

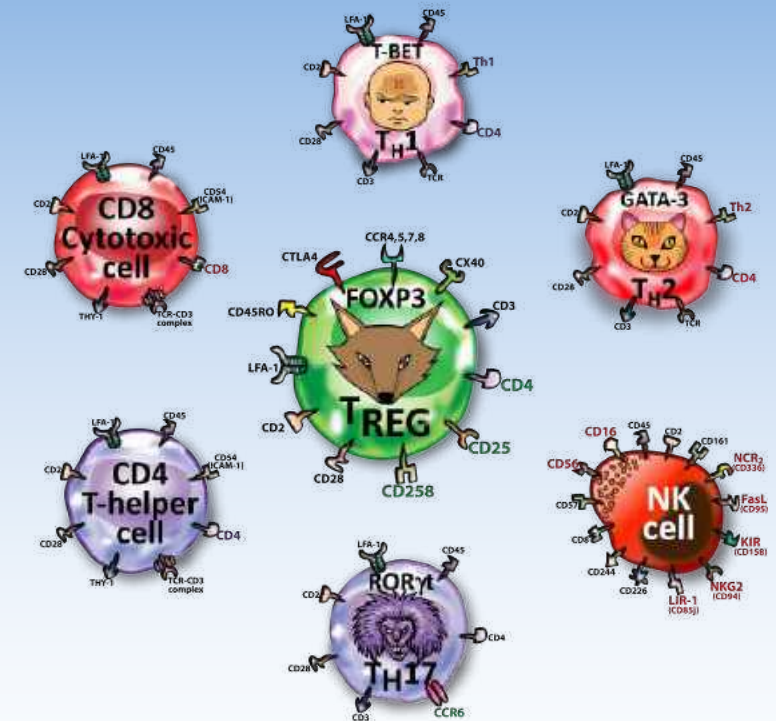


Nutritional Medicine
Institute

Environmental Factors, Inflammation, Immune Dysfunction and Autoimmunity

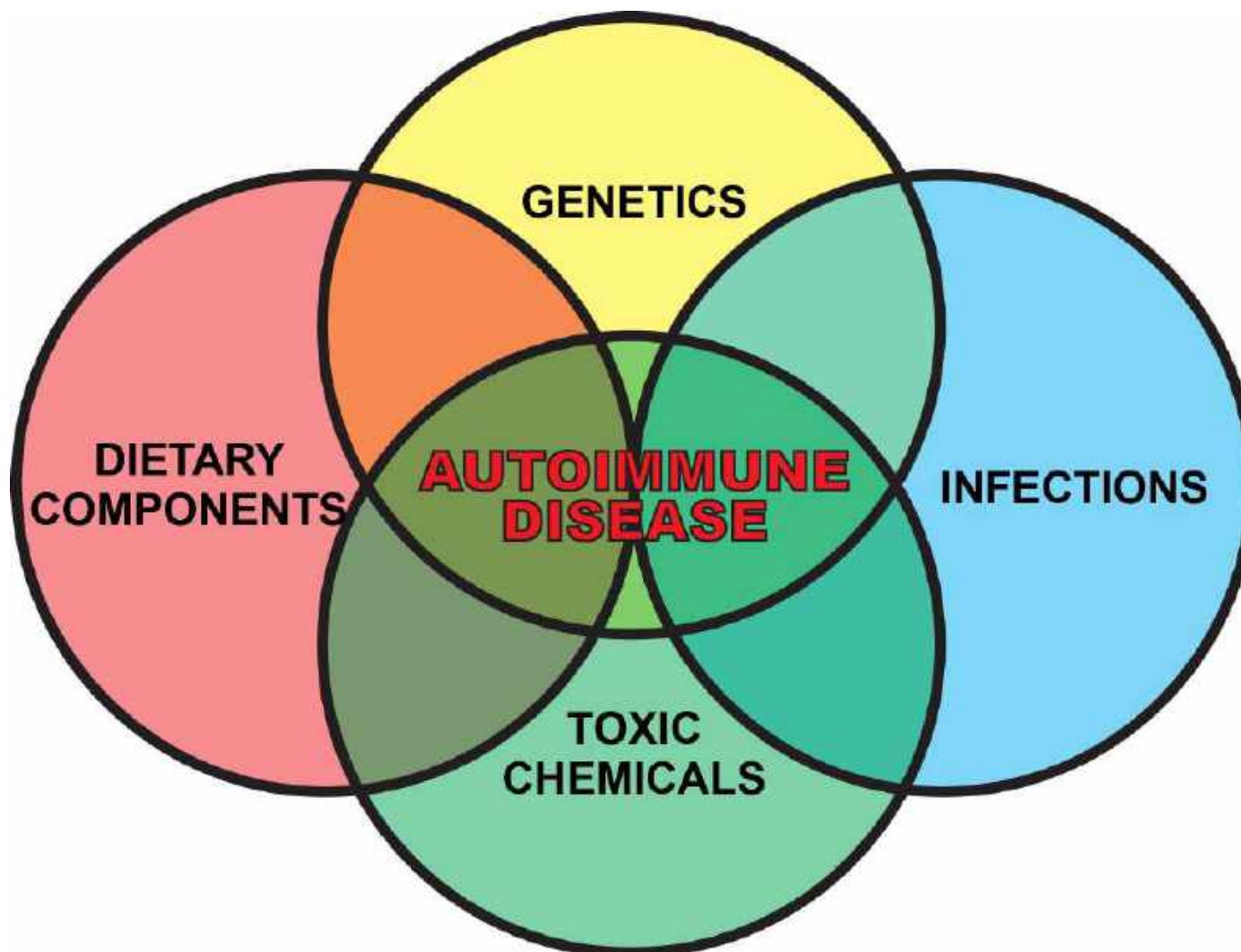
Aristo Vojdani, PhD, MSc, CLS
Cyrex Labs LLC

NMI BANT 2021, May 22, 2021



Objectives

- To learn the mechanisms by which environmental factors can affect various components of the immune system, which can set the stage for various autoimmune diseases that are detected in about 10% of the world population
- To learn how to assess changes in the humoral and cellular components of the immune system at the earliest stages of inflammatory and autoimmune disorders
- To learn how the measurement of changes in various lymphocyte immunotypes and predictive antibodies could be used as an early warning to prevent the induction and progression of inflammatory and autoimmune disorders



Factors that contribute to autoimmune disease

Environmental Exposures and Autoimmune Diseases: Contribution of Gut Microbiome

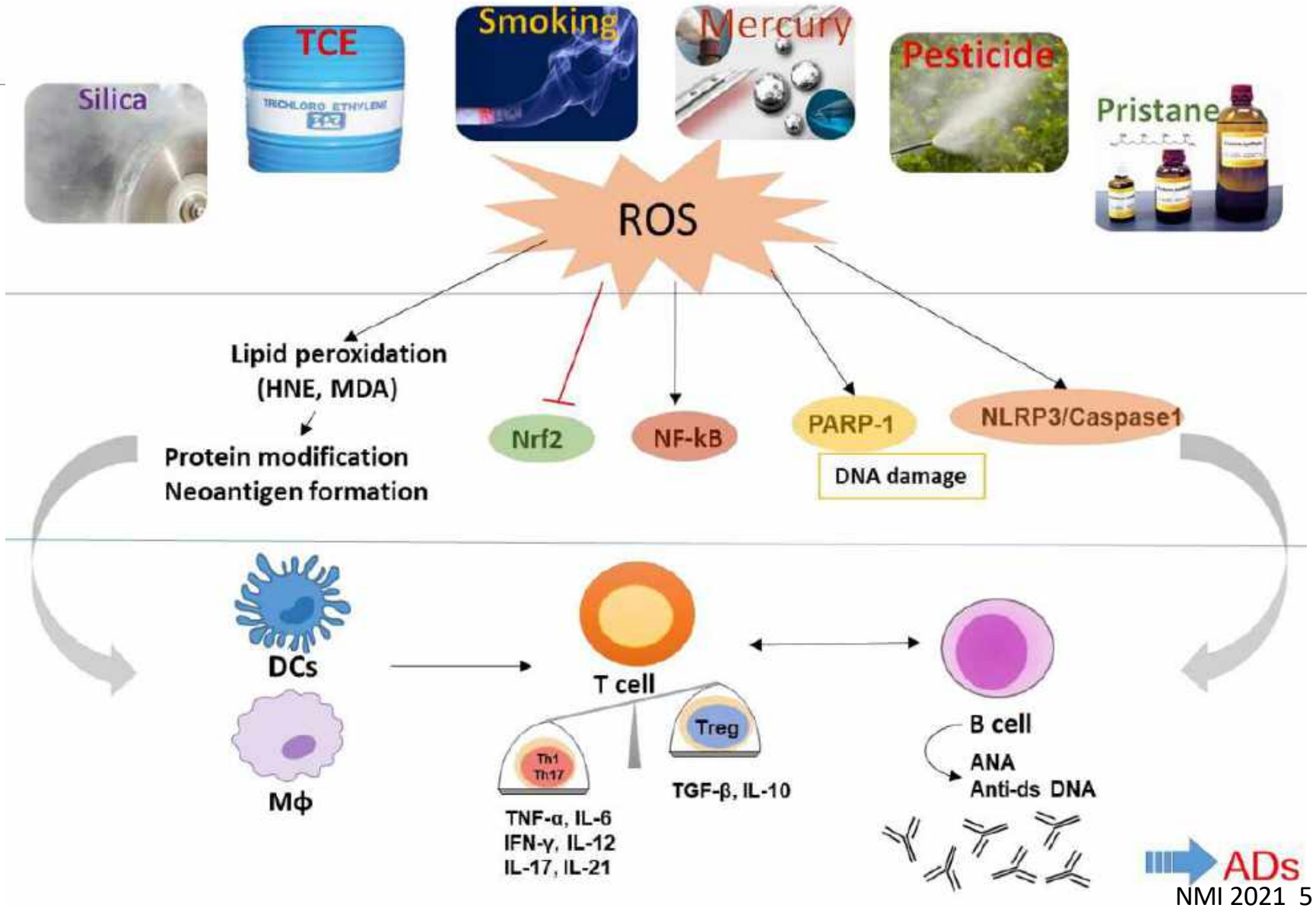
M. Firoze Khan and Hui Wang*

Dysbiosis of the gut microbiome is another important environmental factor that has been linked to the onset of different ADs. Altered microbiota composition is associated with impaired intestinal barrier function and dysregulation of mucosal immune system.

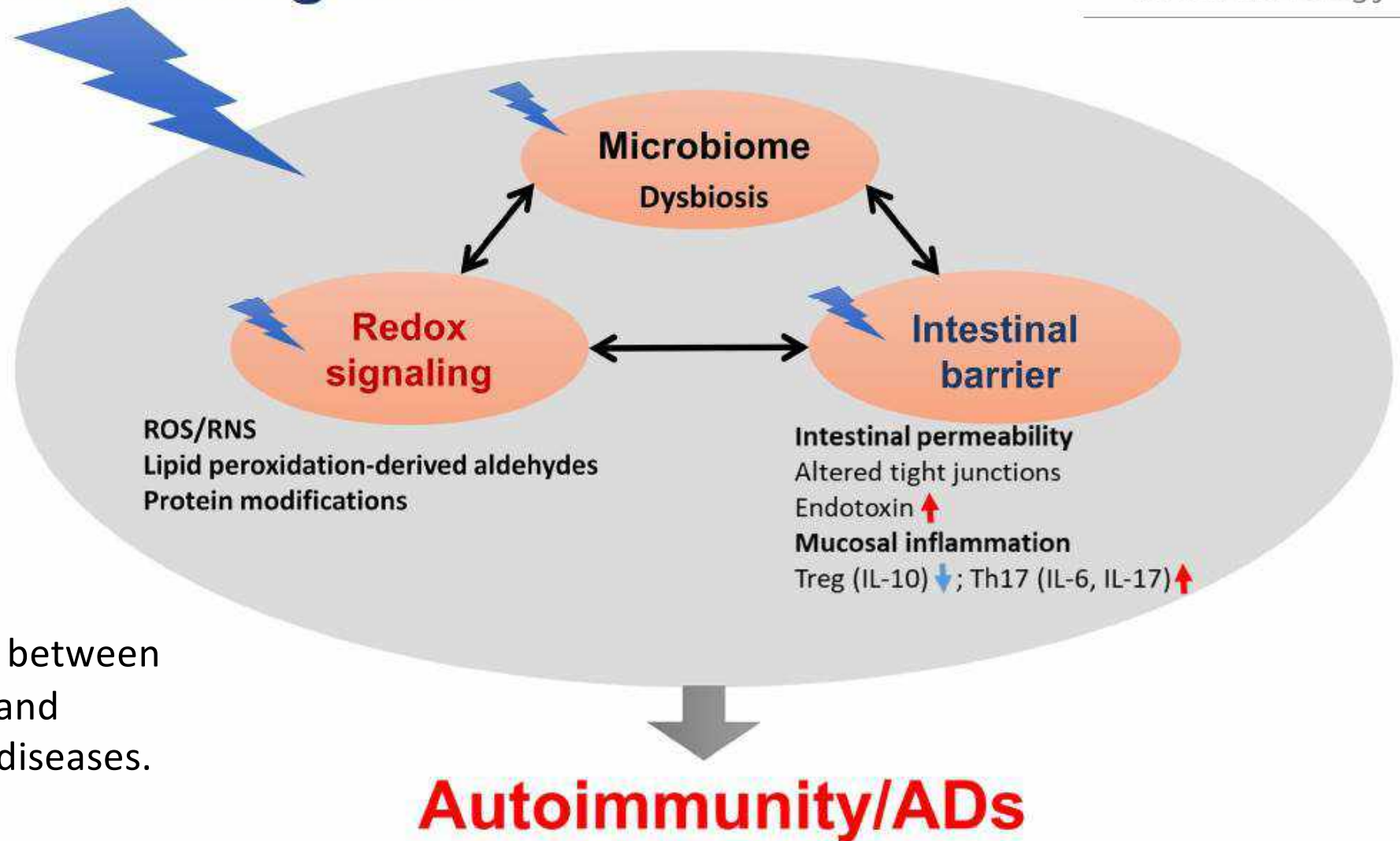
However, potential mechanisms by which these environmental agents contribute to the disease pathogenesis remains largely

The most challenging aspect of autoimmunity is to identify the early events that trigger immune dysregulation and autoimmunity.

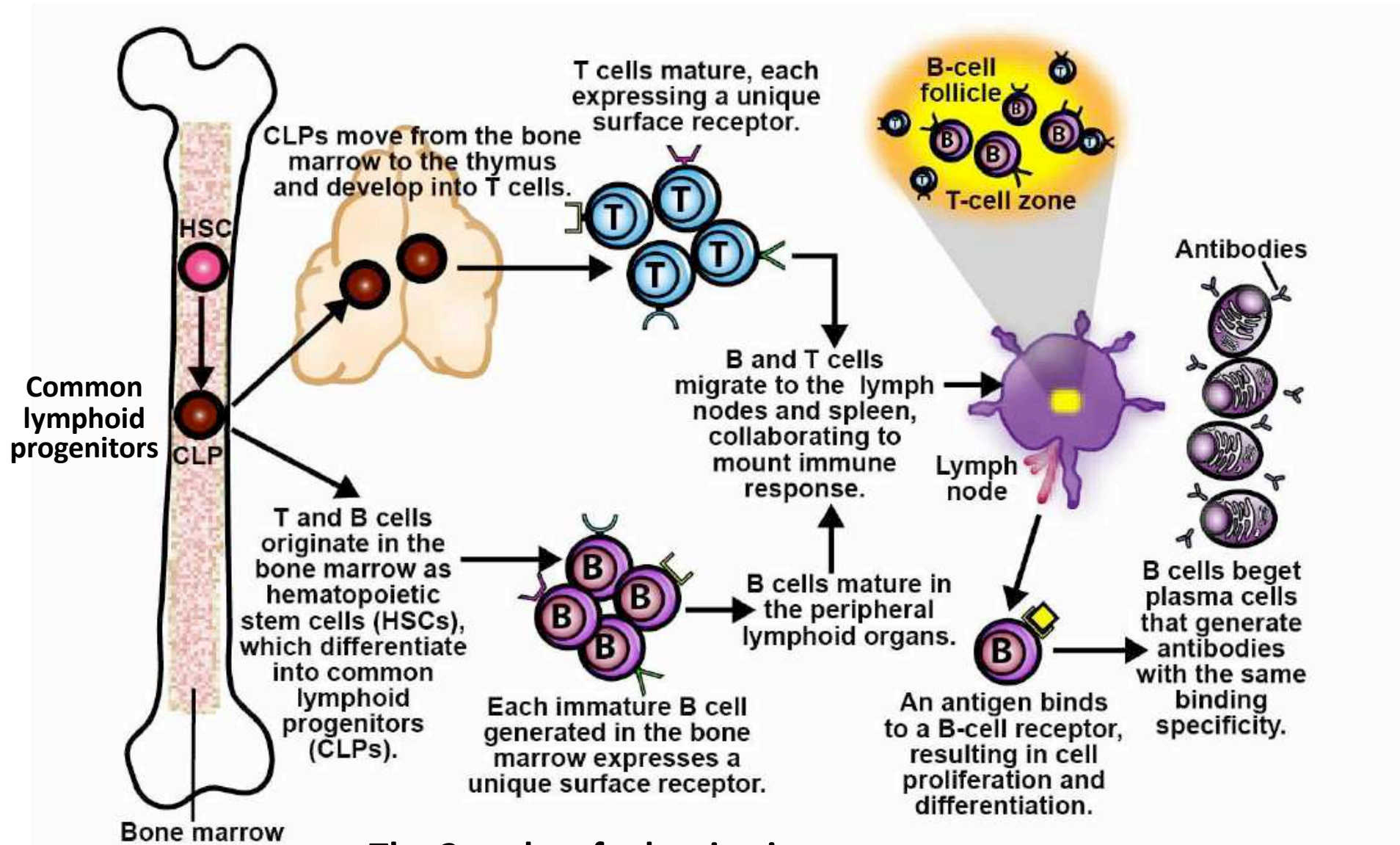
Proposed mechanistic pathways linking environmental agents to the development of **autoimmune diseases**.



Environmental Agents

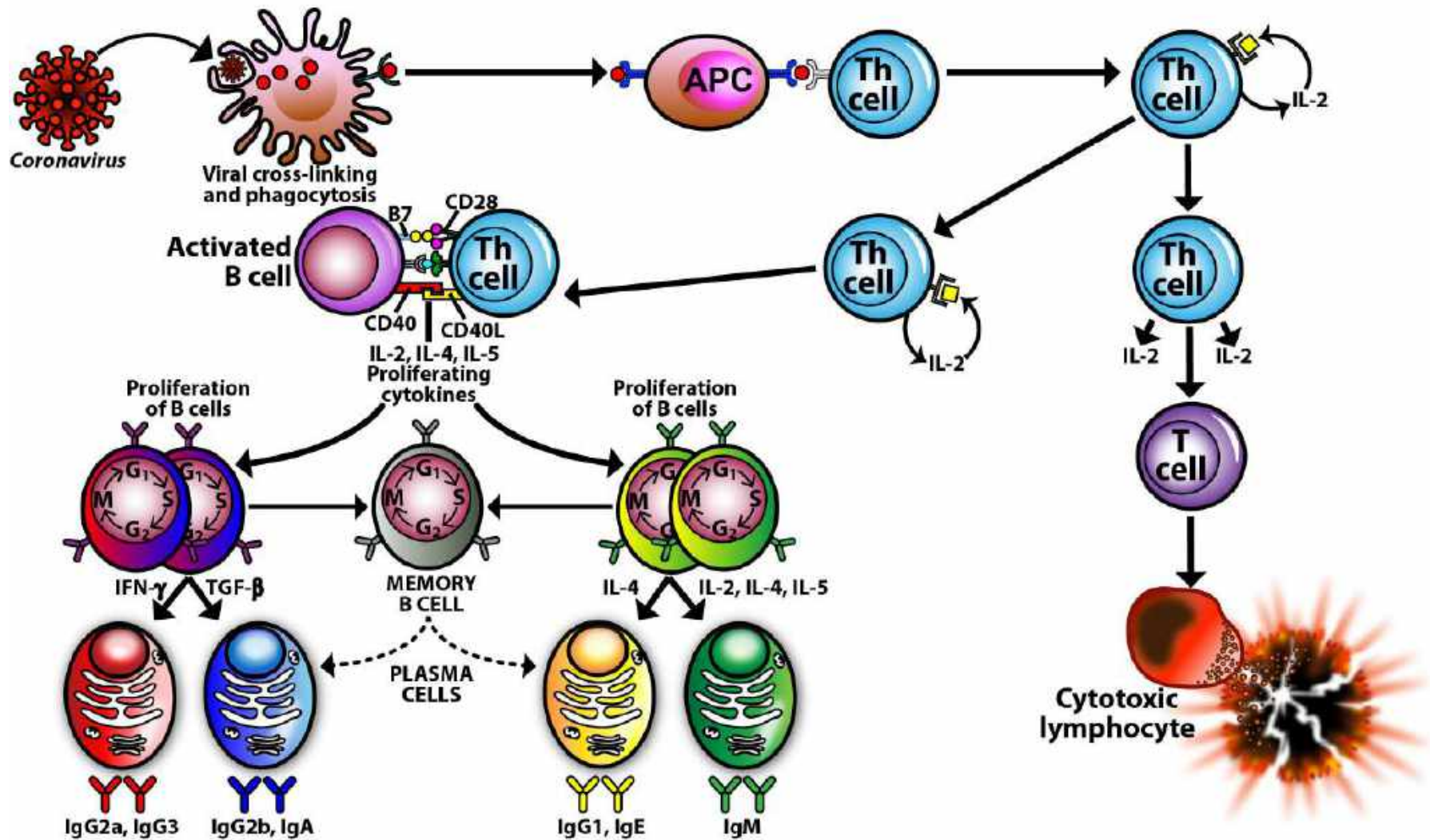


Proposed link between
gut dysbiosis and
autoimmune diseases.



The 2 paths of adaptive immune response





The immune system is a complex network of organs, special cells and substances that interact to protect the body against infections and other diseases.



The immune system in people is as diverse as height, beauty, intelligence and other human features.
Our **genomes**, **lifestyles** and **exposomes** affect our immunotypes.



These immunotypes can be determined by
FLOW CYTOMETRY

Definitions

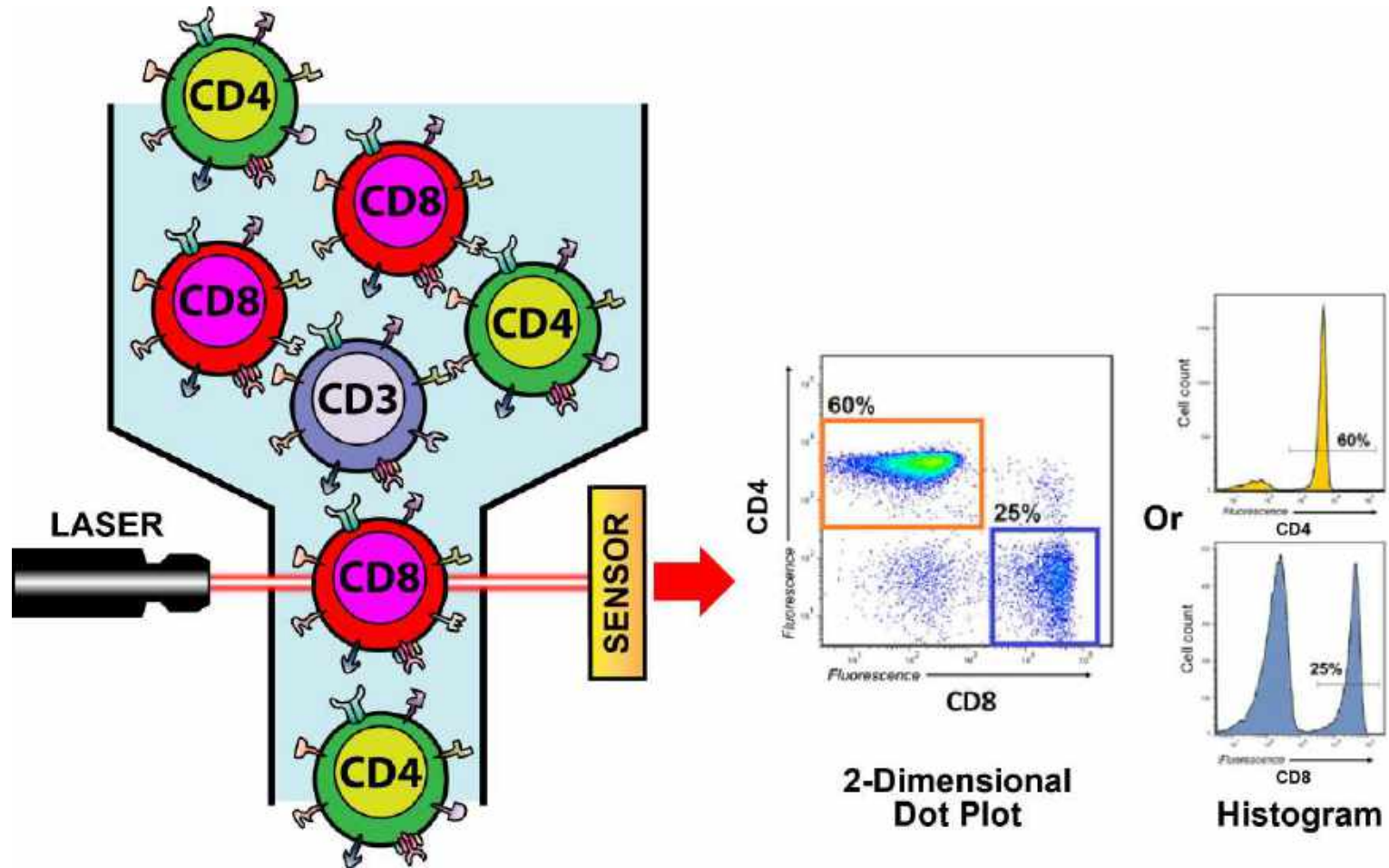
- **Flow cytometry** – the study of cells as they move in fluid suspension, allowing multiple measurements to be made per cell
- **FACS™** – fluorescence-activated cell sorting



How Flow Cytometry Works

- ❖ Cells to be analyzed are suspended in liquid and fluorescently labeled with different fluorescent colors as needed.
- ❖ This sheath fluid is pumped through a narrow aperture tube, forcing the cells to move one by one through a laser beam.
- ❖ Light is refracted around each cell at different angles to specific detectors, enabling various kinds of data to be transmitted.
- ❖ This data is fed into a computer, and can now be read and analyzed as percentages of T cells, B cells and other lymphocyte subtypes.





Flow cytometry can use CD-specific fluorescent labeling to differentiate, classify and count different kinds of cells, such as CD4, CD8, Th1, Th2, Th17, Treg and more.

What is immunotyping?

Quantification by flow cytometry of an individual's lymphocyte subsets into an identifiable pattern.

- *Matthew D et al. Science, 369, 1209, 2020.*

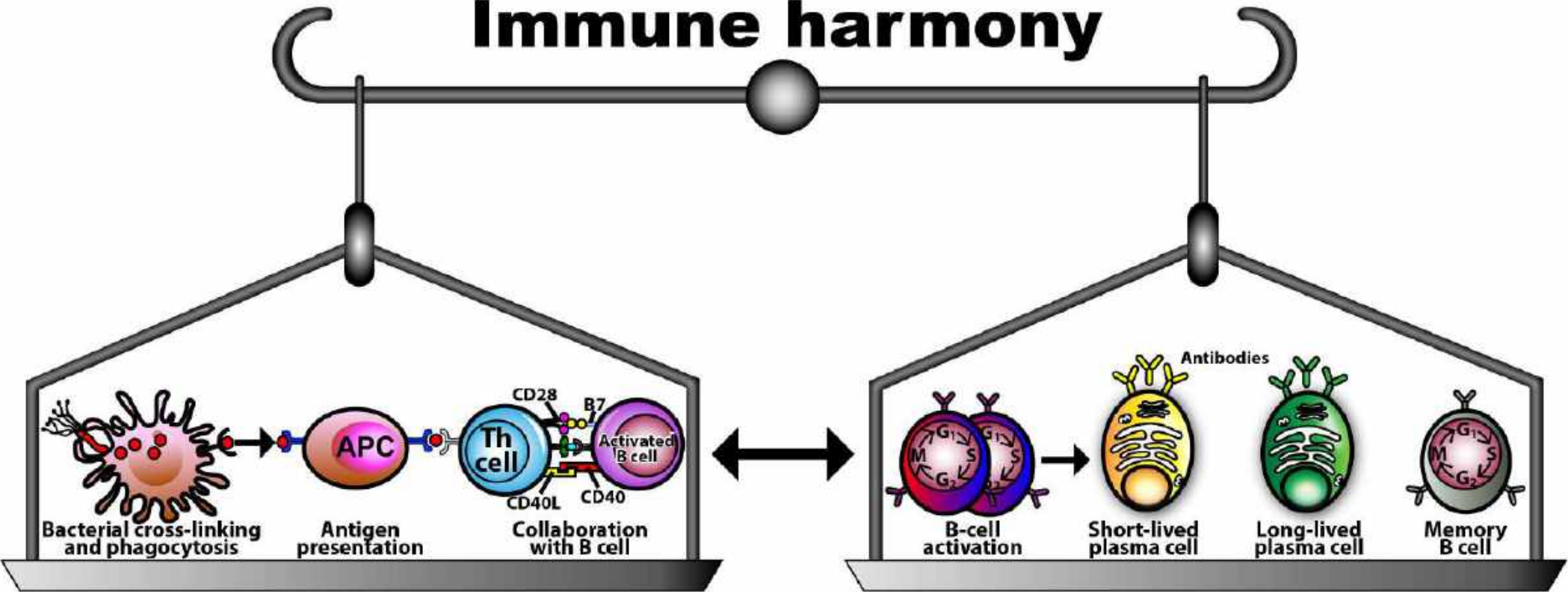


Summary statistics for T cell subsets test

	Discharged	Death
Total T Cells Percentage (%)	64.0	52.7
Total T Cells Counts (cells/ μ l)	773	228
Helper T Cells Percentage (%)	37.2	33.8
Helper T Cells Counts (cells/ μ l)	457	139
Suppressor T Cells Percentage (%)	25.0	17.3
Suppressor T Cells Counts (cells/ μ l)	297	80.9
Th/Tsc (Helper Suppressor Ratio)	1.71	2.41
Total Lymphocyte Counts (cells/ μ l)	1160	425

“Patients with a less damaged immune system at the time of hospitalization had higher chance of recovery.”

Immune harmony



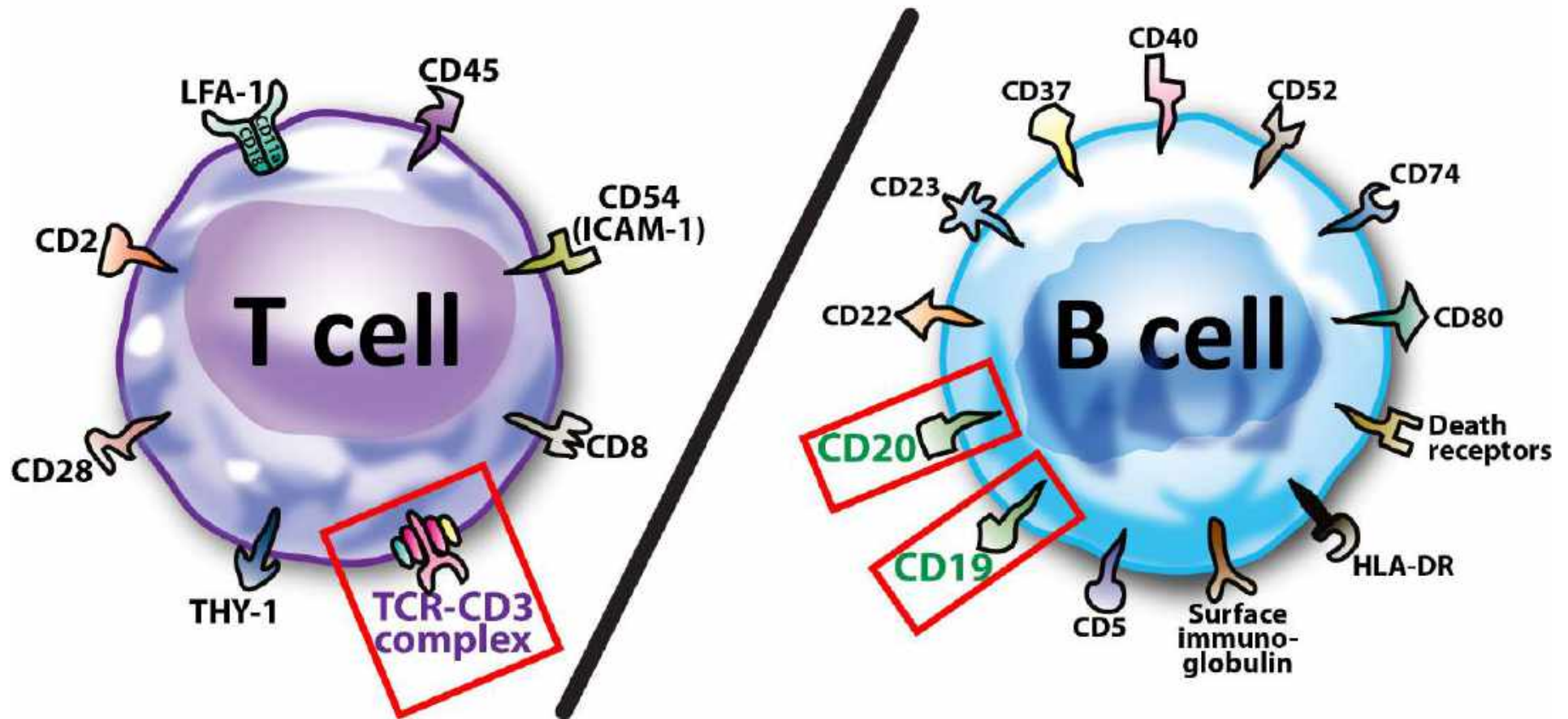
1. Completely normal immunotype.



Normal Results

TEST	RESULTS				Units
	Low	In-range	High	Reference Range	
Lymphocyte MAP Comprehensive Immunophenotyping of Lymphocytes					
Total WBC		3991		3400-9100	Cells/mcl
% Lymphocyte		36.5		20-40	%
Total Lymphocyte		1458		1200-3200	Cells/mcl
% T Cell		72.5		46-82	%
Total T Cell		1057		440-1600	Cells/mcl
% B Cell		12.1		6-18	%
Total B Cell		177		90-400	Cells/mcl
T Cell/B Cell Ratio		6		4-11	Ratio
% T-Helper (CD4) Cell		49.4		28-55	%
Total T-Helper (CD4) Cell		720		500-1100	Cells/mcl
% Cytotoxic (CD8) T Cell		19.9		10-30	%
Total Cytotoxic (CD8) T Cell		290		200-500	Cells/mcl
CD4/CD8 Ratio		2.5		1-4	Ratio
% T-Helper-1 Cell		30.4		18-38	%
Total T-Helper-1 Cell		398		150-550	Cells/mcl
% T-Helper-2 Cell		6.5		6-12	%
Total T-Helper-2 Cell		86		70-150	Cells/mcl
TH1/TH2 Ratio		4.7		1-5	Ratio
% T-Helper-17		4.8		2-7	%
Total T-Helper-17		63		30-90	Cells/mcl
% Regulatory T Cell		2.5		1-4	%
Total Regulatory T Cell		33		10-50	Cells/mcl
TH17/TREG Ratio		1.9		1-3	Ratio
% NK Cell		8.8		3-15	%
Total NK Cell		128		60-220	Cells/mcl
% Cytotoxic NK cells		8		2-10	%
Total Cytotoxic NK cells		116		30-200	Cells/mcl
% NKT		2.4		1-6	%
Total NKT		35		10-120	Cells/mcl

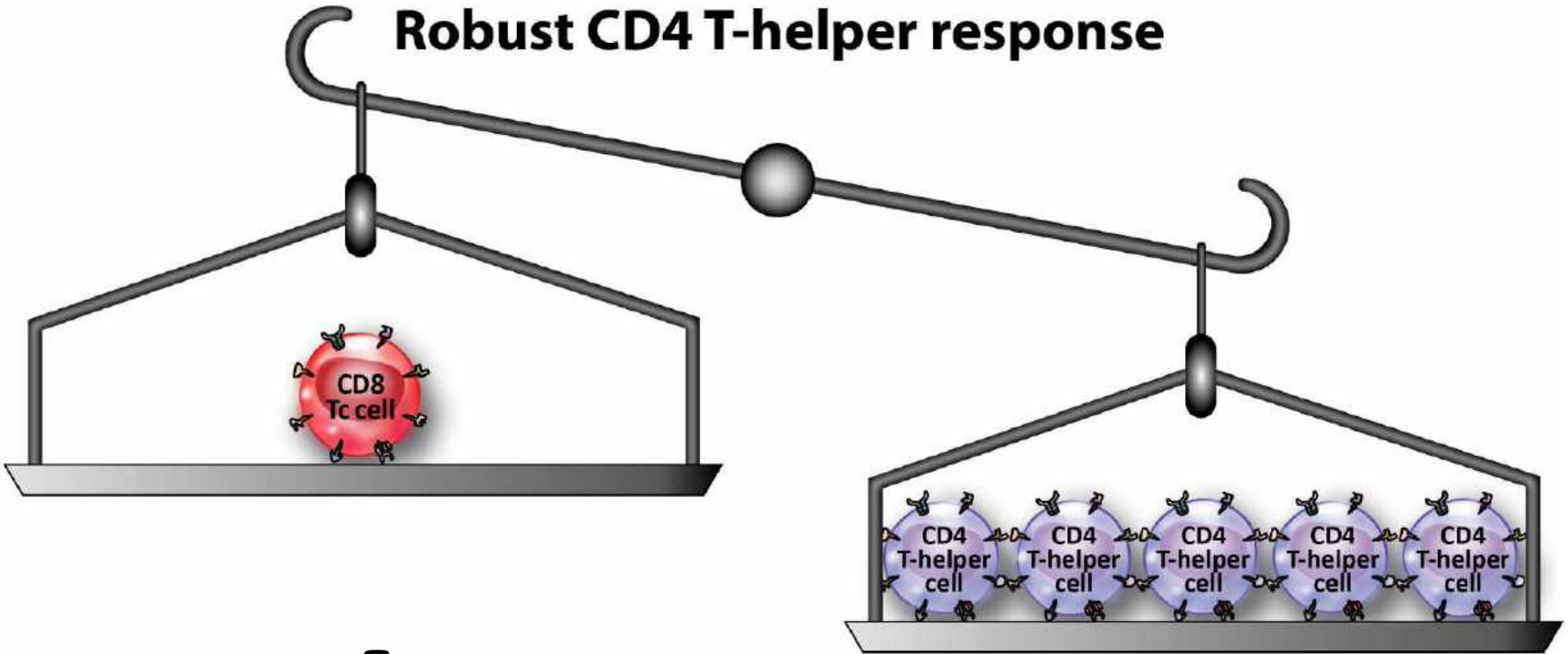
T cell/B cell Ratio



Abnormal T Cell/B Cell Ratio

TEST	Low	In-range	High	Reference Range	Units
Lymphocyte MAP Comprehensive Immunophenotyping of Lymphocytes					
Total WBC		5118		3400-9100	Cells/mcl
% Lymphocyte		33.7		20-40	%
Total Lymphocyte		1722		1200-3200	Cells/mcl
% T Cell			83	46-82	%
Total T Cell		1304		440-1600	Cells/mcl
% B Cell		6.1		6-18	%
Total B Cell		188		90-400	Cells/mcl
T Cell/B Cell Ratio			13.6	4-11	Ratio
% T-Helper (CD4) Cell			55.8	28-55	%
Total T-Helper (CD4) Cell		957		500-1100	Cells/mcl
% Cytotoxic (CD8) T Cell		19		10-30	%
Total Cytotoxic (CD8) T Cell		327		200-500	Cells/mcl
CD4/CD8 Ratio		2.9		1-4	Ratio
% T-Helper-1 Cell		35.8		18-38	%
Total T-Helper-1 Cell			600	150-550	Cells/mcl
% T-Helper-2 Cell		7.9		6-12	%
Total T-Helper-2 Cell		132		70-150	Cells/mcl
TH1/TH2 Ratio		4.5		1-5	Ratio
% T-Helper-17		5.3		2-7	%
Total T-Helper-17		89		30-90	Cells/mcl
% Regulatory T Cell		1.9		1-4	%
Total Regulatory T Cell		32		10-50	Cells/mcl
Th17/Treg Ratio		2.8		1-3	Ratio
% NK Cell		5.9		3-15	%
Total NK Cell		102		60-220	Cells/mcl
% Cytotoxic NK cells		5.1		2-10	%
Total Cytotoxic NK cells		88		30-200	Cells/mcl
% NKT	0.9			1-6	%
Total NKT		16		10-120	Cells/mcl

Robust CD4 T-helper response



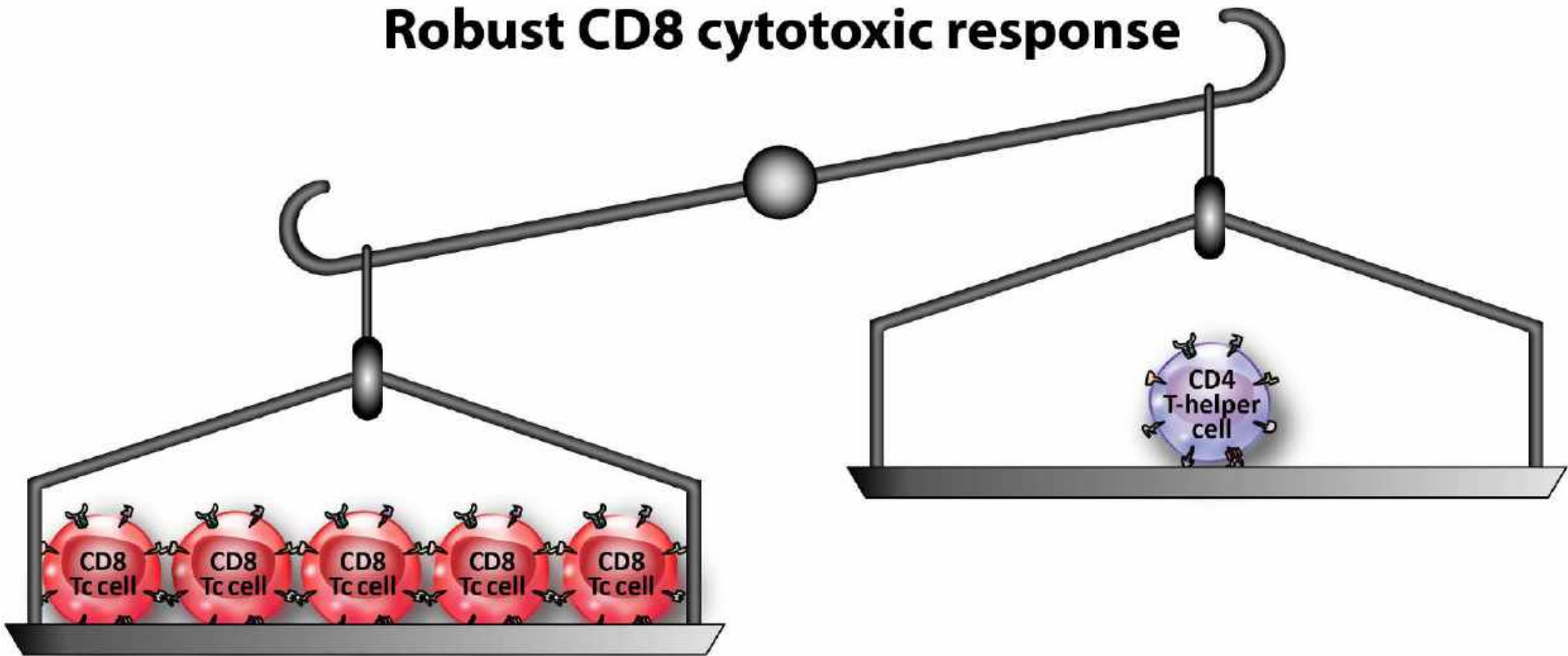
- 4.** Immunotype with high numbers of CD4 Th cells and low numbers of CD8 cytotoxic cells. May develop autoimmune disease years in the future.



High CD4/CD8 Ratio

TEST	RESULTS				
	Low	In-range	High	Reference Range	Units
Lymphocyte MAP Comprehensive Immunophenotyping of Lymphocytes					
Total WBC		6234		3400-9100	Cells/mcl
% Lymphocyte		30.8		20-40	%
Total Lymphocyte		1921		1200-3200	Cells/mcl
% T Cell		75.8		46-82	%
Total T Cell		1455		440-1600	Cells/mcl
% B Cell		9.2		6-18	%
Total B Cell		176		90-400	Cells/mcl
T Cell/B Cell Ratio		8.3		4-11	Ratio
% T-Helper (CD4) Cell			61.9	20-50	%
Total T-Helper (CD4) Cell			1189	500-1100	Cells/mcl
% Cytotoxic (CD8) T Cell		11.2		10-30	%
Total Cytotoxic (CD8) T Cell		214		200-500	Cells/mcl
CD4/CD8 Ratio			5.6	1-4	Ratio
% T-Helper-1 Cell			45.7	18-38	%
Total T-Helper-1 Cell			829	50-400	Cells/mcl
% T-Helper-2 Cell		11.5		6-12	%
Total T-Helper-2 Cell			208	70-150	Cells/mcl
TH1/TH2 Ratio		4		1-5	Ratio
% T-Helper-17	1.4			2-7	%
Total T-Helper-17	25			30-90	Cells/mcl
% Regulatory T Cell		2.4		1-4	%
Total Regulatory T Cell		43		10-50	Cells/mcl
Th17/Treg Ratio	0.6			1-3	Ratio
% NK Cell		8.2		3-15	%
Total NK Cell		158		60-220	Cells/mcl
% Cytotoxic NK cells		7.5		2-10	%
Total Cytotoxic NK cells		144		30-200	Cells/mcl
% NKT	0.9			1-6	%
Total NKT		16		10-120	Cells/mcl

Robust CD8 cytotoxic response



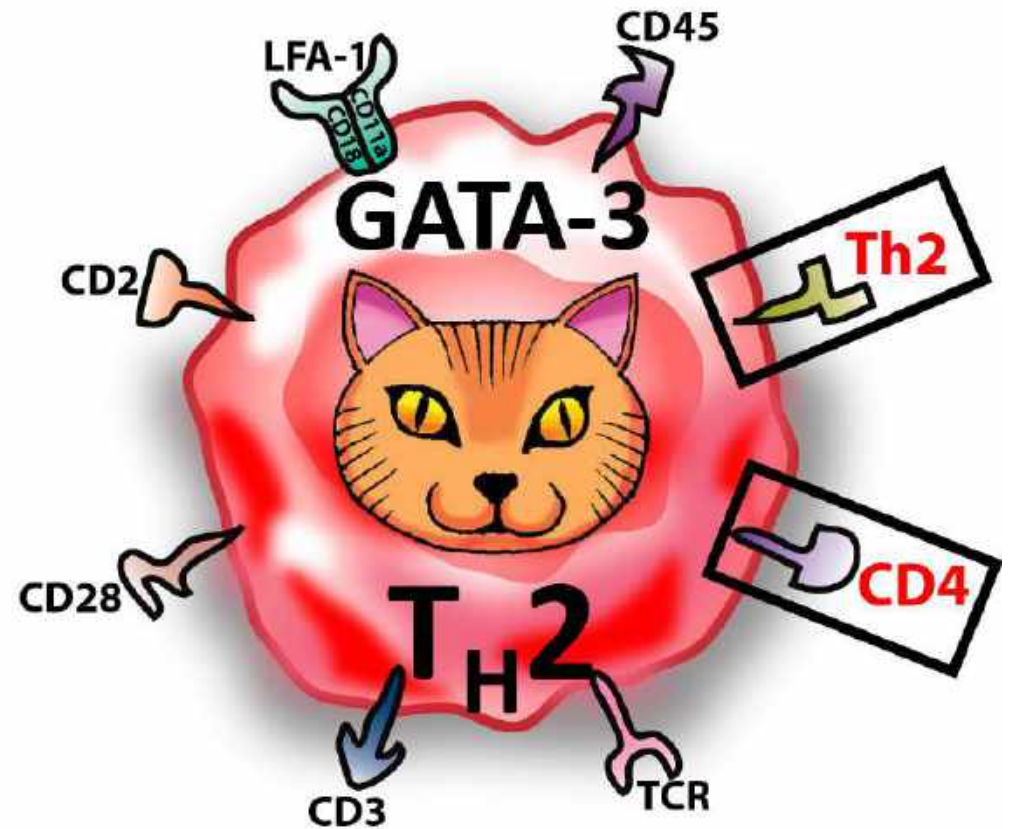
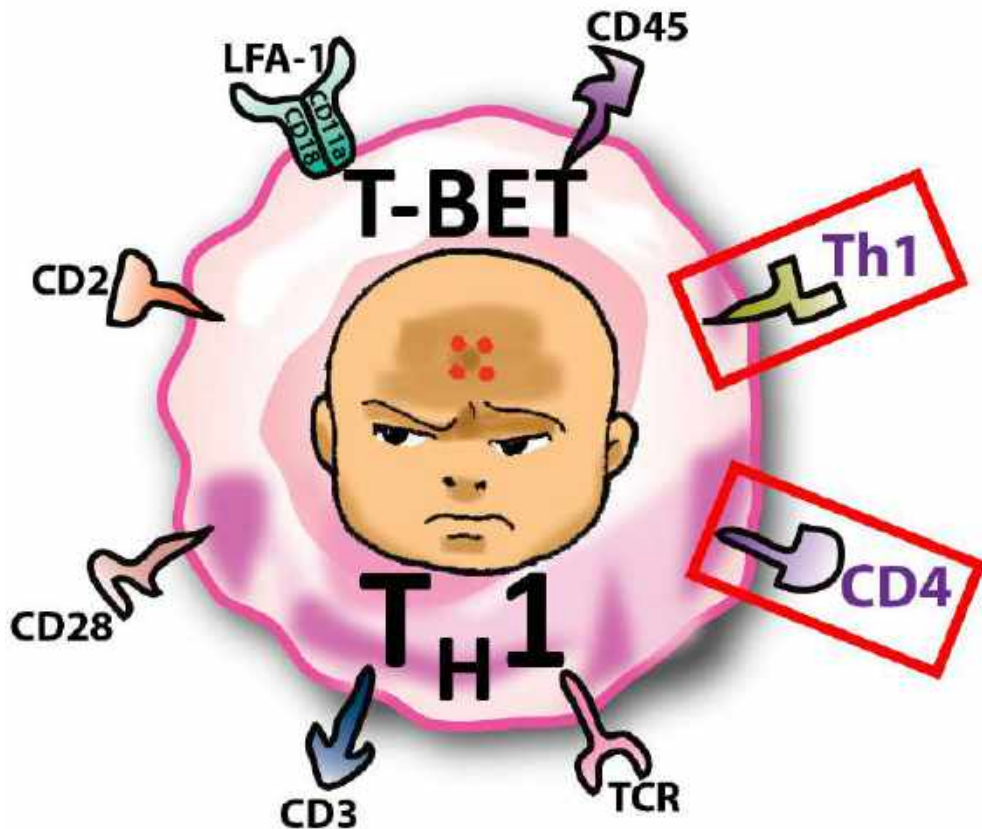
- 5** • Immunotype with high numbers of CD8 cells compared to low numbers of CD4 cells.

Associated with immune dysfunction, immune deficiency (HIV), and cancer



Low CD4/CD8 Ratio

TEST	RESULTS				Units
	Low	In-range	High	Reference Range	
Lymphocyte MAP Comprehensive Immunophenotyping of Lymphocytes					
Total WBC		5118		3400-9100	Cells/mcl
% Lymphocyte		33.7		20-40	%
Total Lymphocyte		1722		1200-3200	Cells/mcl
% T Cell		75.7		46-82	%
Total T Cell		1304		440-1600	Cells/mcl
% B Cell		10.9		6-18	%
Total B Cell		188		90-400	Cells/mcl
T Cell/B Cell Ratio		6.9		4-11	Ratio
% T-Helper (CD4) Cell	17.5			20-50	%
Total T-Helper (CD4) Cell	301			500-1100	Cells/mcl
% Cytotoxic (CD8) T Cell			41	10-30	%
Total Cytotoxic (CD8) T Cell			706	200-500	Cells/mcl
CD4/CD8 Ratio	0.43			1-4	Ratio
% T-Helper-1 Cell		35.8		18-38	%
Total T-Helper-1 Cell			600	150-550	Cells/mcl
% T-Helper-2 Cell		7.9		6-12	%
Total T-Helper-2 Cell		132		70-150	Cells/mcl
TH1/TH2 Ratio		4.5		1-5	Ratio
% T-Helper-17		5.3		2-7	%
Total T-Helper-17		89		30-90	Cells/mcl
% Regulatory T Cell		1.9		1-4	%
Total Regulatory T Cell		32		10-50	Cells/mcl
Th17/Treg Ratio		2.8		1-3	Ratio
% NK Cell		5.9		3-15	%
Total NK Cell		102		60-220	Cells/mcl
% Cytotoxic NK cells		5.1		2-10	%
Total Cytotoxic NK cells		88		30-200	Cells/mcl
% NKT	0.9			1-6	%
Total NKT		16		10-120	Cells/mcl



CD4⁺ T cells are further divided into subsets, including T-helper-1 (Th1) and T-helper-2 (Th2)



Abnormal Th1/Th2 Ratio

TEST	RESULTS				
	Low	In-range	High	Reference Range	Units
Lymphocyte MAP Comprehensive Immunophenotyping of Lymphocytes					
Total WBC		5977		3400-9100	Cells/mcl
% Lymphocyte		37.1		20-40	%
Total Lymphocyte		2219		1200-3200	Cells/mcl
% T Cell		68.4		46-82	%
Total T Cell		1517		440-1600	Cells/mcl
% B Cell		13		6-18	%
Total B Cell		287		90-400	Cells/mcl
T Cell/B Cell Ratio		5.3		4-11	Ratio
% T-Helper (CD4) Cell		45.4		28-55	%
Total T-Helper (CD4) Cell		1007		500-1100	Cells/mcl
% Cytotoxic (CD8) T Cell		19.4		10-30	%
Total Cytotoxic (CD8) T Cell		430		200-500	Cells/mcl
CD4/CD8 Ratio		2.3		1-4	Ratio
% T-Helper-1 Cell		33.1		18-38	%
Total T-Helper-1 Cell			768	150-550	Cells/mcl
% T-Helper-2 Cell	4.1			6-12	%
Total T-Helper-2 Cell		95		70-150	Cells/mcl
Th1/Th2 Ratio			8	1-5	Ratio
% T-Helper-17		3.7		2-7	%
Total T-Helper-17		85		30-90	Cells/mcl
% Regulatory T Cell		1.8		1-4	%
Total Regulatory T Cell		42		10-50	Cells/mcl
Th17/Treg Ratio		2.1		1-3	Ratio
% NK Cell		7.5		3-15	%
Total NK Cell		166		60-220	Cells/mcl
% Cytotoxic NK cells		7		2-10	%
Total Cytotoxic NK cells		154		30-200	Cells/mcl
% NKT			7.3	1-6	%
Total NKT			161	10-120	Cells/mcl

What Do My Th1/Th2 Ratio Test Results Mean?

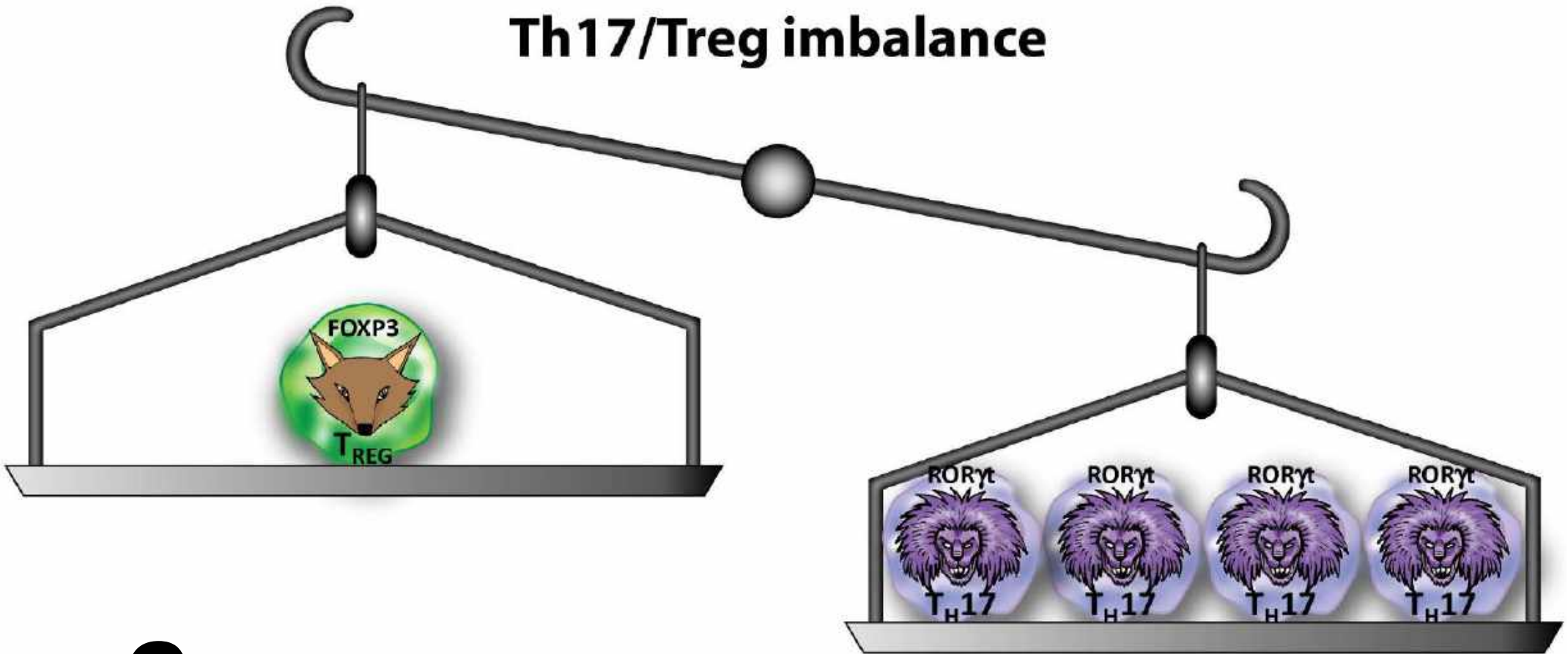


**Th1/Th2
Ratio**

The Th1/Th2 ratio measures the proportion of Th1 cells to Th2 cells. The resulting value can help predict the likely course of a disease. The normal reference range for Th1/Th2 ratio is 1-5. The greater the numbers go higher than 5, i.e., a Th1/Th2 ratio of 6.0 or 8.0, the greater the probability of immune activation and autoimmunity.



Th17/Treg imbalance



- 9** • Immunotype with low Tregs and elevated Th17, producing IL-17 and IL-2, which have broad inflammatory effects.

May result in autoimmunities, allergies, hypersensitivities and inflammatory diseases.



Abnormal Th17/Treg Ratio

TEST	RESULTS				
	Low	In-range	High	Reference Range	Units
Lymphocyte MAP Comprehensive Immunophenotyping of Lymphocytes					
Total WBC		5417		3400-9100	Cells/mcl
% Lymphocyte		38.4		20-40	%
Total Lymphocyte		2080		1200-3200	Cells/mcl
% T Cell		68.4		46-82	%
Total T Cell		1422		440-1600	Cells/mcl
% B Cell		14.4		6-18	%
Total B Cell		299		90-400	Cells/mcl
T Cell/B Cell Ratio		4.8		4-11	Ratio
% T-Helper (CD4) Cell		51.1		28-55	%
Total T-Helper (CD4) Cell		1062		500-1100	Cells/mcl
% Cytotoxic (CD8) T Cell		14		10-30	%
Total Cytotoxic (CD8) T Cell		291		200-500	Cells/mcl
CD4/CD8 Ratio		3.7		1-4	Ratio
% T-Helper-1 Cell		32.3		18-38	%
Total T-Helper-1 Cell			732	150-550	Cells/mcl
% T-Helper-2 Cell		7.2		6-12	%
Total T-Helper-2 Cell			163	70-150	Cells/mcl
TH1/TH2 Ratio		4.5		1-5	Ratio
% T-Helper-17		7		2-7	%
Total T-Helper-17			114	30-90	Cells/mcl
% Regulatory T Cell		1.7		1-4	%
Total Regulatory T Cell		38		10-50	Cells/mcl
Th17/Treg Ratio			4.1	1-3	Ratio
% NK Cell		7.1		3-15	%
Total NK Cell		148		60-220	Cells/mcl
% Cytotoxic NK cells		6.8		2-10	%
Total Cytotoxic NK cells		142		30-200	Cells/mcl
% NKT		5.9		1-6	%
Total NKT			123	10-120	Cells/mcl

What Do My Th17/Treg Ratio Test Results Mean?

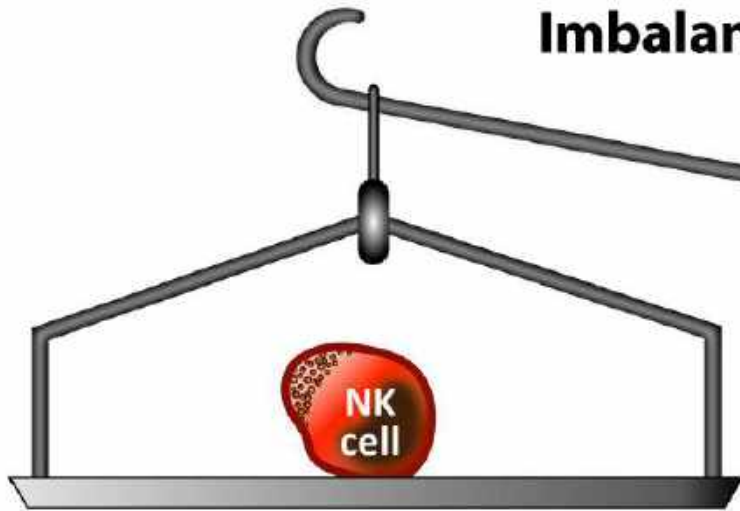


**Th17/Treg
Ratio**

The Th17/Treg ratio measures the proportion of Th17 cells to Treg cells. The resulting value can help predict the likely course of a disease. The normal reference range for Th17/Treg ratio is 1-3. The greater the numbers go higher than 3, i.e., a Th17/Treg ratio of 4.0 or 6.0, the greater the probability of immune activation and autoimmunity.

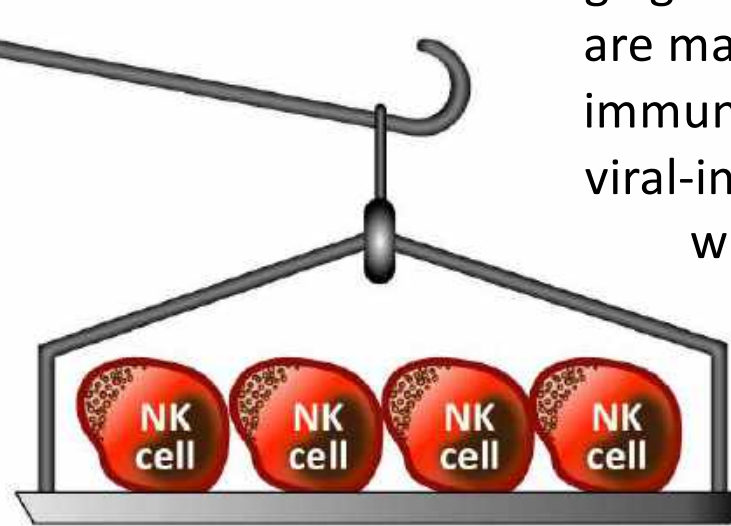


Imbalanced NK cells



Too few NK cells may lead to

- Viral and bacterial infection
- Breakdown in peripheral tolerance
- Autoimmune diseases
- Different types of cancer



Too many NK cells may lead to

- Healthy immunity
- Protection against viruses
- Protection against bacteria
- Prevention of autoimmunities
- Induction of autoimmunities
- Chronic, obstructive, pulmonary disorder
- Loss of pregnancy

Natural Killer (NK) cells are large granular lymphocytes that are major components of the immune system. They can kill viral-infected and tumor cells without pre-stimulation.

If NK cells are soldiers, the cytotoxic NK subset are like ninja assassins, killing even more efficiently than ordinary NK cells.

12.

• Immunotype with imbalanced NK cells.



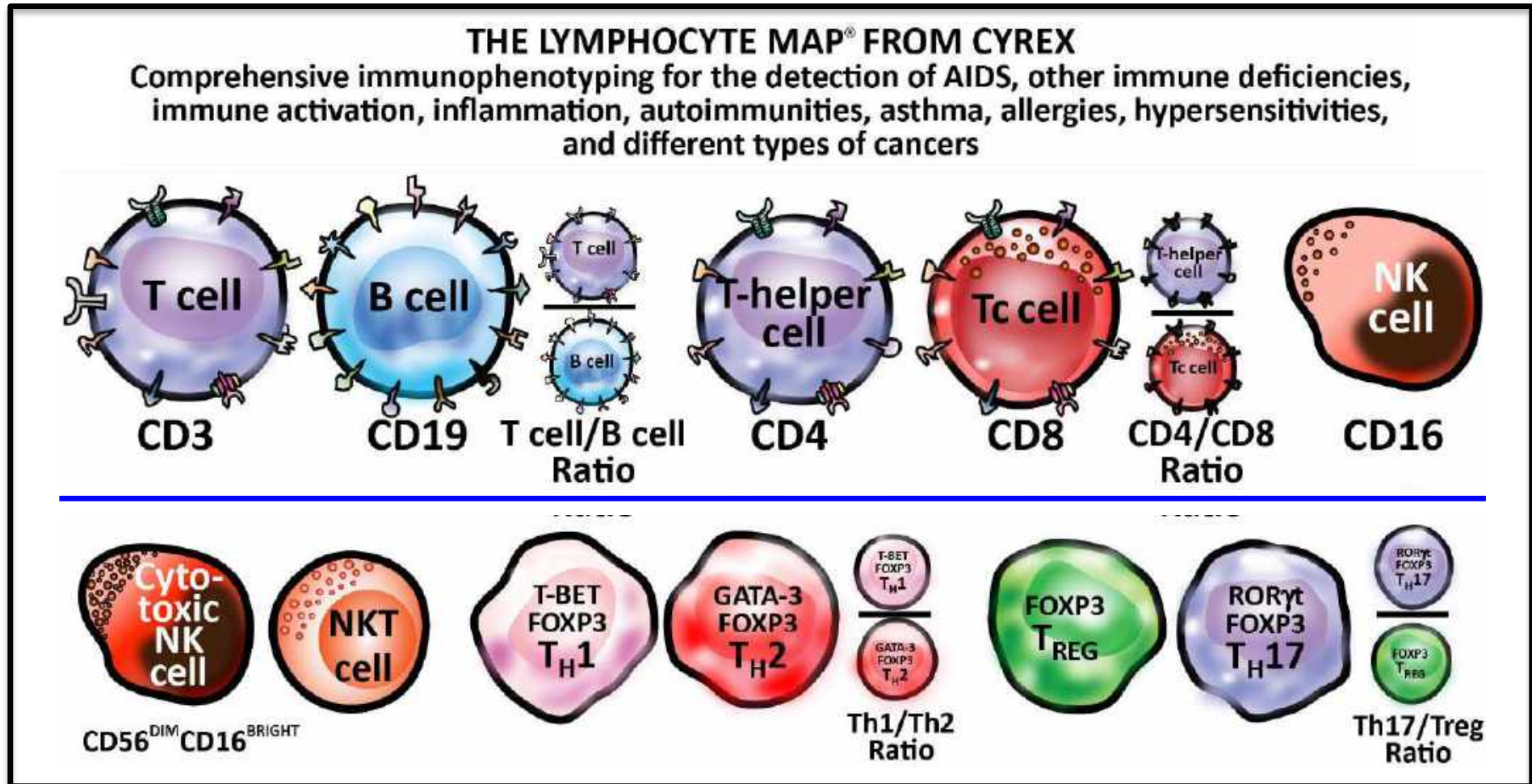
Elevated Cytotoxic NK Cell

TEST	RESULTS				
	Low	In-range	High	Reference Range	Units
Lymphocyte MAP Comprehensive Immunophenotyping of Lymphocytes					
Total WBC		4369		3400-9100	Cells/mcl
% Lymphocyte			42.5	20-40	%
Total Lymphocyte		1856		1200-3200	Cells/mcl
% T Cell		64.4		46-82	%
Total T Cell		1195		440-1600	Cells/mcl
% B Cell		8.8		6-18	%
Total B Cell		126		90-400	Cells/mcl
T Cell/B Cell Ratio		9.5		4-11	Ratio
% T-Helper (CD4) Cell		41.4		28-55	%
Total T-Helper (CD4) Cell		768		500-1100	Cells/mcl
% Cytotoxic (CD8) T Cell		21.1		10-30	%
Total Cytotoxic (CD8) T Cell		391		200-500	Cells/mcl
CD4/CD8 Ratio		2		1-4	Ratio
% T-Helper-1 Cell		24.5		18-38	%
Total T-Helper-1 Cell		423		150-550	Cells/mcl
% T-Helper-2 Cell		6.9		6-12	%
Total T-Helper-2 Cell		120		70-150	Cells/mcl
TH1/TH2 Ratio		3.5		1-5	Ratio
% T-Helper-17		4.5		2-7	%
Total T-Helper-17		77		30-90	Cells/mcl
% Regulatory T Cell		1.6		1-4	%
Total Regulatory T Cell		28		10-50	Cells/mcl
Th17/Treg Ratio		2.8		1-3	Ratio
% NK Cell		13.1		3-15	%
Total NK Cell			242	60-220	Cells/mcl
% Cytotoxic NK cells			12.3	2-10	%
Total Cytotoxic NK cells			228	30-200	Cells/mcl
% NKT		5.2		1-6	%
Total NKT		96		10-120	Cells/mcl

Combination Immunotype

TEST	RESULTS				Units
	Low	In-range	High	Reference Range	
Lymphocyte MAP Comprehensive Immunophenotyping of Lymphocytes					
Total WBC		6234		3400-9100	Cells/mcl
% Lymphocyte		30.8		20-40	%
Total Lymphocyte		1921		1200-3200	Cells/mcl
% T Cell		75.8		46-82	%
Total T Cell		1455		440-1600	Cells/mcl
% B Cell		9.2		6-18	%
Total B Cell		176		90-400	Cells/mcl
T Cell/B Cell Ratio		8.3		4-11	Ratio
% T-Helper (CD4) Cell			61.9	20-50	%
Total T-Helper (CD4) Cell			1189	500-1100	Cells/mcl
% Cytotoxic (CD8) T Cell		11.2		10-30	%
Total Cytotoxic (CD8) T Cell		214		200-500	Cells/mcl
CD4/CD8 Ratio			5.6	1-4	Ratio
% T-Helper-1 Cell			45.7	18-36	%
Total T-Helper-1 Cell			829	50-400	Cells/mcl
% T-Helper-2 Cell		11.5		6-12	%
Total T-Helper-2 Cell			208	70-150	Cells/mcl
TH1/TH2 Ratio		4		1-5	Ratio
% T-Helper-17	1.4			2-7	%
Total T-Helper-17	25			30-90	Cells/mcl
% Regulatory T Cell		2.4		1-4	%
Total Regulatory T Cell		43		10-50	Cells/mcl
Th17/Treg Ratio	0.6			1-3	Ratio
% NK Cell		8.2		3-15	%
Total NK Cell		158		60-220	Cells/mcl
% Cytotoxic NK cells		7.5		2-10	%
Total Cytotoxic NK cells		144		30-200	Cells/mcl
% NKT	0.9			1-6	%
Total NKT		16		10-120	Cells/mcl

The difference between partial immunophenotyping and comprehensive immunophenotyping (The Lymphocyte Map®)

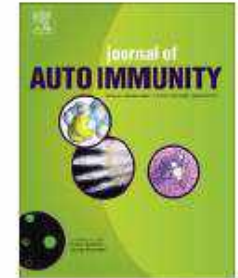




Contents lists available at [ScienceDirect](#)

Journal of Autoimmunity

journal homepage: www.elsevier.com/locate/jautimm



Development of autoantibodies precedes clinical manifestations of autoimmune diseases: A comprehensive review

Wen-Tao Ma^{a, b, c}, Christopher Chang^d, M. Eric Gershwin^{d, **}, Zhe-Xiong Lian^{a, b, e, *}

- **The etiology of autoimmune diseases is due to a combination of genetic predisposition and environmental factors that alter the expression of immune regulatory genes through various mechanisms including epigenetics.**
- **The presence of autoantibodies has been detected in most but not all autoimmune diseases before the appearance of clinical symptoms.**

autoimmune disease, but occasionally the severity as well. This observation is intriguing because it



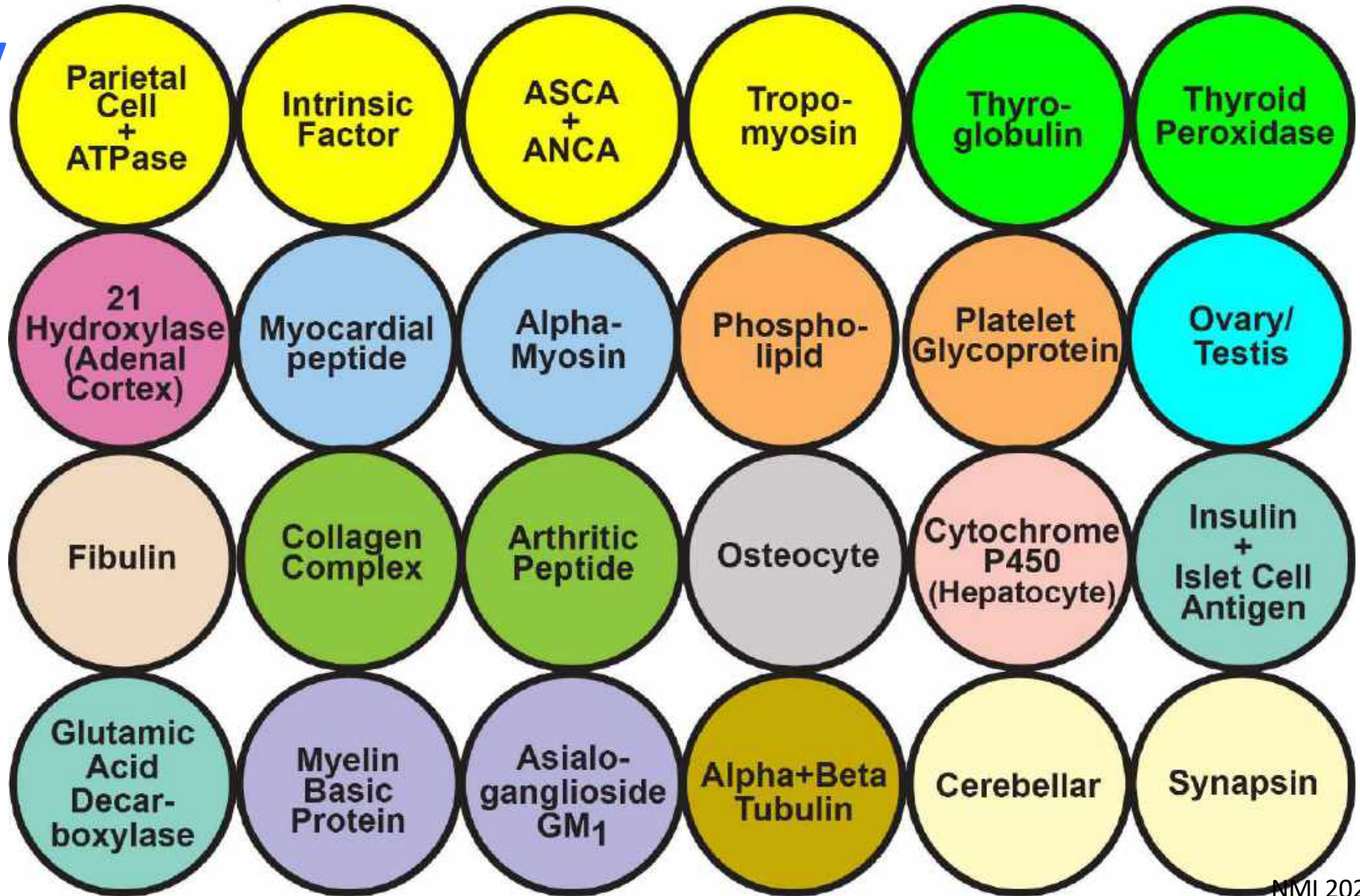
Copyright Aristo Vojdani

Autoantibodies Precede Clinical Manifestation of Autoimmune Diseases

Autoimmune Disease	Detected antibodies	Years preceding clinical disease
Rheumatoid Arthritis	IgM Anti-IgG, Anti-Citrullinated Peptide, Anti-Carbamylated Peptide	13.8 Years
Systemic Lupus Erythematosus	ANA, DSDNA, Ribonucleoprotein, Phospholipid, Type VII Collagen	8.1 Years
Multiple Sclerosis	Anti-Proteosome, Anti-MBP, Anti-MOG	3 Years
Type-1 Diabetes	Anti-Insulin, GAD-65, Tyrosine Phosphatase, ZNT8	10 Years
Autoimmune Thyroiditis	Anti-Thyroglobulin, Anti-Thyroid Peroxidase, Anti-TSHR	7 Years
Adrenal Autoimmunity	Anti-21-Hydroxylase, Anti-17-Hydroxylase	10 Years
Primary Biliary Cirrhosis	Anti-Mitochondrial Antibody	19 Years
Systemic Sclerosis	Anti-Topoisomerase-1, Anti-Centromere, Anti-RNA Polymerase-3	NR
Sjogren's Syndrome	ANA, RF, Anti-SSA, Anti-SSB	7 Years
Celiac Disease	Anti-Tissue Transglutaminases IgA, Anti-Gliadin IgA	NR
Crohn's Disease	ASCA, Outer Membrane-Porin C, Bacterial Flagellin	4.5 Years
Ulcerative Colitis	ANCA, Tropomyosin	4.5 Years

From Ma et al. J Autoimmun 2017; 83: 95-112

Array 5



Research Article

Received: 12 February 2014,

revised: 15 April 2014,

Accepted: 27 April 2014

(wileyonlinelibrary.com) DOI 10.1002/jat.3031

Elevated levels of antibodies against xenobiotics in a subgroup of healthy subjects

Aristo Vojdani^{a*}, Datis Kharrazian^b and Partha Sarathi Mukherjee^c

ABSTRACT: In spite of numerous research efforts, the exact etiology of autoimmune diseases remains largely unknown. Genetics and environmental factors, including xenobiotics, are believed to be involved in the induction of autoimmune disease. Some en-

Detection of antibodies against various protein adducts may indicate chronic exposure to these chemical haptens in about 20% of the tested individuals.

This protein adduct formation could be one of the mechanisms by which environmental chemicals induce autoimmune reactivity in a significant percentage of the population.

Keywords: haptens; autoimmunity; xenobiotics; chemicals; adducts



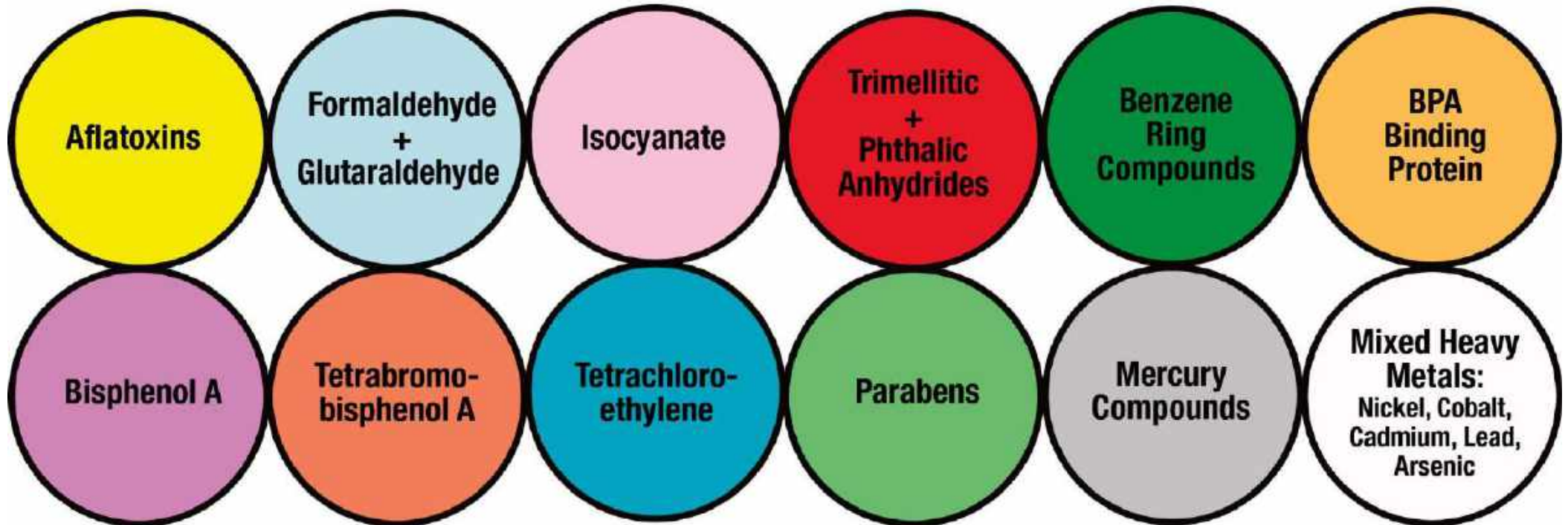
A. Vojdani

USA

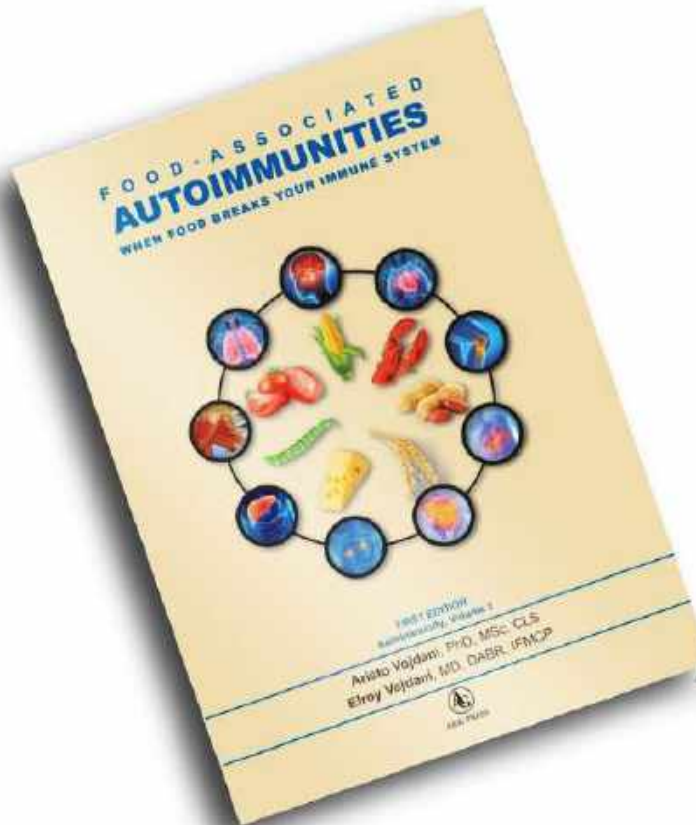
10TH INTERNATIONAL CONGRESS ON AUTOIMMUNITY
APRIL 6-10, 2014, LEIPZIG, GERMANY

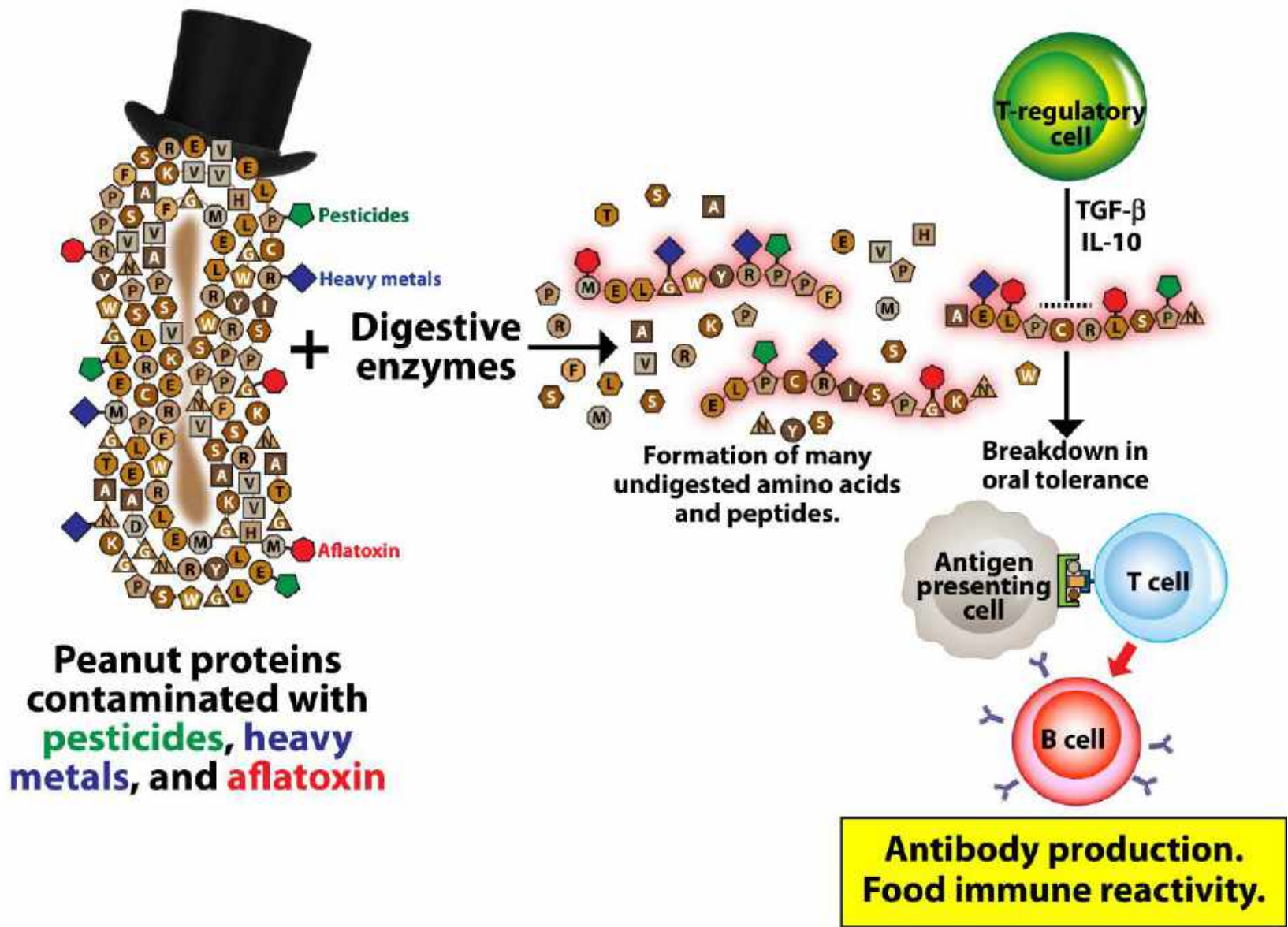
Commonly Exposed Xenobiotics

12 Different Antigens for ARRAY 11



FOOD-ASSOCIATED **AUTOIMMUNITIES** WHEN FOOD BREAKS YOUR IMMUNE SYSTEM





A Food Testing Panel that reflects the patient's actual diet



Raw and Cooked Vegetables



Raw and Cooked Fruits



Raw and Roasted Nuts and Seeds



Cooked Meat and Meat Glue



Raw and Cooked Fish and Shellfish



Gums



Food Coloring



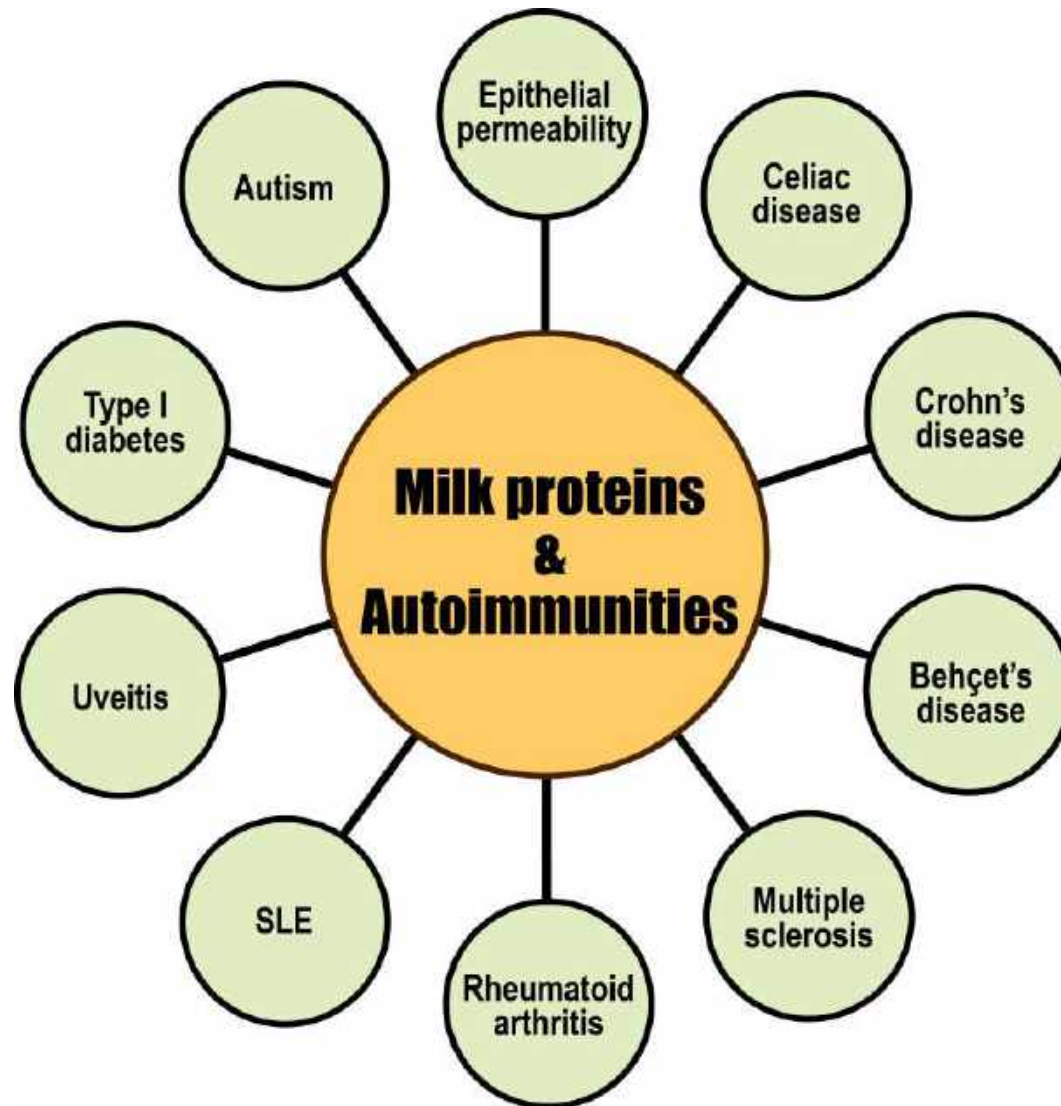
Oleosins



Lectins and Agglutinins



Enzymes and Others



Spectrum of autoimmune disorders that are associated with milk proteins

Case report: Multiple Sclerosis from environmental triggers

- ❖ Individual consumed milk and wheat on a regular basis.
- ❖ At age 38 developed bloating and other GI disorders after meals.
- ❖ Went from doctor to doctor looking for answers
- ❖ A blood test was ordered: IgG and IgA were elevated against milk; only IgG was highly elevated against wheat proteins, particularly against wheat germ agglutinin.
- ❖ She was told that she did **not** have allergy to milk nor dairy and was sent home.
- ❖ For almost 11 years she continued with the same diet.
- ❖ At age 49 she developed fatigue, fibromyalgia, dizziness and inability to concentrate.



Case report: Multiple Sclerosis from environmental triggers

- ❖ One year later, she lost her job and became very stressed about her overall health.
- ❖ When she was 52, her GP finally decided to send her to a neurologist, who, based on her continuing symptomatology, ordered an MRI of the brain and a test for anti-brain antibodies.
- ❖ The MRI revealed several plaques or lesions in her brain's white matter, which was an indication of ongoing active demyelination. This was further confirmed by elevation in anti-brain antibodies.
- ❖ The patient started anti-inflammatory medication and Natalizumab (Tysabri).

How would you have handled this patient differently so that she wouldn't develop Multiple Sclerosis?

Reaction of Human Monoclonal Antibodies to SARS-CoV-2 Proteins With Tissue Antigens: Implications for Autoimmune Diseases

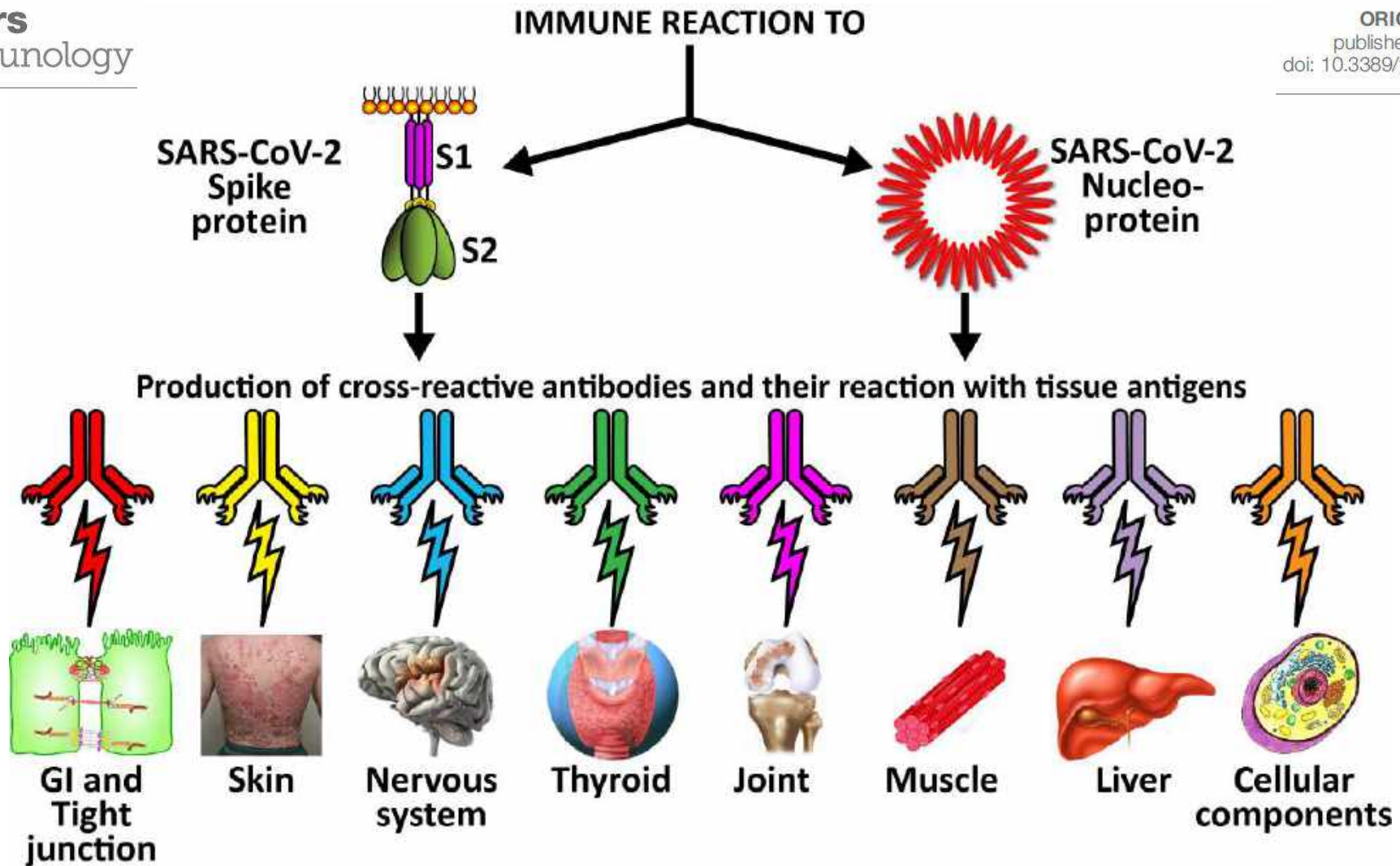
Aristo Vojdani^{1,2*}, Elroy Vojdani³ and Datis Kharratian^{2,4,5}

¹ Department of Immunology, Immunosciences Laboratory, Inc., Los Angeles, CA, United States, ² Department of Preventive Medicine, Loma Linda University School of Medicine, Loma Linda, CA, United States, ³ Regenera Medical, Los Angeles, CA, United States, ⁴ Department of Neurology, Harvard Medical School, Boston, MA, United States, ⁵ Department of Neurology, Massachusetts General Hospital, Charlestown, MA, United States

We sought to determine whether immune reactivity occurs between anti-SARS-CoV-2

We also did selective epitope mapping using BLAST and showed similarities and homology between spike, nucleoprotein, and many other SARS-CoV-2 proteins with the human tissue antigens mitochondria M2, F-actin and TPO.

different tissue antigens. We found that SARS-CoV-2 antibodies had reactions with 28 out of 55 tissue antigens, representing a diversity of tissue groups that included barrier proteins, gastrointestinal, thyroid and neural tissues, and more. We also did selective



Possible relationship between SARS-CoV-2 proteins and autoimmune target proteins,

5 months after Dr V contracted COVID-19

TEST	RESULTS				Units
	Low	In-range	High	Reference Range	
Lymphocyte MAP Comprehensive Immunophenotyping of Lymphocytes					
Total WBC		6610		3400-9100	Cells/mcl
% Lymphocyte			47.2	20-40	%
Total Lymphocyte		3123		1200-3200	Cells/mcl
% T Cell		67.7		46.0-82.0	%
Total T Cell			2114	440-1600	Cells/mcl
% B Cell		12.5		6.0-18.0	%
Total B Cell		391		90-400	Cells/mcl
T Cell/B Cell Ratio		5.4		4.0-11.0	Ratio
% T-Helper (CD4) Cell		50.4		28.0-55.0	%
Total T-Helper (CD4) Cell			>1195	500-1100	Cells/mcl
% Cytotoxic (CD8) T Cell		14.4		10.0-30.0	%
Total Cytotoxic (CD8) T Cell		450		200-500	Cells/mcl
CD4/CD8 Ratio		3.5		1.0-4.0	Ratio
% T-Helper-1Cell			40.9	18-38	%
Total T-Helper-1 Cell			761	150-550	Cells/mcl
% T-Helper-2 Cell		6.0		6.0-12.0	%
Total T-Helper-2 Cell		112		70-150	Cells/mcl
Th1/Th2 Ratio			6.8	1-5	Ratio
% T-Helper-17		3.5		2.0-7.0	%
Total T-Helper-17		65		30-90	Cells/mcl
% Regulatory T Cell	0.6			1-4	%
Total Regulatory T Cell		11		10-50	Cells/mcl
Th17/Treg Ratio			5.9	1-3	Ratio
% NK Cell		6.6		3.0-15.0	%
Total NK Cell		205		60-220	Cells/mcl
% Cytotoxic NK cells		6.3		2.0-10.0	%
Total Cytotoxic NK cells		195		30-200	Cells/mcl
% NKT			7.0	1-6	%
Total NKT			219	10-120	Cells/mcl

8 months
after Dr V
contracted
COVID-19

TEST	RESULTS				Units
	Low	In-range	High	Reference Range	
Lymphocyte MAP Comprehensive Immunophenotyping of Lymphocytes					
Total WBC		5417		3400-9100	Cells/mcl
% Lymphocyte		38.4		20-40	%
Total Lymphocyte		2080		1200-3200	Cells/mcl
% T Cell		68.4		46-82	%
Total T Cell		1422		440-1600	Cells/mcl
% B Cell		14.4		6-18	%
Total B Cell		299		90-400	Cells/mcl
T Cell/B Cell Ratio		4.8		4-11	Ratio
% T-Helper (CD4) Cell		51.1		28-55	%
Total T-Helper (CD4) Cell		1062		500-1100	Cells/mcl
% Cytotoxic (CD8) T Cell		14		10-30	%
Total Cytotoxic (CD8) T Cell		291		200-500	Cells/mcl
CD4/CD8 Ratio		3.7		1-4	Ratio
% T-Helper-1 Cell		32.3		18-38	%
Total T-Helper-1 Cell			732	150-550	Cells/mcl
% T-Helper-2 Cell		7.2		6-12	%
Total T-Helper-2 Cell			163	70-150	Cells/mcl
TH1/TH2 Ratio		4.5		1-5	Ratio
% T-Helper-17		7		2-7	%
Total T-Helper-17			114	30-90	Cells/mcl
% Regulatory T Cell		1.7		1-4	%
Total Regulatory T Cell		38		10-50	Cells/mcl
Th17/Treg Ratio			4.1	1-3	Ratio
% NK Cell		7.1		3-15	%
Total NK Cell		148		60-220	Cells/mcl
% Cytotoxic NK cells		6.8		2-10	%
Total Cytotoxic NK cells		142		30-200	Cells/mcl
% NKT		5.9		1-6	%
Total NKT			123	10-120	Cells/mcl

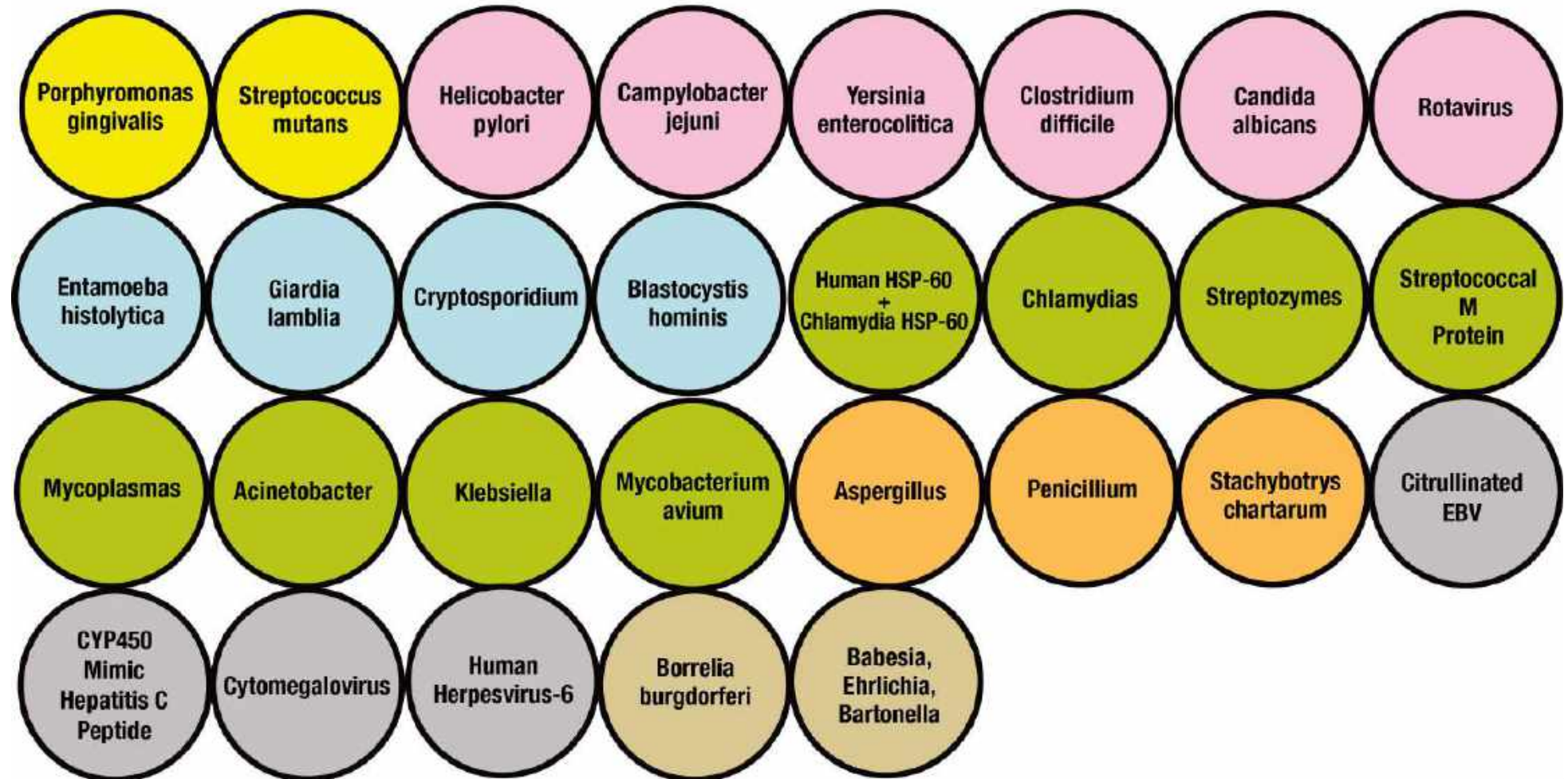
5 months after Elroy contracted COVID-19

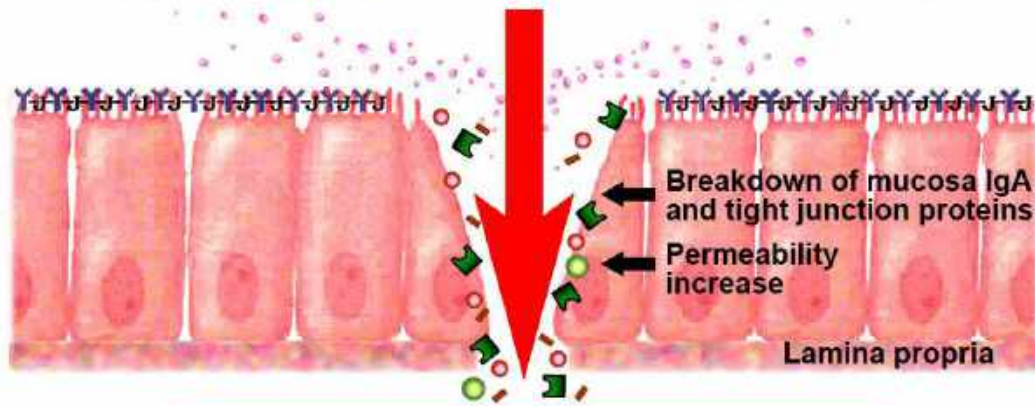
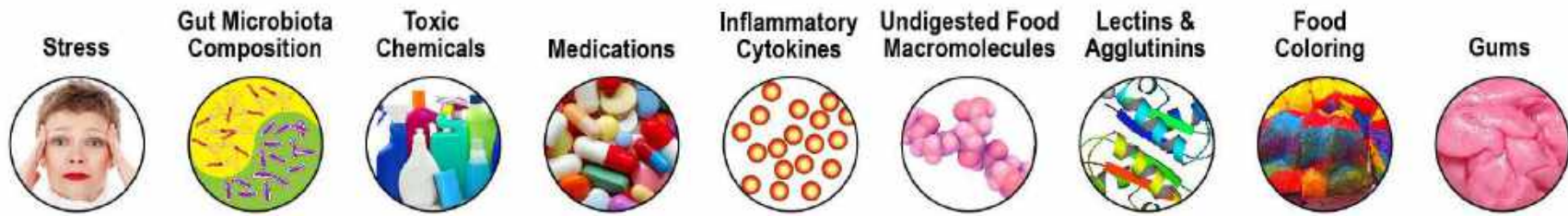
TEST	RESULTS				Units
	Low	In-range	High	Reference Range	
Lymphocyte MAP Comprehensive Immunophenotyping of Lymphocytes					
Total WBC		5482		3400-9100	Cells/mcl
% Lymphocyte			55.6	20-40	%
Total Lymphocyte		3047		1200-3200	Cells/mcl
% T Cell		62.8		46.0-82.0	%
Total T Cell			1912	440-1600	Cells/mcl
% B Cell		14.5		6.0-18.0	%
Total B Cell			440	90-400	Cells/mcl
T Cell/B Cell Ratio		4.3		4.0-11.0	Ratio
% T-Helper (CD4) Cell		36.8		28.0-55.0	%
Total T-Helper (CD4) T Cell			1122	500-1100	Cells/mcl
% Cytotoxic (CD8) T Cell		22.9		10.0-30.0	%
Total Cytotoxic (CD8) T Cell			696	200-500	Cells/mcl
CD4/CD8 Ratio		1.6		1.0-4.0	Ratio
% T-Helper-1 Cell		20.1		18.0-38.0	%
% T-Helper-2 Cell	2.0			6.0-12.0	%
Total T-Helper-2 Cell	36			70-150	Cells/mcl
TH1/TH2 Ratio			10.0	1.0-5.0	Ratio
% T-Helper-17	1.0			2.0-7.0	%
Total T-Helper-17	18			30-90	Cells/mcl
% Regulatory T Cell	0.5			1.0-4.0	%
Total Regulatory T Cell		10		10-50	Cells/mcl
Th17/Treg Ratio		1.9		1.0-3.0	Ratio
% NK Cell		10.9		3.0-15.0	%
Total NK Cell			331	60-220	Cells/mcl
% Cytotoxic NK cells		9.9		2.0-10.0	%
Total Cytotoxic NK Cells			>257	30-200	Cells/mcl
% NKT		1.2		1.0-6.0	%
Total NKT		37		10-120	Cells/mcl

8 months after Elroy contracted COVID-19

TEST	RESULTS				Units
	Low	In-range	High	Reference Range	
Lymphocyte MAP Comprehensive Immunophenotyping of Lymphocytes					
Total WBC		5851		3400-9100	Cells/mcl
% Lymphocyte		33		20-40	%
Total Lymphocyte		1929		1200-3200	Cells/mcl
% T Cell		64.6		46-82	%
Total T Cell		1246		440-1600	Cells/mcl
% B Cell		16		6-18	%
Total B Cell		309		90-400	Cells/mcl
T Cell/B Cell Ratio		4		4-11	Ratio
% T-Helper (CD4) Cell		41.5		28-55	%
Total T-Helper (CD4) Cell		800		500-1100	Cells/mcl
% Cytotoxic (CD8) T Cell		19.8		10-30	%
Total Cytotoxic (CD8) T Cell		382		200-500	Cells/mcl
CD4/CD8 Ratio		2.1		1-4	Ratio
% T-Helper-1 Cell		17.5		18-38	%
Total T-Helper-1 Cell		318		150-550	Cells/mcl
% T-Helper-2 Cell		6.9		6-12	%
Total T-Helper-2 Cell		124		70-150	Cells/mcl
TH1/TH2 Ratio		2.6		1-5	Ratio
% T-Helper-17		5.3		2-7	%
Total T-Helper-17			96	30-90	Cells/mcl
% Regulatory T Cell		2.4		1-4	%
Total Regulatory T Cell		44		10-50	Cells/mcl
Th17/Treg Ratio		2.2		1-3	Ratio
% NK Cell		5.4		3-15	%
Total NK Cell		103		60-220	Cells/mcl
% Cytotoxic NK cells		4.7		2-10	%
Total Cytotoxic NK cells		91		30-200	Cells/mcl
% NKT		1.3		1-6	%
Total NKT		26		10-120	Cells/mcl

ARRAY 12 - Pathogen-Associated Immune Reactivity Screen (PAIRS) IgG in Blood against 29 Antigens





INFLUENCE ON THE BLOOD-BRAIN BARRIER AND NEUROAUTOIMMUNITY

The Cyrex System[®] is a highly interconnected system, focused on barrier integrity and environmental triggers.

ARRAY 2

Intestinal Antigenic Permeability Screen

Permeability/
Dysbiosis

Bacterial Endotoxin (LPS)
IgG, IgM, IgA

Epithelial Cell Damage

Actomyosin Network
IgG

Tight Junction Damage

Occludin/
Zonulin
IgG, IgM, IgA

ARRAY 22

Irritable Bowel/
SIBO and more

Permeability/
Dysbiosis

Bacterial Cytotoxins
IgG, IgM, IgA

Tight Junction Damage

Cytoskeletal Proteins
IgG, IgM, IgA

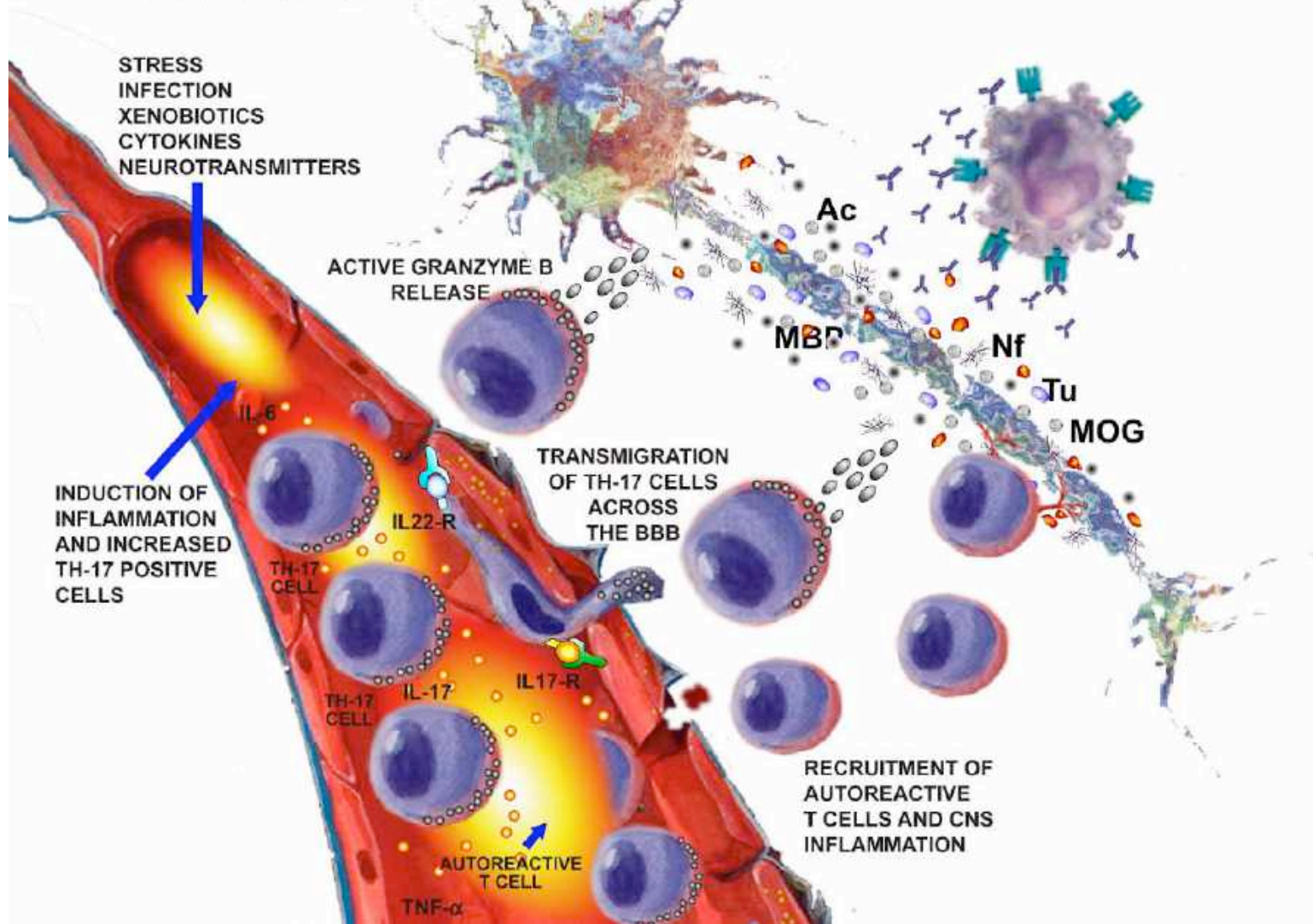
ARRAY 20

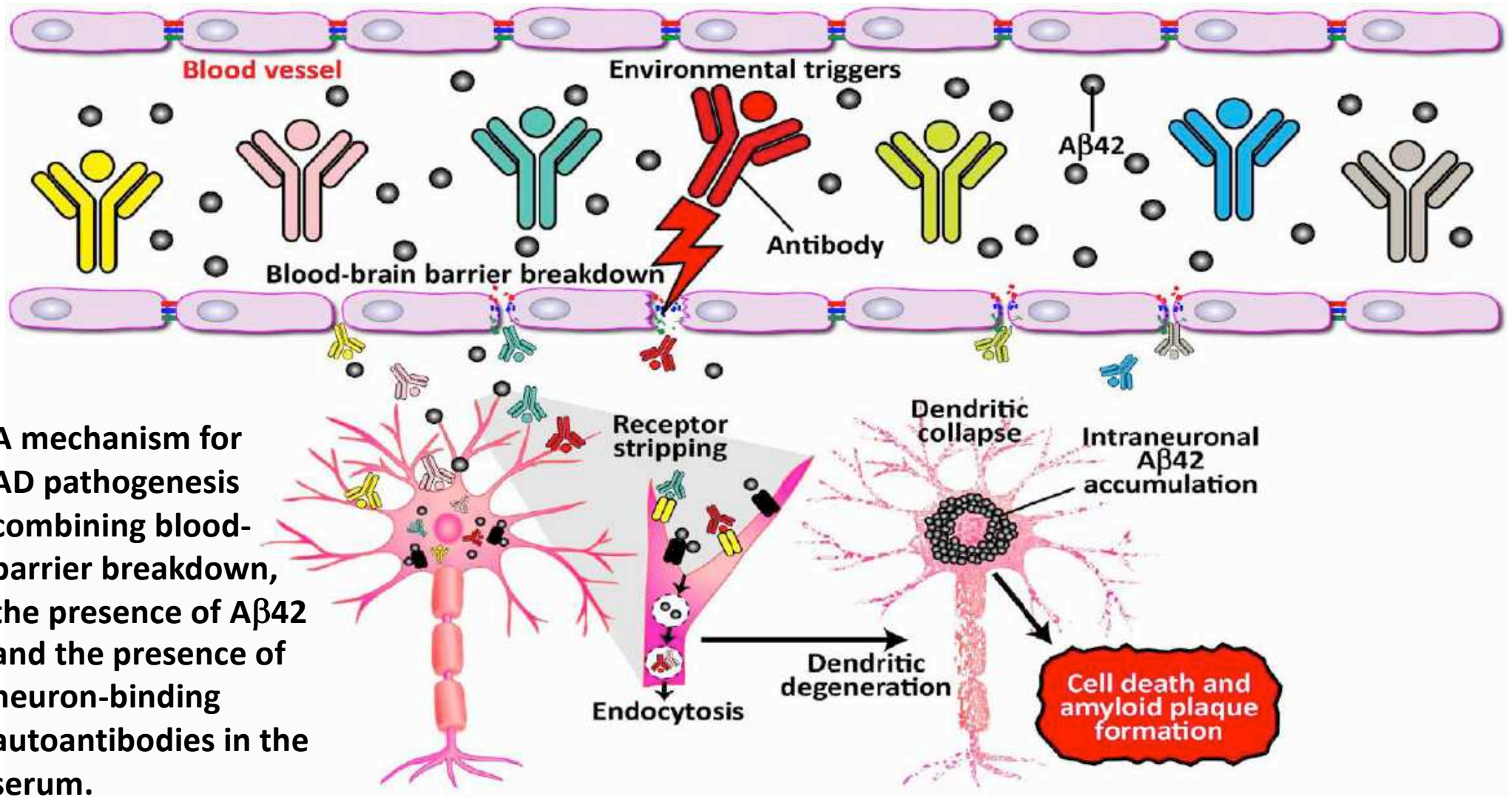
Blood Brain Barrier Permeability

BBB Damage

BBB Protein and Neural Cell Antigens
IgG, IgM, IgA

The Role of Th17 Lymphocytes in the Pathogenesis of Inflammatory and Neuroimmunological Disorders





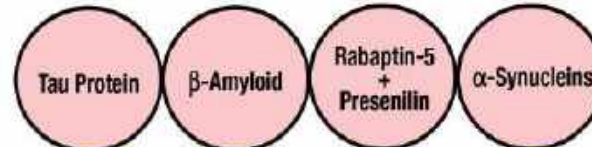
A mechanism for AD pathogenesis combining blood-brain barrier breakdown, the presence of Aβ42 and the presence of neuron-binding autoantibodies in the serum.

Alzheimer's LINX™

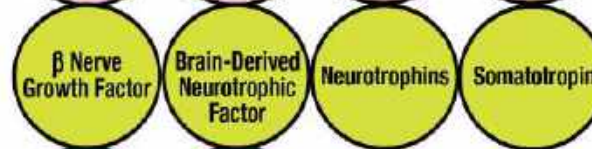
Alzheimer's-Associated Immune Reactivity

ARRAY
18

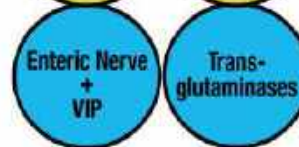
1. Brain Proteins



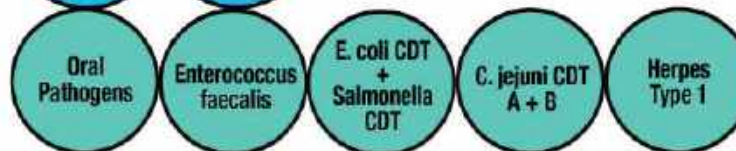
2. Growth Factors



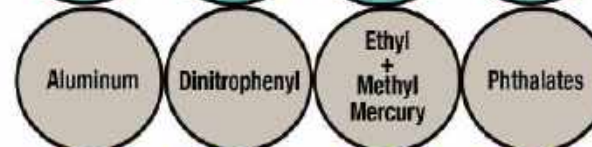
3. Enteric Nerve, Enzymes & Neurological Peptides



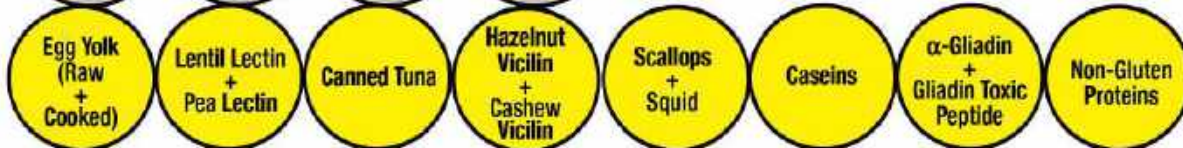
4. Pathogens



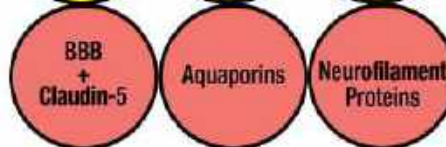
5. Chemicals



6. Foods Cross-Reactive to Amyloid-Beta



7. Blood-Brain Barrier Proteins



TEST	RESULT			
	IN RANGE (Normal)	EQUIVOCAL*	OUT OF RANGE	REFERENCE (ELISA Index)
Alzheimer's LINX™ - Alzheimer's-Associated Immune Reactivity **				
Brain Proteins				
Tau Protein	0.74			0.0-1.2
Amyloid-Beta Peptide		1.31		0.1-1.4
Rabaptin-5 + Presenilin	0.92			0.0-1.4
Alpha-Synuclein			3.74	0.4-1.7
Growth Factors				
Beta Nerve Growth Factor	0.92			0.3-1.5
Brain Derived Neurotrophic Factor		1.00		0.0-1.0
Neurotrophins	0.61			0.0-1.0
Somatotropin			2.32	0.1-1.8
Enteric Nerve, Enzymes and Neurological Peptides				
Enteric Nerve + Vasoactive Intestinal Peptide	0.55			0.0-1.0
Transglutaminases		1.18		0.2-1.3
Pathogens				
Oral Pathogens	0.66			0.2-1.1
Enterococcus faecalis	1.40			0.4-1.8
Escherichia coli CDT + Salmonella CDT		1.52		0.3-1.7
Campylobacter jejuni CDT			2.24	0.0-1.7
Herpes Type-1	0.79			0.2-1.8

Chemicals				
Aluminums			1.52	0.4-1.5
Dinitrophenyl	1.17			0.6-1.9
Ethyl + Methyl Mercury	0.89			0.3-1.3
Phthalates	1.65			0.0-2.4
Foods Cross-Reactive to Amyloid Beta				
Egg Yolk, Raw + Cooked		1.94		0.0-2.1
Lentil Lectin + Pea Lectin	0.56			0.4-1.2
Tuna, Canned	0.52			0.0-1.0
Hazelnut Vicilin + Cashew Vicilin	1.41			0.5-2.1
Scallops + Squid		1.68		0.2-2.0
Caseins	0.42			0.0-3.0
Alpha-Gliadin + Gliadin Toxic Peptide	1.12			0.3-2.1
Non-Gluten Wheat Proteins	0.63			0.3-1.6
Blood Brain Barrier and Neurofilaments				
Blood-Brain Barrier Protein + Claudin-5		1.12		0.2-1.4
Aquaporins			1.03	0.2-1.0
Neurofilament Proteins			2.13	0.4-2.1

Stage 4-5 Alzheimer's

Significant memory impairment

RF positive

RNP positive

Total IgE >1000

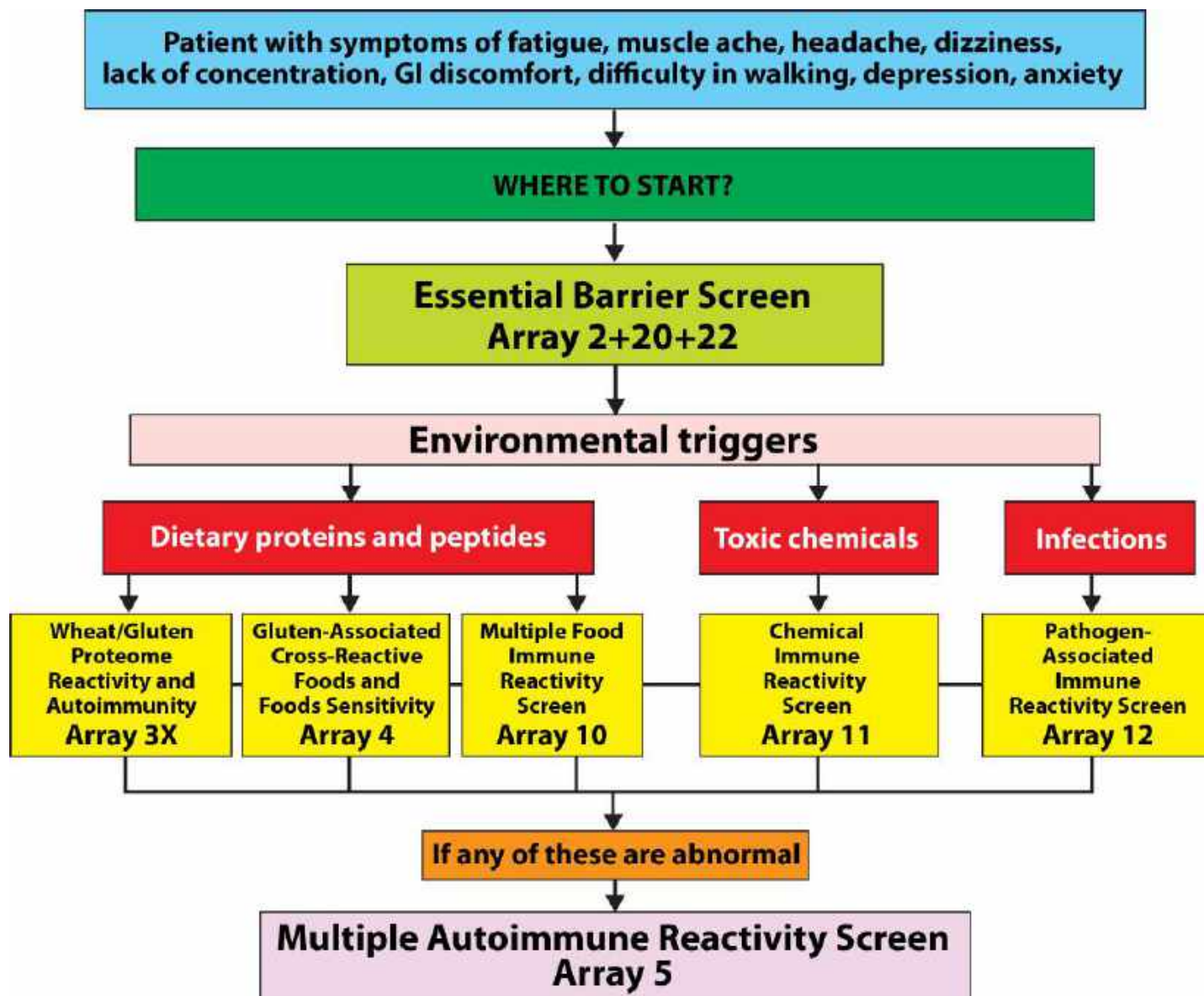
TEST	RESULTS				
	Low	In-range	High	Reference Range	Units
Lymphocyte MAP Comprehensive Immunophenotyping of Lymphocytes					
Total WBC		3409		3400-9100	Cells/mcl
% Lymphocyte		34.9		20.0-40.0	%
Total Lymphocyte	1189			1200-3200	Cells/mcl
% T Cell		68.9		46.0-82.0	%
Total T Cell		819		440-1600	Cells/mcl
% B Cell		8.5		6.0-18.0	%
Total B Cell		101		90-400	Cells/mcl
T Cell/B Cell Ratio		8.1		4.0-11.0	Ratio
% T-Helper (CD4) Cell			56.4	28.0-55.00	%
Total T-Helper (CD4) Cell		671		500-1100	Cells/mcl
% Cytotoxic (CD8) T Cell		11.3		10.0-30.0	%
Total Cytotoxic (CD8) T Cell	135			200-500	Cells/mcl
CD4/CD8 Ratio			5.0	1.0-4.0	Ratio
% T-Helper-1 Cell		24.8		18.0-38.0	%
Total T-Helper-1 Cell		278		150-550	Cells/mcl
% T-Helper-2 Cell			12.6	6.0-12.0	%
Total T-Helper-2 Cell		141		70-150	Cells/mcl
TH1/TH2 Ratio		2.0		1.0-5.0	Ratio
% T-Helper-17			8.6	2.0-7.0	%
Total T-Helper-17			96	30-90	Cells/mcl
% Regulatory T Cell		4.0		1.0-4.0	%
Total Regulatory T Cell		44		10-50	Cells/mcl
Th17/Treg Ratio		2.2		1.0-3.0	Ratio
% NK Cell			15.7	3.0-15.0	%
Total NK Cell		186		60-220	Cells/mcl
% Cytotoxic NK Cells			14.6	2.0-10.0	%
Total Cytotoxic NK cells		174		30-200	Cells/mcl
% NKT	0.6			1.0-6.0	%
Total NKT		7		10-120	Cells/mcl

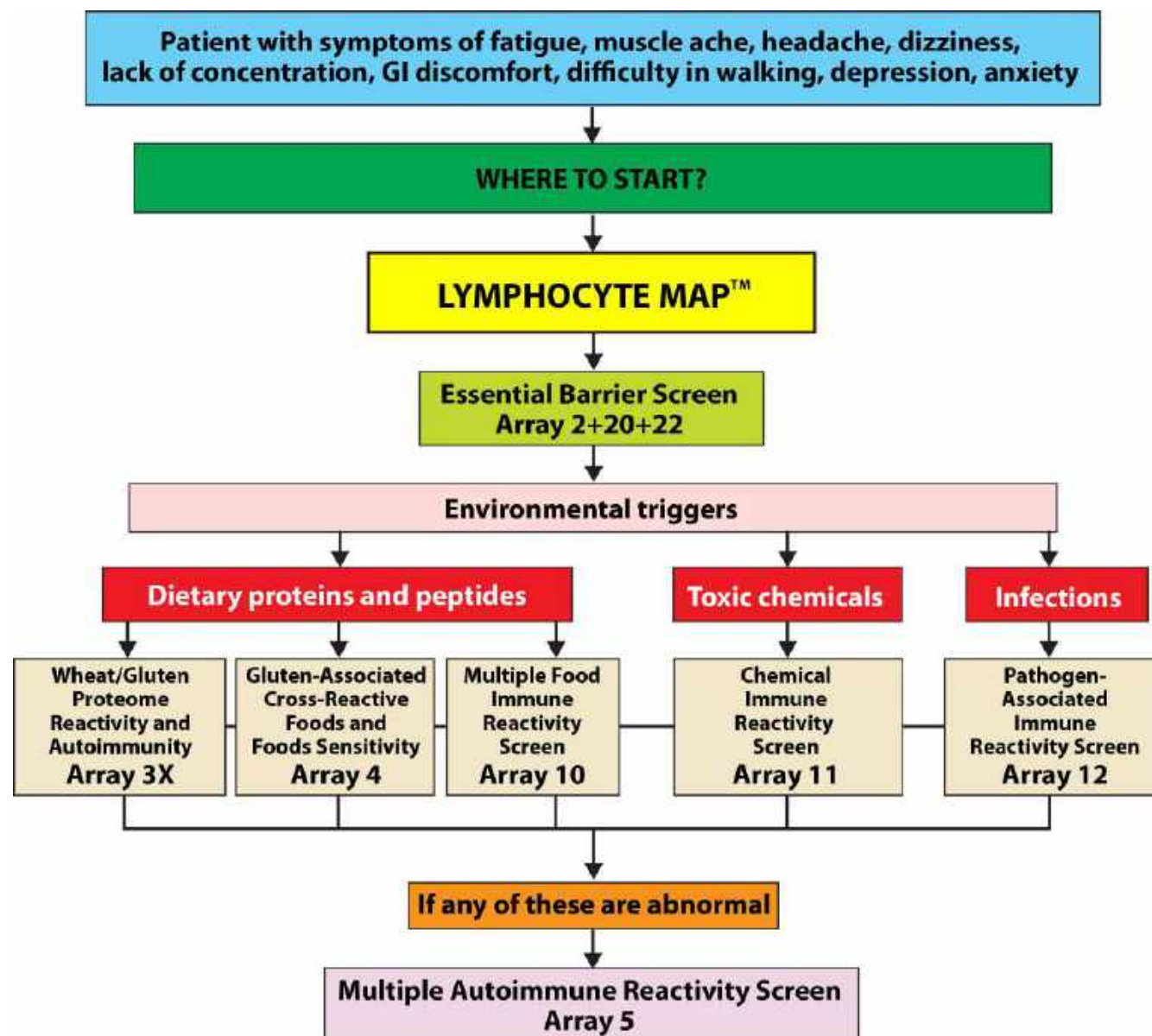
Environmental Exposures and Autoimmune Diseases: Contribution of Gut Microbiome

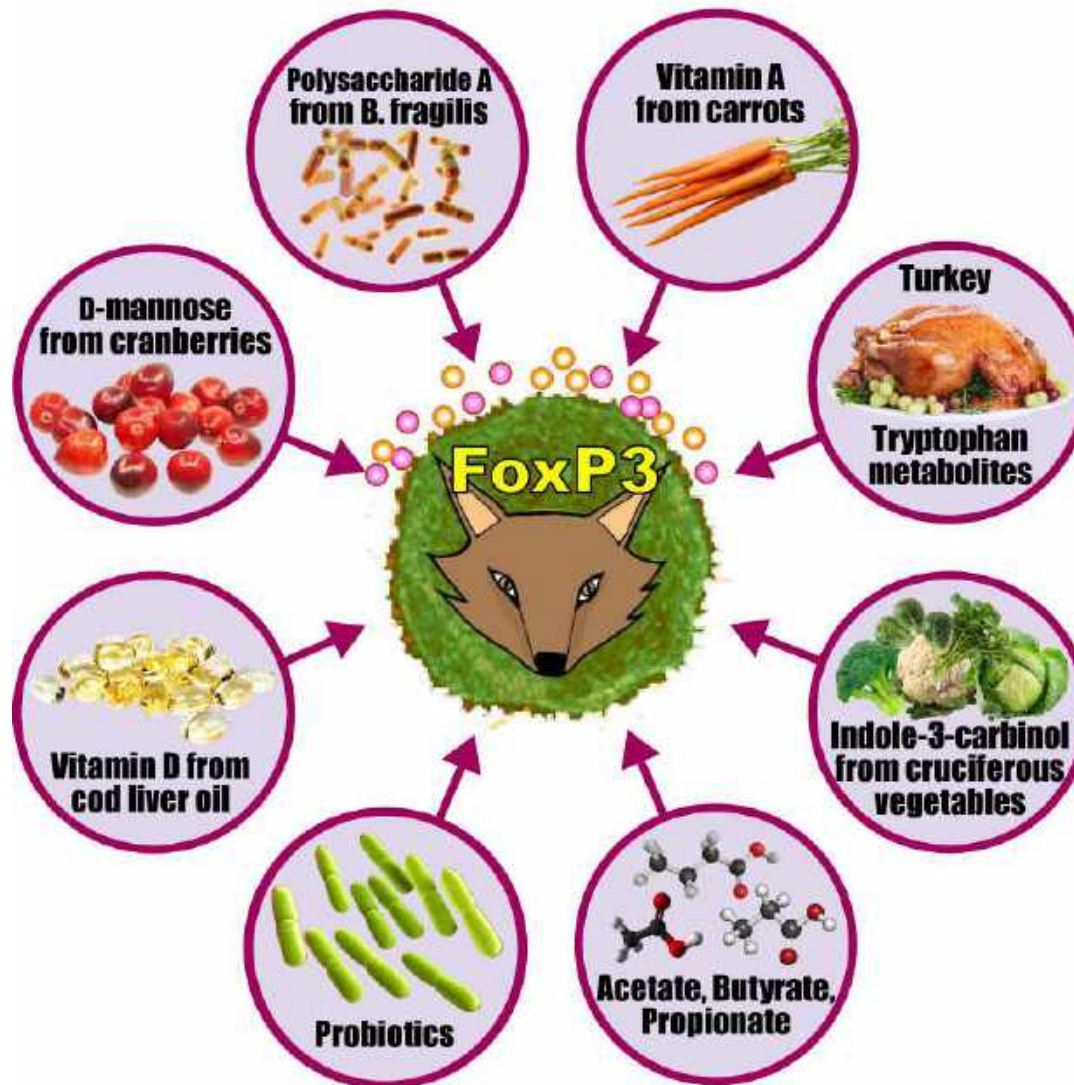
M. Firoze Khan and Hui Wang*

Environmental agents have been gaining more attention in recent years for their role in the pathogenesis of autoimmune diseases (ADs). The most challenging aspect of autoimmunity is to identify the early events that trigger immune dysregulation and autoimmunity.

unknown. Dysbiosis of the gut microbiome is another important environmental factor that has been linked to the onset of different ADs. Altered microbiota composition







Copyright Aniso Vojdani

Factors that regulate Treg cells, repair immune tolerance, and prevent autoimmunity