

# SHEICON2017

## Enzyme Inhibitors

[www.seekinghealth.org](http://www.seekinghealth.org)

# Paying Attention: Inhibitors

by Bernarda Zenker, MD

# Disclaimers

- Consultant, Spectracell Laboratory
- Speaker, Spectracell Laboratory
- Speaker, Xymogen Nutraceuticals

# Objectives

- Participants will learn inhibiting factors of enzyme function.
- Participants will learn symptoms of enzyme inhibition.
- Participants will learn evaluation of inhibitors that may affect enzyme function.

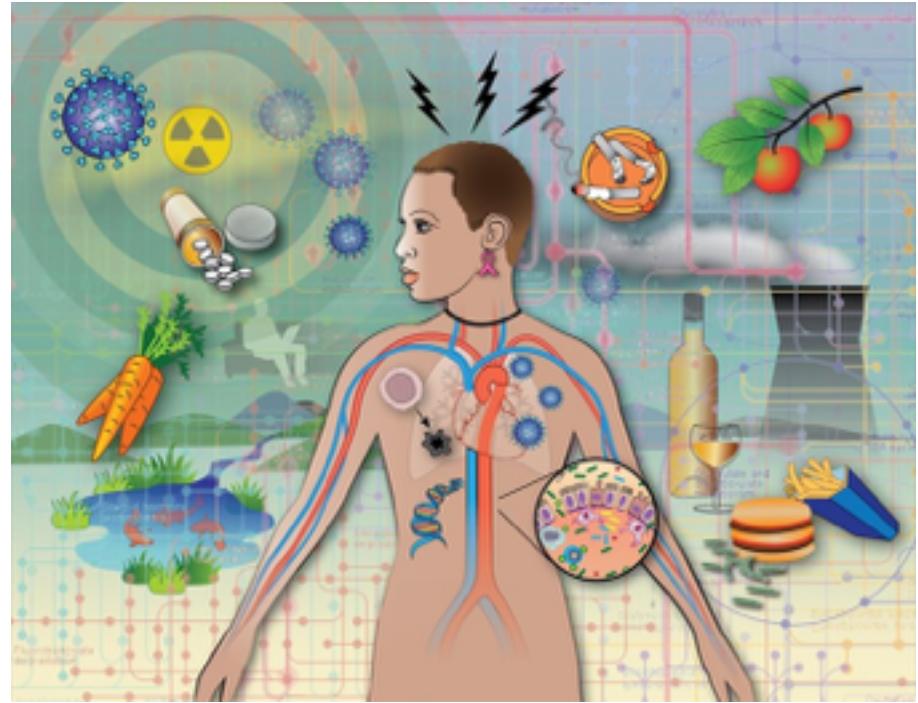
# Influencing Health & Disease

**Genetics 10%**



**Exposome: 90 %**

(Cofactors, precursors, inhibitors)



[https://ysmwebsites.azureedge.net/ysph/ehs/exposome/YPH3%20poster2017b\\_291406\\_36929\\_w744.jpeg?v=1](https://ysmwebsites.azureedge.net/ysph/ehs/exposome/YPH3%20poster2017b_291406_36929_w744.jpeg?v=1)

# *A Focused Sampler:* Enzyme Inhibitors

- LPS: Lipopolysaccharide
- Acetylaldehyde (*Candida*)
- Heavy Metals: Arsenic, Lead, Mercury, Aluminum
- Environmental toxins
  - Endocrine Disrupting Chemicals
  - Glyphosate

**This is only a Sampler. Look... for others.**

**NOTE:** Using *Pathway Planner*  
*4.0*  
*and Pathway Planner 4.1*

- these are already out of date!
- more inhibitors will be known next year,
- and in 5 years,
- and even more in 10 years.

# **Pay Attention: Inhibitors**

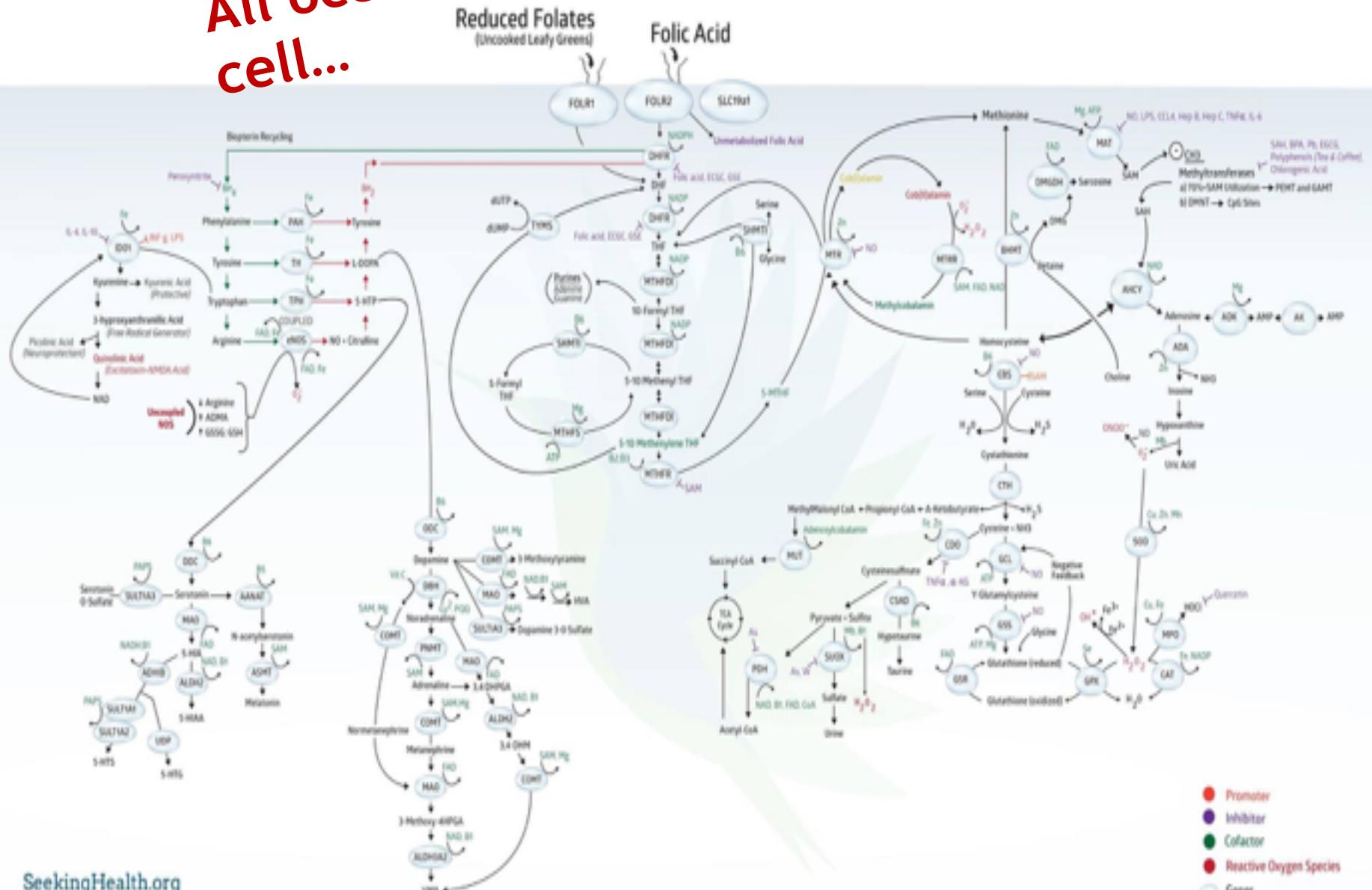
**“...we know what we know...  
AND we do not know what we do not  
know.”**

Bernarda  
Zenker

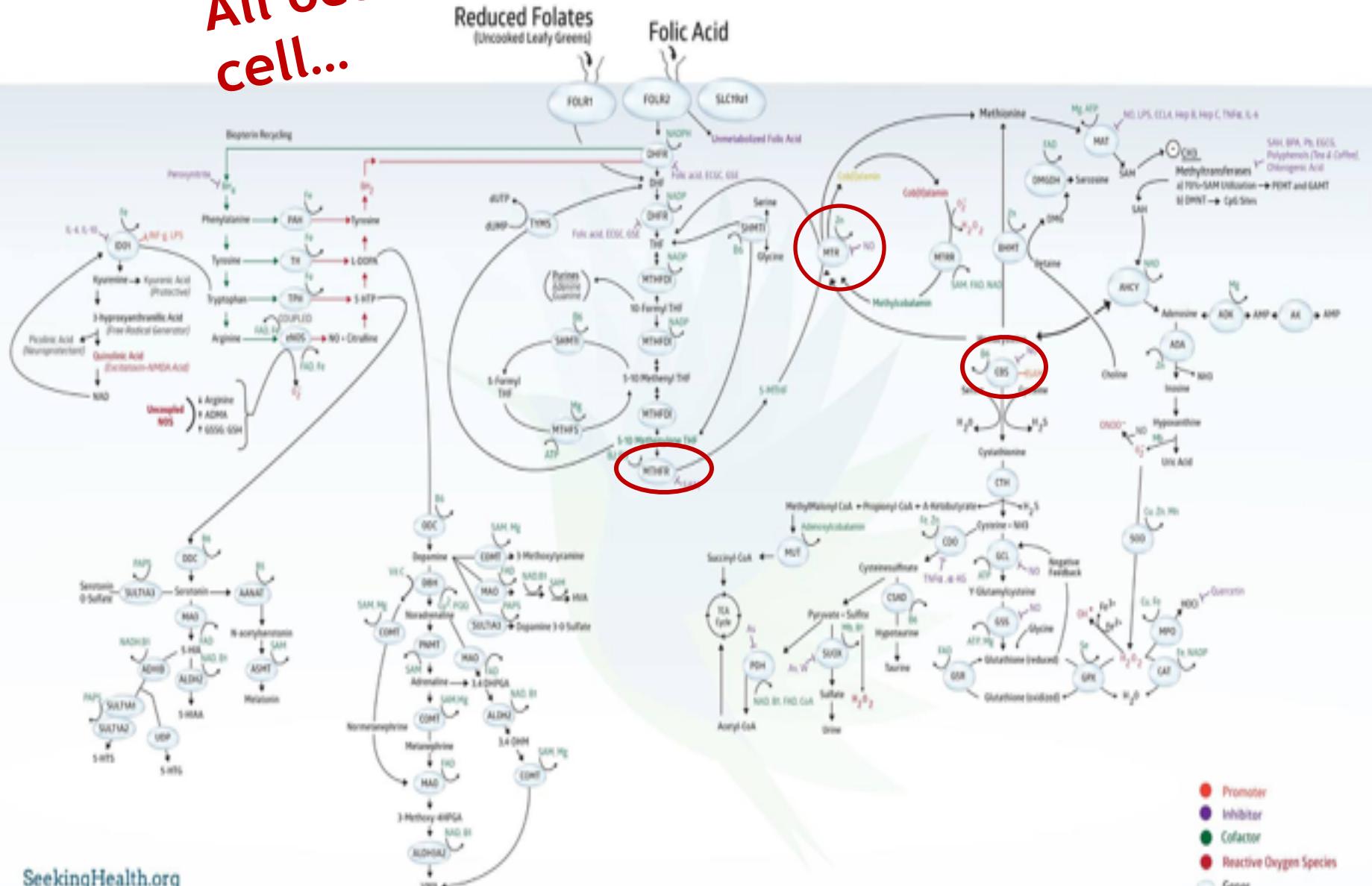
# Testing Pearls: for Inhibitors

- Not all inhibitors are known (more coming)
- Testing may not be feasible, due to cost or patient's health limitations
- Not every test is needed for each inhibitor
- Keep a **HIGH** index of suspicion
- Trust your intuition
- Look for clinical clues

All occurs inside the cell...

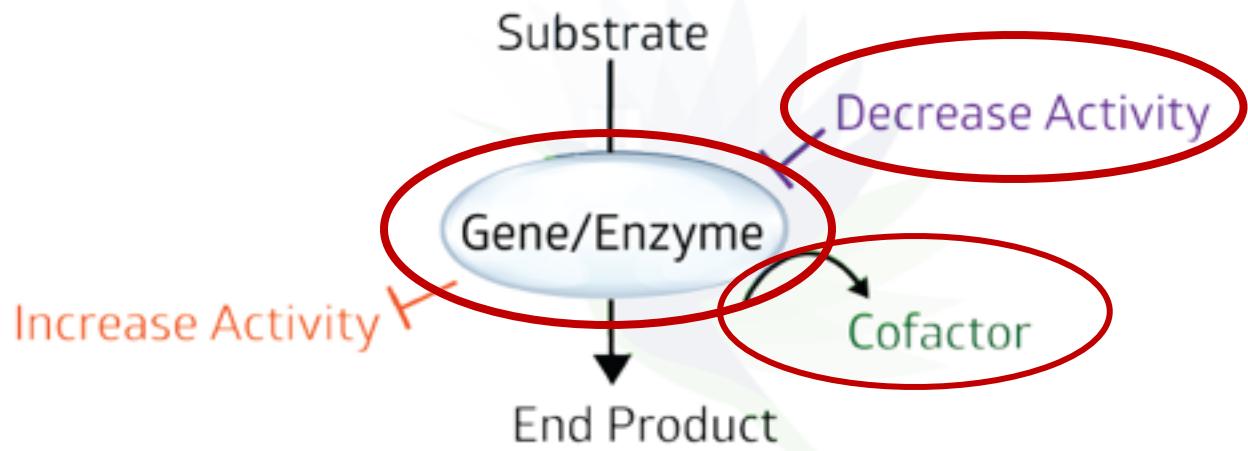


All occurs inside the cell...



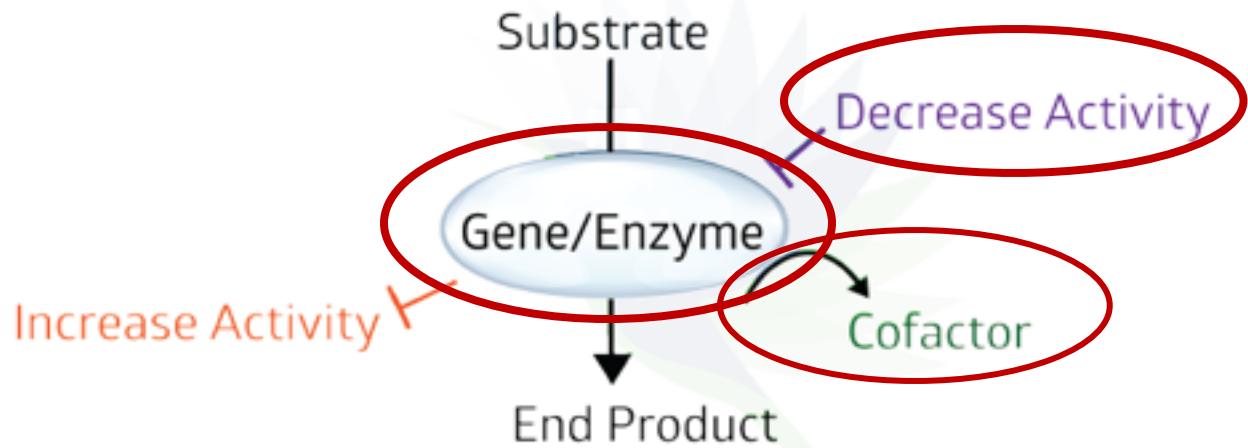
# Assessment:

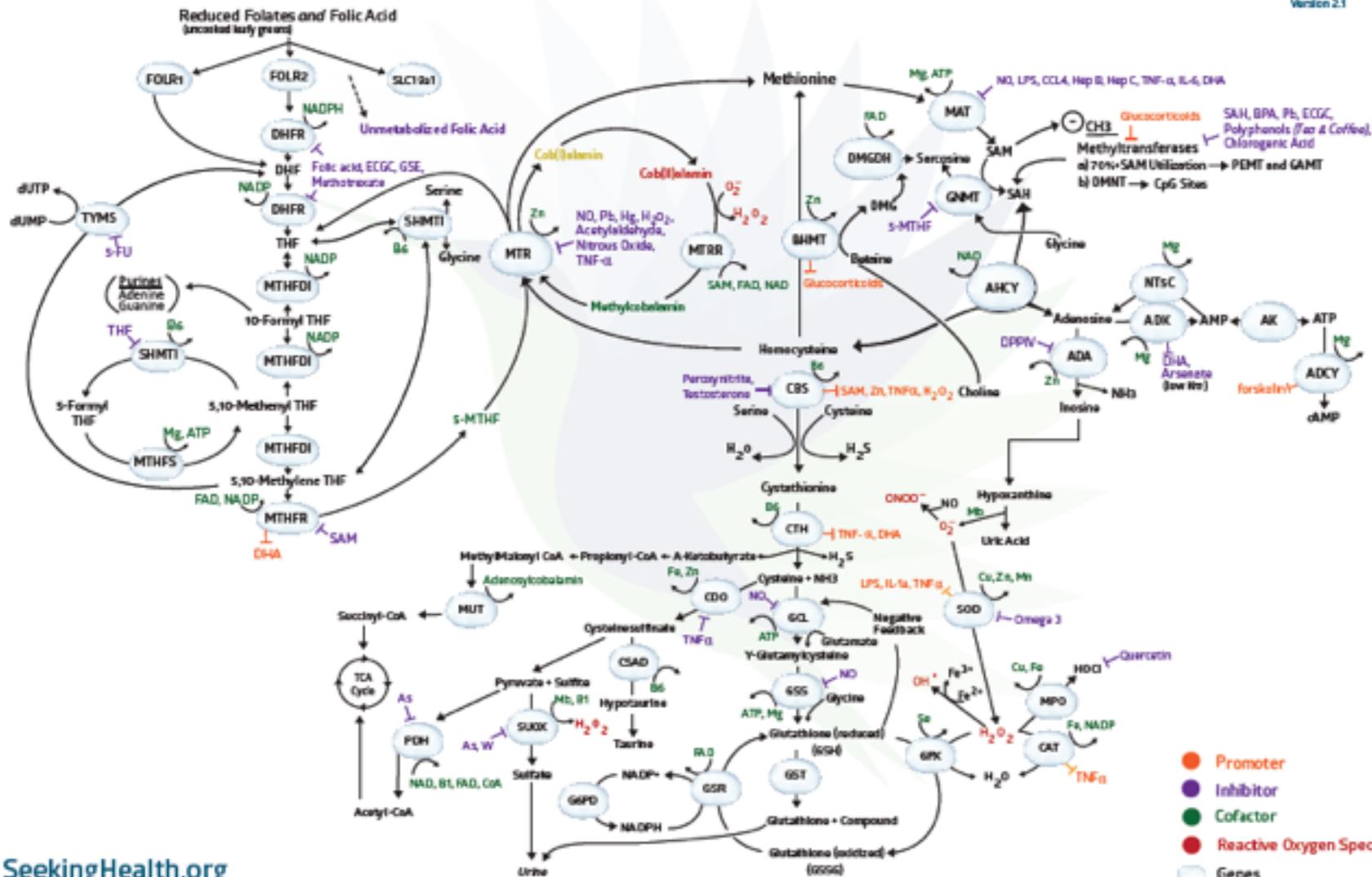
1. Enzyme
2. Cofactor
3. Inhibitor



- Increase Activity
- Decrease Activity
- Cofactor
- Reactive Oxygen Species
- Genes

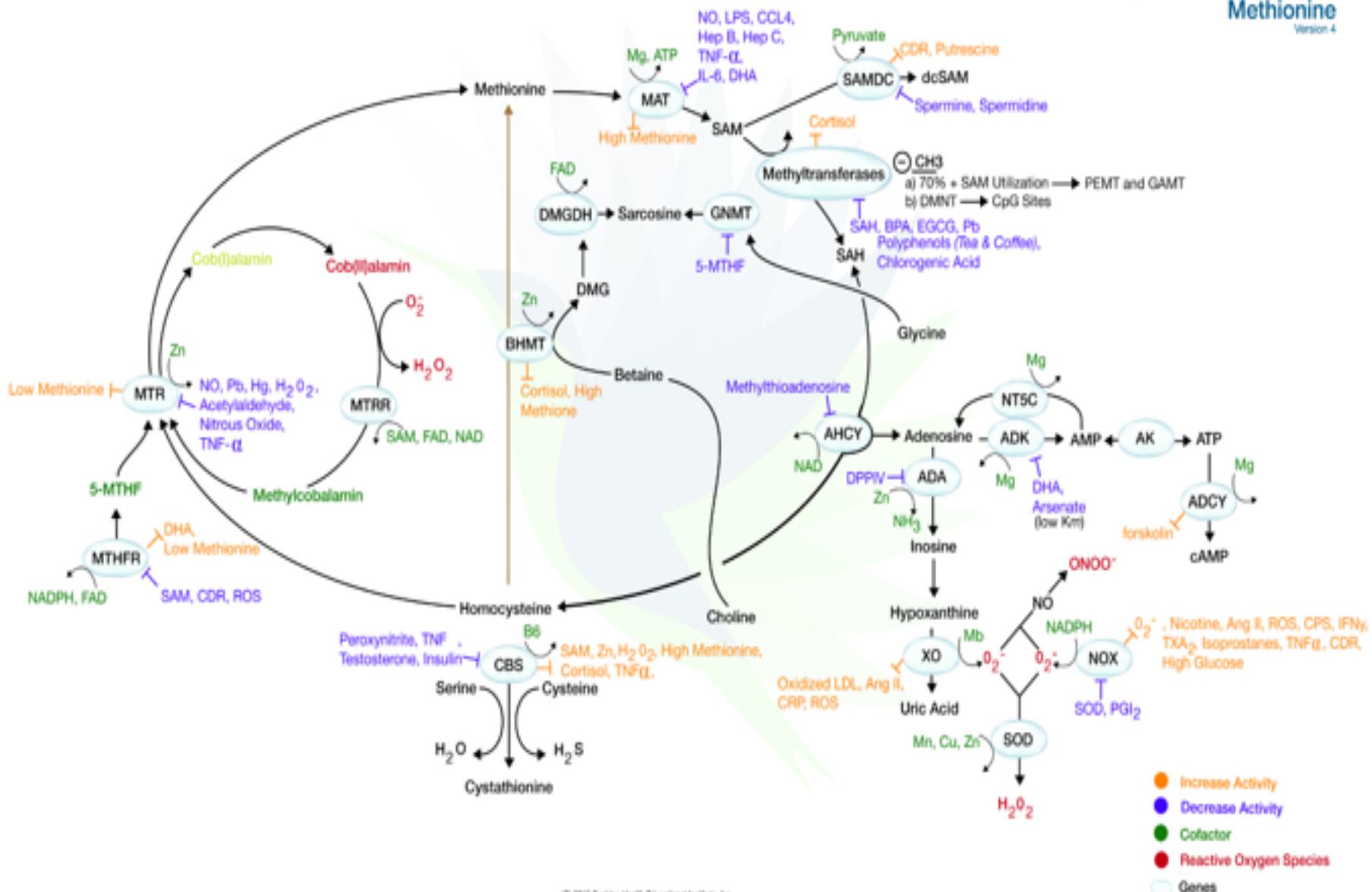
- Assessment:**
1. Enzyme
  2. Cofactor
  3. Inhibitor - PURPLE





# Pathway Planner

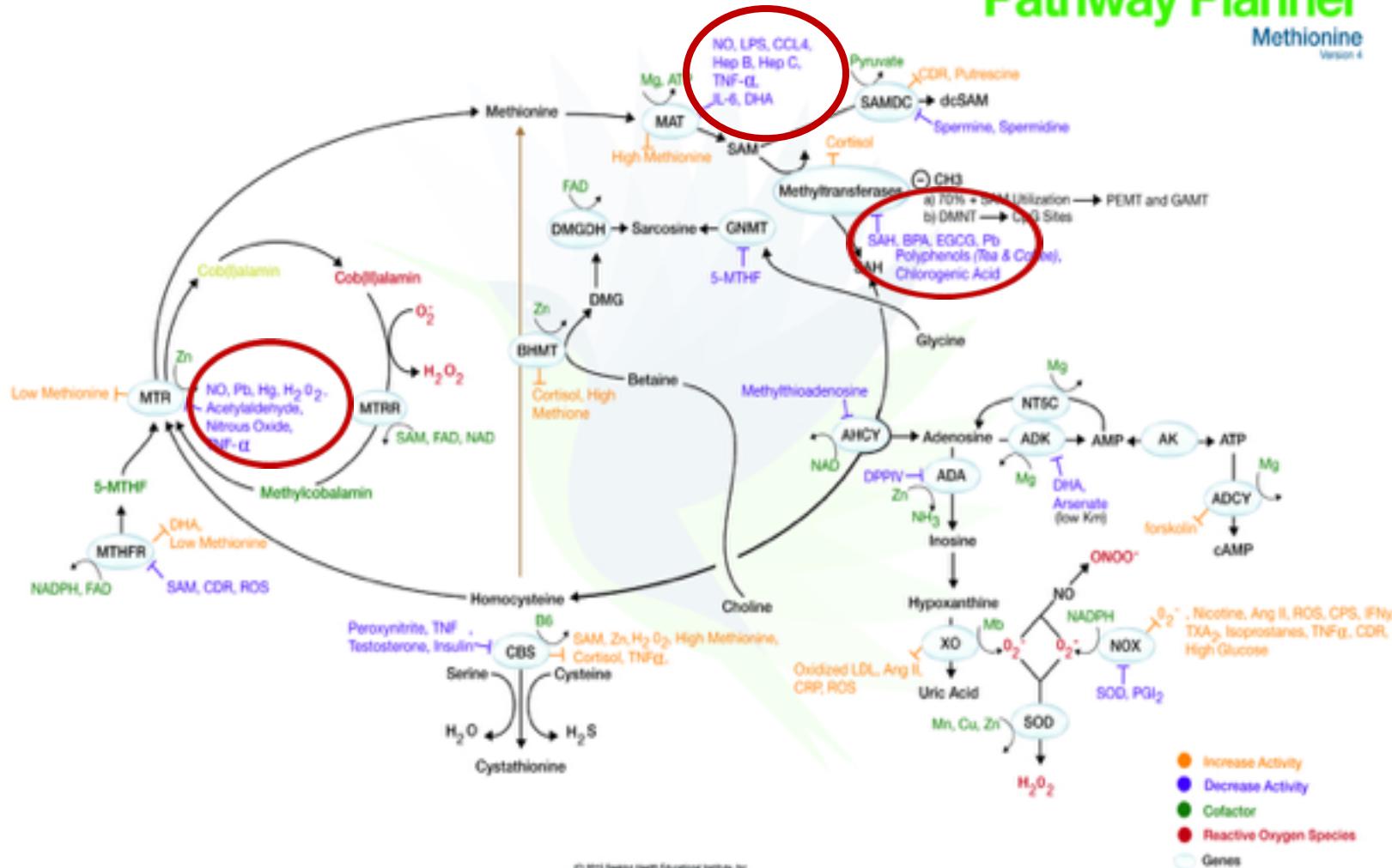
Methionine  
Version 4



# Inhibitors: Look for the Purple

## Pathway Planner

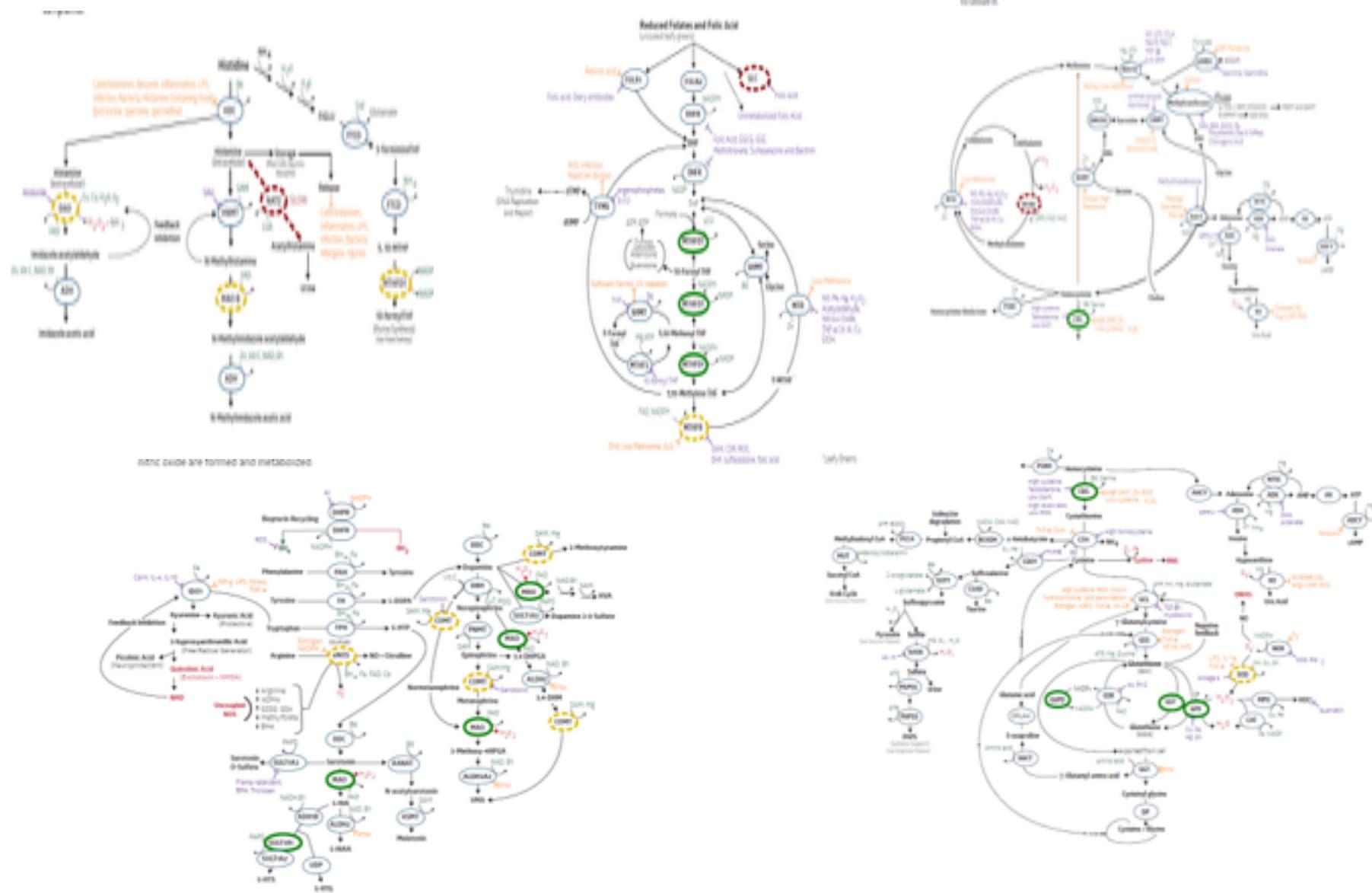
Methionine Version 4



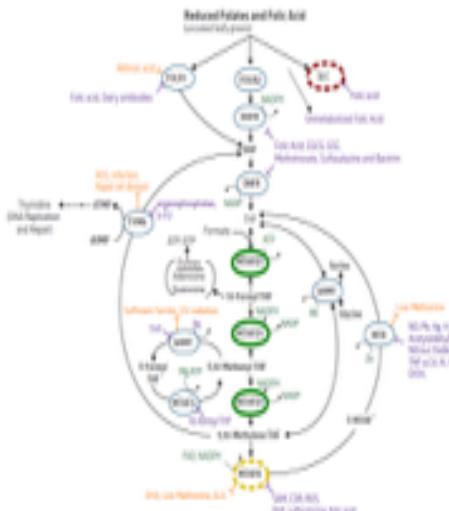
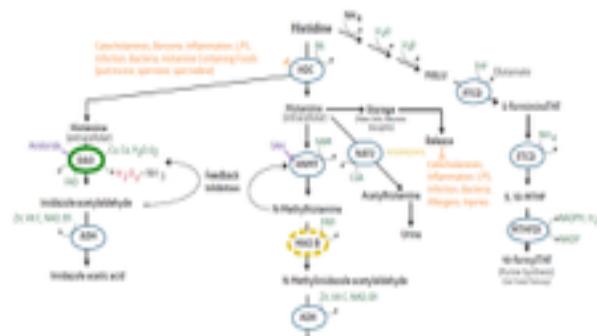
# Examples...

**Importance of Inhibitors:  
Why genetics is only 10% of the  
evaluation!**

# #1 Example: anxiety, insomnia, stomach pain, food sensitivities



## #2 Example: arthritis, insomnia, fatigue



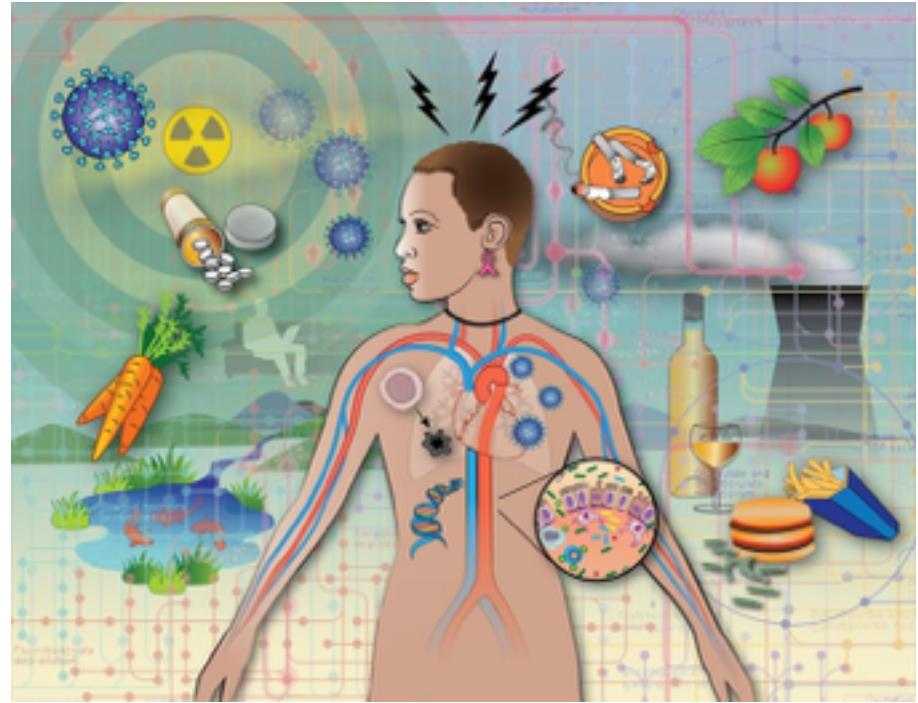
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## Understanding the Enzyme Functions

- Pain / Headaches / Arthralgia:
  - Sulfites? (upregulated CBS?)
  - Glutamate ? (impaired GAD?)
  - Norepinephrine elevated? (impaired COMT?)
  - Histamine? (DAO? HNMT?) Is there enough SAMe?
  - Insufficient SAMe? (dysfunctional MAT?)
- Fatigue / Neuropathy / Mitochondria
  - Kreb's Cycle - enzymes
  - Electron Transport Chain (**MMAB?**, **MUT?**)
- Insomnia:
  - Norepinephrine? SAMe? (COMT?, MAT?)
  - Melatonin? SAMe? (MAT?, AANAT?)
  - GABA ( GDH?)
- Heartburn / Stomach Pain:
  - Norepinephrine elevated? ( Insufficient SAMe? MAT? COMT?)
- Anxiety:
  - Norepinephrine? Sulfites? Glutamate? (COMT?, CBS?, MAT?)
- Additional: **MTHFR?**

# **Enzyme Inhibitors**

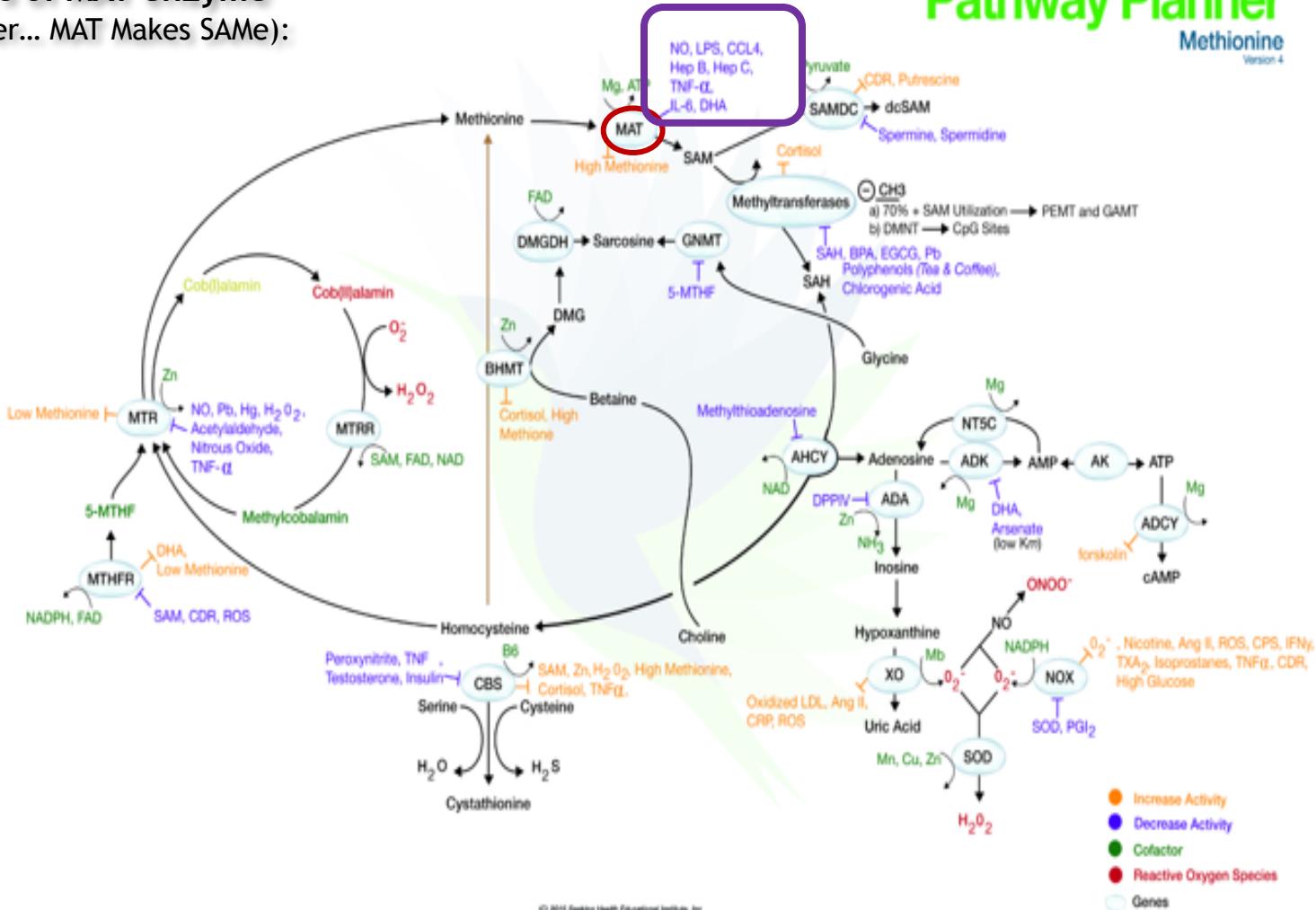
1<sup>st</sup> enzyme: MAT

## Inhibitors of MAT enzyme

(\*\*remember... MAT Makes SAMe):

## Pathway Planner

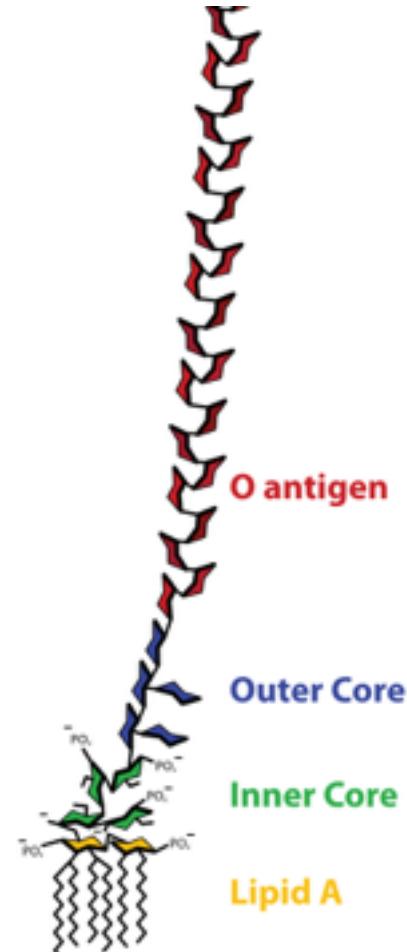
Methionine  
Version 4



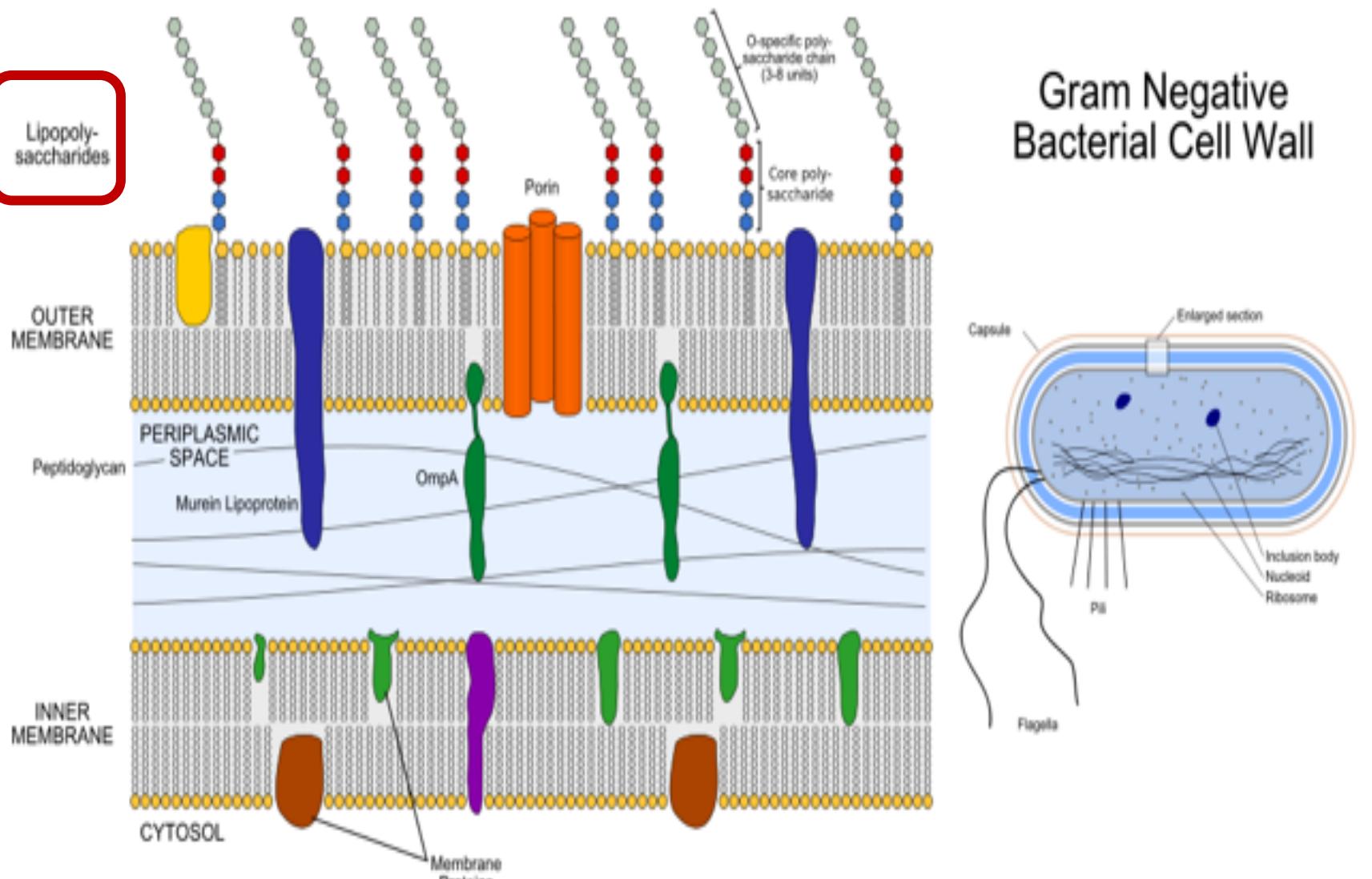
**LPS = Lipopolysaccharide**

# LPS

- *Lipopolysaccharides (LPS)*, also known as lipoglycans and endotoxins, are large molecules consisting of a lipid and a polysaccharide composed of O-antigen, outer core and inner core joined by a covalent bond; they are found in the **outer membrane of Gram-negative bacteria**, and elicit strong immune responses in animals.



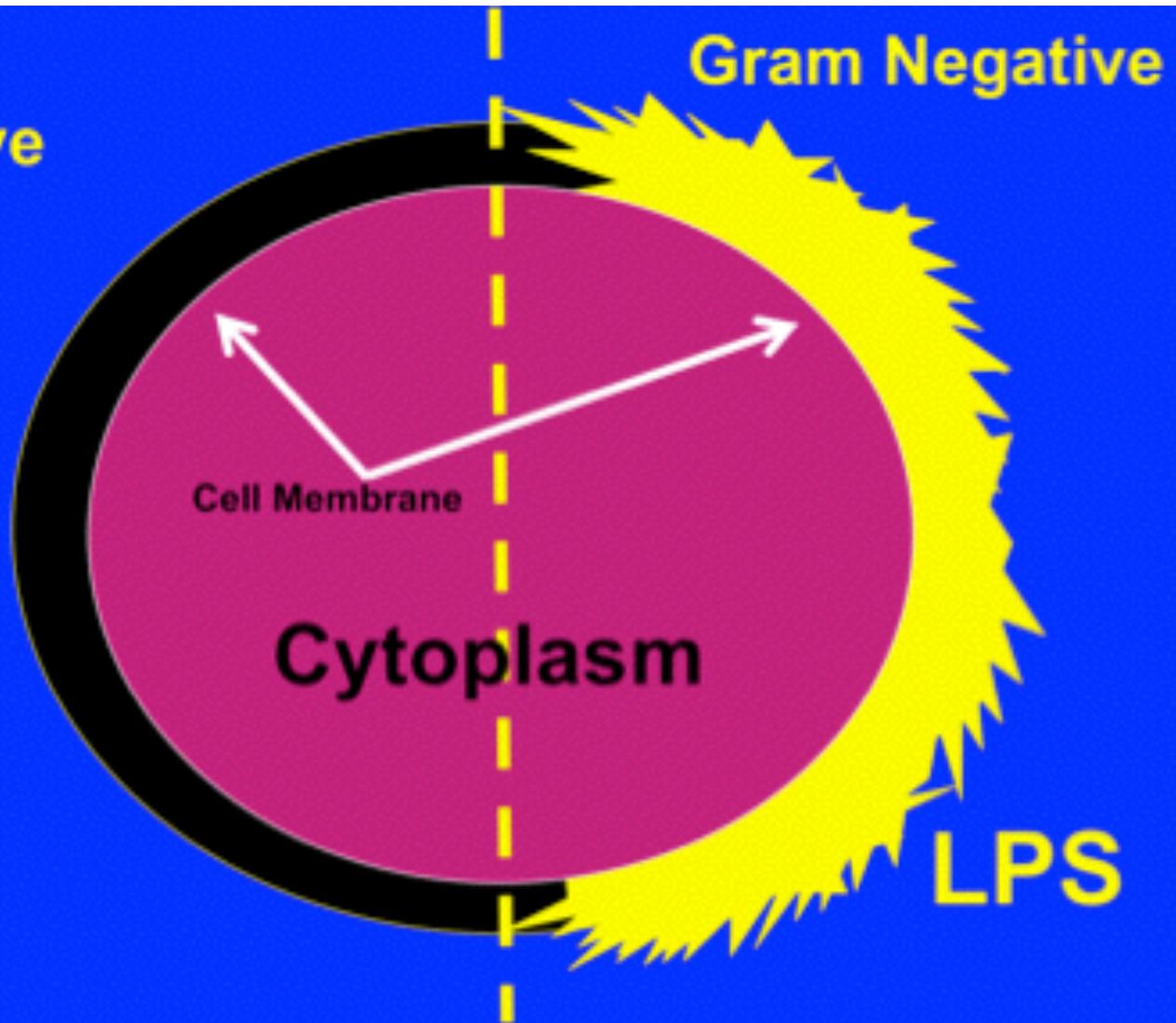
<https://en.wikipedia.org/wiki/Lipopolysaccharide>



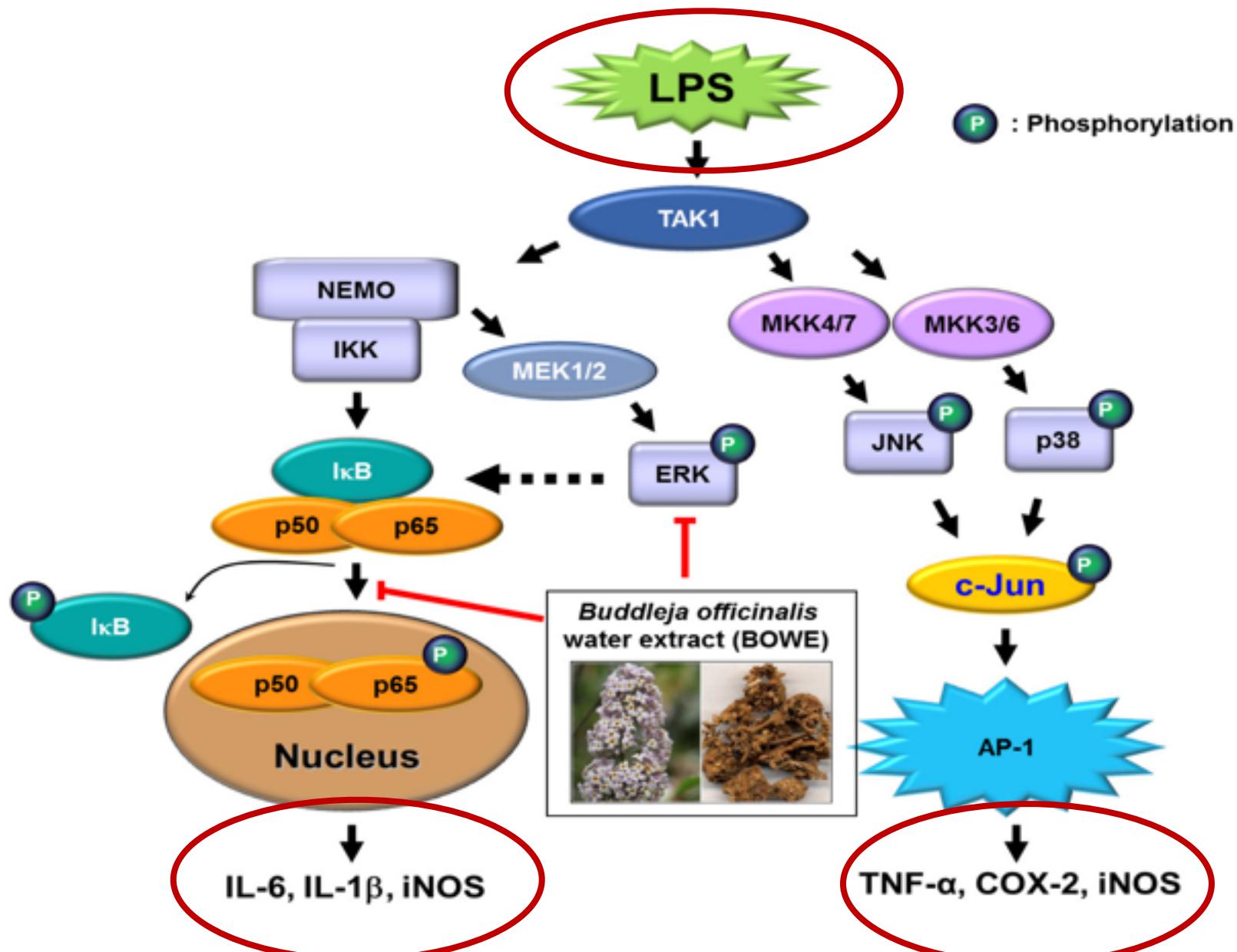
[http://upload.wikimedia.org/wikipedia/commons/thumb/8/8b/Gram\\_negative\\_cell\\_wall.svg/1000px-Gram\\_negative\\_cell\\_wall.svg.png](http://upload.wikimedia.org/wikipedia/commons/thumb/8/8b/Gram_negative_cell_wall.svg/1000px-Gram_negative_cell_wall.svg.png)

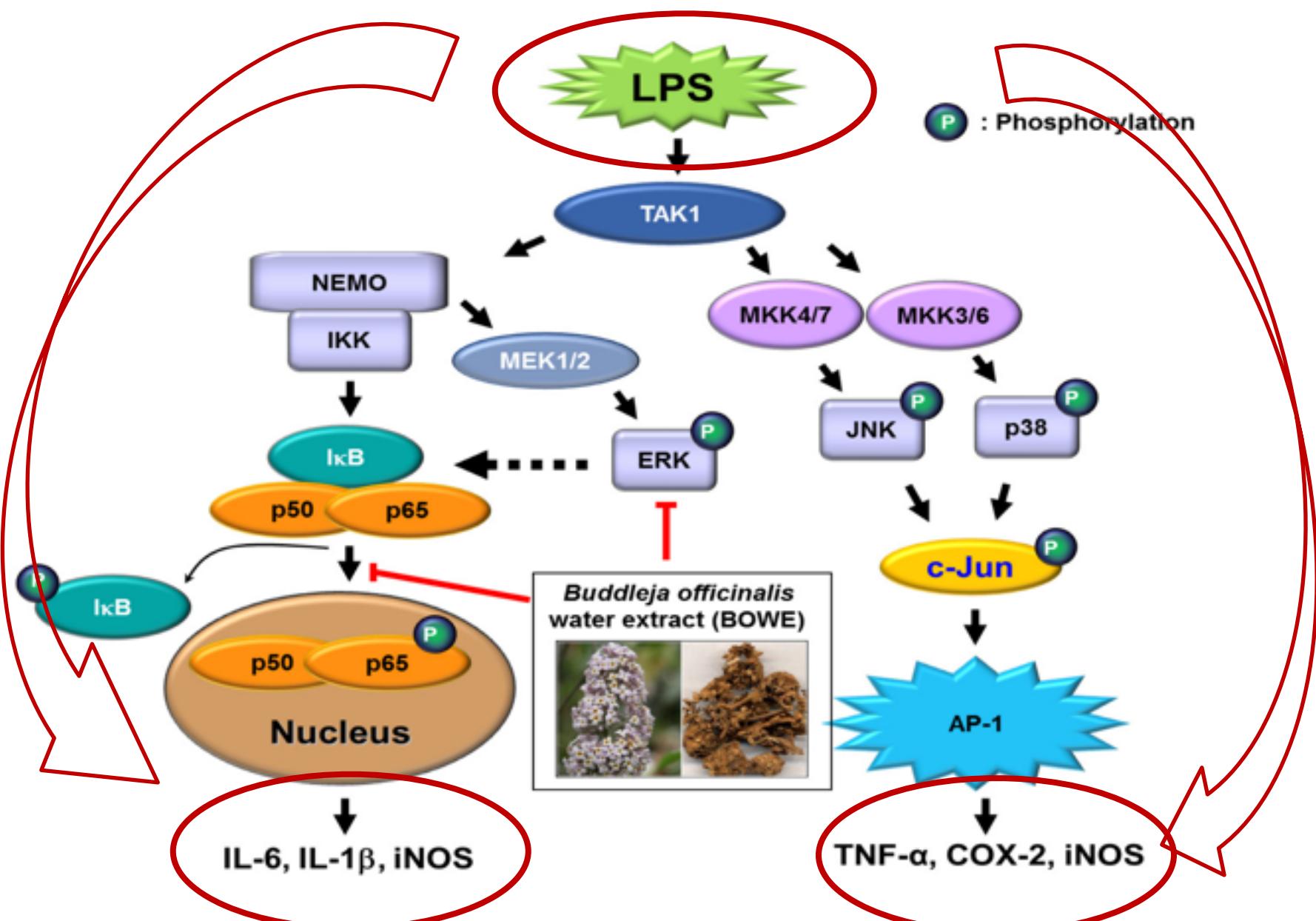
Gram  
Positive

Gram Negative

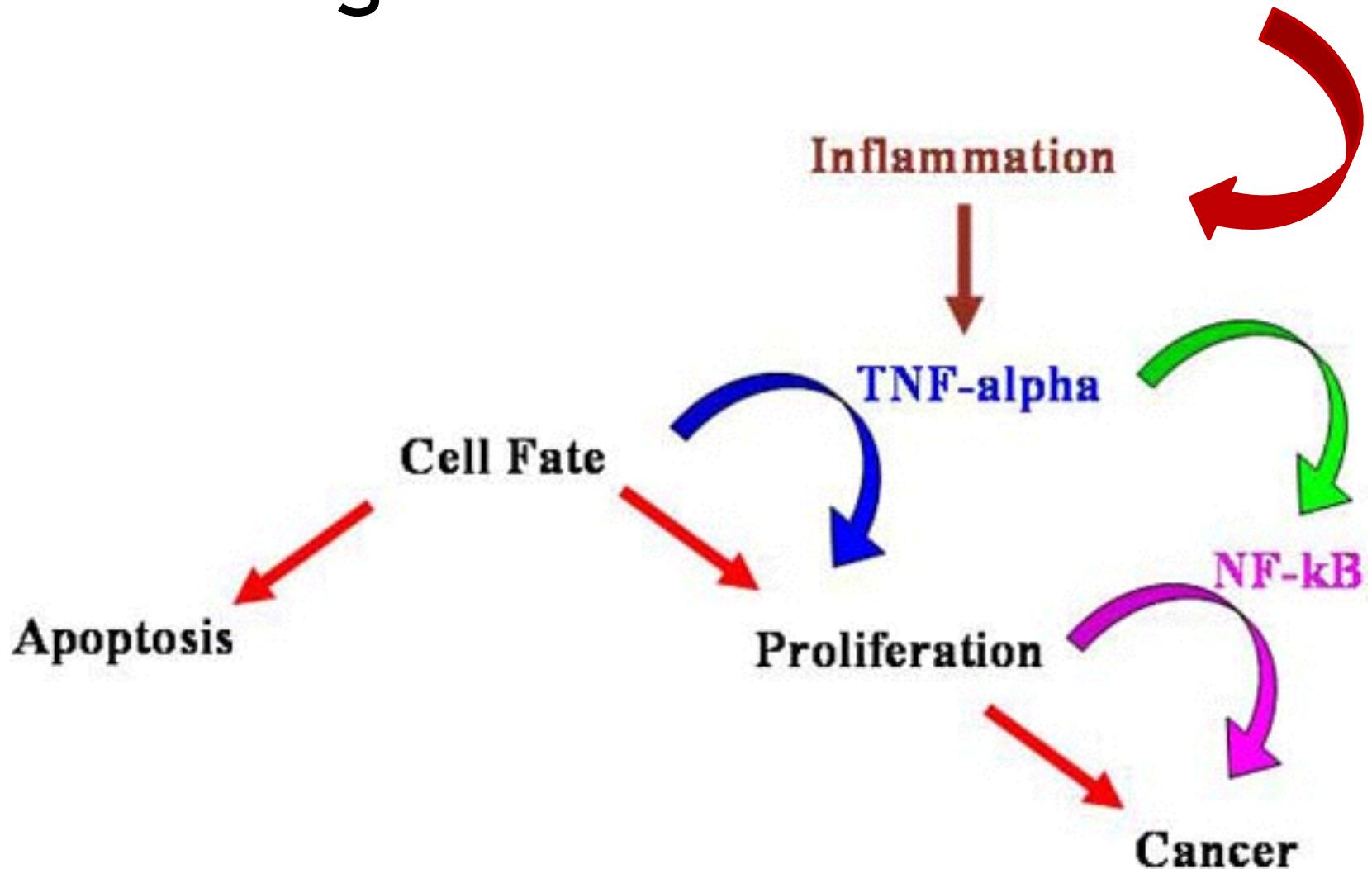


<http://drdanenberg.com/wp-content/uploads/2015/08/LPS-for-Website.png>





# Gram-Neg bacteria... to LPS... to



[http://legacy.lakeforest.edu/images/userImages/vaidyt/Page\\_5419/figure1.jpg](http://legacy.lakeforest.edu/images/userImages/vaidyt/Page_5419/figure1.jpg)

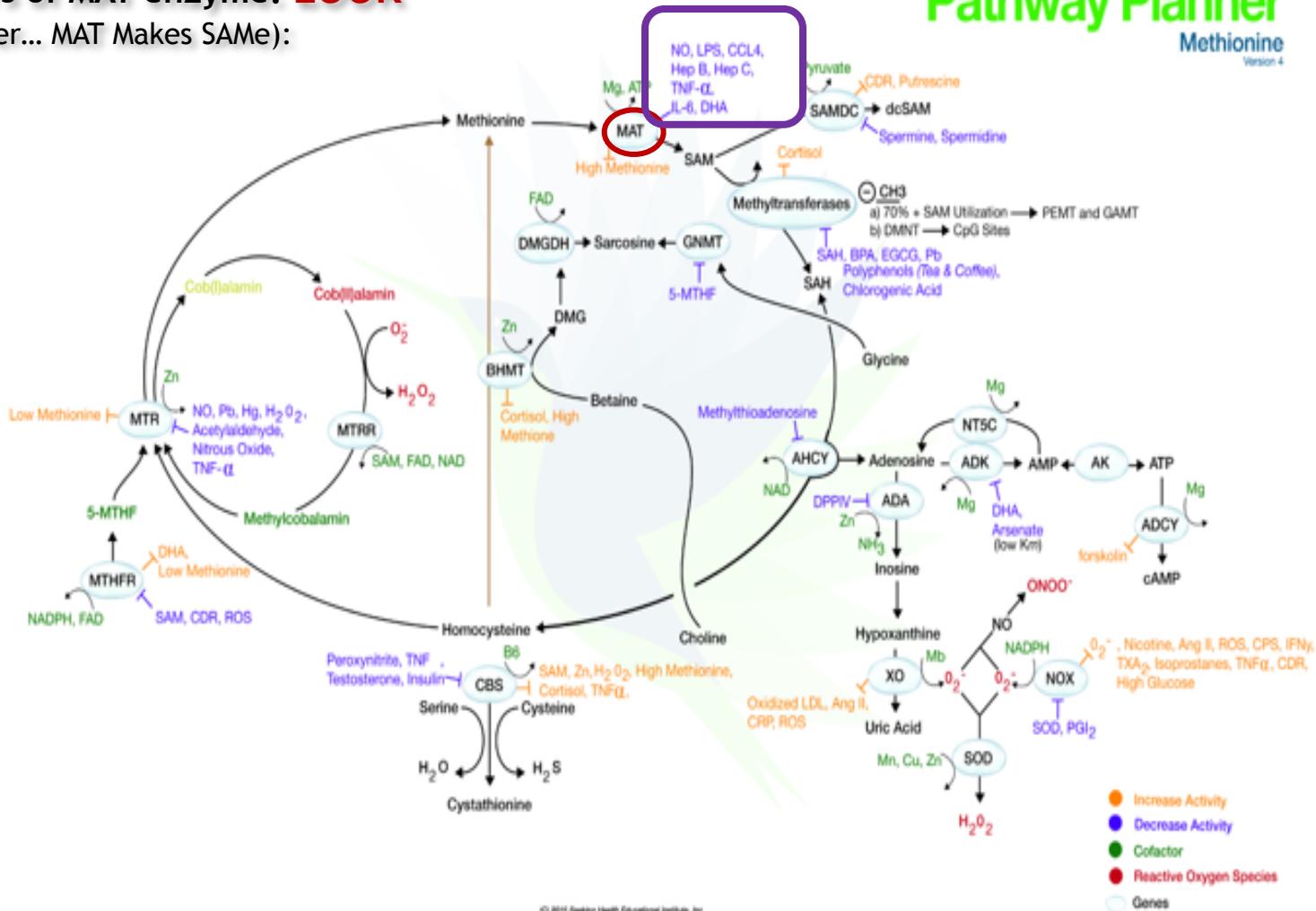
**LPS = Increased TNF-alpha &  
IL-6**

## Inhibitors of MAT enzyme: LOOK

(\*\*remember... MAT Makes SAMe):

## Pathway Planner

Methionine  
Version 4



# Testing: Lipopolysaccharide (LPS) Example

ADVANCED INTESTINAL BARRIER ASSESSMENT: PROFILE 5150 (PLASMA)



LPS IgA



LPS IgG



LPS IgM



ADVANCED INTESTINAL BARRIER ASSESSMENT: PROFILE 5150 (PLASMA)



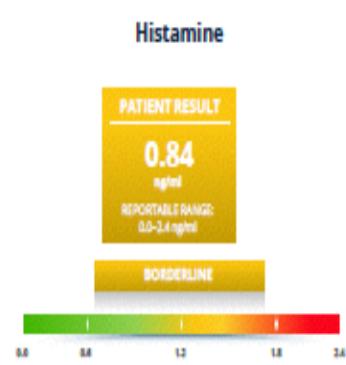
Zonulin



Diamine Oxidase (DAO)



Histamine



A high DAO-to-Histamine ratio suggests that there is sufficient DAO present to degrade any free Histamine.

A low ratio, on the other hand, may be indicative of histamine intolerance. The lower the ratio, and particularly the closer it gets to 1, the stronger that indication.

**Examples:** Actomyosin IgA - Epithelial cell damage (intestinal wall cells)  
 Occludin/Zonulin IgG/IgA/IgM - Tight junction damage  
 LPS (Lipopolysaccharide, Gram Negative Bacteria) Immune response, involved in chronic, systemic inflammation.

TEST	RESULT		
	IN RANGE (Normal)	EQUIVOCAL*	OUT OF RANGE
Array 2 – Intestinal Antigenic Permeability Screen			
Actomyosin IgA **		46.12	0.0-20
Occludin/Zonulin IgG	0.39		0.2-1.5
Occludin/Zonulin IgA		1.80	0.1-1.8
Occludin/Zonulin IgM		2.10	0.1-2.1
Lipopolsaccharides (LPS) IgG	0.72		0.1-1.6
Lipopolsaccharides (LPS) IgA	0.49		0.1-1.8
Lipopolsaccharides (LPS) IgM	1.03		0.1-2.0

TEST	RESULT		
	IN RANGE (Normal)	EQUIVOCAL*	OUT OF RANGE
Array 2 – Intestinal Antigenic Permeability Screen			
Actomyosin IgA **	11.47		0.0-20
Occludin/Zonulin IgG	0.44		0.2-1.5
Occludin/Zonulin IgA	0.79		0.1-1.8
Occludin/Zonulin IgM		1.81	0.1-2.1
Lipopolsaccharides (LPS) IgG	0.47		0.1-1.6
Lipopolsaccharides (LPS) IgA	0.50		0.1-1.8
Lipopolsaccharides (LPS) IgM		1.52	0.1-2.0

If there is LPS...  
...Stool Assessment is needed  
...Look for Gram-Negative Pathogens

BACTERIOLOGY CULTURE		
Expected/Beneficial flora	Commensal (Imbalanced) flora	Dysbiotic flora
3+ Bacteroides fragilis group	2+ Alpha hemolytic strep	
1+ Bifidobacterium spp.	1+ Citrobacter freundii complex	
2+ Escherichia coli	2+ Enterobacter cloacae complex	
2+ Lactobacillus spp.	2+ Enterobacter cloacae complex, isolate 2	
1+ Enterococcus spp.	2+ Enterobacter sakazakii	
2+ Clostridium spp.	2+ Gamma hemolytic strep	
NG = No Growth		

## BACTERIA INFORMATION

**Expected /Beneficial bacteria** make up a significant portion of the total microflora in a healthy & balanced GI tract. These beneficial bacteria have many health-protecting effects in the GI tract including manufacturing vitamins, fermenting fibers, digesting proteins and carbohydrates, and propagating anti-tumor and anti-inflammatory factors.

**Clostridia** are prevalent flora in a healthy intestine. *Clostridium* spp. should be considered in the context of balance with other expected/beneficial flora. Absence of clostridia or over abundance relative to other expected/beneficial flora indicates bacterial imbalance. If *C. difficile* associated disease is suspected, a Comprehensive Clostridium culture or toxigenic *C. difficile* DNA test is recommended.

**Commensal (Imbalanced) bacteria** are usually neither pathogenic nor beneficial to the host GI tract. Imbalances can occur when there are insufficient levels of beneficial bacteria and increased levels of commensal bacteria. Certain commensal bacteria are reported as dysbiotic at higher levels.

**Dysbiotic bacteria** consist of known pathogenic bacteria and those that have the potential to cause disease in the GI tract. They can be present due to a number of factors including consumption of contaminated water or food, exposure to chemicals that are toxic to beneficial bacteria, the use of antibiotics,

## Comprehensive Stool Analysis / Parasitology x3

## Example

BACTERIOLOGY CULTURE		
Expected/Beneficial flora	Commensal (Imbalanced) flora	Dysbiotic flora
3+ Bacteroides fragilis group	2+ Alpha hemolytic strep	
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2+ Escherichia coli	2+ Enterobacter cloacae complex	★
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1+ Enterococcus spp.	2+ Enterobacter sakazakii	★
2+ Clostridium spp.	2+ Gamma hemolytic strep	
NG = No Growth		★ = Gram Negative

### BACTERIA INFORMATION

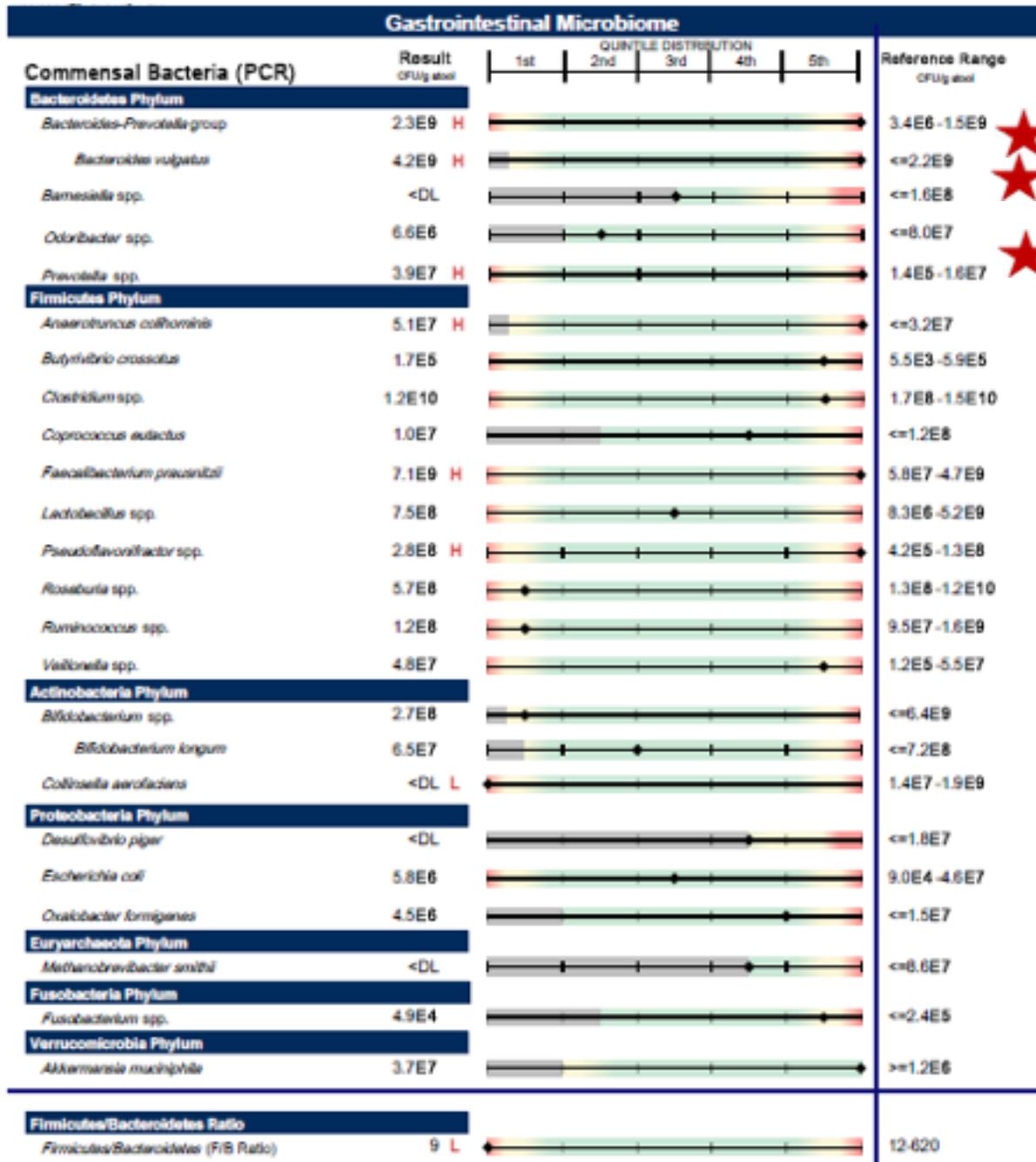
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Example



# Example

**Microbiology**

**Bacteriology**

**12. Beneficial Bacteria**

Lactobacillus species	*NG	(1)
Escherichia coli		(2)
Bifidobacterium		(1)

**13. Additional Bacteria**

Streptococcus agalactiae gp B	NP	(2)
Haemolytic Escherichia coli	NP	(4)

**14. Mycology**

\*NG \*NG

Human microbiota is influenced by environmental factors and the competitive ecosystem of the organisms in the GI tract. Pathological significance should be based upon clinical symptoms and reproducibility of bacterial recovery.

\*NG  
 \*NG

NP

PP

P

No Growth      Non-Pathogen      Potential Pathogen      Pathogen

**Microbiology**

**Bacteriology**

**12. Beneficial Bacteria**

Lactobacillus species	*NG	(1)
Escherichia coli		(2)
Bifidobacterium		(1)

**13. Additional Bacteria**

alpha haemolytic Streptococcus	NP	(2)
gamma haemolytic Streptococcus	NP	(2)
Mucoid Escherichia coli	NP	(3)

**14. Mycology**

\*NG \*NG

Human microbiota is influenced by environmental factors and the competitive ecosystem of the organisms in the GI tract. Pathological significance should be based upon clinical symptoms and reproducibility of bacterial recovery.

\*NG  
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PP

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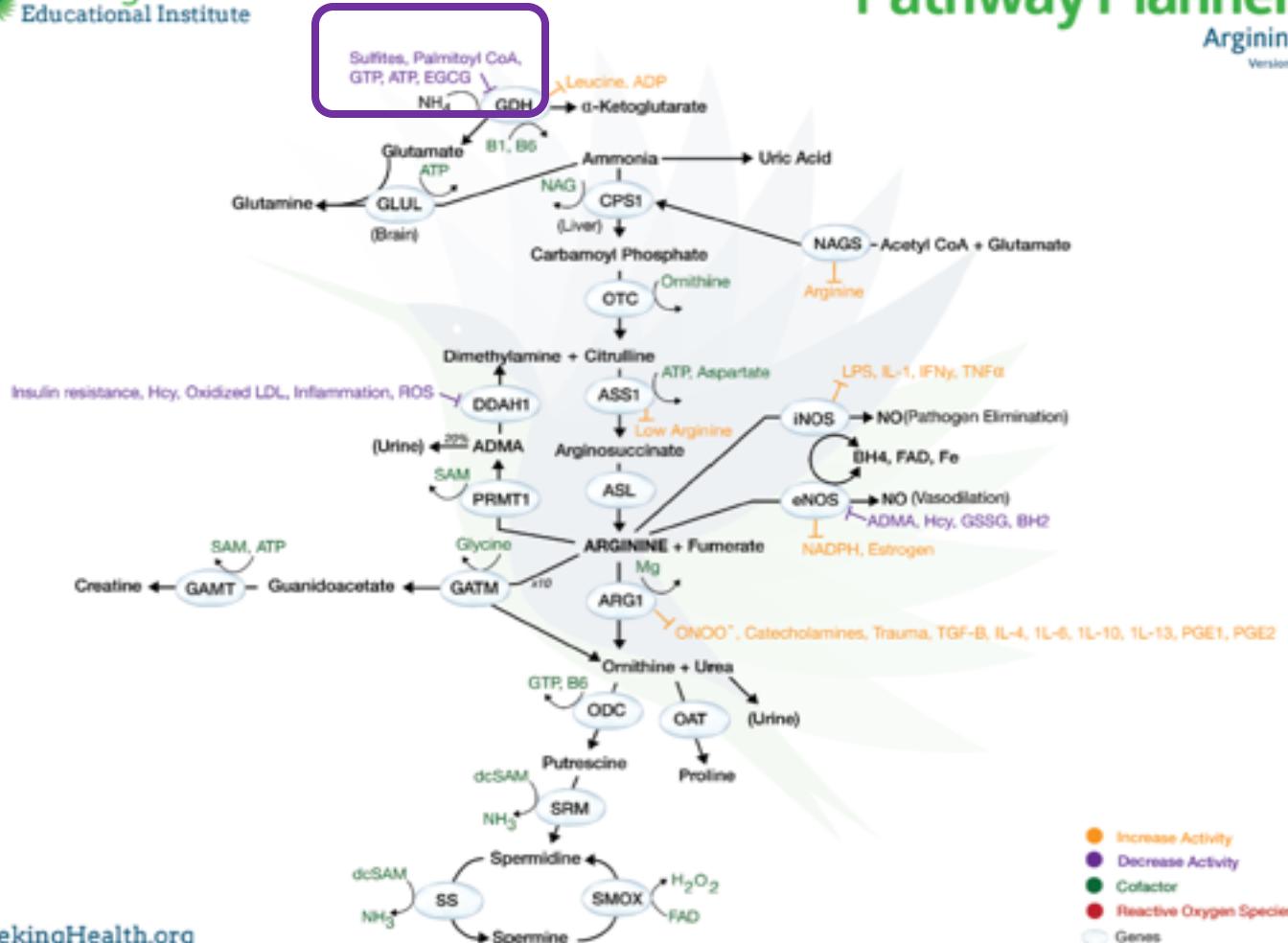
# In addition... “Sulfite-Producing Bacteria”

- The most common species:
  - *Pseudomonas* ★
  - *Citrobacter* ★
  - *Aeromonas* ★
  - *Salmonella* ★
  - *Escherichia coli*★

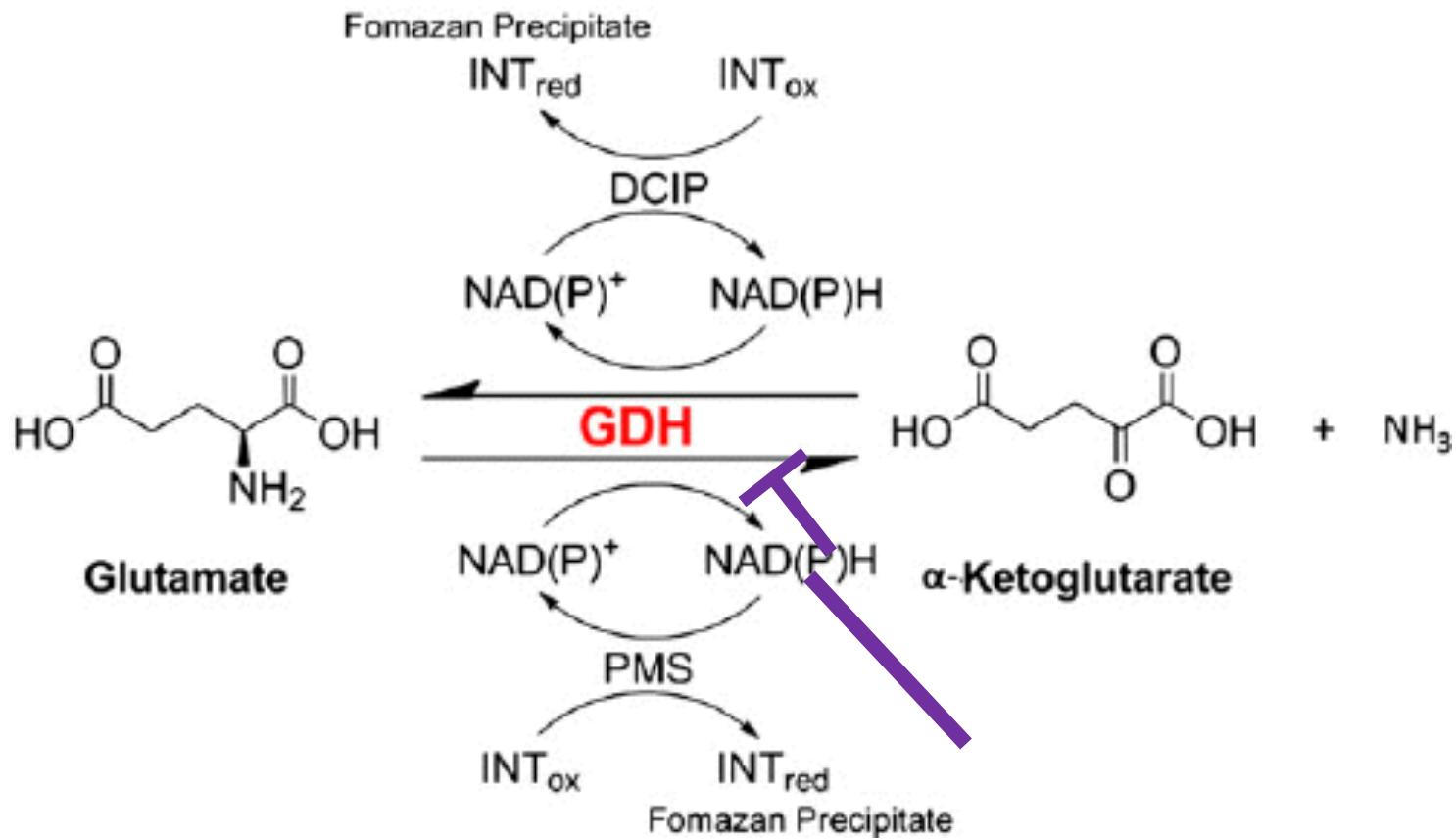
# Sulfites... Block!!



**Pathway Planner**  
Arginine  
Version 4

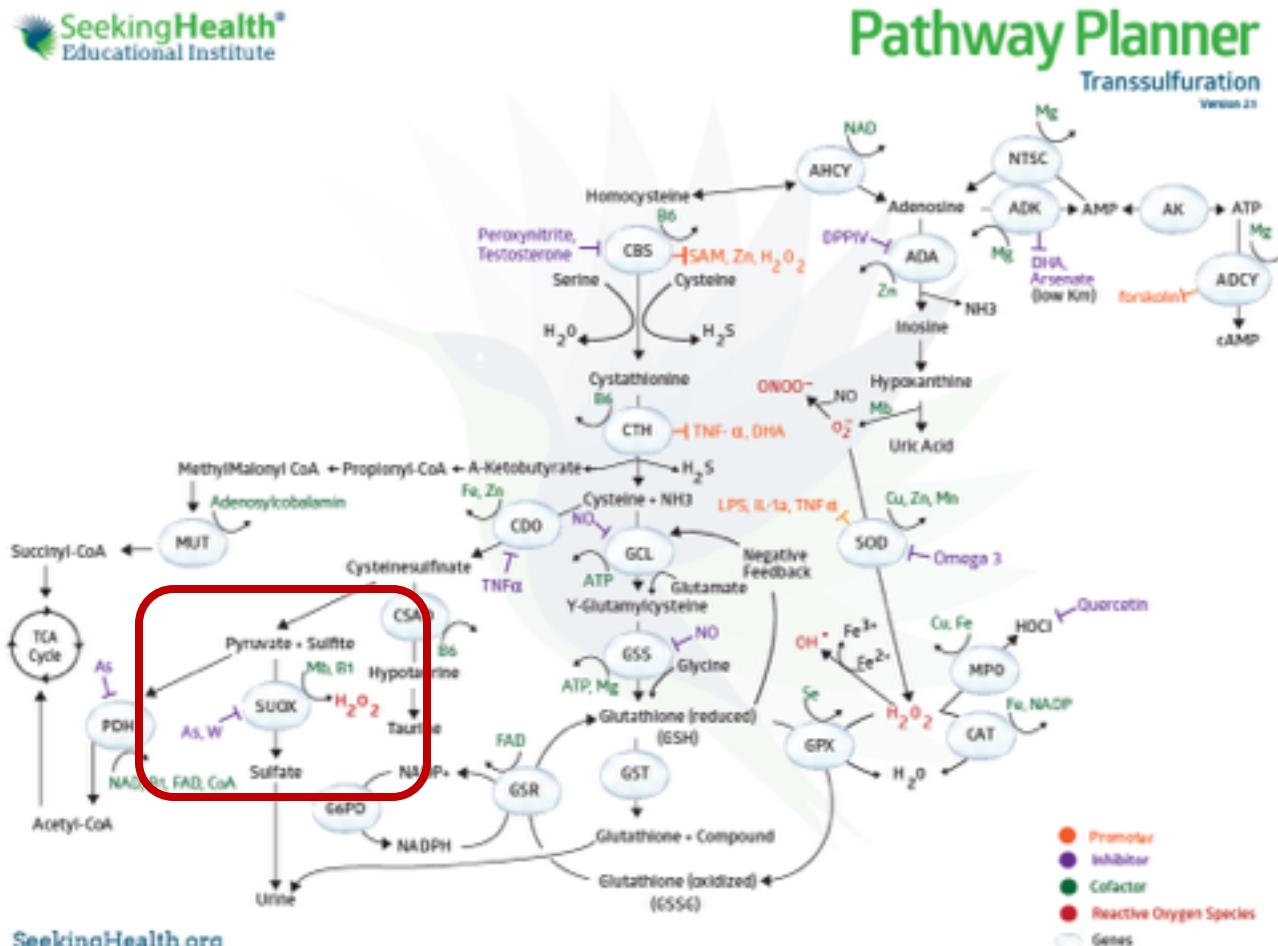


# Sulfites Block...



[https://www.researchgate.net/profile/Christopher\\_Auger/publication/224977072/figure/fig1/AS-302602530115584@1449157473474/Fig-1-A-schematic-representation-of-the-electrophoretic-method-to-detect-GDH-linked.png](https://www.researchgate.net/profile/Christopher_Auger/publication/224977072/figure/fig1/AS-302602530115584@1449157473474/Fig-1-A-schematic-representation-of-the-electrophoretic-method-to-detect-GDH-linked.png)

# Sulfite Metabolism: Molybdenum, B1



# If minerals are low... Suspect abnormal intestinal pathogens

## Pathogen:

- Epstein Barr Virus.....
- Clostridia.....
- Streptococcus.....
- Yeast.....
- Mycoplasma.....
- Mycobacterium TB.....
- E. Coli.....
- Klebsiella, Psuedomonas...

## Nutrient Sufficiency (?):

- Chromium, Aluminum
- Cobalt
- Strontium, Cobalt, Chromium
- Chromium, cobalt, gold
- Thiamine
- Niacin
- Chromium
- Niacin

Tentative findings  
Bernarda Zenker,

MD

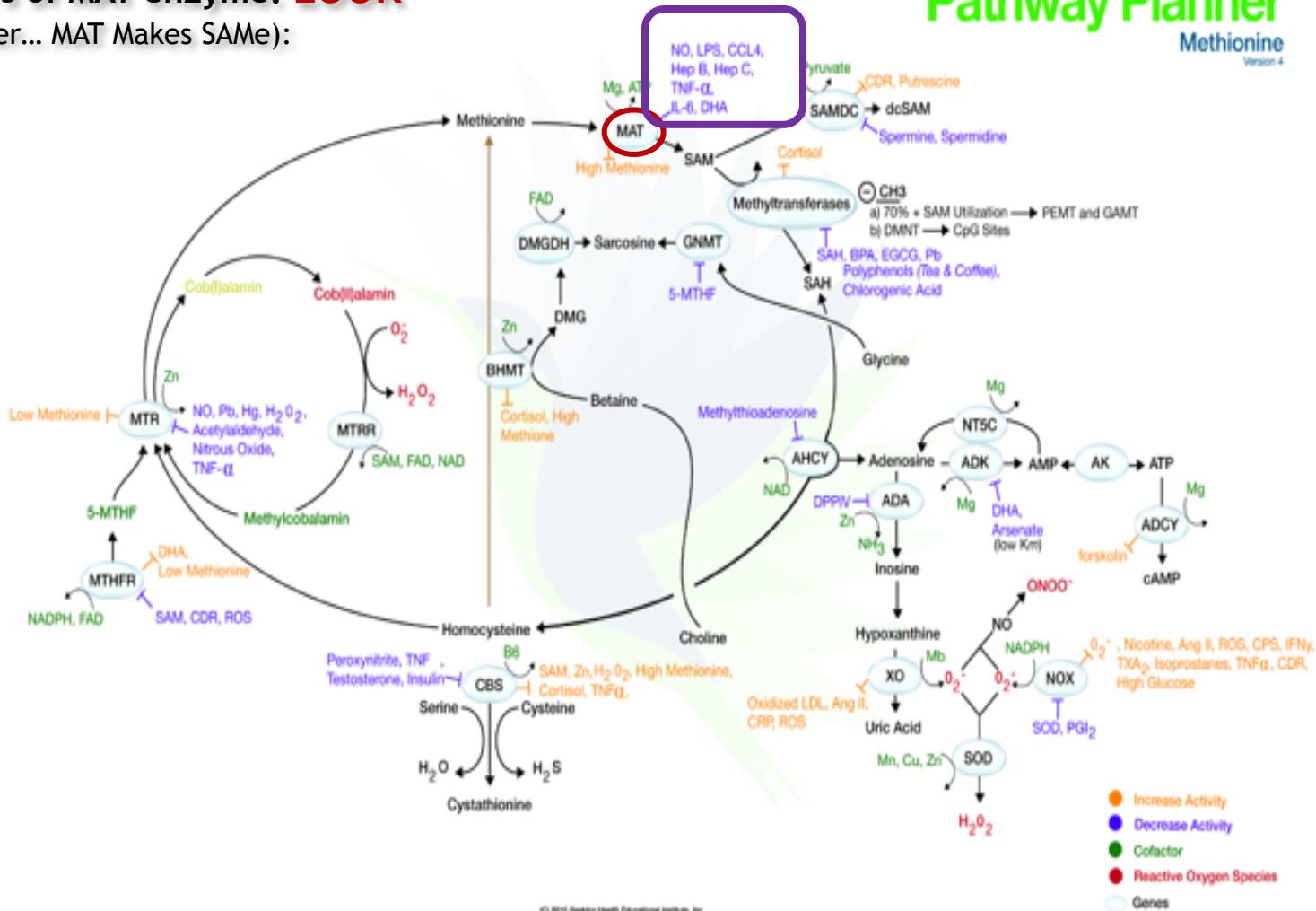
**IL-6 (Interluekin-6)  
TNF-alpha**

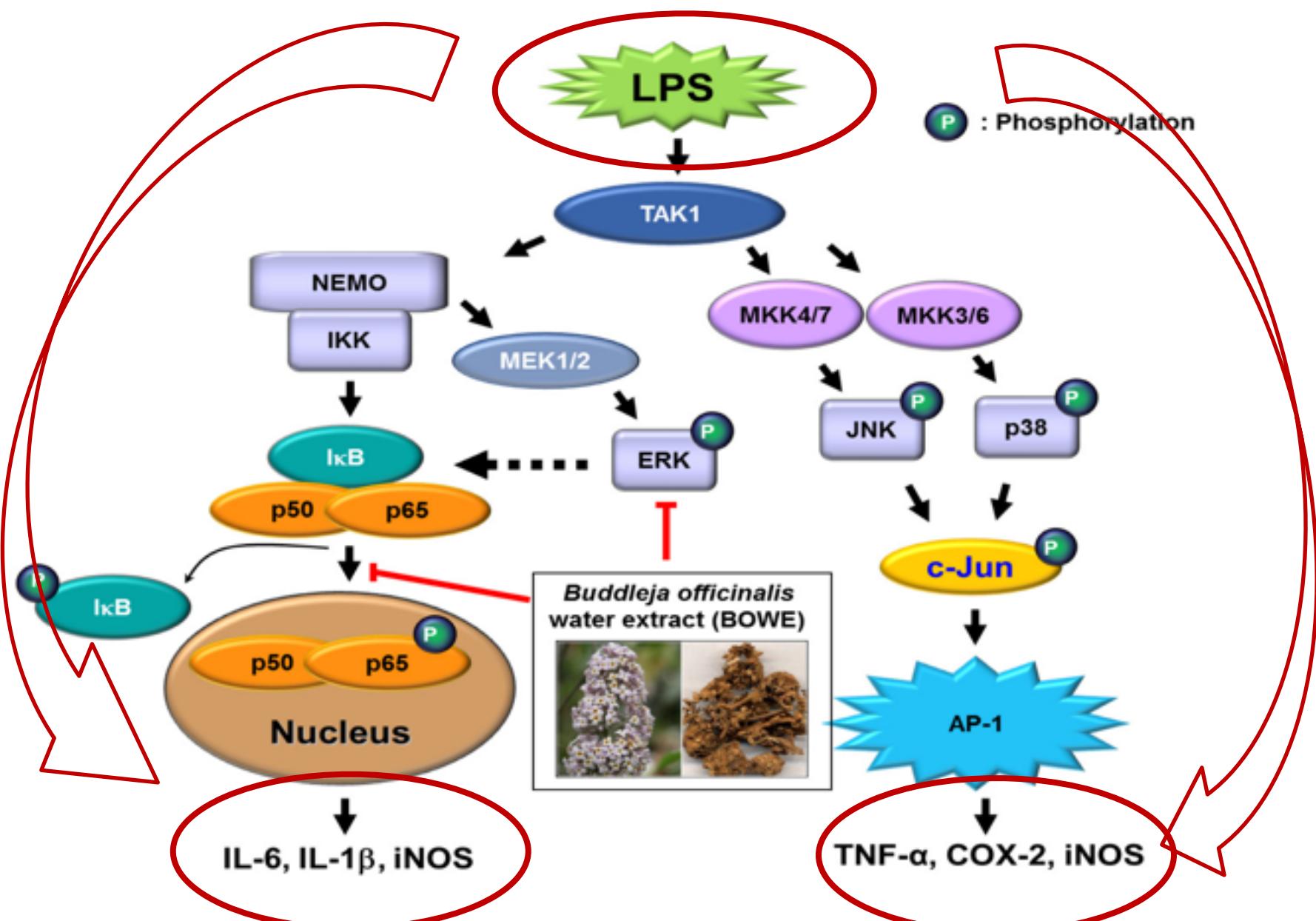
## Inhibitors of MAT enzyme: LOOK

(\*\*remember... MAT Makes SAMe):

## Pathway Planner

Methionine  
Version 4





## Autoimmune diseases



Ankylosing spondylitis  
Multiple sclerosis  
Eczema  
Hidradenitis suppurativa



Inflammatory bowel disease  
Atopic dermatitis  
Rheumatoid arthritis



Psoriasis  
Sarcoidosis  
Scleroderma  
Systemic lupus erythematosus

## Cardiovascular diseases



Atherosclerosis  
Myocardial infarction

LPS

TNF- $\alpha$

IL-6

## Neurologic diseases

Alzheimer's disease  
Epilepsy  
Bipolar disorder  
Parkinson's disease  
Depression



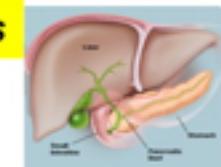
## Osteoporosis



## Cancer



## Non-alcoholic fatty liver disease



## Metabolic diseases

Obesity  
Diabetes, type 2

## Pulmonary diseases



Asthma  
Chronic obstructive pulmonary disease

# Immunologic Networks



playground 1000000000

8F, 58 olog, 1-4-4, Nezu, Bunkyo-ku, Tokyo 113-0031, Japan  
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Email: support@biscole.com Web: [www.biscole.com/](http://www.biscole.com/)

plus several factors by

Ambachtsweg 5, 1422 DS Uithoorn, The Netherlands  
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Email: info@semed.belexcel.com, techsupport@belexcel.com

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Toll-free Phone: 1-877-Bio-Legend (246-5343)  
Phone: (858) 455-9588 Fax: (877) 455-9587  
Email: customerserv@biolog.com, techserv@biolog.com

[www.biolegend.com](http://www.biolegend.com)

[Intertech](http://www.intertech.com) offers numerous online learning opportunities.

You would like to thank Dr. William K. Kauffman of measured medical records for his contributions to this assessment.

# Cytokine testing: Very Expensive Example

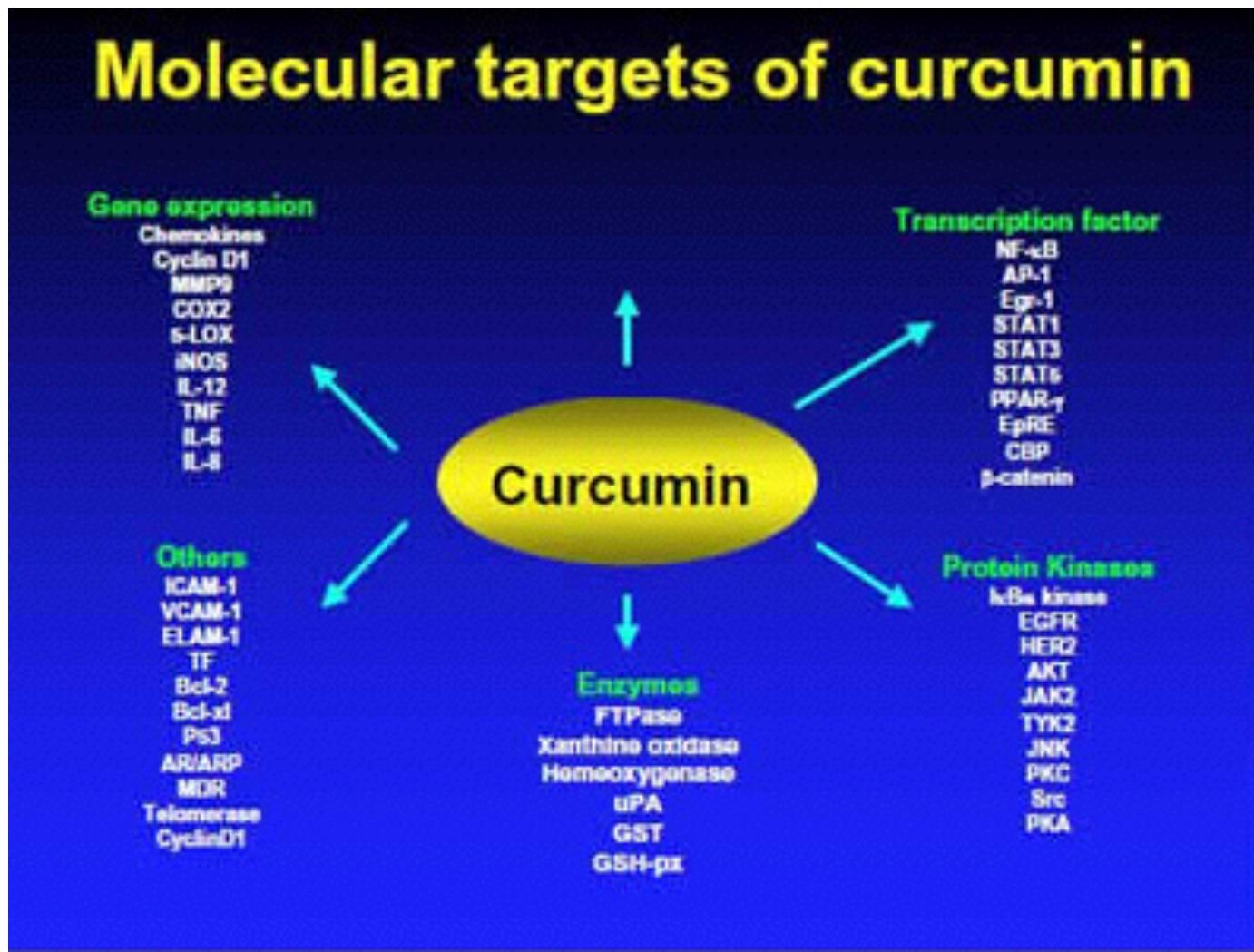
## Test Results

### 5082 - Stim. Cytokine Analysis Comprehensive

#### Stimulated Cytokines



# Molecular targets of curcumin



[http://www.positivehealth.com/img/phfiles/Issue\\_220/Issue\\_220\\_Articles/molecular\\_targets\\_of\\_curcumin.jpg](http://www.positivehealth.com/img/phfiles/Issue_220/Issue_220_Articles/molecular_targets_of_curcumin.jpg)

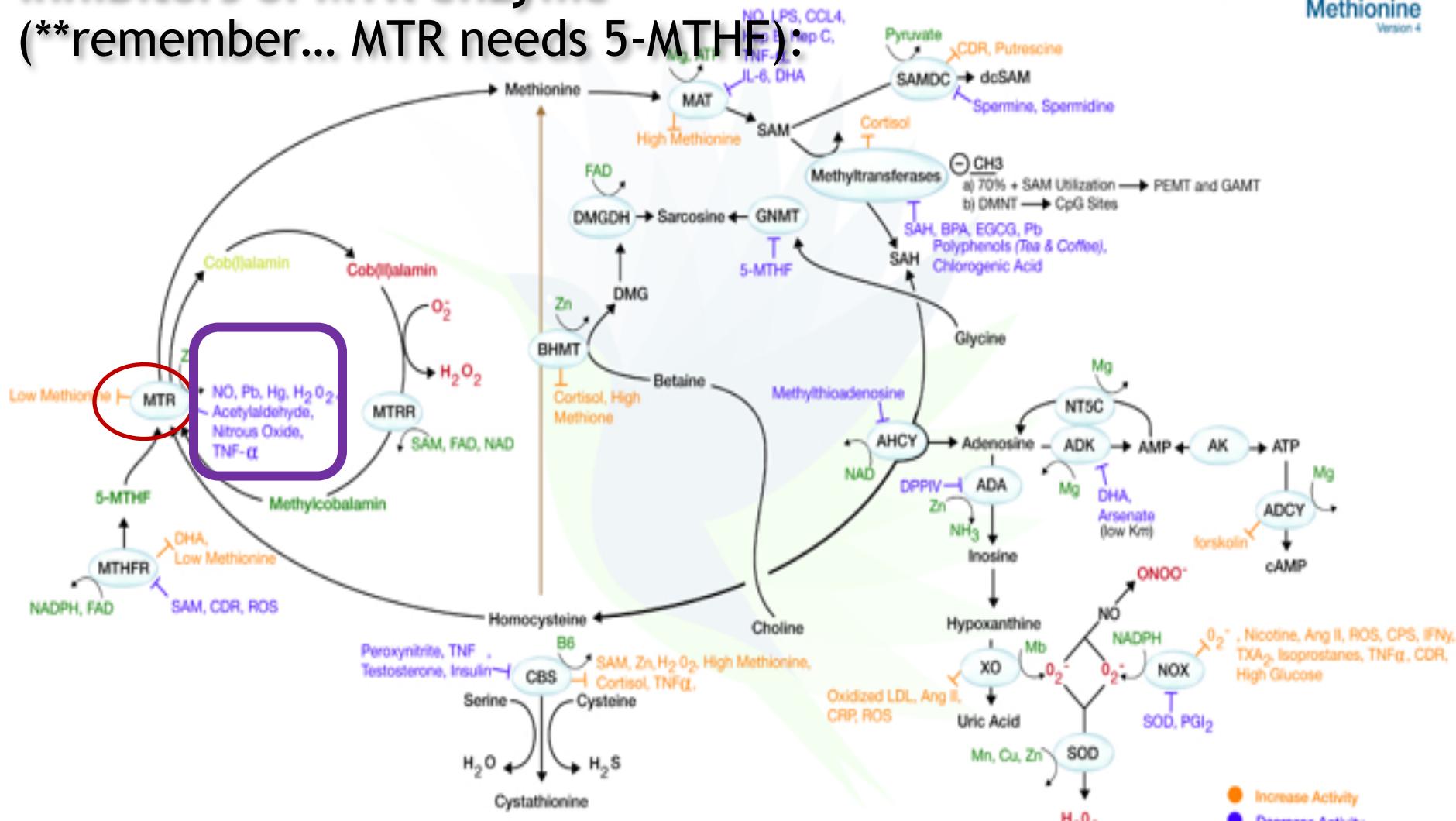
**2<sup>nd</sup> Enzyme: MTR**

# Inhibitors of MTR enzyme

(\*\*remember... MTR needs 5-MTHF):

# Pathway Planner

Methionine  
Version 4



# Acetylaldehyde

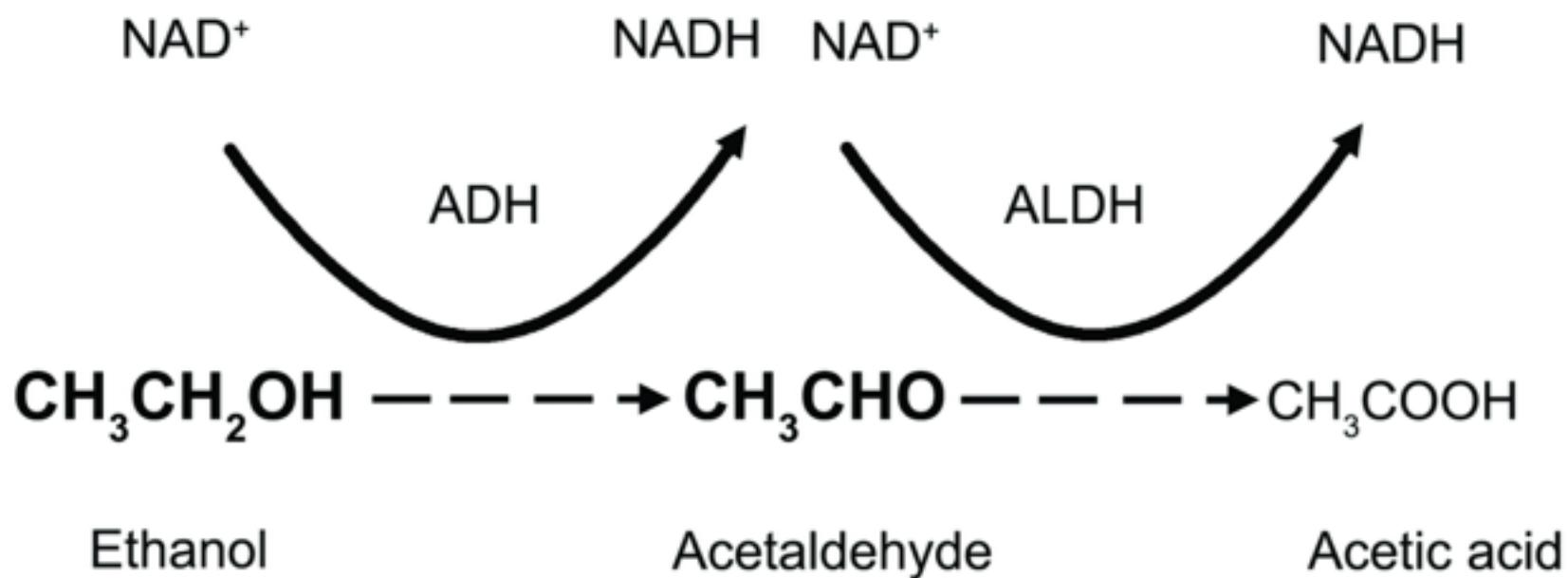
# Acetylaldehyde by *Candida*

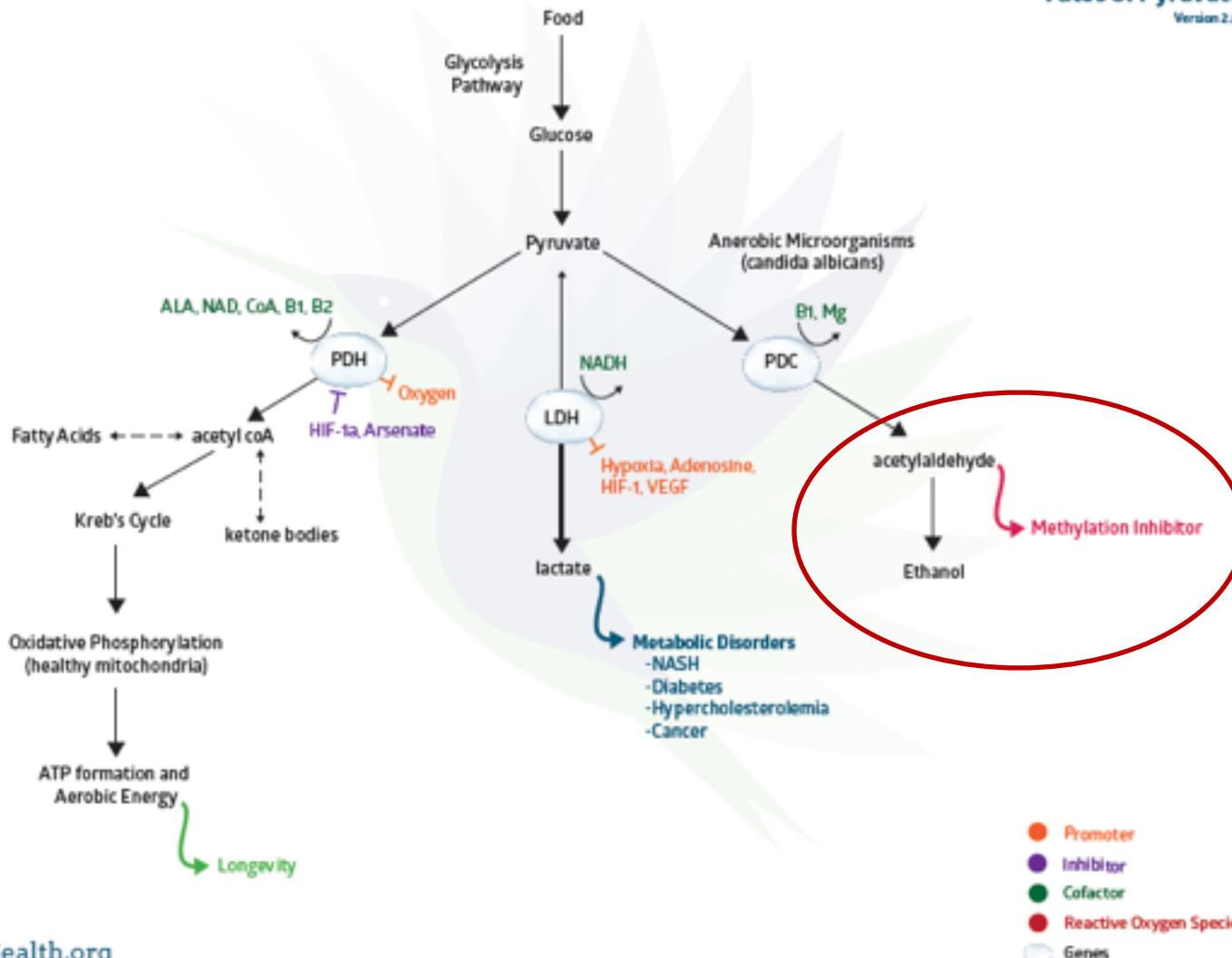


*Candida albicans*

- Brain Fog
- Bloating
- Fatigue
- Weight gain
- Insulin Resistance
- Cold hands and feet
- Yeast infections
- Sugar cravings
- Dystrophic nails

<https://s-media-cache-ak0.pinimg.com/originals/e5/22/b6/e522b6a59aa9b8b491b8ec0a172f3f74.jpg>



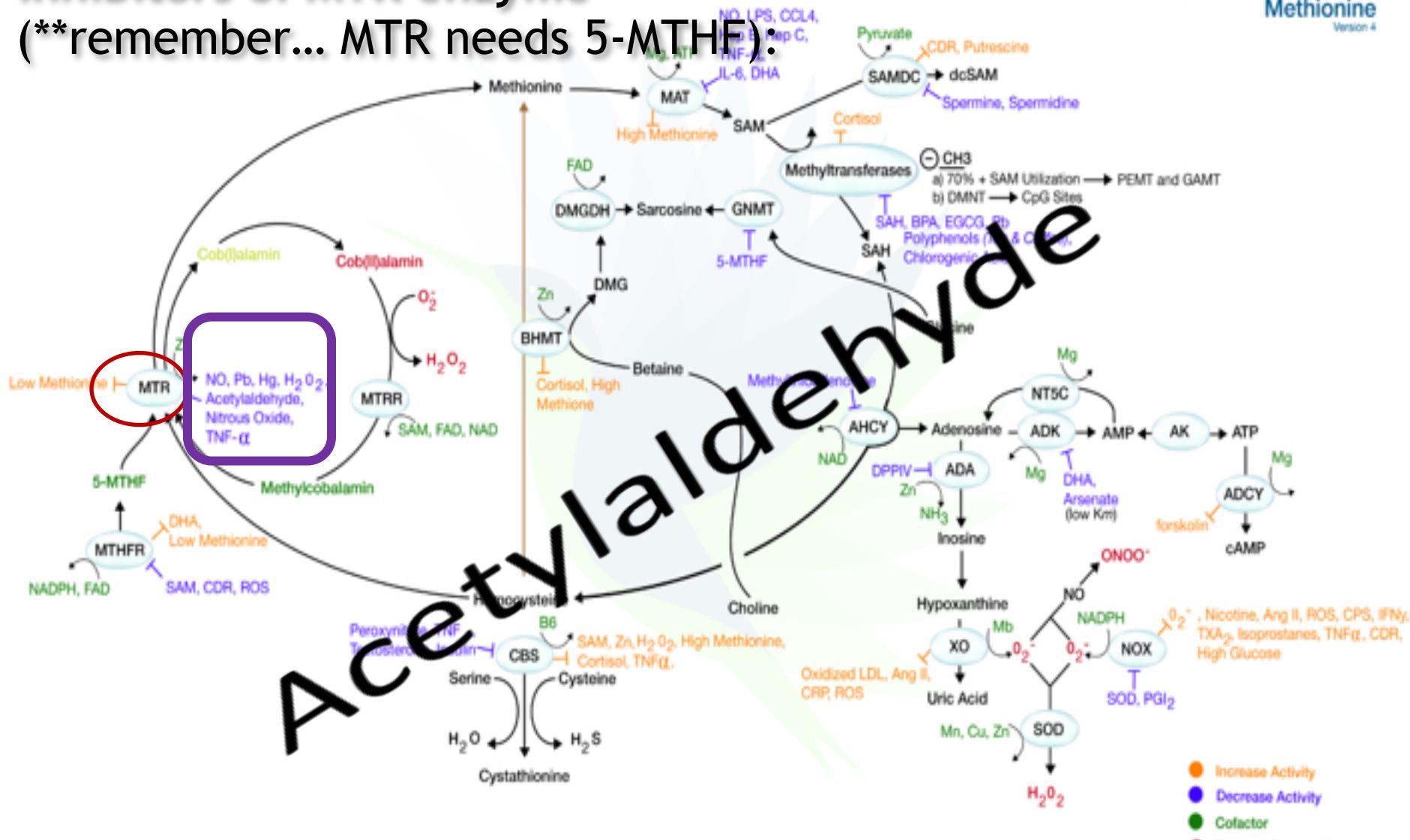


# Inhibitors of MTR enzyme

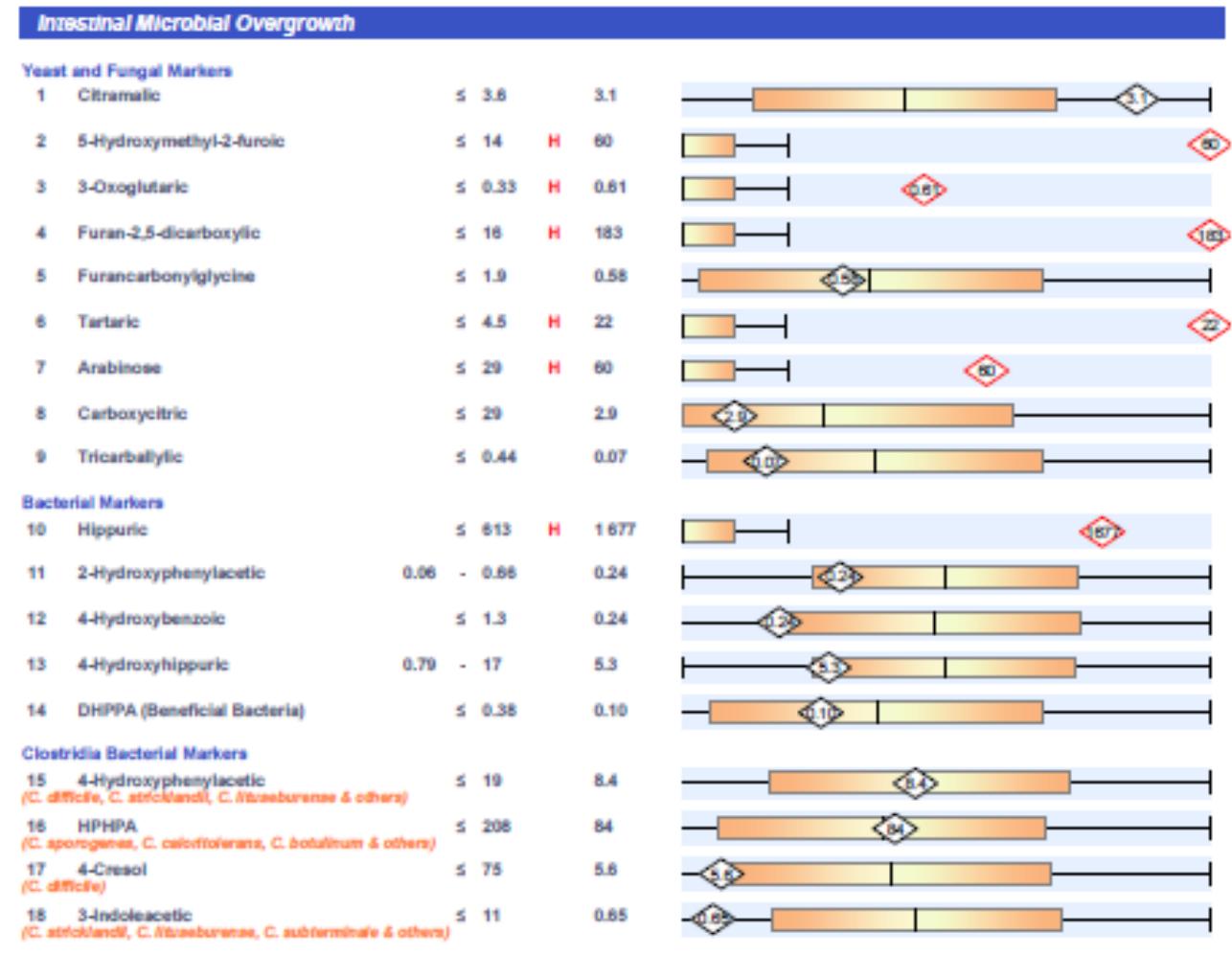
(\*\*remember... MTR needs 5-MTHF)

# Pathway Planner

Methionine  
Version 4



# Testing for Candida: Urine Arabinose Example



# Testing: Candida & Fungus Example

## Procedure Type

Ochratoxin A - Procedure by ELISA  
Aflatoxin Group (B1,B2,G1,G2) - Procedure by ELISA  
Trichothecene Group (Macrocytic) - Procedure by ELISA  
Gliotoxin Derivative - Procedure by ELISA

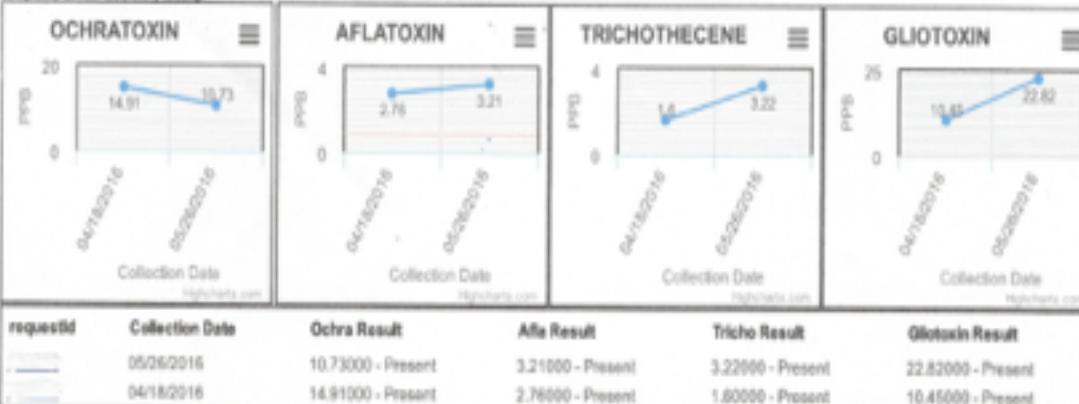
## Results:

Code	Test	Specimen	Value	Result	Not Present if less than	Equivalent if between	Present if greater or equal
E8501	Ochratoxin A	Urine	10.73000 ppb	Present	1.8 ppb	1.8-2.0 ppb	2.0 ppb
E8502	Aflatoxin Group (B1,B2,G1,G2)	Urine	3.21000 ppb	Present	0.8 ppb	0.8-1.0 ppb	1.0 ppb
E8503	Trichothecene Group (Macrocytic)	Urine	3.22000 ppb	Present	0.18 ppb	0.18-0.2 ppb	0.2 ppb
E8510	Gliotoxin Derivative	Urine	22.82000 ppb	Present	0.2 ppb	0.2-0.3 ppb	0.3 ppb

  
Director Signature \_\_\_\_\_

Tests such as this should be used only in conjunction with other medically established diagnostic elements (e.g., symptoms, history, clinical impressions, results from other tests, etc). Physicians should use all of the information available to them to diagnose and determine appropriate treatment for their patients.

**Disclaimer:** This test was developed and its performance characteristics determined by RealTime Lab. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88) as qualified to perform high complexity clinical laboratory testing.



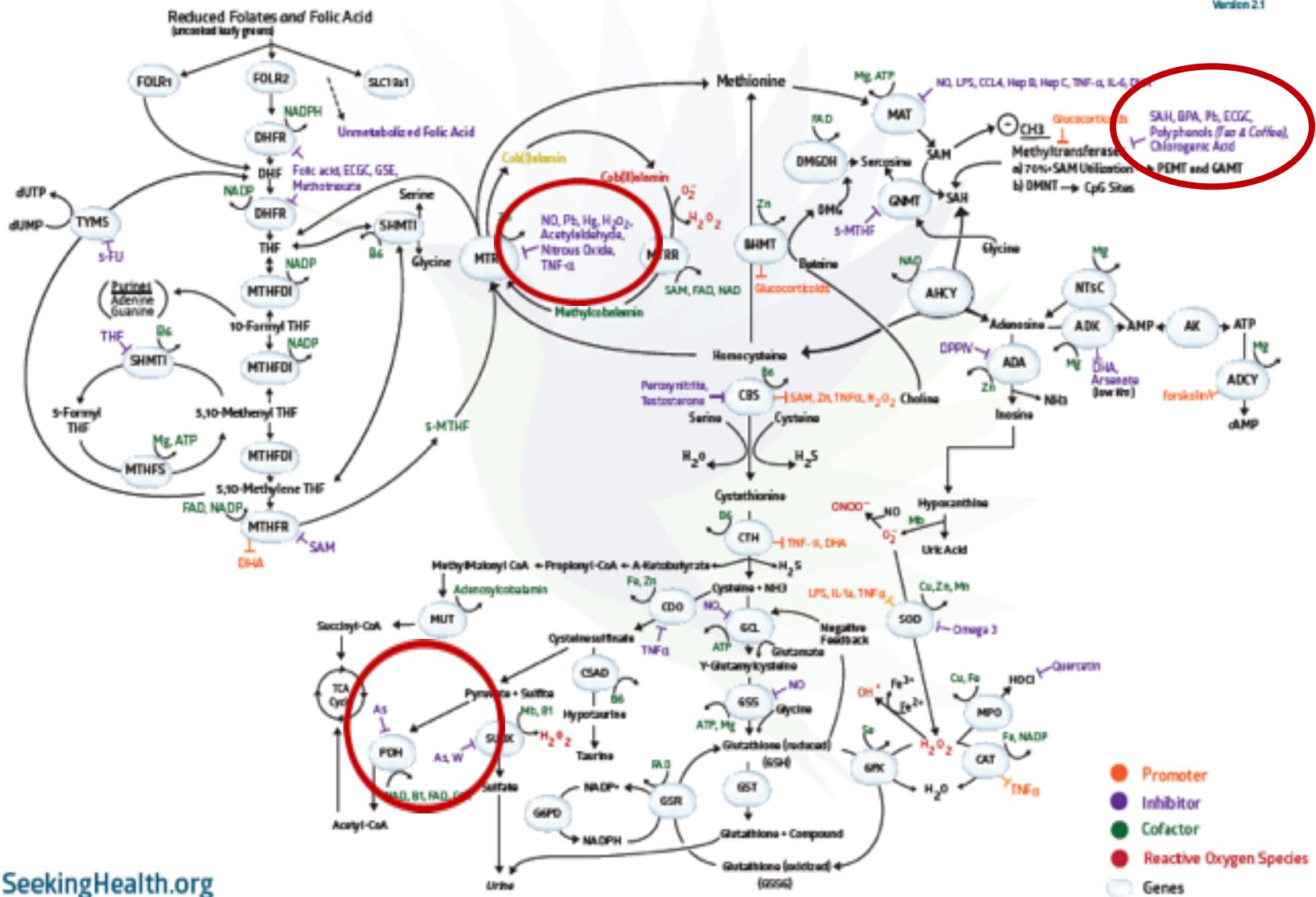
**Heavy Metals: Pb, Hg, Al,  
As,Cd**

There is NO perfect best test.

# Pathway Planner

## Folate, Methionine & Transsulfuration

Version 2.1



**Abstract: The Association between Blood Lead Levels and Osteoporosis among Adults—  
Results from the Third National Health and Nutrition Examination Survey (NHANES III)**  
[James R. Campbell](#) and [Peggy Auinger](#)

[Environ Health Perspect](#). 2007 Jul; 115(7): 1018–1022. Published online 2007 Mar 12.

Osteoporosis is a reduction in bone mass sufficient to increase the risk of fracture. Lead exposure during childhood may be a risk factor for low bone mineral density (BMD). Basic-science research demonstrates that lead exposure is associated with a decrease in BMD in animals. However, human studies are limited.

**Objective:** Our objective was to conduct a secondary analysis of a national database to explore the association between lead exposure and osteoporosis in adult humans.

**Methods:** In this study we used data from the Third National Health and Nutrition Examination Survey (NHANES III). We analyzed subjects who were  $\geq 50$  years of age. A concurrent venous blood lead level defined lead exposure. The primary outcome variable was the BMD of the total hip. We conducted analyses on four groups: non-Hispanic white men, non-Hispanic white women, African-American men, and African-American women. We conducted bivariate analyses between covariates known to be associated with bone density (i.e., age, body mass index, calcium intake, ethanol/tobacco consumption, physical activity, socioeconomic status) and the total hip BMD. The significant covariates were introduced into analysis of covariance to determine the association between BMD and blood lead level

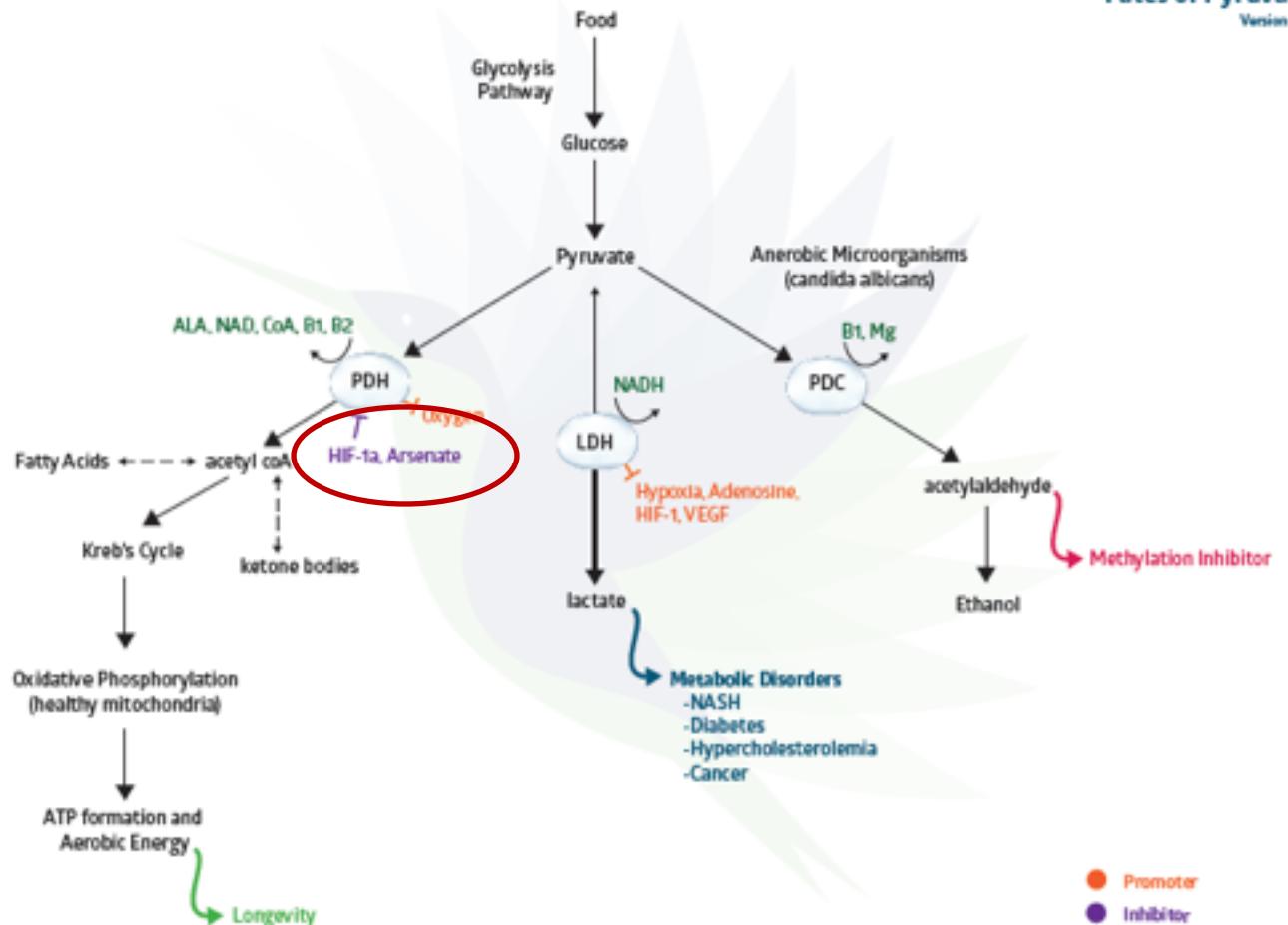
**Results:** The adjusted mean total hip BMD among non-Hispanic white males with a blood lead level in the lowest tercile versus the highest tercile was  $0.961 \text{ g/cm}^2$  and  $0.934 \text{ g/cm}^2$ , respectively ( $p < 0.05$ ). We also found a similar association among white females, but the difference was marginally significant ( $0.05 < p < 0.10$ ).

**Conclusions:** We found a significant inverse association between lead exposure and BMD, but only among white subjects. However, because of the cross-sectional design of NHANES, we cannot make inferences about the temporal sequence of this association. With the large number of adults who had lead exposure in the past and the morbidity associated with osteoporosis, further inquiry is necessary on the possible causal association between lead exposure and osteoporosis in humans.

# Arsenic can inhibit Krebs Cycle

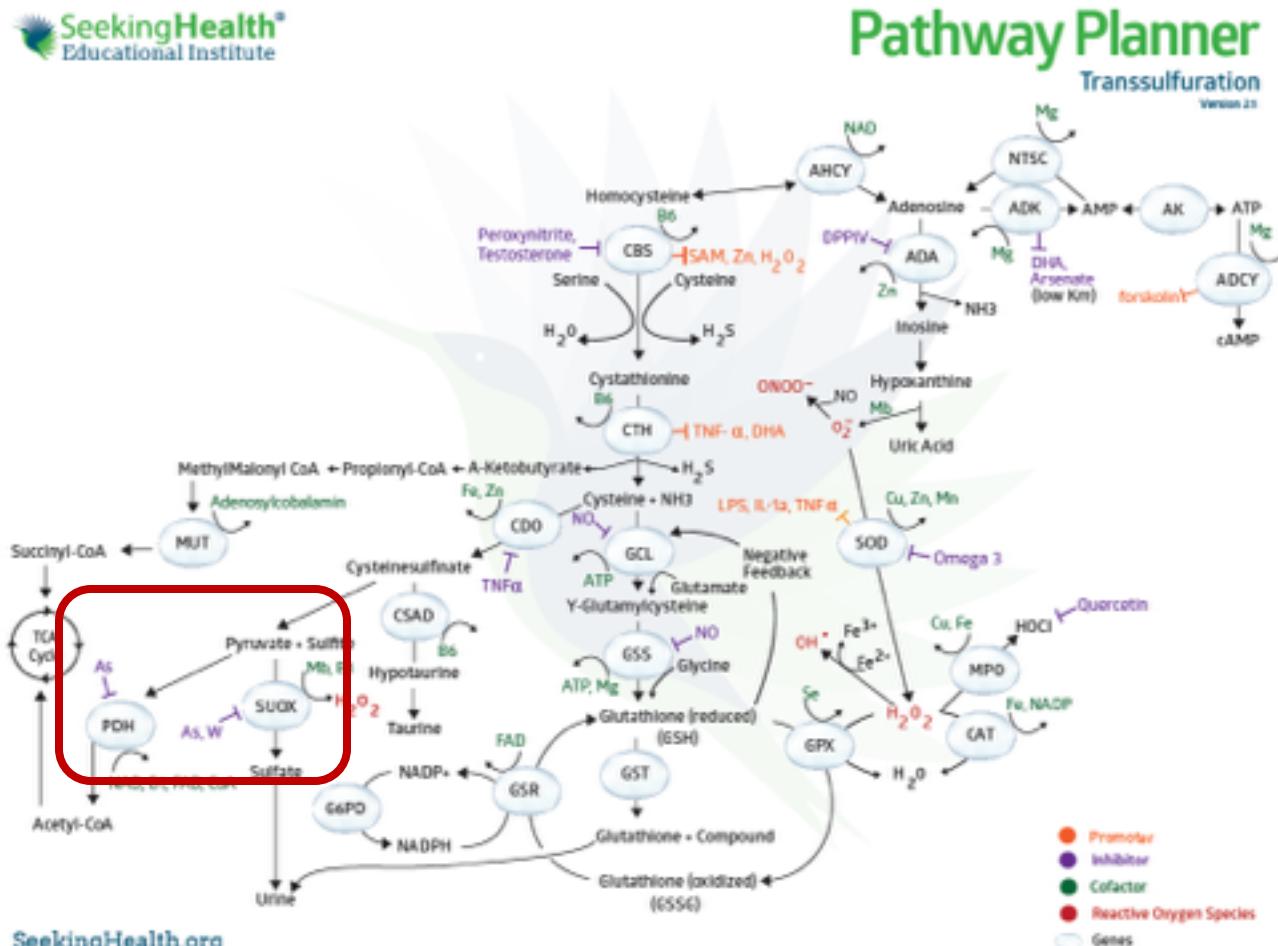


Pathway Planner  
Fates of Pyruvate  
Version 2.0

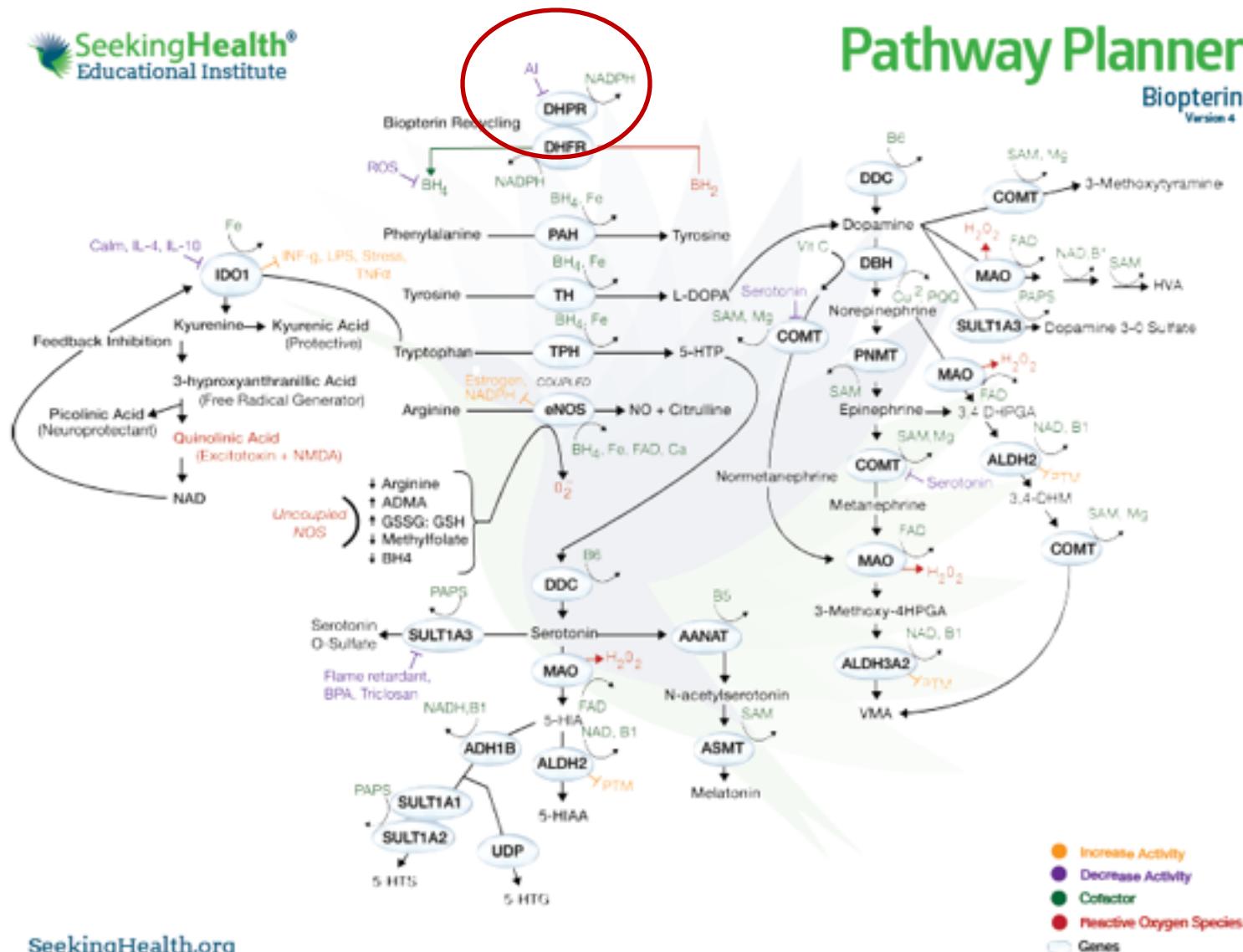


# Arsenic inhibits SUOX

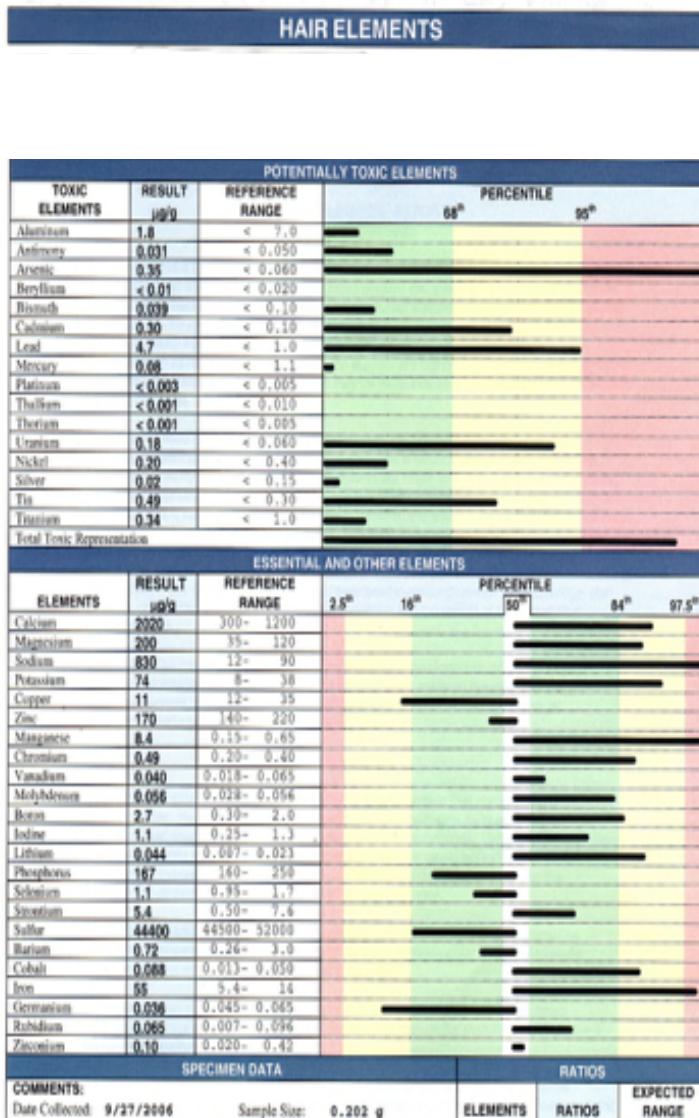
# Arsenic inhibits PDH



# Aluminum blocks BH4 production



# Hair Analysis: Heavy Metals Examples



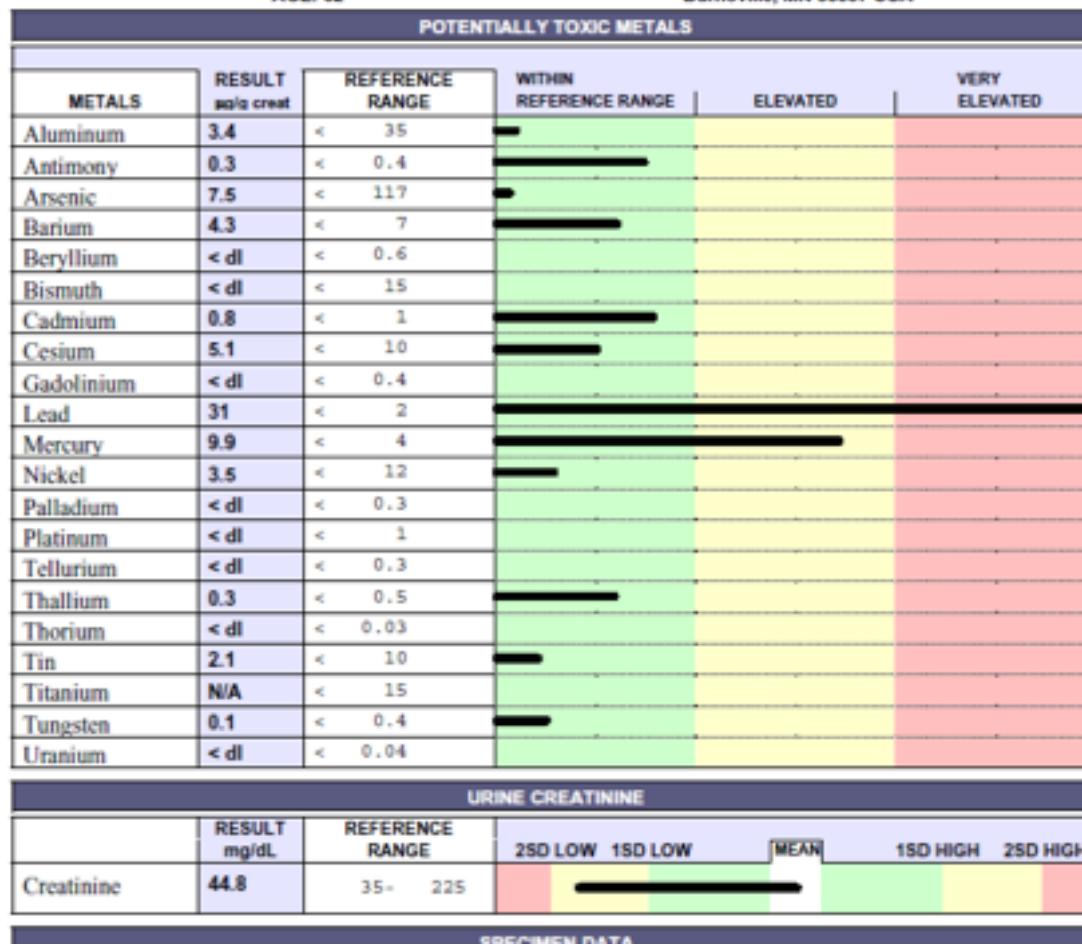
**Toxic Element Exposure Profile: Hair**

TOXIC METALS			
	RESULT µg/g	REFERENCE INTERVAL	PERCENTILE 68 <sup>th</sup> 95 <sup>th</sup>
Arsenic (As)	0.040	< 0.20	—
Lead (Pb)	0.77	< 6.0	—
Mercury (Hg)	0.07	< 2.0	—
Cadmium (Cd)	0.032	< 0.25	—
Chromium (Cr)	0.54	< 1.0	—
Beryllium (Be)	< 0.01	< 0.050	—
Cobalt (Co)	0.040	< 0.050	—
Nickel (Ni)	0.45	< 0.60	—
Zinc (Zn)	86	< 240	—
Copper (Cu)	49	< 35	—
Thorium (Th)	0.004	< 0.005	—
Thallium (Tl)	< 0.001	< 0.005	—
Barium (Ba)	0.94	< 2.0	—
Cesium (Cs)	< 0.002	< 0.010	—
Manganese (Mn)	0.27	< 1.2	—
Selenium (Se)	1.0	< 1.6	—
Bismuth (Bi)	0.078	< 5.0	—
Vanadium (V)	1.1	< 0.30	—
Silver (Ag)	0.15	< 1.0	—
Antimony (Sb)	0.048	< 0.20	—
Palladium (Pd)	< 0.004	< 0.010	—
Aluminum (Al)	62	< 22	—
Platinum (Pt)	< 0.003	< 0.010	—
Tungsten (W)	0.006	< 0.020	—
Tin (Sn)	0.49	< 0.80	—
Uranium (U)	0.029	< 0.20	—
Gold (Au)	0.013	< 0.30	—
Tellurium (Te)	< 0.05	< 0.050	—
Germanium (Ge)	0.042	< 0.045	—
Titanium (Ti)	0.56	< 2.0	—
Gadolinium (Gd)	0.002	< 0.008	—

**SPECIMEN DATA**

Comments:	Date Collected: 9/27/2006	Sample Size: 0.202 g	ELEMENTS	RATIOS	EXPECTED RANGE
Comments:					

# Provoked Urine Heavy Metal Eval: Female, age 60, Example



# Provoked Urine Heavy Metal Eval: Male, age 66, Example

## Toxic Metals; Urine

TOXIC METALS					
		RESULT µg/g creat	REFERENCE INTERVAL	WITHIN REFERENCE	OUTSIDE REFERENCE
Aluminum	(Al)	8	< 25	■	
Antimony	(Sb)	0.2	< 0.3	■	
Arsenic	(As)	9.6	< 108	■	
Barium	(Ba)	1.6	< 7	■	
Beryllium	(Be)	< dl	< 1		
Bismuth	(Bi)	0.3	< 10	■	
Cadmium	(Cd)	0.4	< 0.8	■	
Cesium	(Cs)	5.4	< 9	■	
Gadolinium	(Gd)	< dl	< 0.3		
Lead	(Pb)	52	< 2	■	
Mercury	(Hg)	4.1	< 3	■	
Nickel	(Ni)	1.8	< 10	■	
Palladium	(Pd)	< dl	< 0.3		
Platinum	(Pt)	< dl	< 1		
Tellurium	(Te)	< dl	< 0.8		
Thallium	(Tl)	0.2	< 0.5	■	
Thorium	(Th)	< dl	< 0.03		
Tin	(Sn)	0.8	< 9	■	
Tungsten	(W)	0.08	< 0.4	■	
Uranium	(U)	< dl	< 0.03		

URINE CREATININE						
	RESULT mg/dL	REFERENCE INTERVAL	-2SD	-1SD	MEAN	+1SD +2SD
Creatinine	176	45 - 225			■	

# Urine Porphyrin Test: Heavy Metals Example

	RESULT nmol/g creatinine	REFERENCE INTERVAL	PORPHYRINS		PERCENTILE 95 <sup>th</sup>	99 <sup>th</sup>
			95 <sup>th</sup>	99 <sup>th</sup>		
Uroporphyrins	14	< 17				
Heptacarboxylporphyrins	2.5	< 3				
Hexacarboxylporphyrins	0.81	< 3				
Pentacarboxylporphyrins	0.62	< 2.5				
Coproporphyrin I	23	< 20				
Coproporphyrin III	71	< 60				
Coproporphyrin I/Coproporphyrin III	0.32	< 0.8				
Total Porphyrins	110	< 90				
Precoproporphyrin II*	0.67	< 2				
Precoproporphyrin III*	0	< 1.2				
Precoproporphyrin III**	0.055	< 1.2				
Total Precoproporphyrins*	0.73	< 4				
Precoproporphyrins*/Uroporphyrins	0.054	< 0.1				

INFORMATION	
<p>Urinary porphyrins are oxidized intermediate metabolites of heme biosynthesis and can serve as biomarkers of disorders in heme production. Abnormal porphyrin profiles have been associated with genetic disorders, poor nutritional status, oxidative stress, and high level exposure to toxic chemicals or toxic metals. The ratio of Precoproporphyrins-to-Uroporphyrins is reported to increase the sensitivity for detecting abnormalities in individuals with low heme biosynthesis. Alcohol, sedatives, analgesics, antibiotics, estrogens and oral contraceptives can affect the levels of urinary porphyrins. Anemia, pregnancy, and liver disease can also affect porphyrin metabolism. The Urine Porphyrins test is best used in conjunction with urine toxic metals pre- and post-provocation testing.</p>	<p><u><a href="#">Porphyrins Pattern Recognition Guide:</a></u></p> <p><u>Mercury</u>: ↑ Penta, ↑ Copro III, ↑ Precopros, ↑ Precopros : Uros</p> <p><u>Arsenic</u>: ↑ Uros, ↑ Copro I : Copro III</p> <p><u>Lead</u>: ↑ Copro III</p> <p><u>Hexachlorobenzene, Dioxin</u>: ↑ Uros</p> <p><u>Methylchloride</u>, <u>Polyvinylchloride</u>, <u>TCP</u>: ↑ Copros</p> <p><u>Polybrominated biphenyl</u></p>

# Fecal Heavy Metals: Example

POTENTIALLY TOXIC METALS					
METALS	RESULT mg/kg	REFERENCE RANGE	PERCENTILE		
			68 <sup>th</sup>	95 <sup>th</sup>	
Mercury	<b>0.021</b>	<.05 w/o amalgams*	█		
Mercury	<b>0.021</b>	<.5 with amalgams*	█		
Antimony	<b>0.121</b>	< 0.080	██████████		
Arsenic	<b>0.18</b>	< 0.30	████		
Beryllium	<b>0.067</b>	< 0.009	██████████		
Bismuth	<b>0.611</b>	< 0.050	██████		
Cadmium	<b>0.69</b>	< 0.50	██████		
Copper	<b>55</b>	< 60	████		
Lead	<b>1.14</b>	< 0.50	██████		
Nickel	<b>12.9</b>	< 8.0	██████		
Platinum	<b>&lt; dl</b>	< 0.003	█		
Thallium	<b>0.016</b>	< 0.020	█		
Tungsten	<b>0.338</b>	< 0.090	██████		
Uranium	<b>0.168</b>	< 0.120	████		

% WATER CONTENT						
	RESULT % H <sub>2</sub> O	EXPECTED RANGE	2SD LOW	1SD LOW	MEAN	
% WATER CONTENT	63.4	60-85%		████	72.5%	

# Heavy Metal Testing: Pros and Cons

(1=Poor, 7=Optimal)

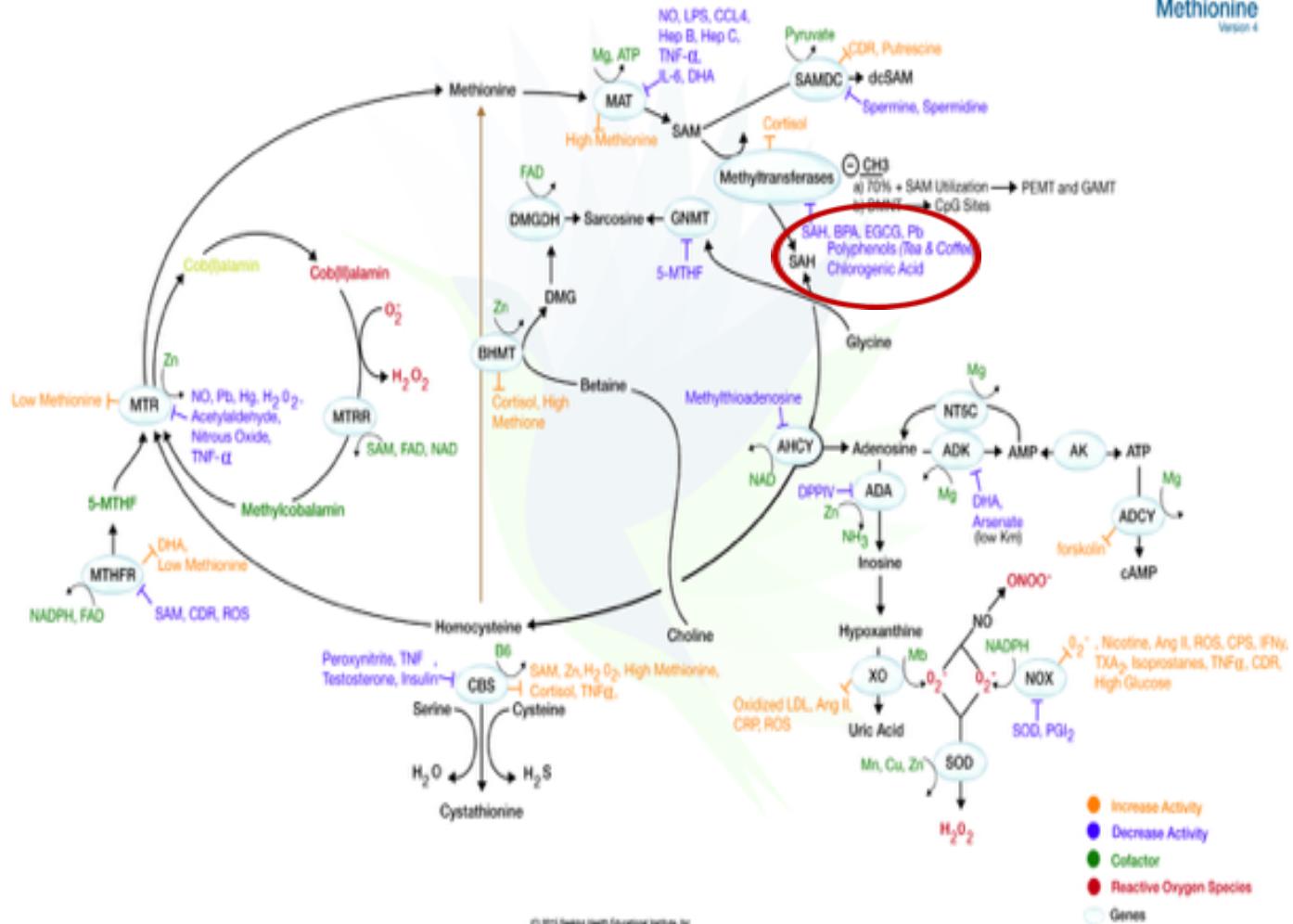
Type of Test	Cost	Invasive/Oral Agent	Reliable Results	Ease of Obtaining
Hair (scalp, pubic)	*****	**	*	***
Provoked Urine (6 hr, or 24 hr)	*****	*	****	**
RBC Blood	*	**	*****	*
Stool	*****	*****	***	****

3rd enzyme:  
**Methyltransferases**

# Inhibitors:

# Pathway Planner

**Methionine**  
Version 4



# Endocrine Disrupting Chemicals

- Bisphenol A (BPA)
- Phthalates: plasticizers
- Atrazine: herbicide
- Organochlorides: pesticides, dioxins
- Glyphosates: pesticide

# Is PON1 working?

# Example



# Example



## Organophosphates - Urine



Percentile values for organophosphates are from the NHANES Fourth National Report on Human Exposure to Environmental Chemicals, CDC, 2009.

\*No national reference ranges are established for atrazine or atrazine mercapturate; percentile ranges are based on patient samples analyzed at Genova Diagnostics.



## Bisphenol A (BPA) - Urine



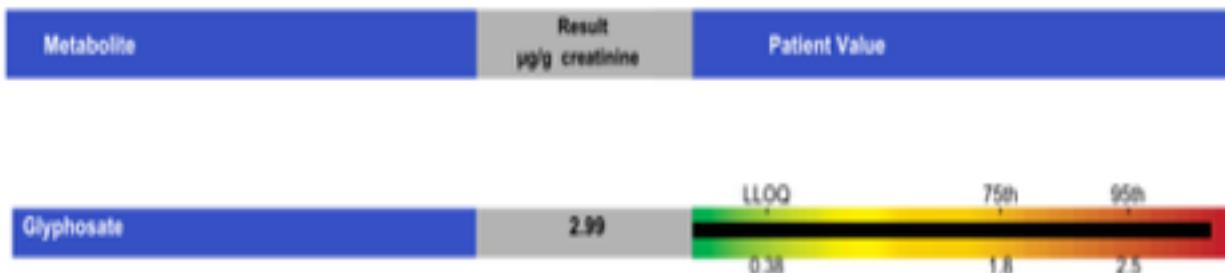
Percentile values are from the NHANES Fourth National Report on Human Exposure to Environmental Chemicals, Updated Tables, CDC, Feb. 2011.

\*\*No national reference ranges are established for 4-Nonylphenol. Percentile ranges are based on patient samples analyzed at Genova Diagnostics.

<DL = less than detection limit

# Glyphosate (Roundup) Example

Glyphosate Profile



**Abstract: Glyphosate, pathways to modern diseases III: Manganese, neurological diseases, and associated pathologies.** [Samsel A<sup>1</sup>](#), [Seneff S<sup>2</sup>](#).

*Surg Neurol Int.* 2015 Mar 24;6:45. doi: 10.4103/2152-7806.153876.

Manganese (Mn) is an often overlooked but important nutrient, required in small amounts for multiple essential functions in the body. A recent study on cows fed genetically modified Roundup(®)-Ready feed revealed a severe depletion of serum Mn. Glyphosate, the active ingredient in Roundup(®), has also been shown to severely deplete Mn levels in plants. Here, we investigate the impact of Mn on physiology, and its association with gut dysbiosis as well as neuropathologies such as autism, Alzheimer's disease (AD), depression, anxiety syndrome, Parkinson's disease (PD), and prion diseases. Glutamate overexpression in the brain in association with autism, AD, and other neurological diseases can be explained by Mn deficiency. Mn superoxide dismutase protects mitochondria from oxidative damage, and mitochondrial dysfunction is a key feature of autism and Alzheimer's. Chondroitin sulfate synthesis depends on Mn, and its deficiency leads to osteoporosis and osteomalacia. Lactobacillus, depleted in autism, depend critically on Mn for antioxidant protection. Lactobacillus probiotics can treat anxiety, which is a comorbidity of autism and chronic fatigue syndrome. Reduced gut Lactobacillus leads to overgrowth of the pathogen, *Salmonella*, which is resistant to glyphosate toxicity, and Mn plays a role here as well. Sperm motility depends on Mn, and this may partially explain increased rates of infertility and birth defects. We further reason that, under conditions of adequate Mn in the diet, glyphosate, through its disruption of bile acid homeostasis, ironically promotes toxic accumulation of Mn in the brainstem, leading to conditions such as PD and prion diseases.

# Antibody testing for Toxins

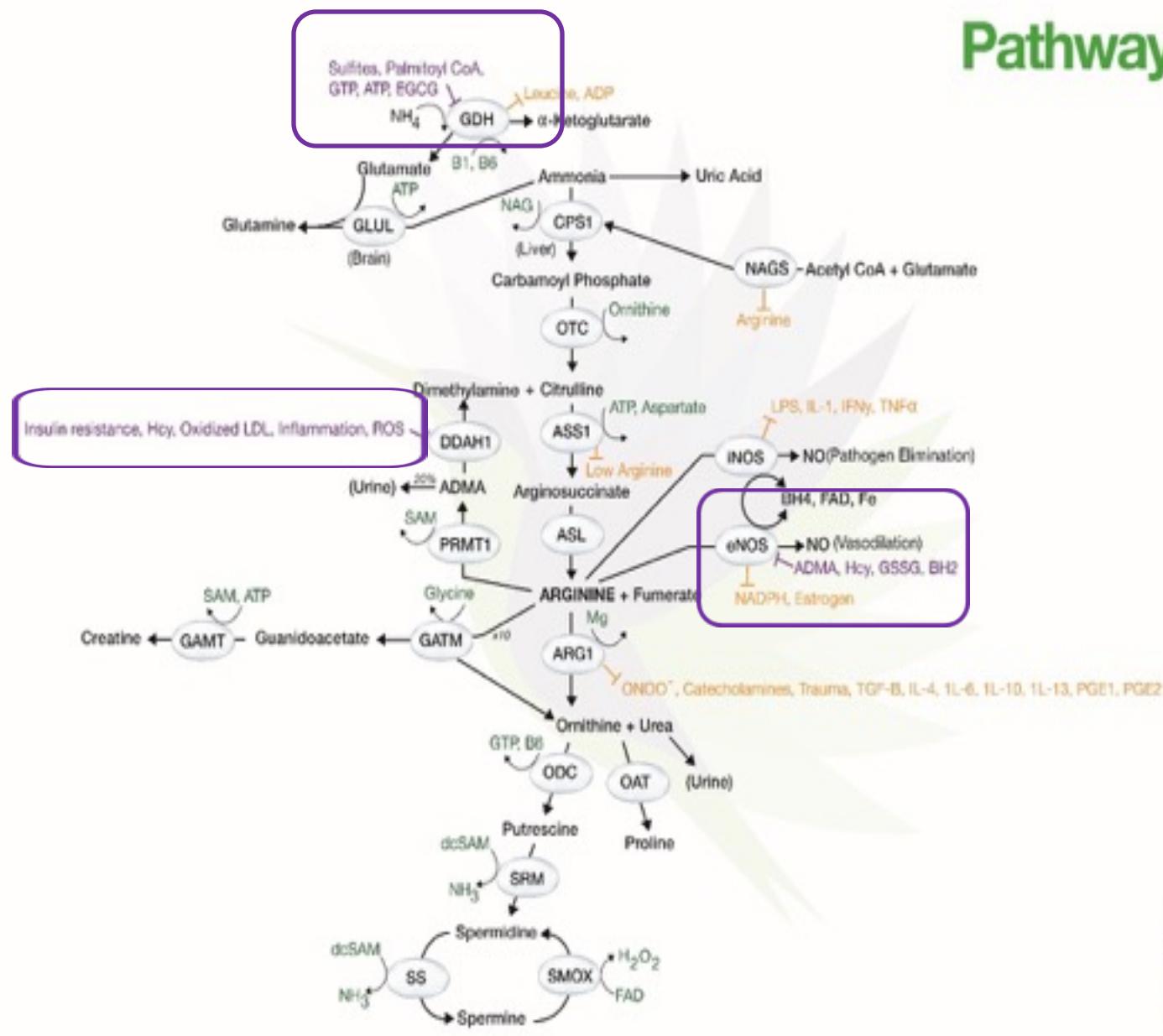
## Example

Array 11 Chemical Immune Reactivity Screen	IN RANGE (Normal)	EQUIVOCAL*	OUT OF RANGE	REFERENCE (ELISA Index)
Aflatoxins IgG+IgA			2.06	0.4-1.8
Aflatoxins IgM	1.30			0.1-1.9
Formaldehyde and Glutaraldehyde IgG+IgA	0.89			0.3-1.4
Formaldehyde and Glutaraldehyde IgM	1.22			0.1-1.8
Isocyanate IgG+IgA		0.96		0.1-1.1
Isocyanate IgM	0.59			0.1-1.2
Trimellitic and Phthalic Anhydrides IgG+IgA		1.08		0.1-1.3
Trimellitic and Phthalic Anhydrides IgM	1.45			0.1-2.0
Benzene Ring Compounds IgG+IgA	0.99			0.2-1.3
Benzene Ring Compounds IgM	1.01			0.1-1.6
BPA Binding Protein IgG+IgA	0.78			0.2-1.8
BPA Binding Protein IgM	0.70			0.1-1.8
Bisphenol A IgG+IgA		1.43		0.1-1.8
Bisphenol A IgM	1.43			0.1-2.0
Tetrabromobisphenol A IgG+IgA	1.16			0.1-1.6
Tetrabromobisphenol A IgM	0.73			0.2-2.0
Tetrachloroethylene IgG+IgA	1.41			0.4-2.0
Tetrachloroethylene IgM	0.96			0.1-2.6
Parabens IgG+IgA		1.53		0.2-1.7
Parabens IgM	0.48			0.1-1.8
Mercury Compounds IgG+IgA		1.47		0.1-1.5
Mercury Compounds IgM	0.94			0.1-2.1
Mixed Heavy Metals IgG+IgA	1.07			0.2-1.8
Mixed Heavy Metals IgM	1.04			0.1-1.8

# Other Enzyme Inhibitors...

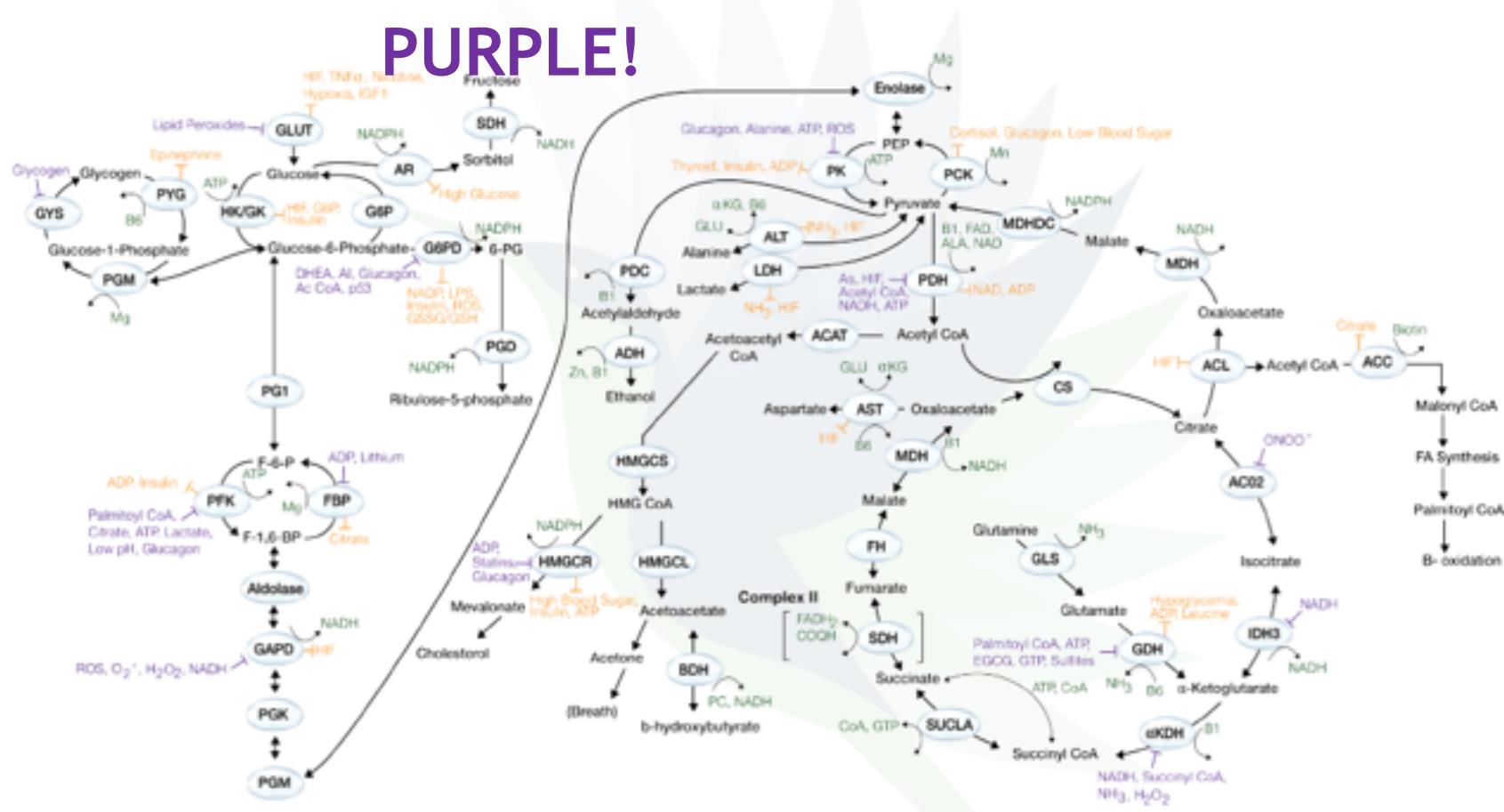
# Pathway Planner

Arginine  
Version 3



- Increase Activity
- Decrease Activity
- Colactor
- Reactive Oxygen Species
- Genes

# Look at all the **PURPLE!**



- Increase Activity
  - Decrease Activity
  - Cofactor
  - Reactive Oxygen Species
  - Genes

# Putting it all together: A Case

Patient Complaints - 30 lb weight gain in one year

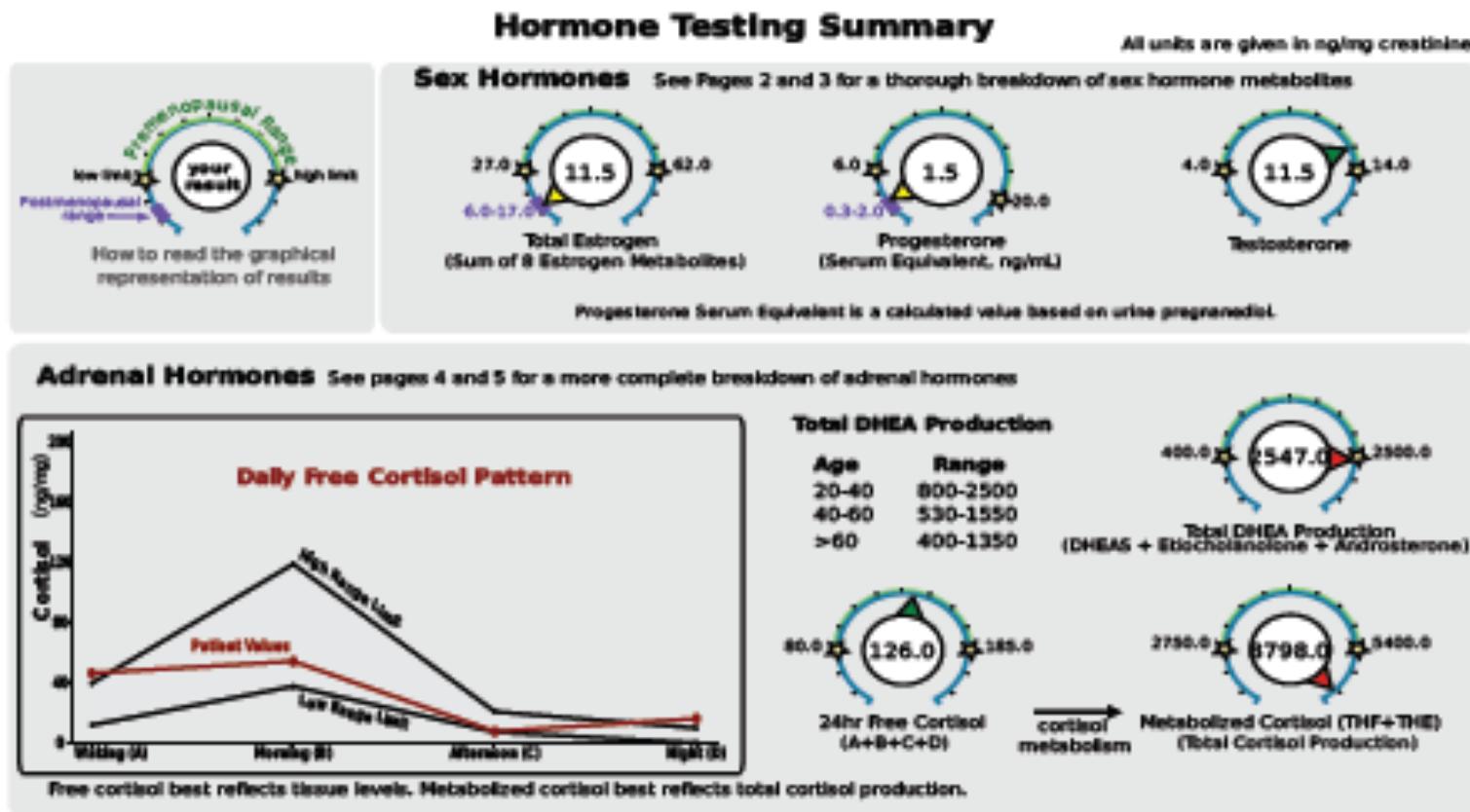
- Fatigue
- Tendonitis
- Decreased zest
- Labs WNL (CBC, CMP,

Thyroid, D3)

\*\* No Genetic Test Results

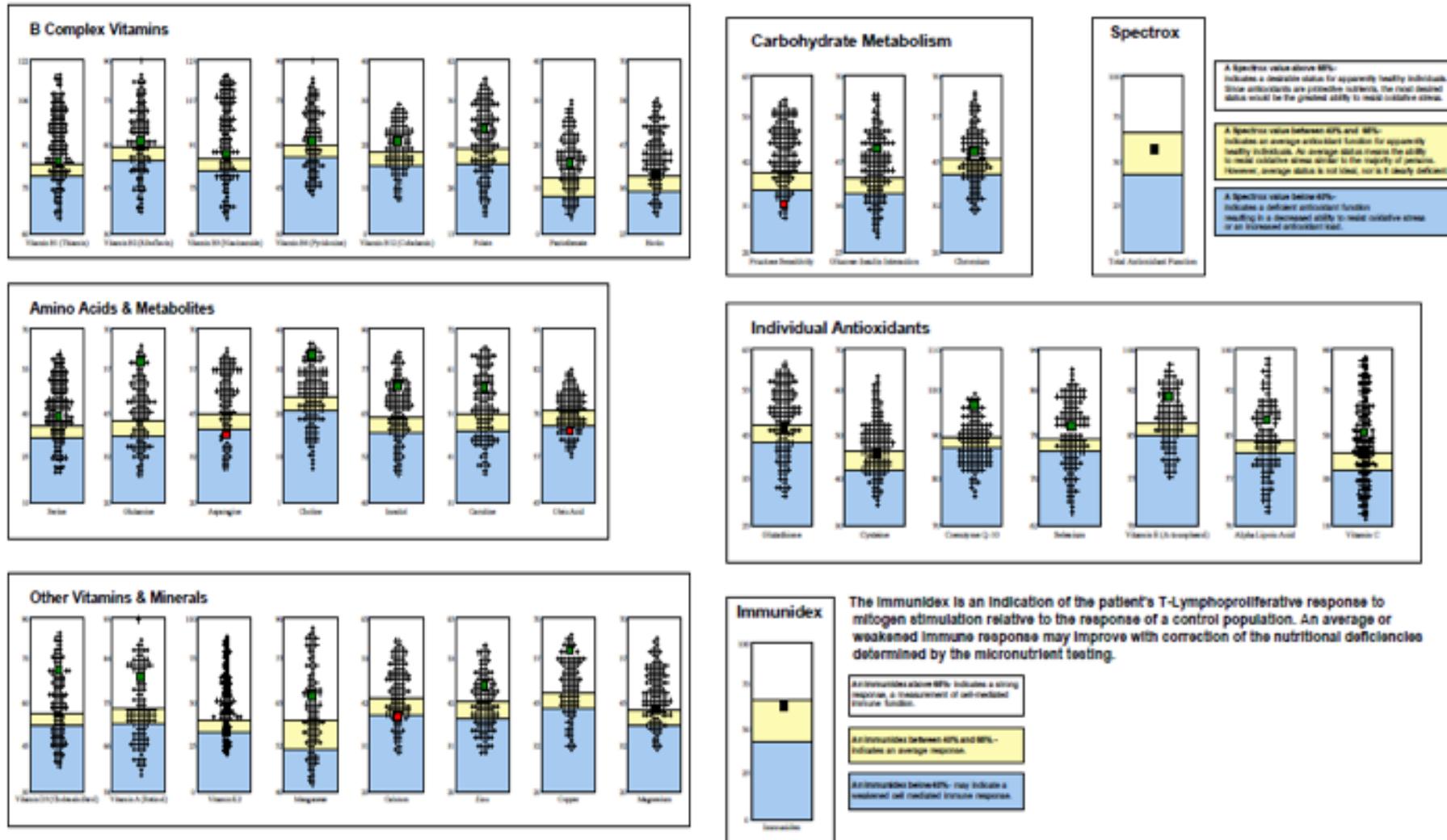
- CASE:** - 30 lb weight gain in one year  
 - Fatigue, - Tendonitis, - Decreased zest

## Hormone Studies:



CASE: - 30 lb weight gain in one year  
 - Fatigue, - Tendonitis, - Decreased zest

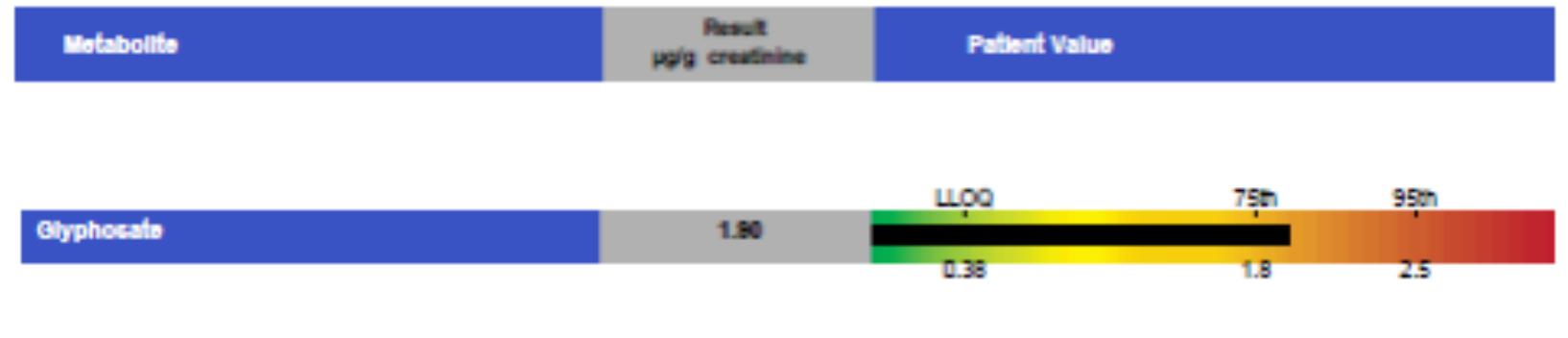
## MicroNutrient Studies:



**CASE:** - 30 lb weight gain in one year  
- Fatigue, - Tendonitis, - Decreased zest

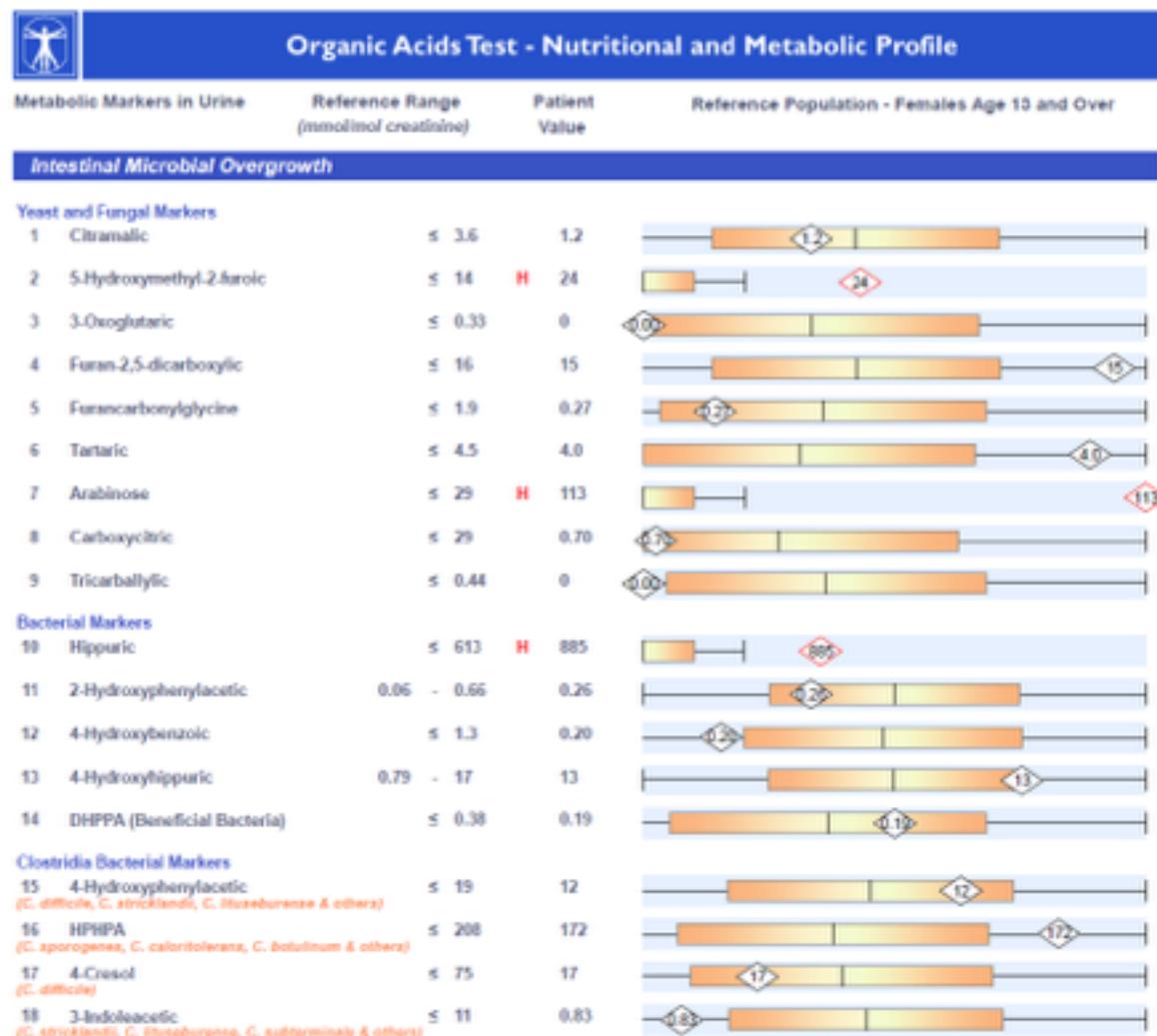
Glyphosate:

[Glyphosate Profile](#)



CASE: - 30 lb weight gain in one year  
 - Fatigue, - Tendonitis, - Decreased zest

# O.A.T Tes

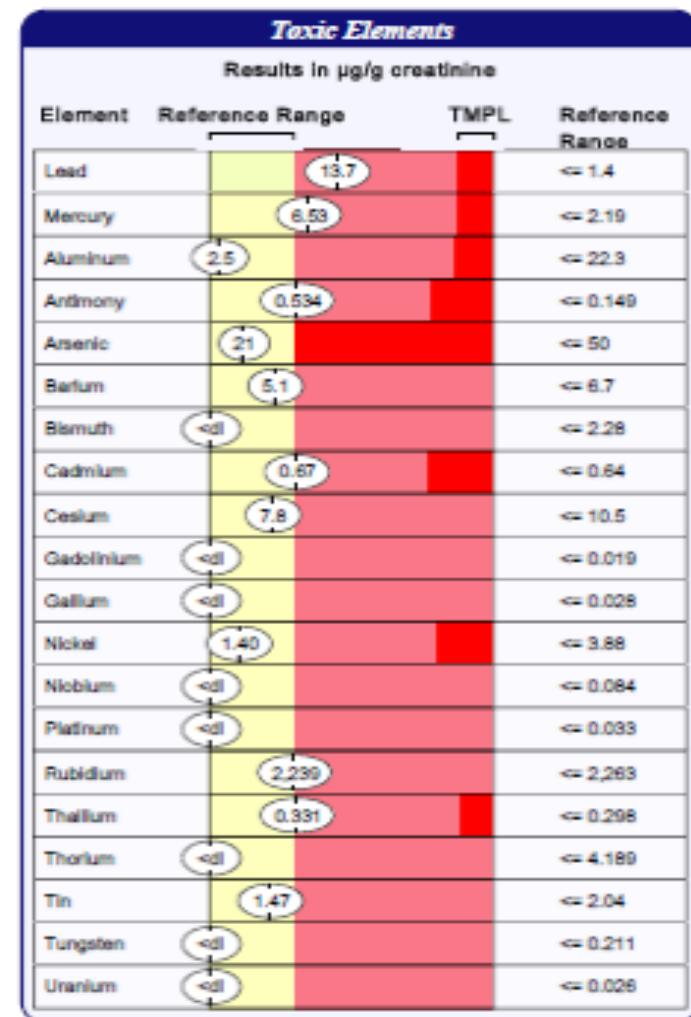


CASE: - 30 lb weight gain in one year  
 - Fatigue, - Tendonitis, - Decreased zest

## DMSA-Provoked Urine Heavy Metals (2 labs):

### Toxic Metals; Urine

TOXIC METALS				
	RESULT mg/g creat	REFERENCE INTERVAL	WITHIN REFERENCE	OUTSIDE REFERENCE
Aluminum (Al)	1.2	< 35	•	
Antimony (Sb)	0.4	< 0.2		—
Arsenic (As)	22	< 80	—	—
Barium (Ba)	5.4	< 7	—	—
Beryllium (Be)	< dl	< 1		
Bismuth (Bi)	0.2	< 4	•	
Cadmium (Cd)	0.8	< 1	—	—
Cesium (Cs)	8.6	< 10	—	—
Gadolinium (Gd)	< dl	< 0.8		
Lead (Pb)	9.9	< 2	—	—
Mercury (Hg)	8.4	< 4	—	—
Nickel (Ni)	6.7	< 10	—	—
Palladium (Pd)	< dl	< 0.15		
Platinum (Pt)	< dl	< 0.1		
Tellurium (Te)	< dl	< 0.5		
Thallium (Tl)	0.3	< 0.5	—	—
Thorium (Th)	< dl	< 0.03		
Tin (Sn)	1.2	< 5	—	—
Tungsten (W)	< dl	< 0.4		
Uranium (U)	< dl	< 0.04		
URINE CREATININE				
	RESULT mg/dL	REFERENCE INTERVAL	-3SD	+3SD
Creatinine	129	30–225	—	—



CASE: - 30 lb weight gain in one year  
 - Fatigue, - Tendonitis, - Decreased zest

# Hair Analysis, Heavy Metals:

Toxic & Essential Elements; Hair

TOXIC METALS			
	RESULT Mg/g	REFERENCE INTERVAL	PERCENTILE 68 <sup>th</sup> 95 <sup>th</sup>
Aluminum (Al)	4.0	< 7.0	-
Antimony (Sb)	0.012	< 0.050	-
Arsenic (As)	0.023	< 0.000	-
Barium (Ba)	5.7	< 2.0	-
Beryllium (Be)	< 0.01	< 0.020	-
Bismuth (Bi)	0.037	< 2.0	-
Cadmium (Cd)	0.050	< 0.010	-
Lead (Pb)	2.1	< 0.60	-
Mercury (Hg)	0.29	< 0.80	-
Platinum (Pt)	< 0.003	< 0.005	-
Thallium (Tl)	< 0.001	< 0.002	-
Thorium (Th)	< 0.001	< 0.002	-
Uranium (U)	0.14	< 0.000	-
Nickel (Ni)	0.71	< 0.30	-
Silver (Ag)	0.07	< 0.15	-
Tin (Sn)	0.13	< 0.30	-
Titanium (Ti)	0.25	< 0.70	-
Total Toxic Representation			
ESSENTIAL AND OTHER ELEMENTS			
	RESULT Mg/g	REFERENCE INTERVAL	PERCENTILE 1 <sup>st</sup> 10 <sup>th</sup> 50 <sup>th</sup> 90 <sup>th</sup> 97.5 <sup>th</sup>
Calcium (Ca)	2160	300- 1200	-
Magnesium (Mg)	360	35- 120	-
Sodium (Na)	310	20- 210	-
Potassium (K)	29	8- 75	-
Copper (Cu)	77	11- 37	-
Zinc (Zn)	180	140- 220	-
Manganese (Mn)	2.1	0.00- 0.60	-
Chromium (Cr)	0.31	0.40- 0.65	-
Vanadium (V)	0.040	0.010- 0.065	-
Molybdenum (Mo)	0.023	0.020- 0.050	-
Boron (B)	0.39	0.25- 1.5	-
Iodine (I)	0.74	0.25- 1.0	-
Lithium (Li)	0.028	0.007- 0.020	-
Phosphorus (P)	115	150- 220	-
Selenium (Se)	0.98	0.15- 1.1	-
Strontrium (Sr)	5.4	0.50- 7.6	-
Sulfur (S)	45000	44000- 50000	-
Cobalt (Co)	0.048	0.035- 0.040	-
Iron (Fe)	10	7.0- 16	-
Germanium (Ge)	0.038	0.030- 0.040	-
Rubidium (Rb)	0.010	0.007- 0.096	-
Zirconium (Zr)	1.5	0.020- 0.42	-

**CASE:** - 30 lb weight gain in one year  
- Fatigue, - Tendonitis, - Decreased zest

## Toxic Metals; Feces

		RESULT making Dry Wt.	REFERENCE INTERVAL	PERCENTILE	
				40 <sup>th</sup>	90 <sup>th</sup>
Mercury	(Hg)	0.057	< 0.06 wt amalgam*	■■■■■	
Mercury	(Hg)	0.057	= 0.6 wt amalgam*	■■■■■	
Antimony	(Sb)	0.029	< 0.080	■■■■■	
Arsenic	(As)	0.26	< 0.30	■■■■■	
Beryllium	(Be)	0.073	< 0.009	■■■■■	
Bismuth	(Bi)	0.028	< 0.050	■■■■■	
Cadmium	(Cd)	0.12	< 0.50	■■■■■	
Copper	(Cu)	18	< 60	■■■■■	
Lead	(Pb)	0.12	< 0.50	■■■■■	
Nickel	(Ni)	4.6	< 8.0	■■■■■	
Platinum	(Pt)	< dl	< 0.003	■■■■■	
Thallium	(Tl)	0.012	< 0.020	■■■■■	
Tungsten	(W)	0.085	< 0.090	■■■■■	
Uranium	(U)	0.055	< 0.120	■■■■■	

## Toxic Metals; Feces

	RESULT mg/kg Dry Wt	REFERENCE INTERVAL	TOXIC METALS	
			PERCENTILE 60 <sup>th</sup>	95 <sup>th</sup>
Mercury	(Hg)	0.134	< 0.05 wth amalgam*	0.134
Mercury	(Hg)	0.134	< 0.6 wth amalgam*	0.134
Antimony	(Sb)	0.054	< 0.080	0.054
Arsenic	(As)	0.24	< 0.30	0.24
Beryllium	(Be)	0.014	< 0.009	0.014
Bismuth	(Bi)	0.100	< 0.050	0.100
Cadmium	(Cd)	0.33	< 0.50	0.33
Copper	(Cu)	24	< 60	24
Lead	(Pb)	0.20	< 0.50	0.20
Nickel	(Ni)	5.3	< 8.0	5.3
Platinum	(Pt)	< 0.8	< 0.003	< 0.8
Thorium	(Th)	0.010	< 0.020	0.010
Tungsten	(W)	0.090	< 0.090	0.090
Uranium	(U)	0.068	< 0.120	0.068

	RESULT % H2O	REFERENCE INTERVAL	WATER CONTENT		
			MEAN	-2SD	+2SD
% Water Content	69.7	60 - 85%	71.3%	-150	+150

**CASE:** - 30 lb weight gain in one year  
 - Fatigue, - Tendonitis, - Decreased zest

## Food IgG/Complement Studies:

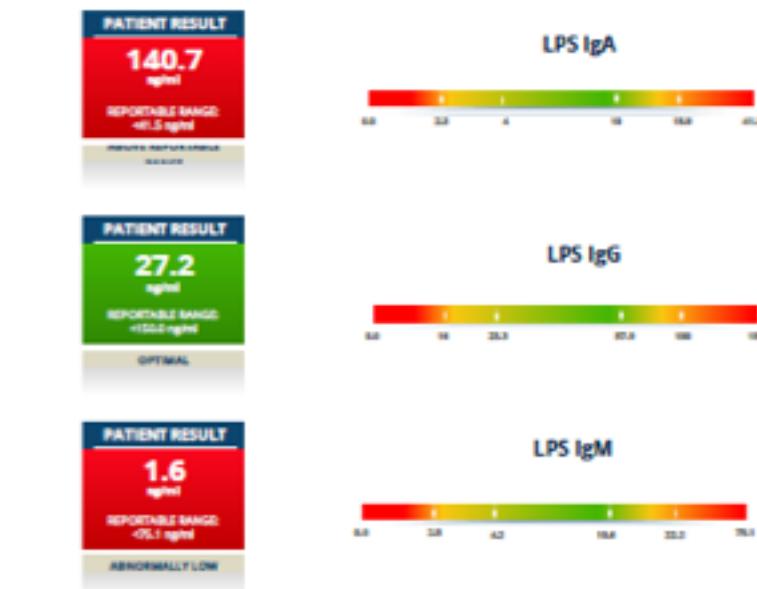
588G: Dietary Antigen Testing: Sensitivity and Complement   3/5					
ALLERGEN	0-100	101-200	201-300	301-400	401-500
	COMPLEMENT				
IgG CONCENTRATION (ng/ml)	REACTIVITY CLASS				
<b>MEATS, DAIRY</b>					
Beef	0	■	■	-	-
Casselin	826	■	■	-	-
Cow's Milk	908	■	■	-	-
Goat's Milk	922	■	■	-	-
Pork	0	■	■	-	-
<b>SHELLFISH</b>					
Clam	0-300 ng/ml	■	■	■	-
Crab	0-710 ng/ml	■	■	■	-
Lobster	0-240 ng/ml	■	■	■	-
Scallops	0-75 ng/ml	■	■	■	-
Shrimp	0-180 ng/ml	■	■	■	-
<b>POULTRY</b>					
Chicken	0	■	■	-	-
Egg Albumin	423	■	■	-	-
Egg Yolk	172	■	■	-	-
Turkey	0	■	■	-	-
<b>FUNGI</b>					
Aspergillus Mix	0-2207 ng/ml	■	■	■	-
Brewer's Yeast	0-811 ng/ml	■	■	■	-
Candida	0-1949 ng/ml	■	■	■	-
Mushroom	0-230 ng/ml	■	■	■	-
<b>SEAFOOD</b>					
Codfish	0	■	■	-	-
Flounder	0	■	■	-	-
Halibut	0	■	■	-	-
Salmon	0	■	■	-	-
Tuna	0	■	■	-	-
<b>LEGUMES, BEANS</b>					
Green Pea	0-240 ng/ml	■	■	■	-
Kidney/Pinto	0-480 ng/ml	■	■	■	-
Navy Bean	0-630 ng/ml	■	■	■	-
Peanut	0-950 ng/ml	■	■	■	-
Soybean	0-620 ng/ml	■	■	■	-

This test was developed and its performance characteristics determined by Biochemistry Labs or third party reference affiliates. This test is not FDA approved, and FDA clearance is not currently required for clinical use. Results are not intended to be used as the sole means for clinical diagnosis. Clinical correlation is required.

CASE: - 30 lb weight gain in one year  
- Fatigue, - Tendonitis, - Decreased zest

## Intestinal Barrier:

ADVANCED INTESTINAL BARRIER ASSESSMENT: PROFILE 5150 (PLASMA)



ADVANCED INTESTINAL BARRIER ASSESSMENT: PROFILE 5150 (PLASMA)



# Treatment

- Remove Pathogens: Candida (herbal antimicrobial)
- Remove Heavy Metals: Lead (Lipophos-EDTA)
- Remove Glyphosate: Eat Organic
- Increase Nutrients needed for Glutathione
- Food Rotation Meal Planning (Off all dairy)
- Fortify GI tract: Glutamine, Aloe, DGL
- Replace: Probiotics & Prebiotics
- Enhanced balance: Sleep, Exercise, Mindfulness

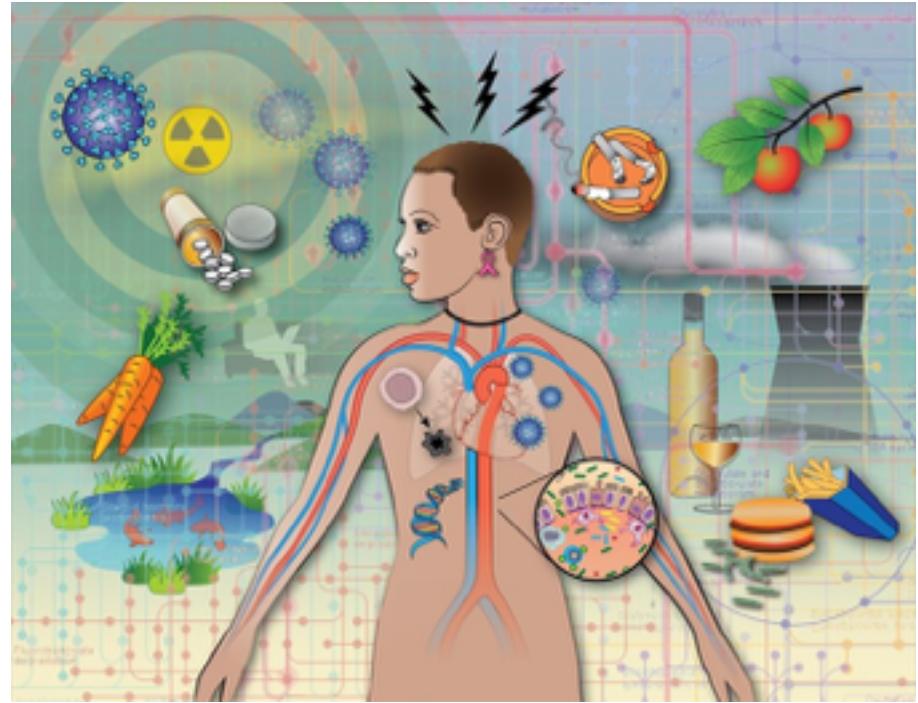
# Influencing Health & Disease

**Genetics 10%**



**Exposome: 90 %**

(Cofactors, precursors, inhibitors)



[https://ysmwebsites.azureedge.net/ysph/ehs/exposome/YPH3%20poster2017b\\_291406\\_36929\\_w744.jpeg?v=1](https://ysmwebsites.azureedge.net/ysph/ehs/exposome/YPH3%20poster2017b_291406_36929_w744.jpeg?v=1)

**Thank you!**