Diagnostic Solutions laboratory

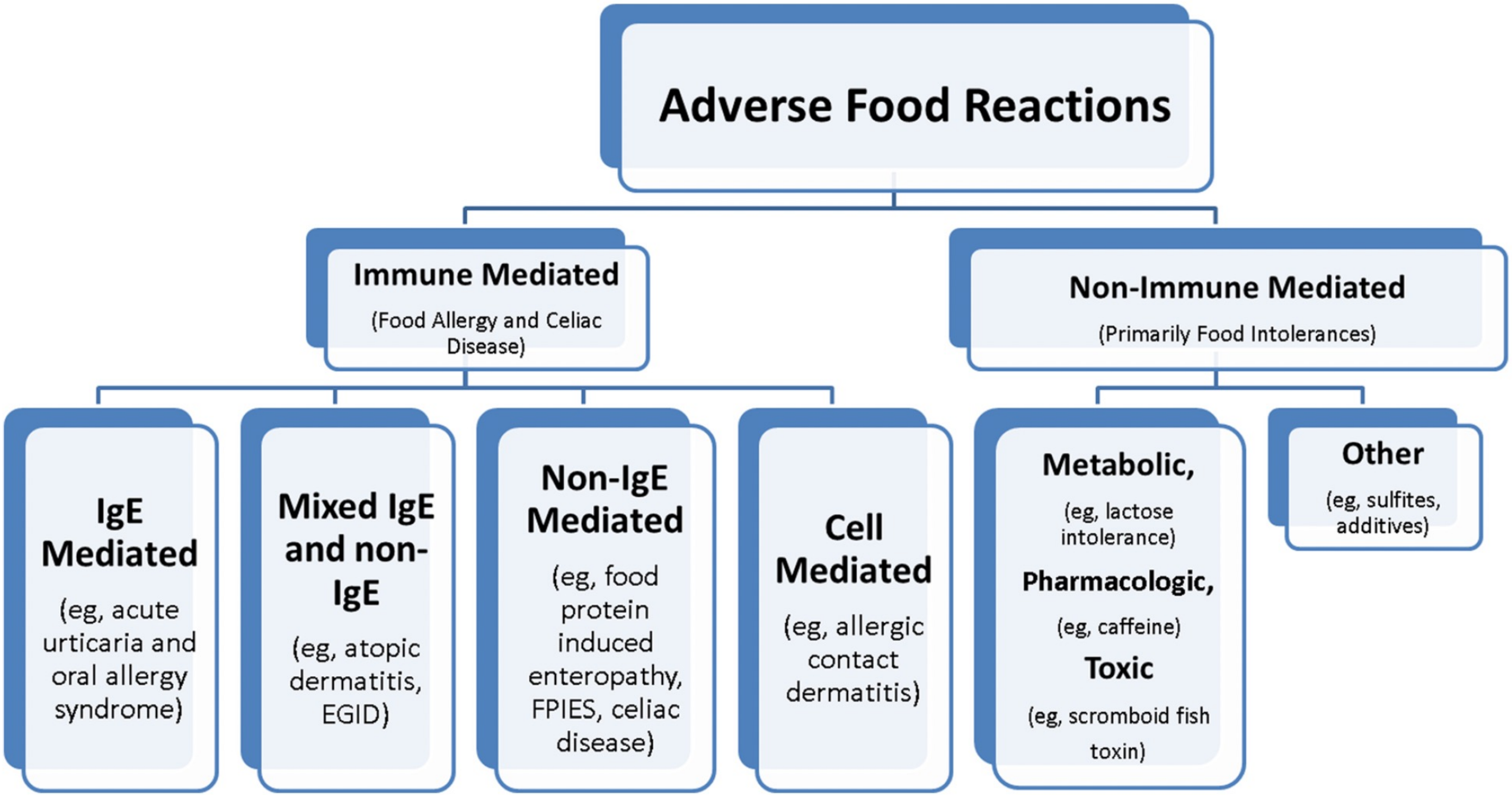
Mast Cells, Histamine & Food Sensitivities

Insights with GI-MAP®

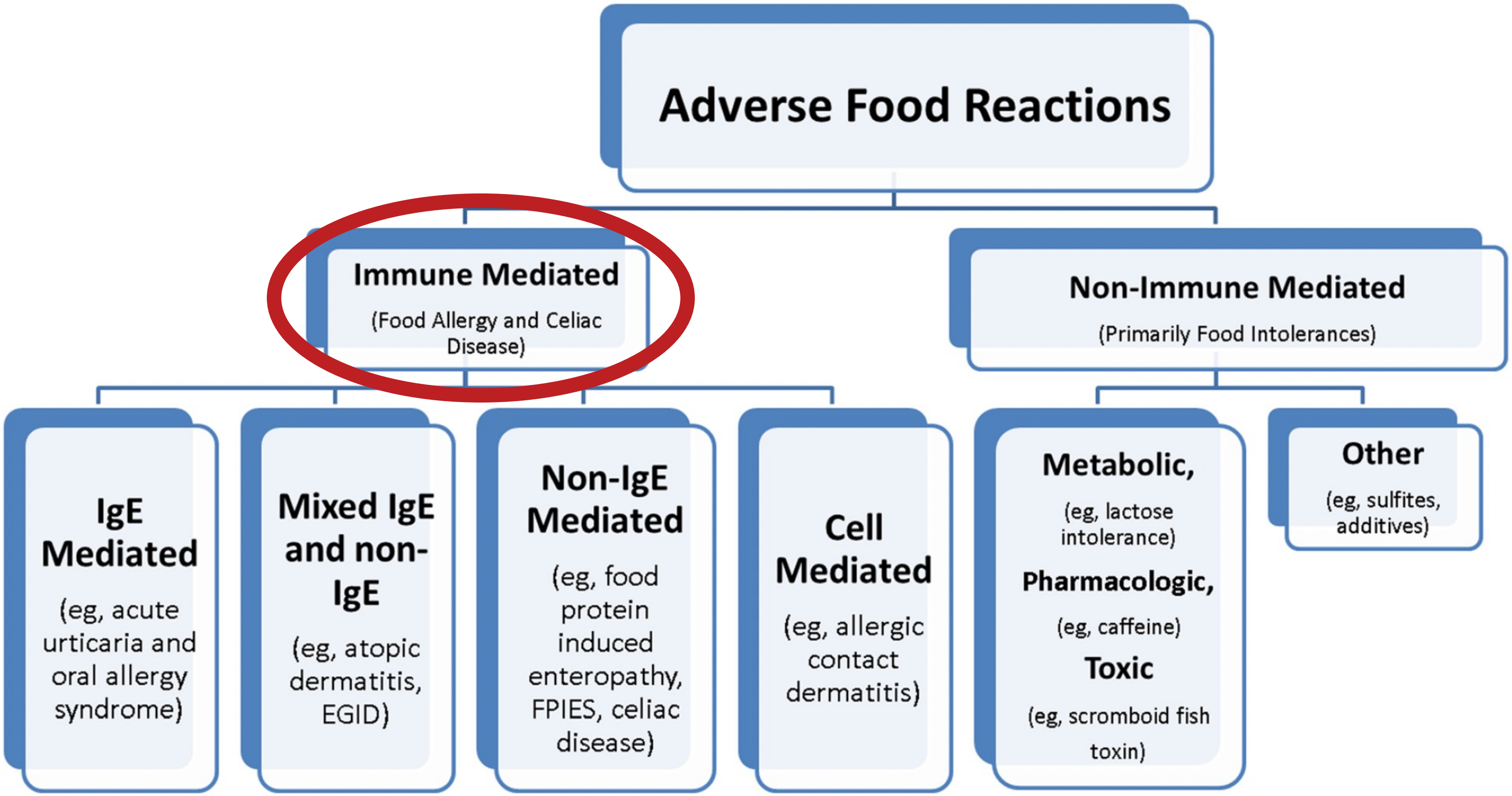
Presented by Thomas Fabian, PhD, CNTP

Presentation Topics

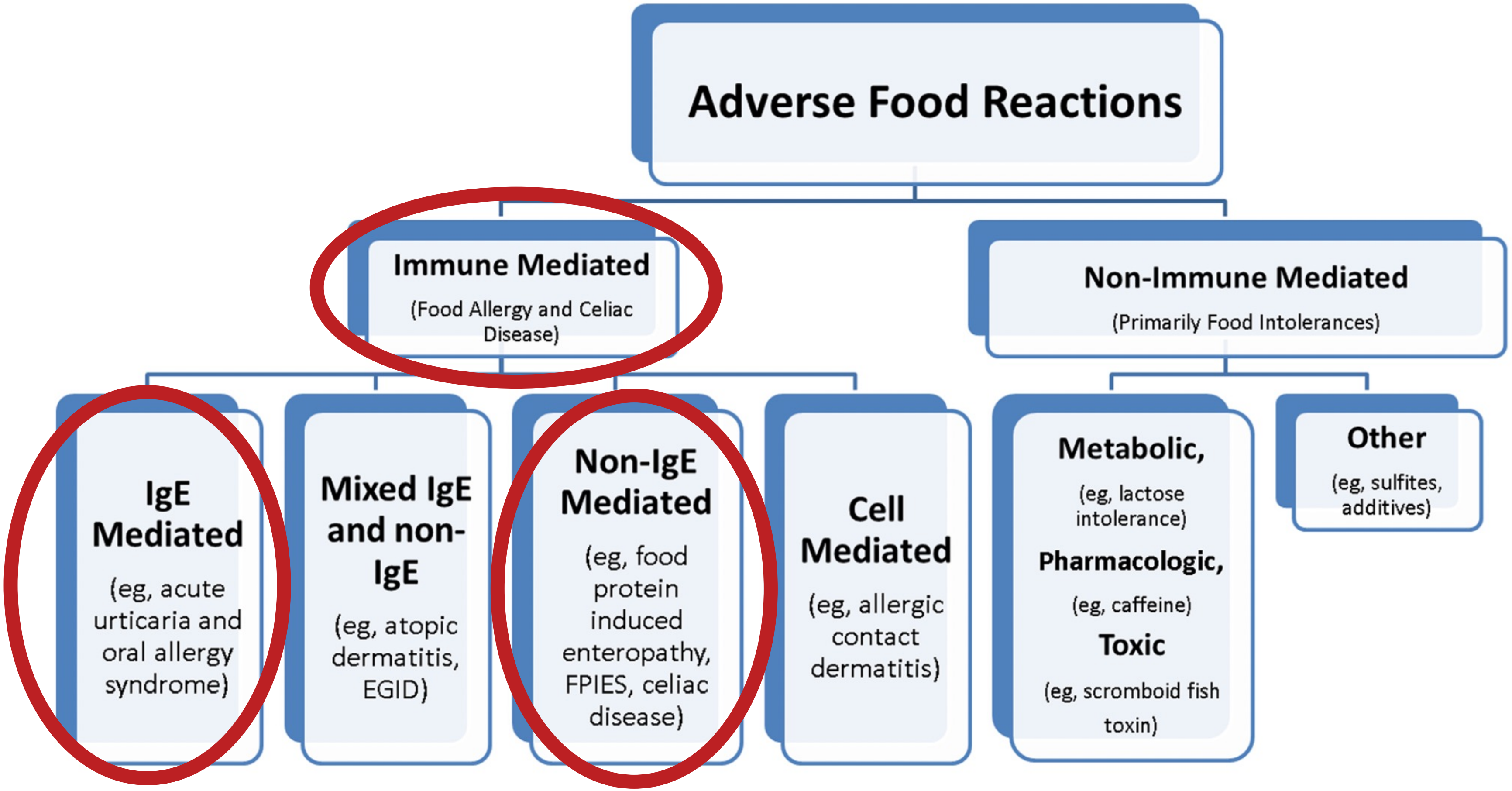
- Key concepts: role of the microbiome, mast cells & histamine in food reactions
- Insights with GI-MAP
- Implications for treatment approaches



Clinic Rev Allerg Immunol (2019) 57:244–260



Clinic Rev Allerg Immunol (2019) 57:244–260



Clinic Rev Allerg Immunol (2019) 57:244–260

Immune-Mediated Food Reactions: Approaches

- Identify potentially problematic foods, elimination diet
- Identify and address GI imbalances that may contribute to immune-mediated food reactions

Diagnostic Solutions laboratory

IgE™

ALLERGY EXPLORER

IgG™

FOOD EXPLORER

Patient A

IgG FOOD EXPLORER™

Milk & Egg

Buttermilk	≤ 5.00 µg/ml
Camembert	≤ 5.00 µg/ml
Emmental	≤ 5.00 µg/ml
Gouda	≤ 5.00 µg/ml
Cottage cheese	5.51 µg/ml
Cow's milk	≤ 5.00 µg/ml
Mozzarella	≤ 5.00 µg/ml
Parmesan	≤ 5.00 µg/ml
Cow's milk Bos d 4 * (Alpha-Lactalbumin)	≤ 5.00 µg/ml
Cow's milk Bos d 5 * (Beta-Lactoglobulin)	≤ 5.00 µg/ml

Cow's milk Bos d 8 * (Casein)	≤ 5.00 µg/ml
Buffalo milk	≤ 5.00 µg/ml
Camel milk	≤ 5.00 µg/ml
Goat cheese	≤ 5.00 µg/ml
Goat milk	≤ 5.00 µg/ml
Quail egg	≤ 5.00 µg/ml
Egg white	33.17 µg/ml
Egg yolk	31.00 µg/ml
Sheep cheese	≤ 5.00 µg/ml
Sheep milk	≤ 5.00 µg/ml

Patient B

IgG™ FOOD EXPLORER

Milk & Egg

Buttermilk	≤ 5.00 µg/ml	●
Camembert	≤ 5.00 µg/ml	●
Emmental	≤ 5.00 µg/ml	●
Gouda	≤ 5.00 µg/ml	●
Cottage cheese	≤ 5.00 µg/ml	●
Cow's milk	≤ 5.00 µg/ml	●
Mozzarella	≤ 5.00 µg/ml	●
Parmesan	≤ 5.00 µg/ml	●
Cow's milk Bos d 4 * (Alpha-Lactalbumin)	≤ 5.00 µg/ml	●
Cow's milk Bos d 5 * (Beta-Lactoglobulin)	≤ 5.00 µg/ml	●
Cow's milk Bos d 8 * (Casein)	≤ 5.00 µg/ml	●
Buffalo milk	≤ 5.00 µg/ml	●
Camel milk	≤ 5.00 µg/ml	●
Goat cheese	≤ 5.00 µg/ml	●
Goat milk	≤ 5.00 µg/ml	●
Quail egg	≤ 5.00 µg/ml	●
Egg white	6.14 µg/ml	●
Egg yolk	≤ 5.00 µg/ml	●
Sheep cheese	≤ 5.00 µg/ml	●
Sheep milk	≤ 5.00 µg/ml	●

Patient C

IgG FOOD EXPLORER™

Milk & Egg

Buttermilk	27.35 µg/ml	●●● (red)	Cow's milk Bos d 8 * (Casein)	42.59 µg/ml	●●● (red)
Camembert	39.03 µg/ml	●●● (red)	Buffalo milk	40.53 µg/ml	●●● (red)
Emmental	36.20 µg/ml	●●● (red)	Camel milk	6.17 µg/ml	● (green)
Gouda	41.37 µg/ml	●●● (red)	Goat cheese	21.32 µg/ml	●●● (red)
Cottage cheese	43.20 µg/ml	●●● (red)	Goat milk	25.25 µg/ml	●●● (red)
Cow's milk	41.60 µg/ml	●●● (red)	Quail egg	8.01 µg/ml	● (green)
Mozzarella	43.65 µg/ml	●●● (red)	Egg white	19.83 µg/ml	●● (yellow)
Parmesan	33.95 µg/ml	●●● (red)	Egg yolk	17.89 µg/ml	●● (yellow)
Cow's milk Bos d 4 * (Alpha-Lactalbumin)	23.04 µg/ml	●●● (red)	Sheep cheese	29.18 µg/ml	●●● (red)
Cow's milk Bos d 5 * (Beta-Lactoglobulin)	26.20 µg/ml	●●● (red)	Sheep milk	33.22 µg/ml	●●● (red)

> J Clin Med. 2021 Sep 23;10(19):4317. doi: 10.3390/jcm10194317.

Igg Food Antibody Guided Elimination-Rotation Diet Was More Effective than FODMAP Diet and Control Diet in the Treatment of Women with Mixed IBS-Results from an Open Label Study

Lucyna Ostrowska [1], Diana Wasiluk [1], Camille F J Lieners [2], Mirosława Gałęcka [2], Anna Bartnicka [2], Dag Tveiten [3]

Affiliations + expand

PMID: 34640335 PMCID: PMC8509634 DOI: 10.3390/jcm10194317

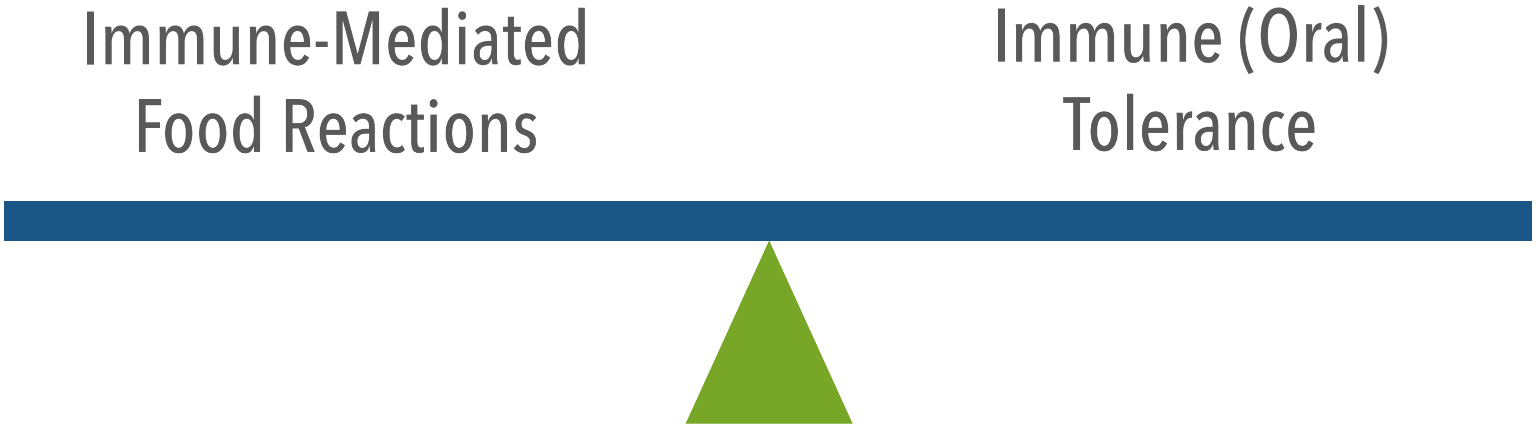
Free PMC article

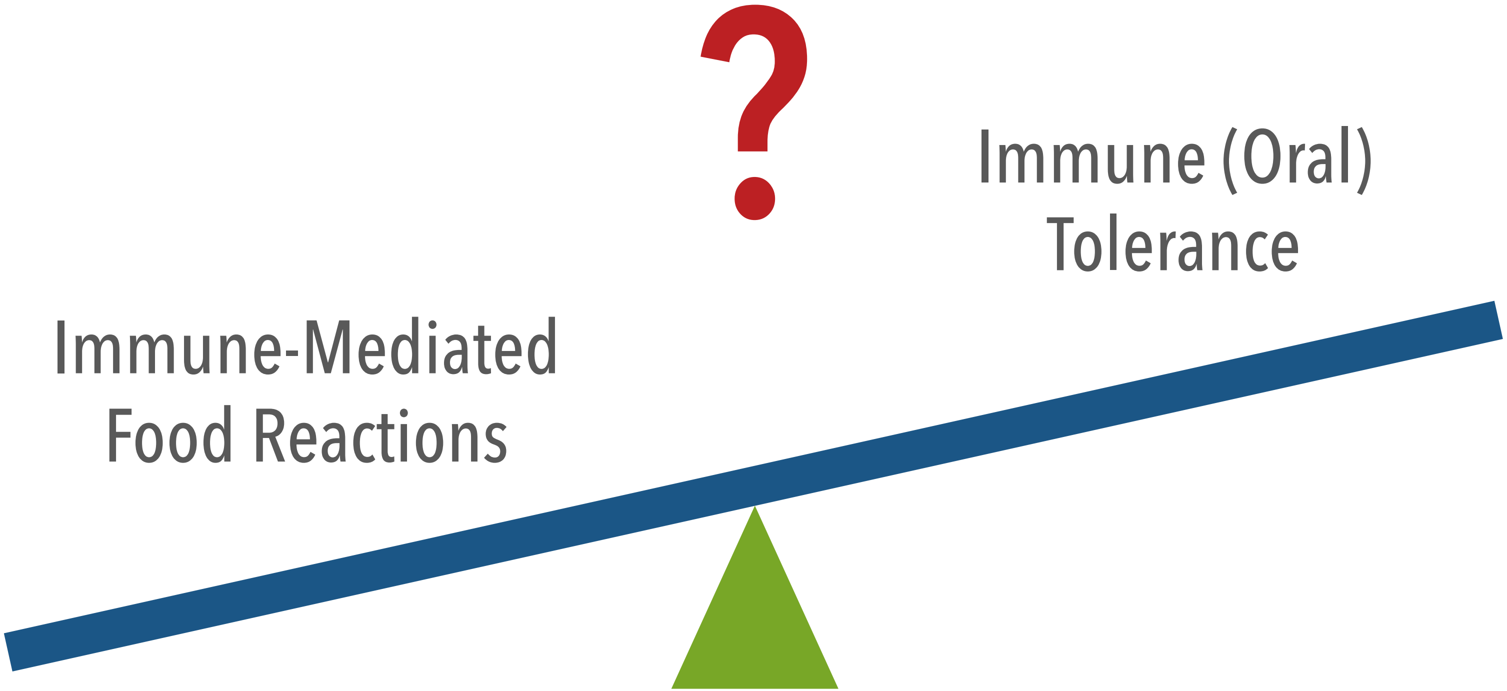
Abstract

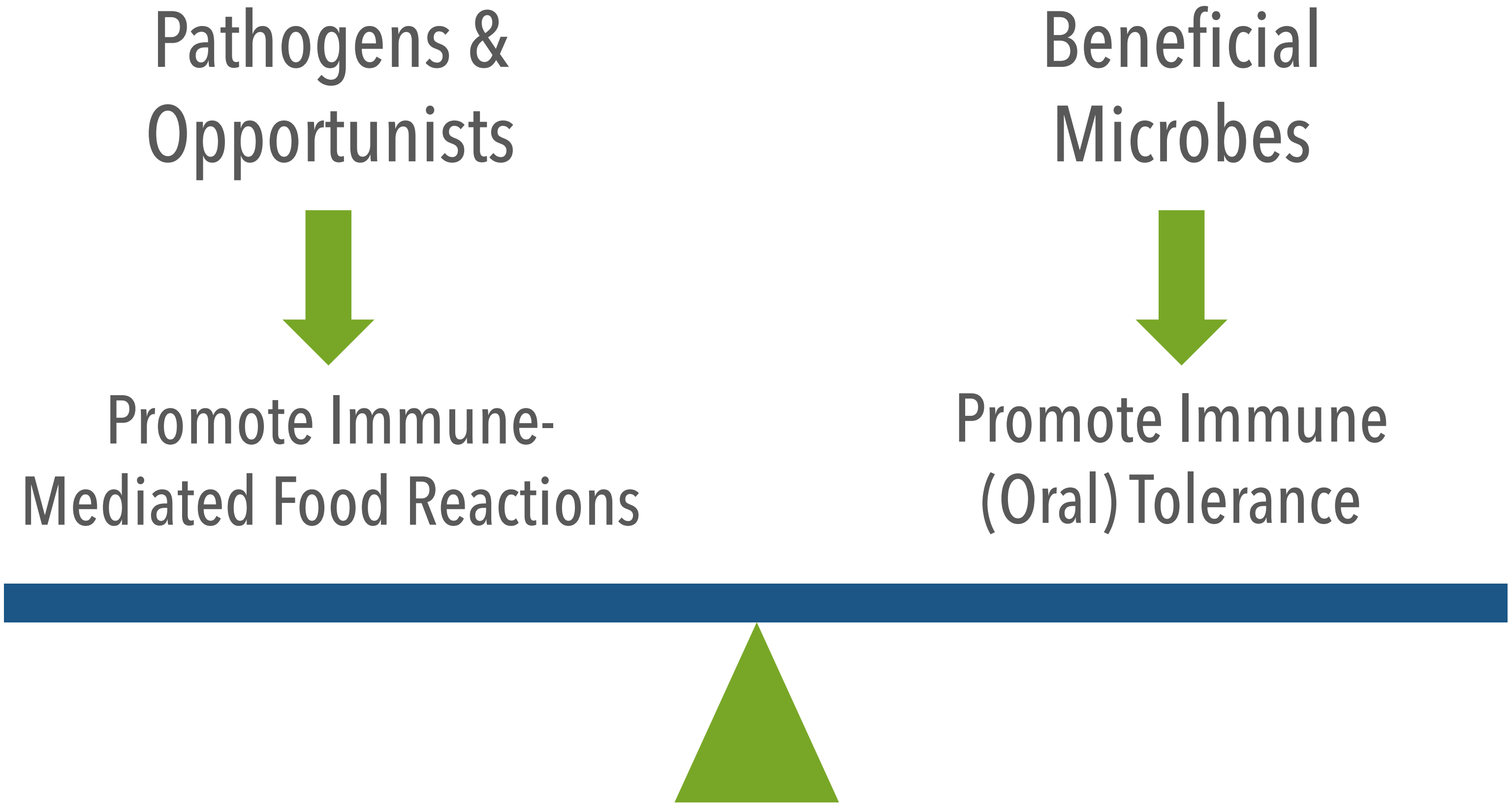
Irritable bowel syndrome (IBS) is a chronic disease with recurrent abdominal pain, disturbed bowel emptying, and changes in stool consistency. We compared the effectiveness of three different dietary treatment plans (G1-FM-low FODMAP diet, G2-IP IgG based elimination-rotation-diet, and as control group, the G3-K control diet recommended by an attending gastroenterologist) in treating patients diagnosed with mixed irritable bowel syndrome. A total of seventy-three female patients diagnosed with a mixed form of irritable bowel syndrome (IBS-M) were enrolled in the study. The diet of each patient in Group 1 (G1-FM) and 2 (G2-IP) was determined individually during

Immune-Mediated Food Reactions: Approaches

- Identify potentially problematic foods, elimination diet
- Identify and address GI imbalances that may contribute to immune-mediated food reactions


Immune-Mediated Food Reactions
Immune (Oral) Tolerance

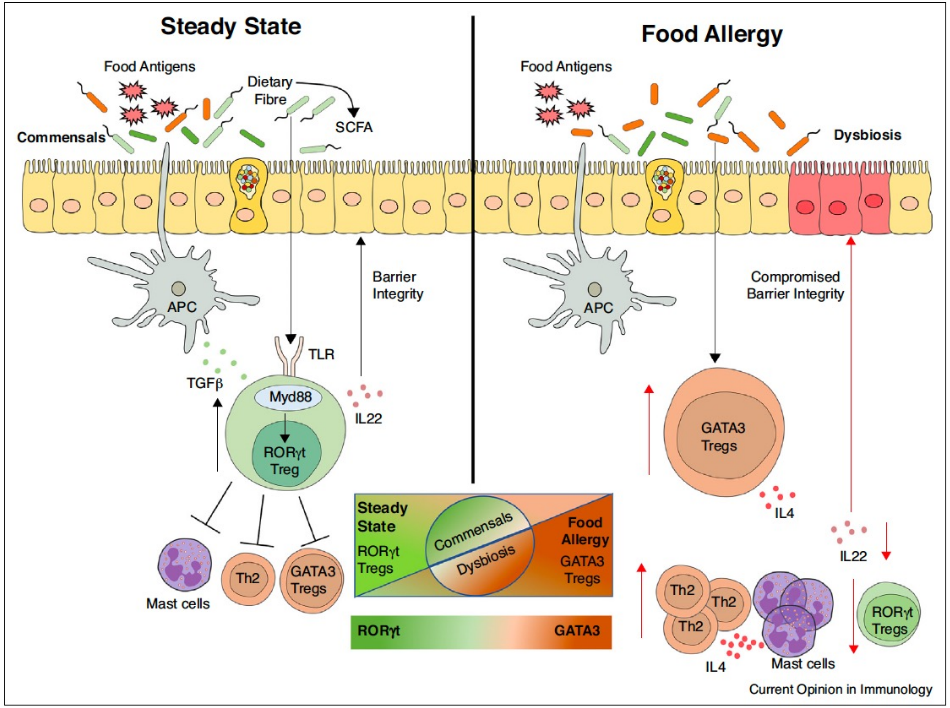

?
Immune (Oral)
Tolerance
Immune-Mediated
Food Reactions

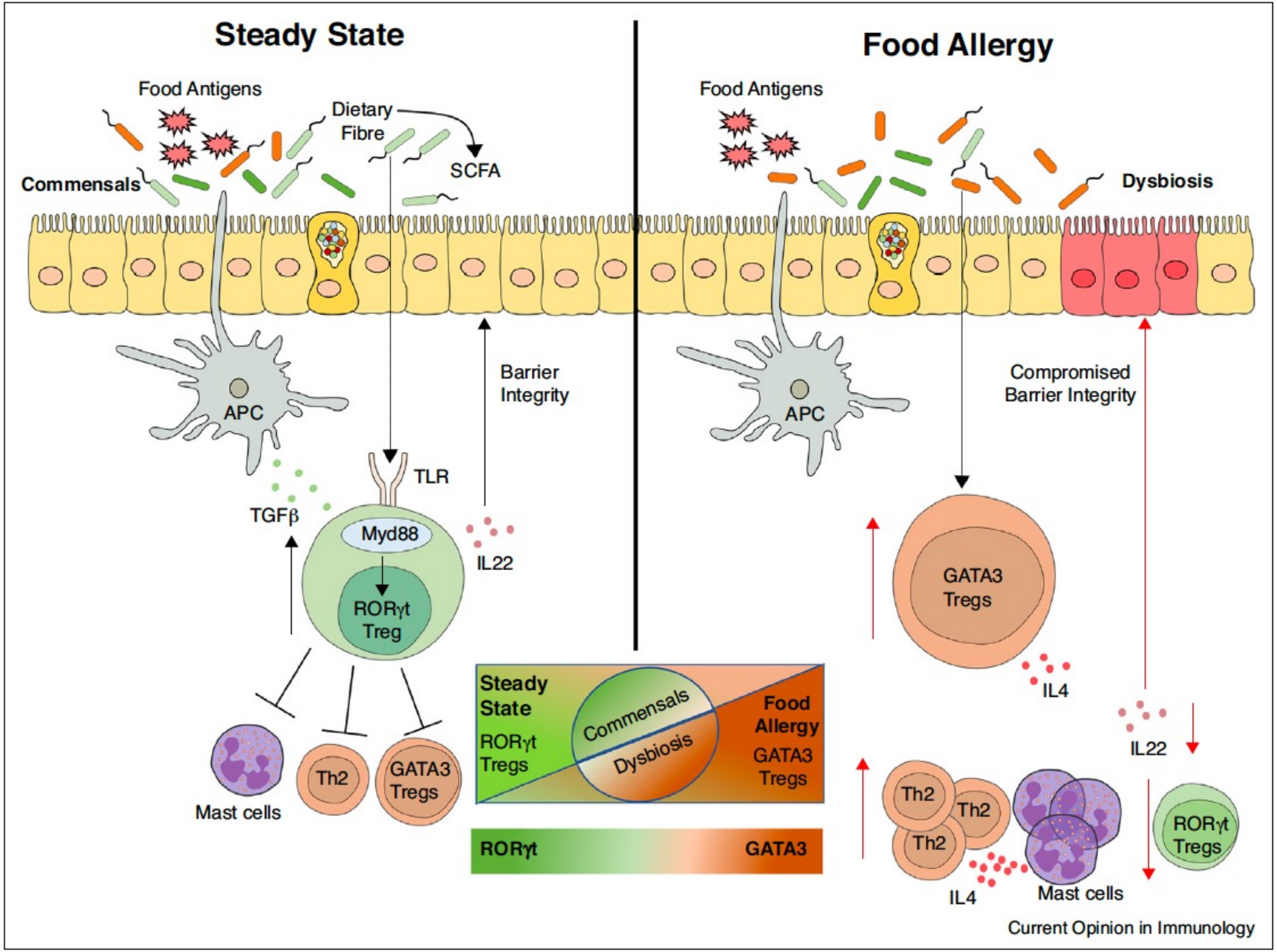


Pathogens & Opportunists
Promote Immune-Mediated Food Reactions
Beneficial Microbes
Promote Immune (Oral) Tolerance

Review > Curr Opin Immunol. 2019 Oct;60:141-147. doi: 10.1016/j.coi.2019.06.001.
Epub 2019 Jul 11.

Regulation of oral immune tolerance by the microbiome in food allergy





Steady State
Food Antigens
Dietary Fibre
SCFA
Commensals
Barrier Integrity
APC
TLR
TGFβ
Myd88
IL22
RORγt Treg
Mast cells
Th2
GATA3 Tregs
Food Allergy
Food Antigens
Dysbiosis
APC
Compromised Barrier Integrity
GATA3 Tregs
IL4
IL22
Th2
Th2
Th2
RORγt Tregs
IL4
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GATA3 Tregs
RORγt
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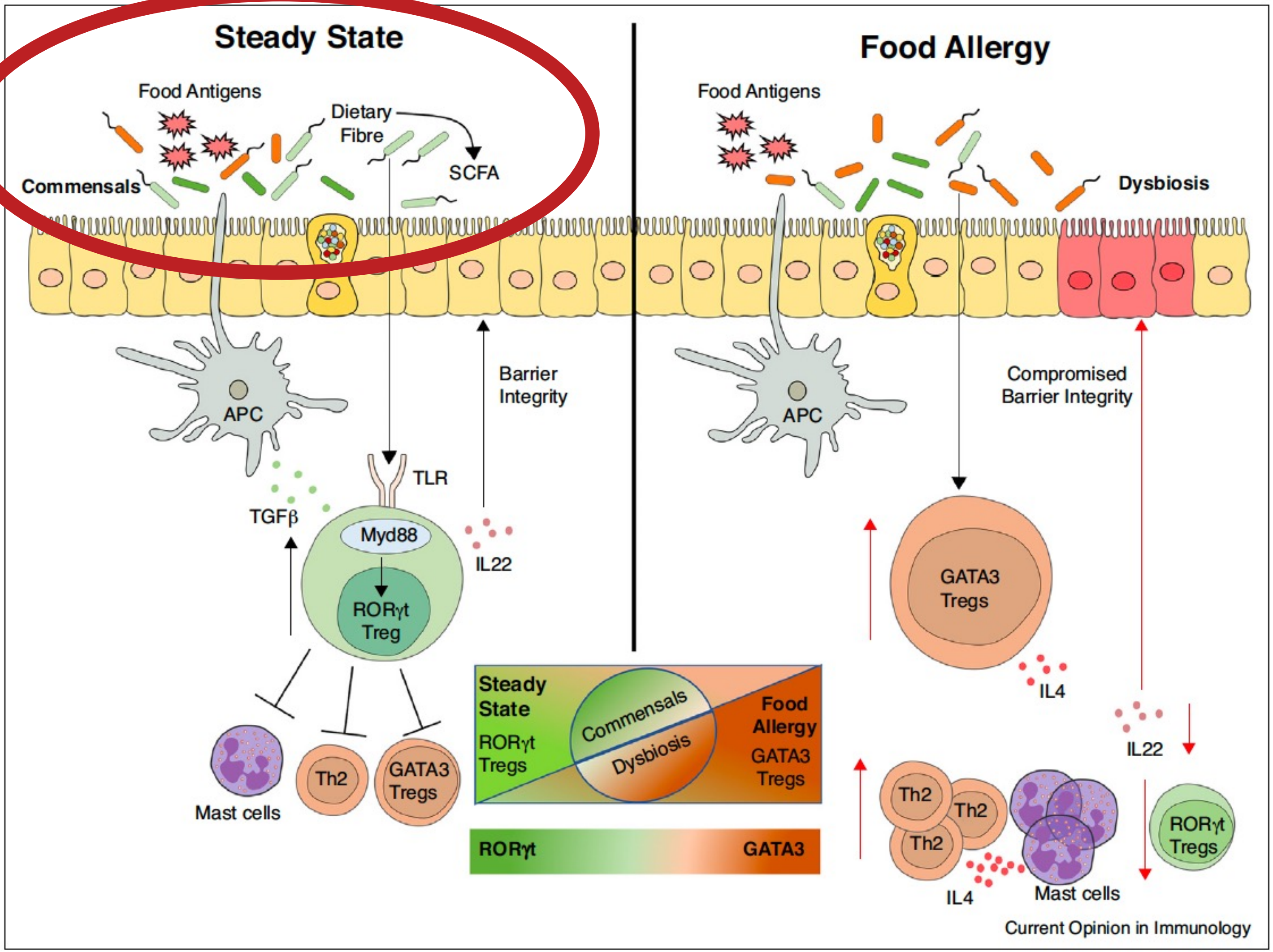
Current Opinion in Immunology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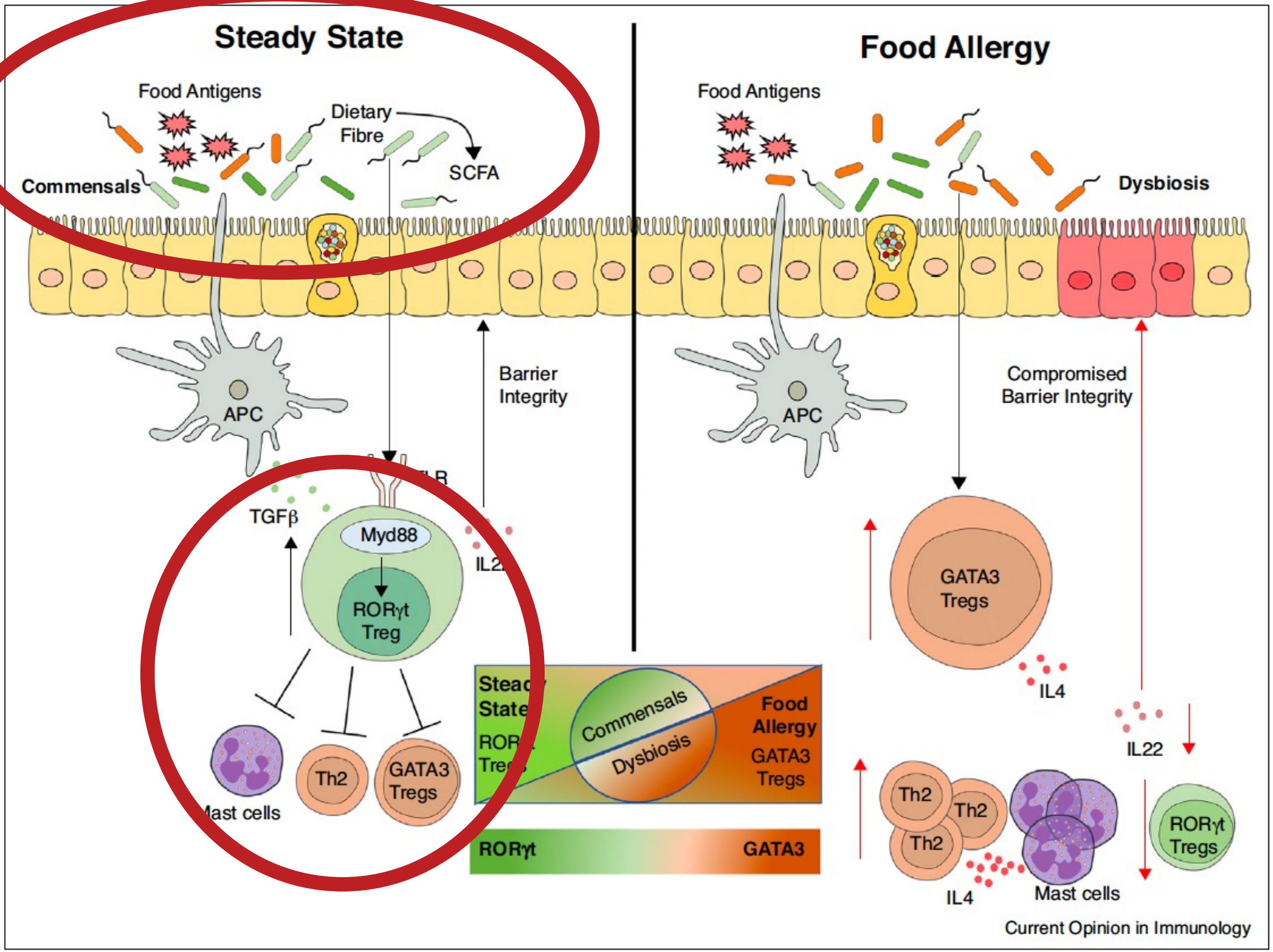

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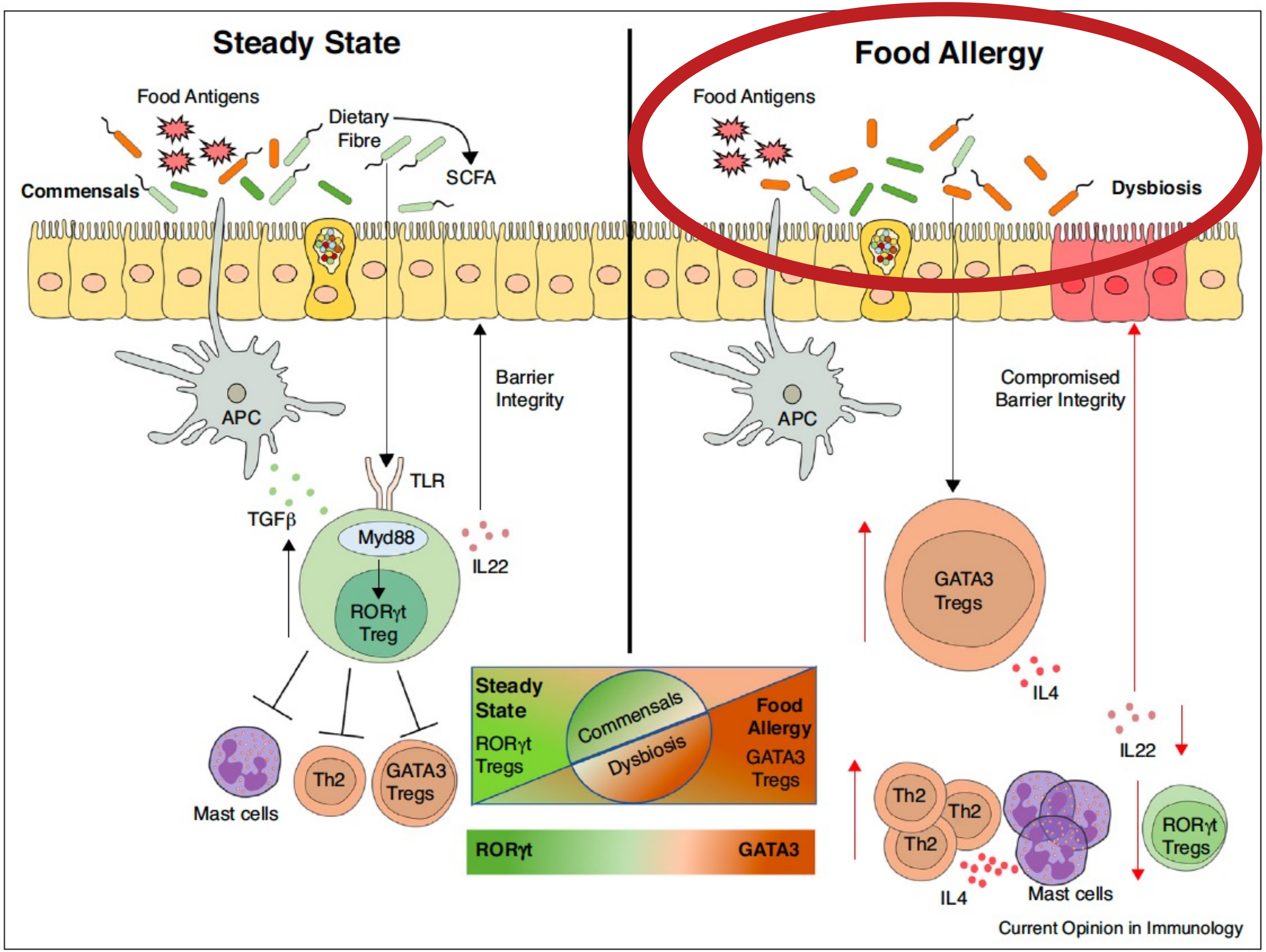

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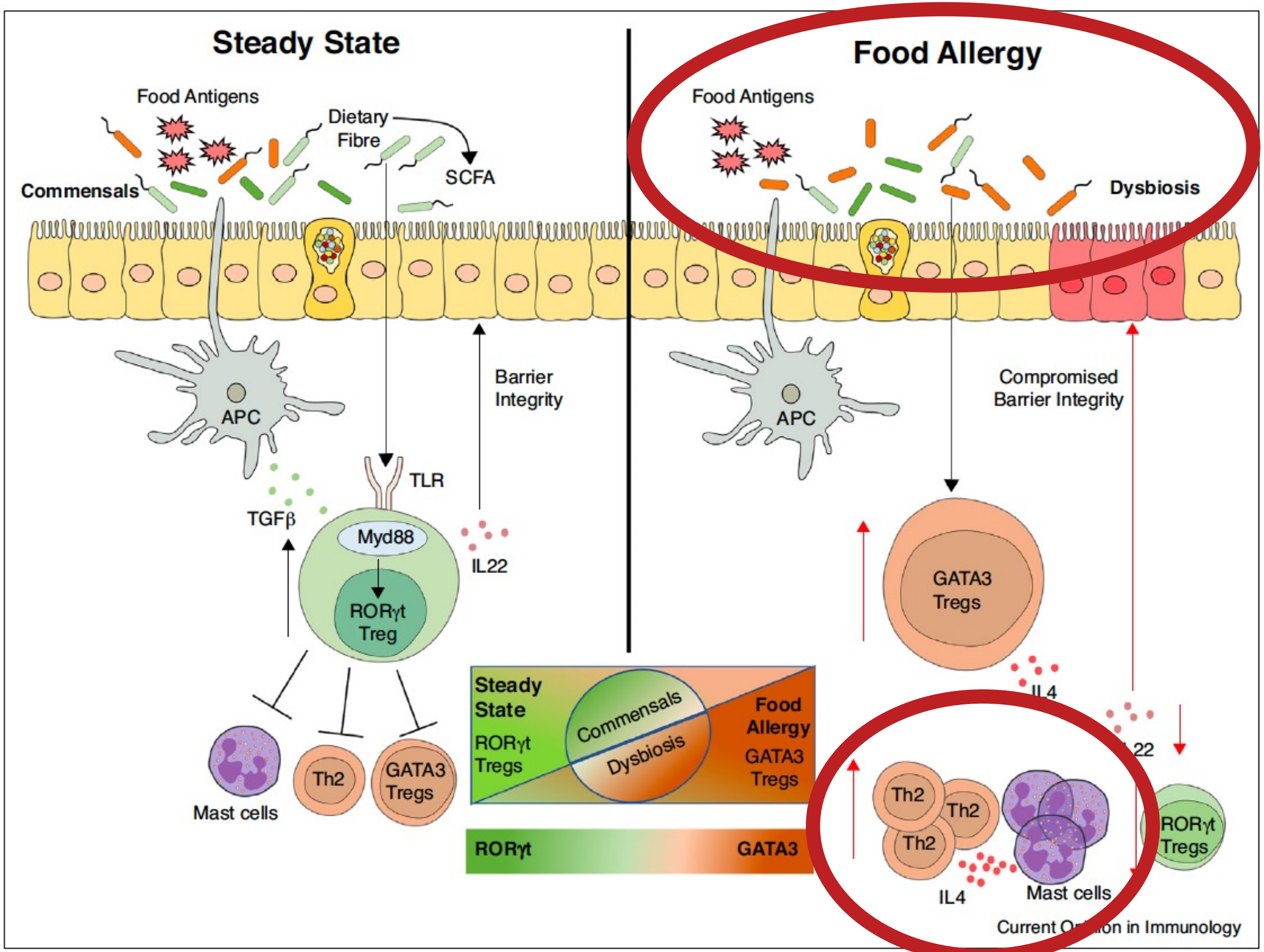


Current Opinion in Immunology

Review > Cells. 2022 Jan 19;11(3):329. doi: 10.3390/cells11030329.

Mucosal Mast Cells as Key Effector Cells in Food Allergies

Nobuhiro Nakano [1], Jiro Kitaura [1]

Affiliations + expand

PMID: 35159139 PMCID: PMC8834119 DOI: 10.3390/cells11030329

Free PMC article

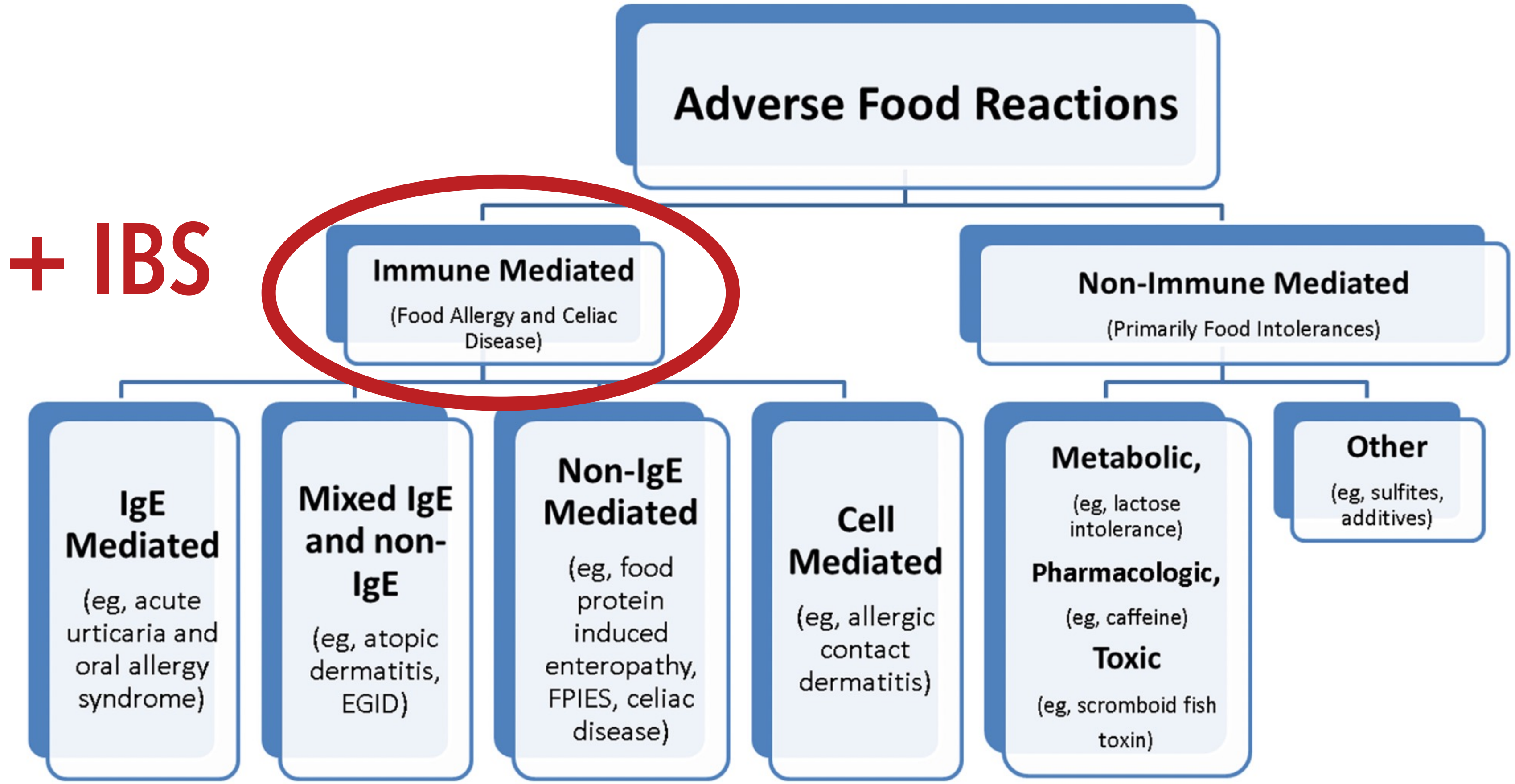
Abstract

Mucosal mast cells (MMCs) localized in the intestinal mucosa play a key role in the development of IgE-mediated food allergies. Recent advances have revealed that MMCs are a distinctly different population from connective tissue mast cells localized in skin and other connective tissues. MMCs are inducible and transient cells that arise from bone marrow-derived mast cell progenitors, and their numbers increase rapidly during mucosal allergic inflammation. However, the mechanism of the dramatic expansion of MMCs and their cell functions are not well understood. Here, we review recent findings on the mechanisms of MMC differentiation and expansion, and we discuss the potential for the inducers of differentiation and expansion to serve as targets for food allergy therapy. In addition, we also discuss the mechanism by which oral immunotherapy, a promising treatment for food allergy patients, induces unresponsiveness to food allergens and the roles of

> Nature. 2021 Feb;590(7844):151-156. doi: 10.1038/s41586-020-03118-2. Epub 2021 Jan 13.

Local immune response to food antigens drives meal-induced abdominal pain

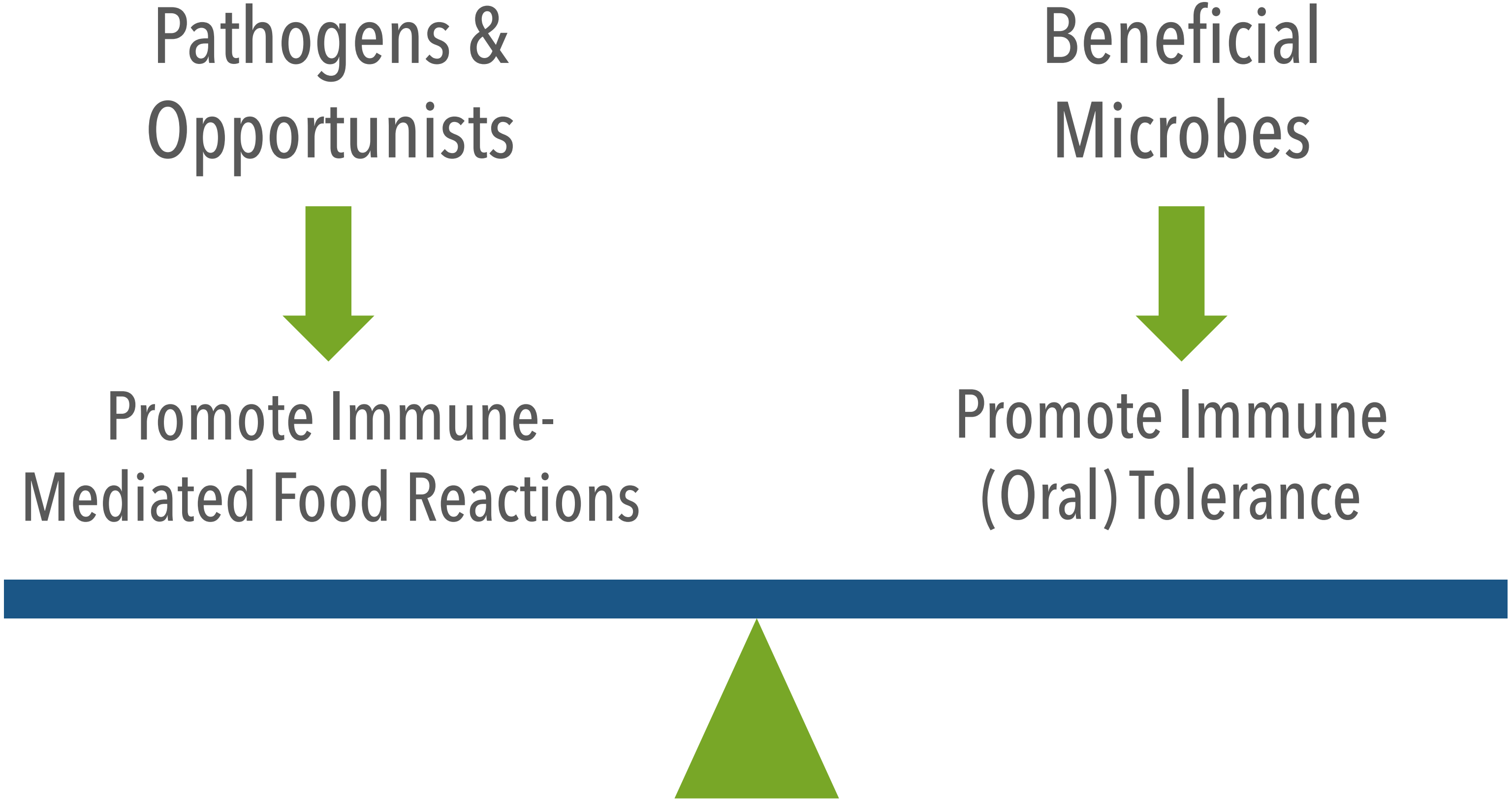
with allergic rhinitis and chronic rhinosinusitis with nasal polyps[22], and they are associated with increased airway reactivity. Based on our data, we propose that IBS, at least in an immunogenetically susceptible subgroup of patients, is part of a spectrum of food-induced disorders mediated by mast cell activation, with systemic food allergy at the extreme end of the spectrum. The risk of developing IBS is likely to depend on genetic make-up, favouring an atopic immune response. This hypothesis is further supported by the association of IBS with atopic diseases such as allergic rhinitis, allergic eczema and asthma[23,24].



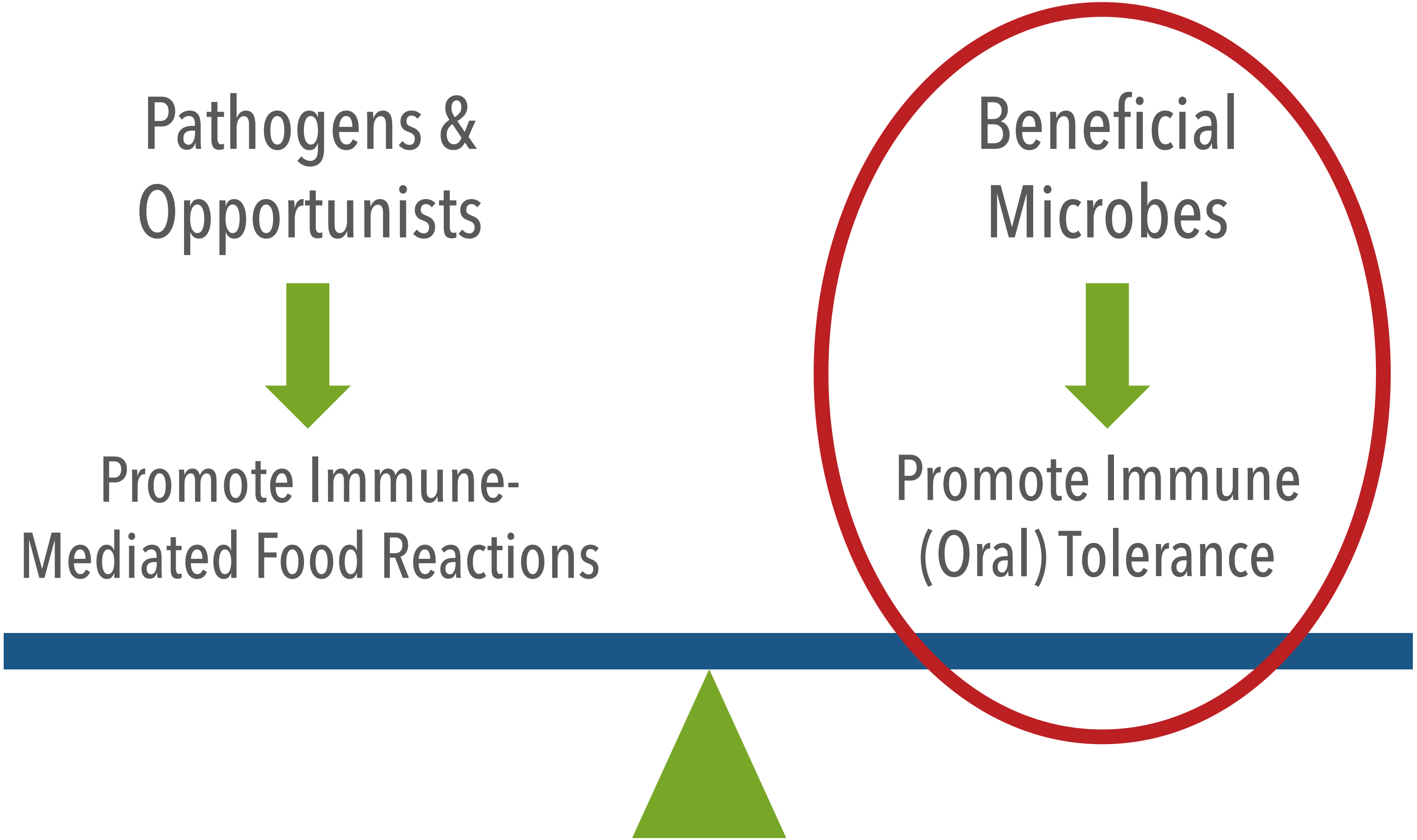
Clinic Rev Allerg Immunol (2019) 57:244–260

GI-MAP™

What are the key imbalances?



Pathogens & Opportunists
Promote Immune-Mediated Food Reactions
Beneficial Microbes
Promote Immune (Oral) Tolerance



Pathogens & Opportunists
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Review > Curr Opin Immunol. 2019 Oct;60:141-147. doi: 10.1016/j.coi.2019.06.001. Epub 2019 Jul 11.

Regulation of oral immune tolerance by the microbiome in food allergy

"Significantly, different immunoprotective commensal bacteria, including members of the ***Clostridiales and Bacteroidales*** orders act to induce the transcription factor RORγt in nascent Treg cells via an upstream MyD88-dependent mechanism to ***promote tolerance to dietary antigens***. "

Normal Bacterial Flora

	Result		Normal
Bacteroides fragilis	**3.70e9**		1.60e9 - 2.50e11
Bifidobacterium spp.	**1.01e10**		>6.70e7
Enterococcus spp.	**3.87e4**	**Low**	1.9e5 - 2.00e8
Escherichia spp.	**7.74e5**	**Low**	3.70e6 - 3.80e9
Lactobacillus spp.	**1.48e6**		8.6e5 - 6.20e8
Clostridia (class)	**3.82e6**	**Low**	5.00e6 - 5.00e7
Enterobacter spp.	**1.09e6**		1.00e6 - 5.00e7
Akkermansia muciniphila	**1.35e6**	**High**	1.00e1 - 5.00e4
Faecalibacterium prausnitzii	**6.98e2**	**Low**	1.00e3 - 5.00e8

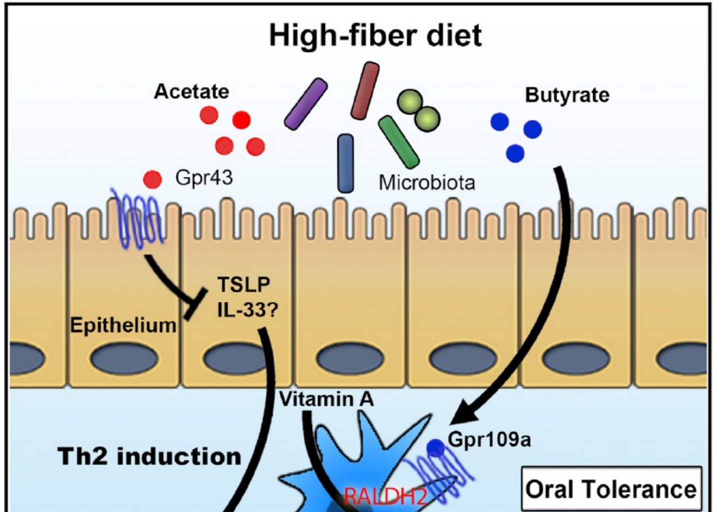
Phyla Microbiota	Result		Normal
Bacteroidetes	**1.10e11**	**Low**	8.61e11 - 3.31e12
Firmicutes	**1.25e10**	**Low**	5.70e10 - 3.04e11
Firmicutes:Bacteroidetes Ratio	**0.11**		<1.00

Cell Reports

Article

Dietary Fiber and Bacterial SCFA Enhance Oral Tolerance and Protect against Food Allergy through Diverse Cellular Pathways

Graphical Abstract



Authors

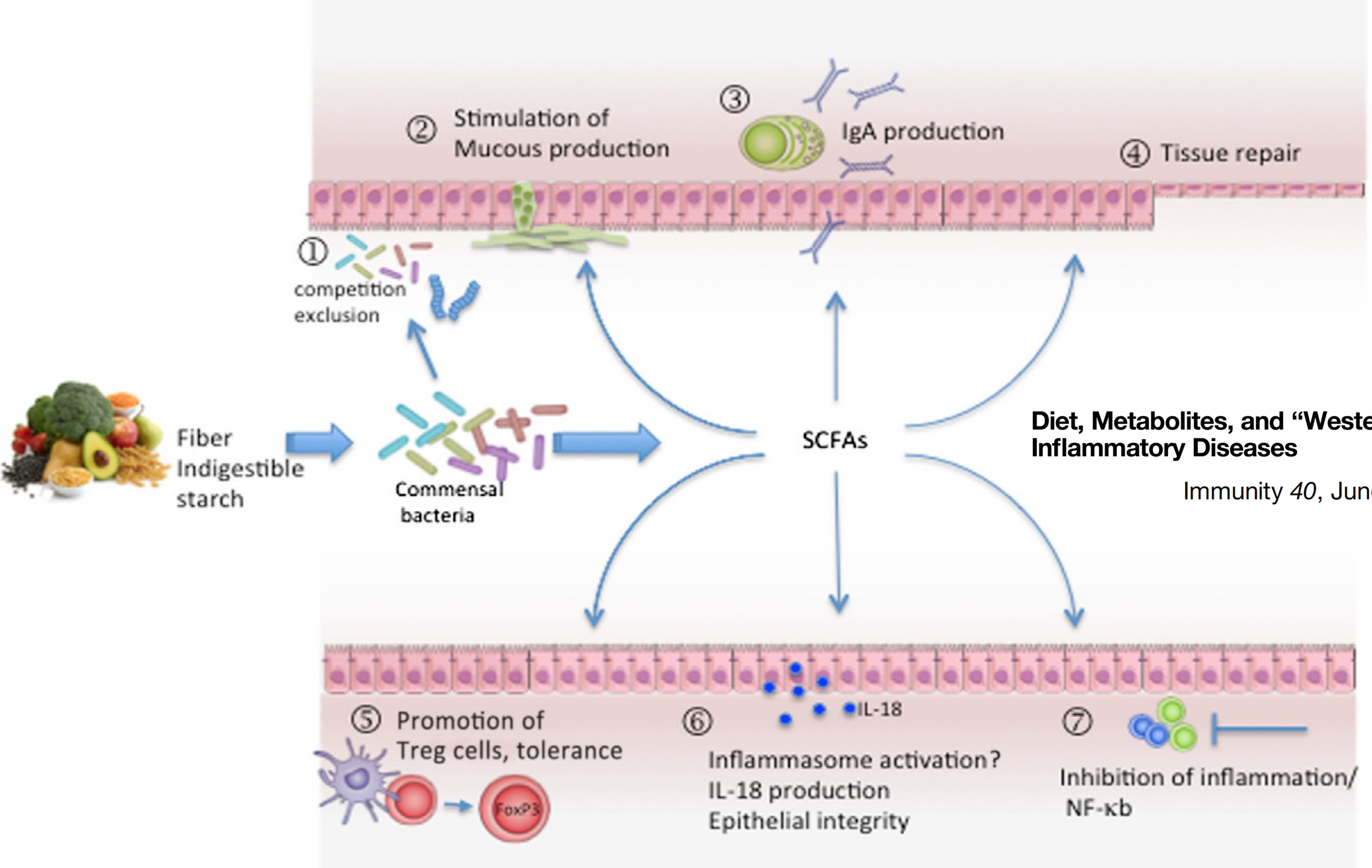
Jian Tan, Craig McKenzie,
Peter J. Vuillermin, ..., Reina E. Mebius,
Laurence Macia, Charles R. Mackay

Correspondence

laurence.macia@sydney.edu.au (L.M.),
charles.mackay@monash.edu (C.R.M.)

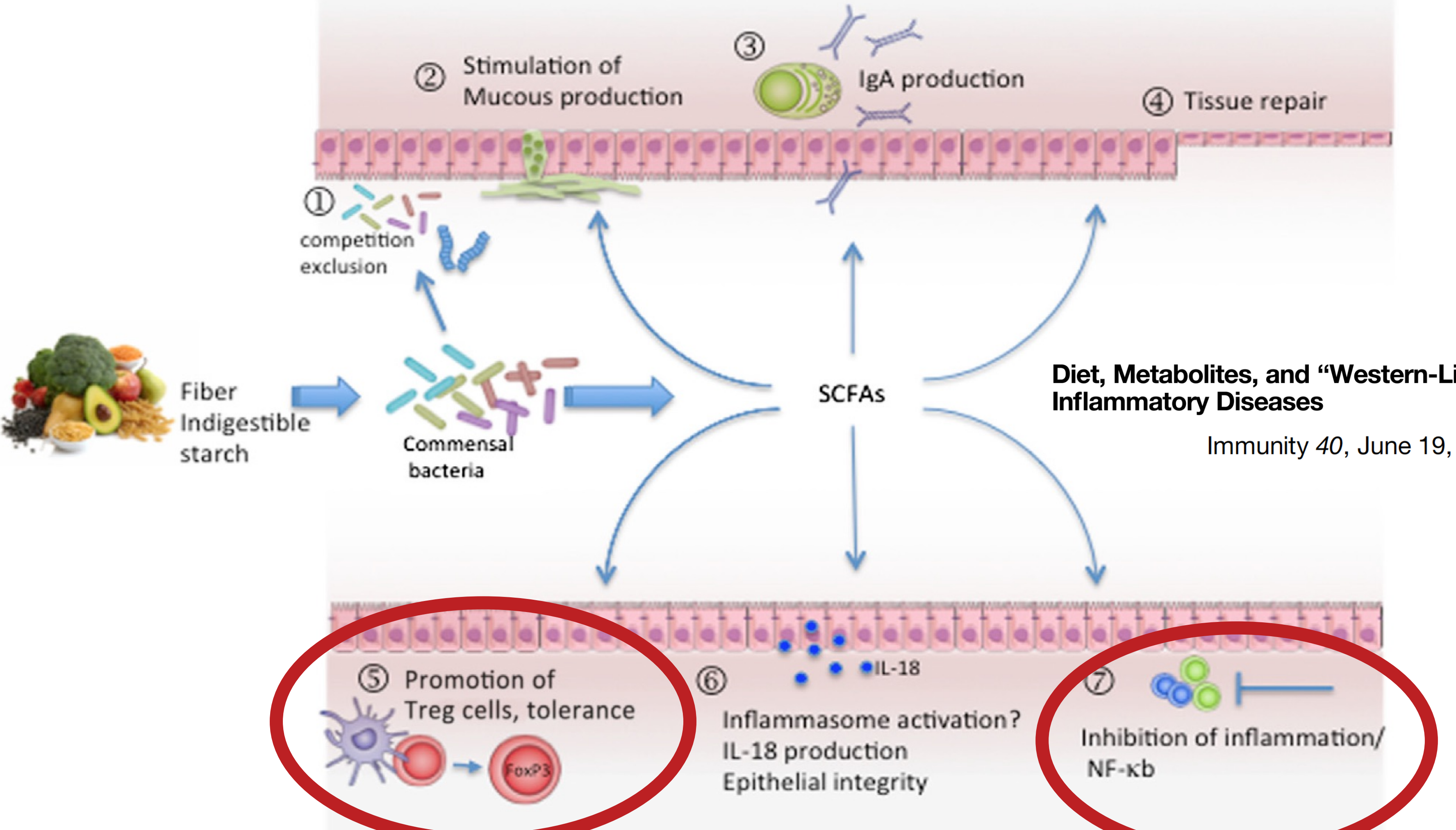
In Brief

Tan et al. examine the beneficial roles of dietary fiber in peanut allergy using mice. The authors find that this effect involves reshaping of the gut microbiota as well as increased levels of short-chain fatty acids and activity of their receptors GPR43 and



Diet, Metabolites, and “Western-Lifestyle” Inflammatory Diseases

Immunity *40*, June 19, 2014



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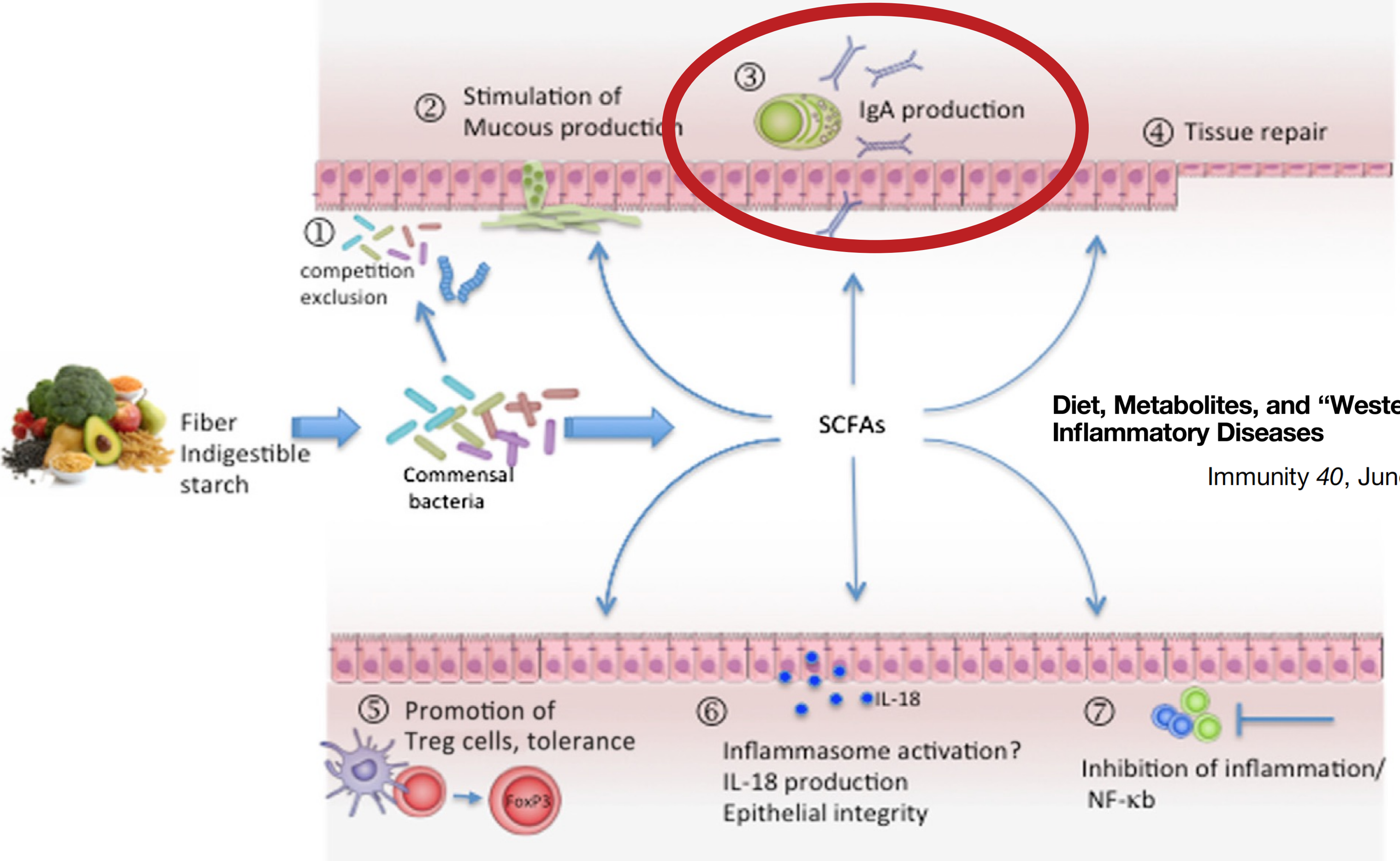


Diet, Metabolites, and "Western-Lifestyle" Inflammatory Diseases

Immunity *40*, June 19, 2014

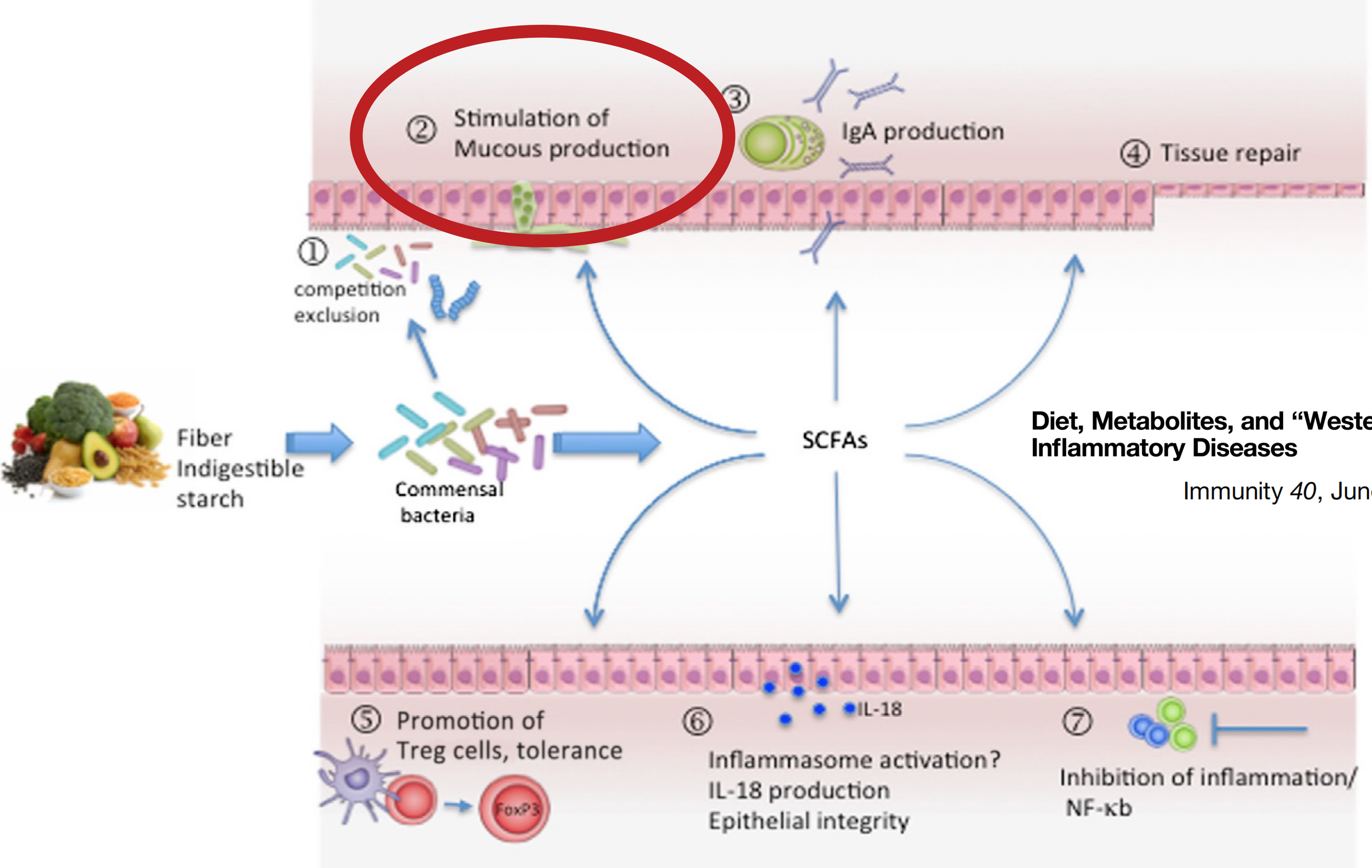
> Ann Allergy Asthma Immunol. 2021 May;126(5):467-468. doi: 10.1016/j.anai.2021.01.028.
Epub 2021 Feb 3.

The role of immunoglobulin A in oral tolerance and food allergy

IgA is thought to have a variety of functions to maintain the epithelial barrier and promote intestinal homeostasis. One of the main forms of mucosal defense is immune exclusion, which limits bacterial colonization and penetration of antigen through the epithelial surface.[1] Immune exclusion is accomplished primarily through secretory IgA, which can trap antigen. This, along with intestinal peristalsis, defensins, and mucin, results in the removal of the antigen from the epithelial surface and hindrance of potential immune responses. IgA also allows for intestinal homeostasis by shaping the composition of commensal microorganisms.[1] Given these reported roles of IgA in the gut against microbes and toxins, it is presumed that IgA might also promote oral tolerance to food antigens.

Intestinal Health

Digestion	Result		Normal
Steatocrit	33	High	<15 %
Elastase-1	187	Low	>200 ug/g
GI Markers	Result		Normal
b-Glucuronidase	**1693**		<2486 U/mL
Occult Blood - FIT	**0**		<10 ug/g
Immune Response	Result		Normal
Secretory IgA	81	Low	510 - 2010 ug/g
Anti-gliadin IgA	**73**		0 - 157 U/L
Inflammation	Result		Normal
Calprotectin	**14**		<173 ug/g



Diet, Metabolites, and "Western-Lifestyle" Inflammatory Diseases

Immunity *40*, June 19, 2014

Review > Trends Mol Med. 2022 Jan;28(1):36-50. doi: 10.1016/j.molmed.2021.10.004.
Epub 2021 Nov 19.

Intestinal mucus barrier: a missing piece of the puzzle in food allergy

Amy Parrish [1], Marie Boudaud [2], Annette Kuehn [2], Markus Ollert [3], Mahesh S Desai [4]

Affiliations + expand

PMID: 34810087 DOI: 10.1016/j.molmed.2021.10.004
Free article

Abstract

The prevalence of food allergies has reached epidemic levels but the cause remains largely unknown. We discuss the clinical relevance of the gut mucosal barrier as a site for allergic sensitization to food. In this context, we focus on an important but overlooked part of the mucosal barrier in pathogenesis, the glycoprotein-rich mucus layer, and call attention to both beneficial and detrimental aspects of mucus-gut microbiome interactions. Studying the intricate links between the mucus barrier, the associated bacteria, and the mucosal immune system may advance our understanding of the mechanisms and inform prevention and treatment strategies in food allergy.

Keywords: allergic sensitization; food allergy; gastrointestinal mucus layer; gut microbiome; mucin-degrading bacteria; mucosal immune system.

Normal Bacterial Flora

	Result		Normal
Bacteroides fragilis	**1.06e11**		1.60e9 - 2.50e11
Bifidobacterium spp.	**3.91e9**		>6.70e7
Enterococcus spp.	**8.16e7**		1.9e5 - 2.00e8
Escherichia spp.	**1.31e8**		3.70e6 - 3.80e9
Lactobacillus spp.	**1.17e7**		8.6e5 - 6.20e8
Clostridia (class)	**1.28e7**		5.00e6 - 5.00e7
Enterobacter spp.	**7.60e6**		1.00e6 - 5.00e7
Akkermansia muciniphila	**<dl**		1.00e1 - 5.00e4
Faecalibacterium prausnitzii	**6.84e1**	**Low**	1.00e3 - 5.00e8

Phyla Microbiota	Result	Normal
Bacteroidetes	**1.84e12**	8.61e11 - 3.31e12
Firmicutes	**8.92e10**	5.70e10 - 3.04e11
Firmicutes:Bacteroidetes Ratio	**0.05**	<1.00

Intestinal Health

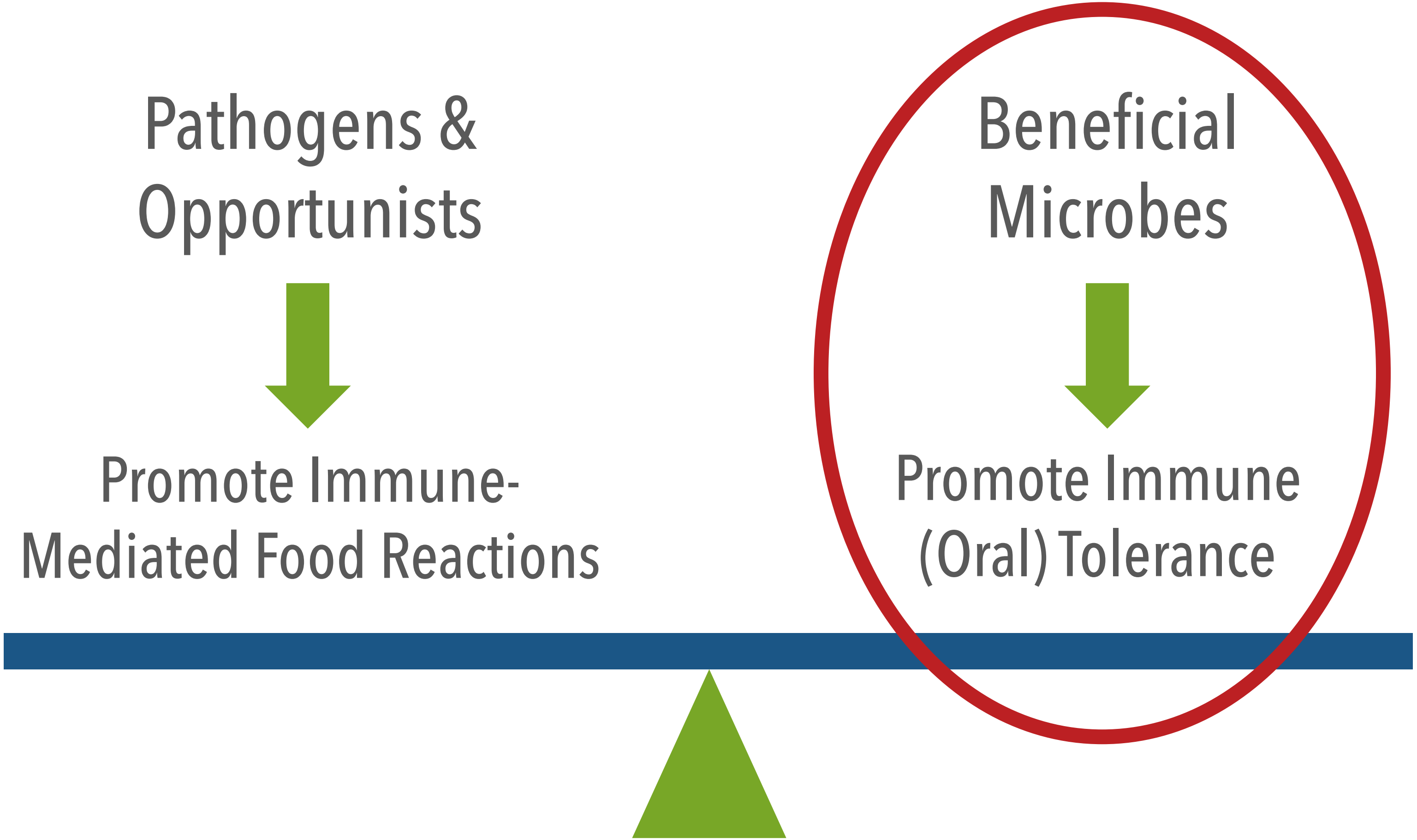
Digestion	Result		Normal
Steatocrit	**<dl**		<15 %
Elastase-1	**>750**		>200 ug/g

GI Markers	Result		Normal
b-Glucuronidase	**1567**		<2486 U/mL
Occult Blood - FIT	**0**		<10 ug/g

Immune Response	Result		Normal
Secretory IgA	**210**	**Low**	510 - 2010 ug/g
Anti-gliadin IgA	**95**		0 - 157 U/L

Inflammation	Result		Normal
Calprotectin	**4**		<173 ug/g

Add-on Test	Result		Normal
Zonulin	**157.3**	**High**	<107 ng/g


Pathogens & Opportunists
Promote Immune-Mediated Food Reactions
Beneficial Microbes
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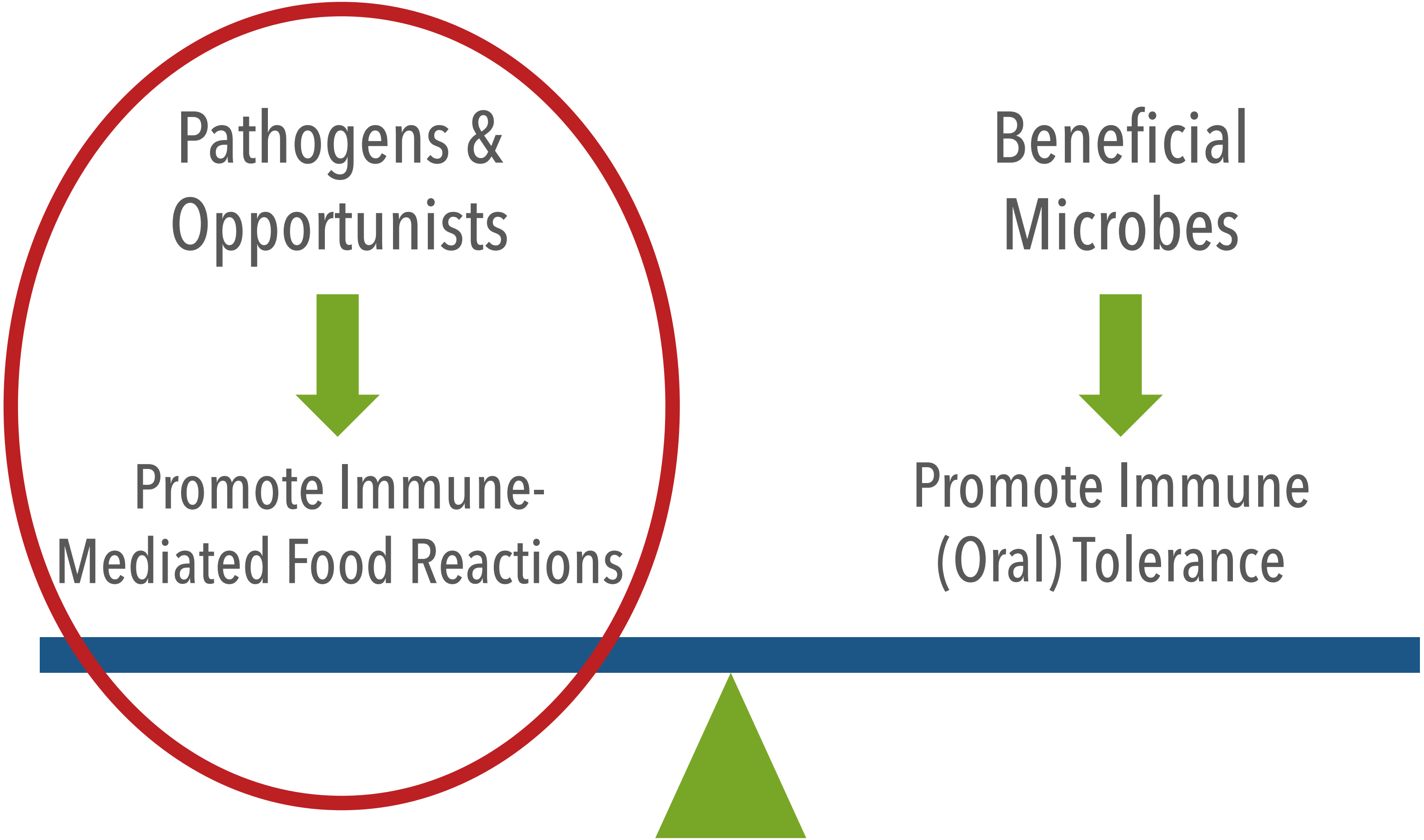
Supporting Beneficial Microbes: 4P's

- **Prebiotics:** wide range of fermentable carbohydrates / fibers
- **Polyphenols:** wide range
- **Probiotics:** Lactobacillus, Bifidobacterium, Akkermansia, etc.
- **Post-biotics:** butyrate and other microbial products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Nat Rev Gastroenterol Hepatol. 2019 Jan;16(1):7-18. doi: 10.1038/s41575-018-0064-z.

Mechanisms by which gut microorganisms influence food sensitivities.

"One mechanism through which bacteria could affect immune responses to dietary components is through bacterial metabolism of antigens. … Indeed, ***depending on the type of bacteria present, the end result will be increased or reduced immunogenicity*** of the produced peptides."

Nat Commun. 2019 Mar 13;10(1):1198. doi: 10.1038/s41467-019-09037-9.

Duodenal bacterial proteolytic activity determines sensitivity to dietary antigen through protease-activated receptor-2.

"Opportunistic pathogens, including members of Proteobacteria such as ***Pseudomonas aeruginosa*** isolated from the duodenum of CeD patients, ***can metabolize gluten predigested by human proteases*** into shorter immunogenic peptides that permeate better through the barrier and ***stimulate human gluten-specific T cells***."

Opportunistic Bacteria

Additional Dysbiotic/Overgrowth Bacteria	Result		Normal
Bacillus spp.	**2.89e6**	**High**	<1.50e5
Enterococcus faecalis	**9.57e4**	**High**	<1.00e4
Enterococcus faecium	**<dl**		<1.00e4
Morganella spp.	**<dl**		<1.00e3
Pseudomonas spp.	**2.05e7**	**High**	<1.00e4
Pseudomonas aeruginosa	**1.47e5**	**High**	<5.00e2
Staphylococcus spp.	**<dl**		<1.00e4
Staphylococcus aureus	**5.34e2**	**High**	<5.00e2
Streptococcus spp.	**3.57e3**	**High**	<1.00e3
Methanobacteriaceae (family)	**9.62e8**		<5.00e9

Gastroenterology. 2016 Oct;151(4):670-83. doi: 10.1053/j.gastro.2016.06.041. Epub 2016 Jun 30.

Duodenal Bacteria From Patients With Celiac Disease and Healthy Subjects Distinctly Affect Gluten Breakdown and Immunogenicity.

"***Lactobacillus spp***. from the duodenum of non-CD [Celiac Disease] controls degraded gluten peptides produced by human and P. aeruginosa proteases, reducing their immunogenicity."

Normal Bacterial Flora

	Result		Normal
Bacteroides fragilis	**2.86e11**	**High**	1.60e9 - 2.50e11
Bifidobacterium spp.	**7.48e10**		>6.70e7
Enterococcus spp.	**2.07e6**		1.9e5 - 2.00e8
Escherichia spp.	**1.02e8**		3.70e6 - 3.80e9
Lactobacillus spp.	**3.96e5**	**Low**	8.6e5 - 6.20e8
Clostridia (class)	**2.90e6**	**Low**	5.00e6 - 5.00e7
Enterobacter spp.	**3.04e7**		1.00e6 - 5.00e7
Akkermansia muciniphila	**8.99e4**	**High**	1.00e1 - 5.00e4
Faecalibacterium prausnitzii	**2.47e3**		1.00e3 - 5.00e8

Phyla Microbiota	Result		Normal
Bacteroidetes	**1.19e13**	**High**	8.61e11 - 3.31e12
Firmicutes	**4.14e11**	**High**	5.70e10 - 3.04e11
Firmicutes:Bacteroidetes Ratio	**0.03**		<1.00

Randomized Controlled Trial > J Allergy Clin Immunol. 2019 Aug;144(2):494-503.
doi: 10.1016/j.jaci.2019.04.025. Epub 2019 May 31.

Association of Staphylococcus aureus colonization with food allergy occurs independently of eczema severity

Olympia Tsilochristou [1], George du Toit [2], Peter H Sayre [3], Graham Roberts [4], Kaitie Lawson [5], Michelle L Sever [5], Henry T Bahnson [6], Suzana Radulovic [2], Monica Basting [2], Marshall Plaut [7], Gideon Lack [8], Immune Tolerance Network Learning Early About Peanut Allergy Study Team

Collaborators, Affiliations + expand

PMID: 31160034 DOI: 10.1016/j.jaci.2019.04.025

Abstract

Background: Staphylococcus aureus has been implicated in the pathophysiology of eczema, allergic rhinitis, asthma, and food allergy. S aureus is a marker of more severe eczema, which is a risk factor for food sensitization/allergy. Therefore it might be that the association between S aureus and food allergy in eczematous patients is related to eczema severity.

Objective: We sought to investigate the association of S aureus colonization with specific IgE

Opportunistic Bacteria

Additional Dysbiotic/Overgrowth Bacteria	Result		Normal
Bacillus spp.	**2.89e6**	**High**	<1.50e5
Enterococcus faecalis	**9.57e4**	**High**	<1.00e4
Enterococcus faecium	**<dl**		<1.00e4
Morganella spp.	**<dl**		<1.00e3
Pseudomonas spp.	**2.05e7**	**High**	<1.00e4
Pseudomonas aeruginosa	**1.47e5**	**High**	<5.00e2
Staphylococcus spp.	**<dl**		<1.00e4
Staphylococcus aureus	**5.34e2**	**High**	<5.00e2
Streptococcus spp.	**3.57e3**	**High**	<1.00e3
Methanobacteriaceae (family)	**9.62e8**		<5.00e9

Review > Front Immunol. 2021 Jun 15;12:685865. doi: 10.3389/fimmu.2021.685865. eCollection 2021.

Responses of Mast Cells to Pathogens: Beneficial and Detrimental Roles

Microbes known to stimulate mast cell responses:

Staphylococcus aureus

Streptococcus spp.

Pseudomonas aeruginosa

Enterococcus faecalis

Candida

H. pylori

Fungi/Yeast

	Result		Normal
Candida spp.	**4.58e5**	**High**	<5.00e3
Candida albicans	**3.32e3**	**High**	<5.00e2
Geotrichum spp.	**<dl**		<3.00e2
Microsporidium spp.	**<dl**		<5.00e3
Rhodotorula spp.	**<dl**		<1.00e3

Viruses

	Result	Normal
Cytomegalovirus	**<dl**	<1.00e5
Epstein Barr Virus	**<dl**	<1.00e7

> Biosci Microbiota Food Health. 2012;31(3):67-70. doi: 10.12938/bmfh.31.67. Epub 2012 Jul 26.

Cell Wall Polysaccharides of Candida albicans Induce Mast Cell Degranulation in the Gut

Abstract

We investigated Candida albicans-induced mast cell degranulation in vitro and in vivo. Cell wall fraction but not culture supernatant and cell membrane fraction prepared from hyphally grown C. albicans induced β-hexosaminidase release in RBL-2H3 cells. Cell wall mannan and soluble β-glucan fractions also induced β-hexosaminidase release. Histological examination of mouse forestomach showed that C. albicans gut colonization induces mast cell degranulation. However, intragastric administration of cell wall fraction failed to induce mast cell degranulation. We propose that cell wall polysaccharides are responsible for mast cell degranulation in the C. albicans-colonized gut.

Opportunistic Bacteria

Additional Dysbiotic/Overgrowth Bacteria	Result		Normal
Bacillus spp.	**2.89e6**	**High**	<1.50e5
Enterococcus faecalis	**9.57e4**	**High**	<1.00e4
Enterococcus faecium	**<dl**		<1.00e4
Morganella spp.	**<dl**		<1.00e3
Pseudomonas spp.	**2.05e7**	**High**	<1.00e4
Pseudomonas aeruginosa	**1.47e5**	**High**	<5.00e2
Staphylococcus spp.	**<dl**		<1.00e4
Staphylococcus aureus	**5.34e2**	**High**	<5.00e2
Streptococcus spp.	**3.57e3**	**High**	<1.00e3
Methanobacteriaceae (family)	**9.62e8**		<5.00e9

Fungi/Yeast

	Result		Normal
Candida spp.	**4.58e5**	**High**	<5.00e3
Candida albicans	**3.32e3**	**High**	<5.00e2
Geotrichum spp.	**<dl**		<3.00e2
Microsporidium spp.	**<dl**		<5.00e3

Review > Dig Dis Sci. 2021 Apr;66(4):965-982. doi: 10.1007/s10620-020-06264-9. Epub 2020 Apr 23.

Mast Cell Activation Syndrome: A Primer for the Gastroenterologist

*"High histamine foods can activate MCs [mast cells] in the gut causing direct and systemic symptoms. … **MCs not only release histamine, but the MCs have receptors for histamine** which then activate other MCs and other cells in the body."*

Review > Biomolecules. 2020 Aug 14;10(8):1181. doi: 10.3390/biom10081181.

Histamine Intolerance: The Current State of the Art

"Specifically, the Enterobacteriaceae species Hafnai aluei, ***Morganella morganii*** and ***Klebsiella pneumoniae*** have been identified as some of the most ***prolific histamine-forming bacteria*** … "

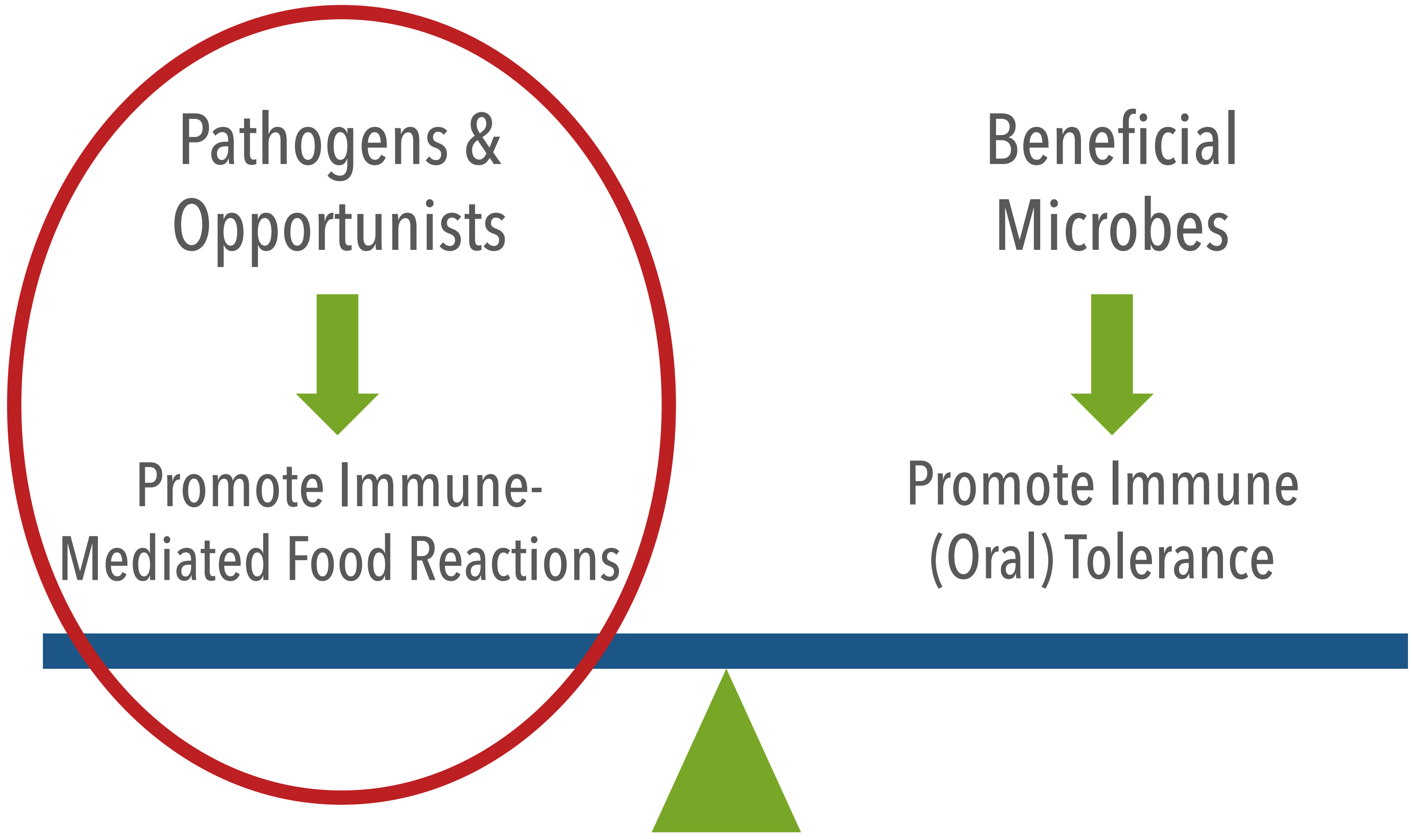
Opportunistic Bacteria

Additional Dysbiotic/Overgrowth Bacteria	Result		Normal
Bacillus spp.	**8.50e5**	**High**	<1.50e5
Enterococcus faecalis	**1.66e3**		<1.00e4
Enterococcus faecium	**1.00e3**		<1.00e4
Morganella spp.	**3.70e4**	**High**	<1.00e3
Pseudomonas spp.	**2.03e3**		<1.00e4
Pseudomonas aeruginosa	**<dl**		<5.00e2
Staphylococcus spp.	**3.32e2**		<1.00e4
Staphylococcus aureus	**1.96e4**	**High**	<5.00e2
Streptococcus spp.	**5.16e4**	**High**	<1.00e3
Methanobacteriaceae (family)	**1.66e10**	**High**	<5.00e9

Histamine Producers	*Morganella*
	Klebsiella
	Klebsiella pneumoniae
	Pseudomonas
	Pseudomonas aeruginosa
	Citrobacter freundii
	Proteus
	Proteus mirabilis

GI-MAP®

GI Microbial Assay Plus

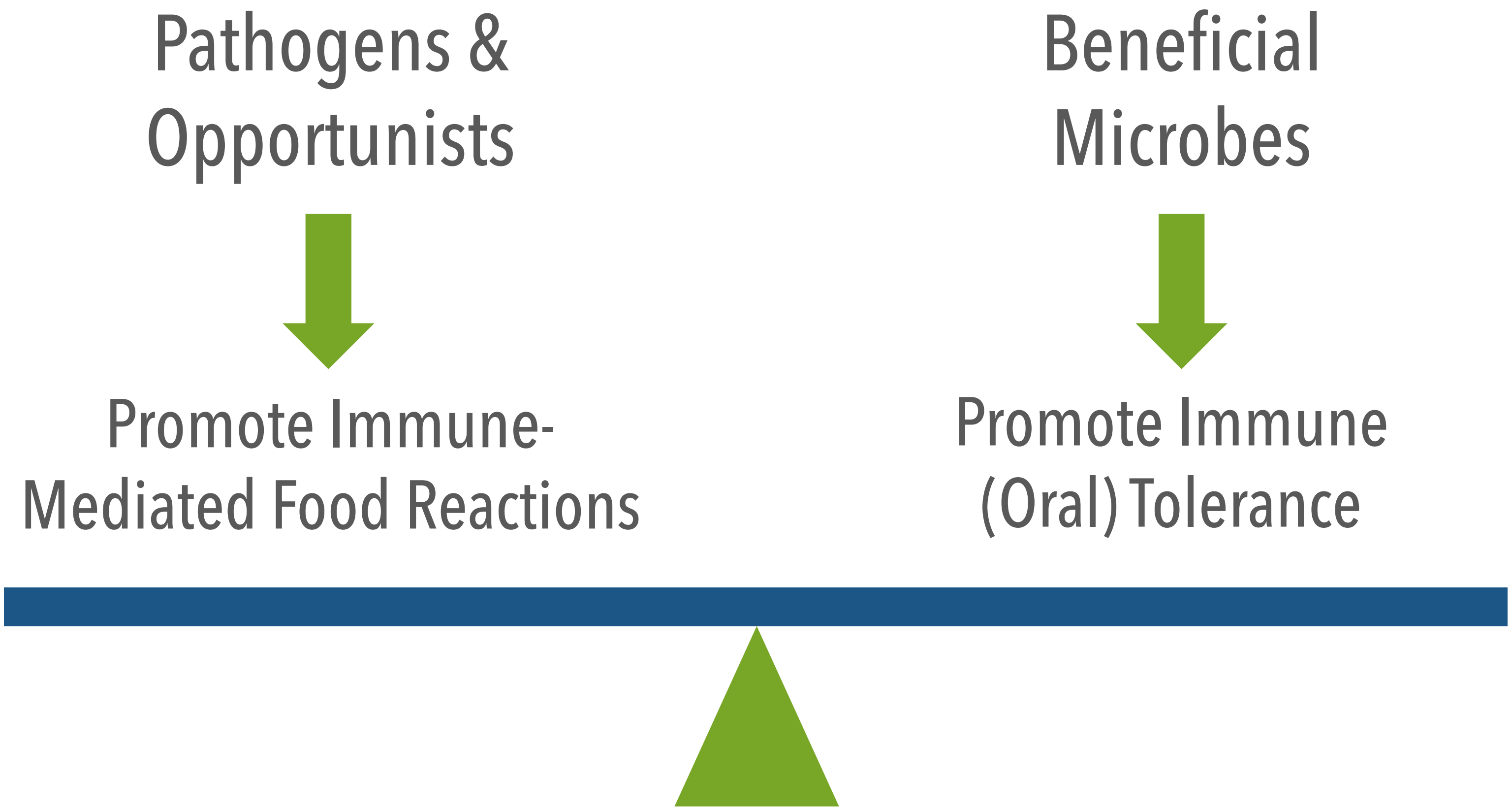


Pathogens & Opportunists
Promote Immune-Mediated Food Reactions
Beneficial Microbes
Promote Immune (Oral) Tolerance

> Allergy. 2020 Aug;75(8):1966-1978. doi: 10.1111/all.14254. Epub 2020 Apr 24.

Butyrate inhibits human mast cell activation via epigenetic regulation of FcεRI-mediated signaling

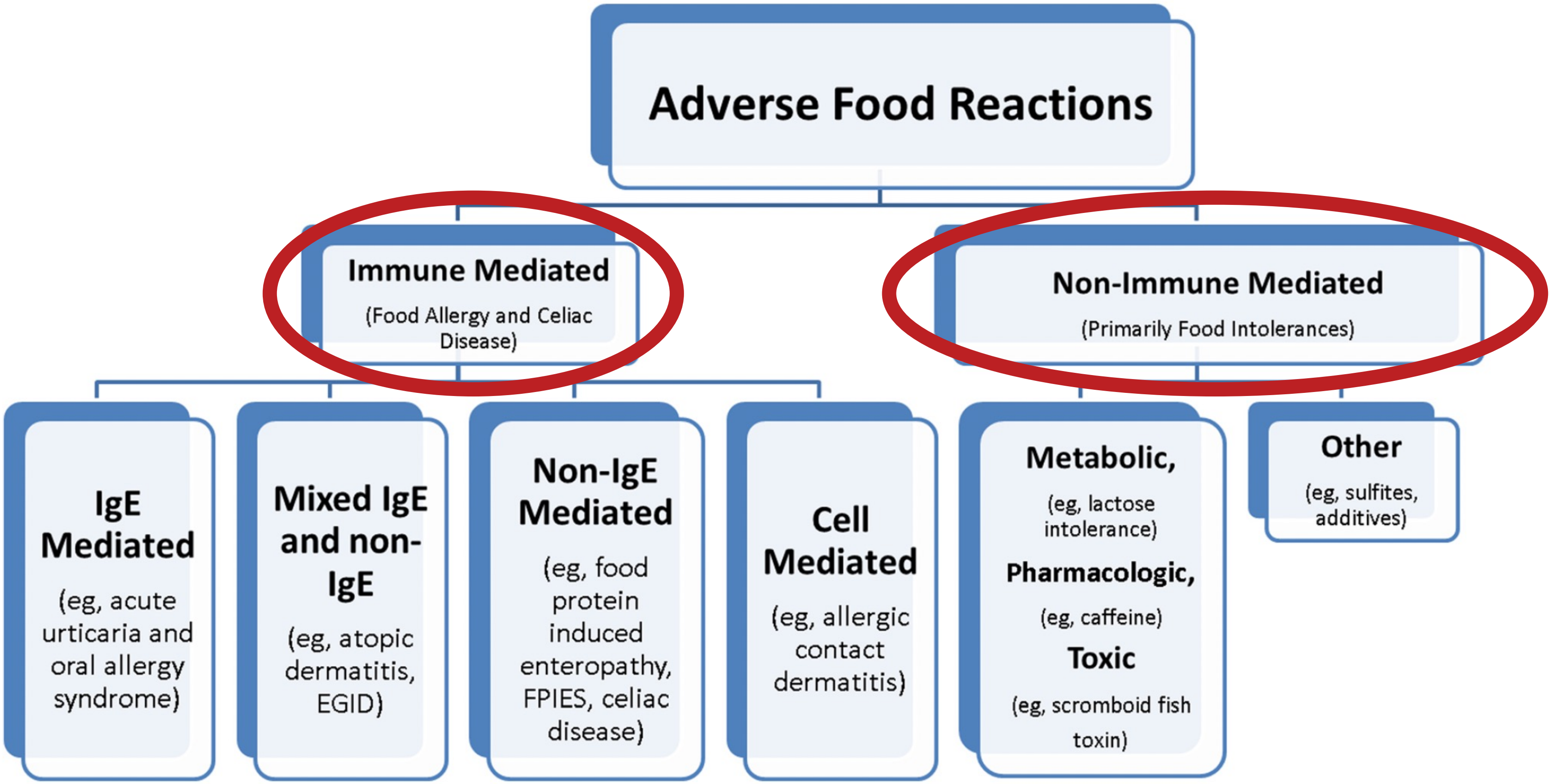
"Short-chain fatty acids (SCFAs) are fermented dietary components that regulate immune responses, promote colonic health, and ***suppress mast cell-mediated diseases***."


Pathogens & Opportunists
Beneficial Microbes
Promote Immune-Mediated Food Reactions
Promote Immune (Oral) Tolerance

Review > Dig Dis Sci. 2021 Apr;66(4):965-982. doi: 10.1007/s10620-020-06264-9.
Epub 2020 Apr 23.

Mast Cell Activation Syndrome: A Primer for the Gastroenterologist

Investigations of the effect of a ***low-FODMAP*** diet in IBS-D patients have shown ***reduction of plasma histamine levels***. Furthermore, ***high-FODMAP*** diet in mice results in increased visceral hypersensitivity and ***increased MC density in the colon***."



Clinic Rev Allerg Immunol (2019) 57:244–260

GI-MAP™

What are the key imbalances?

Case Example 1

- Female, 43
- Abdominal gas, bloating and pain, increasing through the day
- Symptoms associated with meals, but not specific foods yet implicated

Pathogens

Bacterial Pathogens	Result	Normal
Campylobacter	**<dl**	<1.00e3
C. difficile, Toxin A	**<dl**	<1.00e3
C. difficile, Toxin B	**<dl**	<1.00e3
Enterohemorrhagic E. coli	**<dl**	<1.00e3
E. coli O157	**<dl**	<1.00e3
Enteroinvasive E. coli/Shigella	**<dl**	<1.00e2
Enterotoxigenic E. coli LT/ST	**<dl**	<1.00e3
Shiga-like Toxin *E. coli* stx1	**<dl**	<1.00e3
Shiga-like Toxin *E. coli* stx2	**<dl**	<1.00e3
Salmonella	**<dl**	<1.00e4
Vibrio cholerae	**<dl**	<1.00e5
Yersinia enterocolitica	**<dl**	<1.00e5

Parasitic Pathogens	Result	Normal
Cryptosporidium	**<dl**	<1.00e6
Entamoeba histolytica	**<dl**	<1.00e4
Giardia	**<dl**	<5.00e3

Viral Pathogens	Result	Normal
Adenovirus 40/41	**<dl**	<1.00e10
Norovirus GI/II	**<dl**	<1.00e7

H. pylori

	Result	Normal
Helicobacter pylori	**5.5e2**	<1.0e3
Virulence Factor, babA	**Negative**	Negative
Virulence Factor, cagA	**Negative**	Negative
Virulence Factor, dupA	**Negative**	Negative
Virulence Factor, iceA	**Negative**	Negative
Virulence Factor, oipA	**Negative**	Negative
Virulence Factor, vacA	**Negative**	Negative
Virulence Factor, virB	**Negative**	Negative
Virulence Factor, virD	**Negative**	Negative

Normal Bacterial Flora

	Result		Normal
Bacteroides fragilis	**3.70e9**		1.60e9 - 2.50e11
Bifidobacterium spp.	**1.01e10**		>6.70e7
Enterococcus spp.	**3.87e4**	**Low**	1.9e5 - 2.00e8
Escherichia spp.	**7.74e5**	**Low**	3.70e6 - 3.80e9
Lactobacillus spp.	**1.48e6**		8.6e5 - 6.20e8
Clostridia (class)	**3.82e6**	**Low**	5.00e6 - 5.00e7
Enterobacter spp.	**1.09e6**		1.00e6 - 5.00e7
Akkermansia muciniphila	**1.35e6**	**High**	1.00e1 - 5.00e4
Faecalibacterium prausnitzii	**6.98e2**	**Low**	1.00e3 - 5.00e8

Phyla Microbiota	Result		Normal
Bacteroidetes	**1.10e11**	**Low**	8.61e11 - 3.31e12
Firmicutes	**1.25e10**	**Low**	5.70e10 - 3.04e11
Firmicutes:Bacteroidetes Ratio	**0.11**		<1.00

Opportunistic Bacteria

Additional Dysbiotic/Overgrowth Bacteria	Result		Normal
Bacillus spp.	**4.13e5**	**High**	<1.50e5
Enterococcus faecalis	**<dl**		<1.00e4
Enterococcus faecium	**3.41e2**		<1.00e4
Morganella spp.	**<dl**		<1.00e3
Pseudomonas spp.	**7.12e5**	**High**	<1.00e4
Pseudomonas aeruginosa	**3.81e4**	**High**	<5.00e2
Staphylococcus spp.	**<dl**		<1.00e4
Staphylococcus aureus	**6.49e2**	**High**	<5.00e2
Streptococcus spp.	**2.74e3**	**High**	<1.00e3
Methanobacteriaceae (family)	**7.36e7**		<5.00e9

Potential Autoimmune Triggers	Result	Normal
Citrobacter spp.	**1.17e6**	<5.00e6
Citrobacter freundii	**<dl**	<5.00e5
Klebsiella spp.	**<dl**	<5.00e3
Klebsiella pneumoniae	**<dl**	<5.00e4
M. avium subsp. paratuberculosis	**<dl**	<5.00e3
Prevotella spp.	**7.64e6**	<1.00e8
Proteus spp.	**<dl**	<5.00e4
Proteus mirabilis	**<dl**	<1.00e3
Fusobacterium spp.	**1.88e4**	<1.00e8

Fungi/Yeast

	Result		Normal
Candida spp.	**1.09e4**	**High**	<5.00e3
Candida albicans	**<dl**		<5.00e2
Geotrichum spp.	**<dl**		<3.00e2
Microsporidium spp.	**<dl**		<5.00e3
Rhodotorula spp.	**<dl**		<1.00e3

Viruses

	Result	Normal
Cytomegalovirus	**<dl**	<1.00e5
Epstein Barr Virus	**<dl**	<1.00e7

Parasites

Protozoa	Result	Normal
Blastocystis hominis	**<dl**	<2.00e3
Chilomastix mesnili	**<dl**	<1.00e5
Cyclospora spp.	**<dl**	<5.00e4
Dientamoeba fragilis	**<dl**	<1.00e5
Endolimax nana	**<dl**	<1.00e4
Entamoeba coli	**<dl**	<5.00e6
Pentatrichomonas hominis	**<dl**	<1.00e2

Worms	Result	Normal
Ancylostoma duodenale	**Not Detected**	Not Detected
Ascaris lumbricoides	**Not Detected**	Not Detected
Necator americanus	**Not Detected**	Not Detected
Trichuris trichiura	**Not Detected**	Not Detected
Taenia spp.	**Not Detected**	Not Detected

Intestinal Health

Digestion	Result		Normal
Steatocrit	**<dl**		<15 %
Elastase-1	**>750**		>200 ug/g
GI Markers	Result		Normal
b-Glucuronidase	**2048**		<2486 U/mL
Occult Blood - FIT	**0**		<10 ug/g
Immune Response	Result		Normal
Secretory IgA	**300**	**Low**	510 - 2010 ug/g
Anti-gliadin IgA	**200**	**High**	0 - 157 U/L
Inflammation	Result		Normal
Calprotectin	**1**		<173 ug/g
Add-on Test	Result		Normal
Zonulin	**190.0**	**High**	<107 ng/g

Case Example 1 Summary

- H. pylori (low)
- Low normal bacteria
- High opportunists (Pseudomonas, Staphylococcus, Candida)
- Low sIgA, high zonulin, high anti-gliadin IgA

Case Example

- Female, 49
- Extensive food sensitivities
- Rheumatoid arthritis, occasional sinus infections, headaches, nausea

Pathogens

Bacterial Pathogens	Result	Normal
Campylobacter	**<dl**	<1.00e3
C. difficile, Toxin A	**<dl**	<1.00e3
C. difficile, Toxin B	**<dl**	<1.00e3
Enterohemorrhagic E. coli	**<dl**	<1.00e3
E. coli O157	**<dl**	<1.00e3
Enteroinvasive E. coli/Shigella	**<dl**	<1.00e2
Enterotoxigenic E. coli LT/ST	**<dl**	<1.00e3
Shiga-like Toxin *E. coli* stx1	**<dl**	<1.00e3
Shiga-like Toxin *E. coli* stx2	**<dl**	<1.00e3
Salmonella	**<dl**	<1.00e4
Vibrio cholerae	**<dl**	<1.00e5
Yersinia enterocolitica	**<dl**	<1.00e5

Parasitic Pathogens	Result		Normal
Cryptosporidium	**<dl**		<1.00e6
Entamoeba histolytica	**<dl**		<1.00e4
Giardia	**<dl**		<5.00e3

Viral Pathogens	Result		Normal
Adenovirus 40/41	**<dl**		<1.00e10
Norovirus GI/II	**<dl**		<1.00e7

H. pylori

	Result		Normal
Helicobacter pylori	**1.4e3**	**High**	<1.0e3
Virulence Factor, babA	**Negative**		Negative
Virulence Factor, cagA	**Negative**		Negative
Virulence Factor, dupA	**Negative**		Negative
Virulence Factor, iceA	**Negative**		Negative
Virulence Factor, oipA	**Negative**		Negative
Virulence Factor, vacA	**Negative**		Negative
Virulence Factor, virB	**Negative**		Negative
Virulence Factor, virD	**Negative**		Negative

Normal Bacterial Flora

	Result		Normal
Bacteroides fragilis	**5.66e9**		1.60e9 - 2.50e11
Bifidobacterium spp.	**1.15e11**		>6.70e7
Enterococcus spp.	**4.10e5**		1.9e5 - 2.00e8
Escherichia spp.	**2.36e8**		3.70e6 - 3.80e9
Lactobacillus spp.	**3.90e6**		8.6e5 - 6.20e8
Clostridia (class)	**1.16e8**	**High**	5.00e6 - 5.00e7
Enterobacter spp.	**7.21e6**		1.00e6 - 5.00e7
Akkermansia muciniphila	**2.97e6**	**High**	1.00e1 - 5.00e4
Faecalibacterium prausnitzii	**5.82e5**		1.00e3 - 5.00e8

Phyla Microbiota	Result		Normal
Bacteroidetes	**1.64e12**		8.61e11 - 3.31e12
Firmicutes	**1.66e11**		5.70e10 - 3.04e11
Firmicutes:Bacteroidetes Ratio	**0.10**		<1.00

Opportunistic Bacteria

Additional Dysbiotic/Overgrowth Bacteria	Result		Normal
Bacillus spp.	**1.11e6**	**High**	<1.50e5
Enterococcus faecalis	**1.52e4**	**High**	<1.00e4
Enterococcus faecium	**1.89e3**		<1.00e4
Morganella spp.	**1.11e5**	**High**	<1.00e3
Pseudomonas spp.	**9.59e3**		<1.00e4
Pseudomonas aeruginosa	**<dl**		<5.00e2
Staphylococcus spp.	**<dl**		<1.00e4
Staphylococcus aureus	**1.08e3**	**High**	<5.00e2
Streptococcus spp.	**3.40e4**	**High**	<1.00e3
Methanobacteriaceae (family)	**7.14e7**		<5.00e9

Potential Autoimmune Triggers	Result		Normal
Citrobacter spp.	**1.35e8**	**High**	<5.00e6
Citrobacter freundii	**<dl**		<5.00e5
Klebsiella spp.	**<dl**		<5.00e3
Klebsiella pneumoniae	**2.11e2**		<5.00e4
M. avium subsp. paratuberculosis	**<dl**		<5.00e3
Prevotella spp.	**4.61e6**		<1.00e8
Proteus spp.	**<dl**		<5.00e4
Proteus mirabilis	**<dl**		<1.00e3
Fusobacterium spp.	**2.41e5**		<1.00e8

Fungi/Yeast

	Result		Normal
Candida spp.	**2.34e4**	**High**	<5.00e3
Candida albicans	**<dl**		<5.00e2
Geotrichum spp.	**<dl**		<3.00e2
Microsporidium spp.	**<dl**		<5.00e3
Rhodotorula spp.	**<dl**		<1.00e3

Viruses

	Result		Normal
Cytomegalovirus	**<dl**		<1.00e5
Epstein Barr Virus	**<dl**		<1.00e7

Parasites

Protozoa	Result	Normal
Blastocystis hominis	**1.48e3**	<2.00e3
Chilomastix mesnili	**<dl**	<1.00e5
Cyclospora spp.	**<dl**	<5.00e4
Dientamoeba fragilis	**4.10e3**	<1.00e5
Endolimax nana	**<dl**	<1.00e4
Entamoeba coli	**<dl**	<5.00e6
Pentatrichomonas hominis	**<dl**	<1.00e2

Worms	Result	Normal
Ancylostoma duodenale	**Not Detected**	Not Detected
Ascaris lumbricoides	**Not Detected**	Not Detected
Necator americanus	**Not Detected**	Not Detected
Trichuris trichiura	**Not Detected**	Not Detected
Taenia spp.	**Not Detected**	Not Detected

Intestinal Health

Digestion	Result		Normal
Steatocrit	**<dl**		<15 %
Elastase-1	**>750**		>200 ug/g

GI Markers	Result		Normal
b-Glucuronidase	**1567**		<2486 U/mL
Occult Blood - FIT	**0**		<10 ug/g

Immune Response	Result		Normal
Secretory IgA	**210**	**Low**	510 - 2010 ug/g
Anti-gliadin IgA	**95**		0 - 157 U/L

Inflammation	Result		Normal
Calprotectin	**4**		<173 ug/g

Add-on Test	Result		Normal
Zonulin	**157.3**	**High**	<107 ng/g

Case Summary

- High H. pylori
- General overgrowth pattern
- High Morganella, Staphlyococcus aureus and Candida
- Low secretory IgA, high zonulin

Immune-Mediated Food Reactions: Approaches

- Identify potentially problematic foods, elimination diet
- Identify and address GI imbalances that may contribute to immune-mediated food reactions

Immune-Mediated Food Reactions: Approaches

- Identify potentially problematic foods, elimination diet
- Identify and address GI imbalances that may contribute to immune-mediated food reactions

Thank you!

Additional resources:

https://www.diagnosticsolutionslab.com

Diagnostic Solutions laboratory