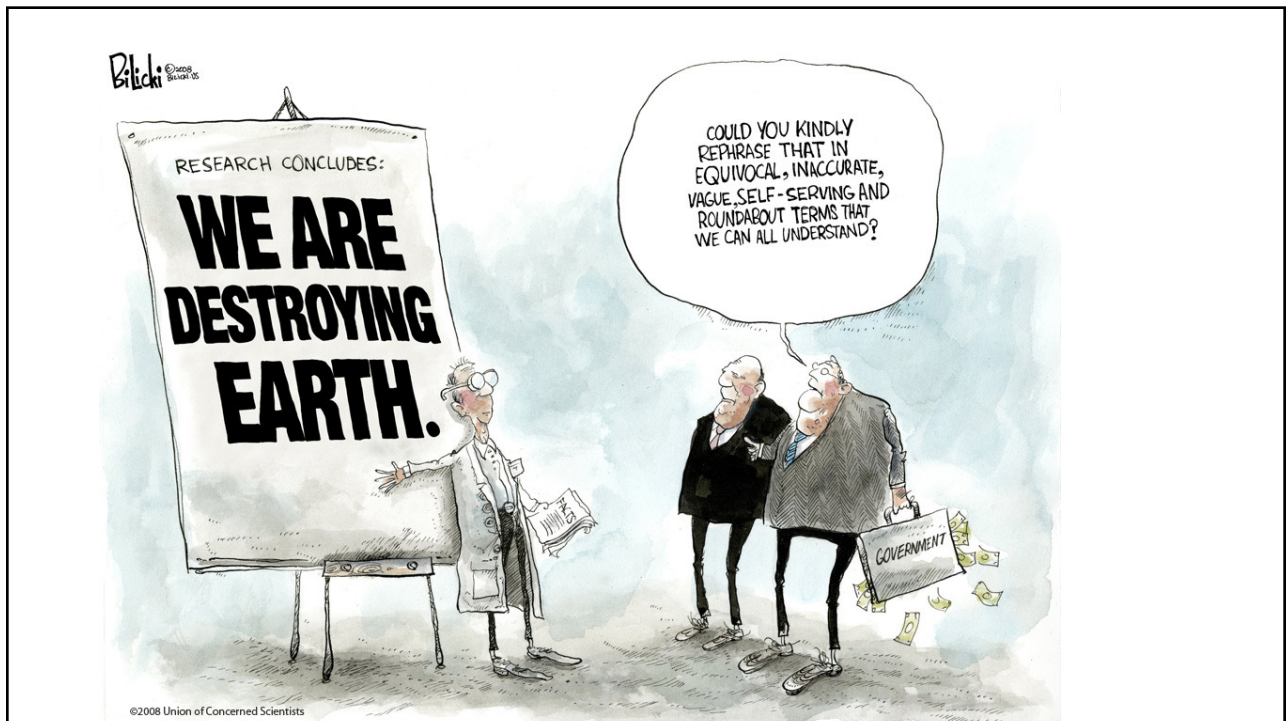


Deutenomics: A Revolution Unfolding in Biology and Medicine

Stephanie Seneff
MIT CSAIL
Real Truth About Health Conference
Tuesday, April 9, 2024

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Outline

- Introduction
- Gut Microbes Supply Deuterium-depleted Nutrients to the Host
- Glyphosate Suppresses Dehydrogenases
- Disrupted Glycolysis Leads to Fatty Liver Disease and Hyperlipidemia
- Methionine Deficiency and Methylation Pathways
- Glyphosate Damages Mitochondria
- Collagen, Proline and Deuterium
- Healthy Lifestyle
- Summary

3

Introduction

4

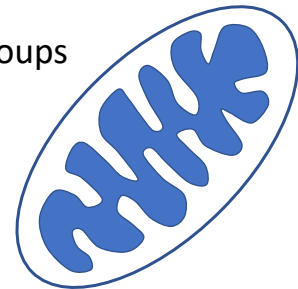
A Personal Time Line

- 2007-2012 – Autism
 - Autism is a complex developmental disorder associated with gut dysbiosis and defective methylation and sulfation pathways. Autism rates are alarmingly on the rise in the United States over the past two decades.
- 2012-2019 – Glyphosate
 - Glyphosate is a pervasive herbicide in our food supply. Autism rates in the US have risen exactly in step with glyphosate usage on core crops. Glyphosate disrupts the gut microbiome and methylation and sulfation pathways.
- 2020-2023 – Deuterium
 - Deuterium is a natural heavy isotope of hydrogen. Deuterium is highly damaging to the mitochondria, which produce ATP as an energy source for the cell. Organisms have developed sophisticated strategies to keep deuterium levels low in the mitochondria. These strategies depend critically on gut microbes and sulfation and methylation pathways.

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The Big Picture

- Deuterium is a natural heavy isotope of hydrogen
 - It is present in the blood at 5x the concentration of calcium
- Deuterium breaks the ATPase pumps in the mitochondria, causing energy loss and generating reactive oxygen species (ROS)
- Nicotinamide Adenine Dinucleotide (NAD) is a major carrier of deuterium-depleted (“depleted”) hydrogen (as NAD^H)
- Methylation pathways preserve low-deuterium methyl groups
- *Glyphosate suppresses many proteins involved in deuterium homeostasis*

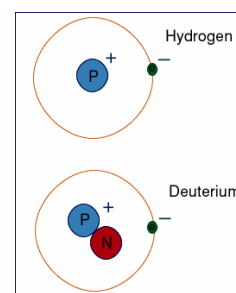


6

Deuterium = “Heavy” Hydrogen

- Hydrogen has one proton and one electron
- Deuterium has one proton, one electron and one neutron
 - ~ Twice as heavy as hydrogen
 - Present in ocean water at 155.8 ppm
 - Has distinct physical and chemical properties compared to hydrogen
 - Fats are low in deuterium compared to other foods

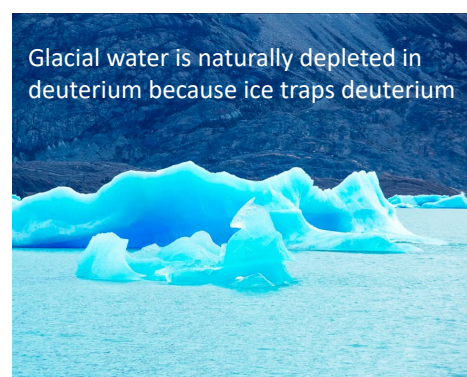
Deuterium management in the body involves trapping deuterium in collagen matrices and invoking specialized enzymes that choose hydrogen over deuterium for their reaction in order to fuel the mitochondria with hydrogen rather than deuterium



7

Ketogenic Diet and DDW: Health Benefits*

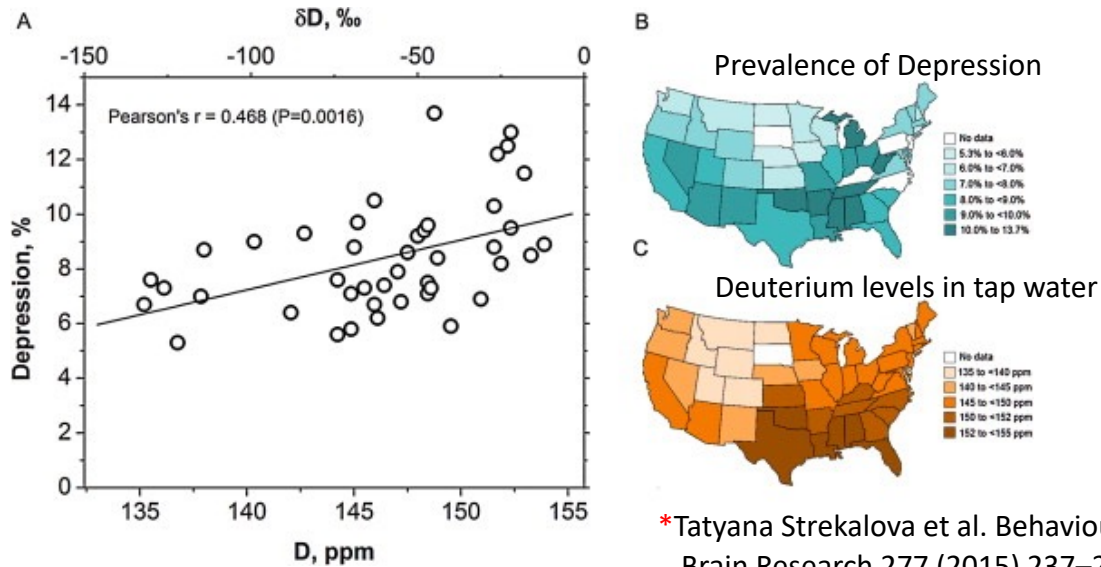
- **Deuterium depleted water** (DDW) is essential for mitochondria to function properly
- People whose water supply is naturally depleted in deuterium are healthier
- Deuterium depletion maintains strong hydrogen bond networks in DNA (keeps it stable)
- DDW inhibits tumor progression
- A ketogenic diet is a deuterium depleted diet



*Laszlo G Boros et al. Medical Hypotheses 2016; 87: 69-74.

8

Deuterium in Water and Depression*

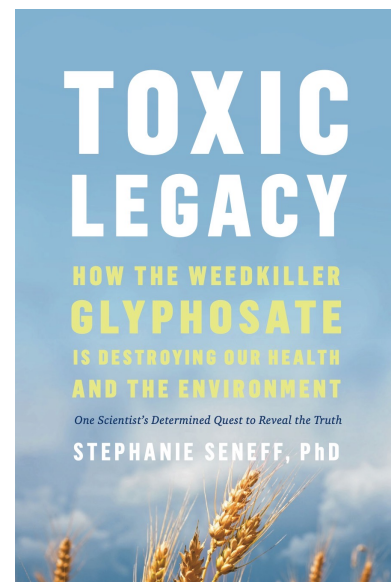


9

My Book on Glyphosate

- Released by Chelsea Green in July 2021
- Presents extensive data on glyphosate toxicity to animals and humans
- Shows how glyphosate interferes with sulfate homeostasis
- Argues that glyphosate is insidiously, cumulatively toxic through its diabolical insertion into proteins by mistake in place of the coding amino acid glycine
 - This unique feature explains why it is causal in so many diseases

This book was selected by Kirkus Reviews as one of the top 100 non-fiction books of 2021



10



Contents lists available at ScienceDirect

Neurotoxicology 2019; 75:1-8.

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

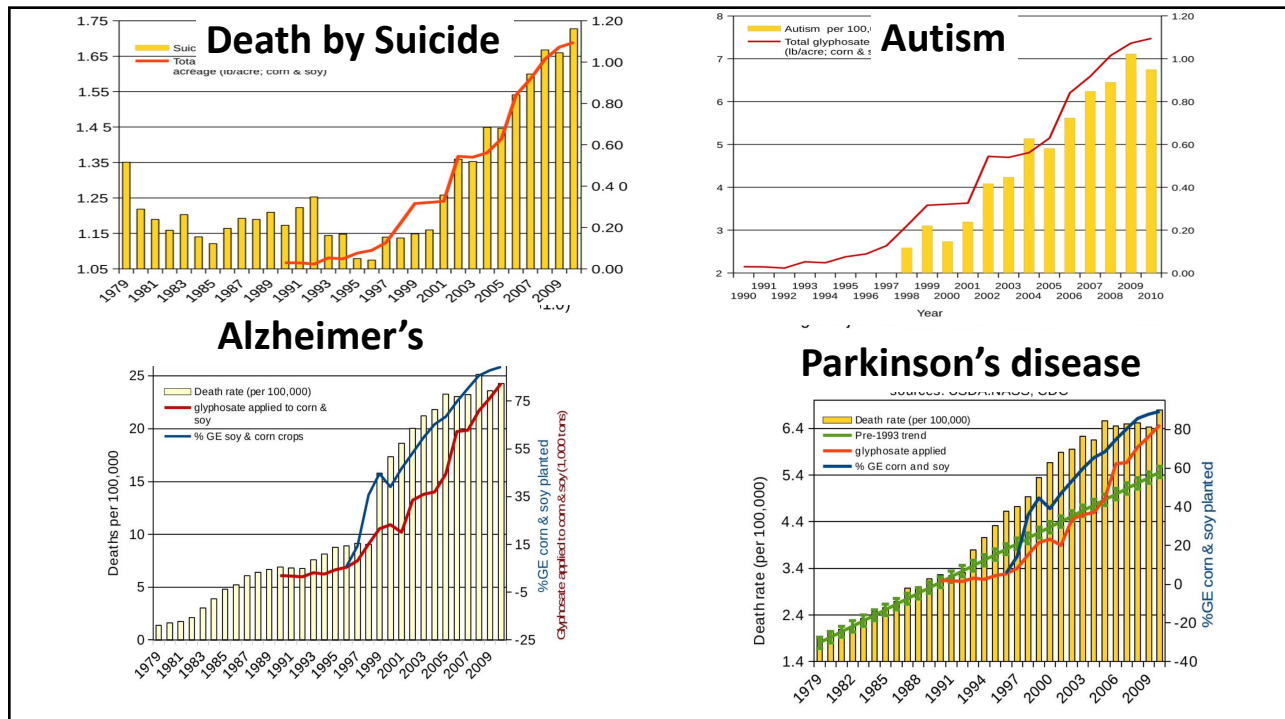
Full Length Article

Gut microbiota and neurological effects of glyphosate

Lola Rueda-Ruzafa^a, Francisco Cruz^b, Pablo Roman^{c,d,e,*}, Diana Cardona^{c,e,f}

“In this work, we state a possible link between Gly[phosate]-induced *dysbiosis* and cognitive and motor aggravations in neurodegenerative and neurodevelopmental pathologies, such as autism spectrum disorder (ASD). Hence, we review the negative impact that Gly-induced dysbiosis may have on *depression/anxiety, autism, Alzheimer’s and Parkinson’s diseases.*”

11



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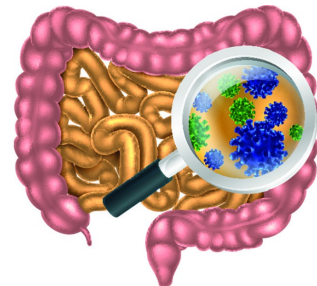
Gut Microbes Supply Deuterium-depleted Nutrients to the Host



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The Big Picture

- Gut microbes produce hydrogen gas that is remarkably depleted in deuterium
 - This gas is recycled back into organic nutrients by other microbes → the nutrients are also deuterium depleted
- The enzymes involved have strong dependencies on glycine residues that could be substituted by glyphosate
 - Intestinal bloating and gas pain may be caused by impaired hydrogen recycling due to glyphosate exposure
- Hydrogen enriched water and other hydrogen therapies show therapeutic promise
 - Is the benefit due to the low deuterium in the hydrogen gas?
- DNA methylation may be a storage mechanism for low-deuterium nutrients



14

Hydrogen gas produced by microbes anaerobically from glucose or formate is depleted down to 30 ppm deuterium*

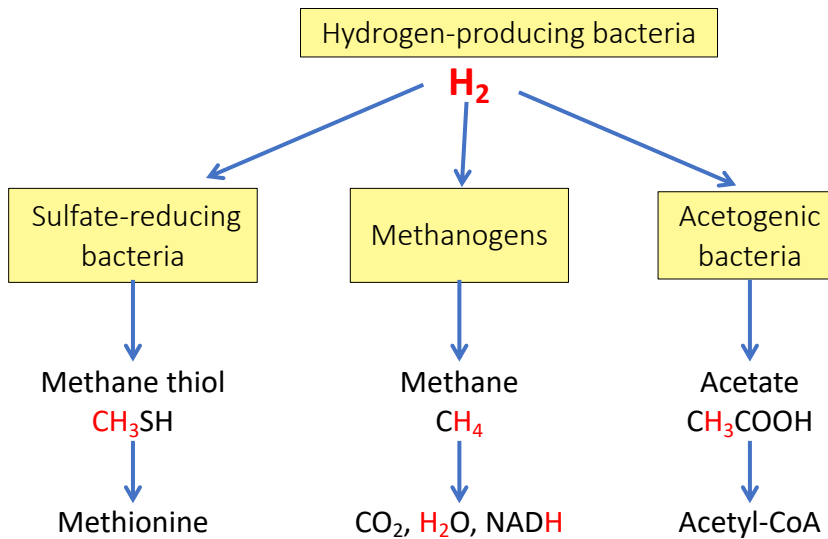
- “Mass spectrometric analyses of the hydrogen produced by growing cells showed a deuterium content of about 30 ppm. (i.e., depleted by a factor of 4.4 to 5.1...)”
- The same was true whether glucose or formate was the substrate.
- The intracellular water and cellular hydrogen were not significantly depleted in deuterium.



*MI Krichevsky et al. JBC 1961 236(9): 2520-2525.

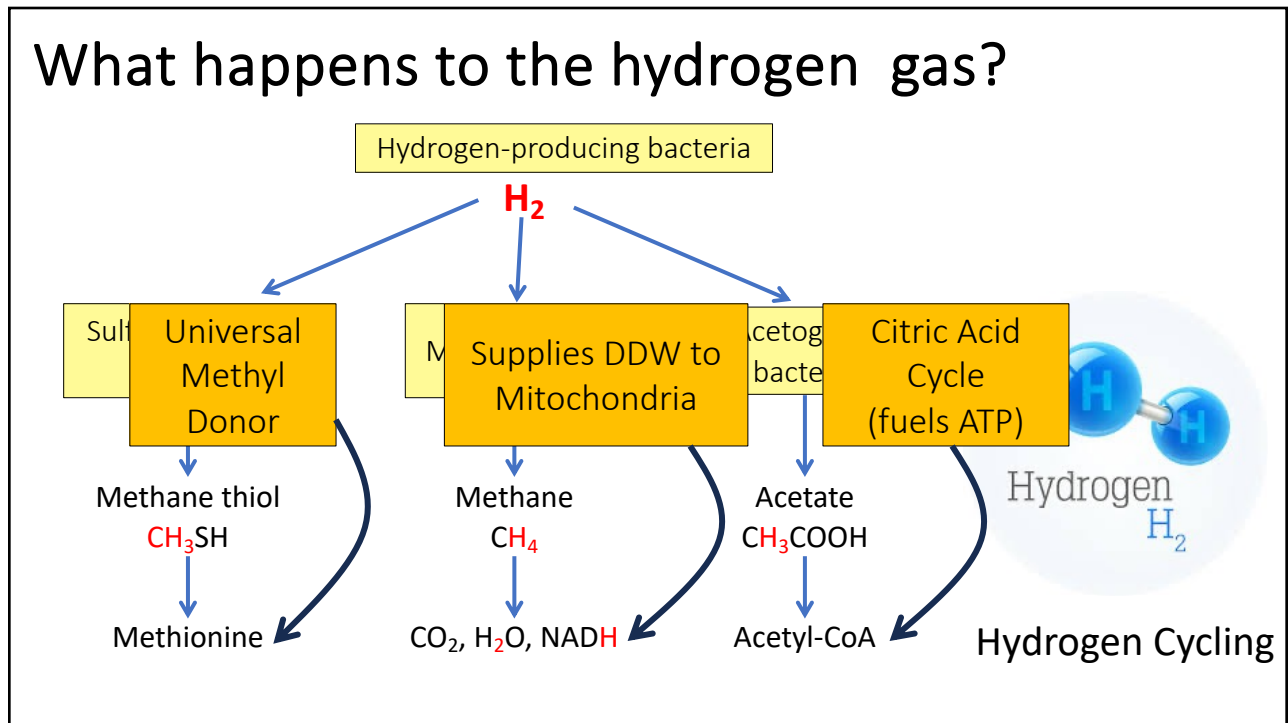
15

What happens to the hydrogen gas?

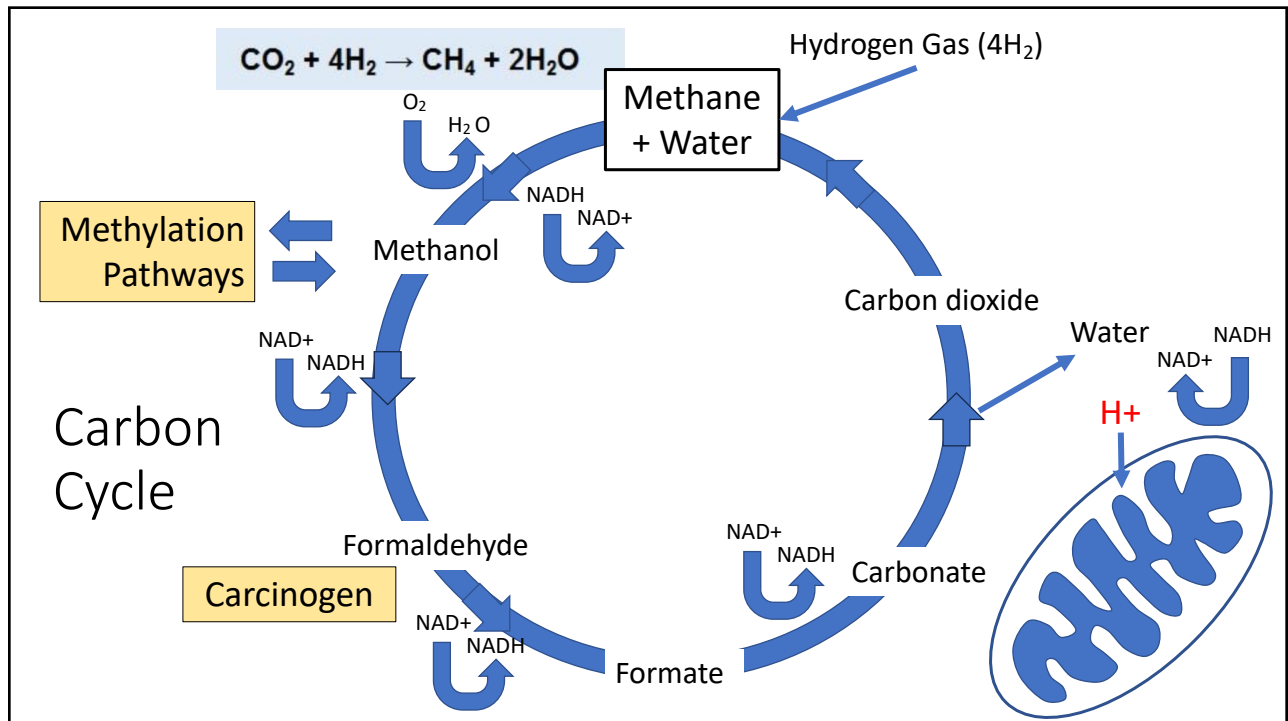


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What happens to the hydrogen gas?

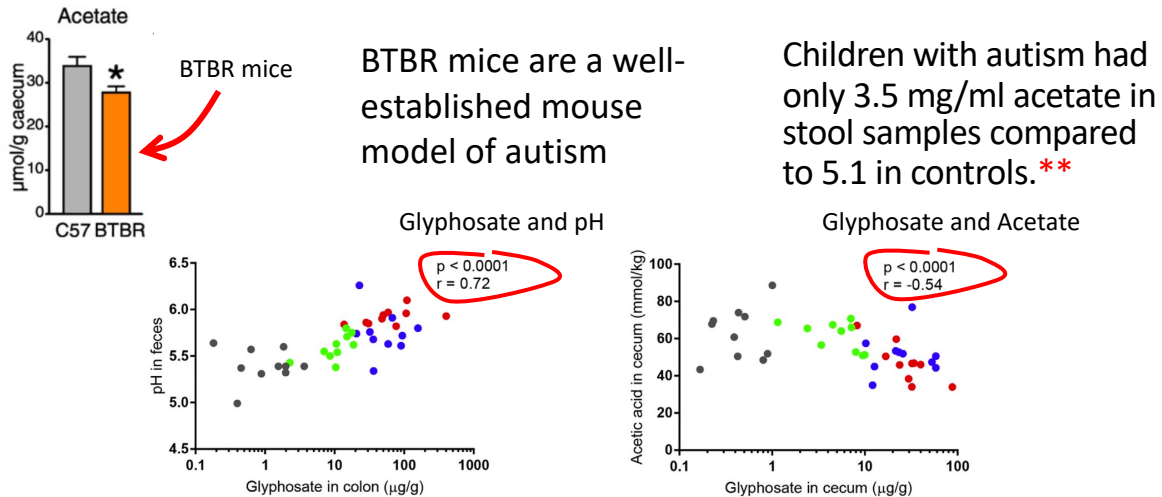


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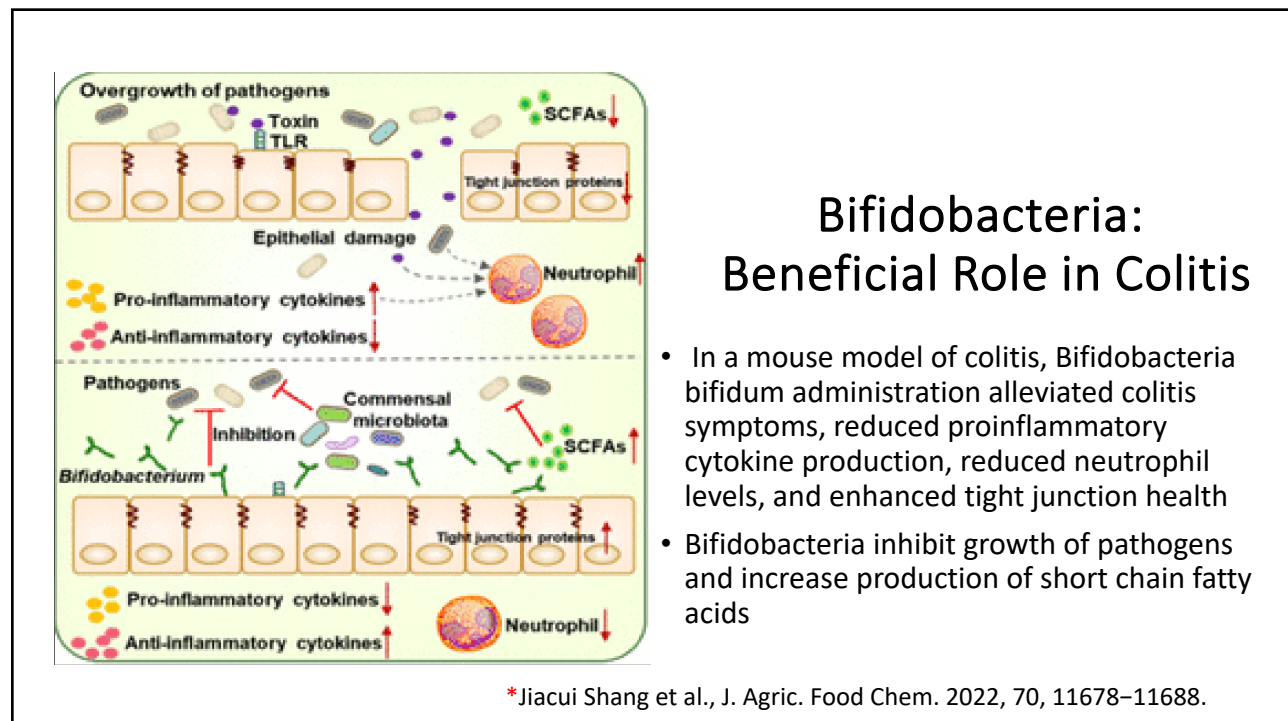
BTBR mice have low acetate, and glyphosate disrupts acetate synthesis in the gut*



*LN Nielsen et al. Environmental Pollution 2018;233:364e376.

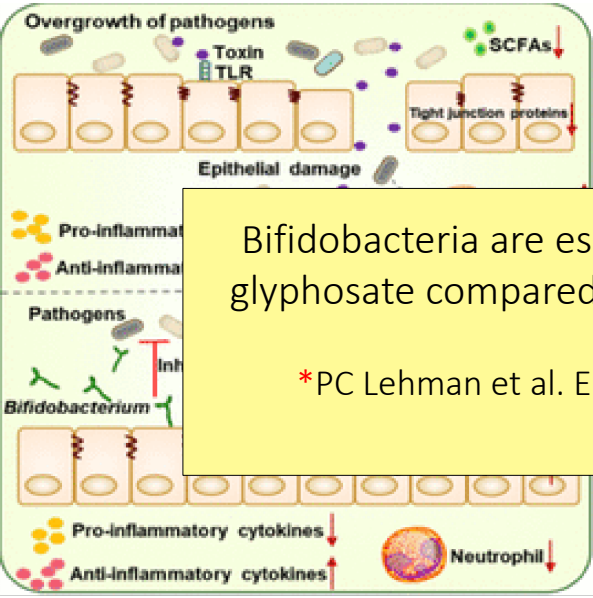
**JB Adams et al. BMC Gastroenterology 2011; 11:22.

21



*Jiacui Shang et al., J. Agric. Food Chem. 2022, 70, 11678–11688.

22



Bifidobacteria:

Bifidobacteria are especially sensitive to glyphosate compared to other microbes*

*PC Lehman et al. Environ Toxicol Pharmacol. 2023 Jun;100:104149.

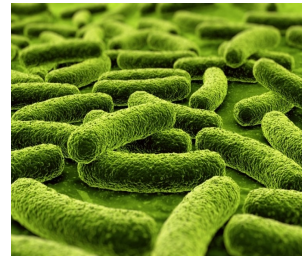
Bifidobacteria inhibit growth of pathogens and increase production of short chain fatty acids

*Jiacui Shang et al., J. Agric. Food Chem. 2022, 70, 11678–11688.

23

Benefits of Bifidobacteria*

- Bifidobacteria metabolize starch to produce lactate and acetate
- Many bacteria, but predominantly Firmicutes and Bacteroidites, produce hydrogen gas from lactate and acetate via hydrogenase enzymes
- Firmicutes are butyrate-producing bacteria that supply the colonocytes with their favorite food
- All these species need to be abundant to support hydrogen recycling
- It is said that approximately 10 liters of hydrogen are produced daily in the human intestines.
- Low hydrogen levels in the breath are linked to Parkinson's disease, rheumatoid arthritis, cardiovascular disease and Crohn's disease



*Yusuke Ichikawa et al., Med Gas Res. 2023 Jul-Sep;13(3):108-111.

24

[Med Gas Res.](#) 2023 Jul-Sep; 13(3): 108–111.

PMCID: PMC9979208

Published online 2022 May 12. doi: [10.4103/2045-9912.344977](https://doi.org/10.4103/2045-9912.344977)

PMID: [36571374](https://pubmed.ncbi.nlm.nih.gov/36571374/)

The overlooked benefits of hydrogen-producing bacteria

[Yusuke Ichikawa](#), PhD,^{1,2,*} [Haru Yamamoto](#),^{2,3} [Shin-ichi Hirano](#),¹ [Bunpei Sato](#),^{1,2} [Yoshiyasu Takefuji](#),^{4,5} and [Fumitake Satoh](#)^{1,2}

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Abstract

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Intestinal bacteria can be classified into “beneficial bacteria” and “harmful bacteria.” However, it is difficult to explain the mechanisms that make “beneficial bacteria” truly beneficial to human health. This issue can be addressed by focusing on hydrogen-producing bacteria in the intestines. Although it is widely known that molecular hydrogen can react with hydroxyl radicals, generated in the mitochondria, to protect cells from oxidative stress, the beneficial effects of hydrogen are not fully pervasive because it is not generally thought to be metabolized *in vivo*. In recent years, it has become clear that there is a close relationship between the amount of hydrogen produced by intestinal bacteria and various diseases, and this report discusses this relationship.

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Hydrogen Gas as a Therapy*

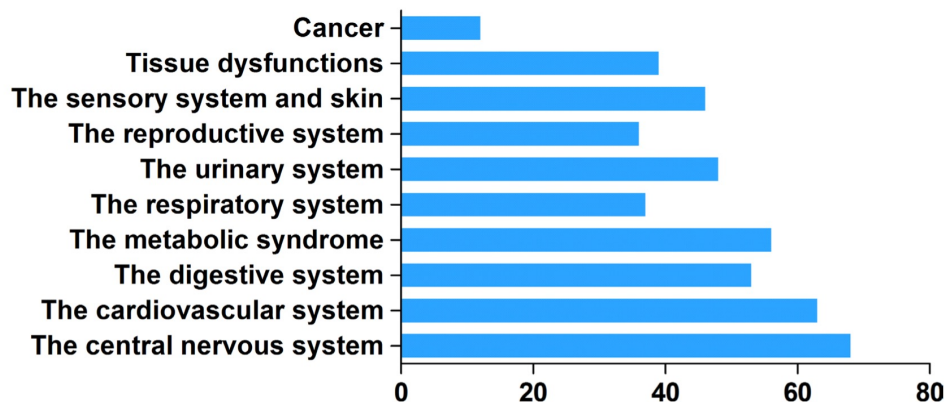


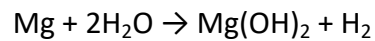
Figure 2: Number of publications on H₂ biological effects in various organ system diseases since 2007.

*L Ge et al. *Oncotarget* 2017; 8(60): 102653-102673.

26

"Pilot study of H₂ therapy in Parkinson's disease: a randomized double-blind placebo-controlled trial"*

- Hydrogen water is water with trapped hydrogen gas in it
- It can be created by dropping tablets of elemental magnesium into tap water



"The results indicated that drinking H₂-water was safe and well tolerated, and a significant improvement in total UPDRS [Unified Parkinson's Disease Rating Scale] scores for patients in the H₂-water group was demonstrated."



*Asako Yoritaka et al. Mov Disord 2013; 28(6): 836-9.

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**Glyphosate
Suppresses
Dehydrogenases**

28

The Big Picture

- Methane gas is converted by gut microbes in a series of steps into methanol, formaldehyde, formate, and ultimately carbon dioxide
- The enzymes that extract hydrogen from methanol, formaldehyde and formate are called *dehydrogenases*.
 - This class of enzymes is suppressed by glyphosate.
- These enzymes generate *NADH* (H originally from hydrogen gas) to fuel the mitochondria with hydrogen that is low in deuterium
- Methionine's methyl group (derived from methane) is the universal methyl donor
- Many methyl groups are attached to large molecules such as DNA, RNA, histones and other proteins
 - Do these methyls serve as a storage form of low-deuterium hydrogens?

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Enzymes Use Hydrogen Tunneling to Avoid Deuterium

- A deuterium kinetic isotope effect (KIE) defines an enzyme's ability to deliver a proton to the product, rather than a deuterium
- Many dehydrogenases have a high deuterium KIE ($\gg 1$)
- An essential aspect of enzymatic action involves hydrogen tunneling (quantum physics)
- Protons are far more efficient at tunneling than deuterons

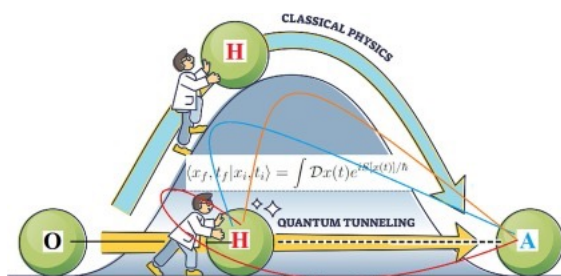


Image credit: Graphical Abstract.
Luca Nanni. Chemical Physics 2023; 574: 112054.

30

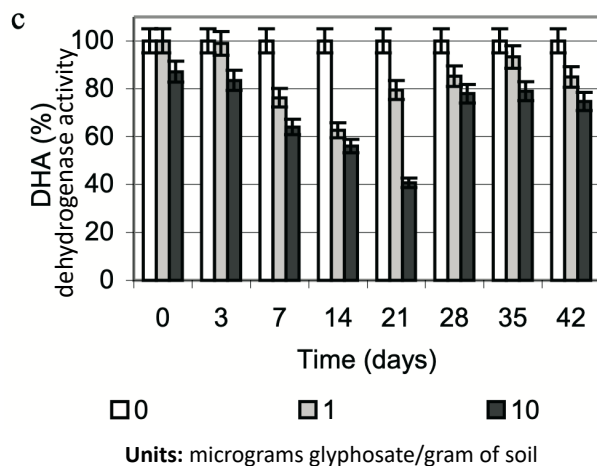
Glyphosate Impairs NAD(P)(H) Pathways*

- NAD(P)(H) is a major carrier of deuterium-depleted protons
- *NAD(P)(H) is derived from tryptophan*
 - Tryptophan is a major product of the shikimate pathway, blocked by glyphosate in plants and microbes
- Glyphosate inhibits *NADH dehydrogenase*, which supplies deuterium-depleted protons to the ATPase pumps in the mitochondria
- Glyphosate inhibits *glucose 6 phosphate dehydrogenase* (G6PD), which restores NADPH from NADP+
- Glyphosate inhibits *succinate dehydrogenase*, the only enzyme that participates in both the citric acid cycle and oxidative phosphorylation in the mitochondria
 - Succinate dehydrogenase deficiency is linked to many cancers

*S Seneff, Toxic Legacy, Chelsea Green Publishers, July 2021.

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Glyphosate Suppresses Dehydrogenases in Soil Microbes*



In mollic gleysols (a type of soil prevalent in meadows and river bottoms), the level of microbial dehydrogenase activity decreased steadily over a three-week period following glyphosate exposure

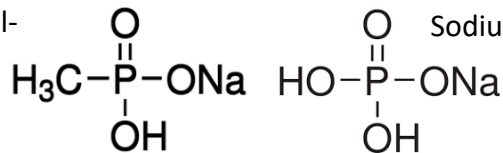
*RP Bennicelli et al. Int. Agrophysics, 2009, 23, 117-122.

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Hypothesis: Glyphosate Disrupts Proteins that Bind Phosphate

- Glyphosate is a glycine molecule with a methylphosphonate unit attached to the nitrogen atom
- Glyphosate kills weeds by suppressing EPSP synthase in the shikimate pathway
- Glyphosate blocks EPSP synthase binding to the phosphate in PEP
- The binding site for PEP has a highly conserved glycine residue
 - If this glycine is swapped out for alanine, the enzyme becomes completely insensitive to glyphosate
 - This is the basis for many GMO glyphosate-resistant crops*

Sodium Methyl-phosphonate



Sodium Phosphate

*T Funke et al. Proc Natl Acad Sci U S A 2006; 103(35): 13010-13015

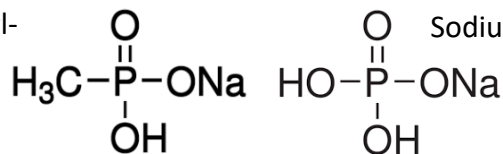
33

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 - This is the basis for many GMO glyphosate-resistant crops*

Many enzymes that glyphosate has been shown to suppress contain a "glyphosate susceptibility motif": they bind phosphate at a site where there is at least one highly conserved glycine residue

Sodium Methyl-phosphonate



Sodium Phosphate

*T Funke et al. Proc Natl Acad Sci U S A 2006; 103(35): 13010-13015

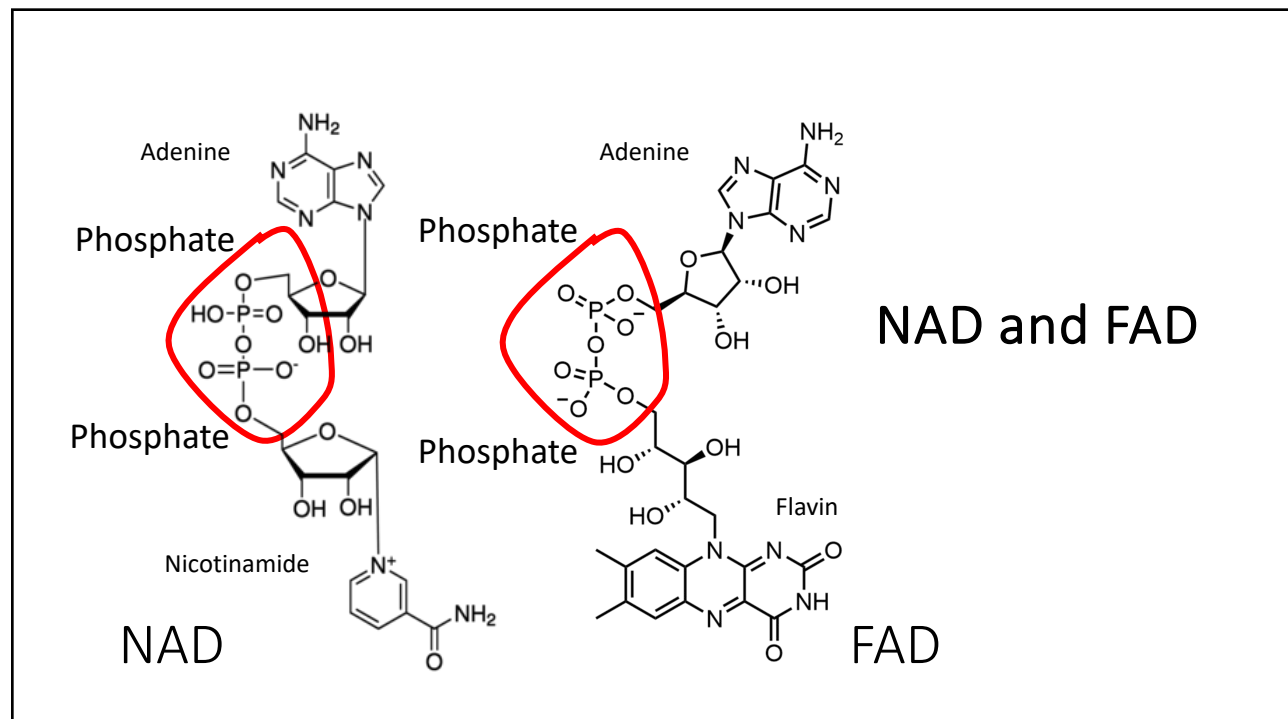
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Does Glyphosate Disrupt FAD binding in Dehydrogenases?

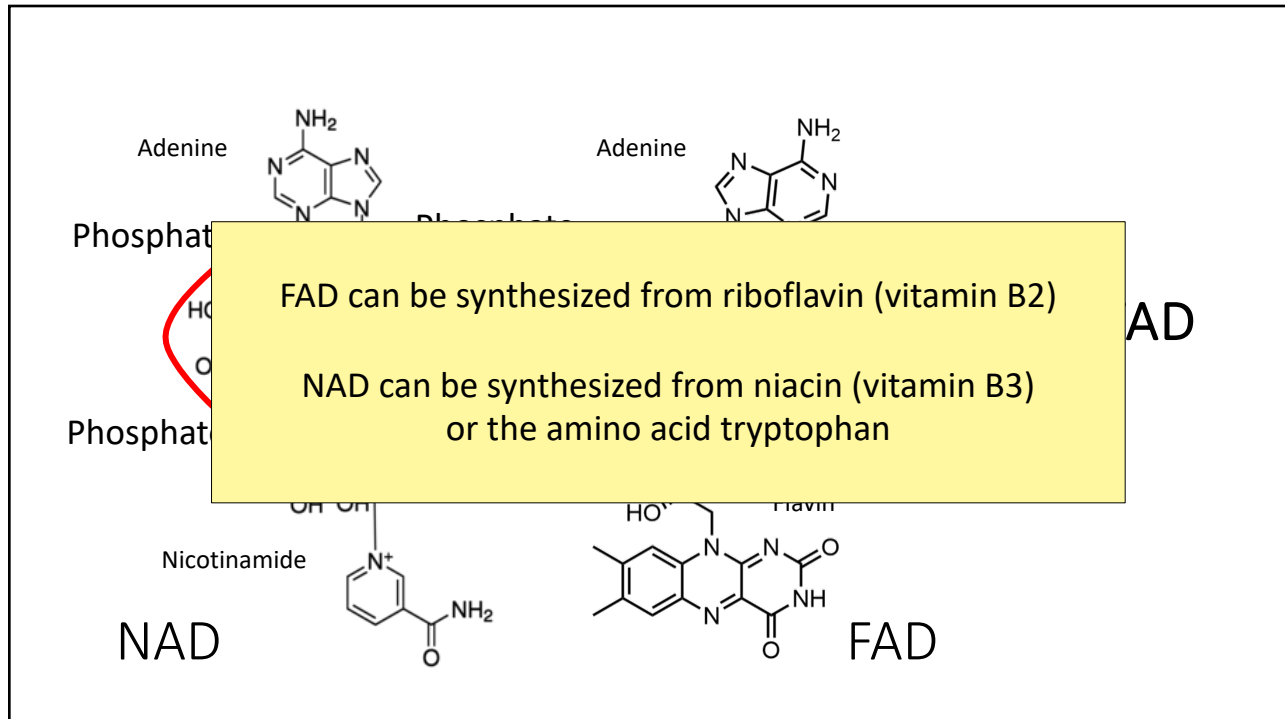
- Many dehydrogenases are *flavoproteins*. They bind flavin-adenine dinucleotide (FAD) at a site with at least one highly conserved glycine residue. FAD facilitates the transfer of protons and electrons
- A region near the carboxyl-terminal segment of FAD-binding dehydrogenases contains a highly conserved glycine-aspartate pair
- Mutation of Gly-478 to alanine in a Bacillus NADH dehydrogenase caused complete loss of activity, due to loss of binding capacity to FAD*
- Gly-478 is preceded by alanine, a small amino acid, leaving room for glyphosate's methylphosphonate unit

*Masato Shiraki and Noriyuki Kayama. Current Microbiology 2003; 46: 432–434.

35



36



37

Some dehydrogenases that are downregulated in *E. coli* when exposed to glyphosate*

- NADH dehydrogenase
- glucose-6-phosphate dehydrogenase
- succinate dehydrogenase
- malate dehydrogenase
- α -ketoglutarate dehydrogenase
- 2-deoxy-D-gluconate dehydrogenase
- acetaldehyde-CoA dehydrogenase
- D-amino acid dehydrogenase
- D-lactate dehydrogenase
- NADP-specific glutamate dehydrogenase
- 3-isopropylmalate dehydrogenase
- D-3-phosphoglycerate dehydrogenase

*Wei Lu et al. *Molecular BioSystems* 2013; 9: 522-530.

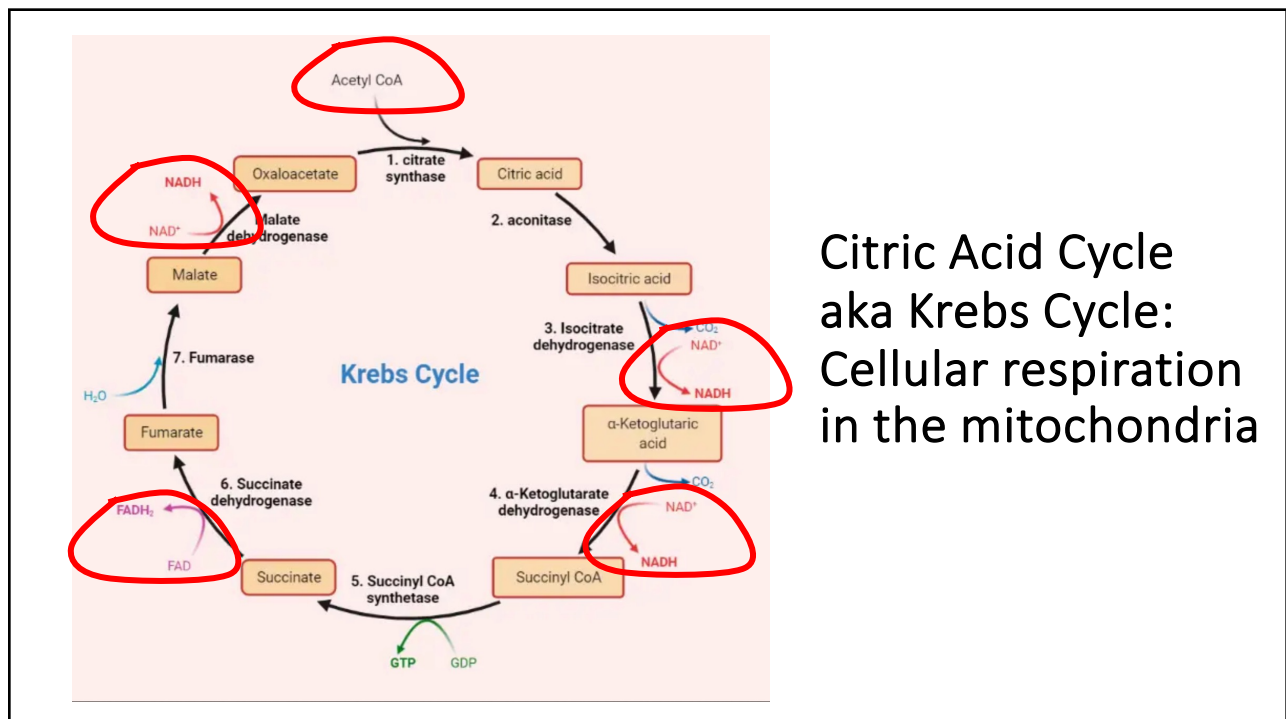
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Some dehydrogenases that are downregulated in *E. coli* when exposed to glyphosate*

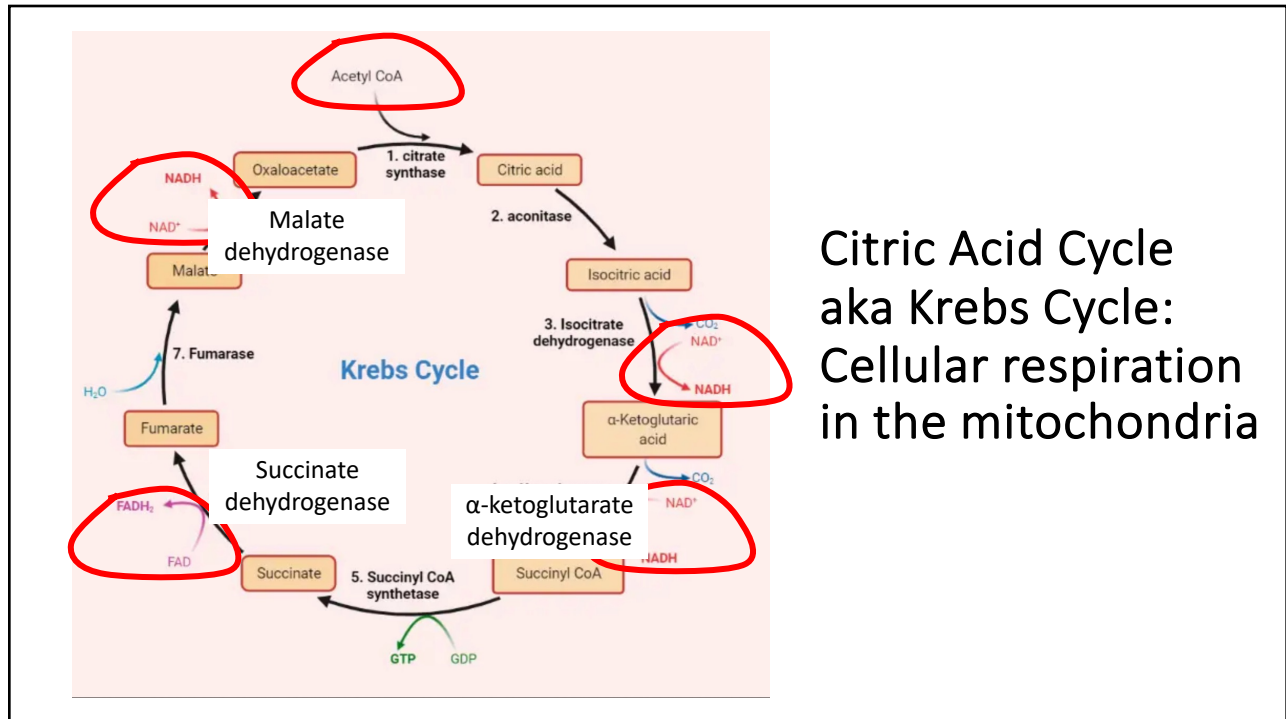
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*Wei Lu et al. Molecular BioSystems 2013; 9: 522-530.

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Citric Acid Cycle
aka Krebs Cycle:
Cellular respiration
in the mitochondria

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**Disrupted Glycolysis
Leads to Fatty Liver
Disease and
Hyperlipidemia**

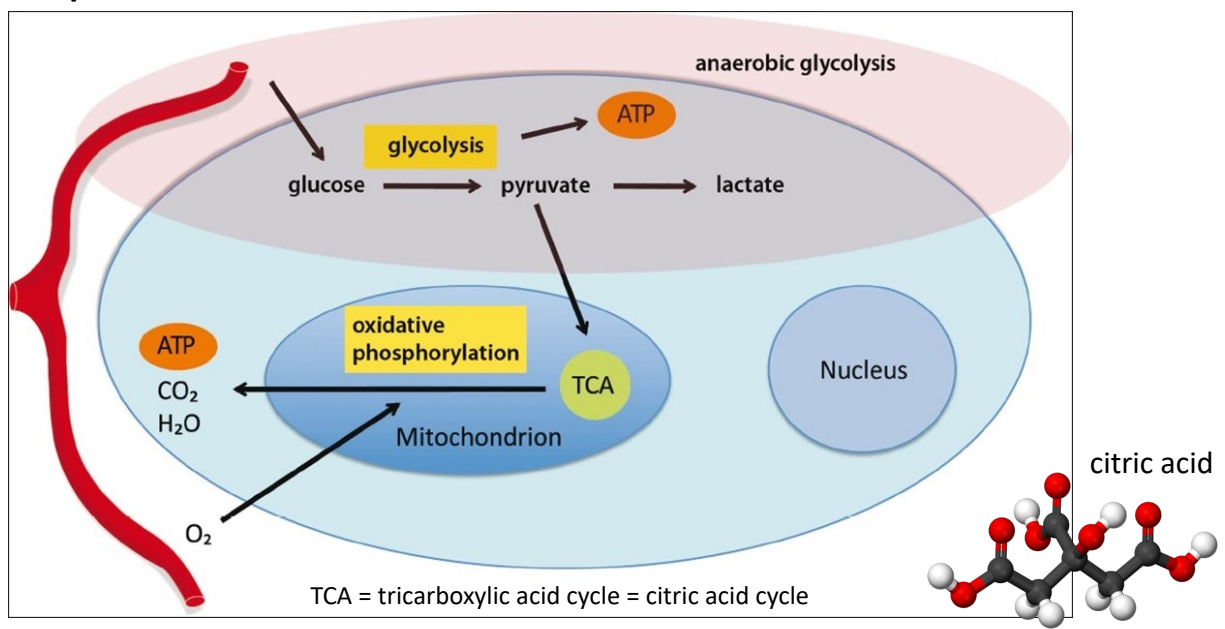
42

The Big Picture

- Glycolysis is the “pre-processing” step that takes place in the cytoplasm and converts glucose into pyruvate
- Many steps in glycolysis help to deplete deuterium in protons
- At least two critical dehydrogenases in glycolysis have strong glyphosate susceptibility motifs
- Genetic mutations in these genes lead to serious health issues, including glycation damage, microcephaly, seizures, cognitive impairment and liver damage

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Simplified Glucose Metabolism



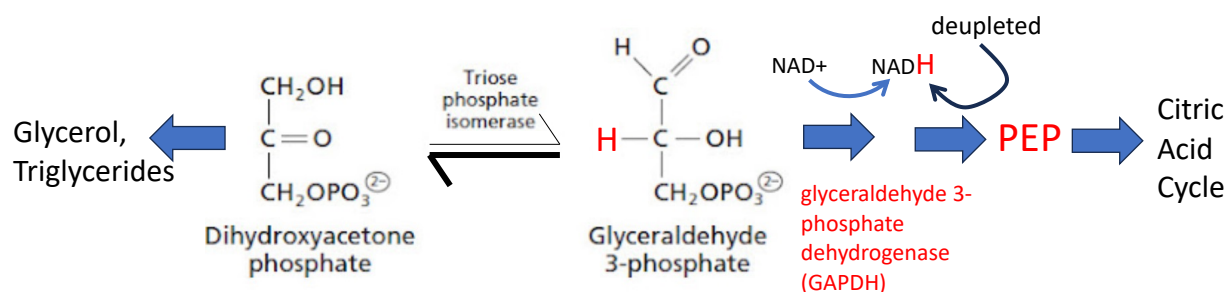
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Glycolysis and Glyphosate

- Glycolysis is the anaerobic pathway in the cytoplasm that converts glucose to pyruvate
- Pyruvate feeds into the citric acid cycle in the mitochondria and gets fully metabolized to carbon dioxide and water
- Glycolysis involves several enzymes that deplete deuterium
- Triosephosphate isomerase is an important enzyme in glycolysis that yields a deuterated proton that is then attached to NAD⁺ to make NADH
- The dehydrogenase that yields NADH has a strong glyphosate-susceptibility motif

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Triosephosphate Isomerase



- GAPDH is a dehydrogenase that has a strong glyphosate-susceptibility motif (highly conserved glycine that binds to NAD)
- PEP = phosphoenolpyruvate – the molecule that EPSPS synthase binds to in the shikimate pathway

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Triosephosphate Isomerase

$\text{H} \quad \text{O} \quad \text{NAD}^+ \quad \text{NADH} \quad \text{depleted}$

Glycerol, Triglycerides ← **If GAPDH is suppressed, triosephosphates are more susceptible to spontaneous conversion to methylglyoxal, possibly the most potent glycating agent known to biology** → P Citric Acid Cycle

- GAPDH is a dehydrogenase that has a strong glyphosate-susceptibility motif (highly conserved glycine that binds to NAD)
- PEP = phosphoenolpyruvate – the molecule that EPSPS synthase binds to in the shikimate pathway

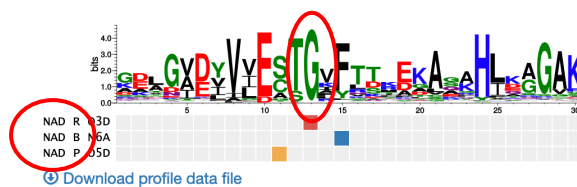
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Highly conserved glycine at NAD binding site of glyceraldehyde 3-phosphate dehydrogenase*

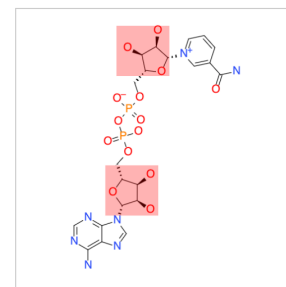
Profile **ESTGFH** with (dihydro)Nicotinamide adenine dinucleotide

Logo and protein-ligand-atom interactions

Click on a table cell to show interaction with a particular ligand moiety



NAD(H)



*<https://www.uniprot.org/uniprotkb/P04406/entry>

*<http://nbd.bii.a-star.edu.sg/search>

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ELSEVIER

Biochimica et Biophysica Acta 1637 (2003) 98–106



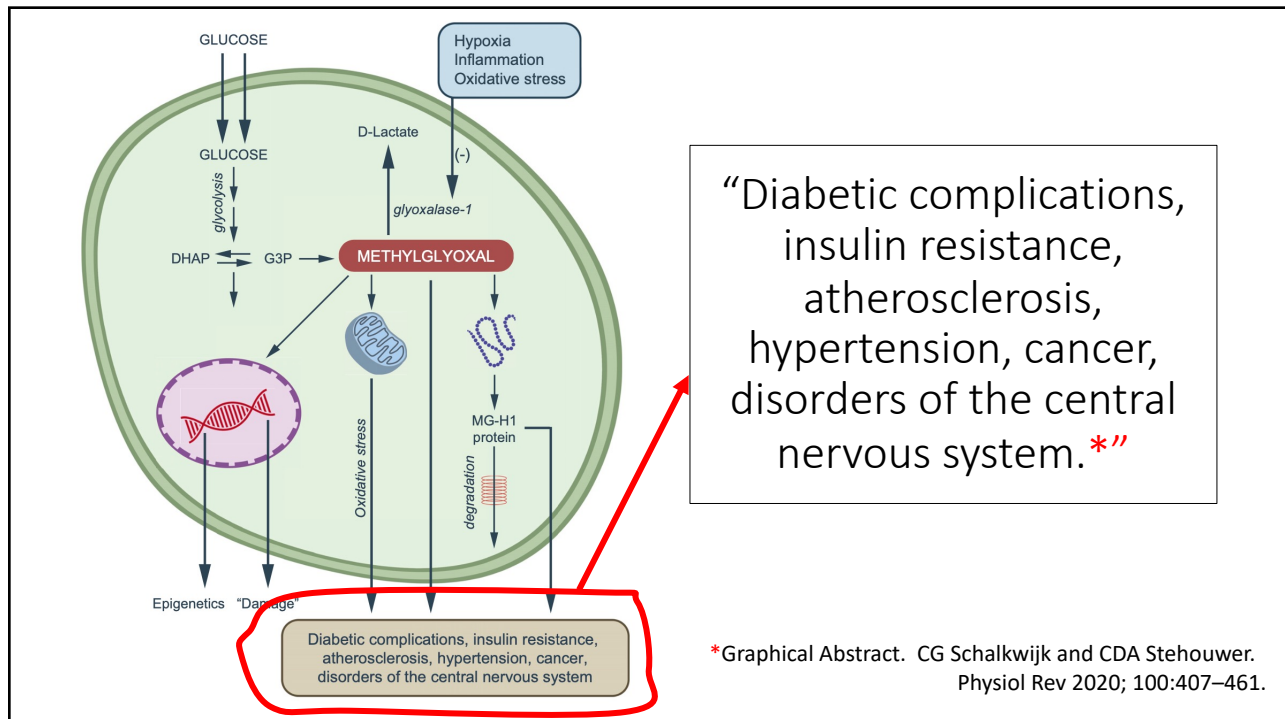
www.bba-direct.com

Glyceraldehyde-3-phosphate dehydrogenase activity as an independent modifier of methylglyoxal levels in diabetes

Paul J. Beisswenger*, Scott K. Howell, Kenneth Smith, Benjamin S. Szwegold

79% reduction of GAPDH activity resulted in a sixfold increase in methylglyoxal

49



*Graphical Abstract. CG Schalkwijk and CDA Stehouwer. *Physiol Rev* 2020; 100:407–461.

50

Toxicol. Res.
Vol. 30, No. 3, pp. 193-198 (2014)
Open Access <http://dx.doi.org/10.5487/TR.2014.30.3.193>
pISSN: 1976-8257 eISSN: 2234-2753 **Original Article**



Toxicological Research
Official Journal of
Korean Society of Toxicology
Available Online at <http://www.ToxicolRes.org>

Methylglyoxal Induces Mitochondrial Dysfunction and Cell Death in Liver

Kyuhwa Seo, Sung Hwan Ki and Sang Mi Shin

- Elevated plasma level of methylglyoxal are associated with diabetes, obesity and fatty liver disease
- Methylglyoxal induces oxidative stress
- Methylglyoxal causes liver toxicity, as indicated by increased levels of ALT and AST
- Methylglyoxal induces mitochondrial impairment and apoptosis in liver cells

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Is Glyphosate Causing an Epidemic in Fatty Liver Disease?

- Worldwide epidemic in fatty liver disease today*
- “Multiomics reveal non-alcoholic fatty liver disease in rats following chronic exposure to an ultra-low dose of Roundup herbicide”**
- Glyphosate correlated with fatty liver disease in humans***



Non-Alcoholic Fatty Liver Disease (NAFLD)

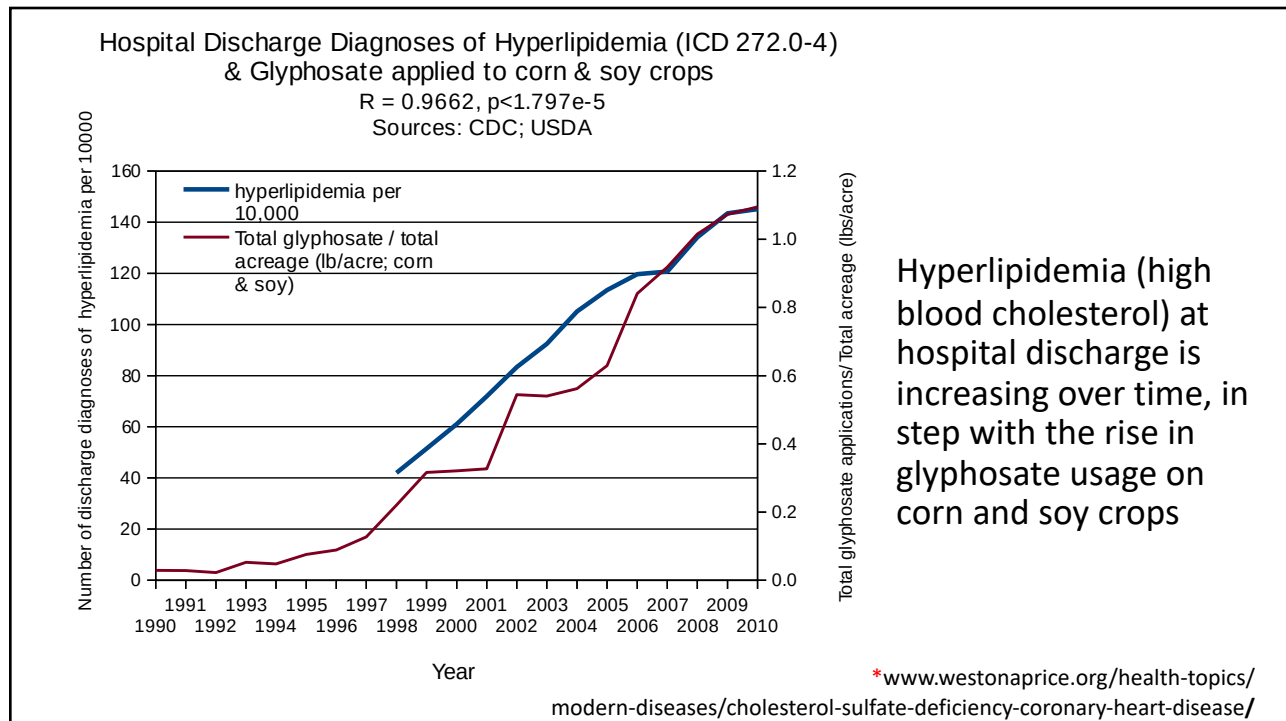


* Chris Estes et al. Hepatology 2018; 67(1): 123-133.

** Robin Mesnage et al. Sci Rep 2017; 7: 39328.

*** PJ Mills et al. Clinical Gastroenterology and Hepatology 2020;18(3):741-743.

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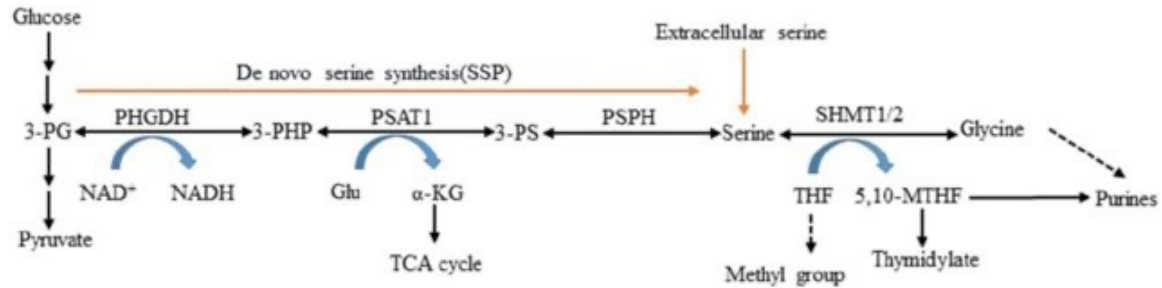
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- NADP-specific glutamate dehydrogenase
- 3-isopropylmalate dehydrogenase
- D-3-phosphoglycerate dehydrogenase

*Wei Lu et al. Molecular BioSystems 2013; 9: 522-530.

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3-phosphoglycerate dehydrogenase

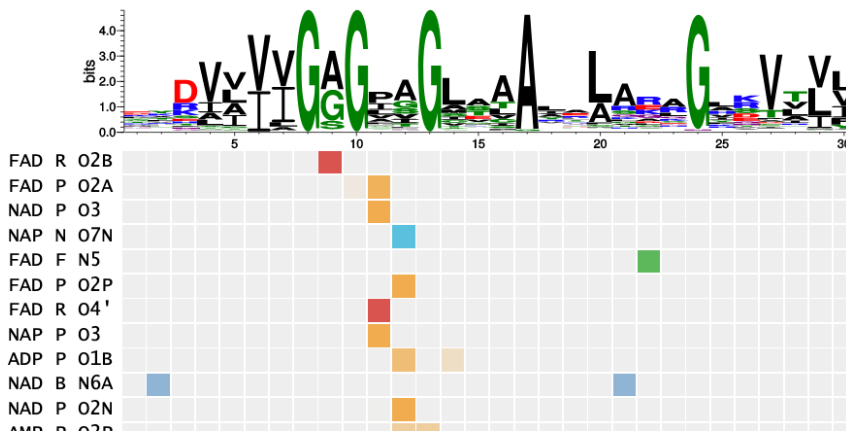


- 3-phosphoglycerate dehydrogenase (PHGDH) pulls an intermediate out of the glycolysis pathway and initiates serine synthesis
- Genetic defects in PHGDH lead to microcephaly, intractable seizures, and motor and cognitive impairments*
- PHGDH has a highly conserved GxGxxG motif at the NAD binding site

*Koning T. Journal of Inherited Metabolic Disease 2006; 29: 347-351.

55

GxGxxG Motif at NAD binding site in 3-phosphoglycerate dehydrogenase



56

Methionine Deficiency and Methylation Pathways

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The Big Picture

- Methylation pathways attach methyl groups to histones and to the cytosines in DNA molecules
- The methylation pattern of histones and DNA greatly influences gene expression
- Cancer is associated with hypomethylated DNA
- Methyls are metabolized while still attached to DNA, and the reaction yields succinate, an important source of protons in the mitochondria
- Methionine is the original source of the methyls, so they are normally severely depleted in deuterium content
- Supplemental methionine is problematic because it is usually synthesized in the chemistry lab rather than biologically synthesized
- Rat studies have shown that methionine deficiency leads to longevity, but these studies are fatally flawed

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Epigenomics. 2009 December ; 1(2): 239–259. doi:10.2217/epi.09.33.

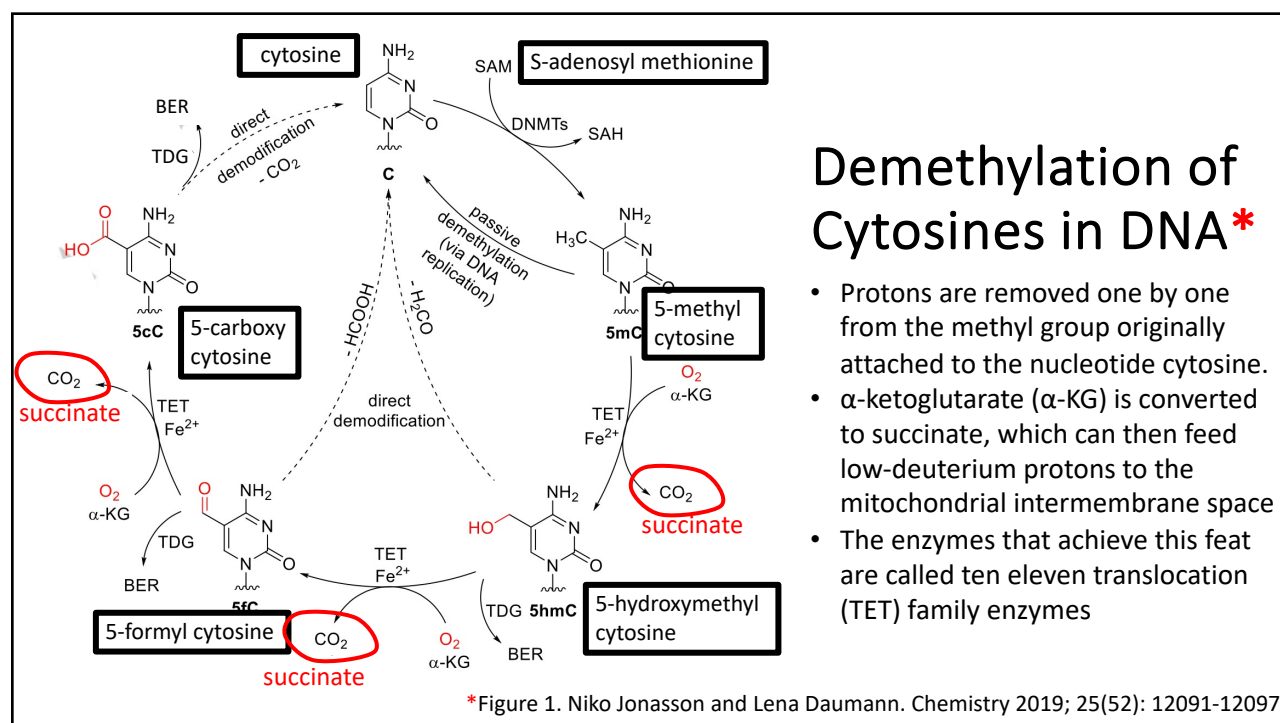
DNA hypomethylation in cancer cells

Melanie Ehrlich

Hayward Genetics Program, Department of Biochemistry, and Tulane Cancer Center, Tulane Medical School, 1430 Tulane Ave., New Orleans, LA 70112, USA, Tel.: +1 504 988 2449, Fax: +1 504 988 1763, ehrlich@tulane.edu

- DNA hypomethylation is a ubiquitous feature of carcinogenesis
- DNA hypomethylation can be found early in carcinogenesis, but can also be associated with tumor progression

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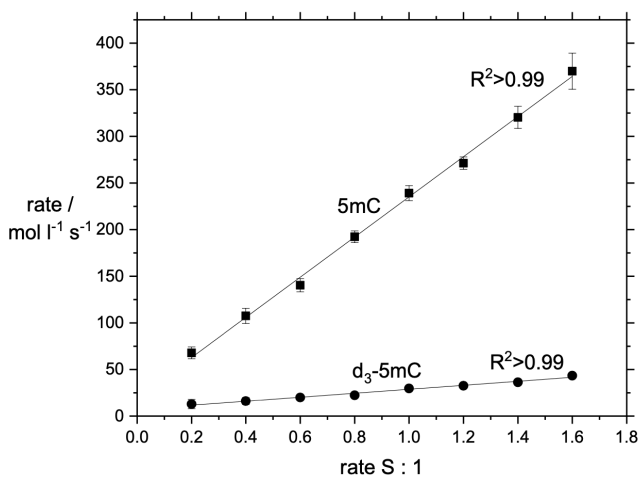


Demethylation of Cytosines in DNA*

- Protons are removed one by one from the methyl group originally attached to the nucleotide cytosine.
- α -ketoglutarate (α -KG) is converted to succinate, which can then feed low-deuterium protons to the mitochondrial intermembrane space
- The enzymes that achieve this feat are called ten eleven translocation (TET) family enzymes

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TET has a high deuterium kinetic isotope effect (KIE)*



When the three protons attached to the methyl group in 5-methyl cytosine are all replaced with deuterium, the reaction rate decreases dramatically

*Figure 6. Niko Jonasson and Lena Daumann. Chemistry 2019; 25(52): 12091-12097.

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Fibromalgia linked with DNA Hypomethylation*

- Fibromalgia has a hypomethylation DNA pattern
- Enriched in genes implicated in stress response and DNA repair/free radical clearance
- This set of genes is also enriched for other disorders, including schizophrenia, mood disorders, bulimia, hyperphagia, and obesity.



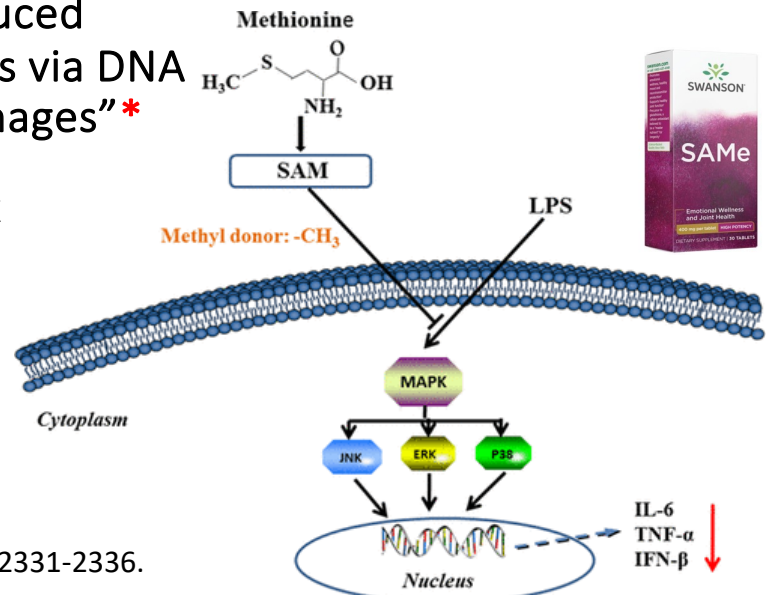
Is depletion of methyl groups in DNA an indicator of mitochondrial dysfunction due to excess deuterium?

*Daniel Ciampi de Andrade et al. Pain. 2017 Aug;158(8):1473-1480.

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“Methionine Attenuates Lipopolysaccharide-Induced Inflammatory Responses via DNA Methylation in Macrophages”*

- Methionine suppresses MAPK signaling via TLR4 through DNA methylation, and reduces production of inflammatory markers
- Reduces inflammatory response to both COVID-19 and the mRNA vaccines



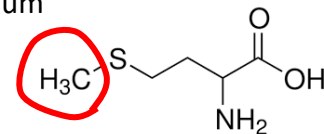
*Jian Ji et al. ACS Omega 2019; 4(1): 2331-2336.

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“Dietary” Methionine Deficiency Induces Longevity

“Forty percent methionine restriction decreases mitochondrial oxygen radical production and leak at complex I during forward electron flow and lowers oxidative damage to proteins and mitochondrial DNA in rat kidney and brain mitochondria.”*

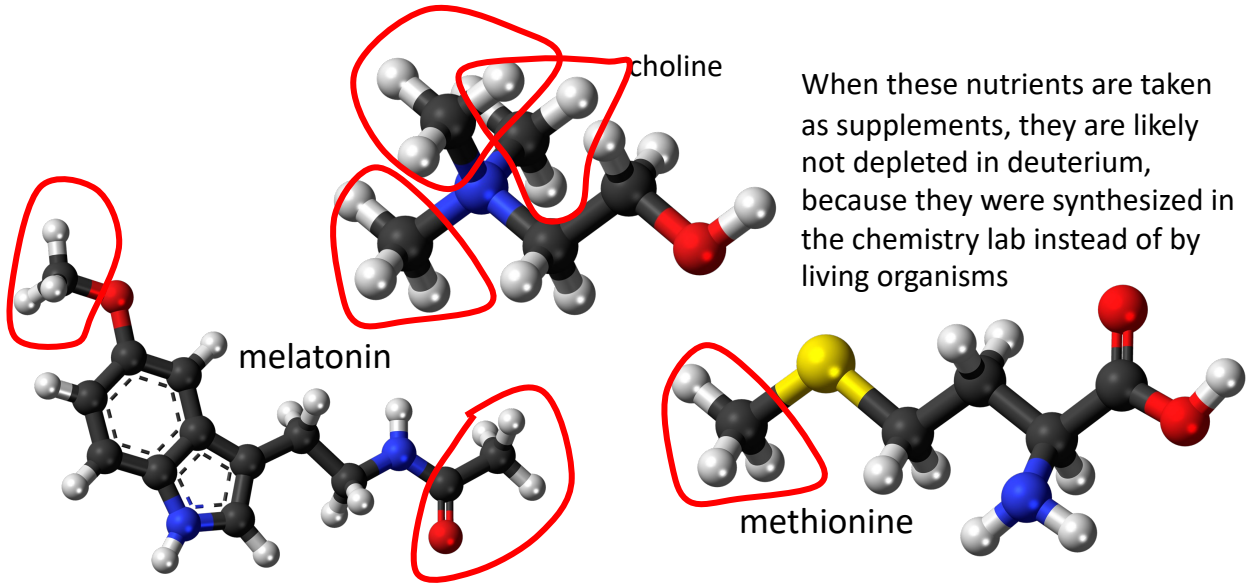
- Rats were fed synthetic amino acids instead of natural proteins
- Treated group got 40% reduced supply of synthetic methionine
 - They relied on methionine synthesized by the gut microbes
 - Their methyl groups were therefore greatly reduced in deuterium
 - Less deuterium in the mitochondria led to reduced ROS



*P Caro et al. Rejuvenation Res. 2009; 12(6): 421-34.

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Problematic Supplements



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Glyphosate Damages Mitochondria

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Glyphosate Suppresses Succinate Dehydrogenase

- Study on glyphosate's effects on E. coli proteins found that glyphosate significantly suppressed three different components of the succinate dehydrogenase complex*
- In vitro study on rat liver mitochondria in isolation exposed to Roundup found significant suppression of succinate dehydrogenase**
- Analysis of mechanism of glyphosate suppression suggested it disrupted *binding of succinate dehydrogenase to FAD****
- Succinate dehydrogenase has the sequence "GAGGAG" (Gly-Ala-Gly-Gly-Ala-Gly) at the site where it binds FAD

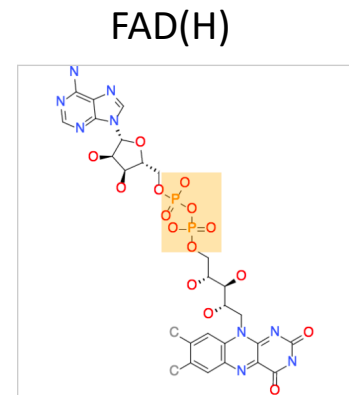
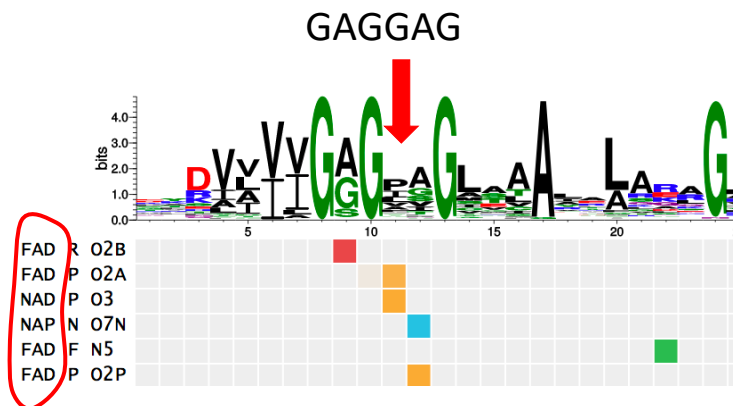
*W Lu et al., Mol. Biosys. 9 (2013) 522–530.

**Francisco Peixoto Chemosphere 61 (2005) 1115-1122.

***R Ugarte. Computational Theor. Chem. 1043 (2014) 54–63.

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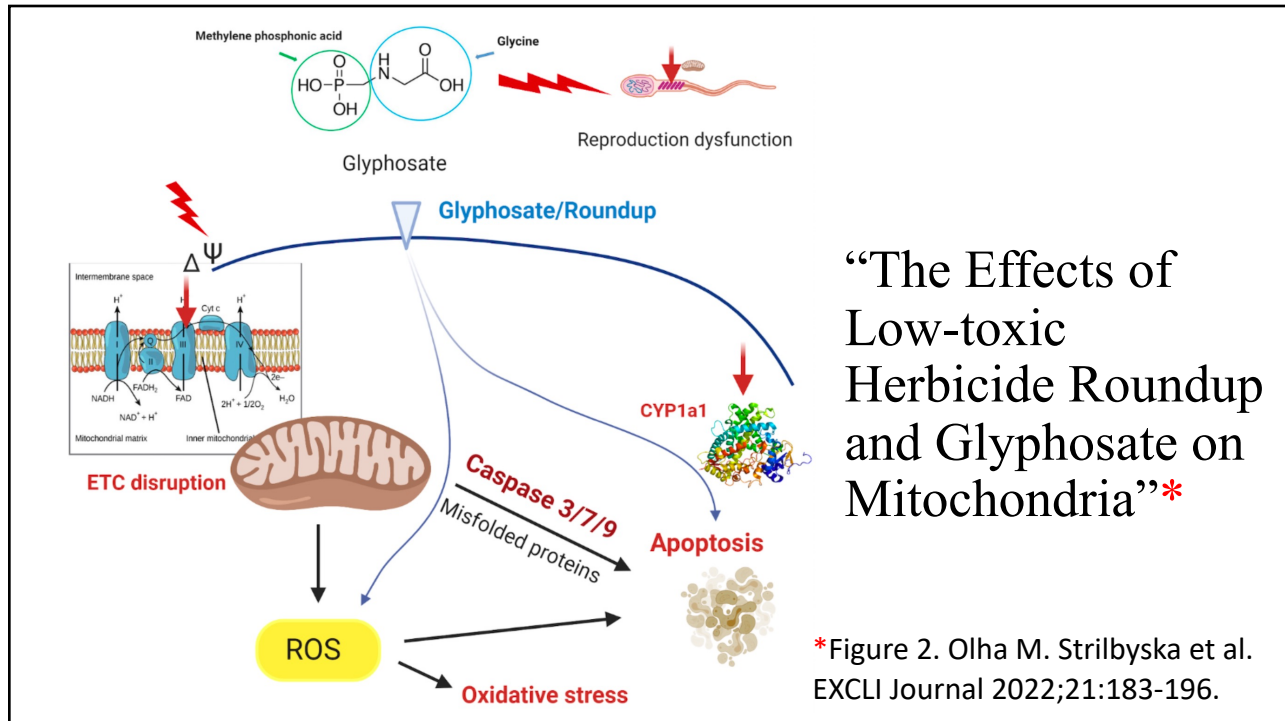
Succinate Dehydrogenase: GxGGxG Motif*



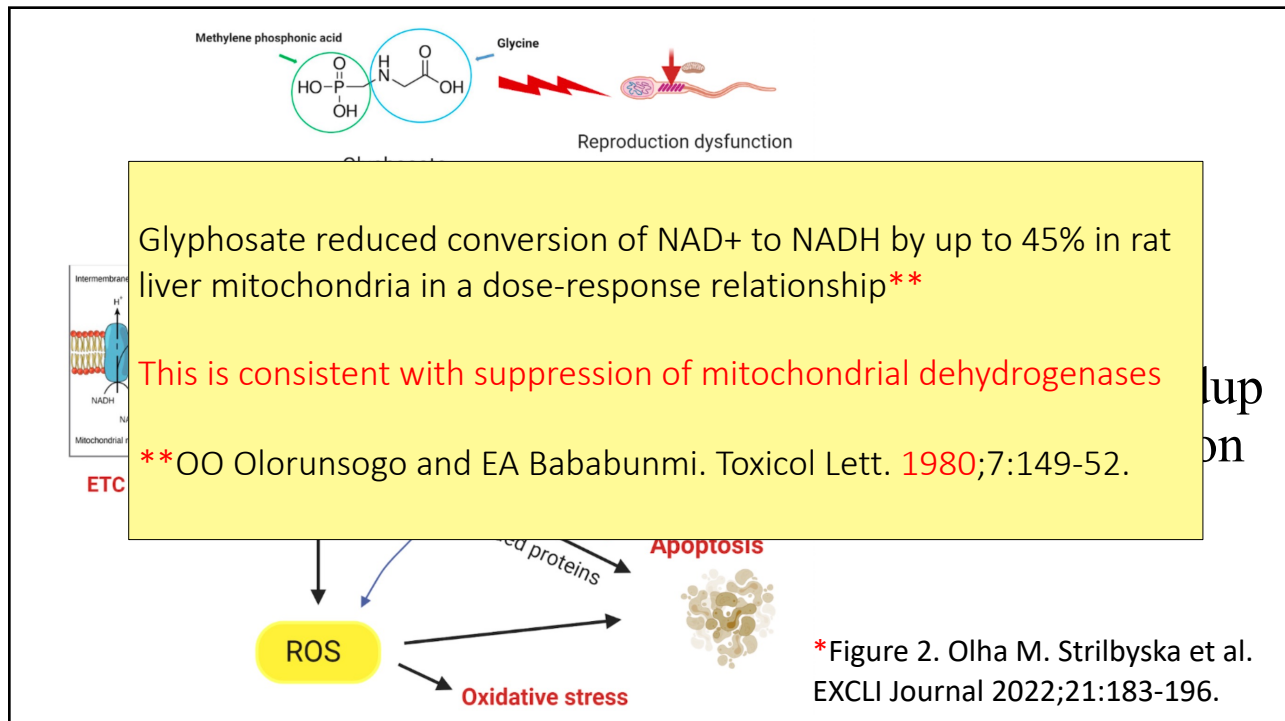
Binds FAD as a cofactor to catalyze electron transport in the mitochondria

*<http://nbd.bii.a-star.edu.sg/search>

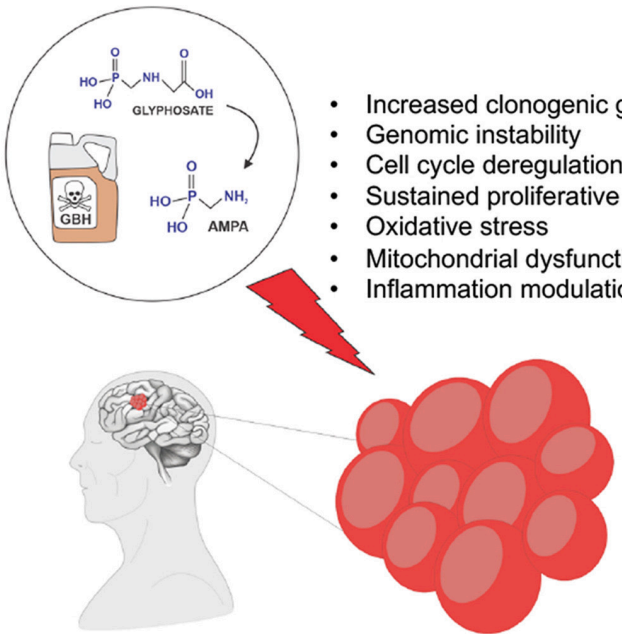
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OC(=O)CNP(=O)(O)O GLYPHOSATE
NC(=O)CNP(=O)(O)O AMPA

- Increased clonogenic growth
- Genomic instability
- Cell cycle deregulation
- Sustained proliferative signaling
- Oxidative stress
- Mitochondrial dysfunction
- Inflammation modulation

Glyphosate caused increased proliferation and mitochondrial dysfunction in human glioblastoma cells.*

Legend
 AMPA: Aminomethylphosphonic acid
 GBH: Glyphosate-based herbicide

*Claudia Daniele Bianco et al. Environmental Pollution 2023; 338: 122695.

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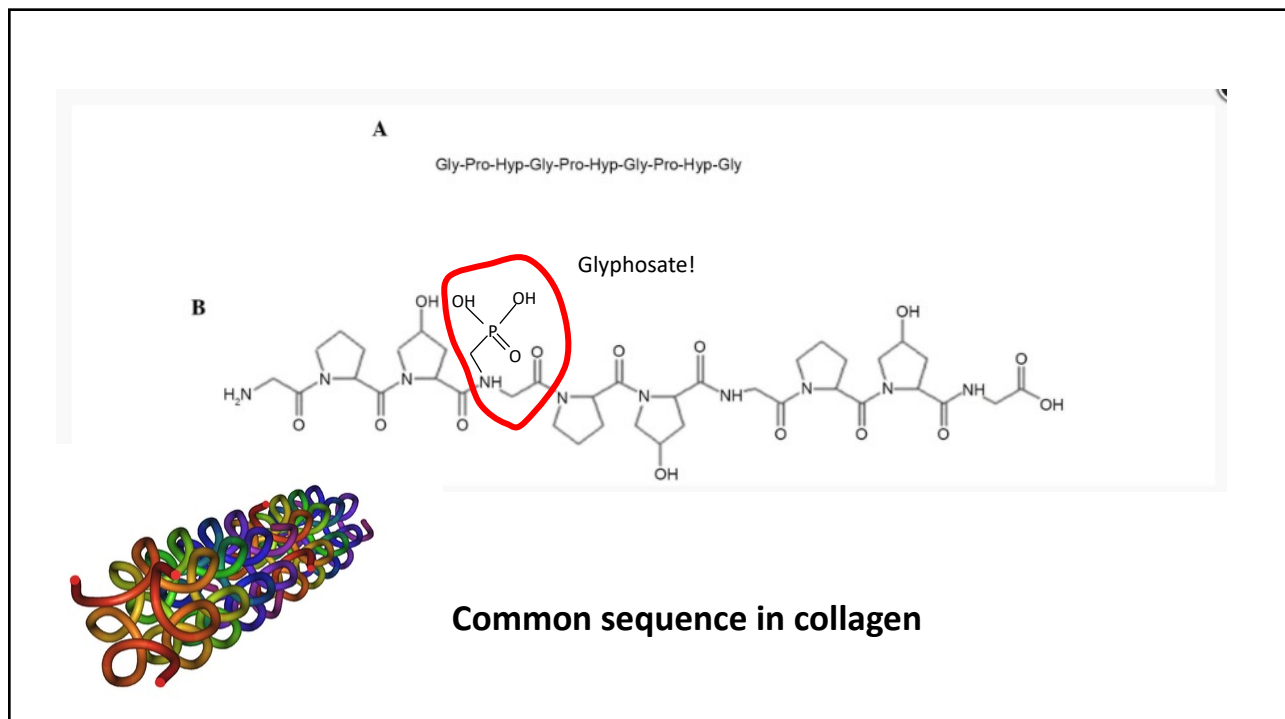
Collagen, Proline and Deuterium

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The Big Picture

- One third of the proteins in the human body are collagen molecules!
- Collagen forms the glue that holds the body together
- Collagen's triple helix structure gives it strength and elasticity
- Collagen has long sequences of GxyGxy... that are susceptible to glyphosate substitution
 - Many glycine mutations lead to connective tissue disorders
- Collagen is highly enriched in proline and hydroxyproline as well
- Proline has special properties that allow collagen to trap and sequester deuterium
- Peptidyl prolyl isomerase (PPIase) is a crucial class of enzymes that orchestrate collagen folding and trap deuterium in the endoplasmic reticulum
- Proline plays a major role in cancer cell metabolism

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Joint Hypermobility Syndrome

- Joint Hypermobility Syndrome is a relatively common genetic condition that often involves mutations in glycine residues in collagen
 - Connective tissue fragility, joint hypermobility, delayed wound healing, thin stretchy skin, abnormal scarring, vascular fragility, risk of aortic aneurism
- Specific heritable disorders include Marfan syndrome (MFS), osteogenesis imperfecta (OI) and Ehlers–Danlos syndrome (EDS)
- A mutation in a single glycine residue can lead to severe disease*
- Caused by impaired folding of the collagen molecule leading to collagen deficiency



*R Inokuchi et al. Medicine (Baltimore). 2014 Dec;93(28):e291.

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Proline Tightly Binds Deuterium*

- "A sample of proline containing 17 atom percent D was boiled with 20% hydrochloric acid for 72 hours."
- "The proline isolated from this solution was found to contain 16.2% D."
- "Thus, even under these relatively drastic conditions exchange, if there is any, is very slow."

Hypothesis:

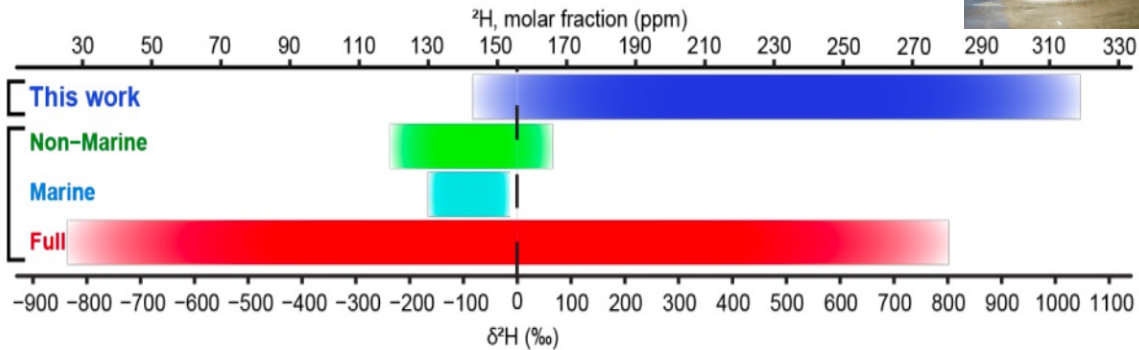
- Collagen folding in the endoplasmic reticulum involves trapping deuterium in proline molecules and ultimately sequestering it in the extracellular matrix and bone.
- This reduces deuterium loading in other proteins.

*Marjorie Roloff Stetten. Doctoral Thesis. Columbia University, 1943.

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Bone Collagen from Seals*

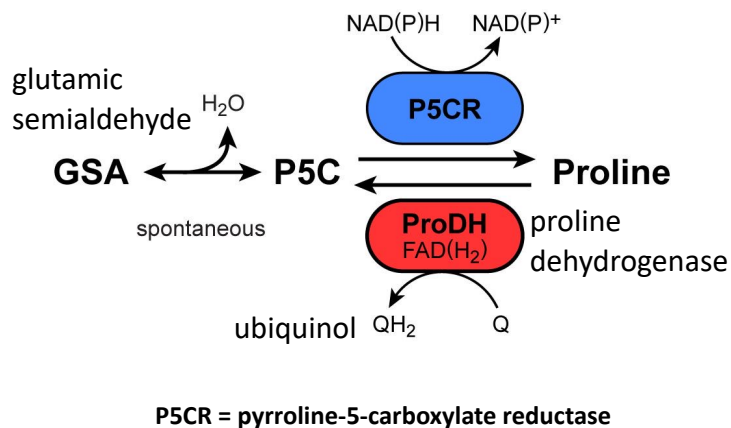
- More than twice as much deuterium in proline and hydroxyproline in the collagen of seals than is found in seawater
- Anomalously high deuterium levels are also found in proline and hydroxyproline in other biological sources



*Hassan Gharibi et al. J. Am. Chem. Soc. 2022, 144, 6, 2484-2487.

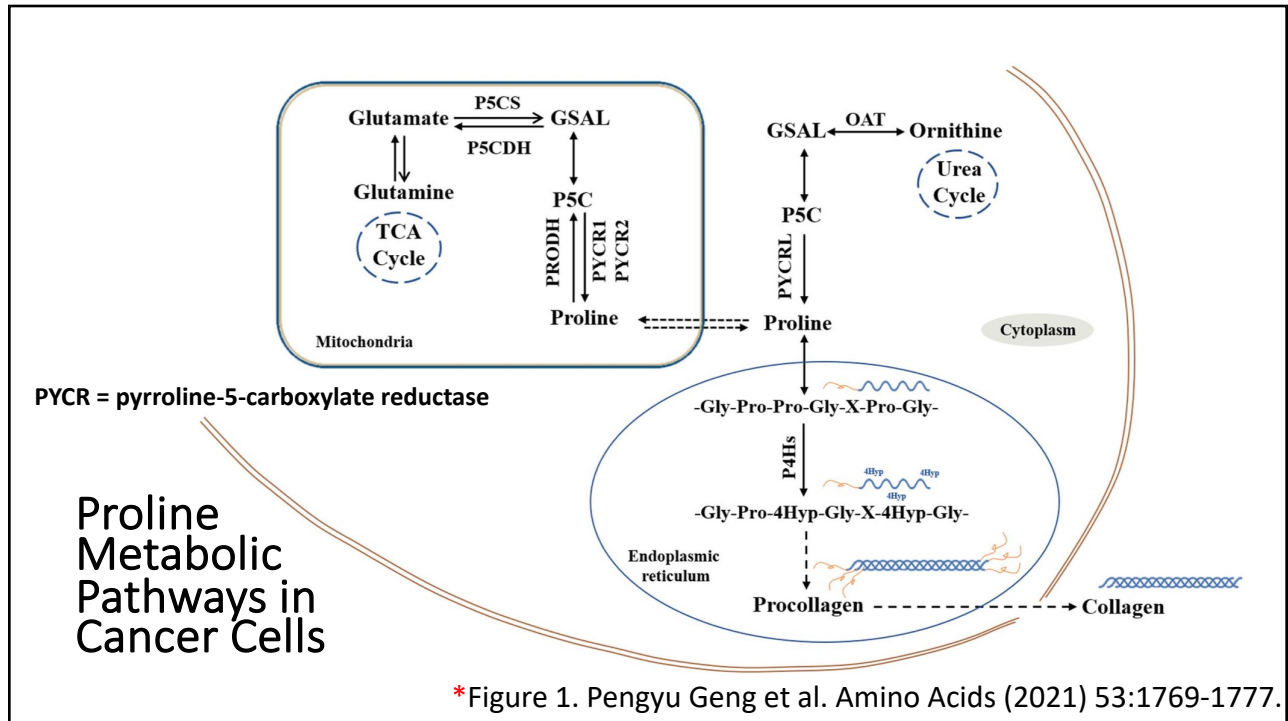
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Proline dehydrogenase replaces succinate dehydrogenase in cancer cells

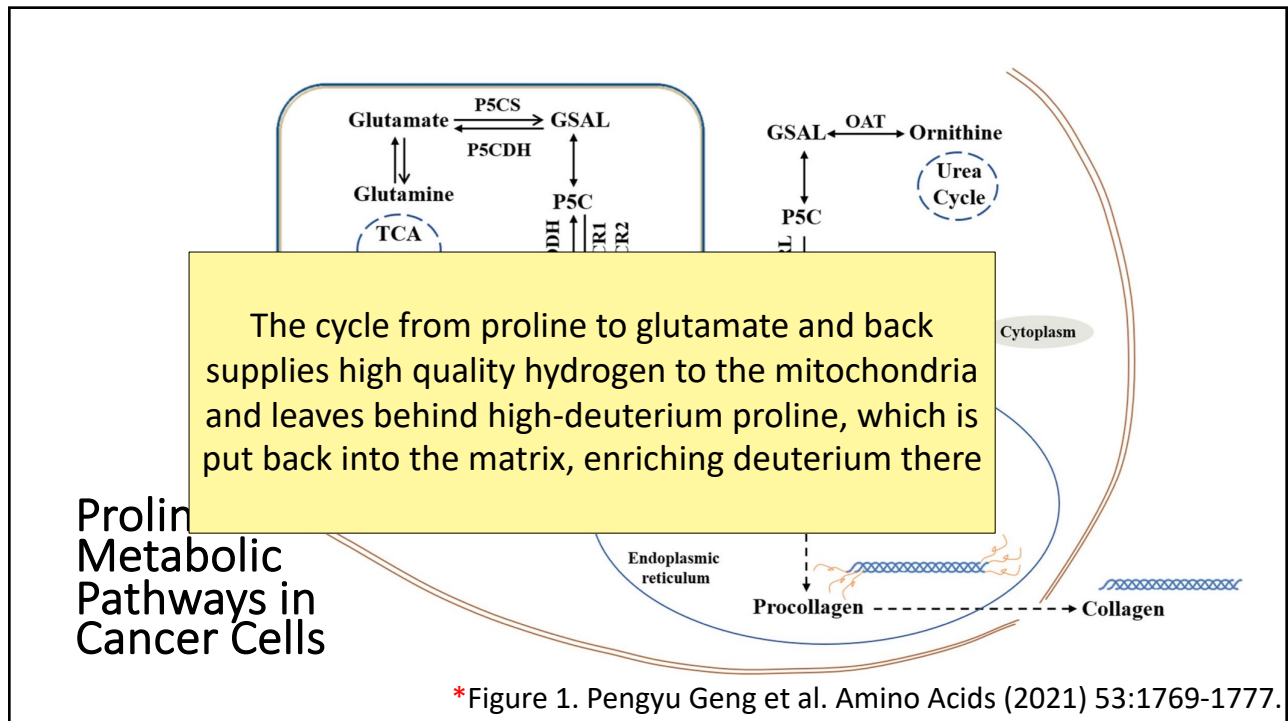


- Proline dehydrogenase (ProDH) substitutes for succinate dehydrogenase in the mitochondria when that enzyme is defective
- This also increases the demand for glutamate in cancer cells, or they can steal proline from the extracellular matrix

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Healthy Lifestyle

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A High-Fat Diet is a Low-Deuterium Diet

- Butter, lard and coconut oil were among the foods with the lowest detected levels of deuterium among foods tested
- The synthesis of fats involves transfer of hydrogen from NADPH into the growing fatty acid chain



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Amounts of Deuterium in Various Foods

Flour: 150 ppm



Sugar: 146 ppm



Cottage Cheese: 136 ppm



Coconut Oil: 110 ppm



Ghee: 112 ppm



Butter: 124 ppm

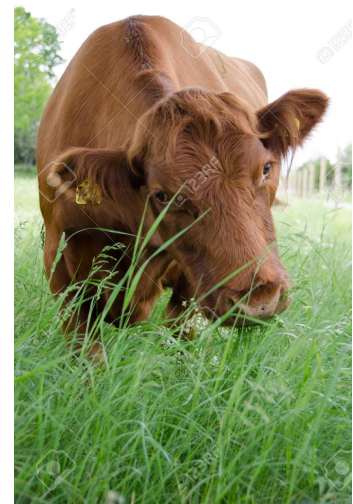


Olive Oil: 130 ppm

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Deuterium in Foods and Mast-Cell Activation Syndrome*

- Mast cells release histamines during an allergic reaction
- Deuterium increases histamine release from mast cells
- Plants get rid of deuterium by storing it in sugar and starch
 - Fruits, root vegetables (potato) and grains are high in deuterium
 - Meats from grain-fed animals are high in deuterium
- Leafy green vegetables, animal fats (lard, tallow, butter) and plant fats (avocado, coconut, olive oil) are low in deuterium
- Grass-fed beef and the dairy products derived from pastured cows are excellent sources of low-deuterium fat



*<https://healinghistamine.com/deuterium-histamine-intolerance/>

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Waterfalls are Therapeutic!*

- Waterfalls produce inhalable, negatively charged nano-water particles known as “Lenard ions” or ballo-electric ions
 - These particles are likely to be deuterium depleted
- “Conclusions: Our study provides new data, which strongly support an “added value” of exposure to waterfall microclimate when combined with a therapeutic sojourn at high altitude including regular physical activity.”
- Ocean waves probably have a similar effect



*C Grafetstätter et al. *Physiol Anthropol.* 2017; 36: 10.

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"Life expectancy in Iceland among the highest in Europe, infant mortality rate is lowest"*

"In 2015 the infant mortality rate in Iceland was 1.9 per 1,000 live births"

"The average in the European Union is 4.0, while the US has an infant mortality rate of 5.87"



Sólheimajökull Glacier



Smoked puffin



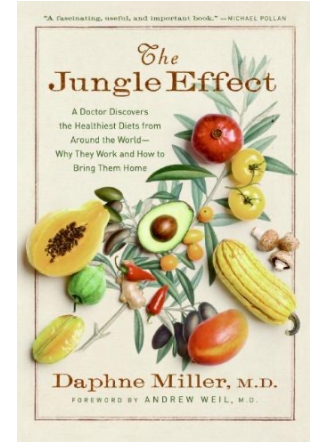
black sand beach of town Vík í Mýrdal in Iceland.

*<https://icelandmag.is/article/life-expectancy-iceland-among-highest-europe-infant-mortality-rate-lowest>

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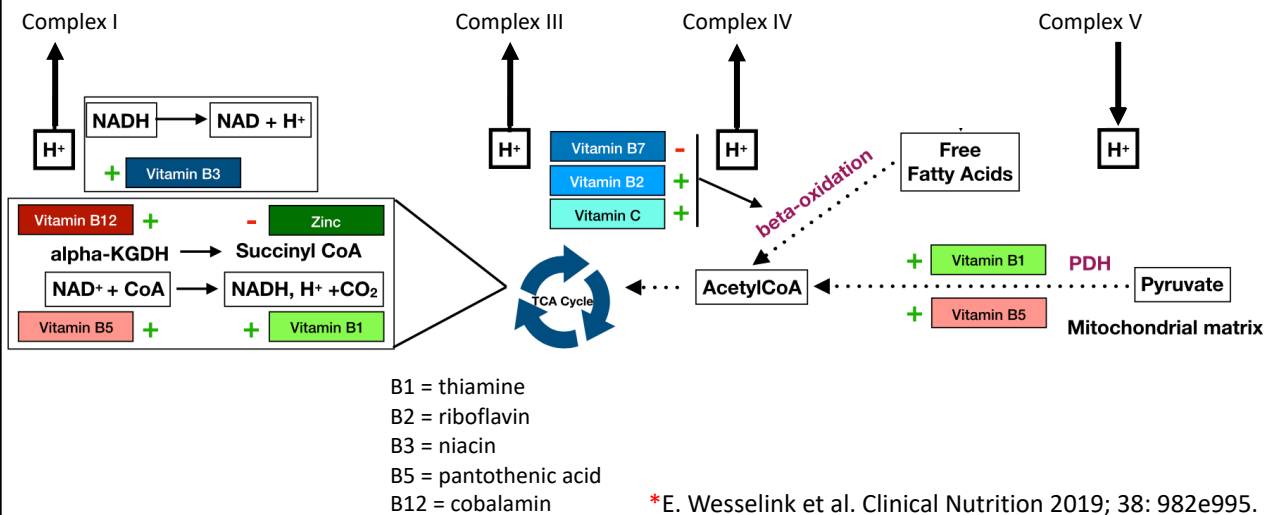
“The Jungle Effect: Healthiest Diets from Around the World” by Daphne Miller, MD

- Iceland was one of the places she studied
- Diet consists of fish, sheep, seabirds, potatoes, and other simple vegetables
- Iceland also has glacier water which is low in deuterium, and basalt which is high in sulfur (maintain sulfate levels)
 - Many sulfur hot springs with therapeutic benefit
- After a major eruption in the 1800’s, many islanders moved to northern Canada
 - They lost their health benefits



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Many Nutrient Deficiencies Contribute to Mitochondrial Dysfunction *



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Supplemental Sources of Sulfur*

- glucosamine sulfate
- chondroitin sulfate
- glutathione
- N-acetylcysteine
- alpha lipoic acid
- taurine
- DMSO, MSM
- S-adenosylmethionine (SAME)
- Epsom salts (Mg-sulfate)

These can have many beneficial effects and are nearly nontoxic

My personal favorite is Epsom salt baths:
Magnesium sulfate uptake through the skin

*S Parcell, Alternative Medicine Review 7(1), 2002, 22-44

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Foods High in Niacin (B3) → NAD(P)(H)

- Many foods are rich in niacin (B3), especially animal products like meat, fish and poultry.
- Vegetarian sources include avocado, peanuts, whole grains, mushrooms, green peas and potatoes.



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Riboflavin (B2): Source for FAD in Flavoproteins

Foods high in riboflavin (B2) include beef, tofu, milk, fish, mushrooms, pork, spinach, almonds, avocados, and eggs



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DDW, Glacier Water and Hydrogen Water



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Flavonoids and Polyphenols!



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Treating Glyphosate Poisoning in Cows*

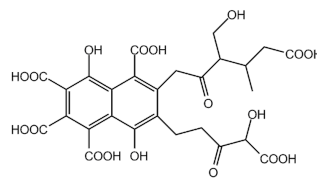


Sauerkraut Juice

Activated charcoal, bentonite clay, humic and fulvic acids, and sauerkraut juice have been shown to be effective in reducing urinary levels of glyphosate and improving animal health



Bentonite Clay



Fulvic Acid



Activated Charcoal

*H Gerlach et al., J Environ Anal Toxicol 2014, 5:2

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Go Organic!

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Summary

- The herbicide glyphosate is pervasive in our food supply, and it is far more toxic than our regulators are willing to admit
- Glyphosate's mechanism of toxicity is unique, and it likely involves substituting for the amino acid glycine by mistake during protein synthesis in susceptible proteins
- Glyphosate disrupts sulfation and methylation pathways, which results in mitochondrial dysfunction due to excessive deuterium accumulation
- Mitochondria exposed to too much deuterium become dysfunctional, spewing out reactive oxygen species and producing insufficient ATP
- Collagen traps deuterium in proline residues, but is highly susceptible to glyphosate toxicity
- Many modern diseases are associated with mitochondrial dysfunction