Personalized Nutrient Interventions in the era of Precision Medicine

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Acknowledgements:

- Jeff Bland, PhD
- Helen Messier, PhD, MD
- Sidney Baker, MD
- David Hagedorn, PhD
- David Cantor, PhD
- Lee Hood, MD, PhD
- Andy Braley PhD
- Richard Lord, PhD
- Stephen Hines, MD
- David Agerter, MD
- Terry Dermody, MD
- Mark Percival, ND, DC
- Gregory Kelly, ND
- Rex Cannon, PhD
- Kara Fitzgerald, ND
- Todd Lepine, MD

Faculty Disclosure

Commercial Interest	Nature of Relevant Financial Relationship (Include all those that apply)	
	What was received	**For what role**
• Xymogen	• Honoraria/ Shares	• Consultant
• BioCeuticals	• Honoraria	• Consultant

Presentation Learning Objectives

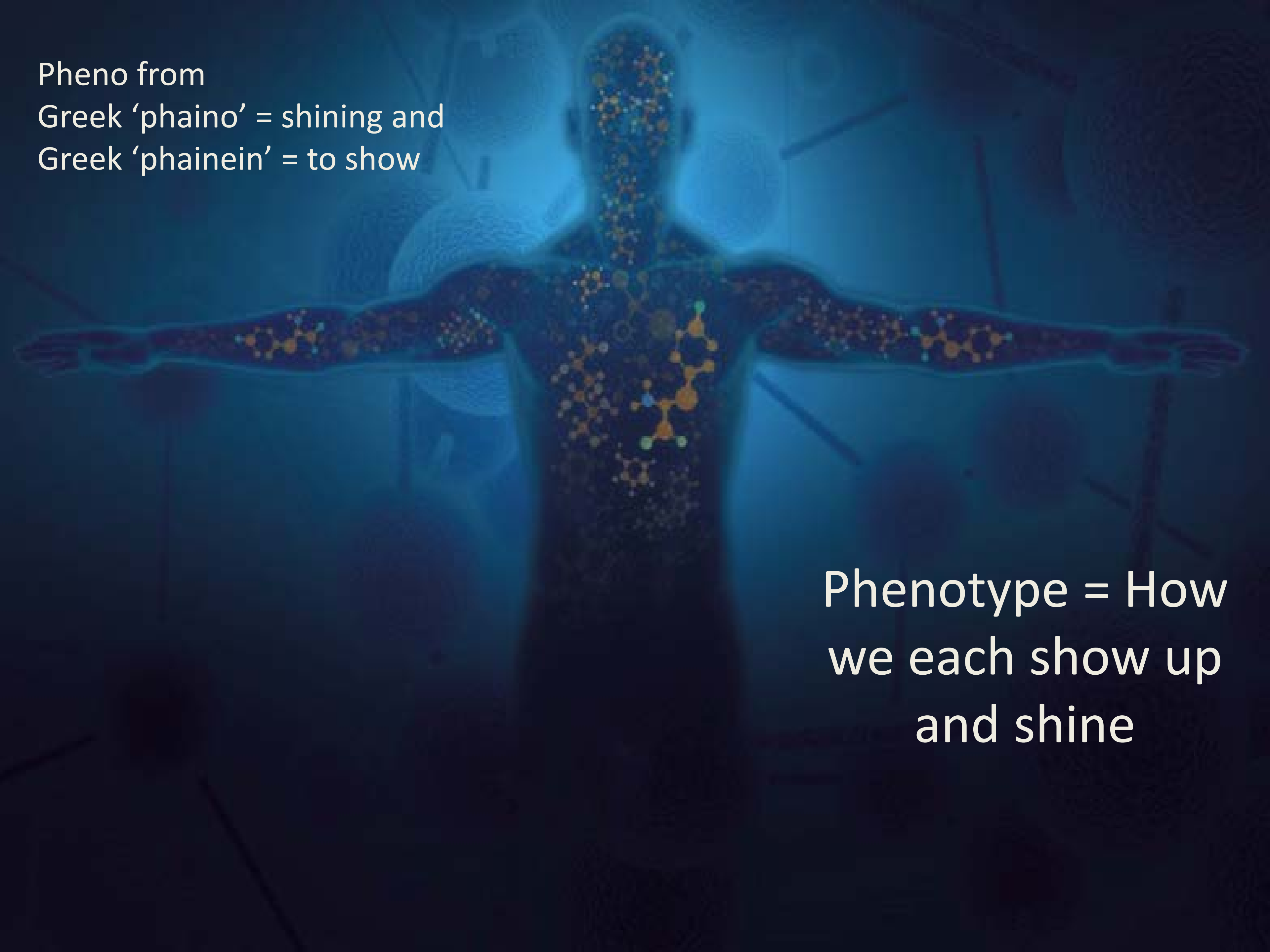
After participating in this presentation, learners should be better able to:

- Use precision medicine to provide insight in assessing toxicity and nutrient insufficiency
- Use data to identify mechanisms of toxic burden
- Employ nutrient interventions to reduce risk of toxicity.

Presentation Clinical Actions

After participating in this presentation, clinicians should be better able to:

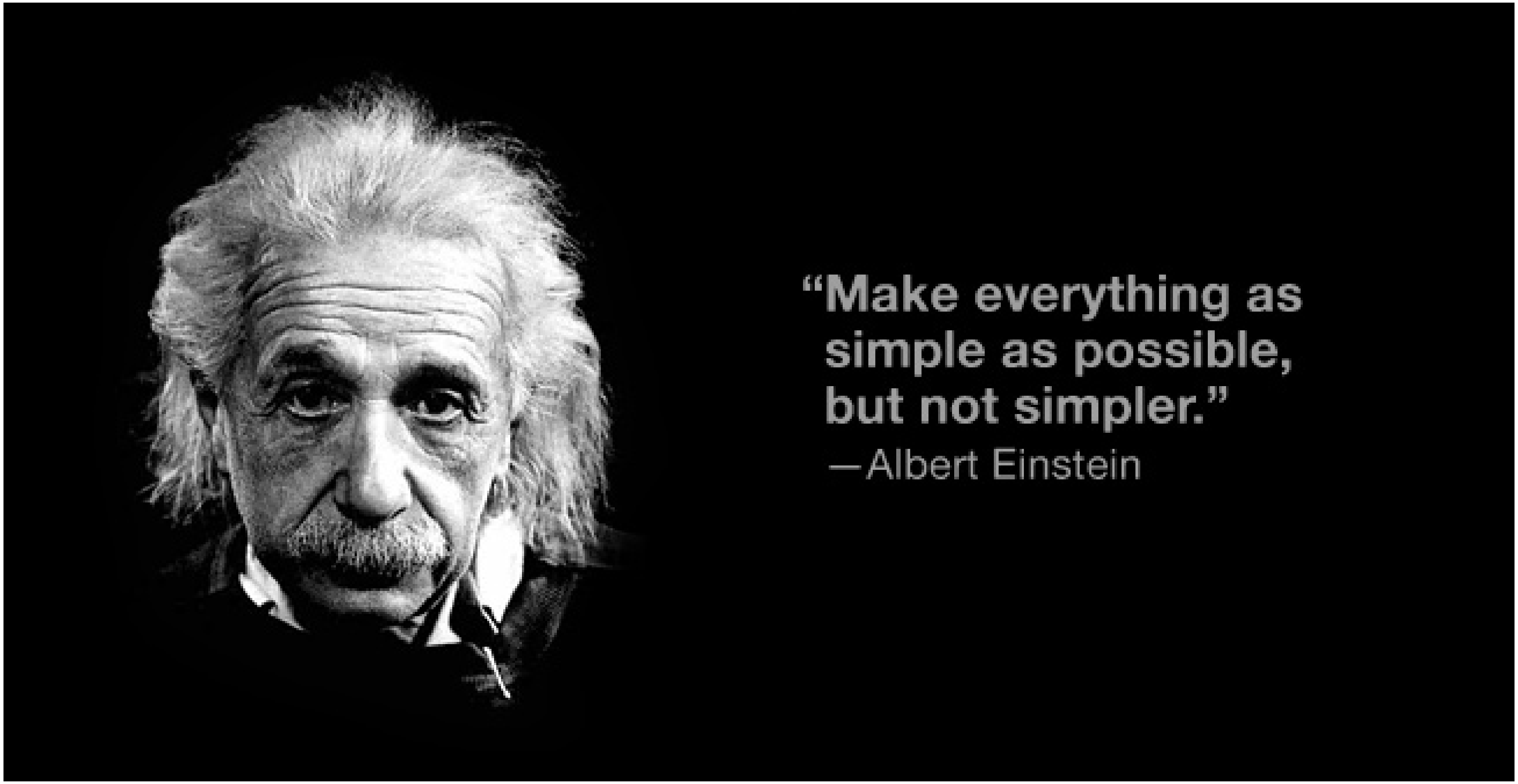
- Recognize that while precision medicine as applied to nutrition has strengths, it also has some pitfalls and that as our knowledge evolves over the next years, so will its application in practice.



Pheno from
Greek ‘phaino’ = shining and
Greek ‘phainein’ = to show

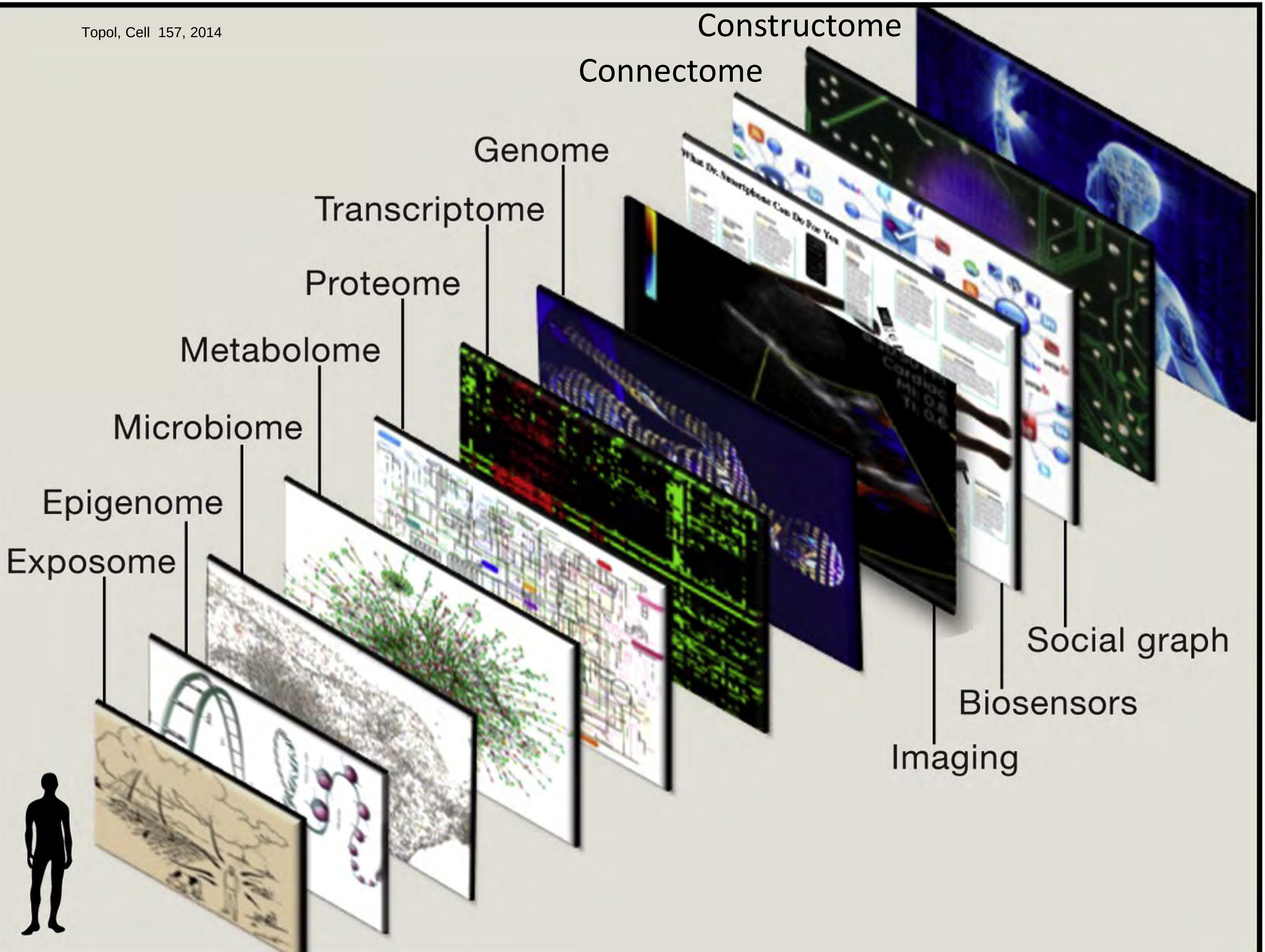
Phenotype = How we each show up and shine

Creating Health…



That we may live as our Highest Potential Phenotype

Topol, Cell 157, 2014



I think that I shall never see
A poem lovely as a tree.

A tree whose hungry mouth is prest
Against the earth's sweet flowing
breast;

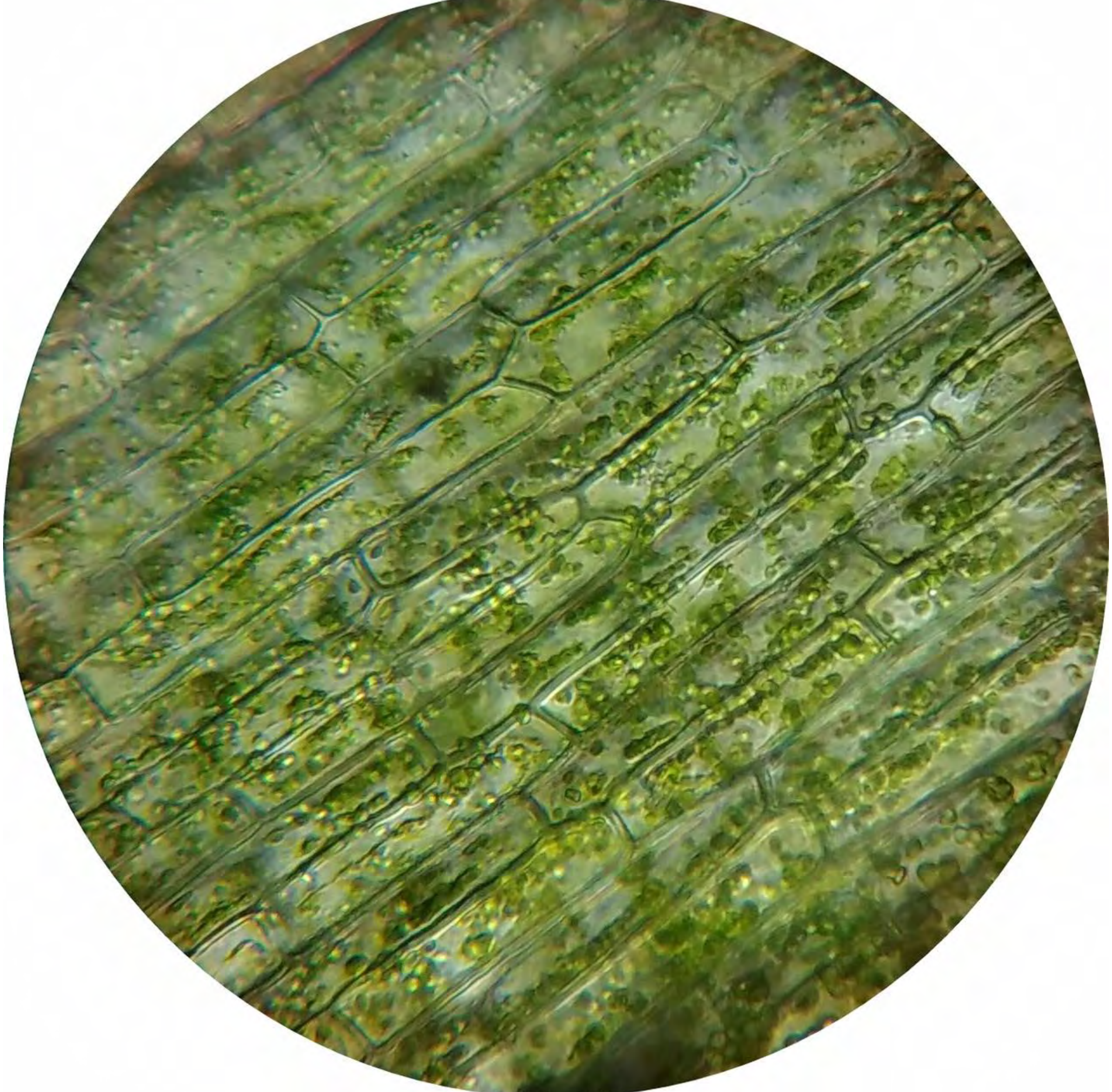
A tree that looks at God all day,
And lifts her leafy arms to pray;

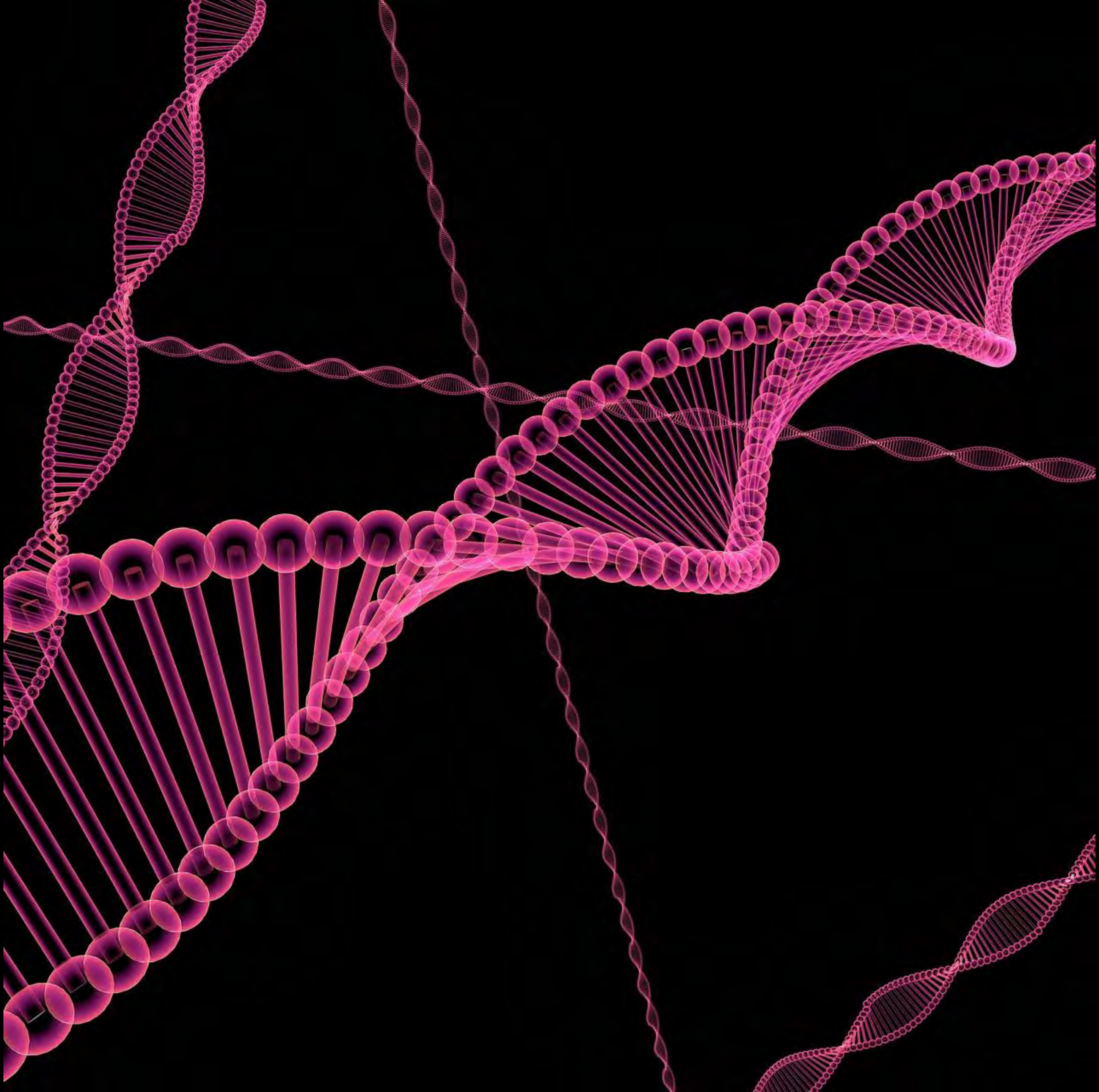
A tree that may in Summer wear
A nest of robins in her hair;

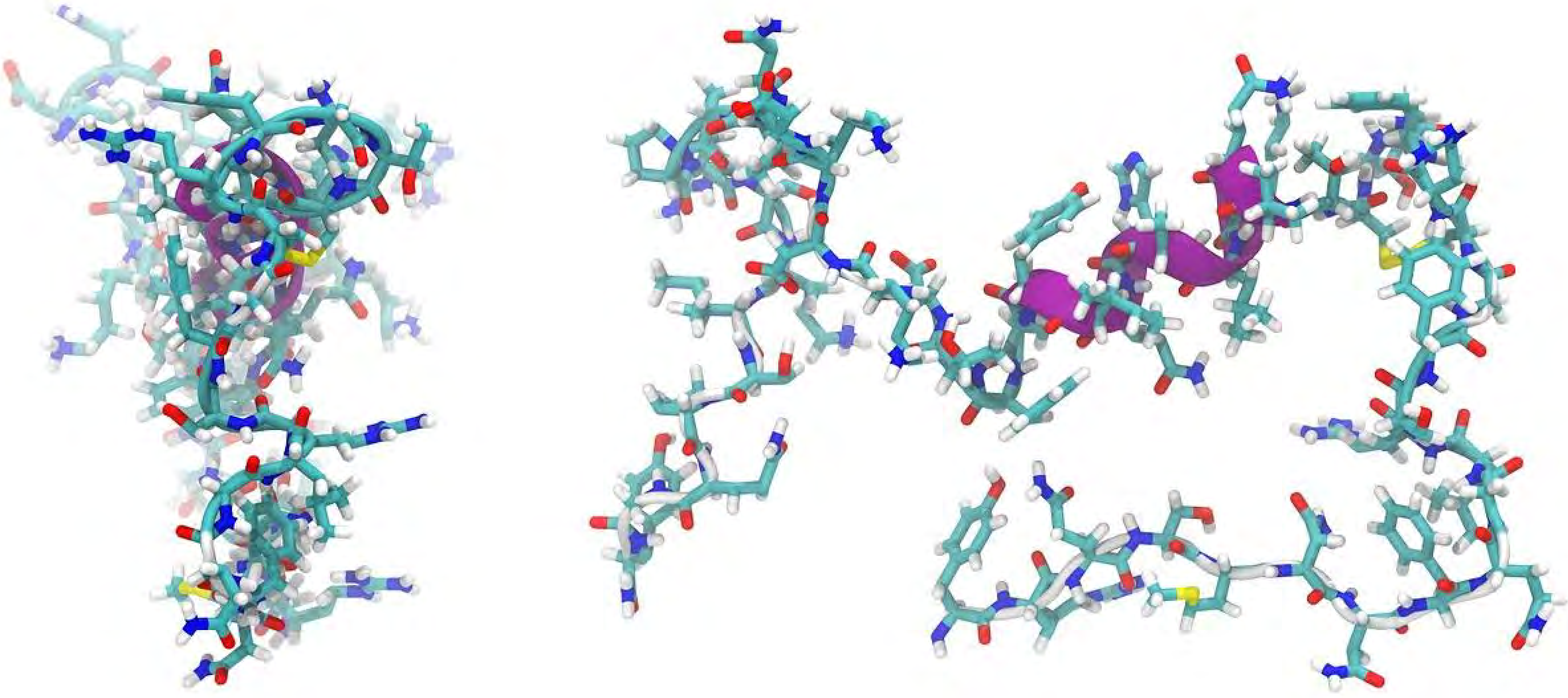
Upon whose bosom snow has lain;
Who intimately lives with rain.

Poems are made by fools like me,
But only God can make a tree.

-Joyce Kilmer








TEMPERED
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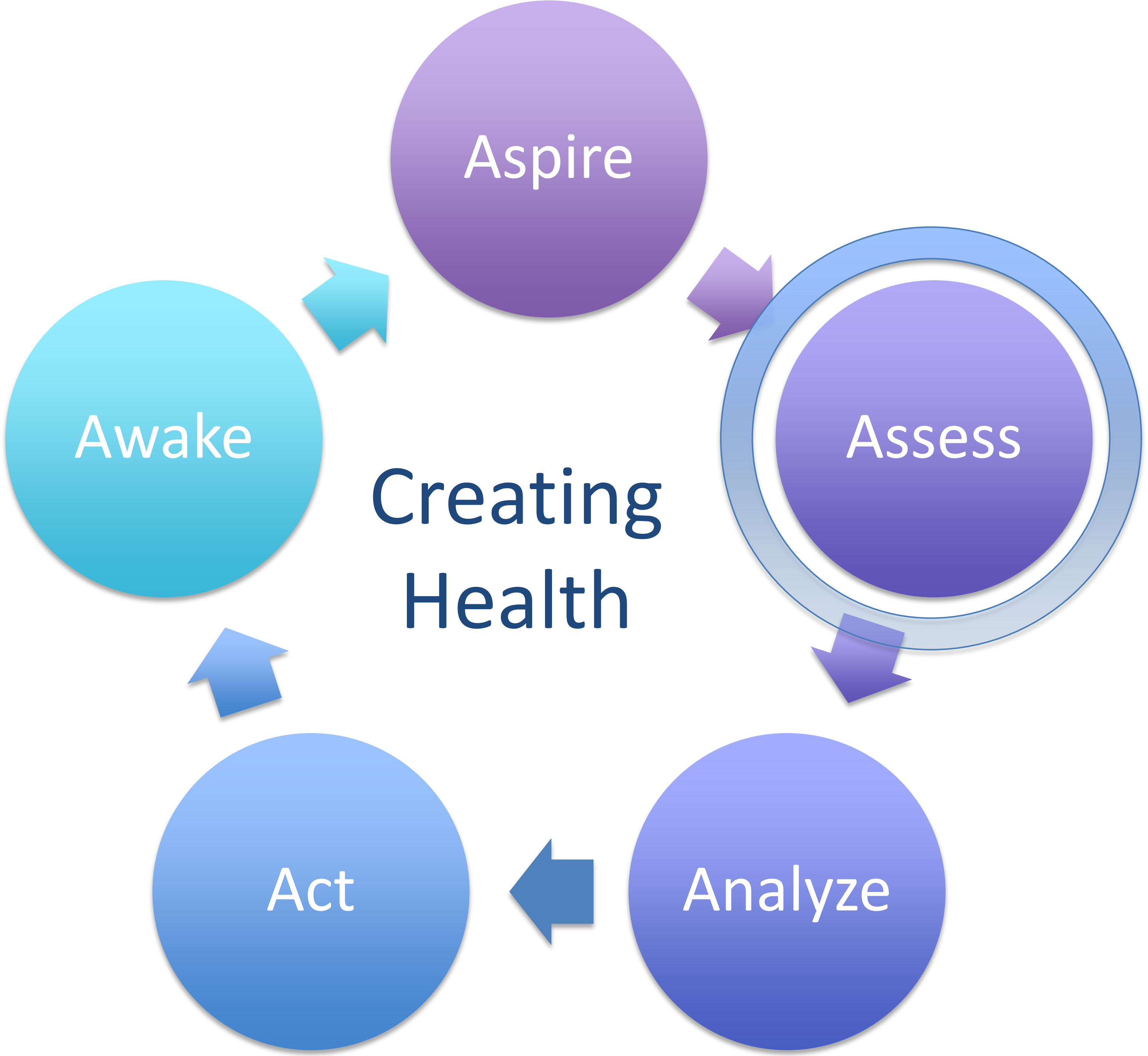
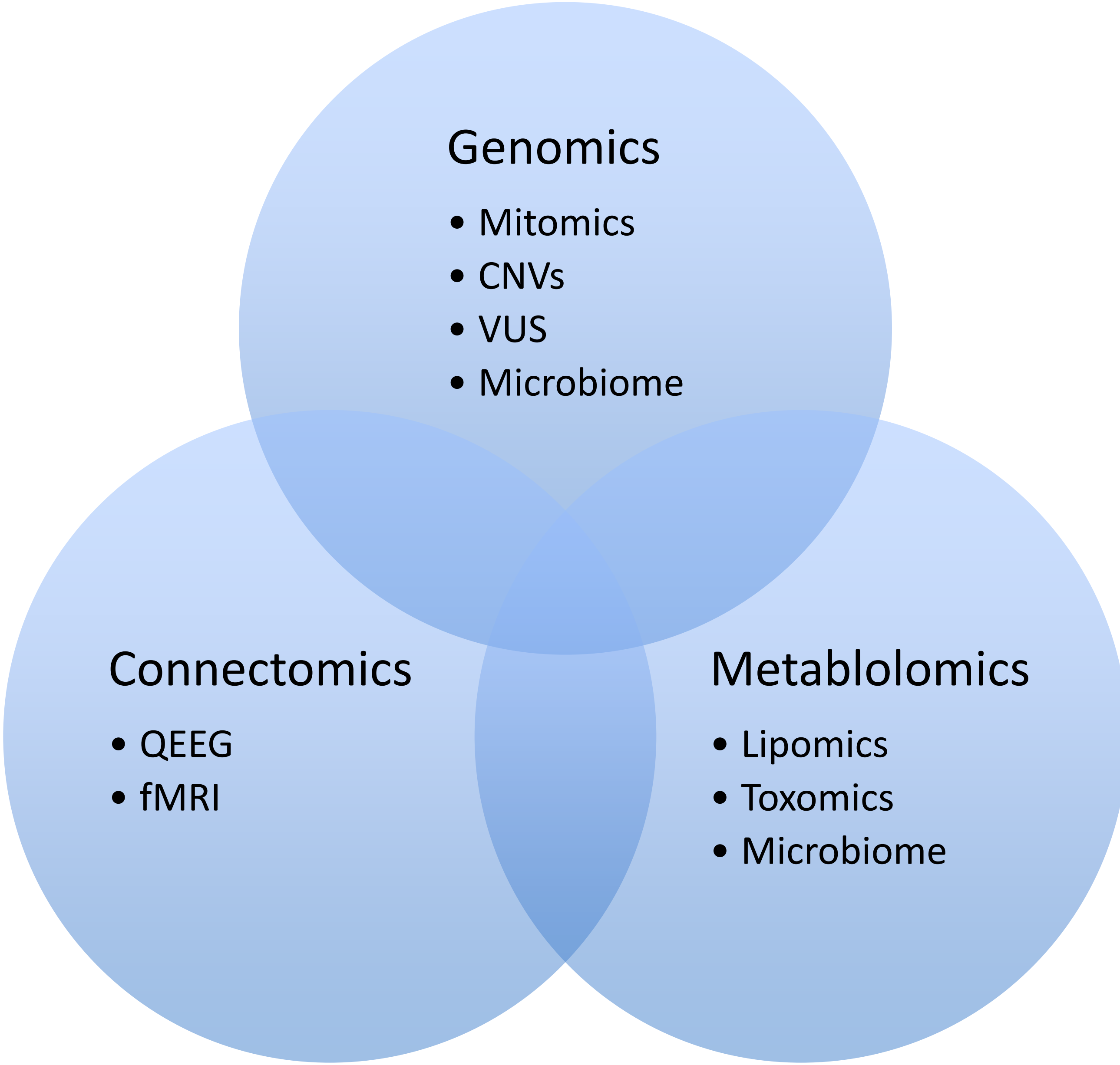
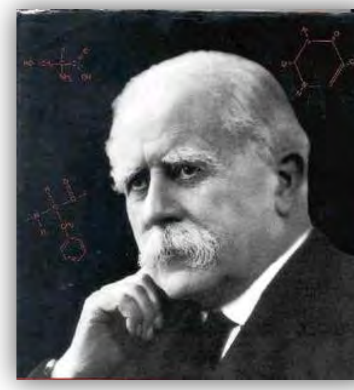

Aspire
Assess
Analyze
Act
Awake
Creating Health

Digging Deeper in Assessment



Genetic Origins of Individual Variations in Metabolism

More than 100 years ago, Archibald Garrod already suggested a link between *chemical individuality* and *predisposition to disease*.



INBORN ERRORS OF METABOLISM

By

ARCHIBALD E. GARROD, K.C.M.G.

D.M., LL.D., F.R.S., F.R.C.P.

Regius Professor of Medicine in the University of Oxford
Consulting Physician to St. Bartholomew's Hospital
and to the Hospital for Sick Children

First Edition 1909

'……merely extreme examples of variations of chemical behaviour which are probably everywhere present in minor degrees' and that this 'chemical individuality [confers] predisposition to and immunities from the various mishaps which are spoken of as diseases'

-**Archibald Garrod**

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A brief History of metabolomics

Quantitative Analysis of Urine Vapor and Breath by Gas–Liquid Partition Chromatography

(orthomolecular medicine/vitamins/controlled diet)

LINUS PAULING*, ARTHUR B. ROBINSON*, ROY TERANISHI†, AND PAUL CARY*

* Department of Chemistry, Stanford University, Stanford, California 94305; and † Western Regional Laboratory, U.S. Department of Agriculture

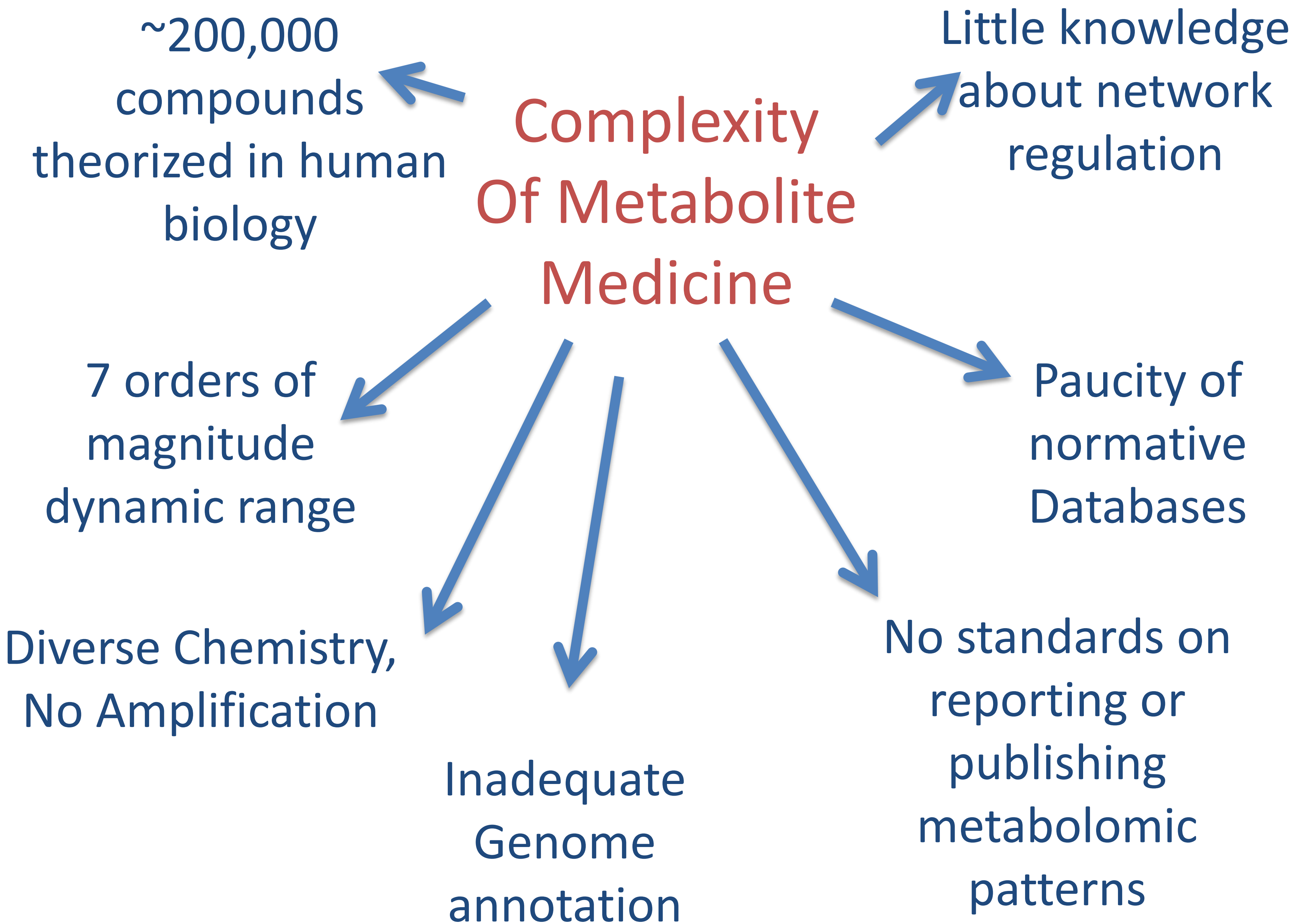
Contributed by Linus Pauling, July 29, 1971

Metabolomics

- **metabolomics developed by Pauling in 1970**
- **the term metabolomics first used in 1998**
  - **Oliver SG et al (1998). Trends Biotechnol 16:373**
- **Metabolomics Society founded 2004**
- **January 23rd, 2007 first draft of the human metabolome “completed”**

Examples of metablolites

- Peptides
- Oligonucleotides
- Sugars
- Nucleosides
- Organic acids
- Ketones
- aldehydes
- Amines
- Amino acids
- Lipids
- Steroids
- Alkaloids
- Drugs
- Xenobiotics


Complexity Of Metabolite Medicine
~200,000 compounds theorized in human biology
Little knowledge about network regulation
7 orders of magnitude dynamic range
Paucity of normative Databases
Diverse Chemistry, No Amplification
Inadequate Genome annotation
No standards on reporting or publishing metabolomic patterns

Sub Pathway	Biochemical Name	KEGG	PUBCHEM	HMDB	Fold of Change																
					DUMMY VS EP_1	DUMMY VS EP_2	DUMMY VS EP_3	DUMMY VS EP_4	DUMMY VS EP_5	DUMMY VS EP_6	DUMMY VS EP_7	DUMMY VS EP_8	DUMMY VS EP_9	IDEP1	IDEP2	IDEP3	IDEP4	IDEP5	IDEP7	IDEP8	ID[illegible]
Glycine, Serine and Threonine Metabolism	glycine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	N-acetylglycine		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	sarcosine (N-Methylglycine)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	dimethylglycine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	betaine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	serine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	N-acetylserine		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	threonine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	N-acetylthreonine	[illegible]	[illegible]		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	allo-threonine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	O-acetylhomoserine	[illegible]	[illegible]		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Alanine and Aspartate Metabolism	alanine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	N-acetylalanine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	aspartate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	asparagine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	N-acetylaspartate (NAA)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Glutamate Metabolism	glutamate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	glutamine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	N-acetylglutamate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	N-acetylglutamine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	N-acetyl-aspartyl-glutamate (NAAG)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	pyroglutamine*		[illegible]		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Histidine Metabolism	histidine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	N-acetylhistidine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	1-methylhistidine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	3-methylhistidine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	N-acetyl-3-methylhistidine*		[illegible]		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	N-acetyl-1-methylhistidine*				[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	trans-urocanate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	cis-urocanate		[illegible]		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	imidazole propionate		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	imidazole lactate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	1-methylimidazoleacetate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Lysine Metabolism	lysine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	N2-acetyllysine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	N6-acetyllysine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	N6-trimethyllysine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	2-aminoadipate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	glutarate (pentanedioate)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	glutarylcarnitine (C5)		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	3-methylglutarylcarnitine (1)		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	3-methylglutarylcarnitine (2)		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	pipecolate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Phenylalanine and Tyrosine Metabolism	phenylalanine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	N-acetylphenylalanine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	phenylpyruvate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	phenyllactate (PLA)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	phenylacetate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	phenylacetylglutamine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	tyrosine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	N-acetyltyrosine		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	4-hydroxyphenylpyruvate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	3-(4-hydroxyphenyl)lactate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	phenol sulfate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	p-cresol sulfate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	o-cresol sulfate		[illegible]		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	vanillylmandelate (VMA)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	3-methoxytyrosine		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	3-methoxytyramine sulfate				[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	gentisate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	3-[3-(sulfooxy)phenyl]propanoic acid		[illegible]		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	3-(3-hydroxyphenyl)propionate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	3-(4-hydroxyphenyl)propionate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	3-phenylpropionate (hydrocinnamate)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	thyroxine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	phenylacetylcarnitine				[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	p-cresol-glucuronide*		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Tryptophan Metabolism	tryptophan	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	N-acetyltryptophan	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	indolelactate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	indoleacetate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	indolepropionate		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	3-indoxyl sulfate		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	kynurenine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	kynurenate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Data

Heat Maps – Need Normative Database Or True Quantitative Measures

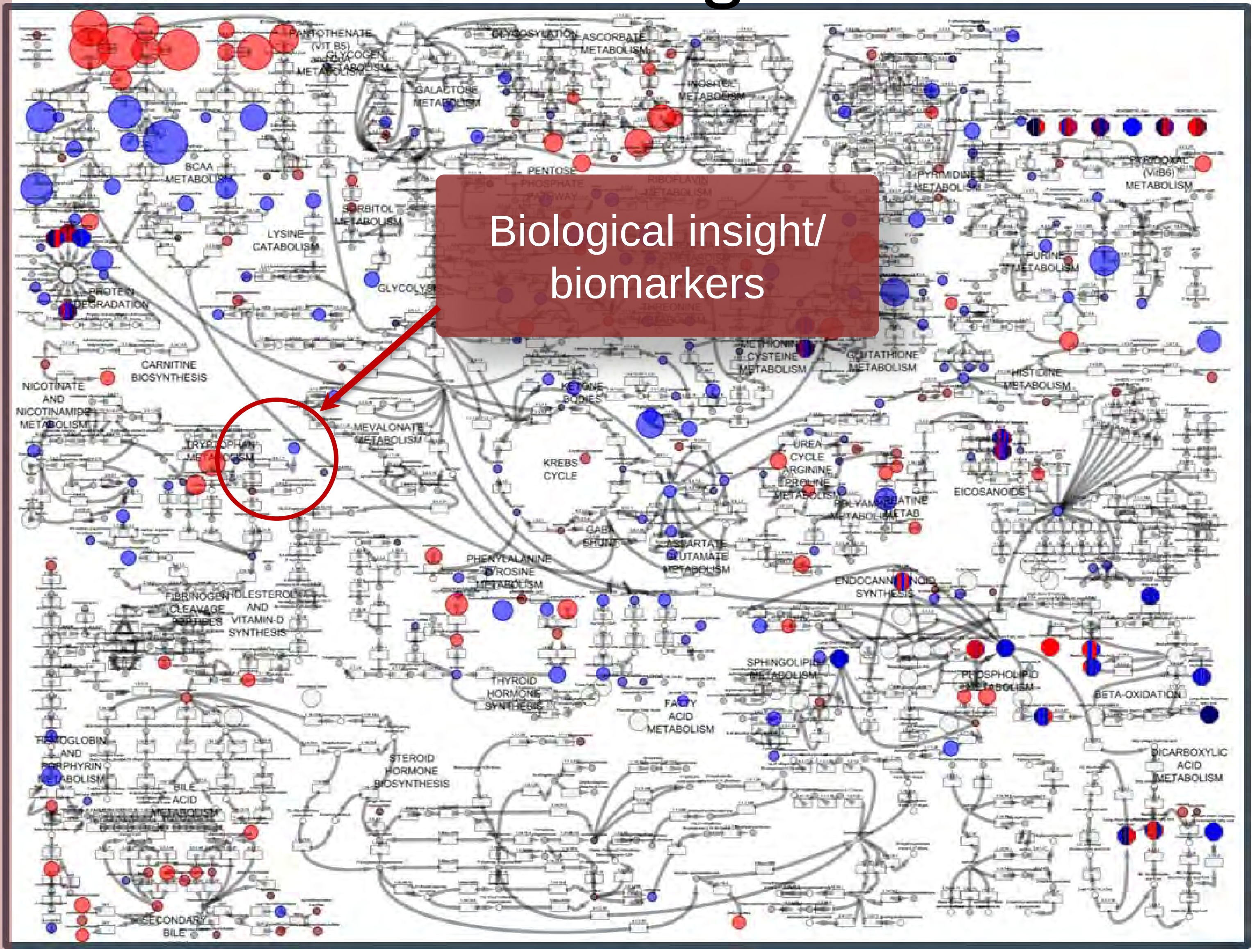
Super Pathway	Sub Pathway ▲	Biochemical Name	Fold Change								
			IDEP1	IDEP2	IDEP3	IDEP4	IDEP5	IDEP6	IDEP7	IDEP8	IDEP9
Amino Acid	Alanine and Aspart...	alanine	0.63	0.49	1.19	1.34	0.87	-1.74	-1.23	-1.13	-0.60
Amino Acid	Alanine and Aspart...	N-acetylalanine	1.83	0.62	-1.31	0.62	-0.36	-1.23	-1.59	1.03	0.34
Amino Acid	Alanine and Aspart...	aspartate	0.03	0.33	0.96	0.35	0.41	-0.42	1.58	-3.74	-0.76
Amino Acid	Alanine and Aspart...	asparagine	-2.15	2.17	0.09	-0.31	-0.04	0.18	-1.54	0.91	0.56
Amino Acid	Alanine and Aspart...	N-acetylaspartate (NAA)	3.14	-1.22	0.42	-0.54	-0.87	-0.78	0.54	0.92	-0.71
Carbohydrate	Aminosugar Metab...	glucuronate	0.63	0.52	-0.29	-0.45	-0.22	-1.34	-0.87	-0.49	4.28
Carbohydrate	Aminosugar Metab...	N-acetylneuraminate	0.80	0.92	-1.59	-1.11	-1.50	0.54	1.68	-0.39	0.52
Carbohydrate	Aminosugar Metab...	erythronate*	0.55	0.06	1.10	1.06	1.45	-1.13	-1.54	-1.60	-0.11
Cofactors and Vitamins	Ascorbate and Ald...	threonate	1.07	1.36	-0.91	-1.39	-1.33	1.00	1.18	-0.24	-0.72
Cofactors and Vitamins	Ascorbate and Ald...	oxalate (ethanedioate)	0.91	1.36	-1.47	-1.49	-0.96	0.88	1.27	-6.40E-3	-0.57
Cofactors and Vitamins	Ascorbate and Ald...	gulonic acid*	1.09	1.20	4.60E-3	-0.35	0.30	-1.24	-2.65	-0.18	1.29
Xenobiotics	Bacterial/Fungal	tartronate (hydroxymalonate)	1.42	1.33	-0.75	-0.42	1.13	-1.04	0.41	-0.11	-2.14
Xenobiotics	Benzoate Metaboli...	hippurate	-0.30	3.15	0.12	-0.40	-0.72	-1.52	-1.00	0.66	0.84
Xenobiotics	Benzoate Metaboli...	2-hydroxyhippurate (salicylurate)	-1.73	-0.89	-0.08	-0.32	-0.45	2.18	-0.64	0.76	1.51
Xenobiotics	Benzoate Metaboli...	3-hydroxyhippurate	0.38	3.10	0.31	0.25	-0.09	-1.27	-2.00	-0.41	0.28
Xenobiotics	Benzoate Metaboli...	4-hydroxyhippurate	-0.13	0.16	0.14	-0.50	3.15	0.32	-2.60	-0.56	0.36
Xenobiotics	Benzoate Metaboli...	benzoate	-0.67	0.49	0.25	1.14	-1.17	0.02	2.68	-0.85	-1.33
Xenobiotics	Benzoate Metaboli...	catechol sulfate	-0.32	4.00	-0.23	-0.28	-0.76	-0.16	-1.70	0.06	0.86
Xenobiotics	Benzoate Metaboli...	O-methylcatechol sulfate	-0.36	4.17	0.19	0.26	-0.54	-0.18	-1.74	-0.73	0.47
Xenobiotics	Benzoate Metaboli...	3-methyl catechol sulfate (1)	0.06	3.05	-0.58	-0.81	-0.71	-0.46	-0.27	-0.89	1.74
Xenobiotics	Benzoate Metaboli...	4-methylcatechol sulfate	1.85	1.93	-0.11	-0.21	-0.87	-1.76	-0.97	0.05	0.38
Xenobiotics	Benzoate Metaboli...	4-ethylphenylsulfate	1.85	0.67	-1.18	-1.13	-1.02	-0.86	0.11	1.71	0.15
Xenobiotics	Benzoate Metaboli...	4-vinylphenol sulfate	-0.86	0.60	0.57	0.35	0.30	1.34	0.83	-3.21	-0.91
Xenobiotics	Benzoate Metaboli...	4-sulfoxy-methylbenzoate	1.41	-0.70	-1.22	-1.33	-1.20	1.09	1.50	0.25	0.26
Cofactors and Vitamin	Biotin Metabolism	biotin	-0.35	-0.35	-0.35	-0.35	-0.35	0.00E0	-0.35	-0.35	-0.35
Lipid	Carnitine Metabolism	deoxycarnitine	-1.42	-0.90	1.20	1.95	1.32	-1.04	-0.58	-0.04	-0.18
Lipid	Carnitine Metabolism	carnitine	-0.18	0.29	1.38	1.84	0.44	0.15	-2.22	-1.18	-0.66
Xenobiotics	Chemical	1,2-propanediol	3.84	-0.77	0.13	-0.44	-0.38	-0.72	-0.57	-0.80	1.32
Xenobiotics	Chemical	2-pyrrolidinone	-0.22	-0.53	-1.22	-0.38	0.76	4.30	-0.94	-0.36	0.40
Xenobiotics	Chemical	sulfate*	2.37	-0.52	-0.42	1.10	0.87	-1.73	0.06	-0.22	-1.19
Xenobiotics	Chemical	O-sulfo-L-tyrosine	2.98	-0.82	-0.19	0.68	-0.56	0.13	-0.95	0.93	-1.46
Xenobiotics	Chemical	2-aminophenol sulfate	-3.11	0.14	1.08	0.85	0.61	1.18	-0.48	-0.06	-1.10
Xenobiotics	Chemical	2-ethylhexanoate	0.20	0.31	0.04	0.48	-0.84	3.37	0.01	-0.79	-1.99
Xenobiotics	Chemical	2-hydroxyisobutyrate	0.65	2.94	-0.92	-0.43	-0.33	-0.92	-0.83	1.37	-0.62
Xenobiotics	Chemical	S-(3-hydroxypropyl)mercapturic ...	0.23	-0.62	1.10	-0.62	-0.62	-0.62	-0.62	-0.62	4.37
Xenobiotics	Chemical	dimethyl sulfone	-0.35	0.05	-0.32	-0.62	-0.33	0.10	10.08	-0.83	-0.47
Xenobiotics	Chemical	EDTA	0.41	1.59	0.20	1.86	0.31	-0.37	-1.03	-1.35	-1.47
Xenobiotics	Chemical	glycolate (hydroxyacetate)	1.98	-0.80	0.29	1.06	-1.00	-2.10	0.85	-0.45	0.14
Xenobiotics	Chemical	iminodiacetate (IDA)	-0.29	-1.18	1.39	1.15	1.04	-0.91	1.11	-1.13	-1.09
Xenobiotics	Chemical	phenylcarnitine*	-1.98	3.09	0.38	0.37	-0.66	-0.95	-0.38	0.24	0.49
Xenobiotics	Chemical	N-methylpipecolate	2.79	0.23	0.53	0.48	0.48	-1.67	-1.23	-0.94	-0.22
Xenobiotics	Chemical	4-hydroxychlorothalonil	1.08	0.24	0.70	0.80	0.73	-3.47	-1.10	-0.55	0.34
Xenobiotics	Chemical	1,2,3-benzenetriol sulfate (2)	-0.70	1.37	0.58	0.14	-0.25	-0.42	-3.05	0.04	1.66
Xenobiotics	Chemical	3-hydroxypyridine sulfate	-0.82	2.23	-0.34	-0.38	-0.04	-0.57	-0.51	-1.05	2.45
Amino Acid	Creatine Metabolism	creatine	1.45	-1.32	-0.58	-0.86	0.88	2.19	-0.32	0.03	-1.06
Amino Acid	Creatine Metabolism	creatinine	0.38	-0.41	1.50	1.47	1.10	-1.73	-1.32	-0.38	-0.59
Amino Acid	Creatine Metabolism	guanidinoacetate	-1.45	0.07	1.04	1.06	-3.28	-0.06	0.44	0.55	0.48
Peptide	Dipeptide	aspartylleucine	-0.38	1.03	-0.70	-0.23	0.70	-3.15	0.33	-0.10	1.80
Peptide	Dipeptide	cyclo(gly-pro)	0.56	1.21	0.77	0.73	0.77	-2.20	-1.86	-0.60	0.02
Peptide	Dipeptide	cyclo(leu-pro)	1.33	1.04	-0.13	-0.92	-0.99	-0.86	-0.14	-1.09	2.25
Peptide	Dipeptide	cyclo(L-phe-D-pro)*	0.66	2.14	-0.73	-0.51	-0.73	-0.73	-0.73	-0.73	2.10

Identifying Hubs of Interest

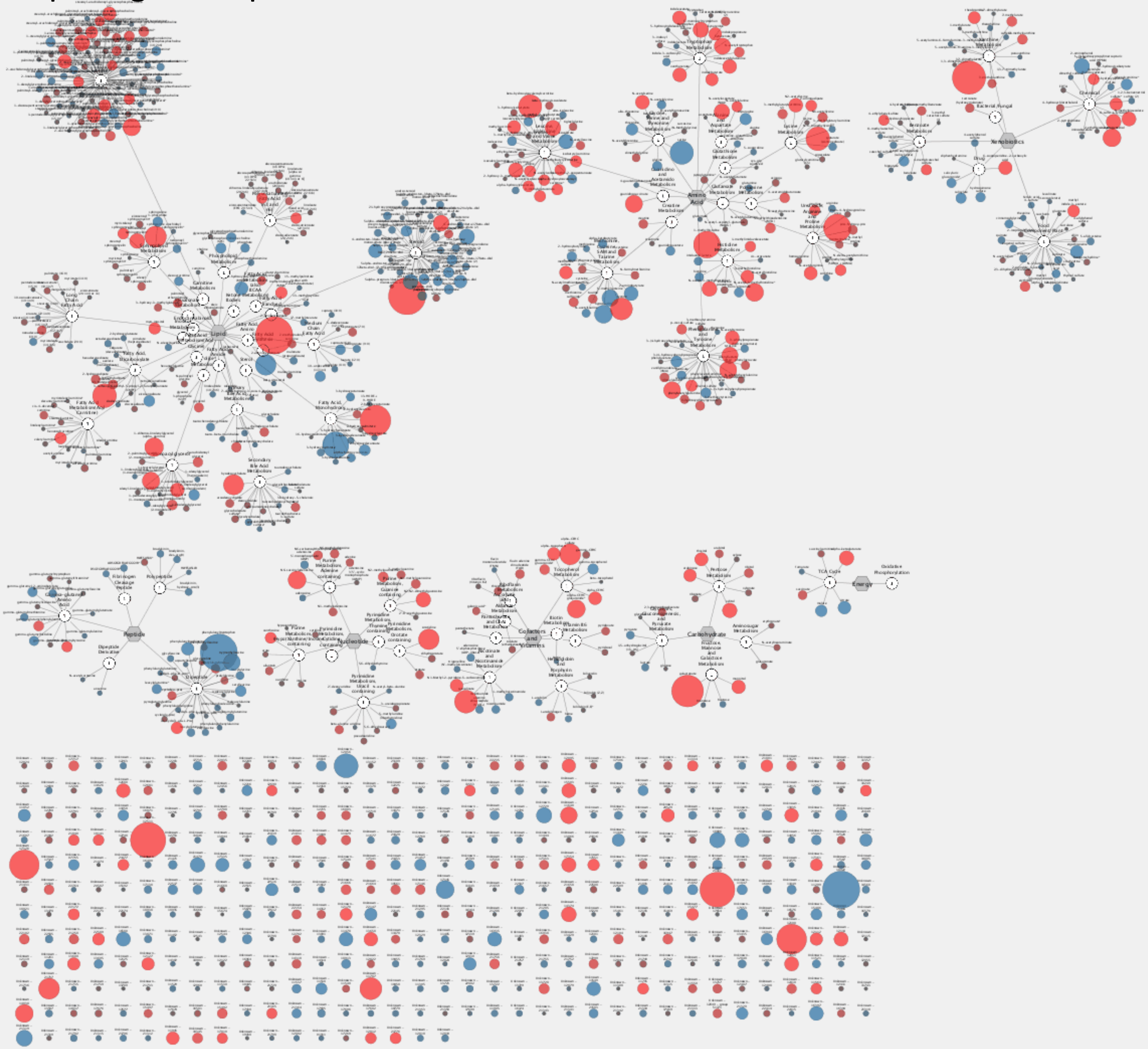
Pathway	IDEP1	IDEP2	IDEP3	IDEP4	IDEP5	IDEP6	IDEP7	IDEP8	IDEP9
Tocopherol Metabolism	3.2	1	1	1	1	1.1	1	1	2.4
Tryptophan Metabolism	2.6	1	2.6	2.7	1	1.5	1.4	1	1.5
Pentose Metabolism	2.4	2	10.9	1	1	1	1	1	1
Leucine, Isoleucine and Valine Metab...	2.2	1.1	1	1.6	1	0.6	1.6	1.4	0.9
Purine Metabolism, (Hypo)Xanthine/I...	1.1	1	7.2	1	1	1	1	1.4	4.2
Sphingolipid Metabolism	1.1	1	1	1	4.5	3.5	1.3	1	1
Long Chain Fatty Acid	1	1	1	1	6.3	1	1	5.4	1
Polyunsaturated Fatty Acid (n3 and n6)	1	1	1	1	1.9	0.6	1	2.9	2.7
Benzoate Metabolism	1	3.3	1	1	1.1	0.7	2	0.7	1
Polypeptide	1	4.8	1	1	1	1	1	1	1.3
Medium Chain Fatty Acid	1	4	1	1	1	1.1	1	2	1
Urea cycle; Arginine and Proline Meta...	1	0.6	1	1	1	1	3.7	1	1.5
Dipeptide	0.9	2.6	1.6	1	1	1.2	1.7	1	1.1
Xanthine Metabolism	0.9	4.8	1	1	1	3.4	1	1	1
Lysolipid	0.6	1.1	0.6	1	0.3	1.6	0.8	1.7	1.1
Secondary Bile Acid Metabolism	0.5	0.6	6.2	3.3	1	0.6	1.7	0.6	0.5
Fatty Acid Metabolism(Acyl Carnitine)	0.5	1.7	3.1	1	5.8	2.4	1	1.2	1

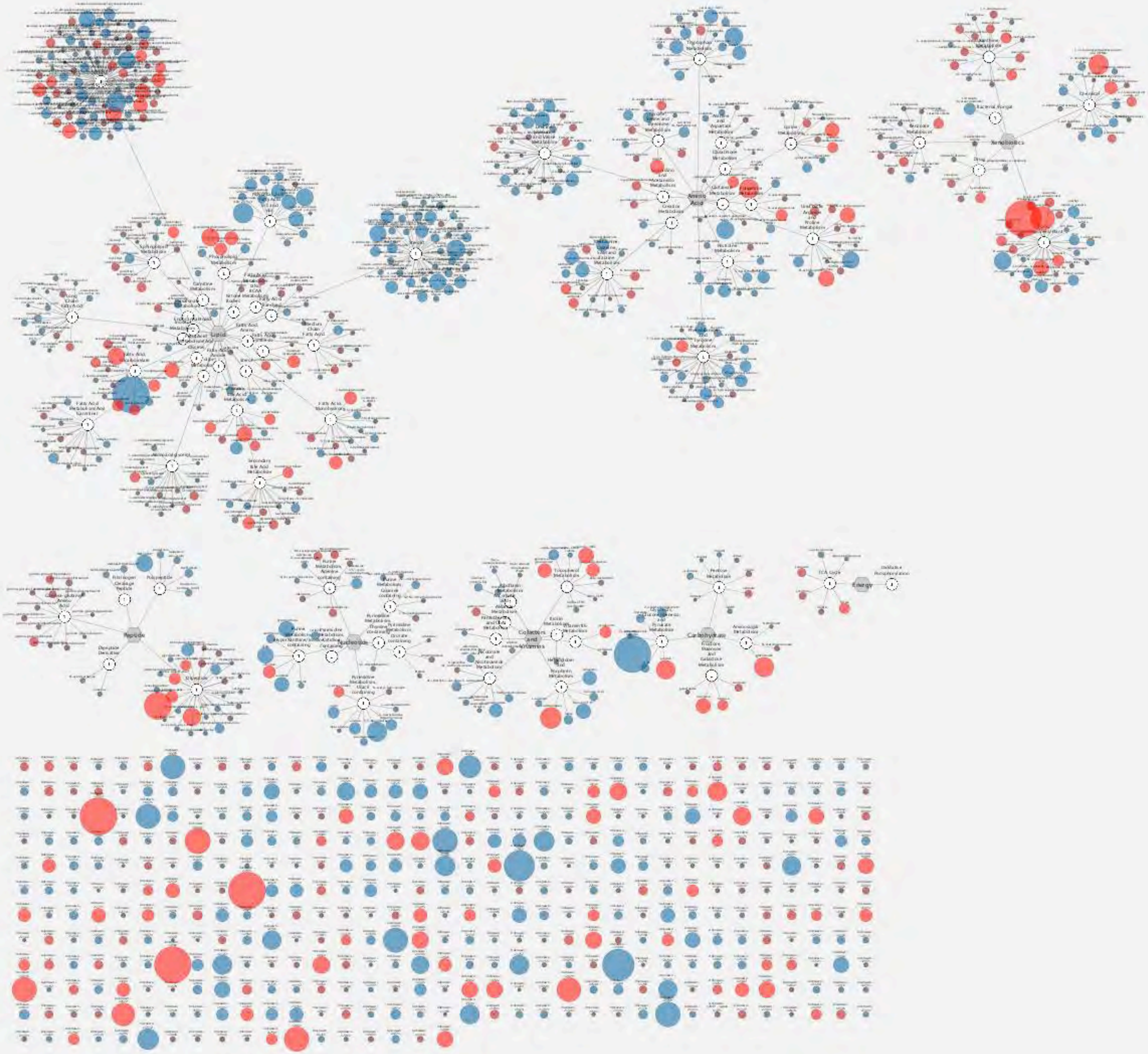
Comparing 9 samples. See the Forest AND the Trees™ Where to ZOOM IN?

Visualizing Data



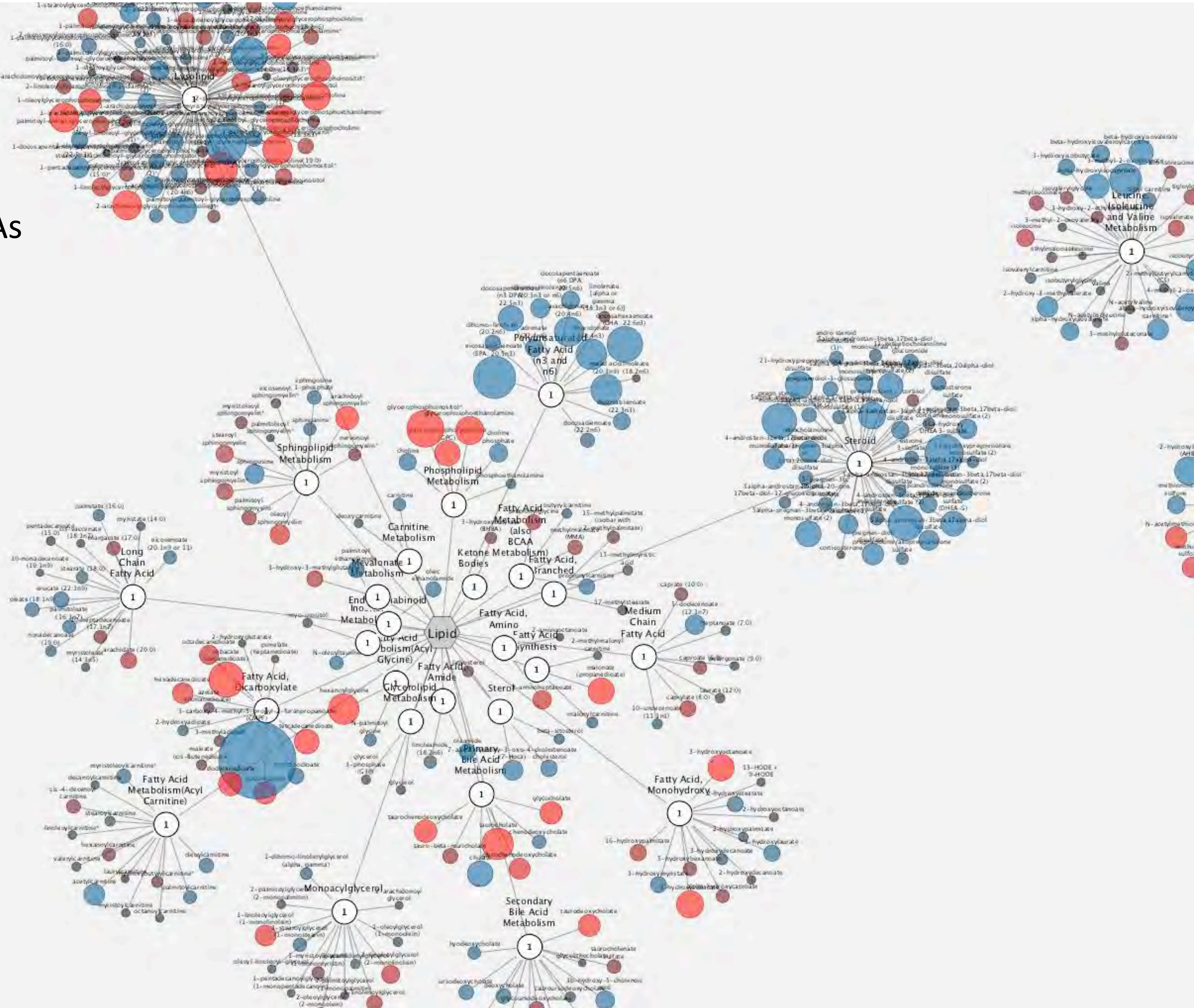
Cluster Analylis - Comparing 9 samples. See the Forest AND the Trees™



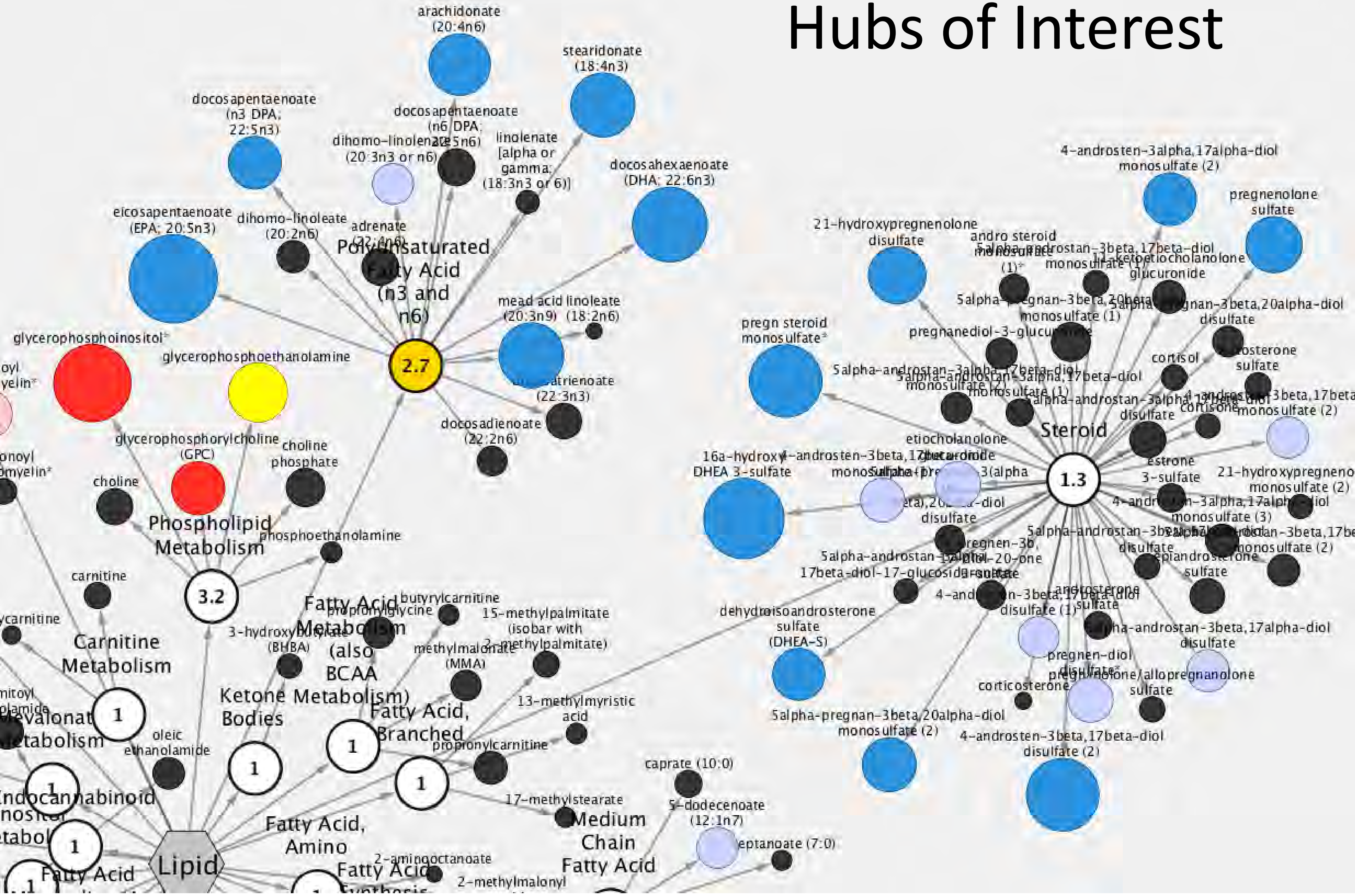

Lipid
Amino Acid
Xenobiotics
Peptide
Nucleotide
Cofactors and Vitamins
Carbohydrate
Energy

Lipid Cluster -
Blue – Low
Red – High

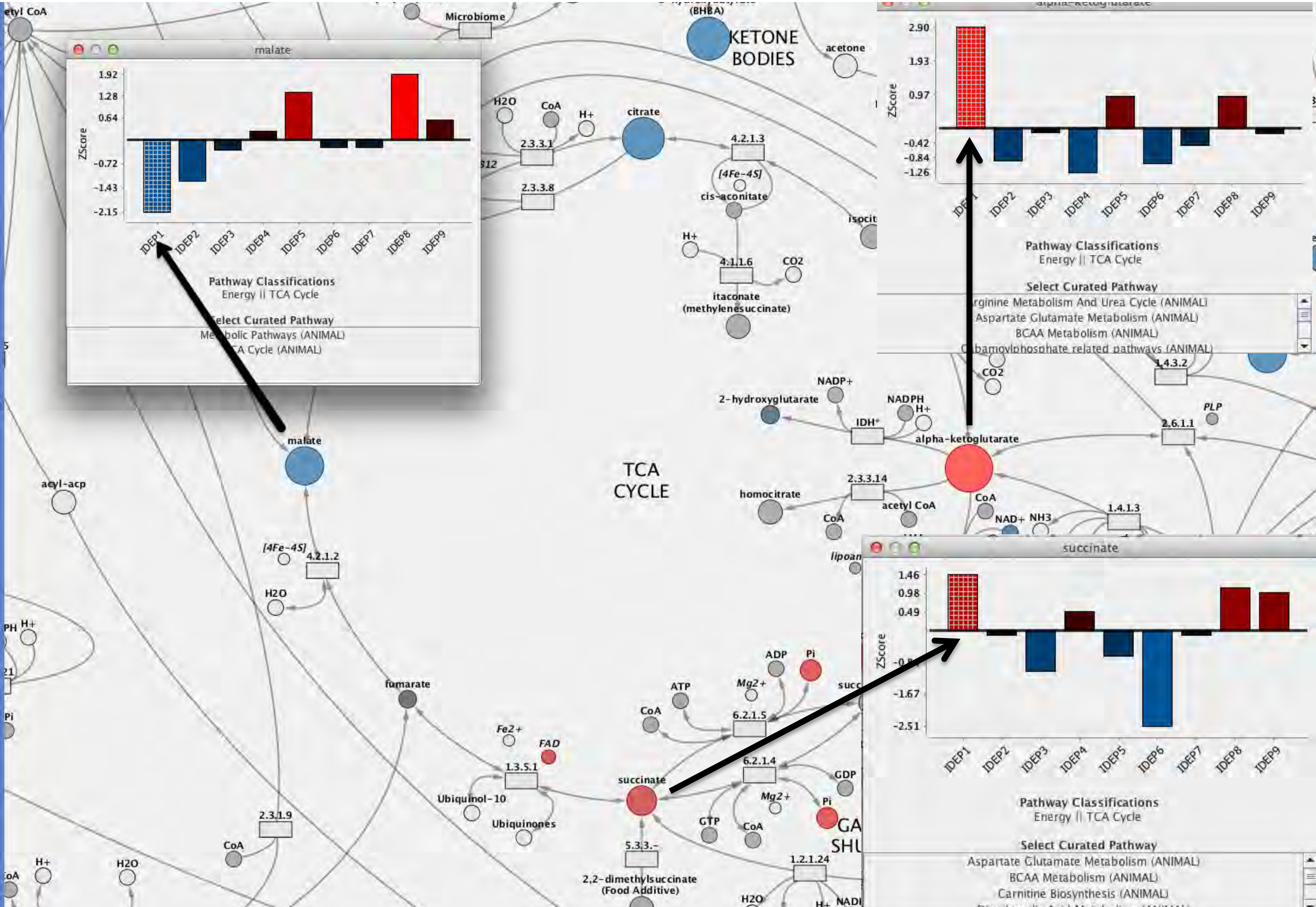
Steroids and PUFAs very low.



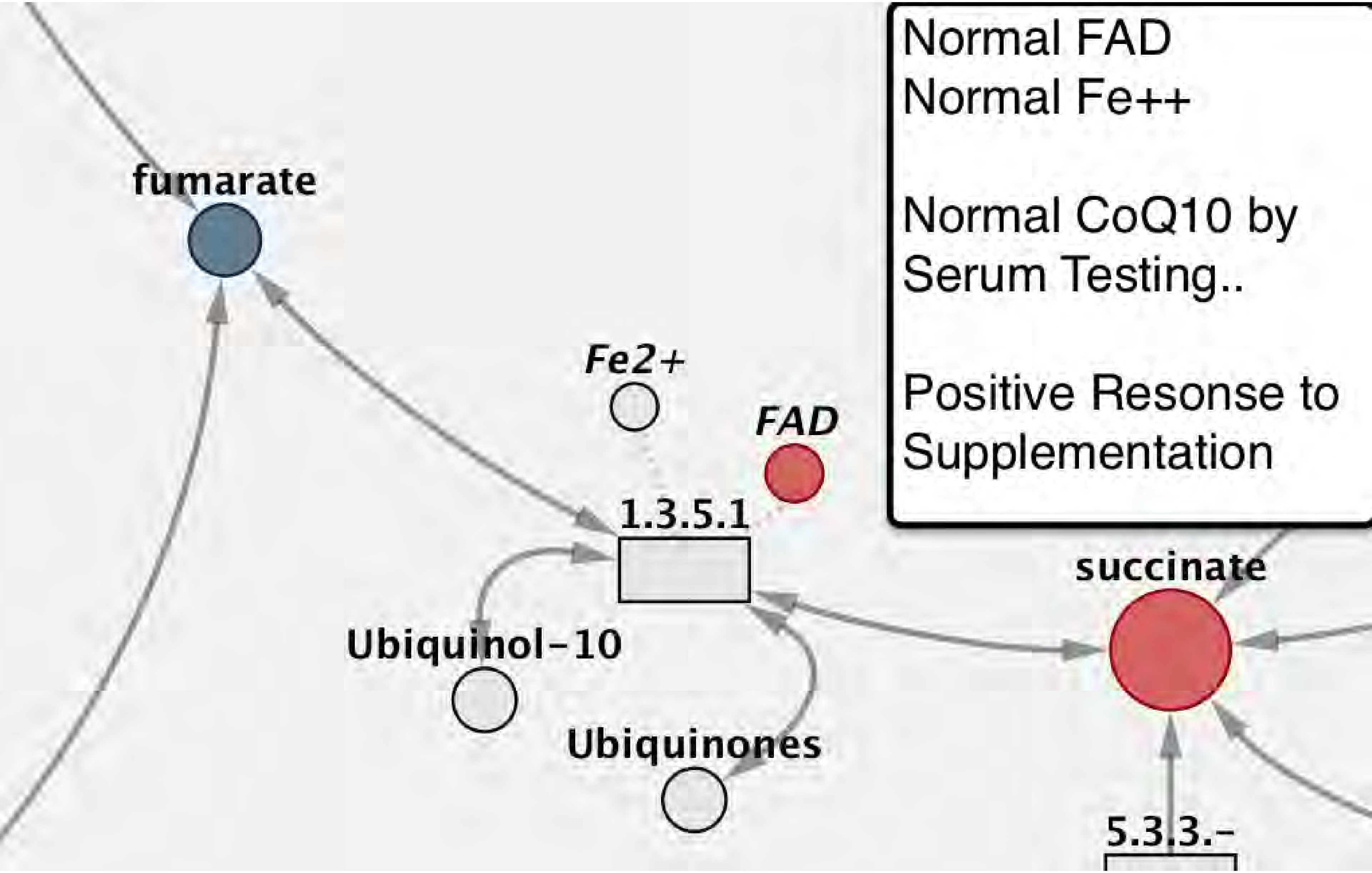
Hubs of Interest



TCA cycle organic acid analysis, with cofactors. Where is the Defect?



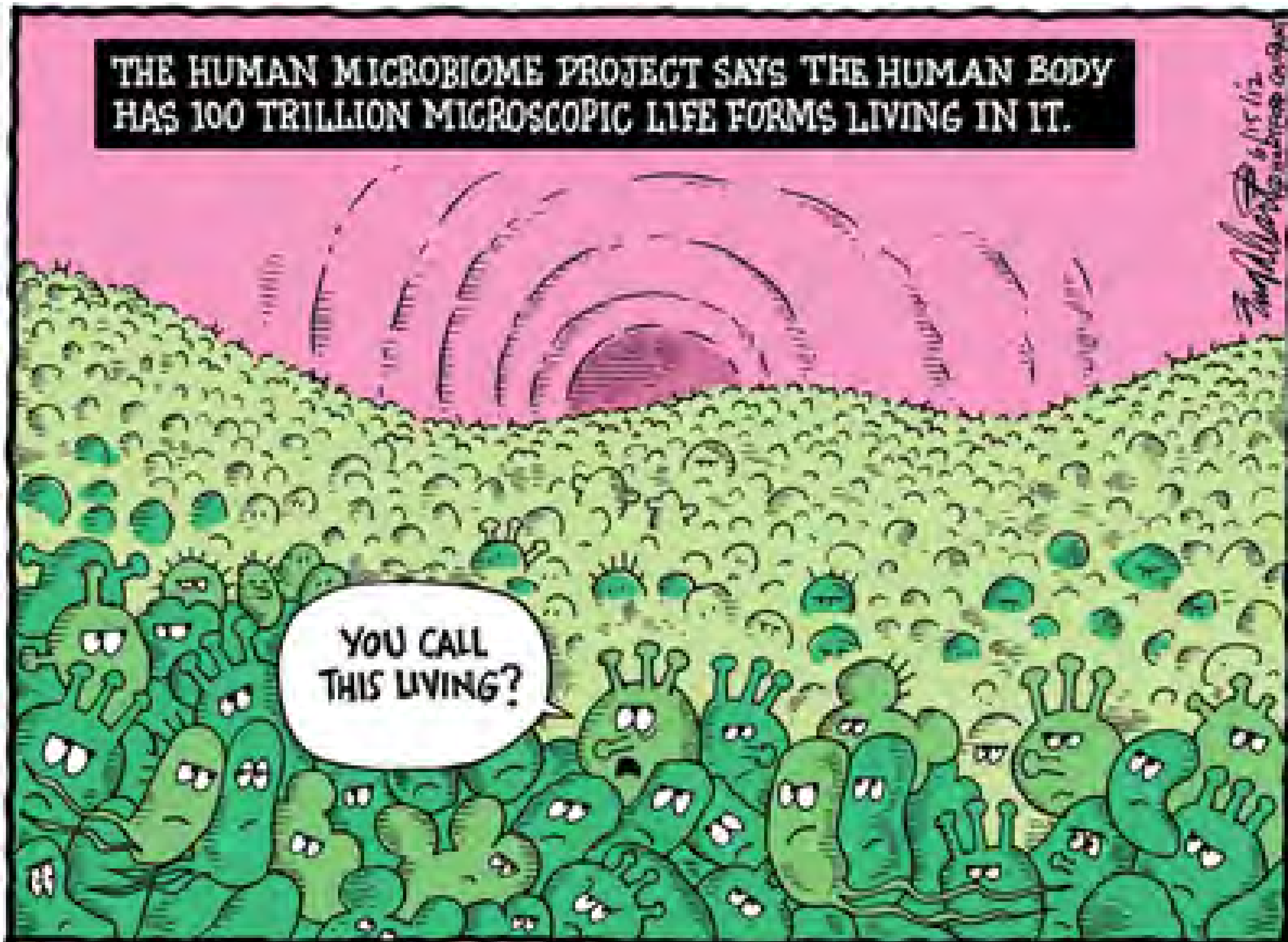
Zoom in on CoQ10.



Normal FAD
Normal Fe++

Normal CoQ10 by
Serum Testing..

Positive Resonse to
Supplementation


THE HUMAN MICROBIOME PROJECT SAYS THE HUMAN BODY HAS 100 TRILLION MICROSCOPIC LIFE FORMS LIVING IN IT.
YOU CALL THIS LIVING?

Comprehensive Coverage of the Microbiome Metabolism

Metabolomic Microbiomics

Short chain FA:
valerate
Isovalerate
Methylpropionate
Lipids:
Lyso-PC, lyso-PE
Monacylglycerol
cholesterol

lipid metabolism

cadaverine
putrescine
spermidine
spermine

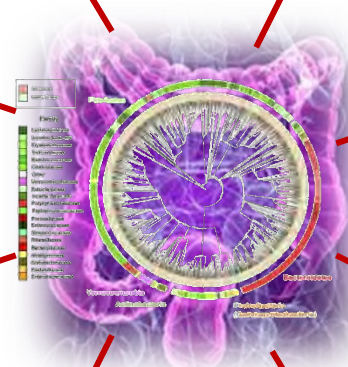
polyamine metabolism

riboflavin
pyridoxine
folate

vitamins

2nd bile acids:
cholate
dehydrocholate
ursodeoxycholate
deoxycholate
glycodeoxycholate
ketodeoxycholate
glycolithocholate sulfate
taurolithocholate
taurolithocholate sulfate
lithocholate
diketolithocholate
ketolithocholate
hyocholate
glycocholenate sulfate
taurocholenate sulfate*
glycoursodeoxycholate
tauroursodeoxycholate

bile acid metabolism



...yphenyl)lactate
...roxyphenylpyruvate
4-hydroxyphenylacetate
3-hydroxyphenylacetate
3,4-dihydroxyphenylacetate
phenylacetylglutamine
phenylacetylglycine
2-(4-hydroxyphenyl)propionate
3-(3-hydroxyphenyl)propionate
3-(4-hydroxyphenyl)propionate
3-phenylpropionate
phenol sulfate
4-hydroxycinnamate
indolelactate
indoleacetate
indole-3-carboxylic acid
n-acetyltryptophan
3-indoxyl sulfate
indolepropionate
skatol
indoleacetylglutamine

aromatic amino acid metabolism

lactate
formate,
succinate
glucose
urea
creatine
creatinine
ketoisovalerate

energy metabolism

choline metabolism

trimethylamine-n-oxide
betaine
dimethylglycine

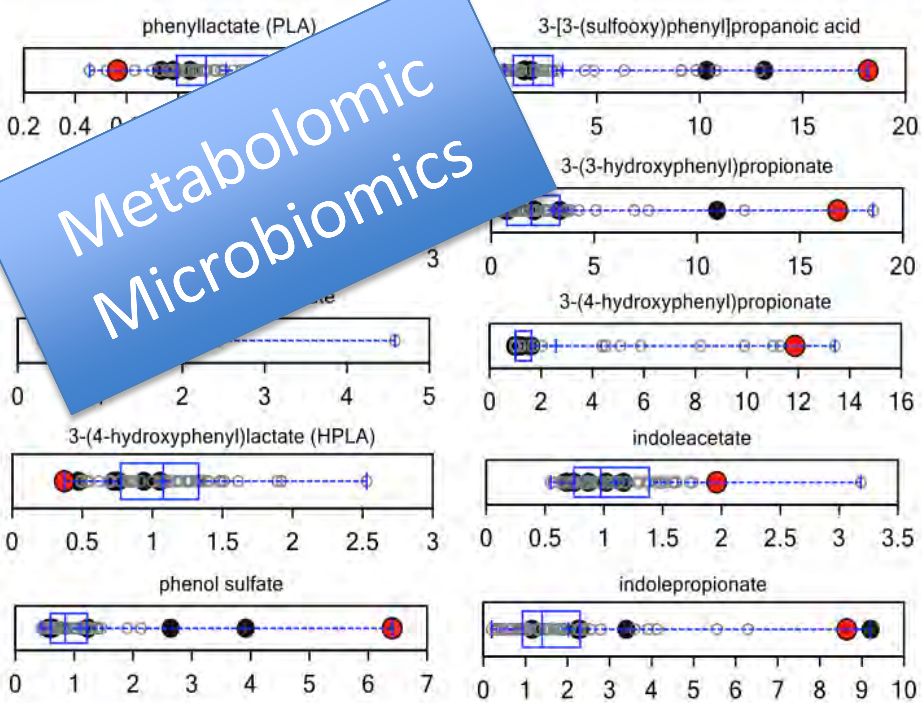
xenobiotic metabolism

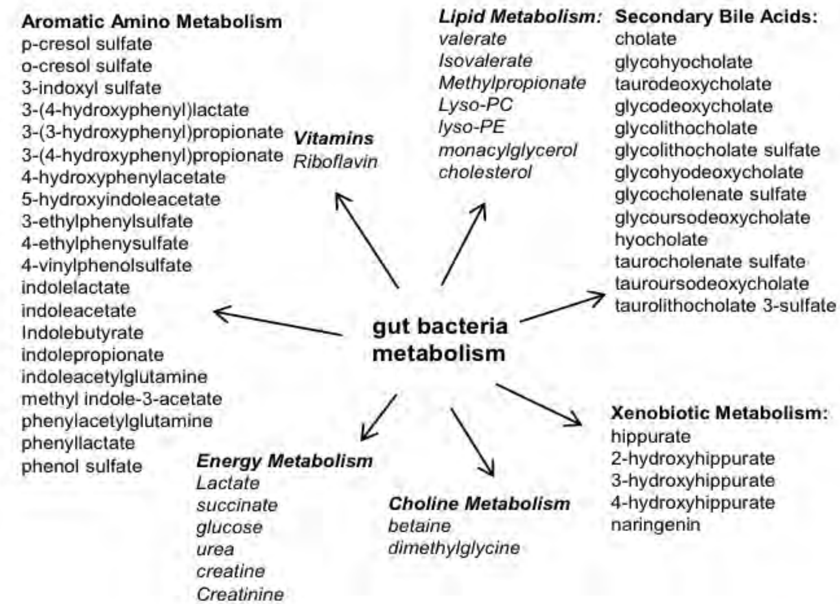
hippurate
2-hydroxyhippurate
3-hydroxyhippurate
4-hydroxyhippurate
3-hydroxybenzoate
4-hydroxybenzoate
3,4-dihydroxybenzoate
2,4,6-trihydroxybenzoate
p-hydroxybenzaldehyde
methyl-4-hydroxybenzoate
3-(2-hydroxyphenyl)propionate
vitexin
daidzein
genistein

exclusively or mainly contributed by bacteria metabolism
contributed by both mammalian cells and bacteria

Gut Bacteria Metabolism

Metabolomic Microbiomics





Biochemical Name	ID 1	ID 2	ID 3	ID 4	ID 5	ID 6
	FASTED POPULATION	FASTED POPULATION	FASTED POPULATION	FASTED POPULATION	FASTED POPULATION	FASTED POPULATION
phenyllactate (PLA)	0.85	-0.88	-0.42	-0.68	1.1	-1.74
phenylacetate	1.06	0.18	1.67	-0.21	0.35	1.14
4-hydroxyphenylpyruvate	0.62	-0.25	-1.18	0.8	-0.07	-1.41
3-(4-hydroxyphenyl)lactate	-0.99	-2.1	-0.31	-0.88	-0.01	-2.74
phenol sulfate	3.61	2.7	0.93	-0.89	-0.64	4.76
3-[3-(sulfooxy)phenyl]propanoic acid	1.87	1.66	-0.1	0.1	-0.08	2.16
3-(3-hydroxyphenyl)propionate	1.8	0.29	0.72	0.3	-0.62	2.18
3-(4-hydroxyphenyl)propionate	0.61		0.49			1.48
indoleacetate	0.01	-1.07	-0.82	0.37	-0.41	1.73
indolepropionate	0.69	2.42	0.71	1.19	-0.13	2.34

Figure 4. Figure of gut microbial produced biochemicals, heat map of Z-scores where dark red and green are Z-scores are significant ($p \leq 0.05$) and light red and light green are Z-scores trending towards significant ($0.05 < p < 0.1$), along with box plots of associated biochemicals as described in **Figure 1**.

Dried Blood Spot Fatty Acid Profiles

Levels of Lipids

- w-3
- w-6
- MUFA
- Saturated FA
- Trans-FA

Lipomics

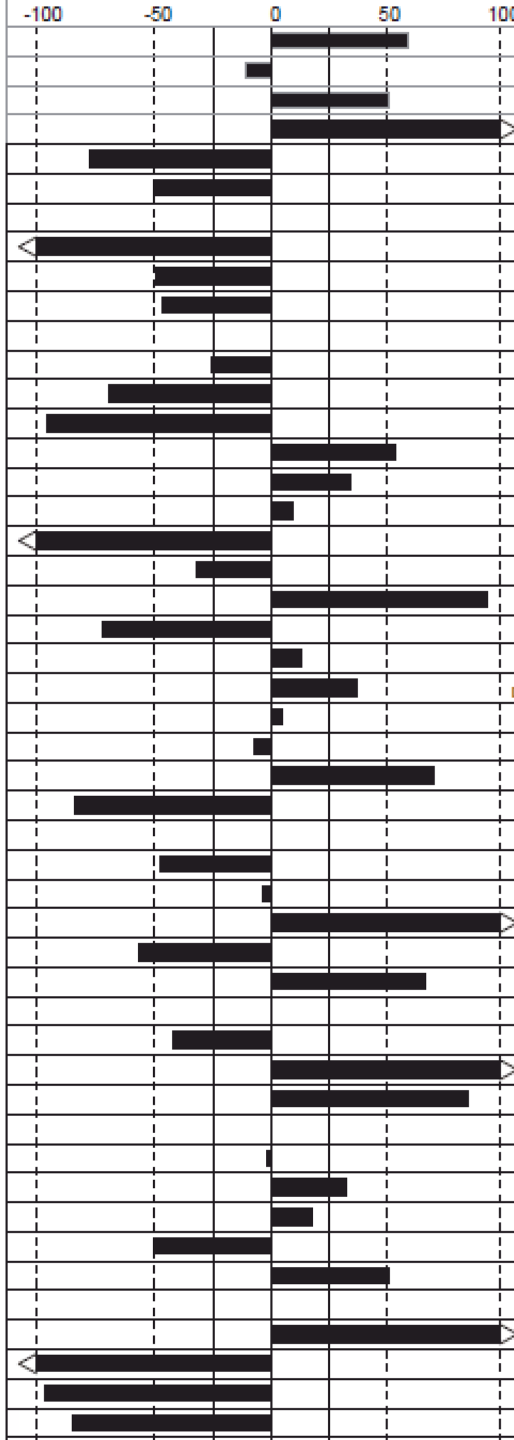
Dried Blood Spot Fatty Acid Profile

Fatty Acid Group	Total	Percentile Rank	Reference Range*
Omega-3 Fatty Acids	**6.56%**	**63rd**	**2.92-13.29%**
Omega 3 Index	6.22%	58th	2.90-12.90%
Alpha-Linolenic (18:3n3)	0.68%		
Eicosapentaenoic (EPA, 20:5n3)	0.75%		
Docosapentaenoic-n3 (22:5n3)	1.57%		
Docosahexaenoic (DHA, 22:6n3)	3.56%		
Omega-6 Fatty Acids	**38.20%**	**52nd**	**26.35-45.15%**
Linoleic (18:2n6)	24.41%		
Gamma-Linolenic (18:3n6)	0.28%		
Eicosadienoic (20:2n6)	0.31%		
Dihomo-y-linolenic (20:3n6)	1.66%		
Arachidonic (AA, 20:4n6)	9.72%		
Docosatetraenoic (22:4n6)	1.45%		
Docosapentaenoic-n6 (22:5n6)	0.37%		
cis-Monounsaturated Fatty Acids	**21.27%**	**51st**	**15.65-32.26%**
Palmitoleic (16:1n7)	0.47%		
Oleic (18:1n9)	19.28%		
Eicosenoic (20:1n9)	0.32%		
Nervonic (24:1n9)	1.20%		
Saturated Fatty Acids	**33.43%**	**47th**	**29.52-37.74%**
Myristic (14:0)	0.40%		
Palmitic (16:0)	19.52%		
Stearic (18:0)	11.72%		
Arachidic (20:0)	0.22%		
Behenic (22:0)	0.70%		
Lignoceric (24:0)	0.87%		
Trans Fatty Acids	**0.58%**	**5th**	**0.35-2.69%**
Trans Palmitoleic (16:1n7t)	0.10%		
Trans Oleic (18:1t)	0.32%		
Trans Linoleic (18:2n6t)	0.16%		
Trans Fat Index	0.48%	5th	0.30-2.42%
Ratios			
AA:EPA	13.0:1	56th	1.4 – 52.6
Omega-6:Omega-3	5.8:1	39th	2.3 – 14.5

Lipomics

Patterns of Carnitine Metabolism

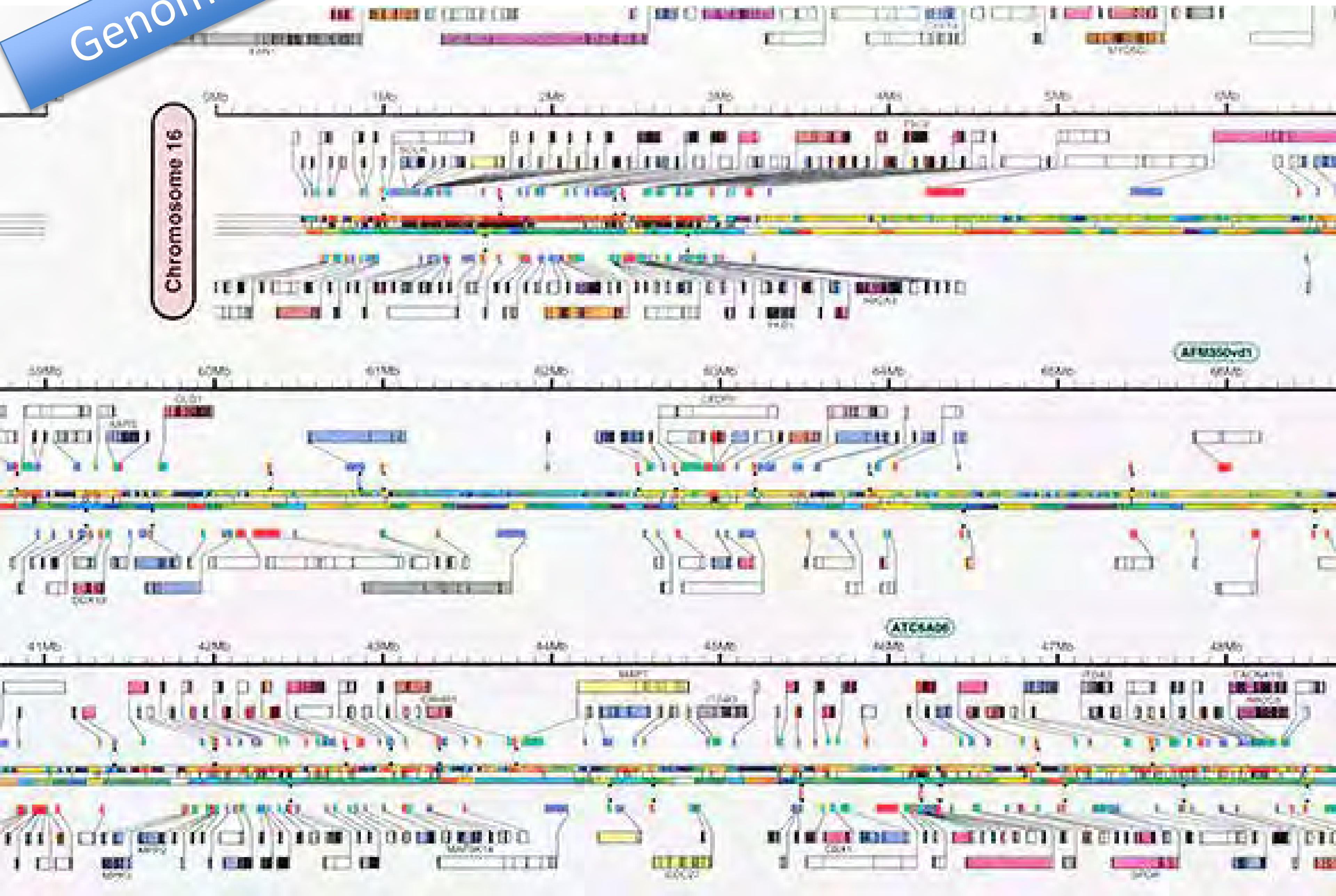
Levels of Lipids
- Saturated
- PUFA
  - w-3
  - w-6
  - w-9
- MUFA
- SCFA
- MCFA
- Trans-
- VLCFA
- Odd Chain
- Renegades
- Omega ox'd



		% Status		Result	Low	High
	16 DMA	**58.62**	**H**	1.81	1.34	1.78
	18:0 DMA	-11.20		2.83	2.55	3.26
	18:1 DMA	**50.00**	**H**	1.07	0.74	1.07
	C10:0 Capric	**250.00**	**H**	0.0080	0.002	0.004
	C14:0 Myristic	**-76.85**	**L**	0.18	0.21	0.31
	C14:1w5 Myristoleic	**-50.00**	**L**	0.0010	0.001	0.003
	C15:0 Pentadecanoic	**-87.21**	**L**	0.07	0.09	0.13
	C16:0 Palmitic	**-102.79**	**L**	17.41	18.54	20.69
	C16:1w7 Palmitoleic	**-49.06**	**L**	0.09	0.09	0.20
	C16:1w9 Hexadecanoic	**-45.83**	**L**	0.05	0.05	0.07
	C17:0 Heptadecanoic	**-60.00**	**L**	0.28	0.29	0.38
	C17:1 Heptadecaenoic	**-25.00**		0.02	0.02	0.03
	C18:0 Stearic	**-68.47**	**L**	14.19	14.57	16.63
	C18:1w5 Octadecanoic	**-95.45**	**L**	0.00	0.06	0.19
	C18:1w7 Vaccenic	**53.35**	**H**	0.84	0.62	0.83
	C18:1w9 Oleic	**34.25**	**H**	11.87	10.47	12.14
LA	C18:2w6 Linoleic	9.03		9.46	7.73	10.65
	C18:2w6 Conj Rumenic	**-110.00**	**L**	0.02	0.04	0.07
ALA	**C18:3w3 Alpha Linolenic**	**-31.25**	**L**	0.09	0.07	0.14
GLA	**C18:3w6 Gamma Linolenic**	**92.11**	**H**	0.05	0.02	0.04
	C20:0 Arachidic	**-71.28**	**L**	0.34	0.36	0.46
	C20:2w6 Eicosadienoic	13.33		0.25	0.19	0.28
DGLA	**C20:3w6 Dihomo-y Lino.**	**37.02**	**H**	1.49	0.99	1.56
	C20:3w9 Mead	5.00		0.04	0.03	0.04
AA	C20:4w6 Arachidonic	-6.68		11.87	10.77	13.31
EPA	**C20:5w3 Eicosapenta.**	**69.46**	**H**	1.19	0.17	1.03
	C22:0 Behenic	**-83.42**	**L**	1.38	1.51	1.90
	C22:1w9 Erucic	0.00		0.05	0.04	0.06
	C22:2w6 Docosadienoic	**-46.67**	**L**	0.05	0.05	0.08
	C22:4w6 Adrenic	-3.71		2.42	1.88	3.04
	C22:5w3 Docosapenta.	**131.01**	**H**	2.75	1.46	2.17
	C22:5w6 Osbond	**-56.01**	**L**	0.34	0.36	0.74
DHA	**C22:6w3 Docosahexa.**	**65.33**	**H**	5.02	2.70	4.71
	C23:0 Tricosanoic	**-90.00**	**L**	0.23	0.26	0.33
	C24:0 Lignoceric	**-41.86**	**L**	4.68	4.61	5.53
	C24:1w9 Nervonic	**167.05**	**H**	5.48	3.23	4.27
	C24:2w6 Tetracosadienoic	**84.02**	**H**	0.76	0.43	0.67
	C25:0 Pentacosanoic	**-46.77**	**L**	0.10	0.09	0.13
	C26:0 Hexacosanoic	-1.95		0.26	0.22	0.30
	C26:1 Lumequic	**31.82**	**H**	0.26	0.17	0.27
	C26:2 Hexacosadienoic	17.31		0.14	0.07	0.17
	C28:0 Octacosanoic	**-50.00**	**L**	0.0030	0.003	0.005
	C30:0 Triacontanoic	**50.00**	**H**	0.0010	0.000	0.001
	Phytanic	0.00		0.0020	0.001	0.003
	Pristanic	**950.00**	**H**	0.0010	0.000	0.000
	Sum C16:1 Trans FAs	**-108.06**	**L**	0.02	0.04	0.07
	Sum C18:1 Trans FAs	**-95.83**	**L**	0.21	0.47	1.03
	Sum C18:2 Trans FAs	**-84.00**	**L**	0.06	0.07	0.12

Genomics

Whole Genome Analysis



Humans have approximately 10 trillion cells

If you were to line all of the DNA found in every cell of a human body it would stretch from the earth to the sun 100 times!

SNV's

- 6 Billion Nucleotides - we sequence ~85%
- SNV's occur one in every 300 nucleotides
- Approximately 20 million in the human genome
- 8000 unique to each person
- If in a exon or regulatory region of a gene can affect the gene function

- Most are Variants of Unknown Significance
- SNPs are SNVs that have >1% prevalence

Whole Genome Analysis

Variant Statistics

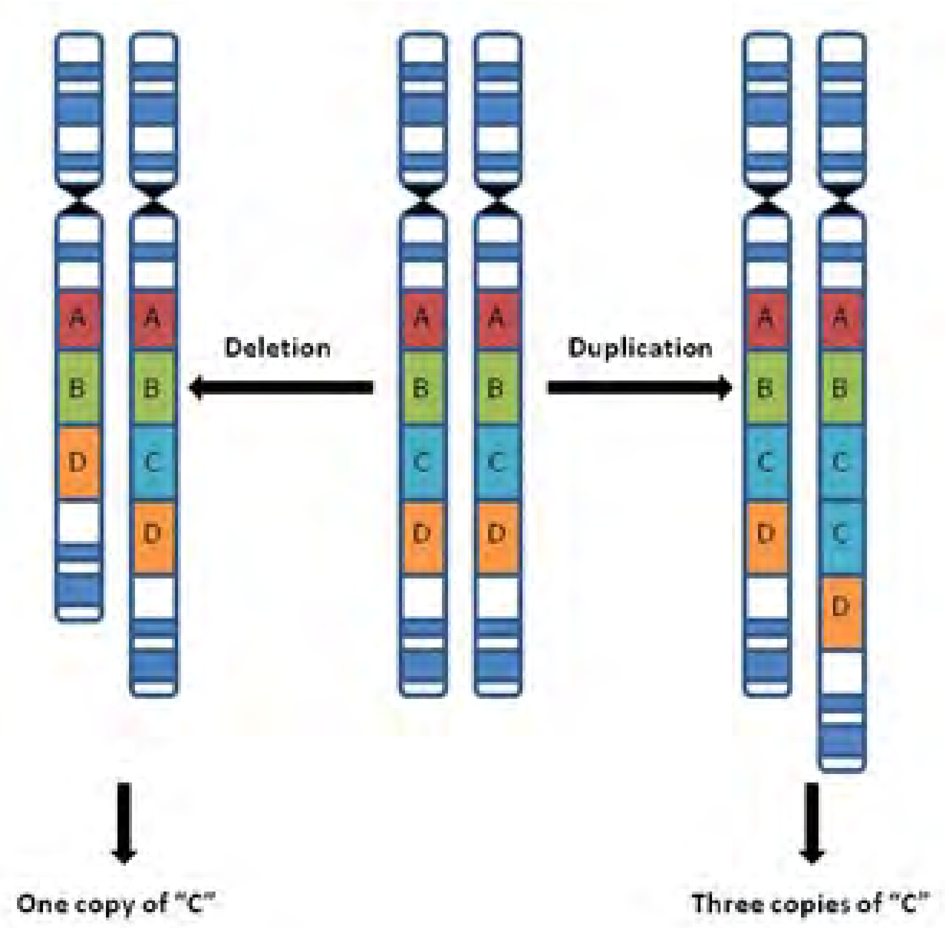
	SNVs	Deletions	Insertions
Total Number	3,507,174	271,870	276,245
Number in Genes	1,346,666	116,847	118,650
Number in Exons	47,010	2,898	3,137
Number in Coding Regions	19,759	235	275
Number in UTR	27,251	2,663	2,862
Splice Site Region	2,483	193	216
Stop Gained	79	0	0
Stop Lost	31	0	0
Frameshift	0	111	152
Non-synonymous	10,470	4	7
Synonymous	9,278	0	0

Genomics

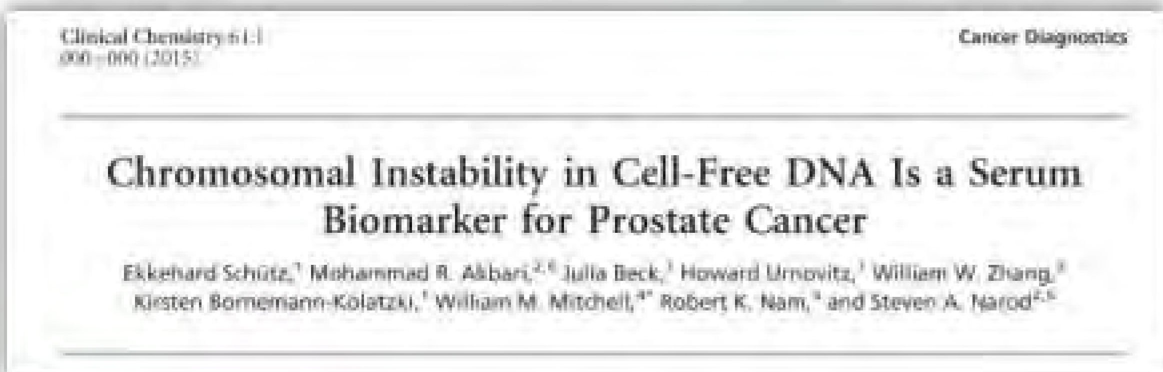
Copy Number Variation

- Accounts for more variation than SNP's
- Deletions, inversions, insertions, and duplications
- 0.4% of the genomes of unrelated people differ with respect to copy number variation
- May be inherited or arise during development
- Variable number of tandem repeats
  - Found throughout genome and show variations in length even between related individuals

Copy Number Variation



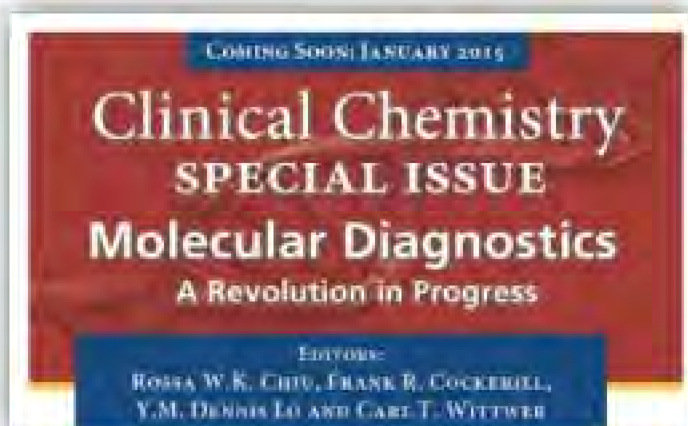
Chromosomal Instability score from CNV Genomics as a Cancer Marker


Clinical Chemistry 61:1
000–000 (2015)

Cancer Diagnostics

Chromosomal Instability in Cell-Free DNA Is a Serum Biomarker for Prostate Cancer

Ekkehard Schütz,[1] Mohammad R. Akbari,[2,6] Julia Beck,[1] Howard Urnovitz,[1] William W. Zhang,[3] Kirsten Bornemann-Kolatzki,[1] William M. Mitchell,[4*] Robert K. Nam,[5] and Steven A. Narod[2,6]



- **Second Opinion™ Validation Study published in high impact January 2015 Special Issue "Molecular Diagnostics: A Revolution in Progress"**

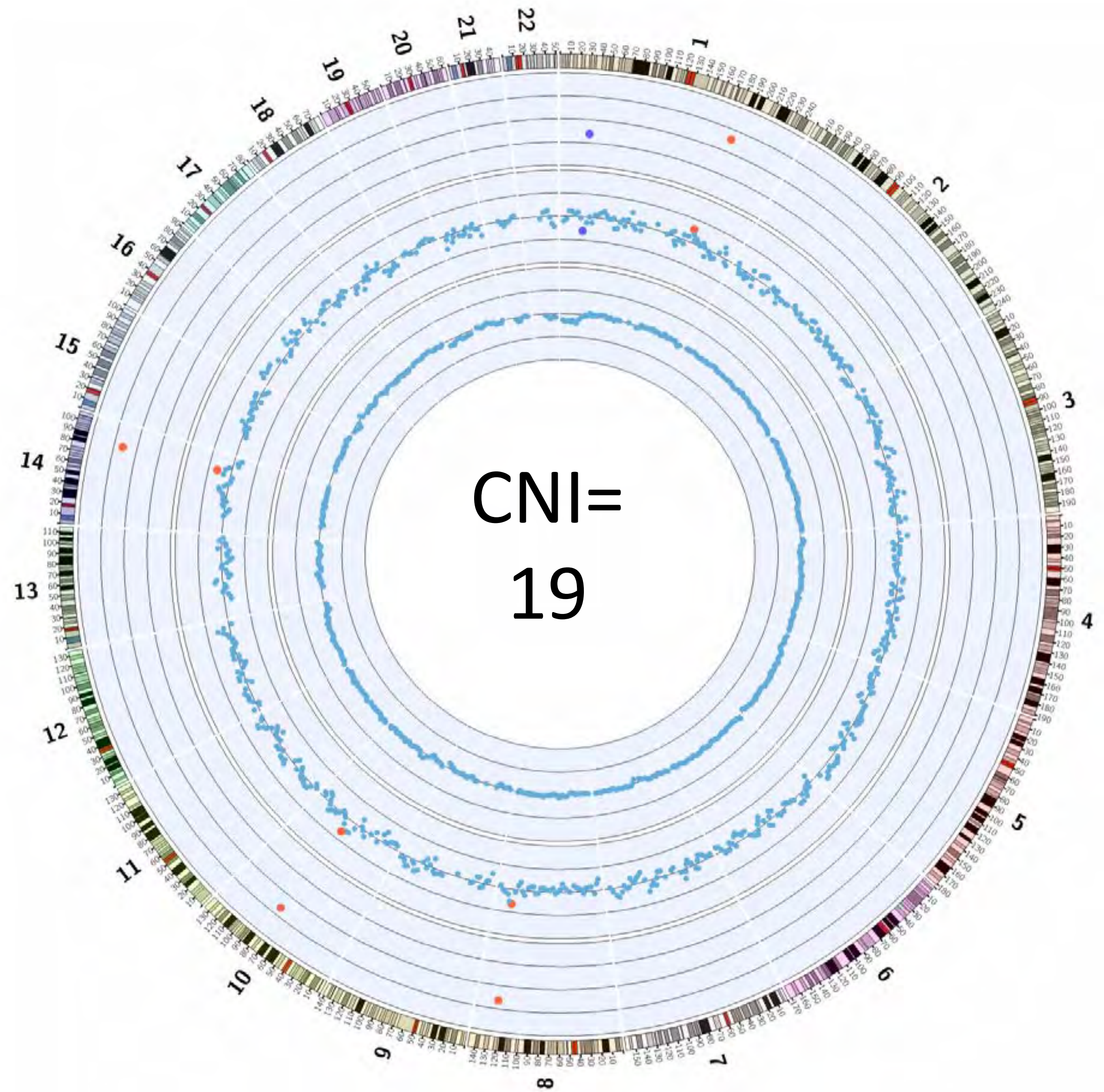
Tumor Load Liquid Biopsy via Copy Number Instability (CNI)

- Circos Plot
  - Red = gain
  - Blue= loss

- Inner circle- PBMC CNI

- Middle Circle – Cell Free DNA CNI (unadjusted)

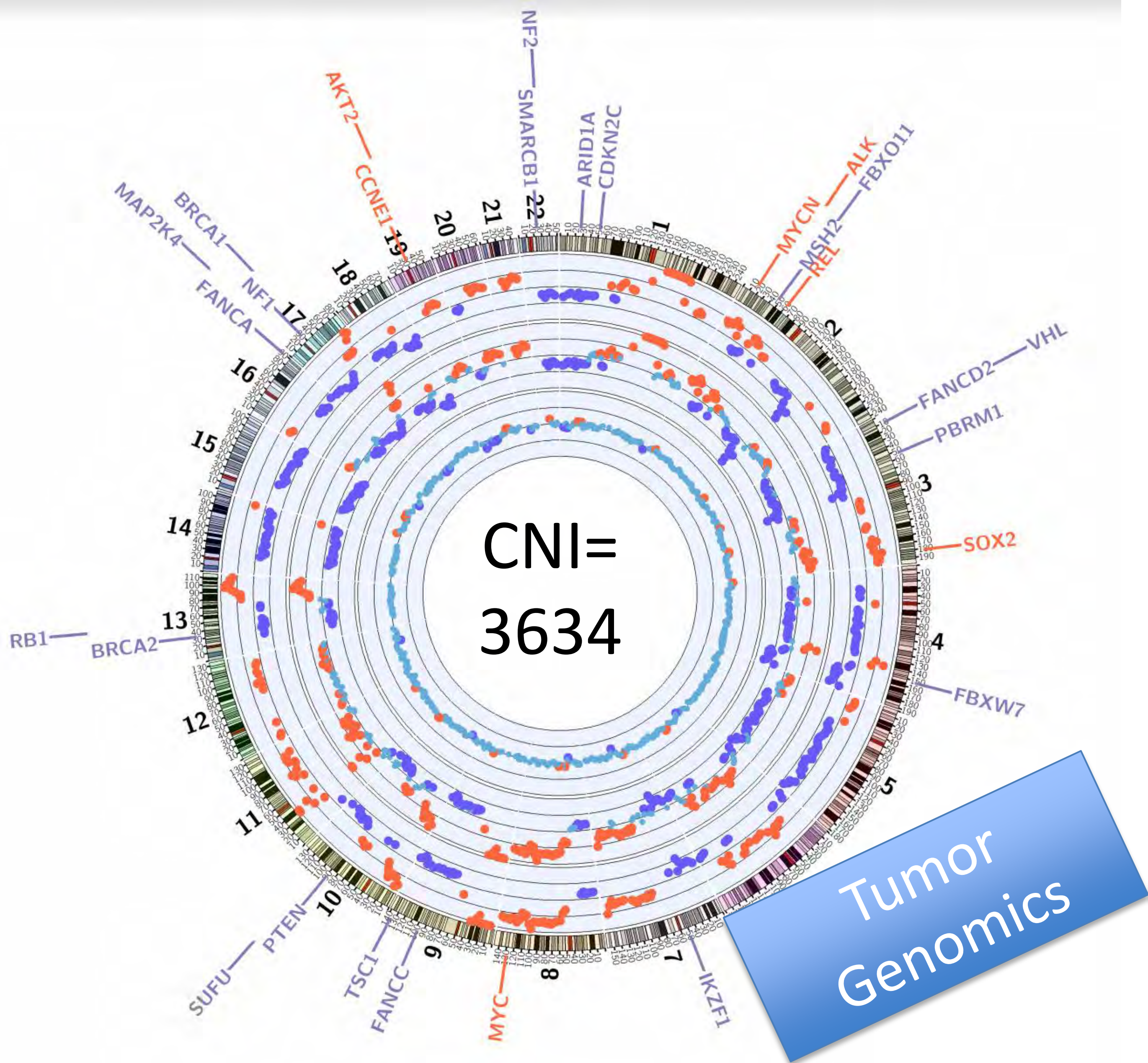
- Outer Circle – CNI remaining after adjustment for PBMC



Tumor Load Liquid Biopsy via CNI

- CNI = Copy Number Instability

- Widely Meta-static Triple Negative Breast Cancer



Examples of the role and the effect of deficiency of specific micronutrients on genomic stability

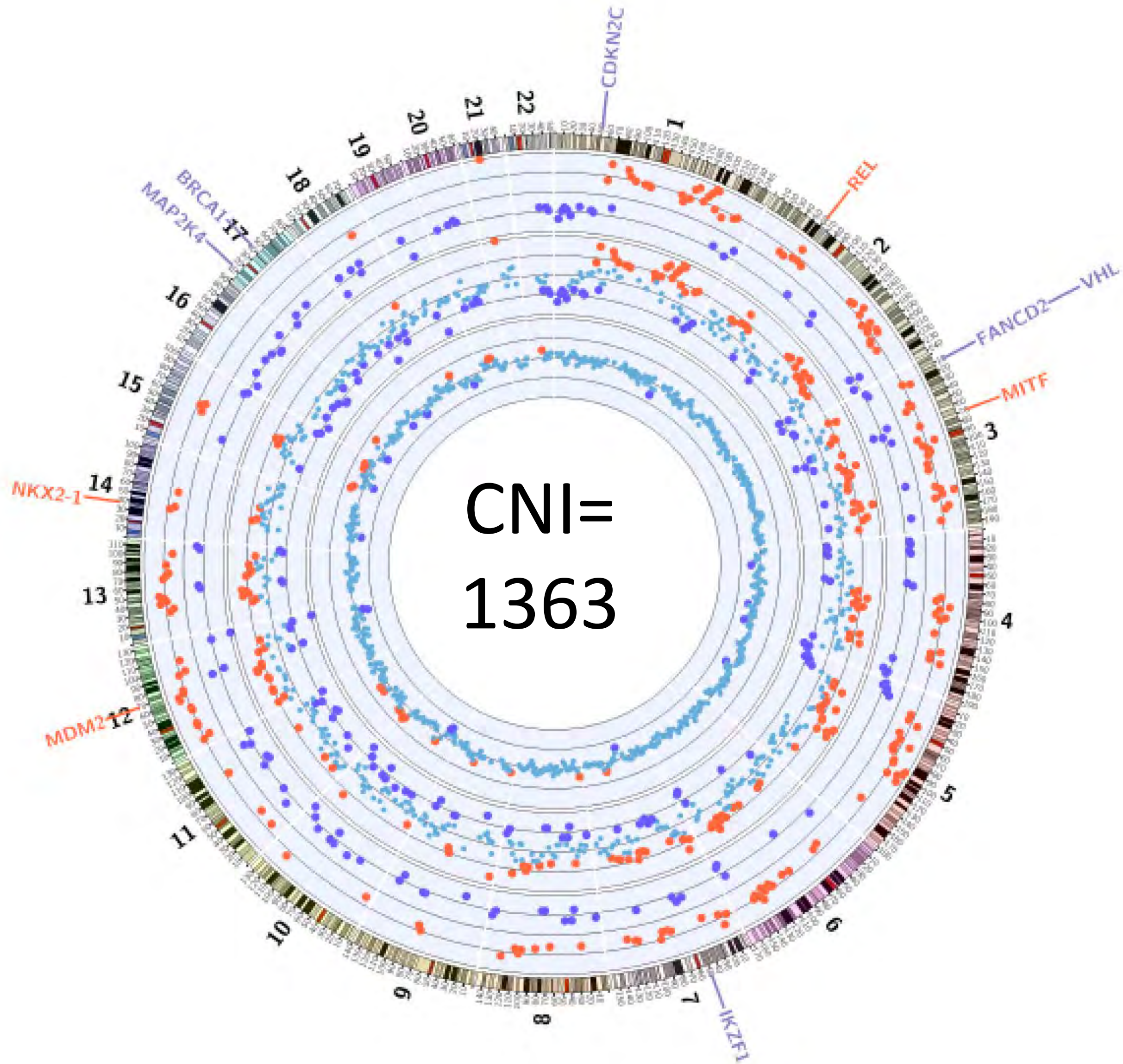
Micronutrients	Role in genomic stability	Consequence of deficiency
Vitamin C, vitamin E	Prevention of oxidation to DNA and lipid oxidation (157,158)	Increased baseline level of DNA strand breaks, chromosome breaks and oxidative DNA lesions and lipid peroxide adducts on DNA (157,158)
Folate and vitamins B2, B6 and B12	Maintenance methylation of DNA; synthesis of dTMP from dUMP and efficient recycling of folate (24)	Uracil misincorporation in DNA, increased chromosome breaks and DNA hypomethylation (24)
Niacin	Required as substrate for poly(ADP-ribose) polymerase (PARP) which is involved in cleavage and rejoining of DNA and telomere length maintenance (61,159)	Increased level of unrepaired nicks in DNA, increased chromosome breaks and rearrangements, and sensitivity to mutagens (61,159)
Zinc	Required as a cofactor for Cu/Zn superoxide dismutase, endonuclease IV, function of p53, Fapy glycosylase and in Zn finger proteins such as PARP (27,28)	Increased DNA oxidation, DNA breaks and elevated chromosome damage rate (27,28)
Iron	Required as component of ribonucleotide reductase and mitochondrial cytochromes (160)	Reduced DNA repair capacity and increased propensity for oxidative damage to mitochondrial DNA (160)
Magnesium	Required as cofactor for a variety of DNA polymerases, in nucleotide excision repair, base excision repair and mismatch repair. Essential for microtubule polymerization and chromosome segregation (50)	Reduced fidelity of DNA replication. Reduced DNA repair capacity. Chromosome segregation errors (50)
Manganese	Required as a component of mitochondrial Mn superoxide dismutase (152,161)	Increase susceptibility to superoxide damage to mitochondrial DNA and reduced resistance to radiation-induced damage to nuclear DNA (152,161)

Fenech, Genome Integr. 2010; 1: 11

Tumor Load Liquid Biopsy via CNI

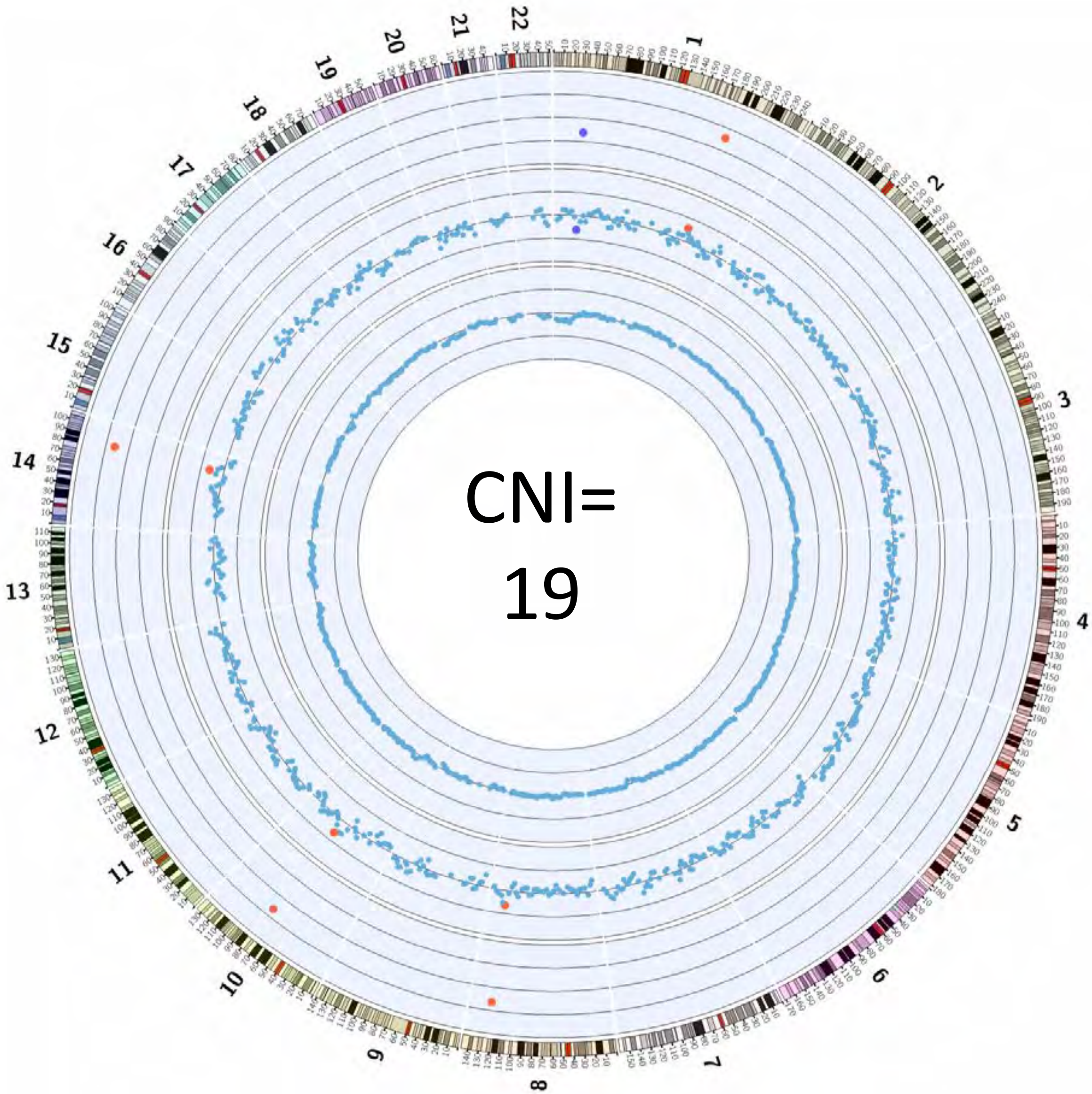
- Colon Cancer – Stage 2 before resection, Chemo, Nutrition Rx.
- BRCA1 loss

- Curcumin,
- 3-6 Beta Glucan,
- w-3 oils,
- WGE- whole glucan extract



Tumor Load Liquid Biopsy via CNI

- Colon Cancer – Stage 2 after resection, chemo, Nutrition Rx.
- CNI down from 1363 to 19.



Clinical Presentation:

- 55 yo male CEO –
- Fatigue, Exercise Intolerance, Brain Fog, Joint Pain, Irritability, Insomnia, Hyperlipidemia
- PastDx: Hashi, Arthritis, Asthma
- FHx: M-Lung Cancer; F – Dementia
- Organic whole-food, gluten & dairy-free diet, Meditates, 10 hrs in Bed (!!!), Exercises as best as possible, Low Caffeine, Stable relationships, Has hobbies and positive mindset.
- Elevated Liver Enzymes- but why?

23&Me derivitive "Detox" Report

GSTP1 I105V	rs1695	AA	-/-
GSTP1 A114V	rs1138272	CC	-/-
SOD2 A16V	rs4880	GG	+/+
NAT1 R187Q	rs4986782	GG	-/-
NAT1 R64W	rs1805158	CC	-/-
NAT2 I114T	rs1801280	CT	+/-
NAT2 R197Q	rs1799930	GG	-/-
NAT2 G286E	rs1799931	GG	-/-
NAT2 R64Q	rs1801279	GG	-/-
NAT2 K268R	rs1208	AG	+/-

Gene	Result
GSTT1	Present

And no GSTM data

Copy Number Variations

Gain/Loss	CytoBand	Location	Size (bp)	# Probes	Ratio	Genes
LOSS	1q44	chr1:248756215-248790932	34,717	6	0.58	OR2T10, OR2T11
LOSS	3q26.1	chr3:162514534-162619141	104,607	13	0.61	
LOSS	4q13.2	chr4:69360187-69512319	152,132	31	0.78	TMPRSS11E, UGT2B17, UGT2B15
LOSS	5p15.33	chr5:702100-820424	118,324	14	0.59	ZDHHC11
LOSS	5p15.2	chr5:12677352-12735332	57,980	6	0.53	
LOSS	6p21.32	chr6:32485374-32551409	66,035	15	0.65	HLA-DRB5, HLA-DRB6, HLA-DRB1
GAIN	8p23.1	chr8:6639145-6949625	310,480	35	1.43	XKR5, DEFB1, DEFA6, DEFA4, DEFA10P, DEFA1, DEFA1B, DEFA3, DEFA5
LOSS	8p11.22	chr8:39233204-39371728	138,524	26	0.74	ADAM5P, ADAM3A
LOSS	9p23	chr9:12031727-12163289	131,562	14	0.53	
GAIN	11q13.2	chr11:67479305-67750341	271,036	20	1.23	LOC645332
LOSS	12p13.31	chr12:9637084-9713425	76,341	9	0.44	
LOSS	15q11.1 - q11.2	chr15:20549990-22589756	2,039,766	82	0.75	GOLGA6L6, GOLGA8C, BCL8, POTEB, NF1P1, LOC646214, CXADRP2, LOC727924, OR4M2, OR4N4, OR4N3P
GAIN	16p11.2 - p11.1	chr16:34468000-34756866	288,866	39	1.83	LOC283914, LOC146481
GAIN	21p11.2 - p11.1	chr21:10751620-10916406	164,786	17	1.32	TPTE
LOSS	22q11.23	chr22:24347959-24395353	47,394	17	0.36	LOC391322, GSTT1, GSTTP2

- **Copy Number Variation Analysis revealed LOSS of GSTT1**
- **Targeted SNP testing revealed NULL GSTM**

Markedly Elevated Aflatoxin IgG+IgA

TEST	RESULT			
Array 11 Chemical Immune Reactivity Screen	**IN RANGE (Normal)**	**EQUIVOCAL***	**OUT OF RANGE**	**REFERENCE** (ELISA Index)
Aflatoxins IgG+IgA			2.69	0.4-1.8
Aflatoxins IgM	1.14			0.1-1.9
Formaldehyde and Glutaraldehyde IgG+IgA	0.72			0.3-1.4
Formaldehyde and Glutaraldehyde IgM	0.91			0.1-1.8
Isocyanate IgG+IgA	0.70			0.1-1.1
Isocyanate IgM	0.85			0.1-1.2
Trimellitic and Phthalic Anhydrides IgG+IgA	0.63			0.1-1.3
Trimellitic and Phthalic Anhydrides IgM	0.92			0.1-2.0
Benzene Ring Compounds IgG+IgA	0.65			0.2-1.3
Benzene Ring Compounds IgM	0.80			0.1-1.6
BPA Binding Protein IgG+IgA	0.87			0.2-1.8
BPA Binding Protein IgM	1.04			0.1-1.8
Bisphenol A IgG+IgA	0.66			0.1-1.8
Bisphenol A IgM	0.88			0.1-2.0
Tetrabromobisphenol A IgG+IgA	0.74			[illegible]
Tetrabromobisphenol A IgM	0.65			[illegible]
Tetrachloroethylene IgG+IgA	0.79			[illegible]
Tetrachloroethylene IgM	1.90			[illegible]

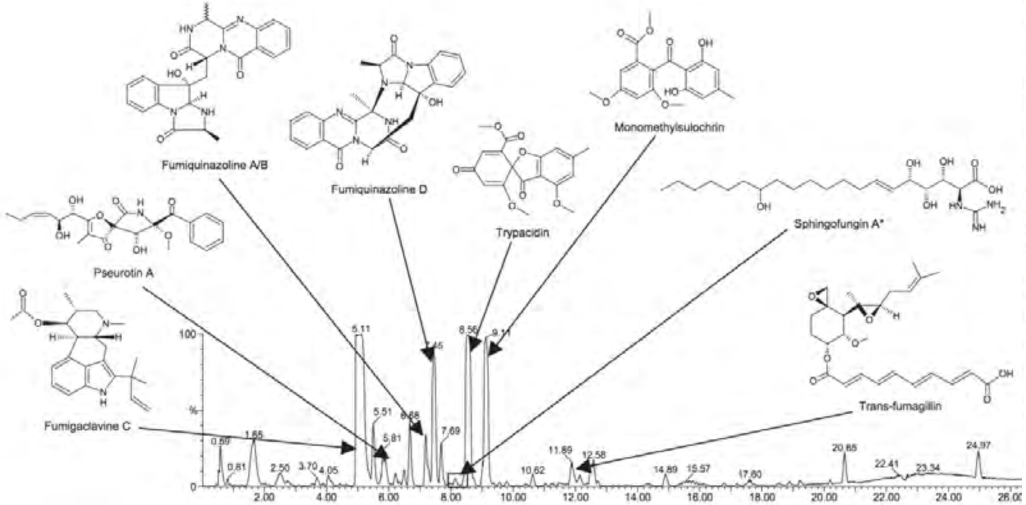
Immunotoxomics

Aspergillus

By S. K. Mohan - http://www.forestryimages.org/browse/detail.cfm?imgnum=5367342, CC BY 3.0, https://commons.wikimedia.org/w/index.php?curid=28824930

Metabolomics of Aspergillus fumigatus

Spinulosin
Spinulosin hydrate
Spinulosin quinol-hydrat
Dihydrospinulosin quino
Phyllostine
Orsellinic acid
Orcinol
m-cresol
3,4-dihydroxytoluquinone
4-hydroxy-3-methoxytoluquinone
3-hydroxytoluquinone
3,6-dihydroxytoluquinone
3-hydroxy-4-methoxy-
Toluquinone 1,6-epoxide
4-carboxy-5,5′-dihydroxy-3,3′-dimethyldiphenyl
Fumiquinone A
Fumiquinone B
Trypacidin
Bisdechlorogeodin
Monomethylsulochrin
Sulochrin-2′-methylether
Asperfumin
Asperfumoid
Emodin
Physcion
2-chloroemodin
2-chloro-1,3,8-trihydroxy-
6-methylanthrone
2-chloro-1,3,8-trihydroxy-
6-hydroxymethylanthrone
YWA1
1,3,6,8-THN
Flaviolin
Scytalone
1,3,8-THN
2-HJ
Vermelone
1,8-DHN
Sphingofungin A-D
Sphingofungins E-F?
Fumifungin
Pseurotin A-E
8-O-demethylpseurotin A
Synerazol
RK-95113
Azaspirene?
FD-839
Pseurotin F2
Ergosterol
Ergosterolperoxide
Ergosterolpalmitat
24-methylenophenol
Ergosta-4,6,8(14),22-tetraen-3-one
Ergosta-4,22-diene-3β-ol 5α,8α-Epidioxy-ergosta-
6,22-diene-3β-ol
Helvolic acid
Helvolinic acid
7-desacetoxyhelvolic acid



Metabolic signatures are possible to elucidate via metabolomics - this guides diagnostic as well as treatment decisions.

5-Demethoxyfumagillol
Fumagiringillin
FR-111142
Sch528647
RK-95113
Ovalicin?
β-*trans*-bergamotene
Hexahydropolyprenyls A-E
Phthioic acid
Teichoic acid
bis(2-hydroxy-3-tert. butyl-5-
Methylphenyl)methane
(= GERI-BP002-A)
Fusigen
Ferrichrome
Gliotoxin
Gliotoxin E
Gliotoxin G
S-methylgliotoxin
bisdethiobis(methylthio)-
Gliotoxin
Agroclavine
Elymoclavin
Chanoclavine I
Festuclavin
Fumigaclavine A-C
Brevianamide F
Fumitremorgin A-C
Verruculogen
15-acetoxyverruculogen
Demethoxyfumitremorgin C
12,13-dihydroxyfumitremorgin C (= TR-3)
12,13-dihydrofumitremorgin C
TR-2
Cyclotryprostatin A-D
Dehydrotryprostatin
Tryprostatin A & B
Spirotryprostatin A & B
'Compound 6′
Alanyl-leucyl and alanyl-isoleucyl, prolyl-phenylalanyl, prolyl-glycyl, prolyl-prolyl, prolyl-valyl, 4-hydroxyprolyl-leucyl, 4-hydroxyprolyl-phenylalanyl, and prolyl-leucyl diketopirazines
Pyripyropene A-R
GERI-BP001-A
Fumiquinazoline A-G
Tryptoquivaline?
Nortryptoquivaline?
Tryptoquivaline E-N?

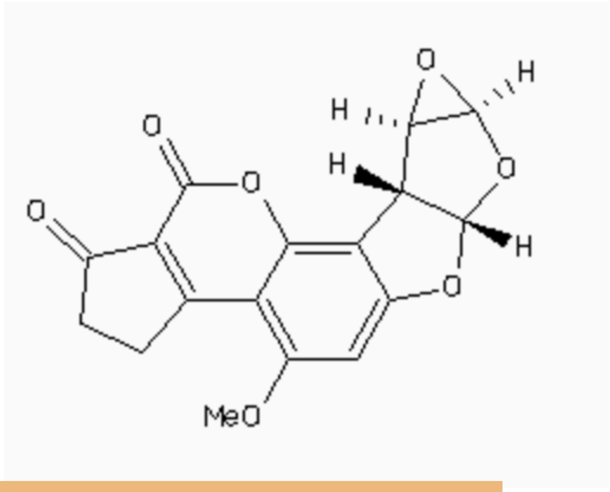
Restrictocin
Mitogillin
Asp F1

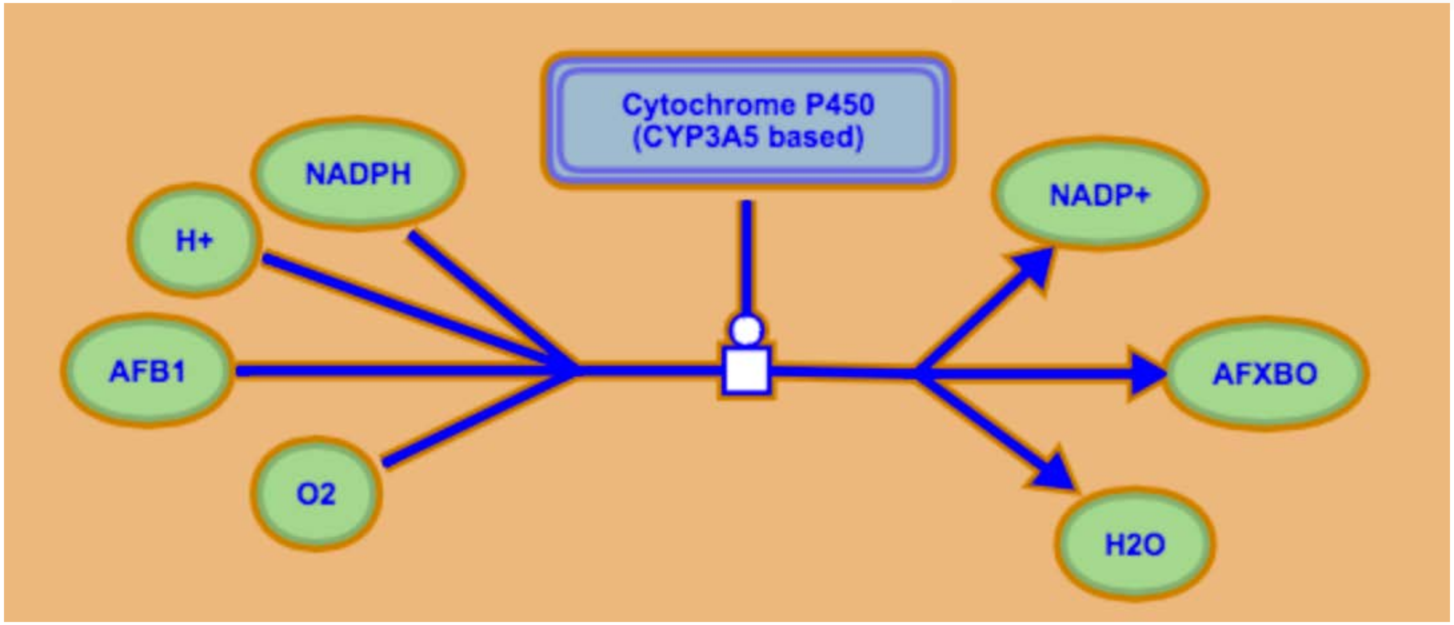
secondary metabolites

Frisvad, Medical Mycology 2009, 47 (Supplement 1), S53-S71

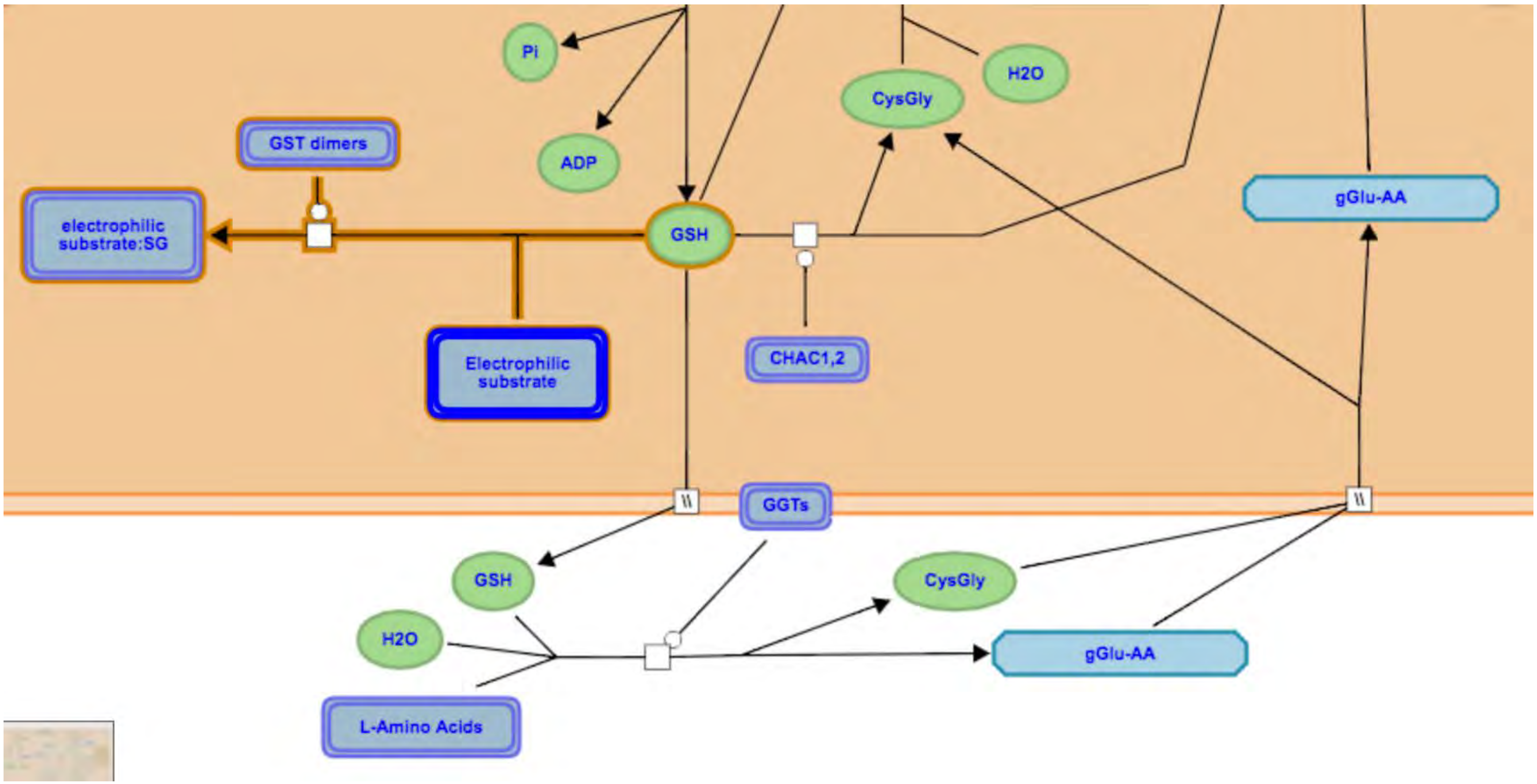
Aflatoxin B1 (**2,3-Epoxyaflatoxin B1**)

Conversion is by
CYP-1A2 and
CYP-3A4 and
CYP-2A13



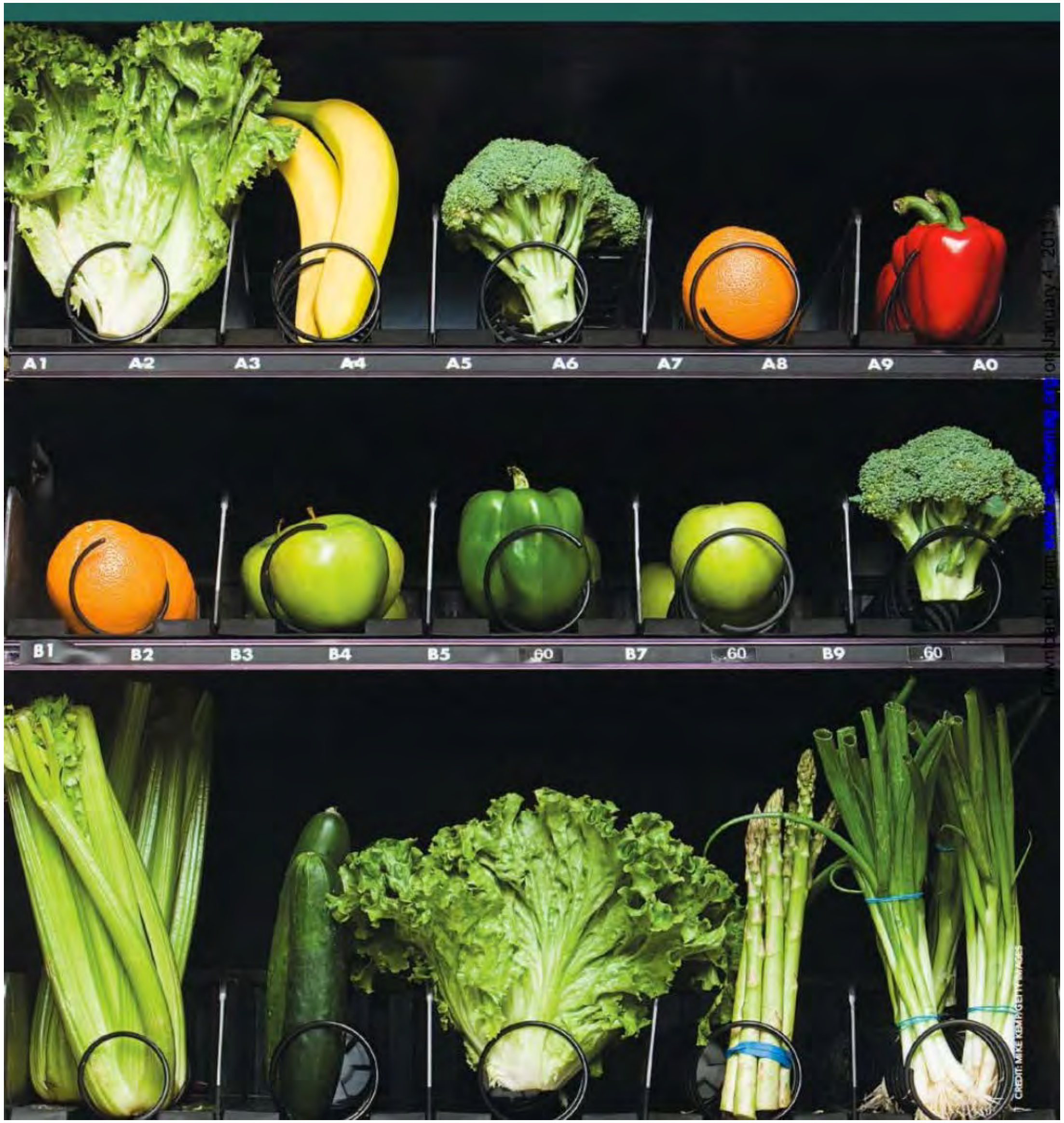


Glutathione Congugates to Electrophilic Substrates via GSTT1



http://www.reactome.org/PathwayBrowser/#/R-HSA-156580&SEL=R-ALL-176070&PATH=R-HSA-1430728,R-HSA-211859&DTAB=MT

More "Good Stuff"



- **Sulforaphane**
  Upregulates NRF-2 and PGC-alpha. This in turn…
- increases
  - Superoxide dismutase
  - Catalase
  - **glutathione S-transferase**
  - expression of heme oxygenase-1
- reduces
  - reactive oxygen species
  - lipid peroxidation
  - COX-2 expression

Fernandez, Mol Cell Biochem, DOI 10.1007/s11010-014-2292-z

Human and Experimental Toxicology
1–7

DOI: 10.1177/0960327115573596
het.sagepub.com
SAGE

Effects of airborne *Aspergillus* on serum aflatoxin B1 and liver enzymes in workers handling wheat flour

A Saad-Hussein[1], MM Taha[1], NN Fadl[2], A-H Awad[3], H Mahdy-Abdallah[1], G Moubarz[1,4], H Aziz[1] and KA El-Shamy[2]

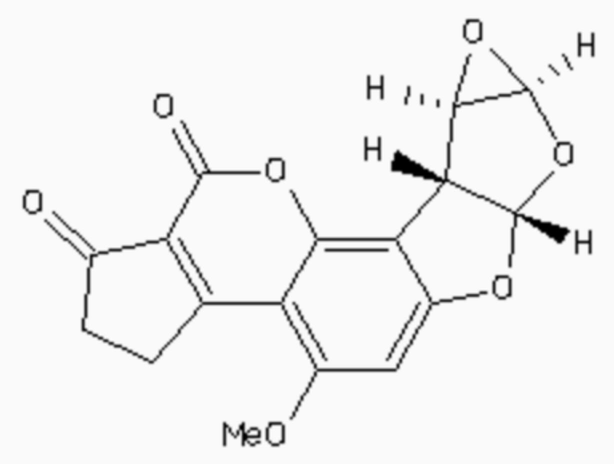
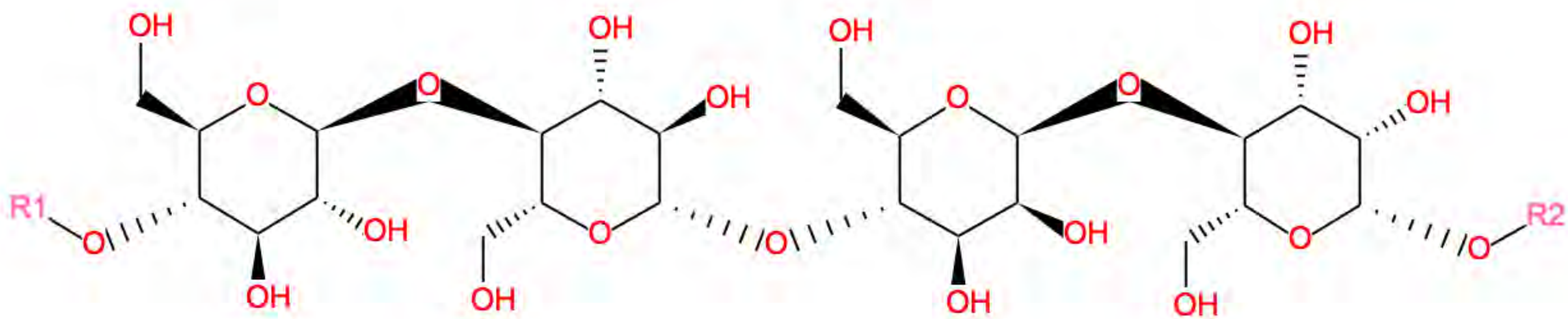


Table 2. Comparison of the AFB_1-Alb levels and the liver enzymes between the milling workers, the bakers, and their controls.

	Controls (100)		Milling workers (100)		Bakers (90)		ANOVA
	Mean	*SD*	Mean	*SD*	Mean	*SD*	*p* Value
AFB_1-Alb (ng/g)	0.04[a,b]	0.008	0.06[c]	0.003	0.10	0.01	$p < 0.0001$
Liver enzymes							
AST (U/L)	16.2[a,b]	10.9	26.5	8.70	26.0	8.33	$p < 0.05$
ALT (U/L)	18.2[a,b]	7.56	37.5	10.66	37.6	11.14	$p < 0.0001$
ALP (IU/L)	77.4[b]	24.50	76.7 [c]	25.71	90.0	32.11	$p = .05$

LSD: least significant difference; AFB_1: aflatoxin B_1; Alb: albumin; ANOVA: analysis of variance; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase.
[a]According to LSD, significant difference between the controls and the milling workers.
[b]According to LSD, significant difference the controls and the bakers.
[c]According to LSD, significant difference between the milling workers and the bakers.

Glucomannan



- In rats fed high fat diet - KGM beneficially reduced
  - malondialdehyde levels of the colon and liver
  - DNA damage in blood lymphocytes
- Upregulated gene expressions of
  - colonic mucosa glutathione peroxidase and catalase
  - hepatic superoxide dismutase and catalase

Wu & Chen, dx.doi.org/10.1021/jf202060p |J. Agric. Food Chem. 2011, 59, 9194–9200

Effect of Glucomannan on Mycotoxins

- Effect of glucomannan on haematological, coagulation and biochemical parameters in male rabbits fed aflatoxin-contaminated ration. –
  - » A. Eisa and A Metwally - World Mycotoxin Journal 2011
  - Human studies of this would be unethical
  - 3 groups
    - Normal Chow
    - Chow spiked with naturally occuring levels of aflatoxin
    - Spiked chow with 1kg/ton glucomannan

DOI: http://dx.doi.org/10.3920/WMJ2010.1273

Effect of glucomannan on Mycotoxins

- Results..
  - Aflatoxin B1 (AFB1) spiked chow caused microcytic anemia, leukopenia, long PT and aPTT, elevated ALT, GGT, Total Bilirubin, BUN, Creatinine, total lipids and cholesterol. Decreased Protein, Albumin, glucose, calcium, phosphorous, and iron.
- Supplementation with glucomannan resulted in the return of the above parameters to normal control values.

DOI: http://dx.doi.org/10.3920/WMJ2010.1273

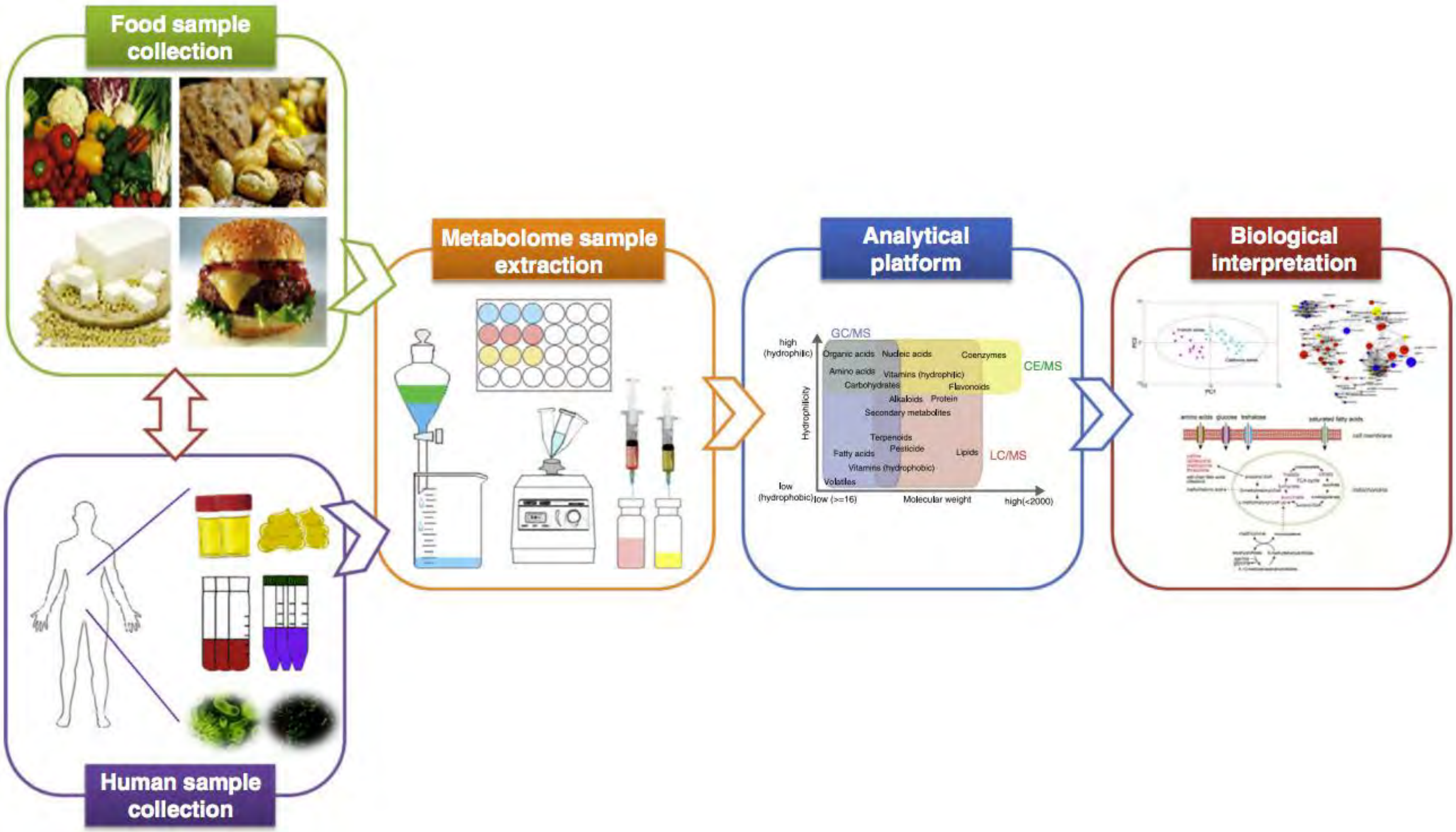
Glucomannan and Aflatoxin B1 and T-2 Toxin

- 0.1% Glucomannan in feed was able to adsorb
  - 75-90% of Aflatoxin (Aspergillus)
  - 30-35% of T2 Toxin (fusarium)

- The longer time Glucomannan was present in the gut, the more Mold Toxins were adsorbed.

Less "Bad Stuff"

Murthy, et. al."Evaluation of glucomannan for its adsorbing ability of Aflatoxin B1 and T-2 Toxin in the gastrointestinal tract of boiler chickens" Mycotoxin research, Volume: 18 Issue: Supplement 1, 2002 March.



Kim, Food Metabolomics - Current Opinion in Biotechnology 2016, 37:16–23

"Susan"

Since 2008, I have had chronic fatigue. Pain and brain fog, neuropathy and weakness. I have been to a large amount of specialist who do not communicate with each other and only prescribe more

[redacted] I struggled for all of these years with sugar. I have hypoglycemia. I lost my will to live in December as I felt my quality of life was so poor and there was little or no hope of improving. [redacted]

“Susan”- Outside MD Note

History of Present Illness:

History of Present Illness provided by patient.

Abdominal pain over the past 9 years. 5 hospitalizations in 2015. GI consultant felt that this is going to be a recurrent situation over the rest of her life. Attributed to damage from cancer treatment. After meditation, prayer and reflection she went to [redacted] and was advised to see psychologist to deal with PTSD and work on diet and yoga. She is eating very healthily. Daily wakes with feeling of being 'hung-over: - dizziness, light-headedness, fatigue, dread, nausea with occasional vomiting, dehydration feeling. Persistent constipation - she has now increased her [redacted] natural laxative) - 8 per day reliably results in daily BM. Dr. [redacted] suggested getting another opinion - EGD with gastritis and colonoscopy with internal hemorrhoids.

Using CPAP nightly with good benefit. Tired of quality of life.

Feels that Savella is helping with fibromyalgia pain. Brain function better with Savella compared to Cymbalta.

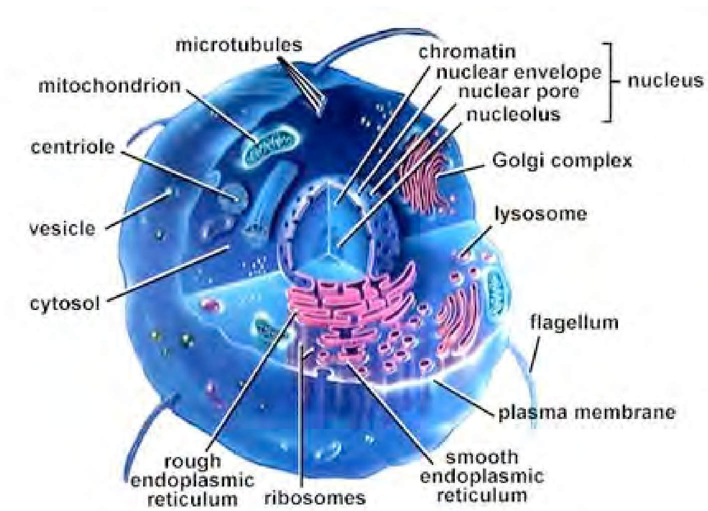
Botox shots for migraines from Dr [redacted] seem to help

Tramadol helps with pain without causing sedation or disorientation.

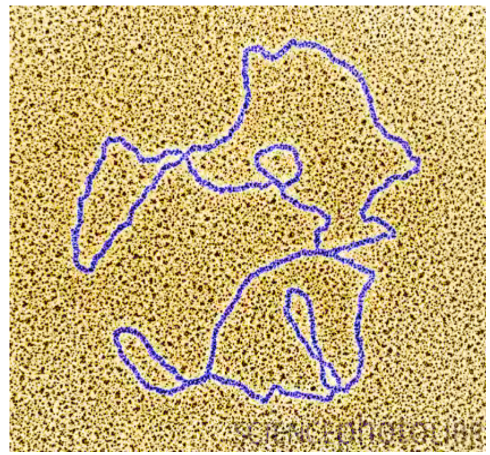
- Tx: Tylenol, Tramadol, Miralax

3590H1	CK	213	+ U/1	< 170	[.......... *>
3591H1	CKMB	37	+ U/1	< 25	[.......... *>

Mito Genetics – The Basics

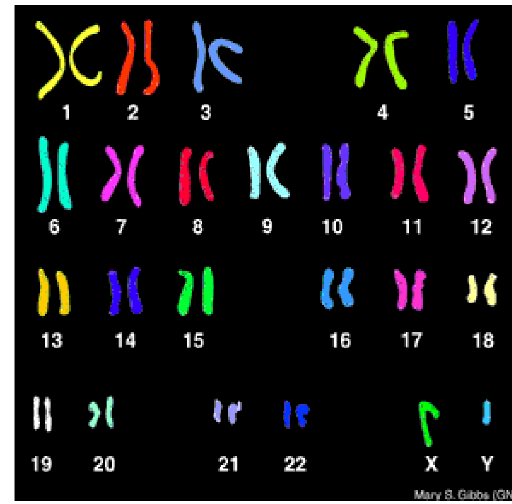


Mitochondrial DNA

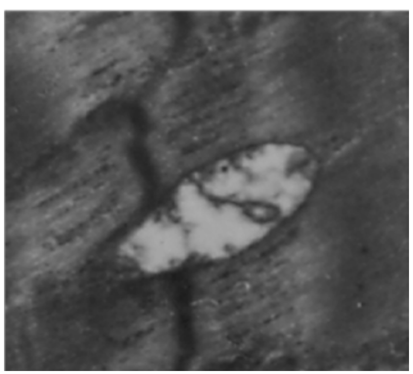


37 genes
16,000 base pairs
- Maternal inheritance
- 13 proteins for OxPhosphorylation
- 22 transfer RNAs
- 2 ribosomal RNAs

Nuclear DNA



1,013 genes
- Autosomal recessive
- Autosomal dominant
- X-linked



Mitochondrion 23 (2015) 64–70

Contents lists available at ScienceDirect

Mitochondrion

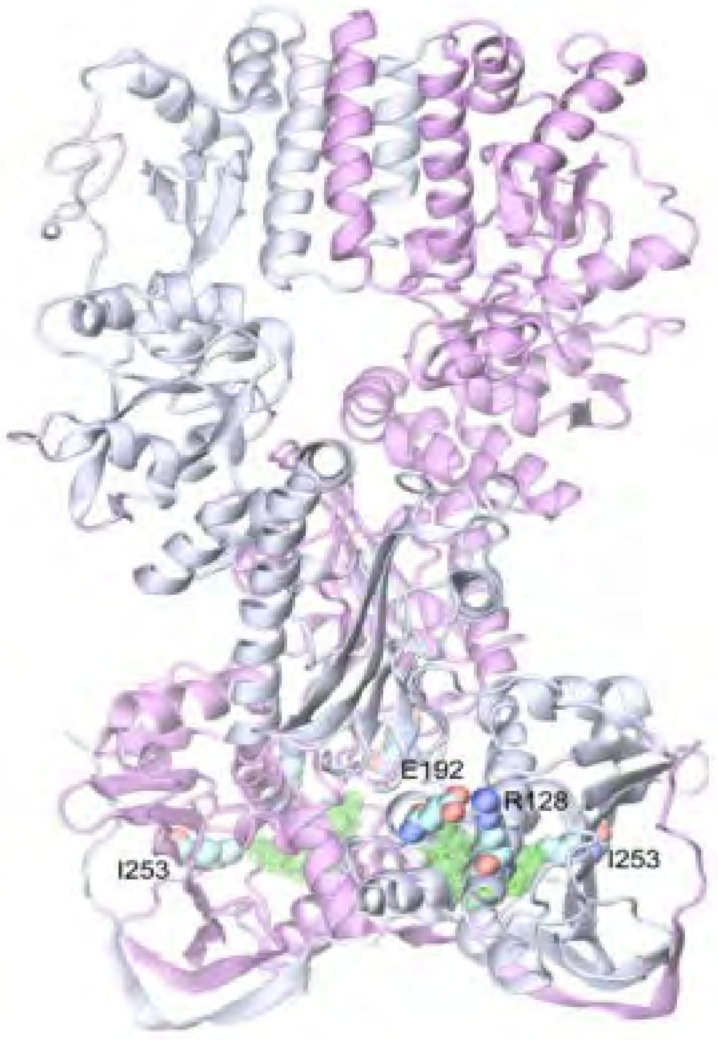
journal homepage: www.elsevier.com/locate/mito

Hurt, tired and queasy: Specific variants in the ATPase domain of the *TRAP1* mitochondrial chaperone are associated with common, chronic "functional" symptomatology including pain, fatigue and gastrointestinal dysmotility

Richard G. Boles [a,*], Holly A. Hornung [a], Alastair E. Moody [a], Thomas B. Ortiz [a], Stacey A. Wong [a], Julie M. Eggington [a], Christine M. Stanley [a], Mu Gao [b], Hongyi Zhou [b], Stephen McLaughlin [a], Amir S. Zare [a], Katherine M. Sheldon [a], Jeffrey Skolnick [b], Kevin J. McKernan [a]

TRAP1-Related Disease (*T1ReD*)

- *TRAP1* encodes a 701-amino acid homodimer protein which is a **mitochondrial chaperone** involved in antioxidant defense.
- An **ATPase domain** (amino acids 108-260) hydrolyze the energy-rich triphosphate bond of ATP to convert into mechanical work of folding proteins.



Boles RG1, Hornung HA1, Moody AE, et al. Hurt, tired and queasy: Specific variants in the ATPase domain of the TRAP1 mitochondrial chaperone are associated with common, chronic "functional" symptomatology including pain, fatigue and gastrointestinal dysmotility. Mitochondrion. 2015 Jul;23:64-70. doi: 10.1016/j.mito.2015.05.002.

TRAP1-Related Disease (*T1ReD*)

- Chronic pain, Fatigue and GI dysmotility.
- Tachycardia/palpitations and dizziness may also be common.
- In these patients, chronic pain and fatigue improved greatly on aggressive antioxidant therapy.

Boles RG1, Hornung HA1, Moody AE, et al. Hurt, tired and queasy: Specific variants in the ATPase domain of the TRAP1 mitochondrial chaperone are associated with common, chronic "functional" symptomatology including pain, fatigue and gastrointestinal dysmotility. Mitochondrion. 2015 Jul;23:64-70. doi: 10.1016/j.mito.2015.05.002.

TRAP1 variants greatly increase the prevalence of functional disease

TRAP1 variants	Pain syndromes	Chronic fatigue	Gastro-intestinal dysmotility	Triad of pain, fatigue & GI	Total number of patients
All conserved in ATPase domain	17 (65%) 4.9 (2.2-11) P = 0.001	16 (62%) 3.3 (1.5-7.3) P = 0.004	14 (54%) 3.1 (1.4-6.8) P = 0.005	12 (46%) 6.4 (2.9-14) P < 0.0001	26
Conserved elsewhere in protein	3 (7%) 0.19 (0.06-0.61) P = 0.005	10 (22%)	11 (24%)	2 (4%)	45
p.Ile253Val	11 (69%) 5.7 (2.0-17) P = 0.001	10 (63%) 3.4 (1.2-9.4) P = 0.02	9 (56%) 3.4 (1.2-9.2) P = 0.02	8 (50%) 7.5 (2.8-20) P = 0.0001	16
Conserved in ATPase excluding p.Ile253Val	7 (64%) 4.6 (1.3-1.6) P = 0.02	7 (64%) 3.6 (1.0-1.2) P = 0.04	6 (55%) *P = 0.06*	5 (45%) 6.2 (1.9-21) P = 0.003	11
Salt bridges: p.Arg128His, p.Glu192Lys	5 (71%) 6.5 (1.3-34) P = 0.03	5 (71%) *P = 0.053*	5 (71%) 6.6 (1.3-34) P = 0.02	5 (71%) 18 (3.6-100) P = 0.0005	7
None	224 (28%)	266 (33%)	222 (27%)	95 (12%)	808

“Susan” TRAP-1 Hetero

TRAP1 - TNF RECEPTOR-ASSOCIATED PROTEIN 1, NM_016292.2 (OMIM® ID: 606219)

Variant 1 (chr16.hg19.g.3740911G>A) c.164C>T	p.Ala55Val	**Heterozygous**	ACMG score 3	

Interpretation	One variant of uncertain significance was identified in this gene. This gene is associated with autosomal recessive and autosomal dominant disease. Clinical correlation is indicated.
Associated disease	*TRAP1-Related Disease (T1ReD)*
Disease inheritance	**Autosomal Dominant or Autosomal Recessive**
Associated literature	PMID 10652318
Gene product/protein function	HSP90 proteins are highly conserved molecular chaperones that have key roles in signal transduction, protein folding, protein degradation, and morphologic evolution. HSP90 proteins normally associate with other cochaperones and play important roles in folding newly synthesized proteins or stabilizing and refolding denatured proteins after stress. TRAP1 is a mitochondrial HSP90 protein.
Variant 1 Classification	**Variant of uncertain significance** *Prevalence:* Rare (0.00% in 1000G; 0.01% in ESP6500 (max subpopulation freq: 0.01%); 0.00% in ExAC (max subpopulation freq: 0.01%)); *Evolutionary Conservation:* Low; *Algorithms of protein function:* SIFT: equivocal, Mutationassessor: benign, Polyphen2: benign, MutationTaster: deleterious

DNA Oxidation Marker: 8-OH DG and Elevated CK in "Susan"

3590H1	CK	213	+ U/l	< 170	[........... *>
3591H1	CKMB	37	+ U/l	< 25	[........... *>

Oxidative Damage and Antioxidant Markers

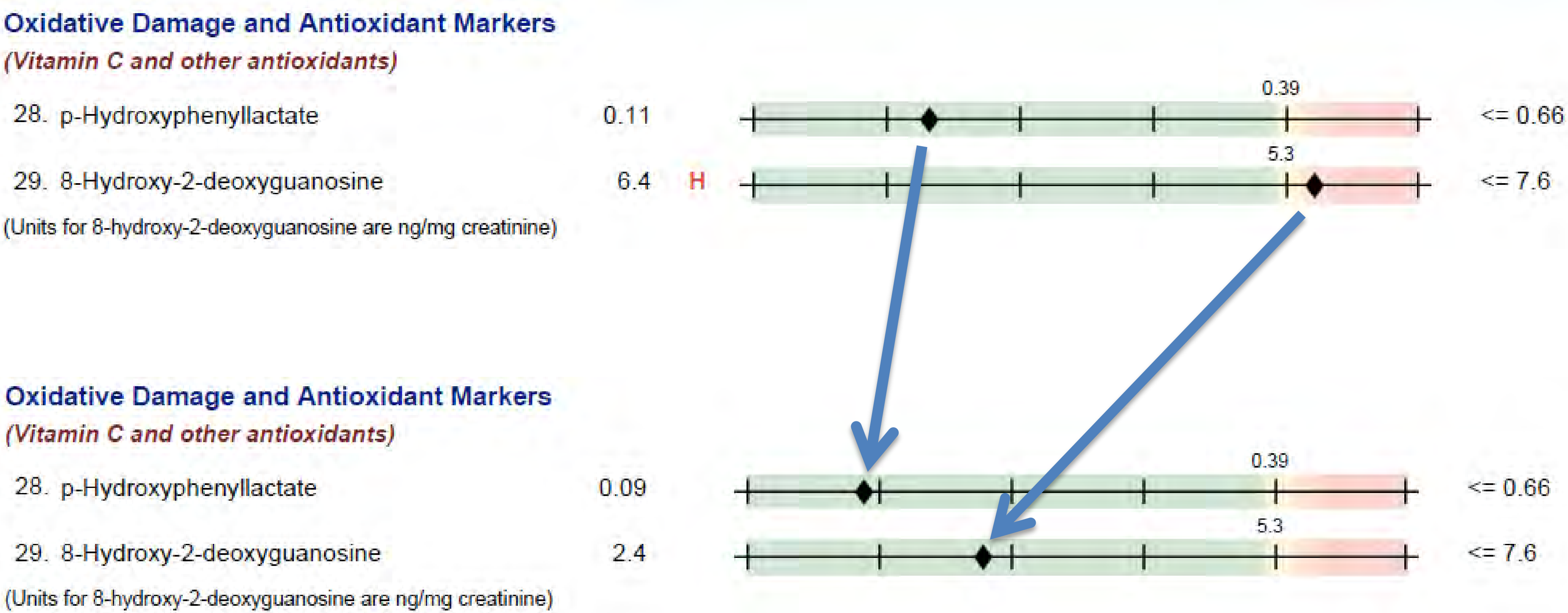
(Vitamin C and other antioxidants)

28. p-Hydroxyphenyllactate	0.11		0.39	<= 0.66
29. 8-Hydroxy-2-deoxyguanosine	6.4	H	5.3	<= 7.6

(Units for 8-hydroxy-2-deoxyguanosine are ng/mg creatinine)

- Context: Organic, "Ideal" diet.
- Tx:
  - Sulphoraphane Glucosinolate, Resveratrol, Curcumin, - All High dose
  - NAC 1200 BID, ALA- 600 mg BID, CoQ10 50mg BID

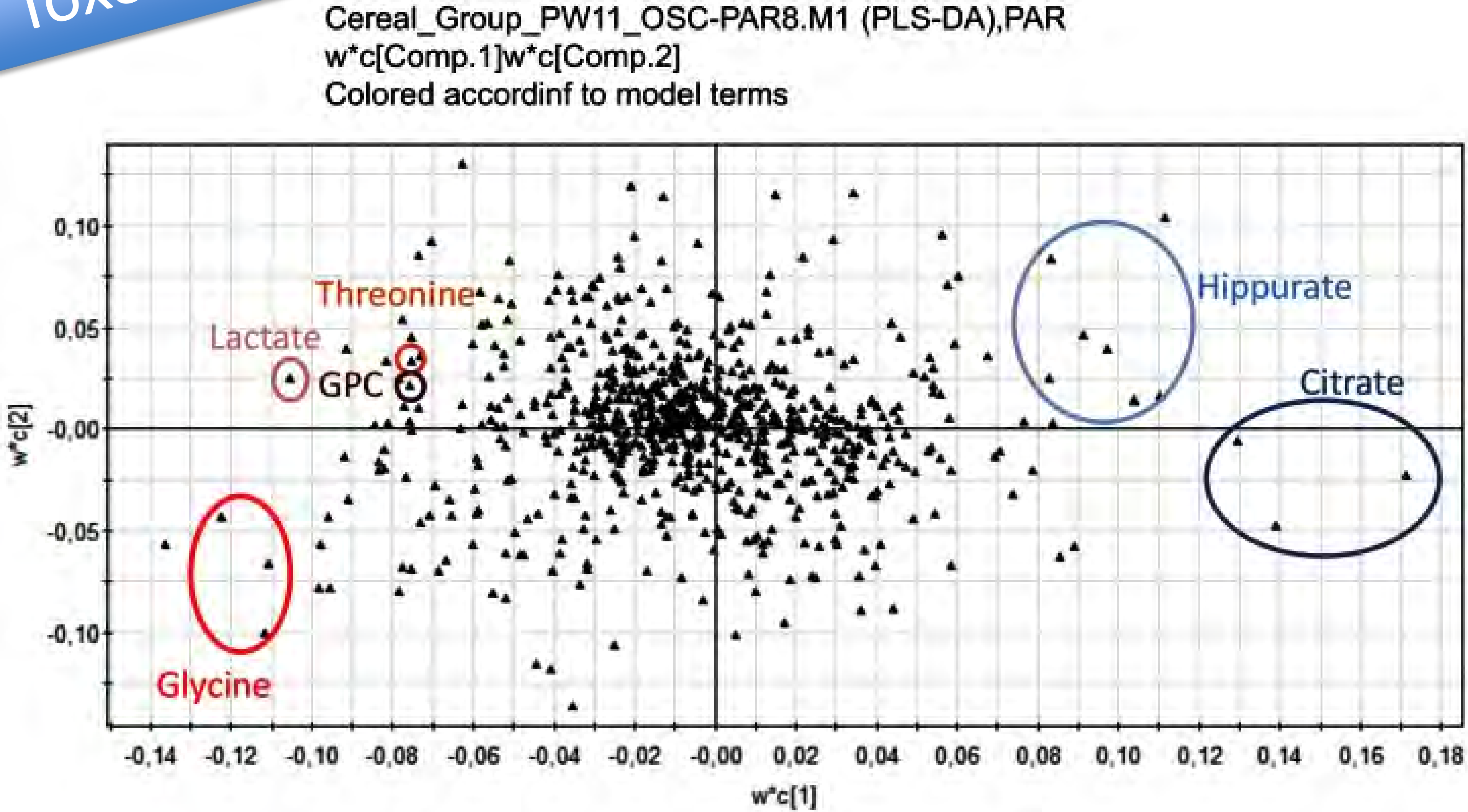
8-OHDG Follow-up
“Susan”



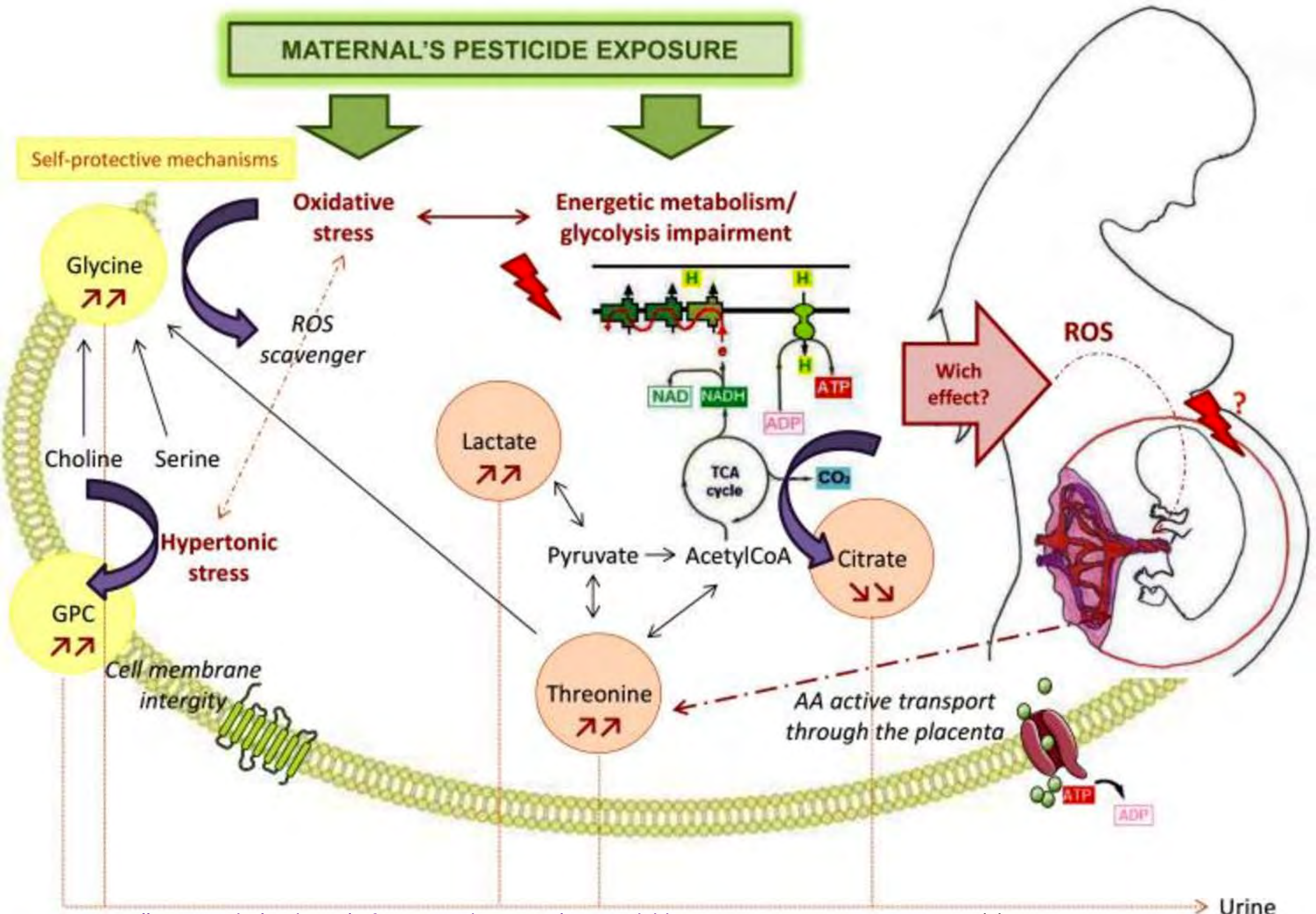
- Subsequent to this… 50 gm IV vitamin C twice a week has been very helpful.

Metabolomics Tools for Describing Complex Pesticide Exposure in Pregnant Women in Brittany (France)

Toxomics



Bonvallote,Metabolomics role for assessing complex Pesticide Exposure, PLoS One. 2013; 8(5): e64433.



Bonvallote,Metabolomics role for assessing complex Pesticide Exposure, PLoS One. 2013; 8(5): e64433.

Integrated ^{1}H NMR-based metabolomics analysis of earthworm responses to sub-lethal Pb exposure

Ting Chen [A], Yan Liu [A], Ming-Hui Li [A], Hua-Dong Xu [A], Ji-Yang Sheng [A], Li Zhang [A B] and Jun-Song Wang [A B]

[A] Centre for Molecular Metabolism, School of Environmental and Biological Engineering, Nanjing University of Science and Technology, Nanjing 210094, China.

[B] Corresponding authors. Email: wang.junsong@gmail.com; njust_zhangli@163.com

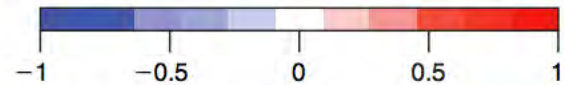
Environmental Chemistry - http://dx.doi.org/10.1071/EN15192

Submitted: 16 September 2015 Accepted: 5 February 2016 Published online: 23 March 2016

… "Pb exposure in earthworms caused widespread metabolic changes, which were associated with oxidative stress, neurotransmitter imbalance, disruption of osmotic equilibrium and interference in energy metabolism and nucleic acid metabolism."

Table 1. Metabolites identified from the aqueous earthworm tissue extracts, their fold change values (control *v.* low, control *v.* medium and control *v.* high) and associated *P* values

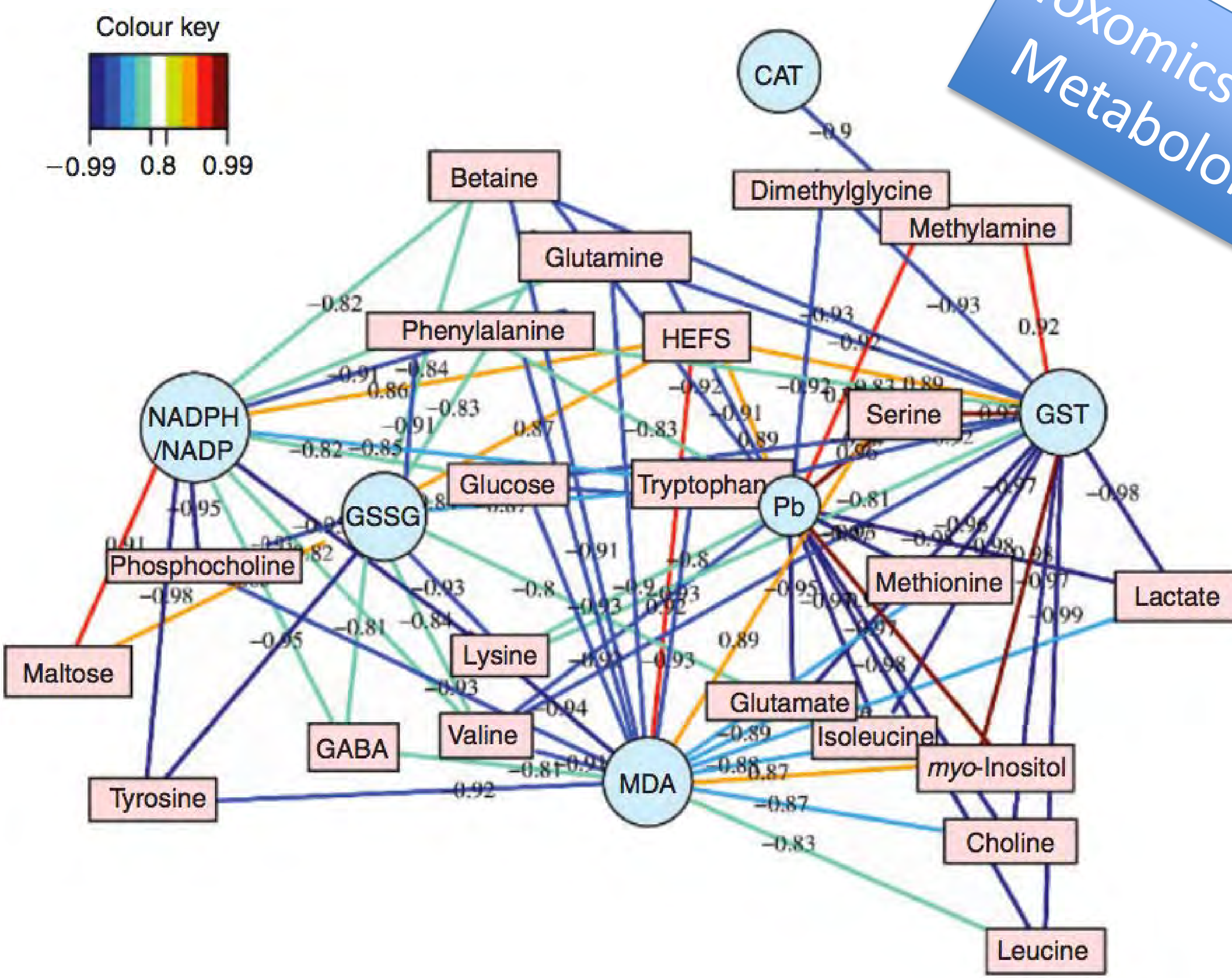
HEFS, 2-hexyl-5-ethyl-3-furansulfonate; GABA, 4-aminobutyrate. Multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Colour coded according to $\log_2$(fold change value), red for decrease and blue for increase in Pb-exposed groups.*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$



Metabolites	Assignments	Chemical shift (ppm)	Control *v.* low		Control *v.* medium		Control *v.* high	
			Fold	*P*	Fold	*P*	Fold	*P*
HEFS		0.85 (t), 2.60 (m), 2.83 (t)	0.92		0.80	*	0.57	**
Leucine	δ-CH_3, δ-CH_3	0.95 (d), 0.96 (d)	1.05		1.11	*	1.99	***
Isoleucine	δ-CH_3, γ-CH_3	0.94 (t), 1.00 (d)	1.09	*	1.16	*	1.76	***
Valine	γ-CH_3, γ-CH_3	0.98 (d), 1.04 (d)	1.06		1.21	**	1.64	***
Lactate	CH_3	1.43 (d)	1.04		1.06		1.25	**
Lysine	CH_2	1.71 (m)	1.06		1.16	*	1.24	**
GABA	CH_2	1.91 (m)	0.94		1.12	*	1.18	*
Glutamate	CH_2	2.05 (m)	1.07		1.09	*	1.26	**
Glutamine	CH_2	2.14 (m)	1.05		1.06		1.13	*
Methionine	CH_2	2.13 (m)	1.08	*	1.16	*	1.69	**
Choline	CH_3	3.20 (s)	1.09	*	1.24	*	2.91	***
Phosphocholine	CH_3	3.21 (s)	1.08	*	1.16	*	1.22	**
Betaine	CH_2, CH_3	3.25 (s), 3.89 (s)	1.07		1.27	**	1.90	***
Dimethylglycine	CH_2	3.71 (s)	1.05		0.99		1.13	*
Serine	CH_2	3.95 (m)	0.93		0.89	*	0.75	**
myo-Inositol	CH	3.54 (dd), 3.63 (t), 4.07 (t)	0.84	*	0.74	**	0.47	***
Glucose		3.45–3.50 (m), 4.65 (d)	1.10	*	1.29	*	1.73	***
Maltose	CH	5.41 (d)	0.91	*	0.88	*	0.89	*
Tyrosine	–CH=	6.90 (m), 7.20 (m)	1.05	*	1.18	**	1.21	**
Phenylalanine	CH=CH	7.33 (d), 7.38 (m), 7.43 (m)	1.12	*	1.20	**	1.33	**
Tryptophan	Ar–H	7.53 (d), 7.73 (d)	1.06		1.15	*	1.35	**
Inosine	O–CH–N, N–CH–N	6.90 (m), 7.20 (m)	1.09	*	1.07		1.18	*

Effects of Lead on Metabolomics

(earthworm)

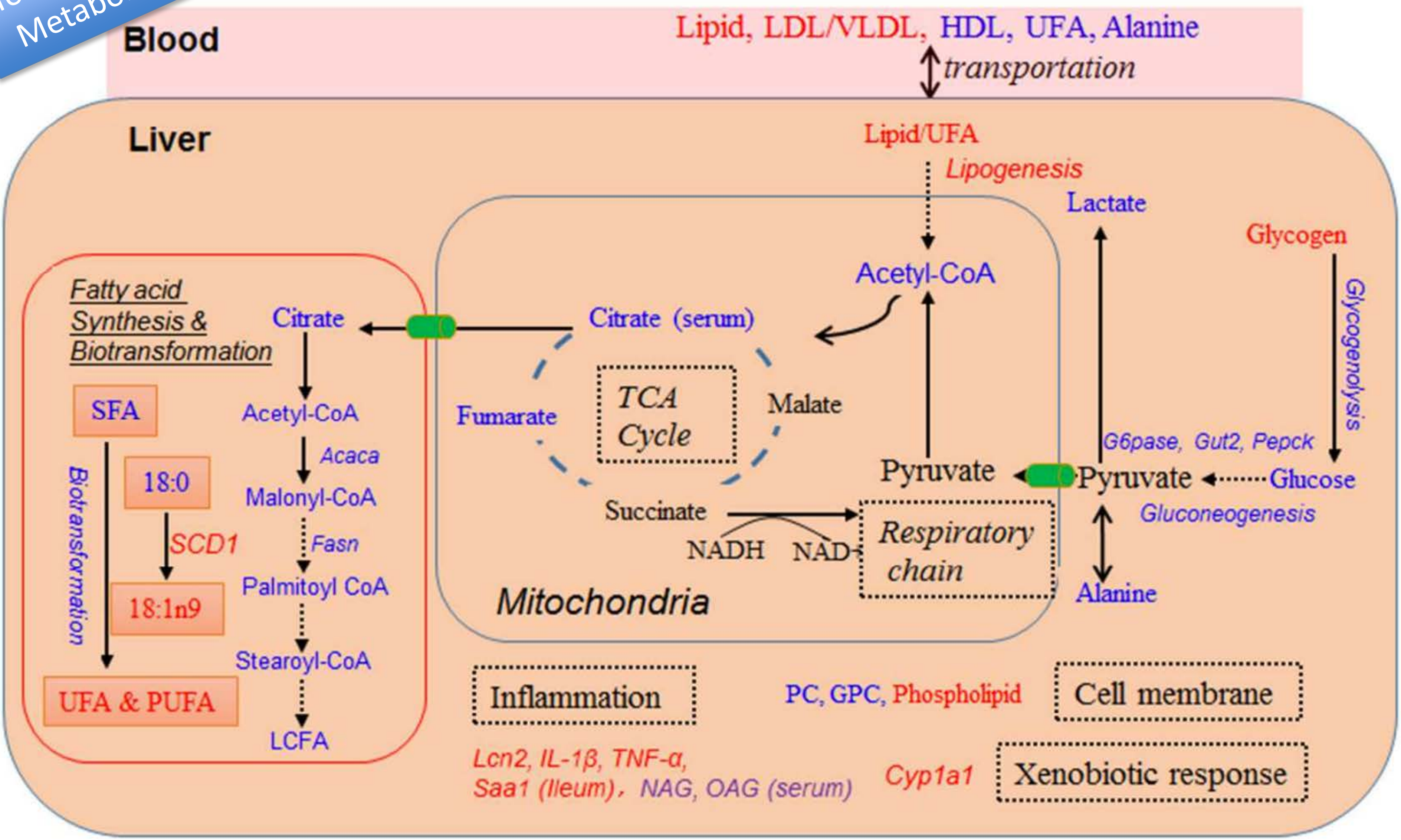


Toxomics meets Metabolomics

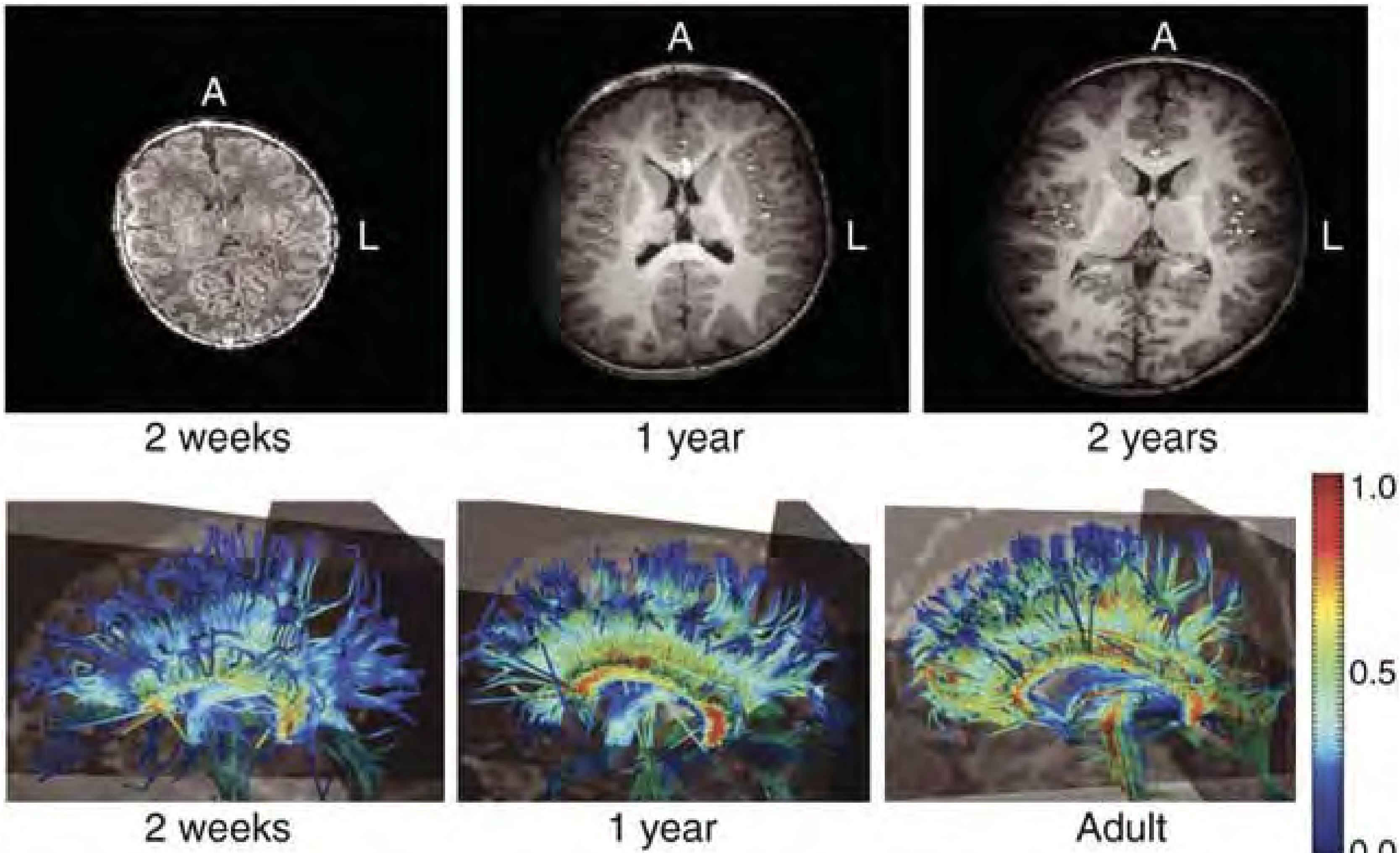
Metabolomics Reveals that Aryl Hydrocarbon Receptor Activation by Environmental Chemicals (dioxin-like) Induces Systemic Metabolic Dysfunction in Mice

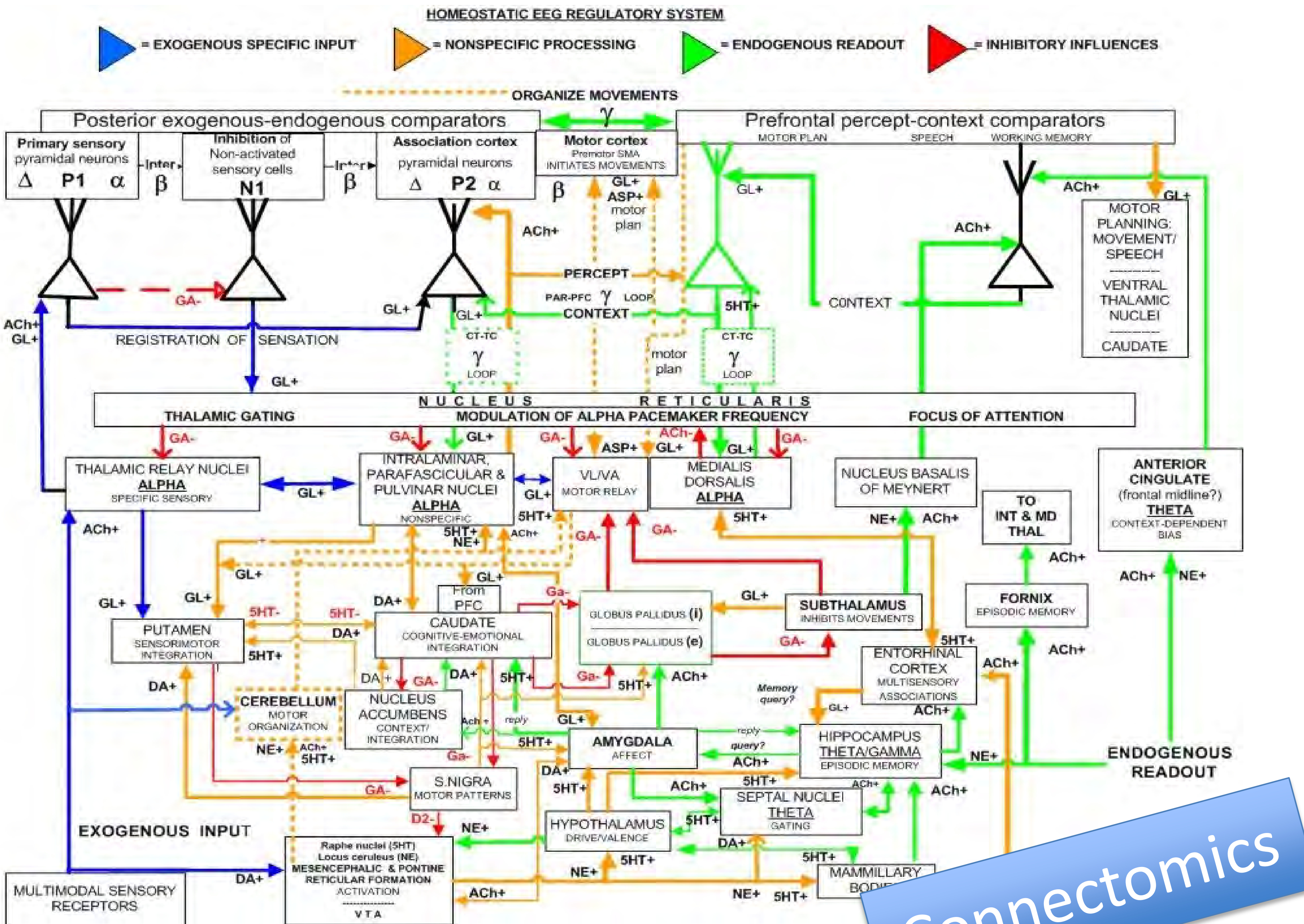
Zhang, Environ. Sci. Technol. 29 May 2015

Toxomics meets Metabolomics



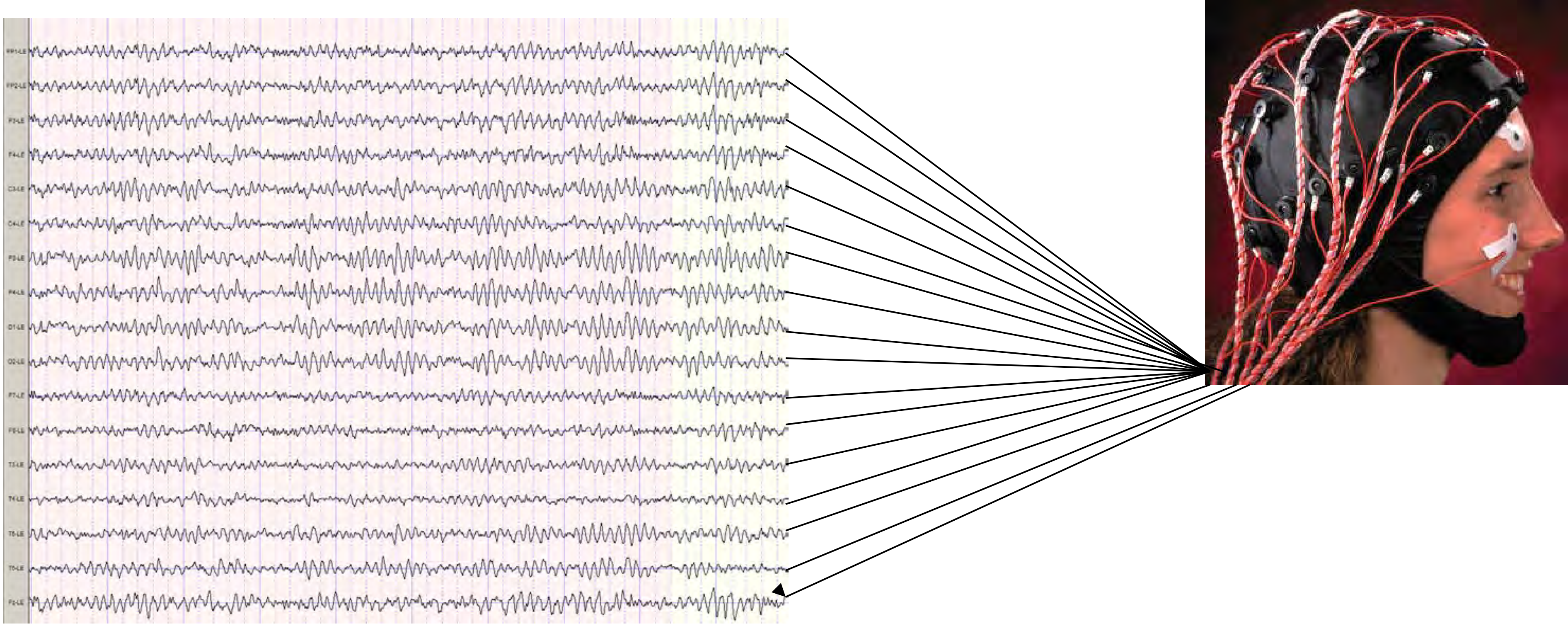
Connectomics

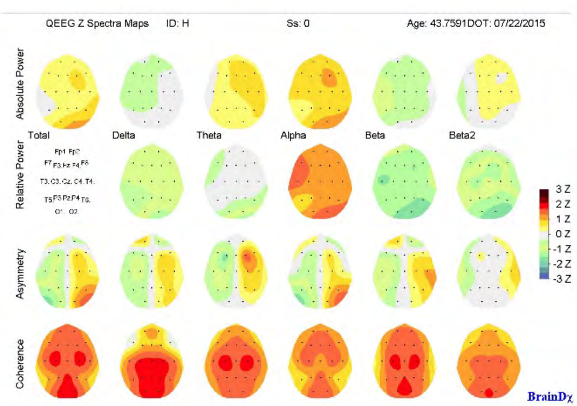


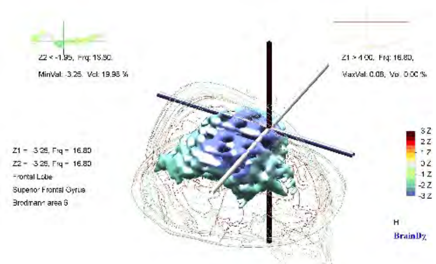


Connectomics

John, ER, Progress in Brain Research 150 (2005)

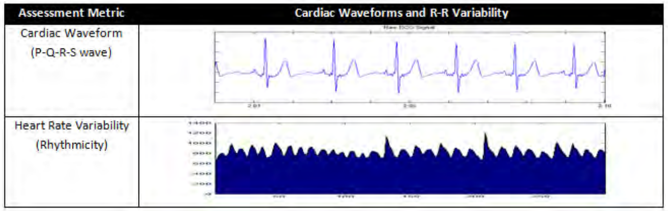






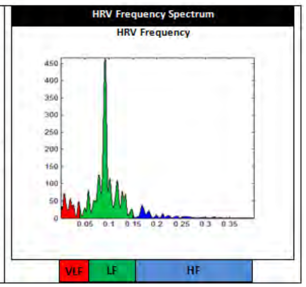
This patient's discriminant scores lie within (p <= 0.025) of the normal limits expected for an individual of this age.

Heart Rate Variability



Neuro-Cardiac Stability	Patient Score	Normal Range
Heart Rate (bpm)	73	55-80
QTc Interval	426.7	male < 440 ms female < 460 ms
QRS duration	0.092	0.06 - 0.12 sec

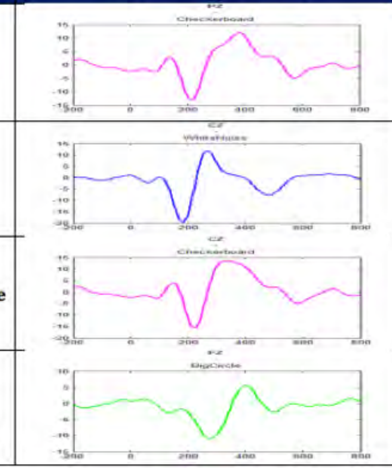
Autonomic Balance	Patient Score	Normal Range
Autonomic Balance (SDNN (ms))	70.25	75-150
Total Power	3394.9	>2000
Very Low Frequency (ms²)	443.7	low
Low Frequency (ms²)	2625.2	highest
High Frequency (ms²)	326.0	low



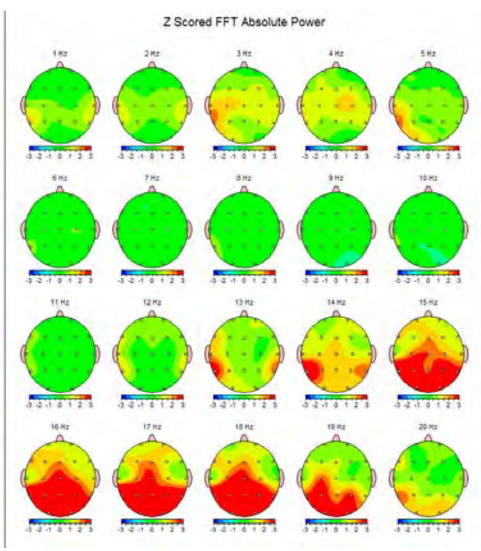
Event Related Potentials

BRAIN PROCESSING SPEED

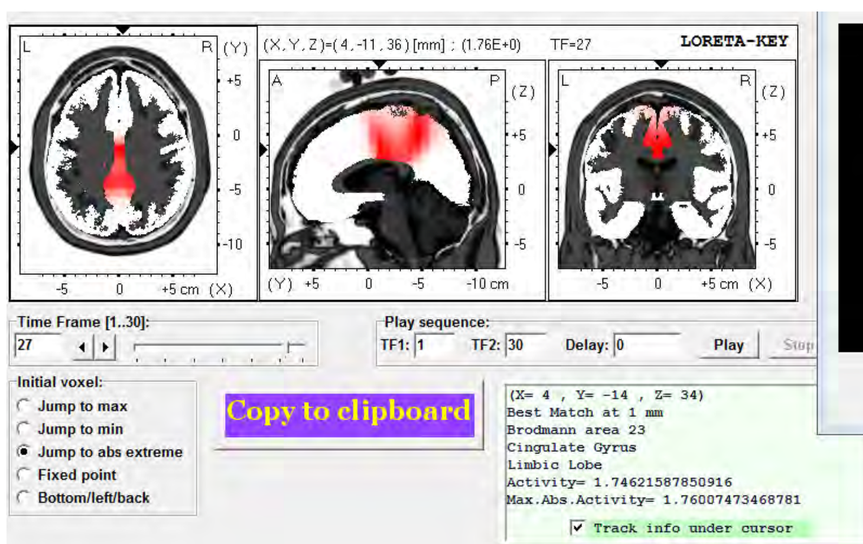
ERP Component	Amplitude and Latency	Patient Score	Suggested Range
Visual processing		212 ms -12.9 uV	< 250ms
Auditory processing		180 ms -19.5 uV	< 250ms
Attention/Vigilance		344 ms 13.5 uV	< 450ms
Information processing / Working memory		400 ms 5.6 uV	< 450ms

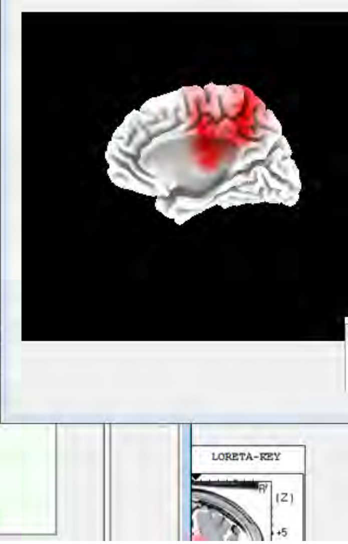


Brain Surface Maps

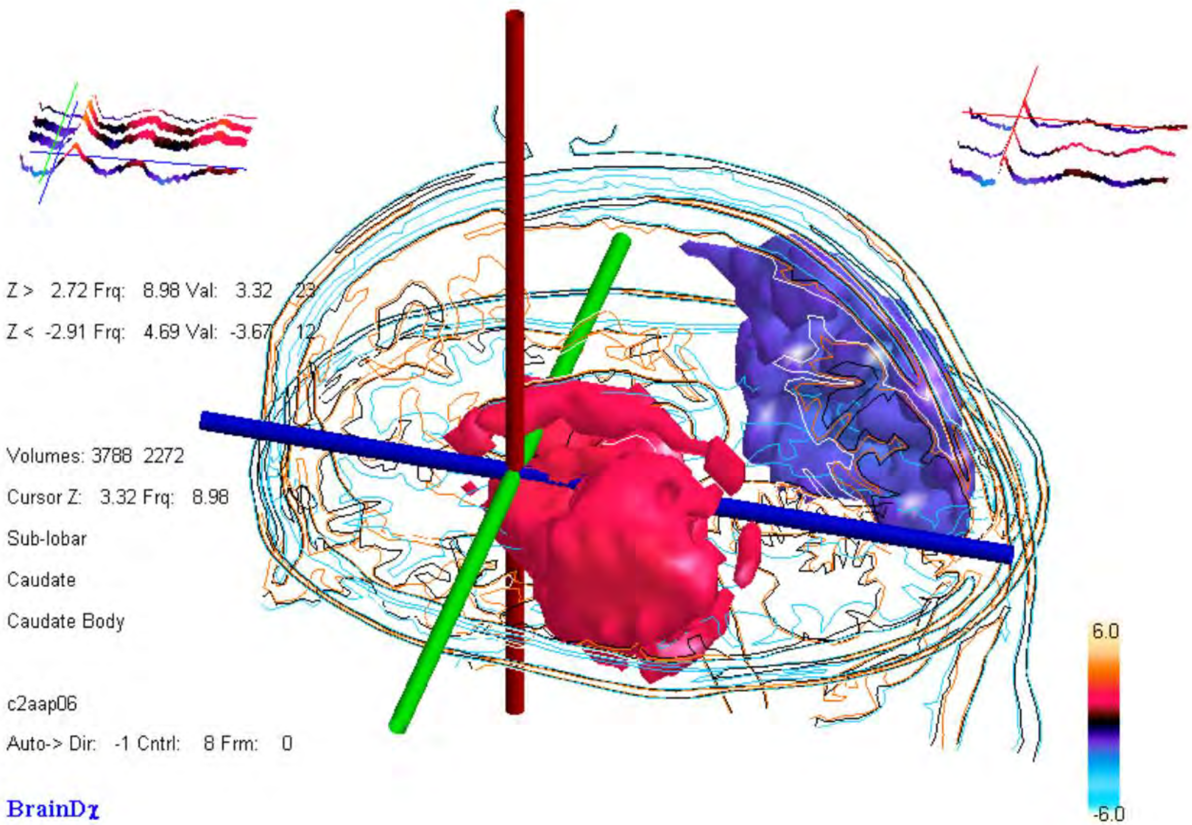


LORETA Brain Imaging





Volumetric 3-D LORETA



This tool can be expanded for use as a real time monitoring device for any intervention that may influence brain function

Three dimensional axial imagery allows high level of specificity in locating brain abnormalities

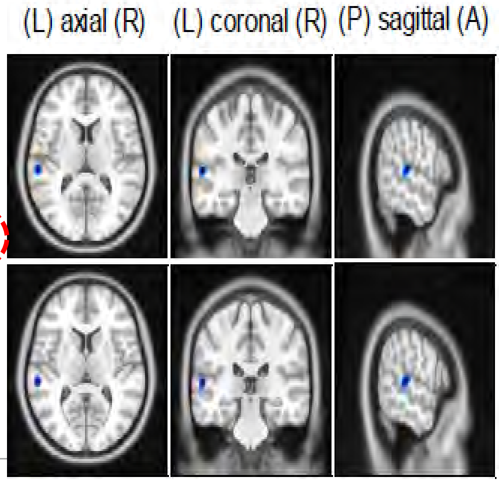
BRAIN FUNCTION: Standard Deviations – Normative database comparison

Severity Eyes Closed

	Pre-Frontal		Frontal					Central			Temporal		Parietal					Occipital	
	Fp1	Fp2	F7	F3	FZ	F4	F8	C3	CZ	C4	T7	T8	P7	P3	PZ	P4	P8	O1	O2
2Hz	-0.2	-0.1	-0.1	-0.3	-0.4	-0.3	-0.3	-0.5	-0.5	-0.5	-0.5	-0.7	-0.7	-0.6	-0.5	-0.7	-0.9	-0.9	-0.9
3Hz	-0.2	-0.1	-0.0	-0.3	-0.3	-0.3	-0.2	-0.3	-0.4	-0.4	-0.4	-0.6	-0.6	-0.5	-0.5	-0.6	-0.8	-0.8	-0.8
4Hz	-0.7	-0.5	-0.3	-0.9	-0.8	-0.7	-0.6	-0.7	-0.6	-0.7	-0.6	-0.8	-0.9	-0.7	-0.7	-0.8	-1.0	-1.0	-1.0
5Hz	-1.0	-1.0	-0.5	-1.1	-1.1	-1.1	-1.0	-0.8	-0.6	-0.8	-0.7	-1.0	-1.0	-0.9	-0.8	-0.9	-1.1	-1.1	-1.1
6Hz	-0.9	-0.9	-0.7	-1.1	-1.2	-1.1	-1.0	-1.1	-1.1	-1.0	-0.7	-1.0	-1.0	-1.1	-0.9	-1.0	-1.1	-1.3	-1.3
7Hz	-0.6	-0.7	-0.3	-0.9	-0.9	-0.9	-0.6	-0.7	-0.7	-0.7	-0.3	-0.7	-0.8	-0.8	-0.7	-0.7	-0.9	-1.0	-1.0
8Hz	0.1	0.2	0.2	0.0	0.1	0.1	0.4	-0.0	0.0	-0.2	0.6	-0.1	-0.5	-0.5	-0.5	-0.6	-0.8	-0.8	-0.8
9Hz	0.1	0.2	0.4	0.2	0.1	0.1	0.3	-0.0	-0.1	-0.2	1.0	0.1	-0.6	-0.8	-0.8	-0.8	-0.7	-1.0	-0.8
10Hz	0.0	0.1	0.2	0.1	0.1	0.1	0.0	-0.0	0.0	-0.1	0.7	-0.0	-0.2	-0.3	-0.3	-0.4	-0.4	-0.7	-0.6
11Hz	1.1	1.0	1.2	1.1	1.0	0.9	0.7	0.8	1.1	0.7	1.3	0.4	0.8	0.8	0.9	0.5	0.6	0.0	0.0
12Hz	0.7	0.7	0.8	0.8	0.7	0.6	0.5	0.7	0.8	0.5	1.0	0.1	0.6	0.2	-0.1	-0.0	0.0	-0.5	-0.6
13Hz	0.3	0.4	0.3	0.2	0.2	0.3	0.1	0.5	0.5	0.3	0.5	-0.3	0.3	0.3	-0.2	-0.3	-0.5	-0.6	-1.0
14Hz	0.3	0.3	0.4	0.3	0.3	0.2	-0.0	0.6	0.7	0.4	0.4	-0.4	-0.1	0.3	0.2	-0.0	-0.5	-0.6	-0.8
15Hz	0.0	0.0	0.2	0.0	-0.1	-0.2	-0.4	0.3	0.3	0.1	0.2	-0.7	-0.2	0.1	0.1	-0.1	-0.6	-0.7	-0.8
16Hz	-0.0	0.0	0.0	-0.1	-0.2	-0.2	-0.3	0.1	0.1	0.1	0.0	-0.7	-0.4	-0.0	-0.1	-0.3	-0.6	-0.7	-0.9
17Hz	-0.6	-0.5	-0.4	-0.6	-0.6	-0.7	-0.8	-0.0	-0.1	-0.1	-0.3	-0.9	-0.7	-0.2	-0.3	-0.4	-0.8	-1.0	-1.2
18Hz	-0.7	-0.6	-0.7	-0.9	-0.9	-1.0	-1.1	-0.2	-0.3	-0.5	-0.6	-1.1	-1.1	-0.5	-0.5	-0.6	-1.1	-1.3	-1.3
19Hz	-0.8	-0.7	-1.0	-1.2	-1.1	-1.1	-1.1	-0.5	-0.5	-0.7	-0.9	-1.2	-1.4	-0.9	-0.7	-0.9	-1.5	-1.6	-1.5
20Hz	-0.7	-0.6	-0.7	-1.1	-1.1	-1.1	-1.0	-0.6	-0.8	-1.0	-0.9	-1.3	-1.5	-0.9	-0.8	-1.0	-1.5	-1.6	-1.5
21Hz	-0.8	-0.7	-0.7	-0.8	-0.9	-0.9	-1.0	-0.5	-0.6	-0.9	-0.8	-1.2	-1.4	-0.8	-0.6	-0.8	-1.3	-1.5	-1.4
22Hz	-0.7	-0.6	-0.6	-0.8	-0.8	-0.8	-0.8	-0.6	-0.7	-0.7	-0.7	-1.0	-1.1	-0.5	-0.4	-0.5	-1.3	-1.4	-1.4
23Hz	-0.5	-0.4	-0.5	-0.6	-0.7	-0.8	-0.8	-0.6	-0.6	-1.0	-0.8	-1.1	-1.5	-0.7	-0.6	-1.1	-1.9	-1.8	-1.7
24Hz	-0.5	-0.4	-0.7	-0.8	-1.0	-1.0	-0.8	-0.8	-0.9	-1.2	-0.8	-1.0	-2.0	-1.1	-1.1	-1.4	-2.2	-2.1	-1.6
25Hz	-0.7	-0.7	-0.9	-0.7	-0.9	-1.0	-0.8	-0.9	-0.8	-1.2	-1.0	-0.9	-2.0	-1.2	-1.2	-1.6	-2.4	-1.9	-1.5
26Hz	-0.8	-0.7	-0.9	-0.9	-1.1	-1.1	-0.8	-1.2	-1.1	-1.3	-1.1	-0.9	-2.3	-1.5	-1.3	-1.8	-2.4	-2.0	-1.6
27Hz	-0.6	-0.6	-0.6	-0.8	-1.0	-1.0	-0.7	-1.3	-1.1	-1.3	-1.0	-0.8	-2.0	-1.4	-1.4	-2.0	-2.4	-2.0	-1.6
28Hz	-0.6	-0.6	-0.6	-0.8	-0.8	-0.9	-0.6	-1.3	-0.9	-1.3	-1.0	-0.8	-1.8	-1.5	-1.6	-2.0	-2.4	-2.2	-1.6
29Hz	-0.6	-0.6	-0.5	-0.7	-0.8	-0.9	-0.6	-1.2	-0.8	-1.2	-1.1	-0.8	-2.1	-1.5	-1.4	-1.8	-2.1	-2.2	-1.5
30Hz	-0.6	-0.5	-0.5	-0.6	-0.7	-0.7	-0.4	-1.2	-0.5	-1.0	-1.1	-0.8	-2.3	-1.7	-1.5	-1.8	-2.1	-2.0	-1.5

Brodmann Areas 22, 40, 42 are nearly 2 standard deviations low power from normal.

Areas govern: performing creative tasks, integer calculation; working/episodic memory, visuo-motor attention, auditory, gesture imitation, language, motor, pain, object and face perception, touch, balance



23-24 Hz

Other Substance Effect

Toxomics meets Connectomics

- Lithium - Generalized Slowing
- Lead –
  - Acute - looks like diffuse encephalopathy
  - Chronic – Inconclusive
- Mercury
  - Nonspecific diffuse slowing reflecting clinical state
- Manganese
  - EEG slowing and fast activity
- Organophosphates
  - Slow wave enhancement, paroxysmal discharges

Mold and the Brain

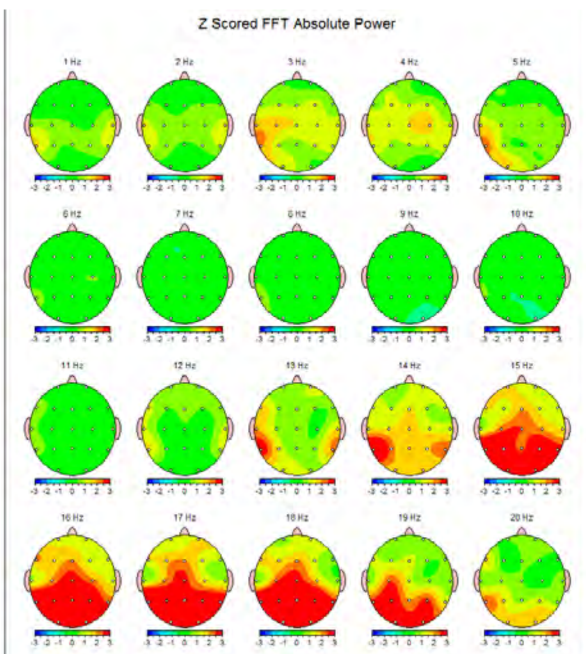
- Measures of toxic mold exposure predicted QEEG measures and neuropsych test performance
  - Impairments similar to mild Traumatic Brain Injury
  - Multiple Cognitive task impairment
- QEEG=
  - Narrowed frequency bands
  - Increased Alpha and Theta frontally
  - Hypoactivation of the cortex
    - Due to Brainstem or Reticular Activating System Dysfunction?

Toxomics meets Connectomics

Crago, Gray, et. al. Archives of Environmental Health: An International Journal Volume 58, Issue 8, 2003 pp 452-463

Severe MDD, Elevated Lead

02-2011
Severe, Chronic Depression.
Past Tx: Prozac, Zoloft, Celexa, Wellbutrin, Paxil, Effexor, Geodon, Cymbalta, Seroquel, Xanax, Klonopin, Adderall, Nuvigil, Provigil, ECT x3.

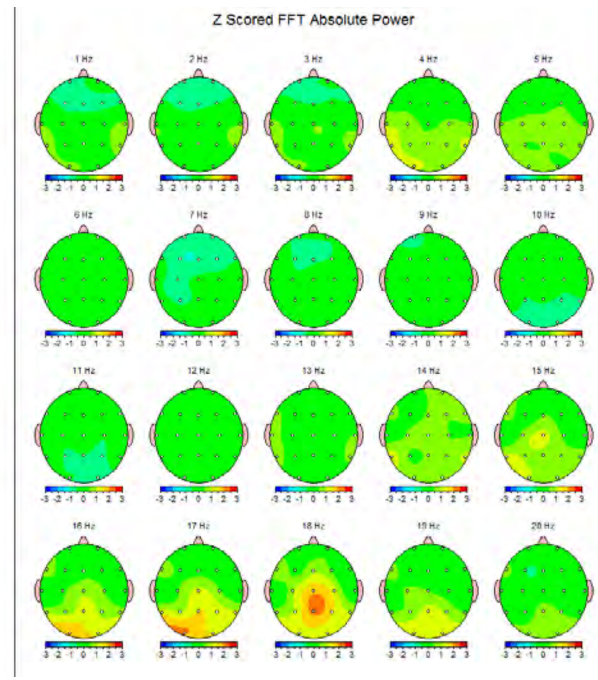


Of note, pt was infertile, and thought herself unfit to be a mother.

Found to have elevated lead on challenge testing.

Underwent QEEG guided Neurofeedback using Z-score 3D training settings. Gut Repair, DMSA Chelation
→

7-2011
Marked improvement on EEG and symptoms.

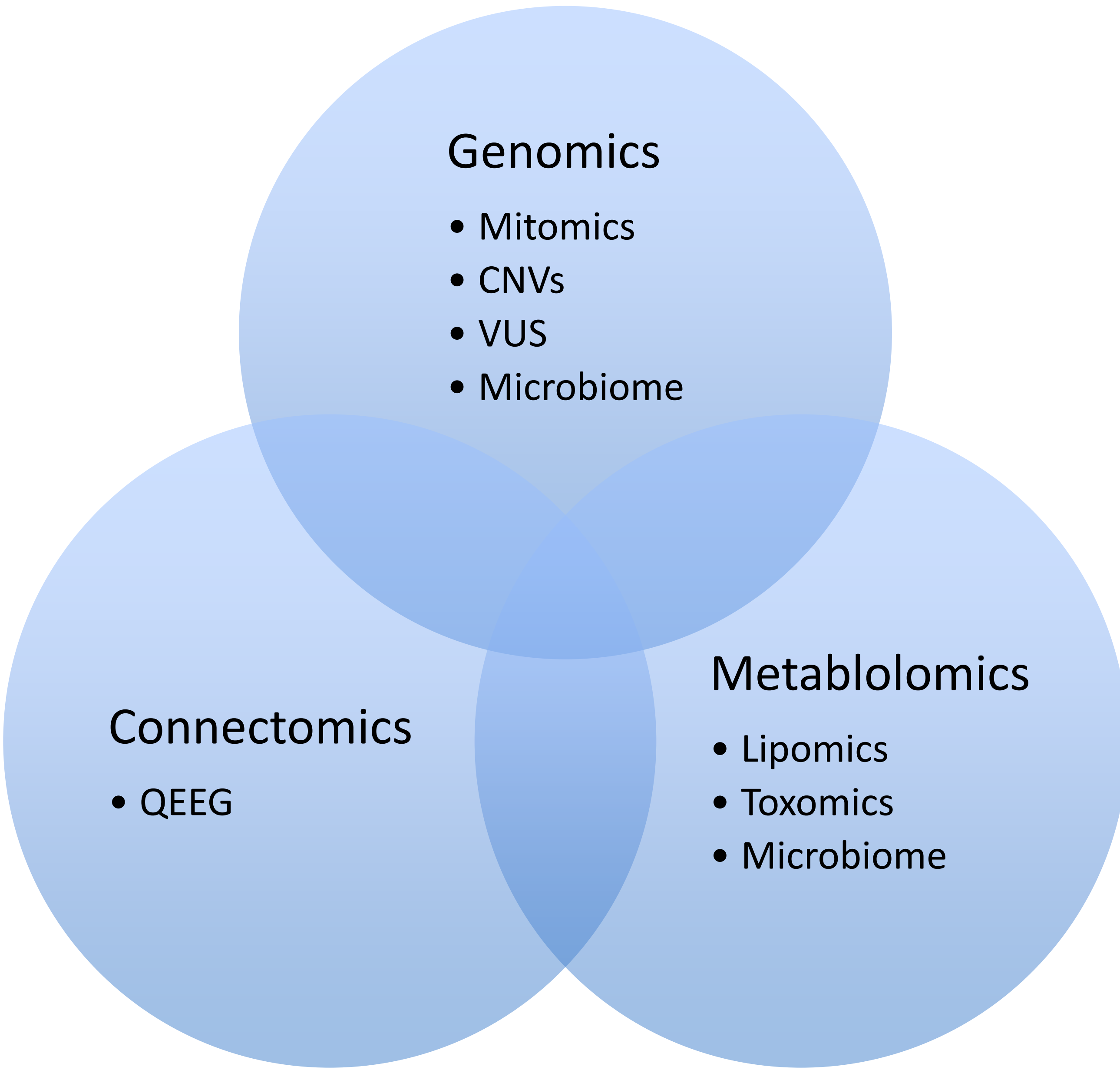


2-2012
“No Depression” Starting career.
Changing Family Dynamics

2015- My Patient and her SECOND child. ☺

Functional Medicine Changes Lives

Digging Deeper in Assessment



Deep Data meets Big Data

Leaves, Trees and Forrests..