Restoring the Gut Instinct
A Paradigm Shift in Disease Prevention and Treatment

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Newton MA

Financial Disclosures
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- Thank you to Aristo Vojdani, PhD, MSc, for use of his slides and diagrams

Learning Objectives

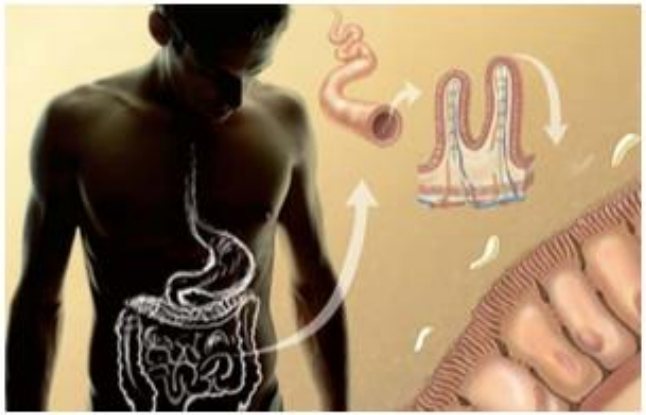
- Explore the relationship of the Gut--Brain Axis and it's role in health and disease
- Identify diagnostic tools and biomarkers to guide the use of conventional and emerging therapies for brain and gut health
- Review clinical case studies, diagnostic and therapeutic options for gut healing and brain health



All disease begins in the gut - Hippocrates 460 BC

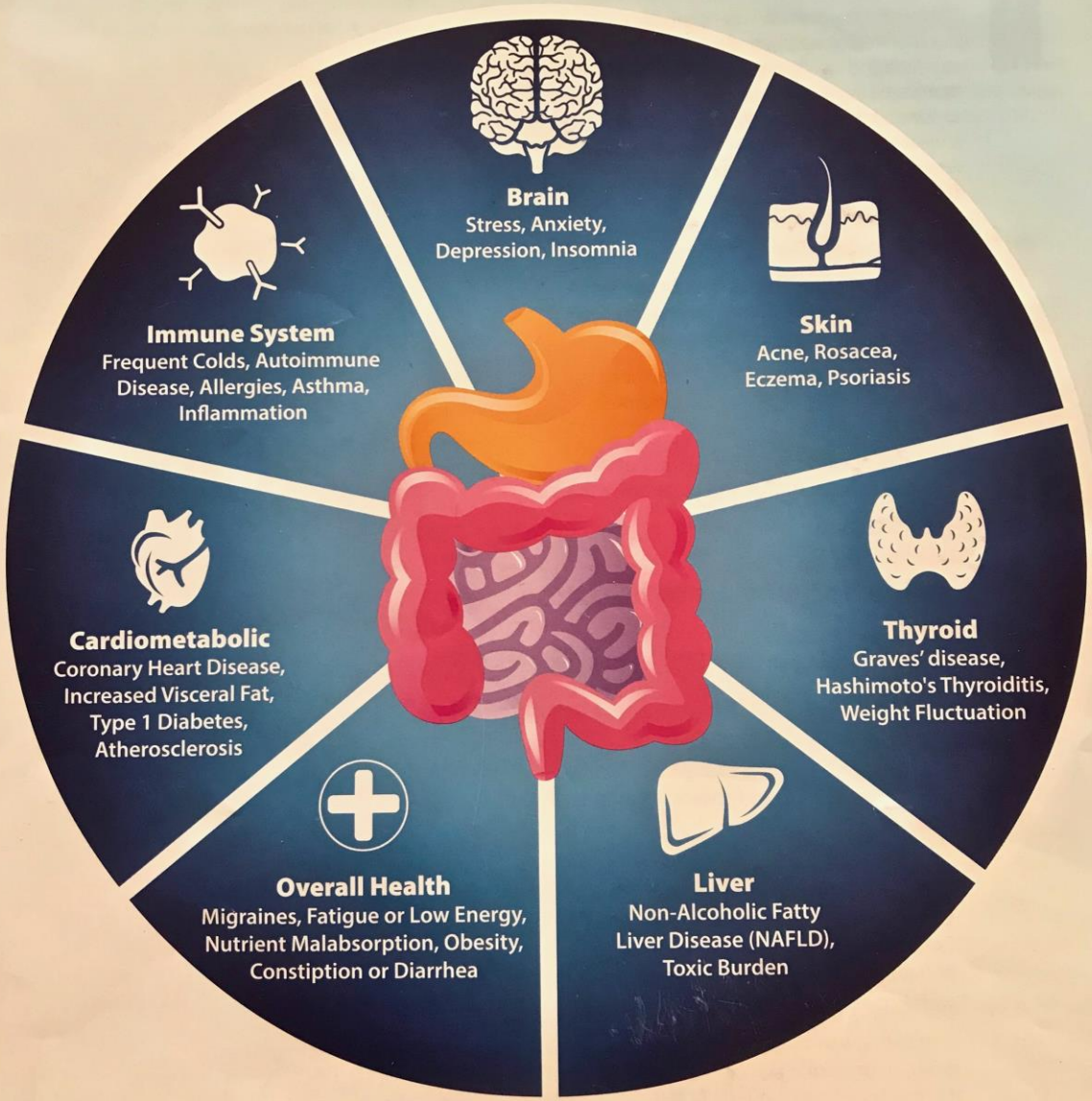
The gut is not like Las Vegas: what happens in the gut does not stay in the gut – A.F. 2010 AC

The intestinal mucosa is the battlefield on which friends and foes need to be recognized and properly managed to find the ideal balance between tolerance and immune response.



How the Gastrointestinal Tract

Affects the Entire Body



The Real Story of Our Genetic Complexity:

We Inherit two Parallel Genomes

Human Genome:

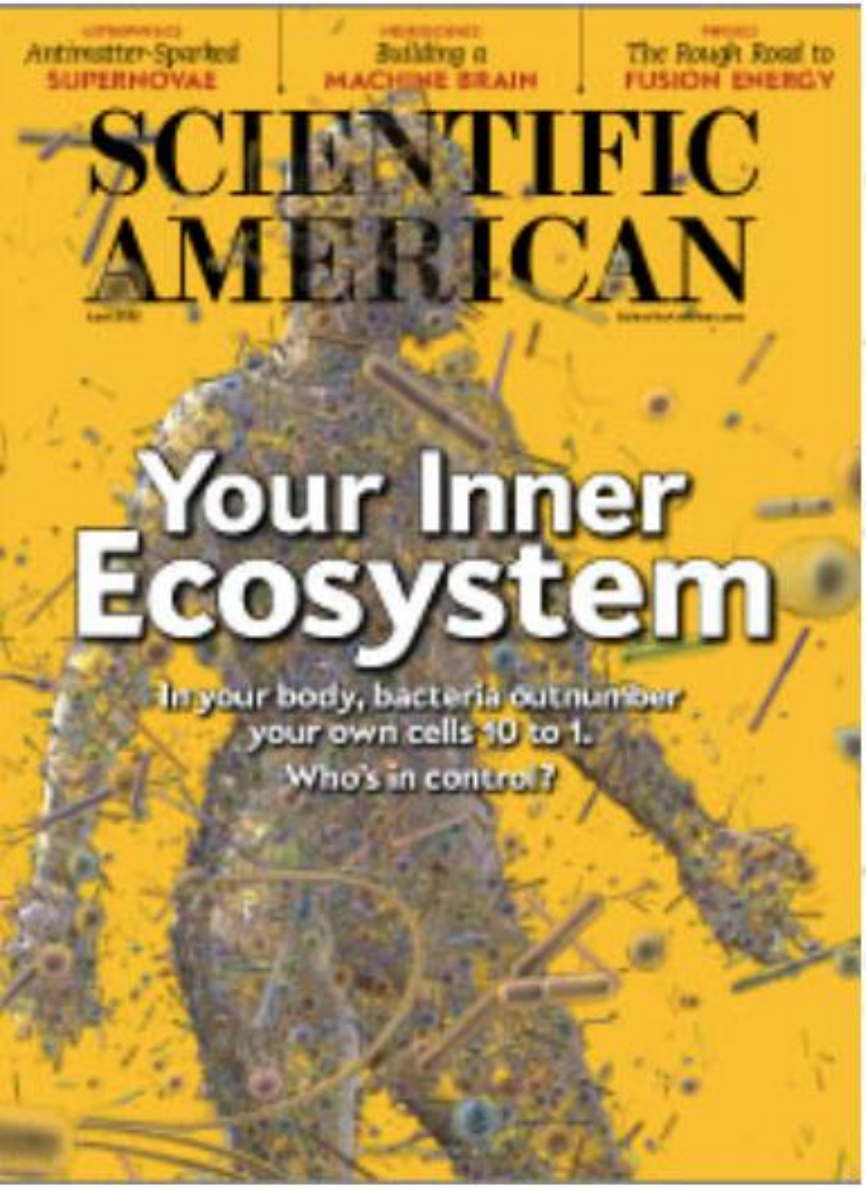
Inherited from both parents, stable, never change in its composition

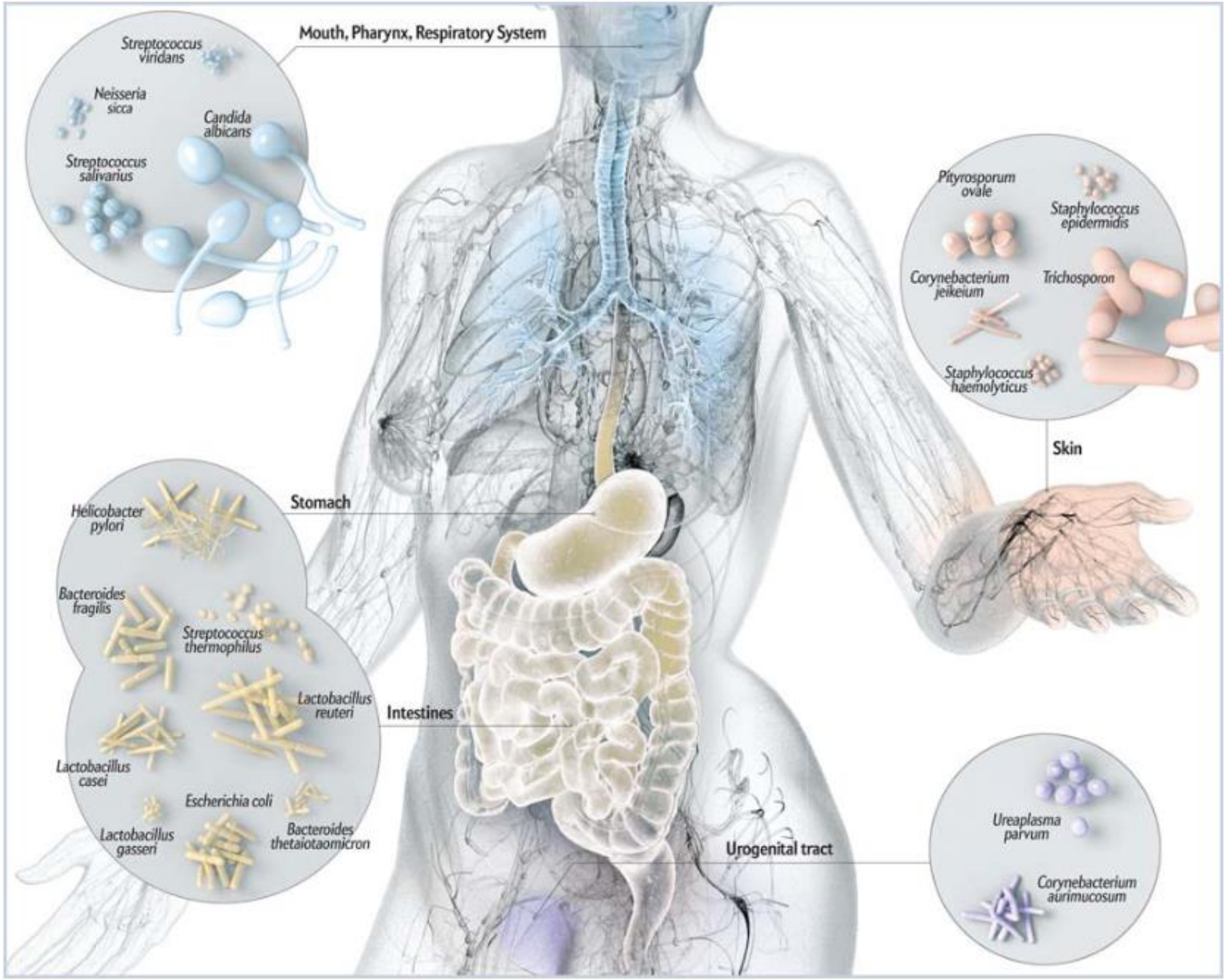
Microbiome:

Inherited from the mother, extremely dynamic, changes from individual to individual and in the same individual over time






Antimatter-Sparked
SUPERNOVAE
Building a
MACHINE BRAIN
The Rough Road to
FUSION ENERGY
SCIENTIFIC AMERICAN
Your Inner Ecosystem
In your body, bacteria outnumber your own cells 10 to 1. Who's in control?


Mouth, Pharynx, Respiratory System
Streptococcus viridans
Neisseria sicca
Candida albicans
Streptococcus salivarius
Pityrosporum ovale
Staphylococcus epidermidis
Corynebacterium jeikeium
Trichosporon
Staphylococcus haemolyticus
Skin
Stomach
Helicobacter pylori
Bacteroides fragilis
Streptococcus thermophilus
Lactobacillus reuteri
Intestines
Lactobacillus casei
Escherichia coli
Lactobacillus gasseri
Bacteroides thetaiotaomicron
Urogenital tract
Ureaplasma parvum
Corynebacterium aurimucosum



Role of Bacteria

- Protection Against Infections
- Improve Digestion
- Immune System Development
- Synthesis of Vitamins



Causes of Microbial Imbalance

- Chronic Stress
- Poor Dietary Intake
- Infections
- Environmental/Lifestyle Toxins
- Antibiotics (Medications and Food Sources)



GI Consequences

- Inflammation
  - Nutrient Malabsorbtion
    - Irregular Bowel Movements
- Intestinal Permeability
  - Negative Food Reactions



Long-Term Effects on the Body

- Obesity
- Depression/Anxiety
- Autoimmune Disease
- Allergies

Recipe For Immune Mediated Diseases

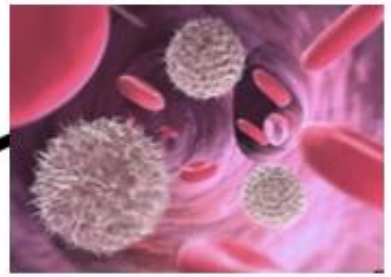
Which Ingredients Are Necessary?



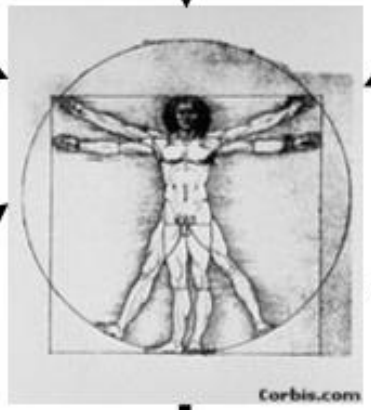
Increased Gut Permeability



Human Genome



Immune Response





Environmental Factors

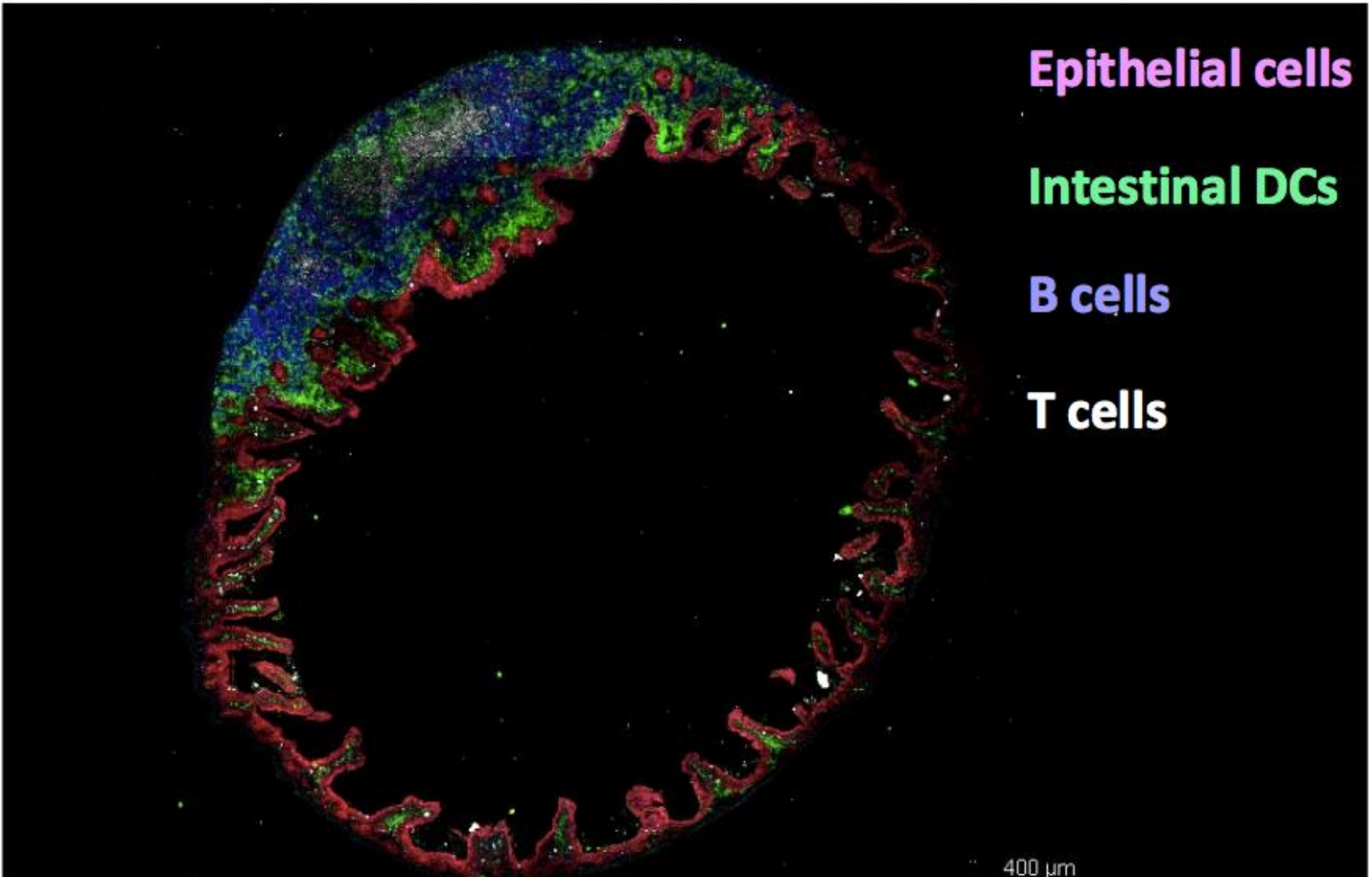


Clinic Outcome

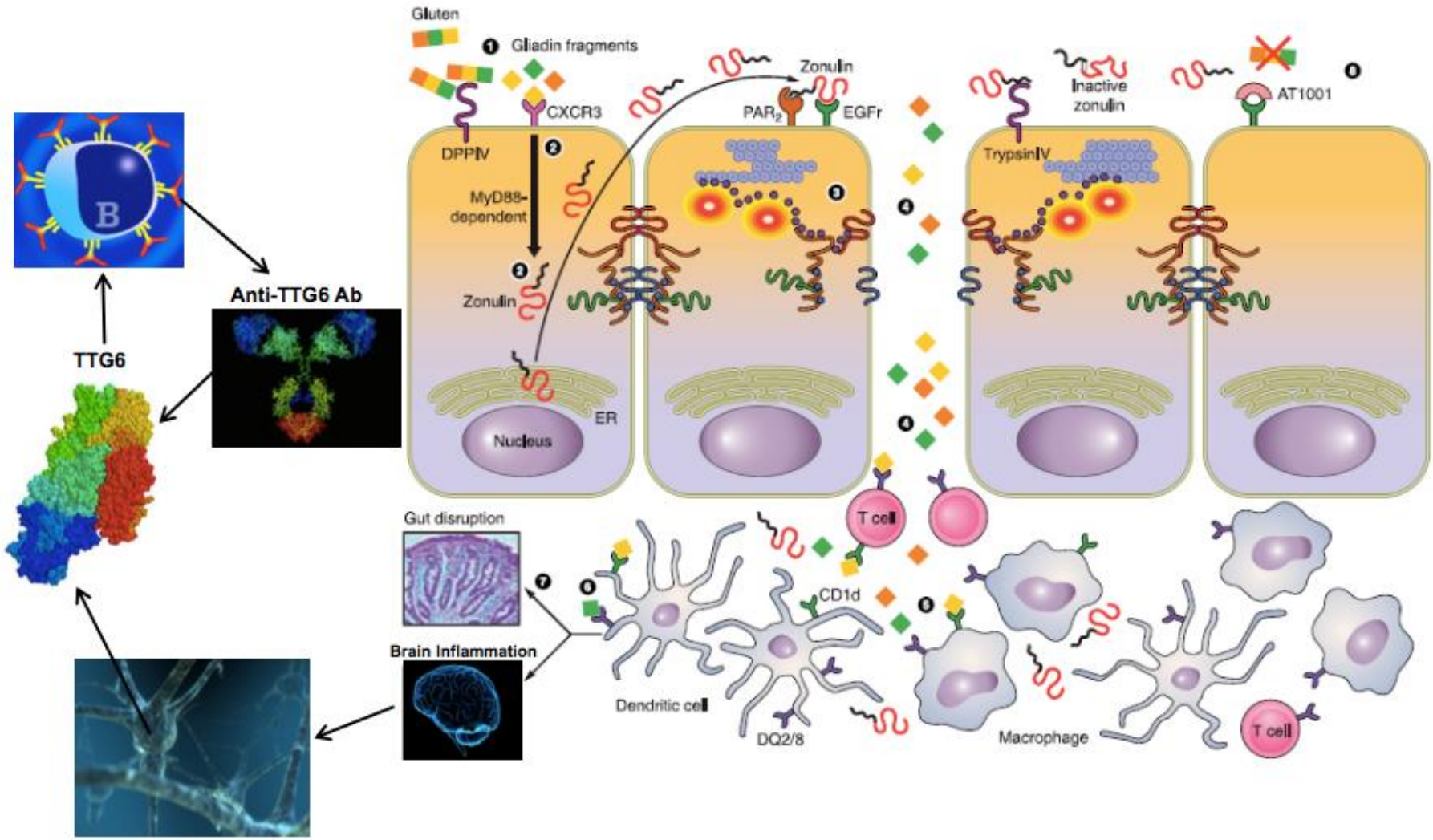


Microbiome

Several Cells Play a Role in Maintaining The Immune Homeostasis



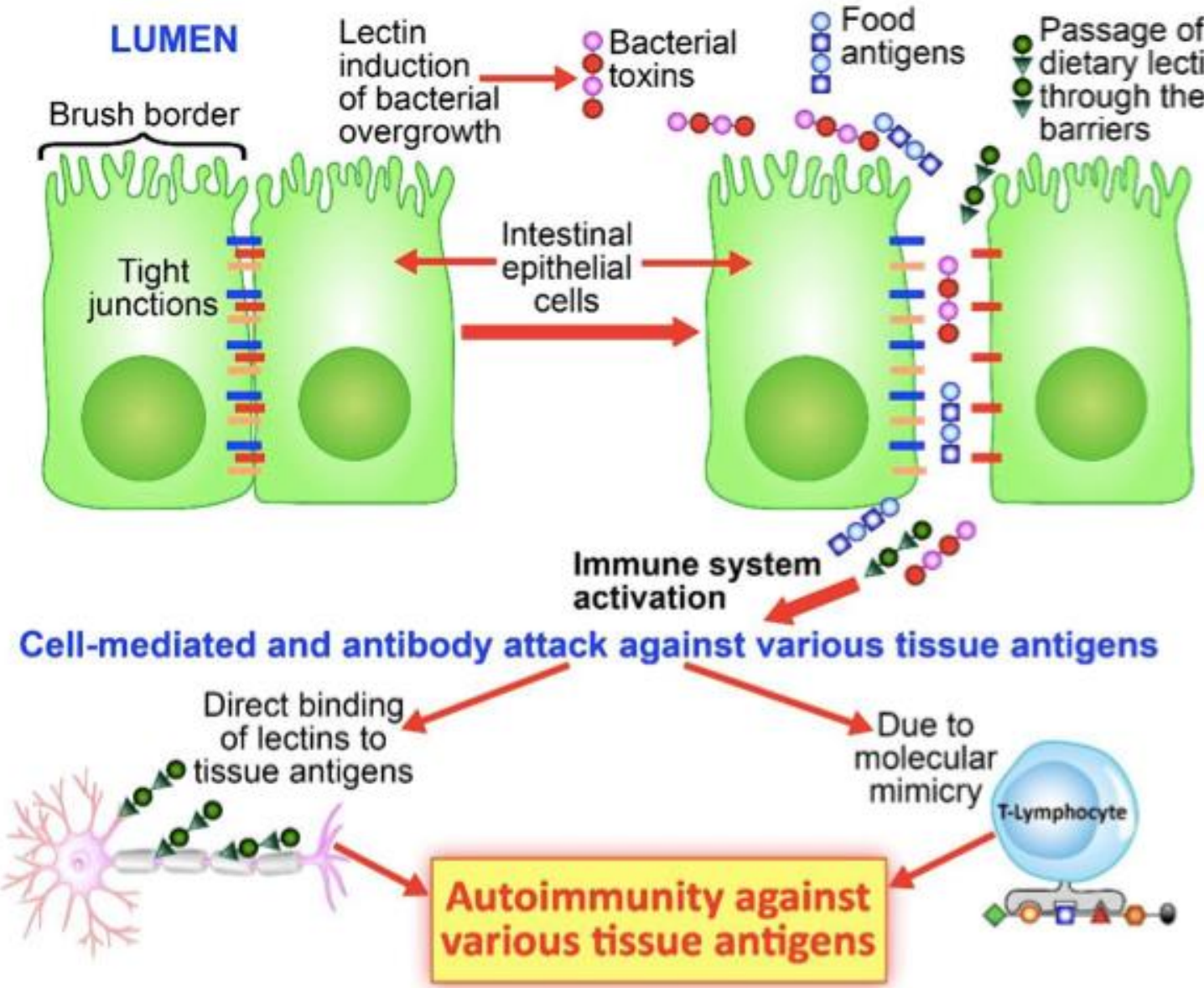
Gluten Causes Leaky Gut and Inflammation by Releasing Zonulin



The Epidemics Of Celiac Disease:
Which Additional Factors are Driving this Epidemics?

- Quality of gluten;
- Quantity of gluten;
- Breast Feeding;
- Maturity of gut functions influencing Ag trafficking and handling:
    - GALT
    - PRRs
    - Mucous production
    - Barrier function
- Timing of gluten introduction.
- Changes in microbiome composition.

n interaction with the gut and immune
m, and their contribution to autoimmunit



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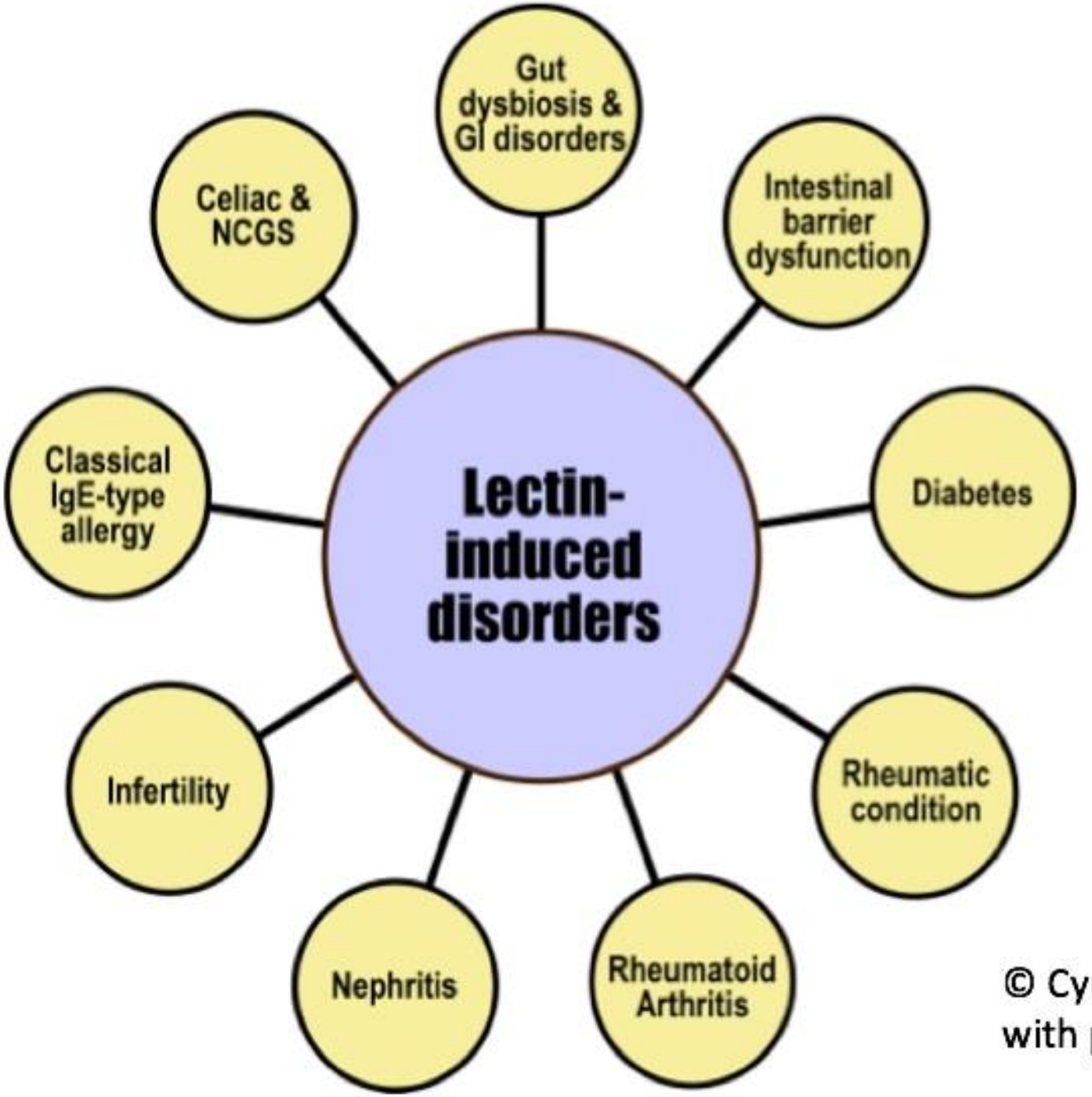

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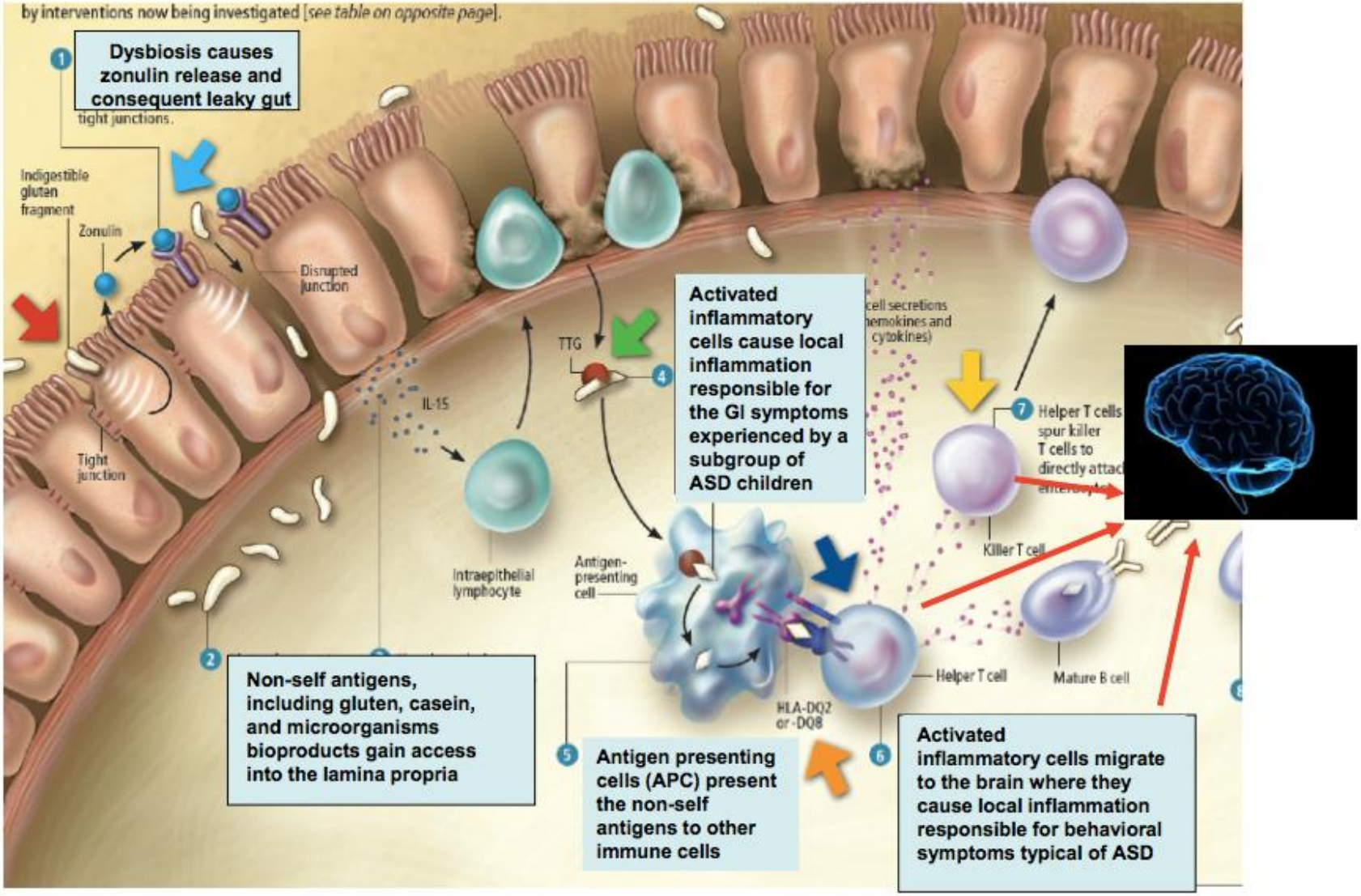
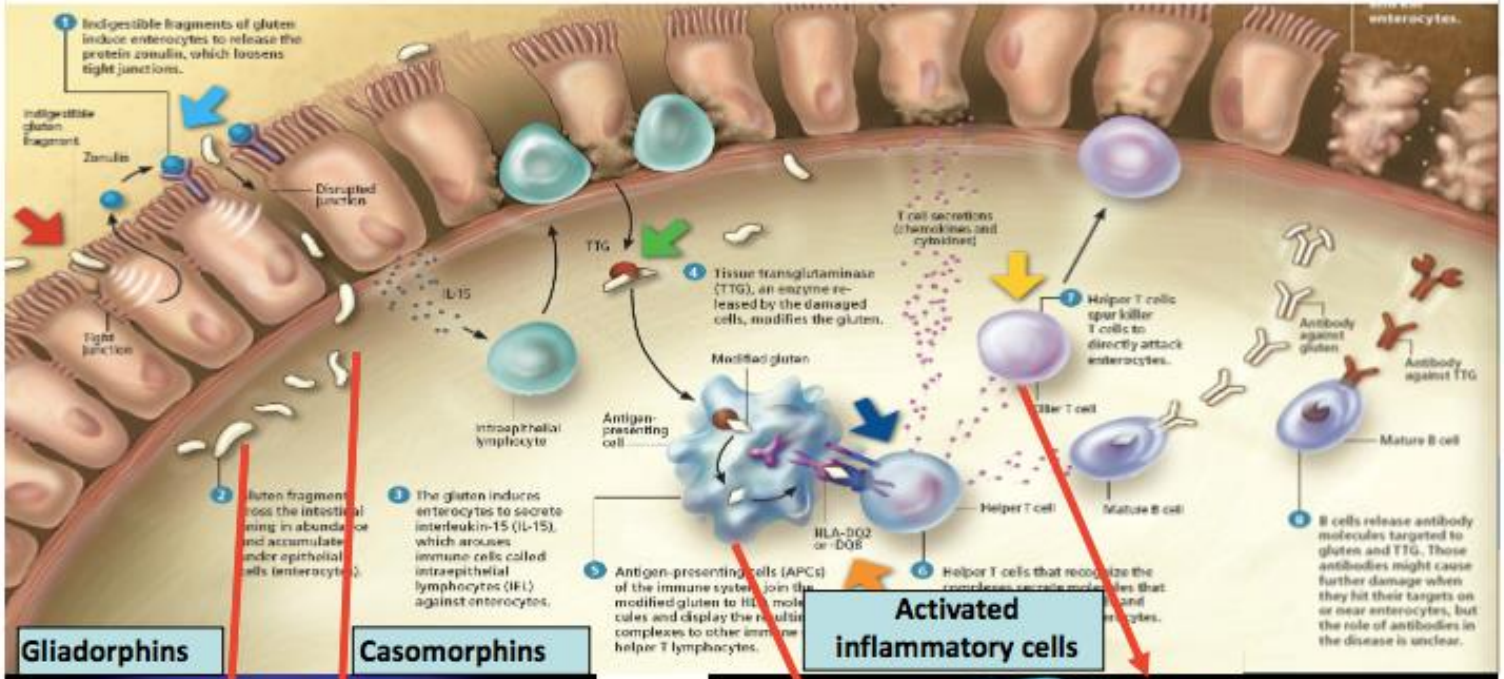
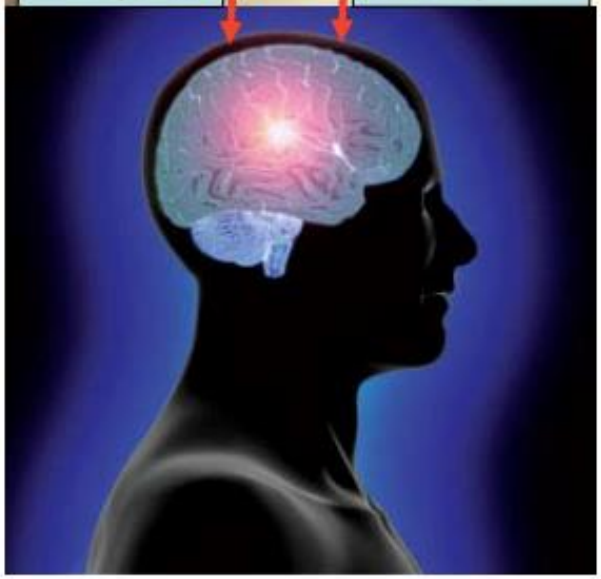
Working Hypothesis: Gastrointestinal Dysfunctions in ASD

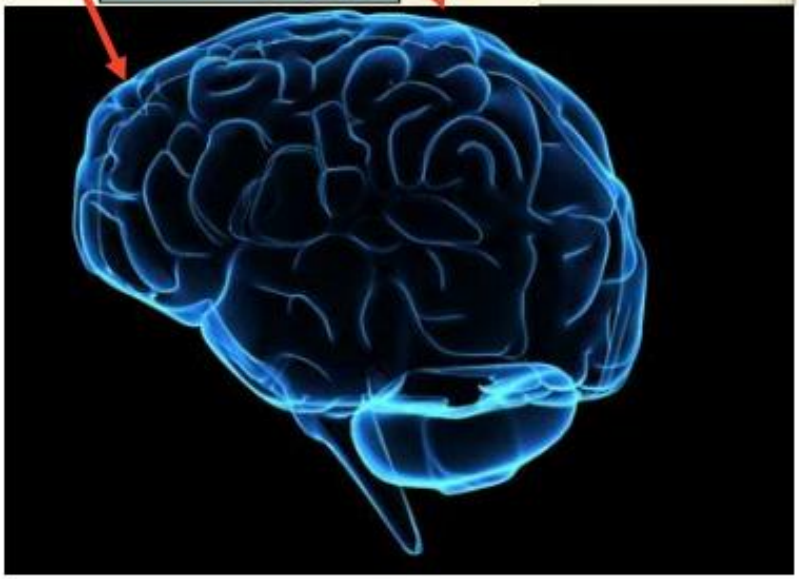


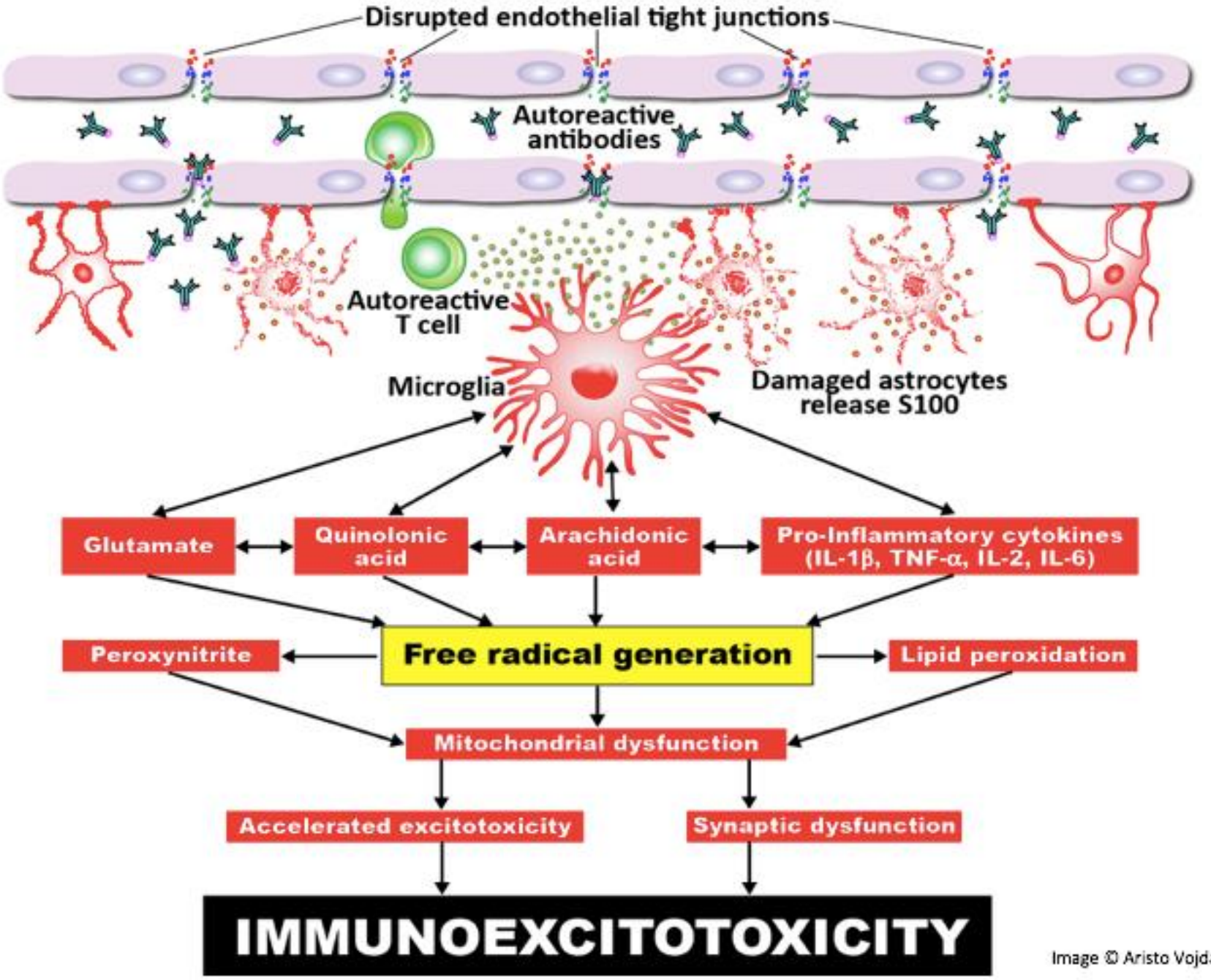
How Zonulin, Gut Permeability and Inflammation Are Relate to Schizophrenia and ASD?



Gliadorphins | **Casomorphins** | **Activated inflammatory cells**







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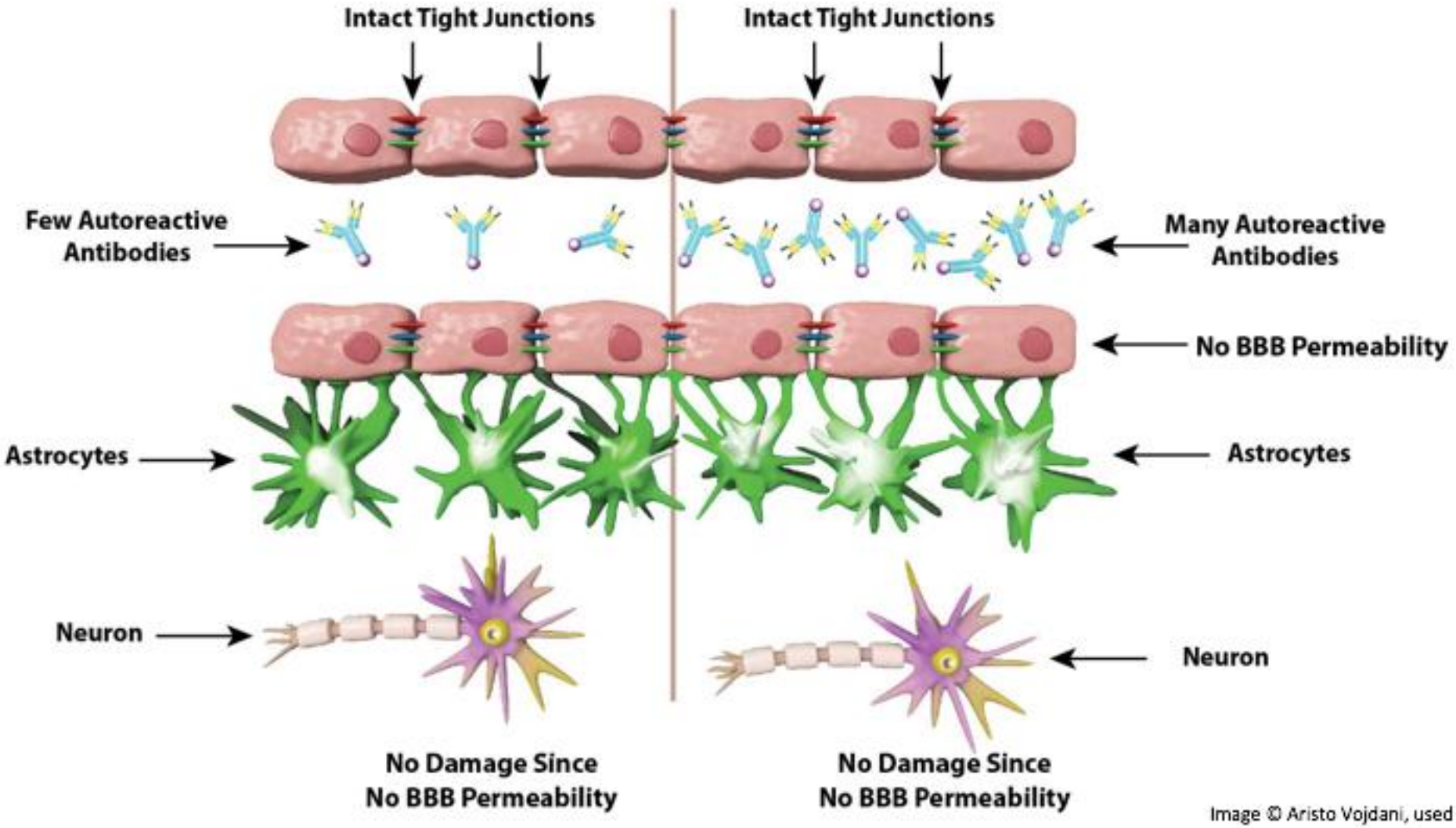
Autoreactive antibodies and intact BBB



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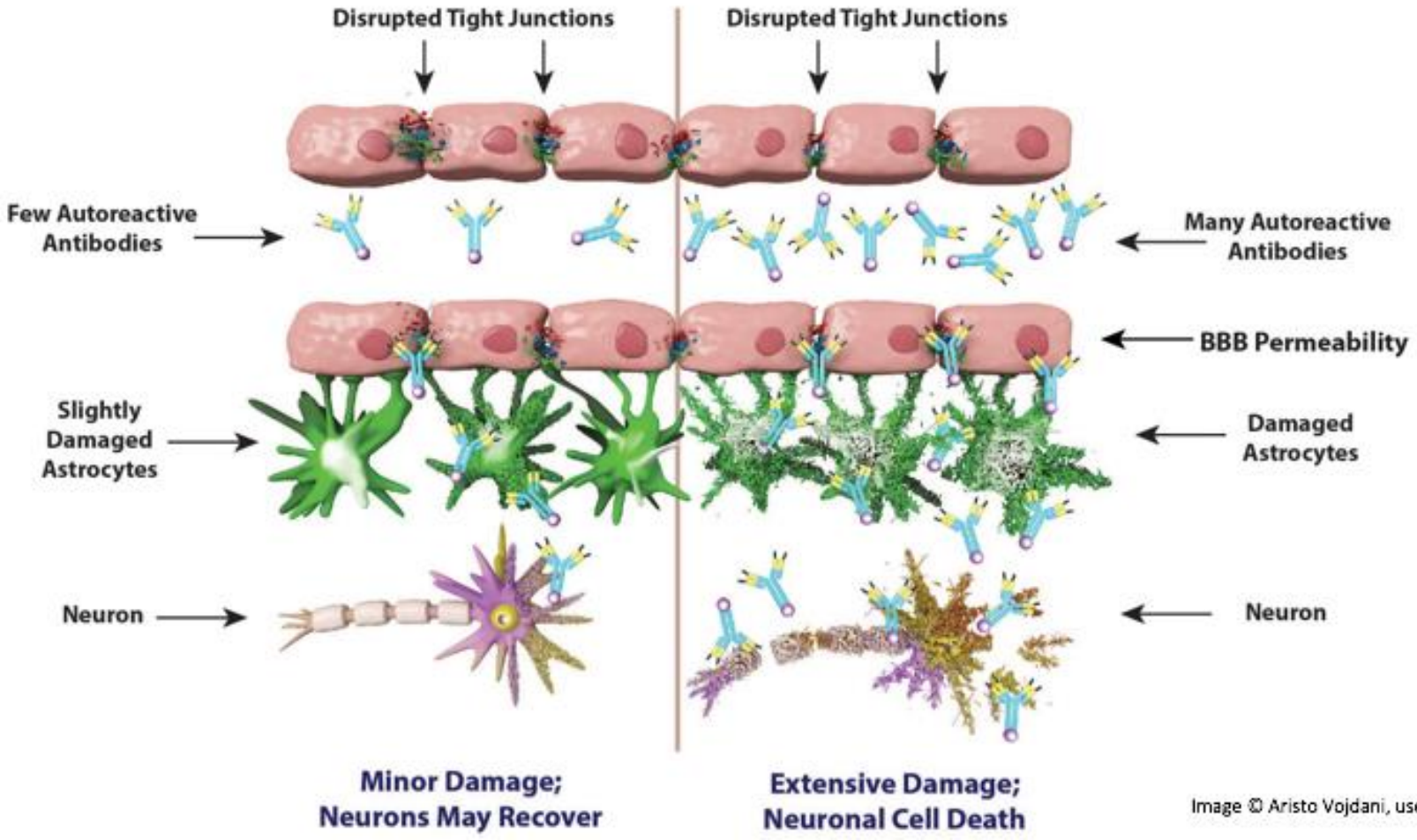
Autoreactive antibodies and disrupted BBB



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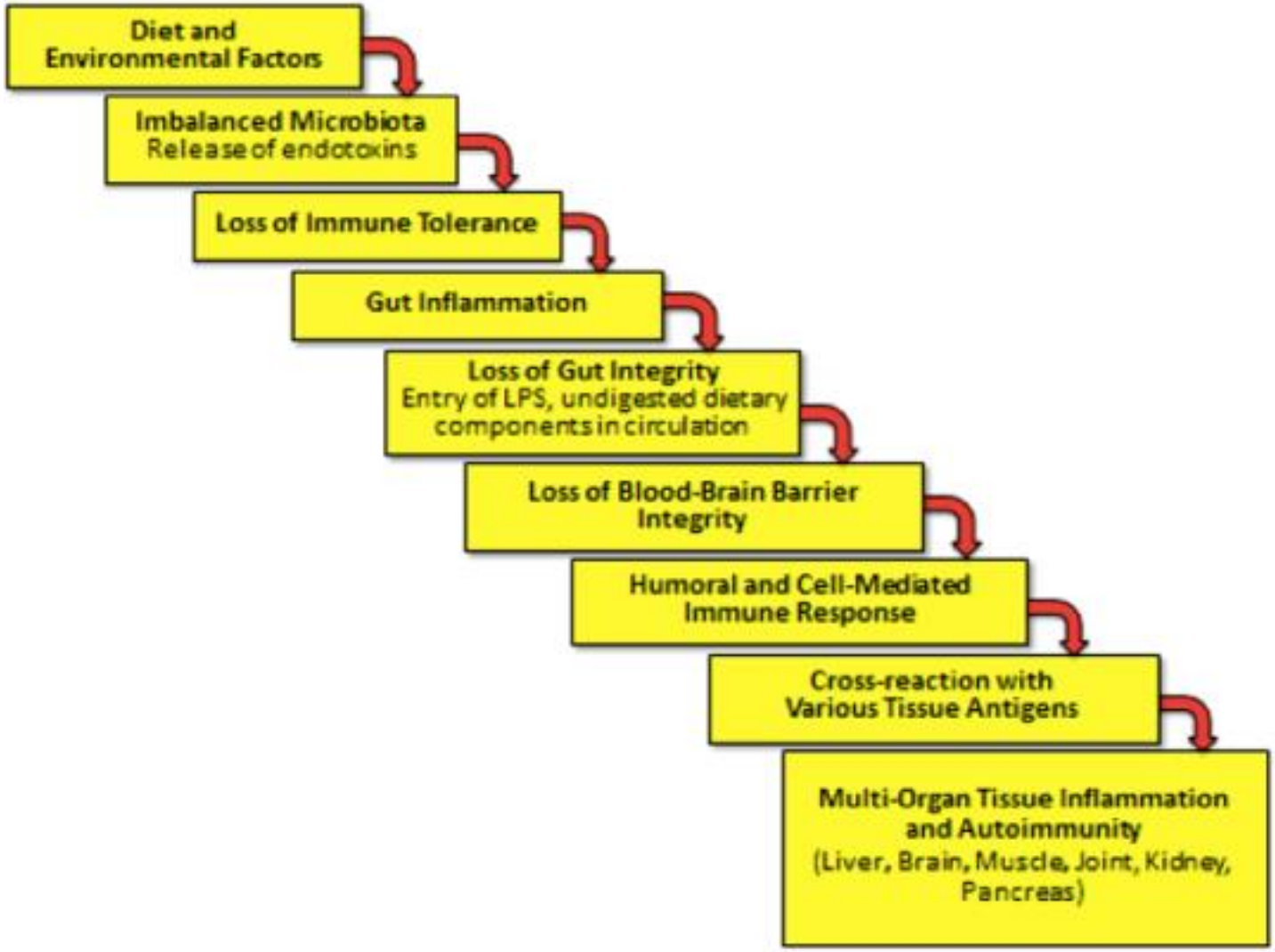

Diet and Environmental Factors
Imbalanced Microbiota Release of endotoxins
Loss of Immune Tolerance
Gut Inflammation
Loss of Gut Integrity Entry of LPS, undigested dietary components in circulation
Loss of Blood-Brain Barrier Integrity
Humoral and Cell-Mediated Immune Response
Cross-reaction with Various Tissue Antigens
Multi-Organ Tissue Inflammation and Autoimmunity (Liver, Brain, Muscle, Joint, Kidney, Pancreas)

Gut—Brain Axis

- Our brain is connected to all organs and to all body functions
- Our gut/microbiome influences all organ function
- Insults to the gut – microbiome - brain can cause a myriad of symptoms and may be primary or secondary
- Gut on fire ➔ Brain on fire →Body on fire

Gut—Brain Axis

- In healing the brain, consider a pleiotropic approach that addresses the brain, the gut, the immune system, the hormones……..
- By choosing a multifactorial systems biology approach, the treatment plan is more likely to be effective at restoring optimal health

Restoring Gut Instinct

- The Gut-Microbiome-Brain axis is an area that is represented in the literature by many reviews and a lesser number of primary papers

- Identifying the signaling molecules and related mechanisms that influence microbiota composition and function will expand our knowledge base helping us to understand how microbes act to influence our health and disease

14 yo F
"Abdominal Migraines"

CC: Anxiety w nausea/vomiting comes on 'like a freight train'

PMH: Abd Migraines, Anxiety, IBS-c, ADD, UARS

Meds: Prilosec 20/d, Propanolol 20/40, Focalin 7.5/d, Culturelle 1/d, D3 1000 iu/d

FHx: Crohn's, Thyroid, FMG

(per mom +FHx of every Auto Immune condition)

June 2017

- ROS: stomach pain, IBS-c BM q3d; “stinky”poop, poor diet (fruit loops, carnation instant breakfast, SAD), anxiety/panic attacks not relieved w Zoloft/SSRI’s; v tired @ school, zones out, migratory generalized pain, snores

- O/E: Tall, thin; BP 86/52; HR 72bpm; unremarkable

- Prior testing: Celiac, SIBO, CBC, CMP, WNL @ PCP
- Food Ab testing (IgG/IgE) unremarkable except 1+ IgG wheat and oyster

Anxiety, N/V
Plan ?

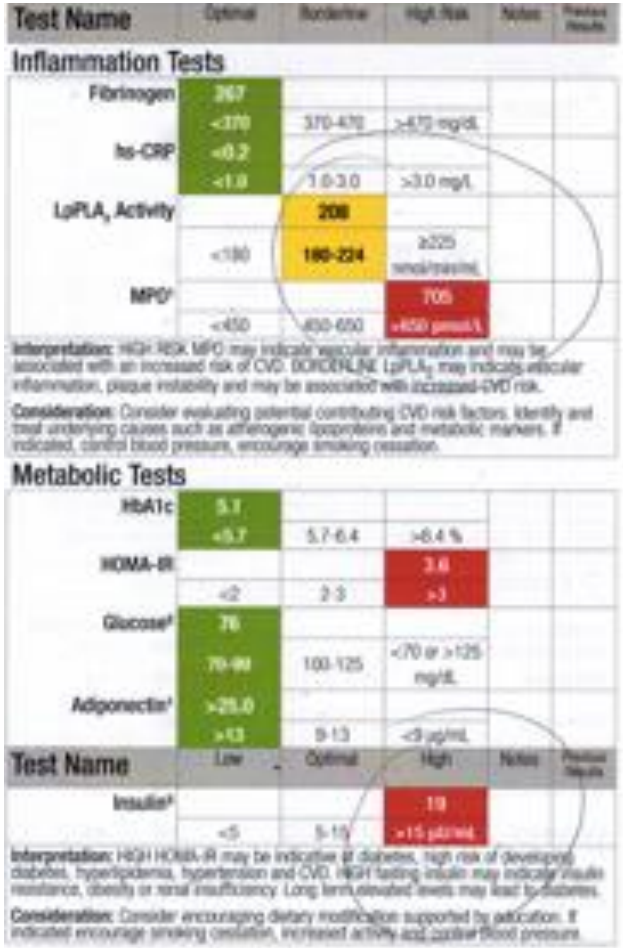
- Biomarker panel: check gums, insulin/glu, TFT..
- Stool Analysis : Assess Microbiome/Pathogens
- Advanced Food Immune Reactivity Screen
- Assess Intestinal Permeability
- Therapeutic Trial: Remove Autoimmune trigger foods*

Autoimmune Trigger Foods

- gliadin/gluten
- lectins (refined, starchy foods, etc)
- agglutinins (pea, bean, lentil, soybean, peanut)
- dairy proteins
- shellfish (shrimp)
- aquaporins (corn, soy, spinach, tomato)

POA June ‘17

- Refused GF trial
- Eliminate dairy, add fiber, healthy food/oils; hydrate
- Supplements: Omega 3, Vitamin C/D3, Culturelle
- F/U in 2 weeks to review labs: Advanced biomarkers, Stool analysis
- Declined Intestinal Permeability, other testing


Test Name
Optimal
Borderline
High Risk
Notes
Previous Results
Inflammation Tests
Fibrinogen
367
<370
370-470
>470 mg/dL
hs-CRP
<0.2
<1.0
1.0-3.0
>3.0 mg/L
LpPLA2 Activity
208
<180
180-224
≥225 nmol/min/mL
MPO
705
<450
450-650
>650 pmol/L
Interpretation: HIGH RISK MPO may indicate vascular inflammation and may be associated with an increased risk of CVD. BORDERLINE LpPLA2 may indicate vascular inflammation, plaque instability and may be associated with increased CVD risk.
Consideration: Consider evaluating potential contributing CVD risk factors. Identify and treat underlying causes such as atherogenic lipoproteins and metabolic markers. If indicated, control blood pressure, encourage smoking cessation.
Metabolic Tests
HbA1c
5.1
<5.7
5.7-6.4
>6.4 %
HOMA-IR
3.6
<2
2-3
>3
Glucose
76
70-99
100-125
<70 or >125 mg/dL
Adiponectin
>25.0
>13
9-13
<9 µg/mL
Test Name
Low
Optimal
High
Notes
Previous Results
Insulin
19
<5
5-15
>15 µU/mL
Interpretation: HIGH HOMA-IR may be indicative of diabetes, high risk of developing diabetes, hypertriglyceridemia, hypertension and CVD. HIGH fasting insulin may indicate insulin resistance, obesity or renal insufficiency. Long term elevated levels may lead to diabetes.
Consideration: Consider encouraging dietary modification supported by education. If indicated encourage smoking cessation, increased activity and control blood pressure.

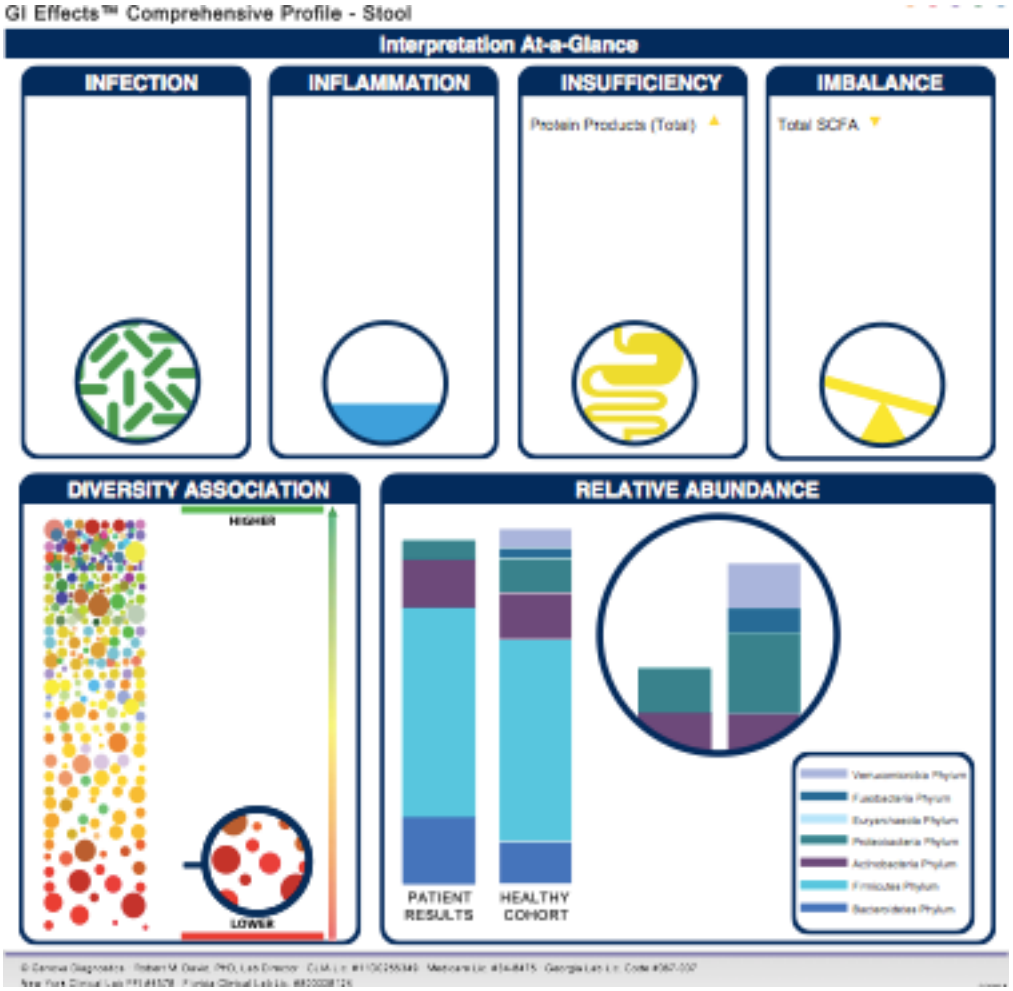
Boston Heart Fatty Acid Balance™ Test[1]

Saturated Fatty Acid Index		**31.1**		Saturated FA Index is BORDERLINE. Higher levels of plasma saturated fatty acids are associated with an increased risk of CVD. Consider restricting dietary intake of saturated fat by choosing poultry without skin, fish, low fat dairy products, lean cuts of meat, and replacing butter with plant based oils.		
	<30.0	**30.0-33.0**	>33.0 %			
Trans Fatty Acid Index	0.38			Trans FA Index is OPTIMAL.		
	<0.50	0.50–0.80	>0.80 %			
	Optimal	Borderline	Low			
Monounsaturated Fatty Acid Index		**20.6**		Monounsaturated FA Index is BORDERLINE. Higher plasma levels of MUFA have been associated with a lower risk of CVD. Consider increasing intake of almonds, avocado or plant based oils (including olive).		
	>22.0	**19.0–22.0**	<19.0 %			
Unsaturated/Saturated Ratio Index		**2.18**		Unsaturated/Saturated Ratio Index is BORDERLINE. A lower Unsaturated/Saturated Ratio Index is associated with a higher LDL-C and increased risk of CVD. Consider increasing intake of plant based fats from nuts, seeds, and their oils along with fatty fish and restricting intake of animal fats like red meat, fatty processed meats, and full fat dairy.		
	>2.25	**2.00–2.25**	<2.00			
Omega-3 Fatty Acid Index			**1.85**	Omega-3 FA Index is LOW. A low Omega-3 FA index is associated with an increased risk for CVD. Eicosapentaenoic Acid (EPA) level is LOW. Increased EPA levels have been associated with lower risk of heart disease. Docosahexaenoic Acid (DHA) level is LOW. Increased DHA levels have been associated with a lower risk of CVD. Consider recommending consumption of at least 2-3 meals of oily fish such as salmon, sardines, herring, tuna, and mackerel weekly or a fish oil or EPA supplement.		
	>4.50	2.00–4.50	**<2.00 %**			
EPA			**<15.6**			
	>50.0	15.6-50.0	**<15.6 µg/mL**			
DHA			**43.0**			
	>100.0	45.0–100.0	**<45.0 µg/mL**			
ALA		**18.2**		Alpha Linolenic Acid (ALA) level is BORDERLINE. Higher levels of ALA have been associated with a lower risk of CVD. Consider recommending increasing intake of walnuts, chia seeds, ground flaxseeds, and canola or flaxseed oil.		
	>30.0	**14.0–30.0**	<14.0 µg/mL			

Fatty Acids and Major Depressive Disorder

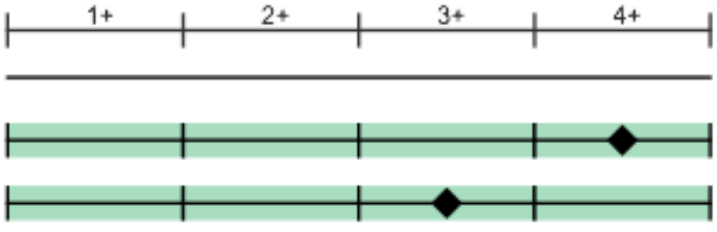
- Overall incidence of depression has increased in Western countries
- Epidemiological studies support a connection between dietary fish/seafood consumption and a lower prevalence of depression
- Clinical symptoms of depression have been found to decrease at higher levels of EPA, and the AA/EPA ratio has been found to positively correlate with the clinical symptoms of depression
- A 1% increase in plasma DHA was associated with a 59% reduction in the reporting of depressive symptoms
- Suicide attempts have also been associated with low levels of RBC EPA

GI Effects™ Comprehensive Profile - Stool



Gastrointestinal Microbiome

Bacteriology (Culture)



Lactobacillus spp.		NG
Escherichia coli	4+	NP
Bifidobacterium	3+	NP

Additional Bacteria

alpha haemolytic Streptococcus	1+	NP
Citrobacter species	2+	NP
Mucoid Escherichia coli	3+	NP

Mycology (Culture)

NG

Methodology: Vitek 2® System Microbial Antibiotic susceptibility, Manual Minimum Inhibition Concentration

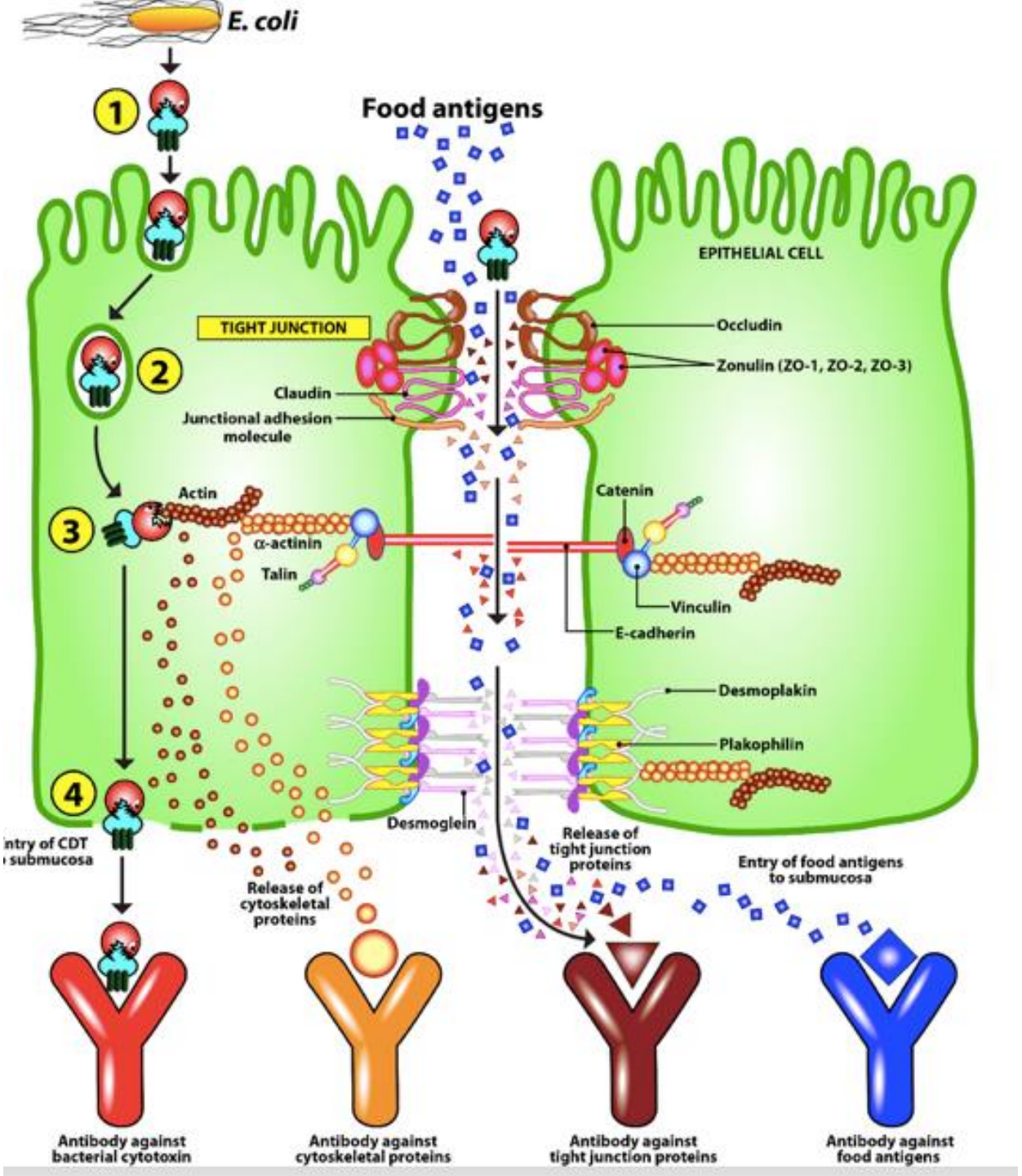
Bacteria Sensitivity

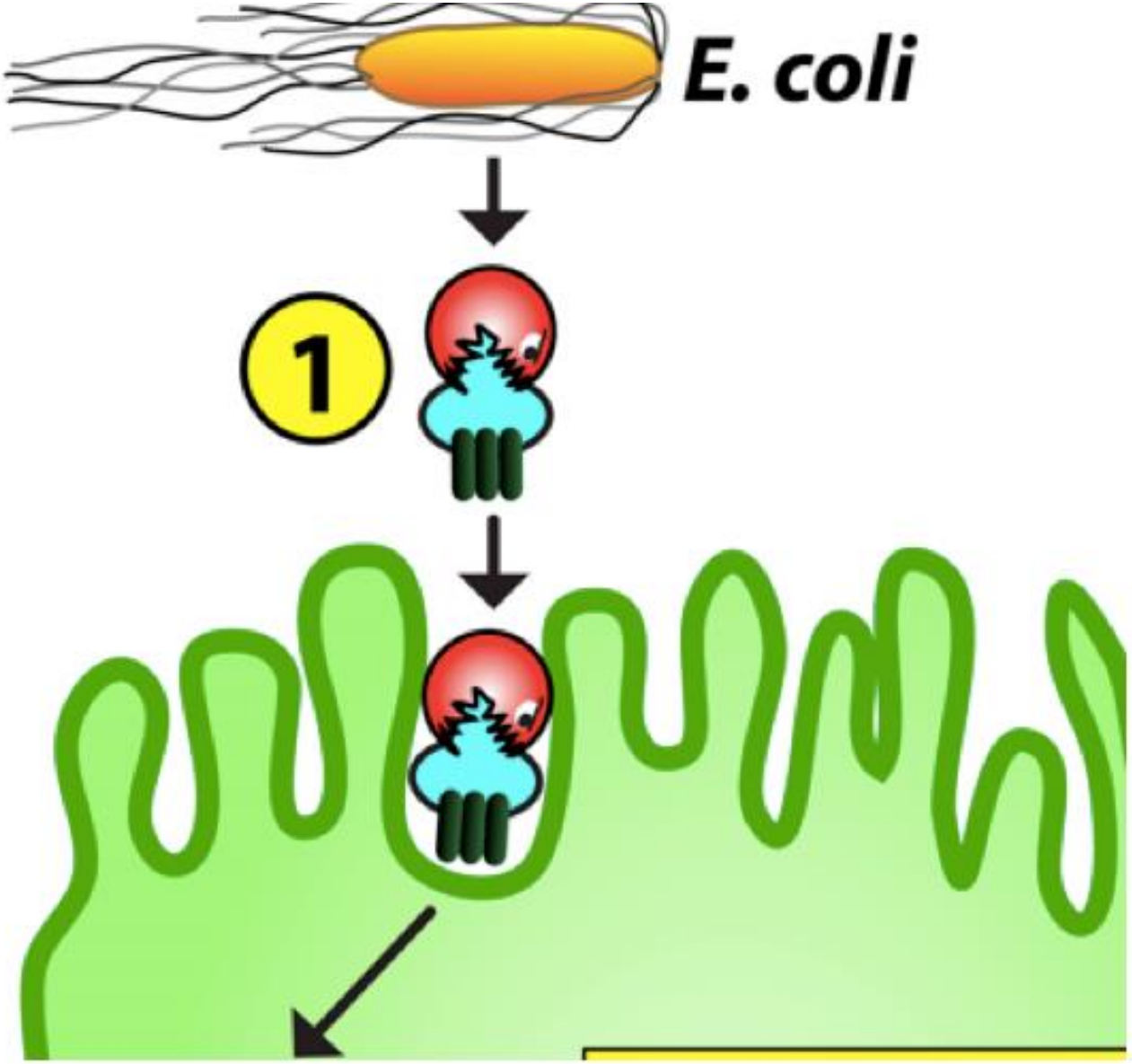
Prescriptive Agents

Citrobacter species	R	I	S-DD	S	NI
Ampicillin	R				
Amox./Clavulanic Acid	R				
Cephalothin	R				
Ciprofloxacin				S	
Tetracycline				S	
Trimethoprim/Sulfa				S	

Natural Agents

Citrobacter species	LOW INHIBITION	HIGH INHIBITION
Berberine		
Oregano		
Plant Tannins		
Uva-Ursi		


E. coli
1
Food antigens
EPITHELIAL CELL
TIGHT JUNCTION
Occludin
Zonulin (ZO-1, ZO-2, ZO-3)
2
Claudin
Junctional adhesion molecule
Actin
3
α-actinin
Talin
Catenin
Vinculin
E-cadherin
Desmoplakin
Plakophilin
4
Desmoglein
ntry of CDT
submucosa
Release of cytoskeletal proteins
Release of tight junction proteins
Entry of food antigens to submucosa
Antibody against bacterial cytotoxin
Antibody against cytoskeletal proteins
Antibody against tight junction proteins
Antibody against food antigens



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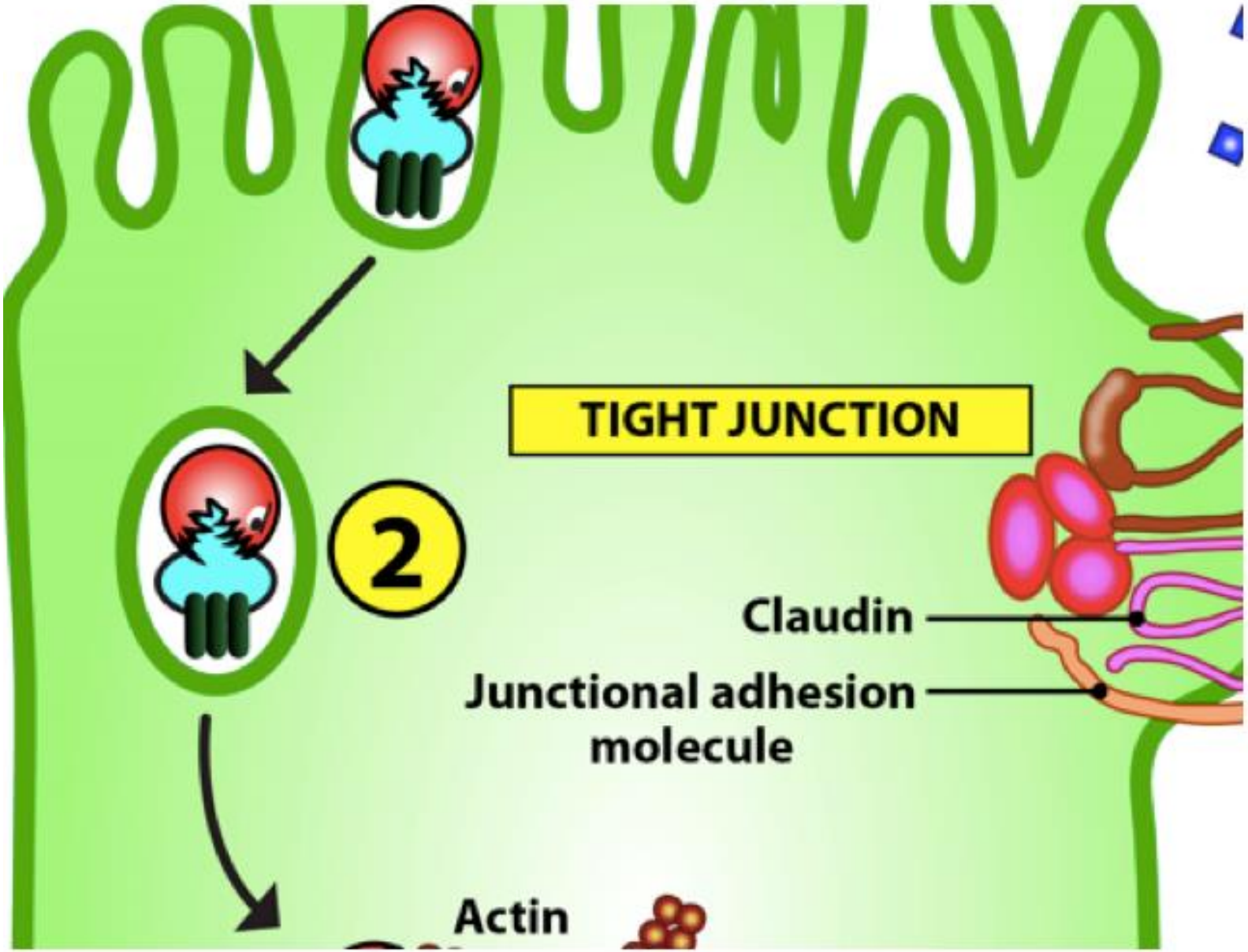

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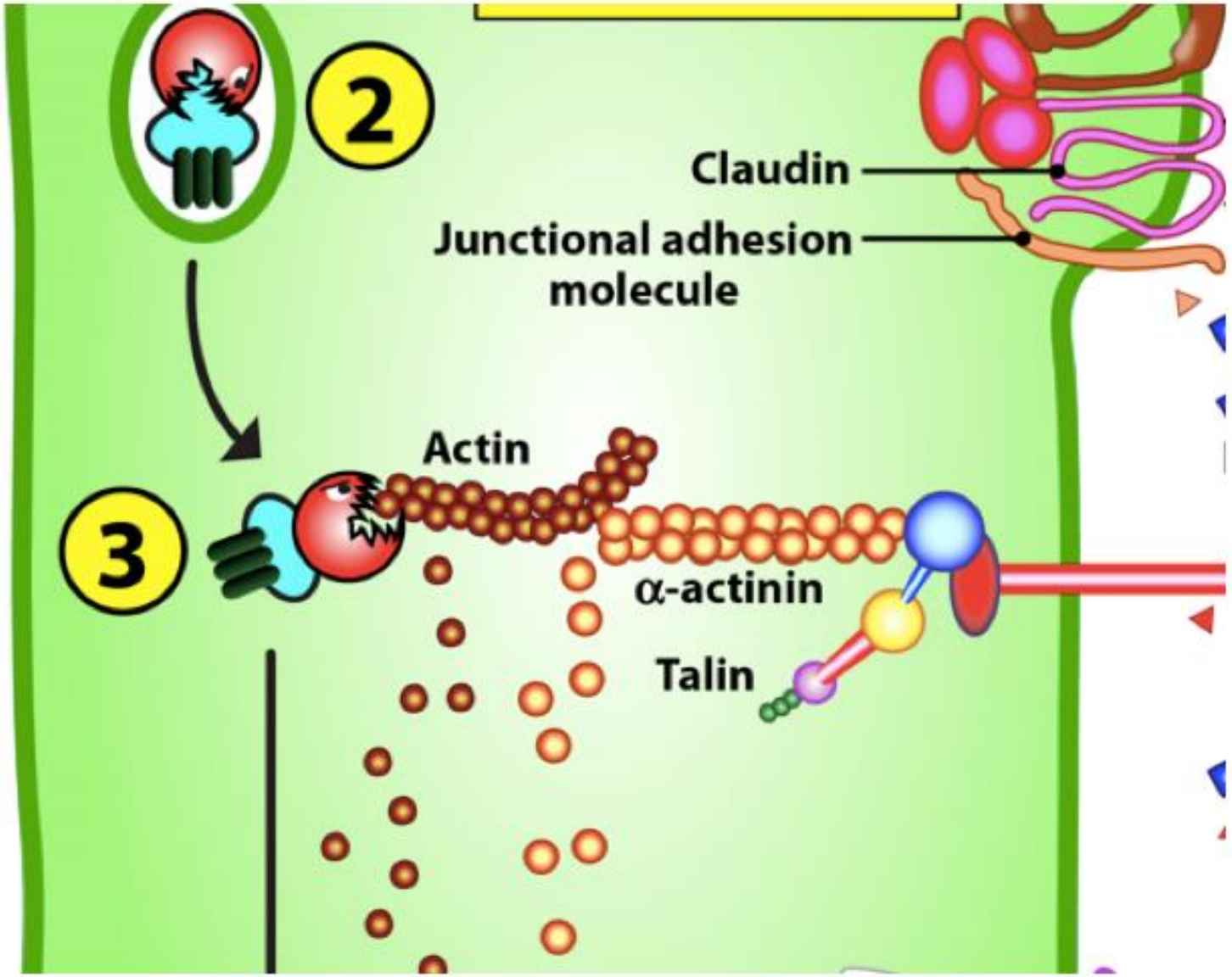

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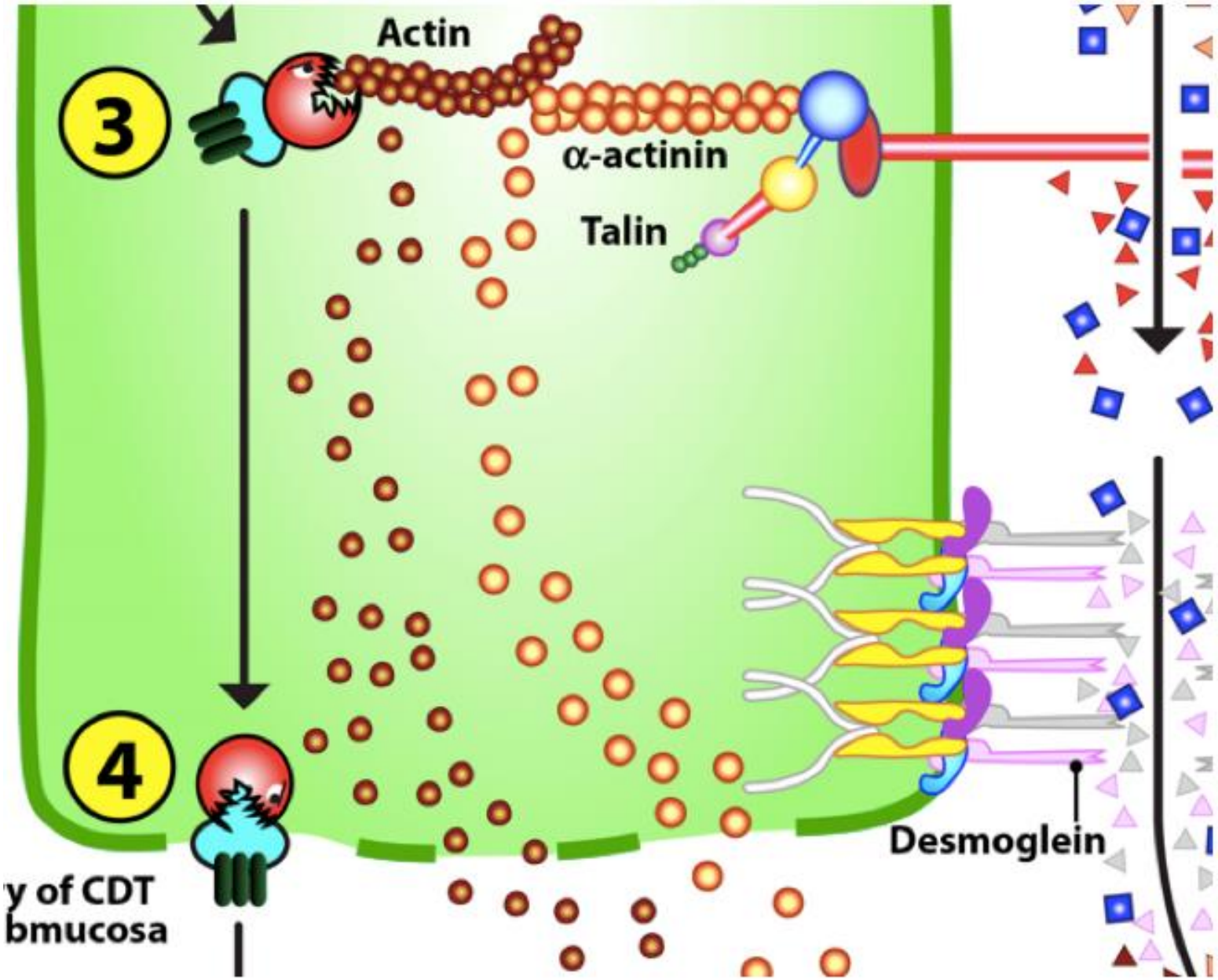

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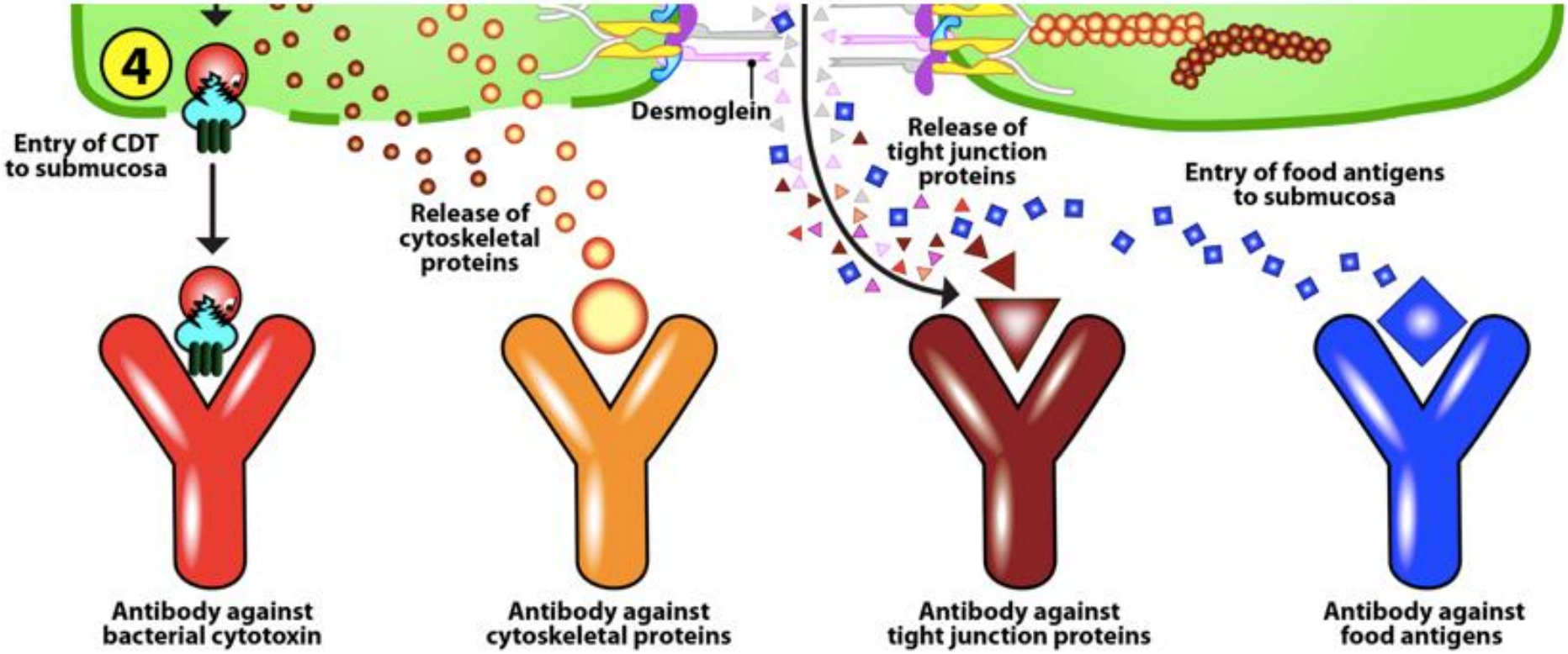

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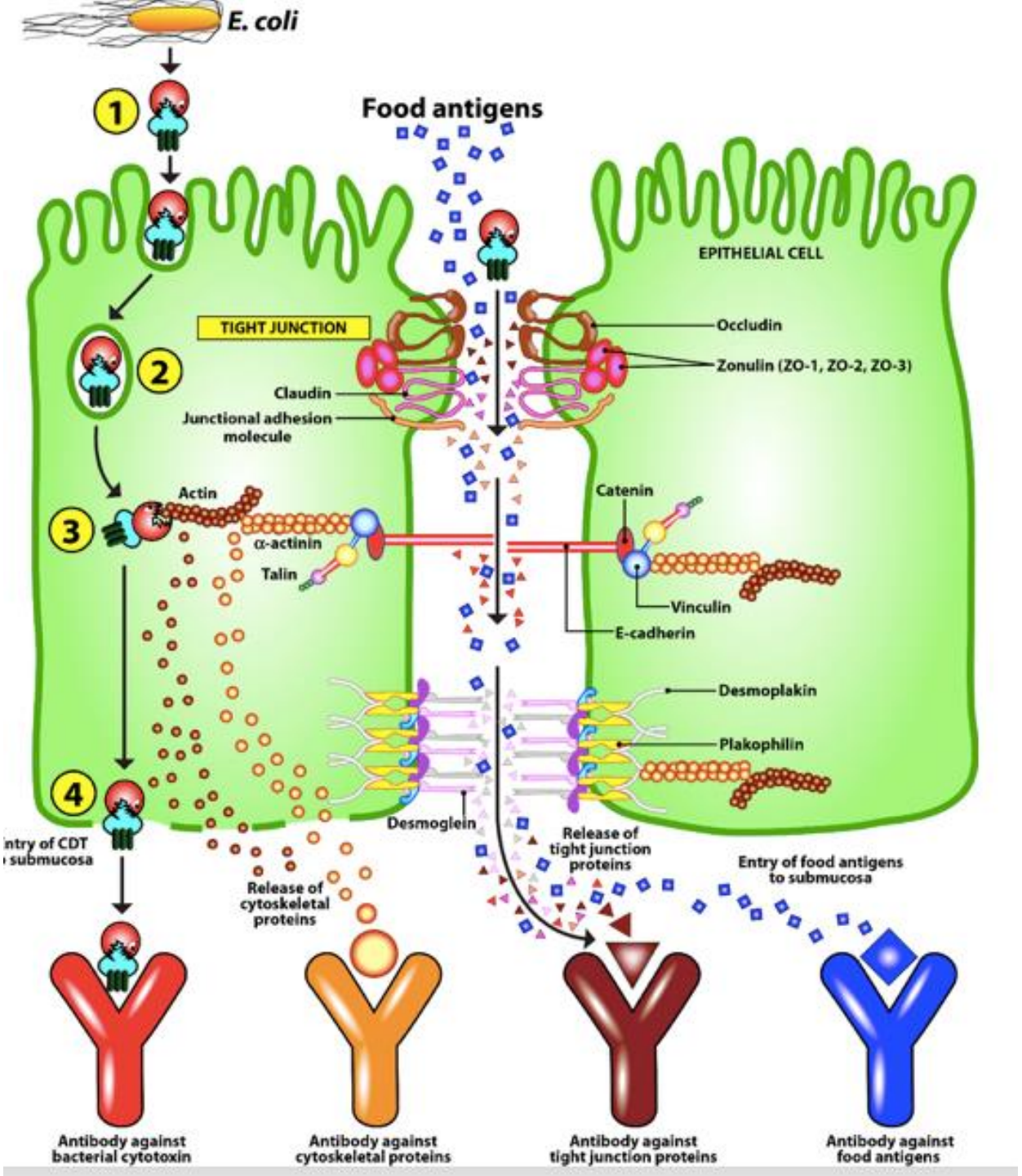

E. coli
1
Food antigens
EPITHELIAL CELL
TIGHT JUNCTION
Occludin
Zonulin (ZO-1, ZO-2, ZO-3)
2
Claudin
Junctional adhesion molecule
Actin
3
α-actinin
Talin
Catenin
Vinculin
E-cadherin
Desmoplakin
Plakophilin
4
Desmoglein
ntry of CDT
submucosa
Release of cytoskeletal proteins
Release of tight junction proteins
Entry of food antigens to submucosa
Antibody against bacterial cytotoxin
Antibody against cytoskeletal proteins
Antibody against tight junction proteins
Antibody against food antigens

July ’17

- Less stomach pain when Dairy Free
- Improved BM→ q3d to qod
- Cont’d anxiety, stomach pain, generalized pain

- Retest abnormal labs

July 2017

- POA: DF, fiber, hydration, good fats, Vit C, Vit D3, Omega 3, Probiotic
- Dental visit
- Rx: Ciprofloxcin x 7d
- Probiotic: VSL / S Boulardi
- Trial Gluten Free

Sept '17

- Rpt tests: WNL MPO, LpPLA2, Insulin/glucose

- Substantially better when DF and GF→ NO meltdowns or stomach issues per mom
- Still on Prilosec prn (most days); now Propanolol 1x/d

- Counsel on importance of addressing root causes; not relying on meds ie; Prilosec and Propanolol
- Declines additional testing

Jan ‘18

- Continues substantially better when GF→ no meltdowns or stomach issues except if indiscretions, but impossible to do and maintain

- Mom asks…Does she need to remain GF?
- Recommended Testing:
- Advanced Food Immune Reactivity Screen
- Assess Intestinal Permeability

TEST	RESULT			
Array 2 – Intestinal Antigenic Permeability Screen	**IN RANGE (Normal)**	**EQUIVOCAL***	**OUT OF RANGE**	**REFERENCE** (ELISA Index)
Actomyosin IgA **	1.64			0.0-20
Occludin/Zonulin IgG	0.83			0.2-1.5
Occludin/Zonulin IgA	0.39			0.1-1.8
Occludin/Zonulin IgM	1.30			0.1-2.1
Lipopolysaccharides (LPS) IgG	1.10			0.1-1.6
Lipopolysaccharides (LPS) IgA	0.47			0.1-1.8
Lipopolysaccharides (LPS) IgM	0.92			0.1-2.0

TEST	RESULT			
Array 3 – Wheat/Gluten Proteome Reactivity & Autoimmunity	**IN RANGE (Normal)**	**EQUIVOCAL***	**OUT OF RANGE**	**REFERENCE** (ELISA Index)
Wheat IgG	1.03			0.3-1.5
Wheat IgA	0.25			0.1-1.2
Wheat Germ Agglutinin IgG			1.38	0.4-1.3
Wheat Germ Agglutinin IgA	0.22			0.2-1.1
Native & Deamidated Gliadin 33 IgG	0.31			0.2-1.2
Native & Deamidated Gliadin 33 IgA	0.13			0.1-1.1
Alpha Gliadin 17-mer IgG	0.42			0.1-1.5
Alpha Gliadin 17-mer IgA	0.19			0.1-1.1
Gamma Gliadin 15-mer IgG	0.63			0.5-1.5
Gamma Gliadin 15-mer IgA	0.12			0.1-1.0
Omega Gliadin 17-mer IgG	0.58			0.3-1.2
Omega Gliadin 17-mer IgA	<0.10			0.1-1.2
Glutenin 21-mer IgG	0.69			0.1-1.5
Glutenin 21-mer IgA	0.12			0.1-1.3
Gluteomorphin + Prodynorphin IgG	0.61			0.3-1.2
Gluteomorphin + Prodynorphin IgA	0.15			0.1-1.2
Gliadin-Transglutaminase Complex IgG	0.44			0.3-1.4
Gliadin-Transglutaminase Complex IgA	<0.20			0.2-1.5
Transglutaminase-2 IgG	0.47			0.3-1.6
Transglutaminase-2 IgA	0.13			0.1-1.6
Transglutaminase-3 IgG	0.82			0.2-1.6
Transglutaminase-3 IgA	0.18			0.1-1.5
Transglutaminase-6 IgG	0.48			0.2-1.5
Transglutaminase-6 IgA	0.15			0.1-1.5

Jan ‘18

- Array 2 WNL ; No evidence of Intestinal Permeability
- Array 3 : Wheat Germ Agglutinin IgG 1.38 o/w WNL

Tissue	Wheat Germ Agglutinin	Soybean Agglutinin	Peanut Agglutinin	Lentil Lectin	Pea Lectin	Bean Agglutinins
Skin	*	*	*	*		*
Buccal mucosa	*	*	*	*		
Stomach	*					
Parietal cells		*	*			
Intestinal brush border	*	*				*
Colonic mucosa	*			*		
Connective tissue	*			*	*	*
Thyroid	*	*		*		*
Cartilage	*	*	*			
Liver	*	*	*			*
Pancreas	*					*
Kidney	*			*		*
Prostate	*		*	*		
Skeletal muscle	*	*	*		*	
Cardiac muscle	*	*				
Breast	*	*	*			
Pituitary			*			
Eye	*	*	*		*	*
Brain (myelin)	*			*		*

Lambert and Vojdani, J Clin Cell Immunol 2017, 8:5 DOI: 10.4172/2155-9899.1000521

February ‘18

POA:

Lectin free, Wheat Free, Gluten Free, Dairy Free

Continue Omega, probiotic, Vit C/D3

Continue on Focalin

Trial: hold Prilosec and Propanolol after 2 weeks of food elimination

F/U 1 – 2 months

March ‘18

Quick telephone check in:

Continues Dairy Free & Wheat (includes WGA) Free ..patient notes that she “feels like crap when eats gluten, wheat of any kind”

Now off Prilosec and Propanolol

17 yo F Depression
Nov ‘17

- CC: Referred by therapist for worsening depression, concerned that needs hospitalization
- PMH: Complex Aura Migraines 2011, Headaches, Dizziness, Tinnitus
- Meds: None
- NB: Fa deceased 47yoa 1 ½ yrs prior (Dec ‘16)
- FHx: Sjogrens, Hashimotos, Raynauds, Achalasia



ROS

- IBS-d with 3BM/d
- Nausea +/- vomiting with frequent headaches
- Fatigue → naps after school for 30-60 min
- Chest pain all my life →sob w tightening,
- Complex migraines→ like 'CVA'→ unable to write or talk→ to ER CT scan WNL
- Anxiety issues all my life→ OCD->GAD-> now constant depression since 2014
- Gluten Free "helps my brain fog"

Depression
Plan ?

- Biomarker Panel: Inflammation Panel, Insulin/Glucose, Essential Fatty Acids, TFT's, etc
- Nutrient Eval'n: Nutreval, OAT, Spectracell
- Stool Analysis: Assess Microbiome, Digestion
- Assess Intestinal Permeability and Food Immune Reactivity

POA Nov ‘17

- 28 day Dairy Free trial along w/Gluten Free
- Omega3 3000mg QHS
- Activity / Movement qd
- F/U to review labs
- Prn, consider Nutrient Evaluation: Nutreval, OAT, Spectracell, Stool Analysis: Microbiome/(DIG), Intestinal Permeability and Food Immune Reactivity

Boston Heart Fatty Acid Balance™ Test[1]

Saturated Fatty Acid Index		**32.7**		Saturated FA Index is BORDERLINE. Higher levels of plasma saturated fatty acids are associated with an increased risk of CVD. Consider restricting dietary intake of saturated fat by choosing poultry without skin, fish, low fat dairy products, lean cuts of meat, and replacing butter with plant based oils.
	<30.0	**30.0-33.0**	>33.0 %	
Trans Fatty Acid Index		**0.53**		Trans FA Index is BORDERLINE. Higher levels of plasma trans fatty acids are associated with an increased risk of CVD. Consider restricting dietary intake of fried foods, foods containing partially hydrogenated fats, shortening, or stick margarine, and replacing with plant based oils.
	<0.50	**0.50–0.80**	>0.80 %	
	Optimal	Borderline	Low	
Monounsaturated Fatty Acid Index	**25.2**			Monounsaturated FA Index is OPTIMAL.
	>22.0	19.0–22.0	<19.0 %	
Unsaturated/Saturated Ratio Index		**2.00**		Unsaturated/Saturated Ratio Index is BORDERLINE. A lower Unsaturated/Saturated Ratio Index is associated with a higher LDL-C and increased risk of CVD. Consider increasing intake of plant based fats from nuts, seeds, and their oils along with fatty fish and restricting intake of animal fats like red meat, fatty processed meats, and full fat dairy.
	>2.25	**2.00–2.25**	<2.00	
Omega-3 Fatty Acid Index		**2.24**		Omega-3 FA Index is BORDERLINE. A lower Omega-3 FA Index is associated with an increased risk for CVD. Eicosapentaenoic Acid (EPA) level is LOW. Increased EPA levels have been associated with lower risk of heart disease. Docosahexaenoic Acid (DHA) level is LOW. Increased DHA levels have been associated with a lower risk of CVD. Consider recommending consumption of at least 2-3 meals of oily fish such as salmon, sardines, herring, tuna, and mackerel weekly or a fish oil or EPA supplement.
	>4.50	**2.00–4.50**	<2.00 %	
EPA			**<15.6**	
	>50.0	15.6-50.0	**<15.6 µg/mL**	
DHA			**35.3**	
	>100.0	45.0–100.0	**<45.0 µg/mL**	
ALA			**10.3**	Alpha Linolenic Acid (ALA) level is LOW. High levels of ALA have been associated with a lower risk of CVD. Consider recommending increasing intake of walnuts, chia seeds, ground flaxseeds, and canola or flaxseed oil.
	>30.0	14.0–30.0	**<14.0 µg/mL**	
	Low	Mid	High	
Omega-6 Fatty Acid Index	**38.2**			Values are reported according to the lowest, middle and highest thirds of our reference population. Some authorities have recommended a goal below the 10th percentile for the Omega-6/Omega-3 Ratio Index (a value of 9.0) and the AA/EPA Ratio Index (a value of 5.0).
	<41.0	41.0–46.0	>46.0 %	
Linoleic Acid (LA)	**605.5**			
	<825.0	825.0–1040.0	>1040.0 µg/mL	
Arachidonic Acid (AA)	**157.1**			
	<220.0	220.0–290.0	>290.0 µg/mL	
AA/EPA Ratio Index		**14.2**		
	<13.0	13.0–25.0	>25.0	
Omega-6/Omega-3 Ratio Index	**13.99**			
	<15.0	15.0–24.0	>24.0	

Genetic Tests by Genotyping[1,4]

Test Name	Test Result	Interpretation	Notes
Reported Date: 11.22.17			
Statin Induced Myopathy (SLCO1B1)[7]	**T/C**	Decreased statin transporter. Patients with a T/C genotype have a decreased ability to transport statins; associated with reduced statin efficacy and up to a 4.5-fold increased risk of developing muscle pain on statin therapy. Consider recommending moderate to low doses of water soluble statins (in order of solubility: pravastatin, pitavastatin, rosuvastatin or fluvastatin).	
Reported Date: 11.22.17			
ApoE	**E3/E4**	Genotype associated with higher LDL-C levels than the common E3/E3. E4 individuals can have greater intestinal absorption and delayed clearance of cholesterol than E3 leading to elevated LDL-C. If cholesterol lowering is indicated consider recommending lifestyle modification and combination therapy with statin and ezetimibe.	
Reported Date: 11.22.17			
Clopidogrel Response (CYP2C19)	***1/*1**	Normal clopidogrel metabolizer.	

Test Name	Test Result	Interpretation	Notes
Reported Date: 11.22.17			
Factor V Leiden	**-/-**	Normal risk of clot formation.	
Reported Date: 11.22.17			
MTHFR	**677 C/C**	677(C/C) genotype – no variant. 1298(A/C) genotype – single copy of variant.	11
	1298 A/C	Due to elevated homocysteine consider nutritional therapy and/or folate and other B vitamin supplementation.	

Chemistry Tests

Test Name	Low	Normal	High	Notes	Previous Results
BUN		7.3			
	<3.0	3.0-25.0	>25.0 mg/dL		
Creatinine	0.42				
	<0.51	0.51-0.95	>.95 mg/dL		
Sodium		138		9	
	<135	135-146	>146 mmol/L		
Potassium		4.1		9	
	<3.5	3.5-5.3	>5.3 mmol/L		
Chloride		100			
	<98	98-110	>110 mmol/L		
CO_2		22			
	<20	20-31	>31 mmol/L		
Anion Gap		16			
	<3	3-16	>16 mmol/L		
Total Protein		7.4			
	<6.6	6.6-8.7	>8.7 g/dL		
Albumin			5.1		
	<3.2	3.2-4.5	>4.5 g/dL		
Calcium		9.9		9	
	<8.6	8.6-10.4	>10.4 mg/dL		
Uric Acid	3.9				
	<6	6-10	>10 mg/dL		
Total Bilirubin		0.4		9	
		0.0-1.2	>1.2 mg/dL		
Direct Bilirubin		0.1			
		0.0-0.3	>0.3 mg/dL		

Test Name	Optimal	Borderline	High Risk	Notes	Previous Results
Glucose[2]	93				
	70-99	100-125	<70 or >125 mg/dL		
AST	12				
	<40	40-120	>120 U/L		
ALT	9				
	<40	40-120	>120 U/L		
Alkaline Phosphatase	55				
	<130	130-200	>200 U/L		

Other Kidney Tests

Cystatin C	0.66				
	<=1.20		>1.20 mg/L		
Magnesium		2.2		9	
	<1.6	1.6-2.6	>2.6 mg/dL		
Phosphorus		3.2		9	
	<2.5	2.5-4.5	>4.5 mg/dL		

Test Name	Optimal	Borderline	High	Notes	Previous Results
BUN/Creatinine	17.4				
	<=23		>23		
eGFR / Non-African American	151			14	
	>60	30-60	<30 mL/min/1.73 m²		
eGFR / African American	175			14	
	>60	30-60	<30 mL/min/1.73 m²		
eGFR / Cystatin C	127.46			14	
	>60	30-60	<30 mL/min /1.73m²		

Muscle Tests

Creatine Kinase (CK)	66				
	<200	200-1000	>1000 U/L		
NT-proBNP	<20			10	
	<125	125-450	>450 pg/mL		

Test Name	Low	Normal	High	Notes	Previous Results
Iron Tests					
Iron		74			
	<37	37-145	>145 µg/dL		
Ferritin		32			
	<15	15-150	>150 ng/mL		

Test Name	Low	Mid	High	Notes	Previous Results
Other Tests					
B12		492		10	
	300-450	451-946	<300 or >946 pg/mL		
Vitamin D, 25-OH	29				
	<30	30-100	>100 ng/mL		

Test Name	Low	Optimal	High	Notes	Previous Results
Thyroid Tests					
TSH		1.07		10	
	<0.27	0.27-4.2	>4.2 µIU/mL		
Total T4		7.6		10	
	<4.5	4.5-11.7	>11.7 ug/dL		
Free T4		1.28		10	
	<0.93	0.93-1.70	>1.70 ng/dL		
Total T3		1.7		10	
	<0.8	0.8-2.0	>2.0 ng/mL		
Free T3		4.0		10	
	<2.0	2.0-4.4	>4.4 pg/mL		
TPO		18		10	
		<40	≥40 IU/mL		

Test Name	Optimal	Borderline	High	Notes	Previous Results
CoQ10[1]			0.42	6	
	>1.40	0.70-1.40	<0.70 mg/L		
Homocysteine		11.4			
	<10	10-14	>14 µmol/L		

Test Name	Test Results	Range	Notes	Previous Results
Female Hormone Tests				
Estradiol	74.4	See below	10	
Progesterone	7.10	See below	10	
LH	1.6	See below	10	
FSH	2.1	See below	10	
SHBG	TNP		13	

Test Name	Test Results	Range	Notes	Previous Results
Total Testosterone	28.0	See below	9,10	
Free Testosterone	TNP		10	
DHEA-S	248.3	65.1-368.0 µg/dL	9,10	
Cortisol	4	See below	10	

Female Hormone Reference Ranges by Phase

	Follicular	Ovulation	Luteal	Postmenopausal
Estradiol	12.4-233.0	41.0-398.0	22.3-341.0	<=138.0 pg/mL
Progesterone	0.06-0.89	0.12-12.0	1.83-23.9	<0.05-0.13 ng/mL
LH	2.4-12.6	14.0-95.6	1.0-11.4	7.7-58.5 mIU/mL
FSH	3.5-12.5	4.7-21.5	1.7-7.7	25.8-134.8 mIU/mL

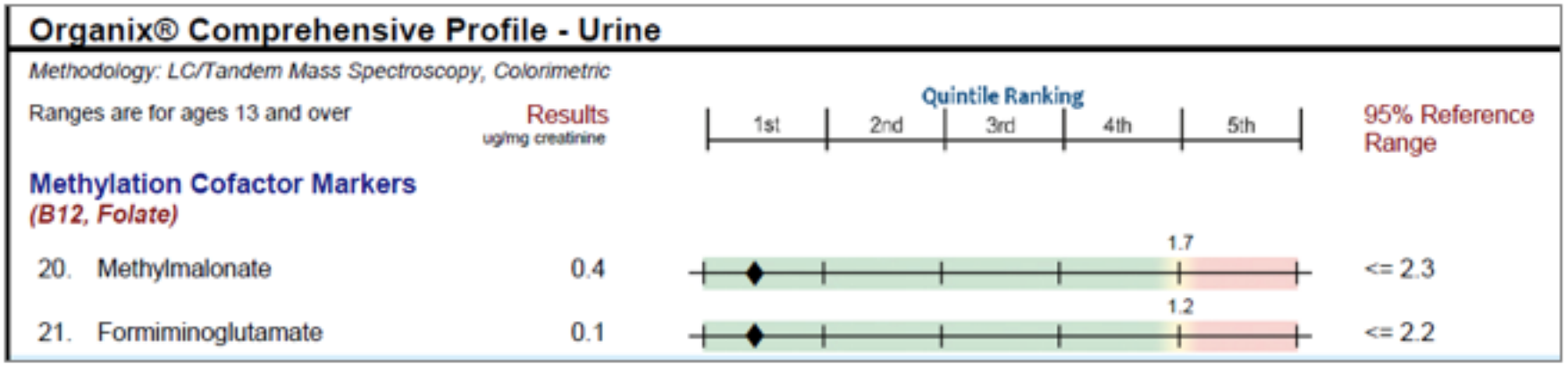
Cortisol Reference Ranges by Collection Time

	Low	Optimal	High
Cortisol (7-10AM)	<6	6-19	>19 µg/dL
Cortisol (4-8PM)	<2	2-12	>12 µg/dL

Female Pediatric Reference Ranges

	Stage	Range
Total Testosterone	Tanner 1	<2.50-6.12 ng/dL
	Tanner 2	<2.50-10.40 ng/dL
	Tanner 3	<2.50-23.70 ng/dL
	Tanner 4	<2.50-26.80 ng/dL
	Tanner 5	4.60-38.30 ng/dL

Mood Disorders: Folate and Vitamin B12



Organix® Comprehensive Profile - Urine

Methodology: LC/Tandem Mass Spectroscopy, Colorimetric

Ranges are for ages 13 and over	Results ug/mg creatinine	Quintile Ranking 1st 2nd 3rd 4th 5th	95% Reference Range
Methylation Cofactor Markers *(B12, Folate)*			
20. Methylmalonate	0.4	1.7	<= 2.3
21. Formiminoglutamate	0.1	1.2	<= 2.2

Folate and Vitamin B12 are key components of the methylation cycle.
Folate is required for the synthesis of dopamine, norepinephrine, and serotonin.

People with folate deficiency were more likely to suffer from depression, and were 6 times less likely to respond to antidepressant drugs.

Testing homocysteine-induced neurotransmitter deficiency, and depression of mood hypothesis in clinical practice

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Abstract

Background: high total plasma homocysteine (tHcy) levels may cause neurotransmitter deficiency, and consequently depression of mood. We have recently shown that mixed oral nutritional supplements containing B-group vitamins led to a statistically significant benefit on depressive symptoms. The aim of this report was to examine the association between elevated plasma tHcy and symptoms of depression in older patients.

Methods: two-hundred and thirty-six hospitalised acutely ill older patients, who were part of a randomised double-blind placebo-controlled trial, were assigned to receive daily mixed oral nutritional supplements containing B-group vitamins or a placebo for 6 weeks. Outcome measures included symptoms of depression measured using Geriatric Depression score and plasma tHcy levels.

Results: the mean tHcy concentration fell by 22% among patients given the supplements compared with the placebo group (mean difference 4.1 μmol/l (95% CI: 0.14–8.03), $P = 0.043$). tHcy concentrations was divided into four quartiles and analysed against depression scores. tHcy concentrations in the first relative to the fourth quartile of the distribution were associated with a lower depression symptoms at the end of the supplement period (Geriatric depression score $r = -0.20$, $P = 0.042$).

Conclusions: lower plasma tHcy concentrations were associated with reduced depression symptoms in older patients recovering from acute illness.

Homocysteine-induced Neurotransmitter Deficiency *(continued)*

Key points

- B-group vitamin deficiencies and raised plasma Homocysteine (tHcy) are associated with increased symptoms of depression.
- High tHcy levels may cause neurotransmitter deficiency, and consequently depression of mood.
- Mixed nutrient supplements containing physiological amount of B vitamins significantly reduced plasma tHcy concentrations in older patients.
- Lower plasma tHcy concentrations were associated with reduced depression symptoms.

Dec ’17
Summary of Labs

- Essential Fatty Acids: Omega 3 index 2.24 ; EPA <15.6, DHA 35, ALA 10
- Genetic SNP’s : E3E4, MTHFR 1298A/C
- Vitamin D3 29, B12 490, Coq10 0.42
- Cortisol 4 ; Total protein 5.1
- Homocysteine 11.4

Dec ‘17

- POA: Continue Gluten Free/Dairy Free, increase healthy fats→ nuts, seeds, oils
- Omega 3 →3000mg bid
- Flaxseed Oil 1 qd
- D3 5000 IU qd
- PQQ (CoQ10) 200 mg/day
- B12 sq x 1; meFolate 1000 mcg/day
- Adrenal Support



Jan ‘18

- “A different person”
- Patient notices + difference; mom too
- Mood “really good”; no depression
- No anxiety d holidays (Xmas/ NY) or since
- No nausea
- No h/a’s , no aura
- No naps→ energy good
- No mania

March ‘18

- Continues symptom free
- Continues on health/good fat diet; GF/DF
- No change in supps
- F/U late spring or prn

63 yo F C Diff
Feb ‘18

- CC: Aug ‘17 in Aruba--Norovirus and my gut has never been the same; bloats, explosive loose stool, fatigue
- Scope Nov’17→ f/b Flagyl x 10d → no improvement
- Allergy testing→+ casein IgG→ FODMAPS diet → no improvement
- Stool Cx Jan ‘18→ C Diff tox B + → Vanco x 10d
- PCP recs 2nd course of Vanco→ reluctant
- Fecal Microbiota Translant?

63yo F CDiff

- PMH: Hyperlipidemia, LBP, Sleep disturbance, Migraine
- Meds: Atorvastatin, Aleve, Amitriptyline, Align/Culturelle
- ROS: IBS-m, bloating/gas/distention, nocturnal stools, fatigue, muscle pain, hair loss, mood swings/irritability, weight gain 12#

63 yo F C Diff

- POA:
- Gut rest→ Physicians Elemental Diet
- Probiotics→ VSL #3 ½ packet bid
- Sacc B. 1 po qd

- Lab testing pending……

63 yo F C Diff

- F/U 6 days later→ “I had 5 good days”
- No diarrhea, No nocturnal BM, good energy
- D#6 4 soft formed stools f/b complete watery diarrhea x 5
- NB: night prior had bread + stew with cooked veggies; Breakfast is always a shake
- Review testing : Food AB

Positive		Moderate		Negative			
IgG	IgA	IgG	IgA				
Fruits Avocado Cherry Pear Pineapple **Gluten containing grains** Rye **Vegetables** Cabbage		**Fruits** Coconut Strawberry Tomato **Miscellaneous** Cocoa **Vegetables** Broccoli Lettuce		**Dairy**			
				Beta-Casein Whey Protein	Casomorphin	Cow's Milk	Goat's Milk
				Fish			
				Catfish Mackerel	Codfish Perch	Halibut Salmon	Lake Trout Tuna
				Mollusks			
				Clam	Oyster	Scallops	
				Shellfish			
				Crab	Lobster	Shrimp	
				Fruits			
				Apple Blueberry Grapefruit Peach	Apricot Cantaloupe Lemon Raspberry	Banana Cranberry Olive Watermelon	Blackberry Grape Orange
				Gluten containing grains			
				Barley	Malt	Oats	
				Gluten free grains			
				Amaranth	Brown Rice	Buckwheat	Corn
				Legumes			
				Kidney Bean	Navy Bean	Peanut	Soybean
				Meat			
				Beef Lamb	Chicken Pork	Egg White Turkey	Egg Yolk
				Miscellaneous			
				Coffee Yeast	Hops	Rosemary	Vanilla Bean
				Spices			
				Black pepper	Cinnamon	Nutmeg	
				Nuts(Tree)			
				Almond Pecan	Black Walnut	Cashews	English Walnut
				Seeds			
				Mustard	Sesame		
				Nightshades			
				Green Pepper	White Potato		
				Vegetables			
				Carrot	Cauliflower	Celery	Cucumber

Total Immunoglobulins

Test name	In Control	Moderate	High Risk	In Control Range	Moderate Range	High Risk Range	Previous
Total IgG (mg/dL)	723			635~1741		≤634 ≥1742	
Total IgA (mg/dL)			62	66~433		≤65 ≥434	

Celiac

Test name	In Control	Moderate	High Risk	In Control Range	Moderate Range	High Risk Range	Previous
Transglutaminase 2 IgG	0.71			≤0.89	0.90~1.10	≥1.11	
Transglutaminase 2 IgA	0.35			≤0.89	0.90~1.10	≥1.11	
DGP IgG	0.25			≤0.89	0.90~1.10	≥1.11	
DGP IgA	0.19			≤0.89	0.90~1.10	≥1.11	

tTG/DGP Complex

Test name	In Control	Moderate	High Risk	In Control Range	Moderate Range	High Risk Range	Previous
tTG/DGP Fusion Peptide IgG	0.09			≤0.89	0.90~1.10	≥1.11	
tTG/DGP Fusion Peptide IgA	0.17			≤0.89	0.90~1.10	≥1.11	

Intestinal Permeability Panel

Test name	In Control	Moderate	High Risk	In Control Range	Moderate Range	High Risk Range	Previous
Zonulin (ng/mL)	44.9			≤45.3	45.4~55.3	≥55.4	
Anti-Zonulin IgG		1.09		≤0.89	0.90~1.10	≥1.11	
Anti-Zonulin IgA	0.38			≤0.89	0.90~1.10	≥1.11	
Anti-Actin IgG			1.75	≤0.89	0.90~1.10	≥1.11	
Anti-Actin IgA	0.46			≤0.89	0.90~1.10	≥1.11	
Anti-LPS IgA (U/ml)	12.7			≤30.0		≥30.1	
Anti-LPS (IgG + IgM) (U/ml)	81.3			≤281.0		≥281.1	

Transglutaminase Panel

Test name	In Control	Moderate	High Risk	In Control Range	Moderate Range	High Risk Range	Previous
Transglutaminase 3 IgG	0.49			≤0.89	0.90~1.10	≥1.11	
Transglutaminase 3 IgA	0.17			≤0.89	0.90~1.10	≥1.11	
Transglutaminase 6 IgG	0.65			≤0.89	0.90~1.10	≥1.11	
Transglutaminase 6 IgA	0.10			≤0.89	0.90~1.10	≥1.11	

Wheat Germ Panel

Test name	In Control	Moderate	High Risk	In Control Range	Moderate Range	High Risk Range	Previous
Wheat Germ Agglutinin IgG		0.90		≤0.89	0.90~1.10	≥1.11	
Wheat Germ Agglutinin IgA	0.46			≤0.89	0.90~1.10	≥1.11	

Gliadin Panel

Test name	In Control	Moderate	High Risk	In Control Range	Moderate Range	High Risk Range	Previous
Alpha Gliadin IgG		1.01		≤0.89	0.90~1.10	≥1.11	
Alpha Gliadin IgA	0.54			≤0.89	0.90~1.10	≥1.11	
Alpha-Beta Gliadin IgG			1.11	≤0.89	0.90~1.10	≥1.11	
Alpha-Beta Gliadin IgA	0.51			≤0.89	0.90~1.10	≥1.11	
Gamma Gliadin IgG		1.03		≤0.89	0.90~1.10	≥1.11	
Gamma Gliadin IgA	0.61			≤0.89	0.90~1.10	≥1.11	
Omega Gliadin IgG			1.11	≤0.89	0.90~1.10	≥1.11	
Omega Gliadin IgA	0.54			≤0.89	0.90~1.10	≥1.11	
Gluteomorphin IgG	0.73			≤0.89	0.90~1.10	≥1.11	
Gluteomorphin IgA	0.30			≤0.89	0.90~1.10	≥1.11	
Prodynorphin IgG	0.72			≤0.89	0.90~1.10	≥1.11	
Prodynorphin IgA	0.25			≤0.89	0.90~1.10	≥1.11	

Glutenin Panel

Test name	In Control	Moderate	High Risk	In Control Range	Moderate Range	High Risk Range	Previous
HMW Glutenin IgG		0.94		≤0.89	0.90~1.10	≥1.11	
HMW Glutenin IgA	0.72			≤0.89	0.90~1.10	≥1.11	
LMW Glutenin IgG	0.77			≤0.89	0.90~1.10	≥1.11	
LMW Glutenin IgA	0.35			≤0.89	0.90~1.10	≥1.11	

Non-Gluten Wheat Panel

Test name	In Control	Moderate	High Risk	In Control Range	Moderate Range	High Risk Range	Previous
Serpin IgG	0.83			≤0.89	0.90~1.10	≥1.11	
Serpin IgA	0.50			≤0.89	0.90~1.10	≥1.11	
Farinins IgG			1.22	≤0.89	0.90~1.10	≥1.11	
Farinins IgA	0.57			≤0.89	0.90~1.10	≥1.11	
Amylase/Protease Inhibitors IgG		1.04		≤0.89	0.90~1.10	≥1.11	
Amylase/Protease Inhibitors IgA	0.47			≤0.89	0.90~1.10	≥1.11	
Globulins IgG		0.90		≤0.89	0.90~1.10	≥1.11	
Globulins IgA	0.51			≤0.89	0.90~1.10	≥1.11	
Purinin IgG	0.83			≤0.89	0.90~1.10	≥1.11	
Purinin IgA	0.45			≤0.89	0.90~1.10	≥1.11	

✓ Detected ○ Not Detected

BACTERIA

Test Name	Current Result	Previous Result
Clostridium difficile toxin A	o	
Clostridium difficile toxin B	o	
Campylobacter spp (jejuni, coli and upsaliensis)	o	
Plesiomonas shigelloides	o	
Salmonella	o	
Yersinia enterocolitica	o	
Vibrio parahaemolyticus	o	
Vibrio cholerae	o	
Vibrio vulnificus	o	
Enteroaggregative E.Coli(EAEC)	o	
Enteropathogenic E.Coli(EPEC)	o	
Enterotoxigenic E.Coli(ETEC)lt/st	o	
Shiga-like toxin producing E.Coli(STEC)stx1/stx2	o	
E.Coli O157	o	
Shigella/Enteroinvasive E.Coli (EIEC)	o	
Helicobacter pylori	o	
Listeria	o	
Klebsiella pneumoniae	o	
Edwardsiella tarda	o	

Gut Microbiome and Intestinal Permeability

Genus/Species	Abundance	Previous	Rating	Potential Associated Risk*
Bacteroides	OPTIMAL↔		★★★	Lower SCFA production
Bifidobacterium	OPTIMAL↔		★★★	
Propionibacterium	OPTIMAL↔		★★★	
Eubacterium	LOW↓		★★★	
Lactobacillus	OPTIMAL↔		★★★	
Clostridium	OPTIMAL↔		★★★	
Roseburia	LOW↓		★★★	
Prevotella	OPTIMAL↔		★★★	
Eubacterium rectale	OPTIMAL↔		★★★	
Butyrivibrio	OPTIMAL↔		★★★★	
Blautia	OPTIMAL↔		★★★	
Enterobacteriaceae (family)	OPTIMAL↔		★★★★	Tight junction integrity impaired
Akkermansia muciniphila	OPTIMAL↔		★★★★★	
Lactobacillus rhamnosus	LOW↓		★★★★	
Lactobacillus reuteri	LOW↓		★★★★	
Lactobacillus plantarum	OPTIMAL↔		★★★	
Streptococcus thermophilus	LOW↓		★★★	
Lactobacillus bulgaricus	OPTIMAL↔		★★★	
Lactobacillus acidophilus	LOW↓		★★★	
Bifidobacterium longum	OPTIMAL↔		★★★	

Potential Risk Mitigation Choices

Prebiotics

Consider taking prebiotic fibers

Probiotics

Consider taking probiotics containing Lactobacillus reuteri, Lactobacillus rhamnosus, Bifidobacterium infantis and Lactobacillus plantarum

Gut Microbiome and Intestinal Health

Genus/Species	Abundance	Previous	Rating	Potential Associated Risk*
Dorea	OPTIMAL↔		★★★★★	IBS
Ruminococcus	OPTIMAL↔		★★★★★	
Faecalibacterium prausnitizii	LOW↓		★★★	
Bifidobacterium	OPTIMAL↔		★★★	
Coprobacillus	HIGH↑		★	
Ruminococcus productus	OPTIMAL↔		★★★★★	
Bifidobacterium catenulatum	OPTIMAL↔		★★★★★	
Desulfovibrio piger	HIGH↑		★★★★★	
Coprococcus eutactus	OPTIMAL↔		★★★★★	
Escherichia coli	HIGH↑		★★	
Clostridium leptum	OPTIMAL↔		★★	IBD
Enterobacterium	OPTIMAL↔		★★★	
Akkermansia muciniphila	OPTIMAL↔		★	
Lachnospira	OPTIMAL↔		★★★★★	
Phascolarctobacterium	LOW↓		★★★★★	
Gardnerella	OPTIMAL↔		★★	
Bacillus	OPTIMAL↔		★★★	
Lactobacillus	OPTIMAL↔		★★★★★	IBS-D
Veillonella	OPTIMAL↔		★★★★★	IBS-C

Potential Risk Mitigation Choices

Probiotics

Consider taking multi-strain probiotics containing Lactobacillus reuteri, Lactobacillus plantarum and Lactobacillus salivarius

Considerations

Possible supplements include curcumin, omega 3's, and Quercetin. Consider working with a Vibrant clinical dietitian to follow an anti-inflammatory diet.
Consider prebiotic fibers based on individual symptoms and evaluate possible food sensitivities.

Diet

Consider increasing the intake of polyphenols and reducing the dietary antibiotics (organic meats/dairy/produce).
Consider avoiding diets excessively high in protein, and ensure adequate intake of plant-based fibers.

Gut Microbiome and Cardiovascular Health

Genus/Species	Abundance	Previous	Rating	Potential Associated Risk*
Collinsella	HIGH↑		★★★★★	Atherosclerosis
Eubacterium	LOW↓		★★★★★	
Lactobacillus reuteri	LOW↓		★★★★★	High LDL-Cholesterol
Lactobacillus acidophilus	LOW↓		★★★★★	
Lactobacillus plantarum	OPTIMAL↔		★★★★★	Atherosclerosis and Triglyceride levels
Prevotella	OPTIMAL↔		★★★★★	Potentially increased TMAO levels leading to atherosclerosis
Sporobacter	HIGH↑		★★★★★	
Peptostreptococcaceae (family)	OPTIMAL↔		★★★★★	
Peptostreptococcaceae incertae sedis	OPTIMAL↔		★★★★★	
Clostridiaceae	HIGH↑		★★★★★	
Fusibacter	OPTIMAL↔		★★★★★	
Lachnospira	OPTIMAL↔		★★★★★	
Clostridium	OPTIMAL↔		★★★★★	
Clostridiales incertae sedis XII (family)	HIGH↑		★★★★★	
Anaerococcus hydrogenalis	OPTIMAL↔		★★★★	
Clostridium asparagiforme	OPTIMAL↔		★★★★	
Clostridium hathewayi	OPTIMAL↔		★★★★	
Clostridium sporogenes	OPTIMAL↔		★★★★	
Escherichia fergusonii	HIGH↑		★★★★	
Proteus penneri	HIGH↑		★★★★	
Providencia rettgeri	OPTIMAL↔		★★★★	
Edwardsiella tarda	LOW↔		★★★★	

Potential Risk Mitigation Choices

Prebiotics

Consider prebiotic supplements inulin and fructooligosaccharide fibers.

Probiotics

Consider taking probiotics containing Lactobacillus reuteri, Lactobacillus acidophilus and Bifidobacterium lactis

Gut Microbiome and Autoimmune Health

Genus/Species	Abundance	Previous	Rating	Potential Associated Risk*
Helicobacter	OPTIMAL↔		★★★★★	Celiac Disease
Serratia	OPTIMAL↔		★★	
Lactobacillus	OPTIMAL↔		★★	
Bifidobacterium	OPTIMAL↔		★★★	
Streptococcus	OPTIMAL↔		★★★	
Papilibacter	OPTIMAL↔		★★	
Prevotella	OPTIMAL↔		★★★★★	
Tannerella	OPTIMAL↔		★★★	Rheumatoid Arthritis (RA)
Yersinia	LOW↔		★★	
Aggregatibacter	OPTIMAL↔		★★★	
Porphyromonas	HIGH↑		★★★	
Coprococcus	OPTIMAL↔		★	Psoriasis and Psoriatic Arthritis
Pseudobutyrivibrio	LOW↓		★	Psoriatic Arthritis
Klebsiella pneumoniae	LOW↔		★★★	Crohn's Disease
Veillonella	OPTIMAL↔		★★	
Dialister	OPTIMAL↔		★★★★★	

Potential Risk Mitigation Choices

Considerations

Consider further testing for RA specific antibodies

Gut Microbiome and Metabolic Health

Genus/Species	Abundance	Previous	Rating	Potential Associated Risk*
Lactobacillus reuteri	LOW↓		★★★★	Obesity
Lactobacillus casei	OPTIMAL↔		★★★	
Lactobacillus paracasei	OPTIMAL↔		★★★★★	
Methanobacteriales	OPTIMAL↔		★	
Bifidobacterium Animalis	OPTIMAL↔		★★★★	
Methanobrevibacter smithii	OPTIMAL↔		★★★★	
Staphylococcus	OPTIMAL↔		★★★	
Blautia	OPTIMAL↔		★★	
Oscillospira	OPTIMAL↔		★★★★★	
Alistipes	OPTIMAL↔		★★★	
Roseburia	LOW↓		★★★★★	Type II Diabetes
Eubacterium	LOW↓		★★★★★	
Eggerthella	OPTIMAL↔		★★★★★	

Potential Risk Mitigation Choices

Probiotics

Consider taking probiotics containing Lactobacillus reuteri, Lactobacillus paracasei, Lactobacillus rhamnosus, and Bifidobacterium animalis.

Gut Microbiome and Nutrition I

Genus/Species	Abundance	Previous	Rating	Potential Associated Risk*
Bifidobacterium bifidum	OPTIMAL↔		★★★★	K Vitamins and B Vitamins Production affected
Bifidobacterium longum	OPTIMAL↔		★★★★	
Lactobacillus plantarum	OPTIMAL↔		★★★	
Bifidobacterium breve	OPTIMAL↔		★★★★	
Bifidobacterium adolescentis	OPTIMAL↔		★★★★	
Bacillus subtilis	OPTIMAL↔		★★	Vitamin K2 production affected
Lactobacillus reuteri	LOW↓		★★	Vitamin B12 production affected
Propionibacterium freudenreichii subsp. shermanii	OPTIMAL↔		★★	
Lactobacillus fermentum	OPTIMAL↔		★★	

Gut Microbiome and Nutrition II

Genus/Species	Abundance	Previous	Rating	Potential Associated Risk*
Bifidobacterium animalis subspe lactis	OPTIMAL↔		★★★	Oxalate metabolism affected
Lactobacillus animalis	OPTIMAL↔		★	
Eggerthella lenta	OPTIMAL↔		★★	
Enterococcus faecalis	LOW↓		★★	
Providencia rettgeri	OPTIMAL↔		★★	
Streptococcus thermophilus	LOW↓		★★	
Lactobacillus plantarum	OPTIMAL↔		★★	
Lactobacillus gasseri	OPTIMAL↔		★★	
Lactobacillus casei	OPTIMAL↔		★★	
Lactobacillus acidophilus	LOW↓		★★	
Lactobacillus rhamnosus	LOW↓		★★	
Lactobacillus salivarius	OPTIMAL↔		★★	
Lactobacillus johnsonii	OPTIMAL↔		★★	
Bifidobacterium infantis	OPTIMAL↔		★★	
Bifidobacterium animalis	OPTIMAL↔		★★	
Oxalobacter formigenes	OPTIMAL↔		★★	
Allisonella	OPTIMAL↔		★★★	Potential gut inflammation - High Histamine production
Methanobrevibacter smithii	OPTIMAL↔		★★★★★	Extraction of nutrients affected

Gut Microbiome and Phylum	Abundance	Previous
Actinobacteria	HIGH↑	
Bacteroidetes	HIGH↑	
Firmicutes	HIGH↑	
Proteobacteria	LOW↓	

Gut Microbiome and Ratios	Floral Balance	Result	Previous	Rating	Potential Associated Risk*
	Firmicutes/ Bacteriodetes	HIGH↑		★★★★	Obesity
	Gram+/ Gram-	OPTIMAL↔		★★★	
	Diversity Index	LOW↓		★★★★	Gut Dysbiosis

Free T4		1.06		9	
	<0.93	0.93-1.70	>1.70 ng/dL		
Free T3		3.0		9	
	<2.0	2.0-4.4	>4.4 pg/mL		
TPO		13		9	
		<40	≥40 IU/mL		

B12		520		9	
	300-450	451-946	<300 or >946 pg/mL		
Vitamin D, 25-OH	27				
	<30	30-100	>100 ng/mL		

Test Name	Test Results	Range	Notes	Previous Results
Female Hormone Tests				
Estradiol	<25.0	See below	9	
Progesterone	0.13	See below	9	
LH	31.3	See below	9	
FSH	83.7	See below	9	
SHBG	41.1	17.3-125.0 nmol/L	9	

Test Name	Test Results	Range	Notes	Previous Results
Total Testosterone	<2.5	2.9-40.8 ng/dL	9	
DHEA-S	54.3	18.9-205.0 µg/dL	9	
Cortisol	6	See below	9	

Female Hormone Reference Ranges by Phase

	Follicular	Ovulation	Luteal	Postmenopausal
Estradiol	12.4-233.0	41.0-398.0	22.3-341.0	<=138.0 pg/mL
Progesterone	0.06-0.89	0.12-12.0	1.83-23.9	<0.05-0.13 ng/mL
LH	2.4-12.6	14.0-95.6	1.0-11.4	7.7-58.5 mIU/mL
FSH	3.5-12.5	4.7-21.5	1.7-7.7	25.8-134.8 mIU/mL

Cortisol Reference Ranges by Collection Time

	Low	Optimal	High
Cortisol (7-10AM)	<6	6-19	>19 µg/dL
Cortisol (4-8PM)	<2	2-12	>12 µg/dL

Test Name	Low	Normal	High	Notes	Previous Results
Complete Blood Count (CBC)					
WBC		5.70			
	<3.50	3.50-10.50	>10.50 x10E3/µL		
RBC		4.15			
	<3.80	3.80-5.10	>5.10 x10E6/µL		

Test Name	Low	Normal	High	Notes	Previous Results
MCV		88.2			
	<80.0	80.0-100.0	>100.0 fL		
MCH		29.9			
	<27.0	27.0-33.0	>33.0 pg		
MCHC		33.9			
	<32.0	32.0-36.0	>36.0 g/dL		

Test Name	Optimal	Borderline	High	Notes	Previous Results
Folate		11.7		9	
	>14.0	10.0-14.0	<10.0 ng/mL		
CoQ10[1]		1.32		6	
	>1.40	0.70-1.40	<0.70 mg/L		
Homocysteine	8.3				
	<10	10-14	>14 µmol/L		

63 yo F C Diff
Summary of Labs

- Celiac HLA genetics and Ab: normal
- IgA (first line of defense) : low
- Intestinal Permeability panel: positive --Anti-Actin IgG 1.75, Anti-Zonulin IgG 1.09
- Gliadin Panel: positive reaction
- Glutenin Panel: positive reaction
- Non-Gluten Wheat Panel: Farinins positive
- Gut Dysbiosis, Low Diversity

Feb ‘18

- Colostrum 2 tspns bid w/water
- BPC 2000mcg/ml. 0.1ml sq qd
- VSL #3 1 packet bid
- Wheat free, Casein free food plan
- L-Glutamine, Curcumin, Digestive Enzymes
- Omega 3 2000mg qd, B12 1000 mcg sq , meFolate 1000mcg/day, D3 2000 iu/day
- Gut Restoration Program

BPC 157

- *"Stable gastric pentadecapeptide BPC 157*
- *is an anti-ulcer agent.....*
- *is safe in inflammatory bowel disease clinical trials and wound healing.....*
- *has no reported toxicity.....*
- *it has a prominent effect on alcohol-lesions and NSAIDs-lesions...*
- *it acts as a free radical scavenger and exhibits neuro-protective properties."*

BPC 157

- BPC 157 has no primary/single effect; pleiotrophic effects with multiple uses
- MOA unclear: novel mediator of cytoprotection
- Administered sq, po and intra-articular

BPC 157
Clinical Effects

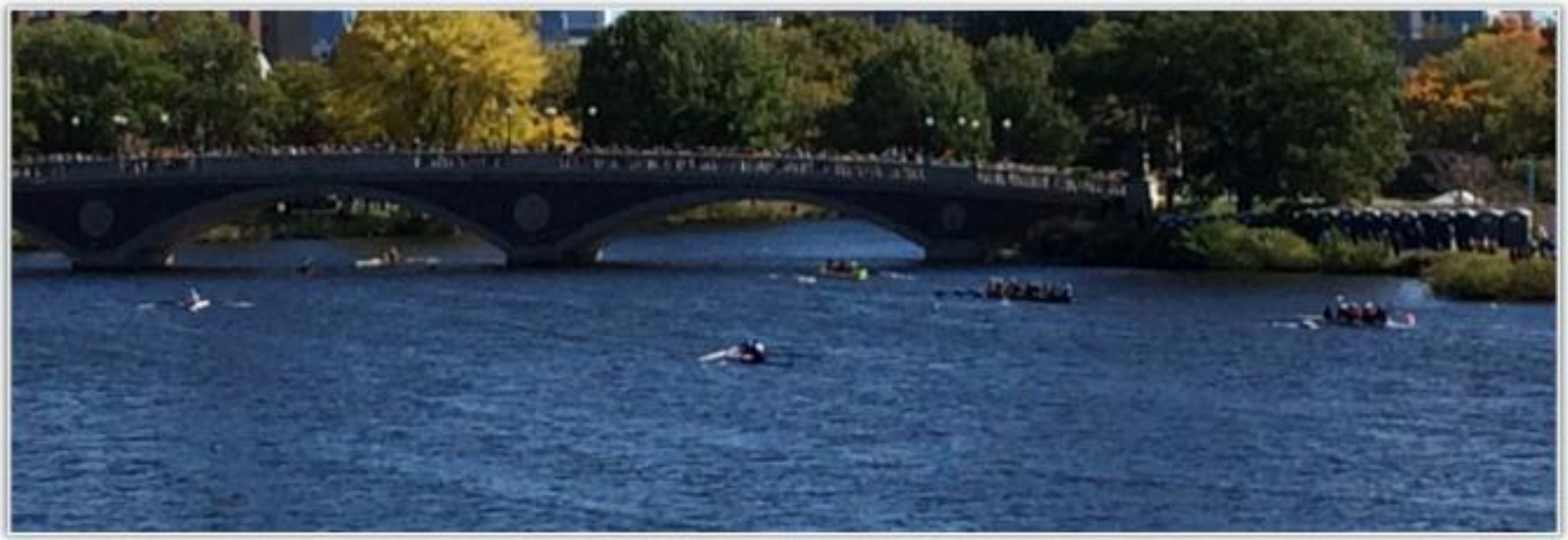
- Potent angio-modulatory agent: regulates gene expression (NO, VEGF, etc)→ promotes angiogenesis and vasculogenesis
- Cytoprotective: maintains GI mucosal integrity
- Repairs tissue: GIT, tendons, ligaments, brain, bone, etc

BPC 157 Therapeutic Uses

- Protects and prevents gastric ulcers (PUD)
- Eosinophilic esophagitis (EE)
- Protects and heals inflamed intestinal epithelium (LGS)
- Used in Inflammatory bowel disease (IBD) exacerbations/flares

Supporting the Pillars of Gut and Brain Health

- Sometimes the best medicine is no medicine at all
- Address Healthy Lifestyle: Movement/Activity
- Personalized Healthy Food Plan
- Replenish Nutrient Deficiencies
- Restore Gut : Gut Rest, Probiotics, Prebiotics, etc
- Restore Immune System
- Restore Hormonal System



Thank you!!

Kathleen ONeil Smith, MD, FAARM
Treat Wellness
Newton, MA

References in the following slides

REFERENCE/ABSTRACT

Alessio Fasano.Zonulin and Its Regulation of Intestinal Barrier Function: The Biological Door to Inflammation, Autoimmunity, and Cancer.
This review talks about the increased interest in the role of a "leaky gut" in the pathogenesis of several pathological conditions targeting both the intestine and extra intestinal organs.

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This review talks about the increased interest in the role of a "leaky gut" in the pathogenesis of several pathological conditions targeting both the intestine and extra intestinal organs.

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The study examines the humoral immune response to various wheat proteins and peptides in patients with gluten sensitivity or Crohn's disease. In gluten-sensitive patients, IgG reacted most against transglutaminase, prodynorphin, wheat extract, and -, -, and -gliadin; IgA reacted most against wheat then transglutaminase, glutenin, and other peptides. In Crohn's disease patients, IgG reacted most against wheat and wheat germ agglutinin then transglutaminase, prodynorphin, -, and -gliadin; IgA reacted foremost against prodynorphin then transglutaminase and -gliadin.

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The study aims to investigate the level and molecular specificity of antibody response to wheat non gluten proteins in celiac disease. The results demonstrate that, in addition to the well-recognized immune reaction to gluten, celiac disease is associated with a robust humoral

CLINICAL–ALIMENTARY TRACT

The Fecal Microbiota of Irritable Bowel Syndrome Patients Differs Significantly From That of Healthy Subjects

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See editorial on page 340.

Background & Aims: **Irritable bowel syndrome (IBS) is a significant gastrointestinal disorder with unknown etiology. The symptoms can greatly weaken patients' quality of life and account for notable economical costs for society. Contribution of the gastrointestinal microbiota in IBS has been suggested. Our objective was to characterize putative differences in gastrointestinal microbiota between patients with IBS and control subjects. These differences could potentially have a causal relationship with the syndrome.** ***Methods:*** **Microbial genomes from fecal samples of 24 patients with IBS and 23 controls were collected, pooled in a group-wise manner, and fractionated according to their guanine cytosine content. Selected fractions were analyzed by extensive high-throughput 16S ribosomal RNA gene cloning and sequencing of 3753 clones. Some of the revealed phylogenetic differences were further confirmed by quantitative polymerase chain reaction assays on individual samples.** ***Results:*** **The coverage of the clone libraries of IBS subtypes and control subjects differed significantly ($P < .0253$). The samples were also distinguishable by the Bayesian analysis of bacterial population structure. Moreover, significant ($P < .05$) differences between the clone libraries were found in several bacterial genera, which could be verified by quantitative polymerase chain reaction assays of phylotypes belonging to the genera *Coprococcus*, *Collinsella*, and *Coprobacillus*.** ***Conclusions:*** **The study showed that fecal microbiota is significantly altered in IBS. Further studies on molecular mechanisms underlying these alterations are needed to elucidate the exact role of intestinal bacteria in IBS.**

Irritable bowel syndrome (IBS) is a common functional gastrointestinal (GI) disorder with a worldwide prevalence of 10%–20%.[1] Although IBS does not predispose patients to severe illness, it can have significant effects on their well-being and need for medical consultation. The symptoms of IBS vary with affected individuals and include abdominal pain or discomfort, irregular bowel movements, flatulence, and constipation or diarrhea. Patients with IBS can be grouped into 3 subtypes according to their bowel habit.[1,2] These are diarrhea predominant (IBS-D), constipation predominant (IBS-C), and mixed subtype (IBS-M), which refers to patients with symptoms of both diarrhea and constipation. The etiology of IBS is poorly understood. Miscellaneous causes, including physiologic features such as altered GI motility and visceral hypersensitivity, psychological stress and disturbances, low-grade inflammation, and bacterial gastroenteritis, have been associated with IBS.[3]

The microbiota of the human GI tract constitutes a complex ecosystem that is involved in the health and physiologic functions of the host. Alterations of the normal GI microbiota have been shown to take place as a result of antibiotic therapies[4] and the use of probiotics,[5] in connection with various dietary strategies,[6] and with obesity.[7,8] Moreover, bacteria belonging to the normal microbiota seem also to be capable of causing disease in some individuals and may have a role in certain disorders, such as inflammatory bowel disease,[9–11] allergies,[12,13] and IBS.[14–17] Conventional culture-based methods provide an incomplete and biased picture of the biodiversity of intestinal microbiota, because the majority of the GI tract bacterial species cannot be cultivated.[18] To overcome these drawbacks, culture-independent molecular methods have been introduced. These methods are mainly based on ribosomal RNA (rRNA) genes that reflect the natural evolutionary relationships among different organisms. The microbial composition of human intestinal microbiota has been studied, for example, by

Abbreviations used in this paper: bp, base pairs; G+C, guanine plus cytosine; %G+C, percent guanine plus cytosine; IBS, irritable bowel syndrome; IBS-C, constipation-predominant irritable bowel syndrome; IBS-D, diarrhea-predominant irritable bowel syndrome; IBS-M, mixed-type irritable bowel syndrome; OTU, operational taxonomic unit; PCR, polymerase chain reaction; qPCR, quantitative real-time polymerase chain reaction; RDP II, Ribosomal Database Project II; rRNA, ribosomal RNA.

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Probiotics in the management of irritable bowel syndrome and inflammatory bowel disease

Kevin Whelan[a] *and Eamonn M.M. Quigley*[b]

Purpose of review
There is direct evidence that the pathogenesis of inflammatory bowel disease (IBD) involves the gastrointestinal microbiota and some evidence that the microbiota might also play a similar role in irritable bowel syndrome (IBS). The aim of this article is to review the emerging evidence for the mechanisms and effectiveness of probiotics in the management of these disorders.

Recent findings
The composition of the gastrointestinal microbiota is strongly influenced by factors including age, diet and disease. Probiotics may be effective through their impact on the host gastrointestinal microbiota and promotion of mucosal immunoregulation. Probiotics are considered to be well tolerated, although the quality of studies and health claims has been variable. There are many short-term studies demonstrating the effectiveness of probiotics in IBS, although recommendations should be made for specific strains and for specific symptoms. Within IBD, a number of trials have shown the benefits of a range of probiotics in pouchitis and in ulcerative colitis, although current evidence in Crohn's disease is less promising.

Summary
Clearly, some probiotics have considerable potential in the management of IBS and IBD; however, the benefits are strain specific. High-quality trials of probiotics in gastrointestinal disorders as well as laboratory investigations of their mechanism of action are required in order to understand who responds and why.

Keywords
inflammatory bowel disease, irritable bowel syndrome, microbiota, probiotics

INTRODUCTION

The gastrointestinal microbiota are a complex and metabolically active ecosystem that play an important role in health and disease. Genotypic sequencing studies have been used to demonstrate that the human gastrointestinal tract can be populated by any of 1000–1150 different species, with individuals harbouring at least 160 [1]. Despite this diversity, a core of 18 species was found in all individuals and 57 species were found in 90% of individuals, indicating considerable dominance and interindividual stability of these species across humans [1].

Many of these bacteria cluster within individuals. In a recent study across four countries, the sequenced metagenomes were shown to fit into three distinct clusters ('enterotypes'), each characterized by variations in numbers of *Bacteroides* (enterotype 1), *Prevotella* (enterotype 2) and *Ruminococcus* (enterotype 3) [2▪▪]. The abundance of these genera correlated positively or negatively with other genera, indicating a propensity for coexistence or avoidance of other species, respectively. Overall, this describes a microbial ecosystem whose structure is determined, at least in part, by the abundance of species that together contribute to a limited number of preferred compositions.

The composition of the microbiota is strongly influenced by factors including age, disease and diet. In one study [3▪], the microbiota of people aged 65–96 years was different from younger adults, with higher *Bacteroides* and Clostridia cluster IV, as well as some signature sequences that were present only in older people. Numerous diseases have been associated with alterations in the microbiota (dysbiosis), ranging from gastrointestinal disorders such as

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The gut-brain barrier in major depression: intestinal mucosal dysfunction with an increased translocation of LPS from gram negative enterobacteria (leaky gut) plays a role in the inflammatory pathophysiology of depression.

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Author information

Abstract

There is nov…natory response system (IR…ive symptoms. The aim of the p… increased translocatio…oward this end, the present stuc… enterobacteria, Hafnia Alvei,…oseri, and Klebsiella Pneumoniae…es for serum IgM and IgA against L…nteers. These differences a… area under the ROC curve is 90.1%… gastro-intestinal symptoms an…ction characterized by an increased tran…flammatory pathophysiology of depression. It …y mount an immune response and thus IRS activation in some patien…ckiness behaviour" symptoms. It is suggested that patients with MDD should be…means of the IgM and IgA panel used in the present study and accordingly should be treat…gut.

The results show that intestinal mucosal dysfunction characterized by an increased translocation of gram-negative bacteria (leaky gut) plays a role in the inflammatory pathophysiology of depression.

Health Matters

Connecting you to the sources of health

by Robert J. Hedaya, M.D.

Mood, Gut Bacteria, and the Immune System

Does the gut, immune system and stress interact?

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Many people would be surprised that the immune system, the gastro-intestinal tract and stress interact, but that is what the most recent of a number of studies shows. In this study on mice, (Brain, Behavior, and Immunity Volume 25, Issue 3, March 2011, Pages 397-407) researchers demonstrated that psychological stress causes almost immediate changes to the gut bacterial population, and that some of these affected sub-populations strongly influence the effect that stress has on immunity. In the study, the researchers exposed mice to social disruption, which is known to cause increases in circulating cytokines (hormones of the immune system), which themselves induce enhanced reactivity in the immune system. The researchers found that social disruption altered bacterial counts of some gut bacteria sub-populations, particularly when the bacteria were assessed immediately after stress exposure. Stress-exposure increased the relative abundance of bacteria in

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Melancholic microbes: a link between gut microbiota and depression?

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Abstract

There is a growing awareness of the potential for microbiota to influence gut-brain communication in health and disease. A variety of strategies have been used to study the impact of the microbiota on brain function and these include antibiotic use, probiotic treatments, fecal microbiota transplantation, gastrointestinal infection studies, and germ-free studies. All of these approaches provide evidence to support the view that the microbiota can influence brain chemistry and consequently behavior. Efforts are now turning to investigate the role of microbiota in animal models of psychopathology. Animal models of depression are thus essential in studying the complex interplay between the microbiota and brain. Recent studies published in this Journal and elsewhere demonstrate that there is a distinct perturbation of the composition of gut microbiota in animal models of depression and chronic stress. This has direct implications for the development of psychobiotic-based therapeutic strategies for psychiatric disorders. Moreover, given that affective co-morbidities, such as major depression and anxiety states, are common in patients presenting with irritable bowel syndrome (IBS), it may have implications for functional bowel disorders also. Further studies require appropriately phenotyped patients with depression and/or IBS using a judicious use of techniques including functional imaging and in depth microbial pyrosequencing.

Testing homocysteine-induced neurotransmitter deficiency, and depression of mood hypothesis in clinical practice

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Abstract

Background: high total plasma homocysteine (tHcy) levels may cause neurotransmitter deficiency, and consequently depression of mood. We have recently shown that mixed oral nutritional supplements containing B-group vitamins led to a statistically significant benefit on depressive symptoms. The aim of this report was to examine the association between elevated plasma tHcy and symptoms of depression in older patients.

Methods: two-hundred and thirty-six hospitalised acutely ill older patients, who were part of a randomised double-blind placebo-controlled trial, were assigned to receive daily mixed oral nutritional supplements containing B-group vitamins or a placebo for 6 weeks. Outcome measures included symptoms of depression measured using Geriatric Depression score and plasma tHcy levels.

Results: the mean tHcy concentration fell by 22% among patients given the supplements compared with the placebo group (mean difference 4.1 μmol/l (95% CI: 0.14–8.03), $P = 0.043$). tHcy concentrations was divided into four quartiles and analysed against depression scores. tHcy concentrations in the first relative to the fourth quartile of the distribution were associated with a lower depression symptoms at the end of the supplement period (Geriatric depression score $r = -0.20$, $P = 0.042$).

Conclusions: lower plasma tHcy concentrations were associated with reduced depression symptoms in older patients recovering from acute illness.

CNS Inflammation: Common Pathway to Schizophrenia and Major Depression

'These mechanisms include the immunological balance between type-1 and type-2 immune activation which influences the tryptophan-degradating enzyme indoleamine 2,3-dioxygenase (IDO) in opposite ways, leading to an imbalance in favor of the production of the NMDA-receptor agonist quinolinic acid in depression and of the NMDA-receptor antagonist kynurenic acid in schizophrenia.'

'By means of findings from the field of psychoneuroimmunology and inflammation it will be shown that different pathological mechanisms in depression and schizophrenia may lead to the same final common pathway of inflammation.'