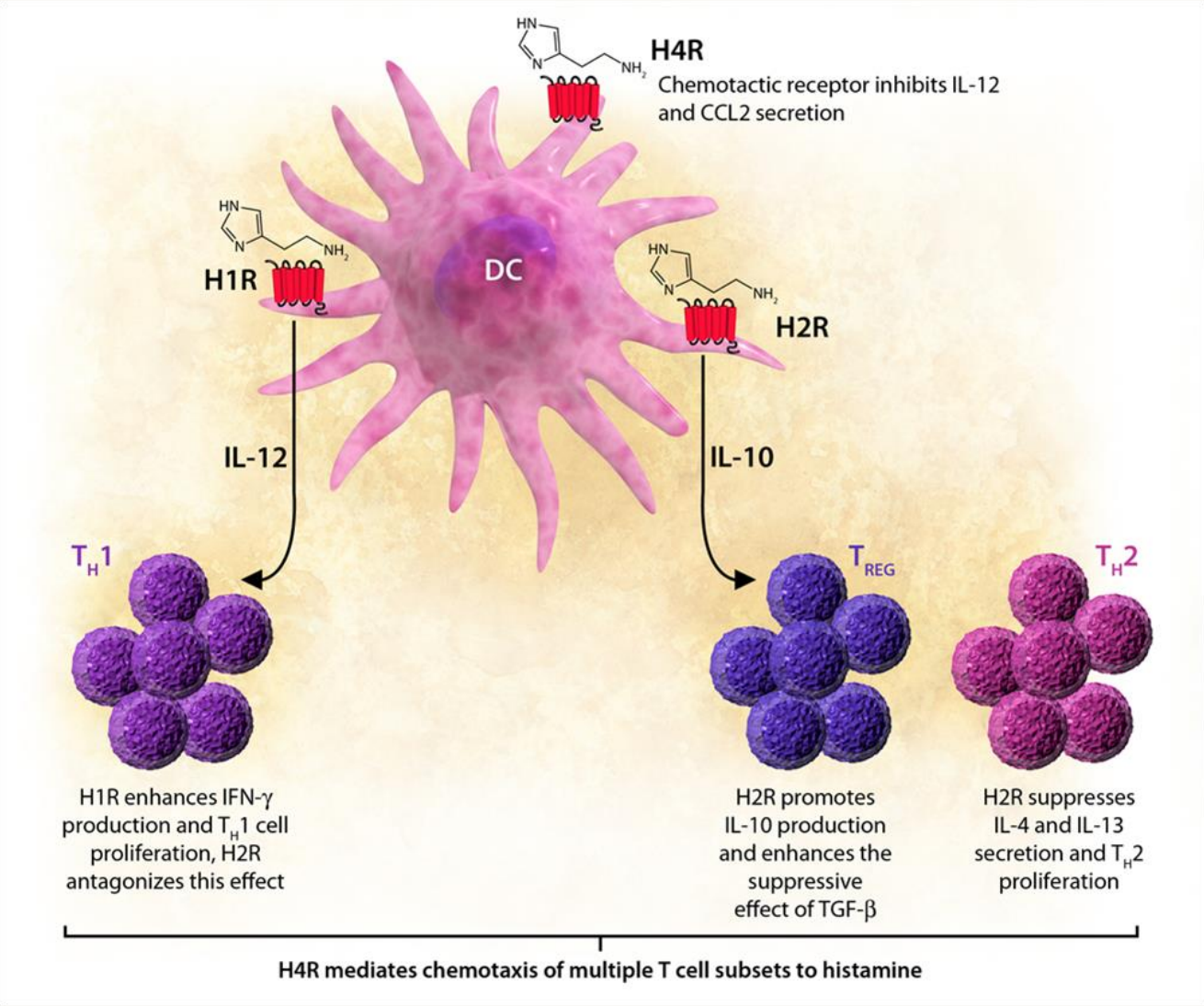
M. morgani Increased in Asthma Patients





Barcik et al., JACI 2016

Immunoregulatory Activities of Histamine Receptors



O'Mahony et al., JACI 2011; Frei et al., JACI 2013; Ferstl et al., JACI 2014

How Do We Modify the Microbiome?

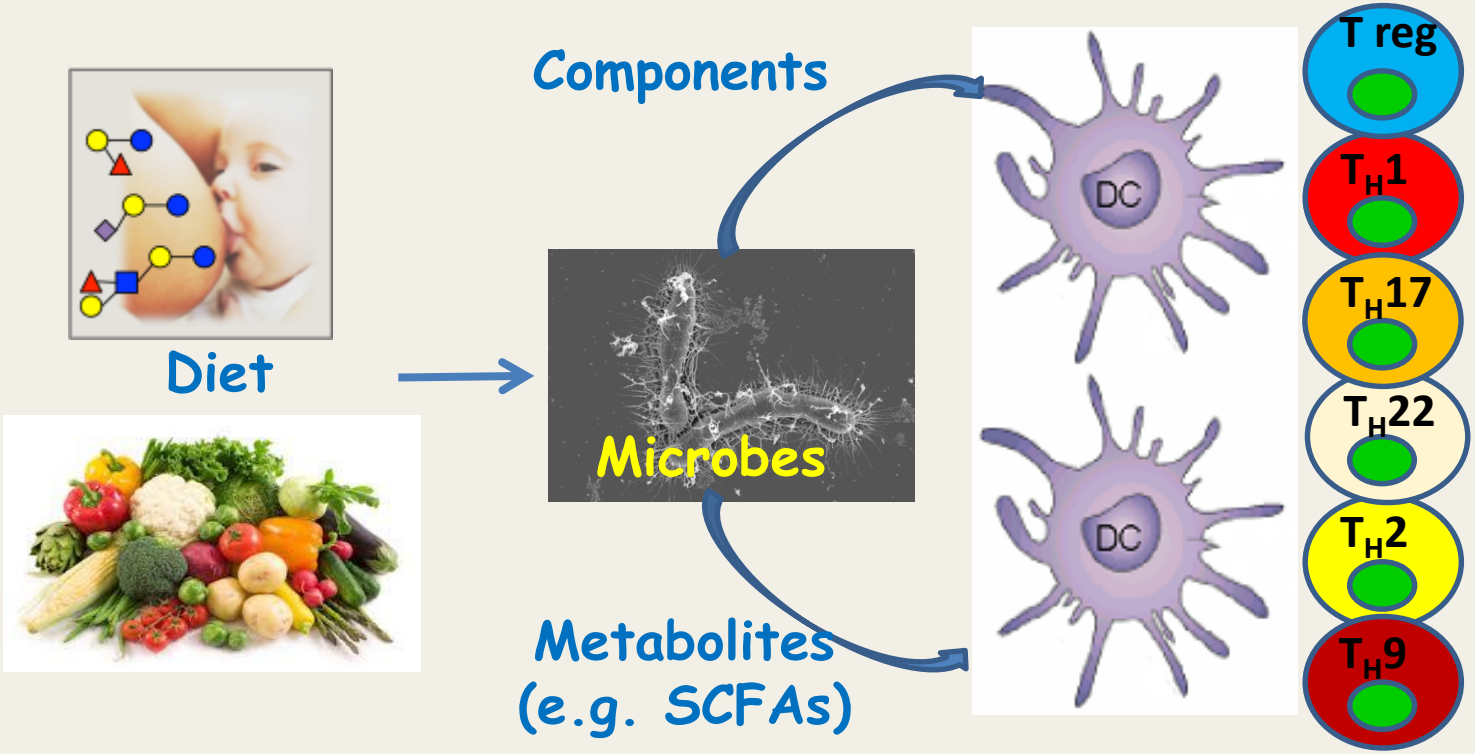
Diet
Probiotics
Prebiotics
Synbiotics
Bacteriophages
Microbiome transplant (FMT)
Antimicrobials

Current Opportunities for Practical Clinical Intervention

Clinical intervention	Rationale
Reduce elective cesarean sections	Microbial dysbiosis can be mitigated to reduce the risk of allergic immune responses and inflammation.
Reduce indiscriminate use of antibiotics during infancy/ perinatal period	
Encourage breast-feeding, when possible	
Increase dietary intake of fermentable fiber	Microbial fermentation produces SCFAs, which *in vitro* and *in vivo* data suggest can mitigate allergic responses, including in the lung.

Huang et al., JACI 2017

Diet-Microbes-Immune Health



Can we prevent allergy by improving early life nutrition?