

**Description**

Acetaldehyde, glycolysis, TCA cycle flux and other mitochondrial matrix NADH generators (not shown - see Figure 17) decrease the mitochondrial NAD+ pool and increase NADH pool sizes.

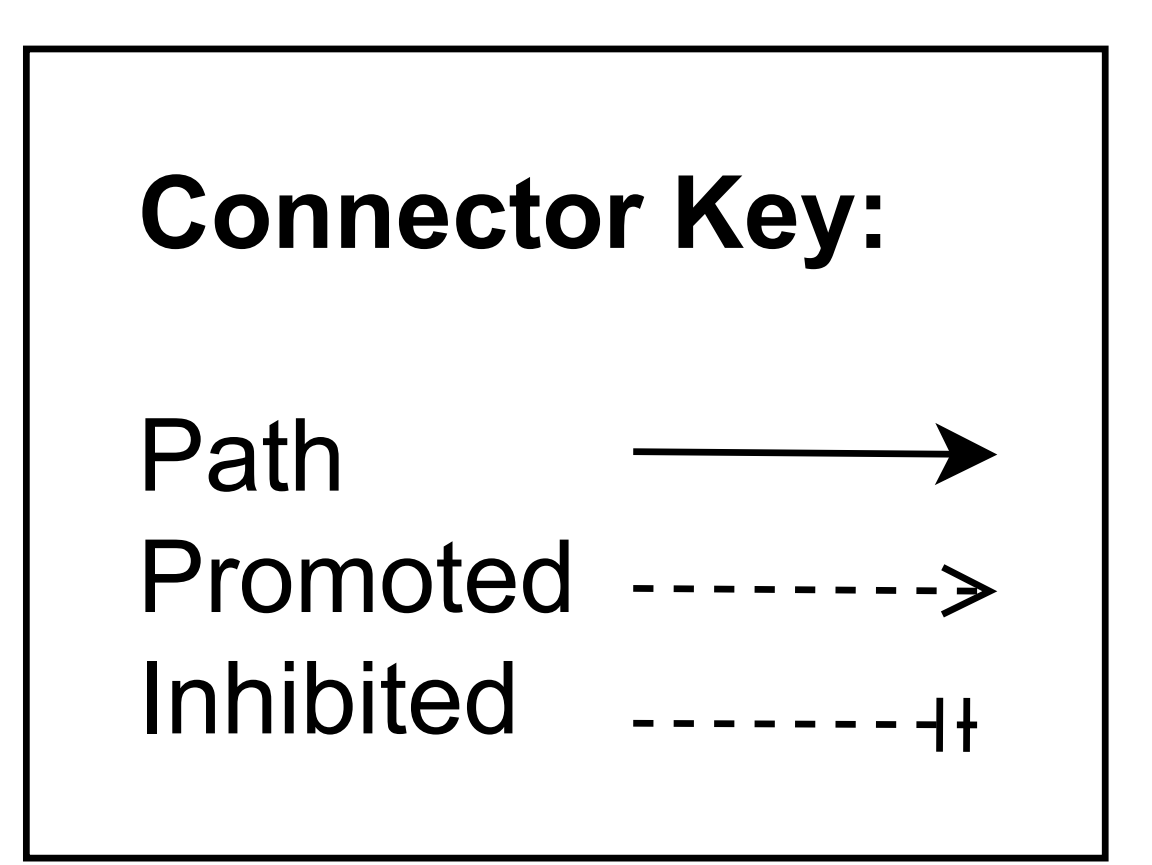
Complex I (NADH Dehydrogenase) normally balances NAD+:NADH redox, however is inhibited by reactive oxygen and nitrogen species, generated by mitochondrial activity and additionally by uncoupled NOS and NOX activity - promoted by interferon signalling cascades and acetaldehyde directly.

As Mitochondrial Complex I is progressively inhibited, proportional NADH pool elevation inhibits TCA cycle substrate pathways, whilst GDH + NADPT activity is increased, increasing glutamate and NADPH, thereby promoting regulatory glutathione peroxidase and reductase activity - unless inhibited by low glycine, cysteine, FAD, total NADP:NADPH pool size and/or excess heavy metals.

Methylene blue concentrates in the mitochondrial matrix, providing a narrow therapeutic window for creating a parallel electron pathway to Cytochrome c and NAD+ redox support.

**Ag** - Silver  
**α-KGDH** - Alpha-Ketoglutarate Dehydrogenase  
**ALDH** - Aldehyde Dehydrogenase  
**ADP** - Adenosine Diphosphate  
**ATP** - Adenosine Triphosphate  
**Au** - Gold  
**cAMP-PKA** - Cyclic Adenosine Monophosphate - Protein Kinase A  
**Cd** - Cadmium  
**CD38** - Cluster of Differentiation 38 (NAD<sup>+</sup> glycohydrolase)  
**CDR** - Cell Danger Response  
**COMPLEX I** - NADH:Ubiquinone Oxidoreductase  
**DHAP** - Dihydroxyacetone Phosphate  
**DOPAL** - 3,4-Dihydroxyphenylacetaldehyde  
**eATP** - Extracellular Adenosine Triphosphate  
**FAD** - Flavin Adenine Dinucleotide  
**G3P** - Glycerol 3-Phosphate  
**GCL** - Glutamate-Cysteine Ligase  
**GLS** - Glutathione Synthase  
**GPD** - Glycerol-3-Phosphate Dehydrogenase  
**GPx** - Glutathione Peroxidase  
**GR** - Glutathione Reductase  
**GDH** - Glutamate Dehydrogenase  
**GHB** - gamma-Hydroxybutyrate  
**GSH** - Glutathione, Reduced  
**GSSG** - Glutathione, Oxidised (Disulfide)  
**H<sub>2</sub>O** - Water  
**H<sub>2</sub>O<sub>2</sub>** - Hydrogen Peroxide  
**Hg** - Mercury  
**IDH** - Isocitrate Dehydrogenase  
**IDO1** - Indoleamine 2,3-Dioxygenase 1  
**IFN** - Interferon  
**LDH** - Lactate Dehydrogenase  
**LPA** - Lipoamide  
**MB<sup>+</sup>** - Methylene Blue  
**MBH<sub>2</sub>** - Leucomethylene Blue  
**MDH** - Malate Dehydrogenase  
**Mo<sup>2+</sup>** - Molybdenum Ion  
**Mg<sup>2+</sup>** - Magnesium Ion  
**NAD<sup>+</sup>** - Nicotinamide Adenine Dinucleotide (oxidised)  
**NADH** - Nicotinamide Adenine Dinucleotide (reduced)  
**NADP<sup>+</sup>** - Nicotinamide Adenine Dinucleotide Phosphate (oxidised)  
**NADPH** - Nicotinamide Adenine Dinucleotide Phosphate (reduced)  
**NADPT** - NAD(P) Transhydrogenase  
**NMNAT** - Nicotinamide Mononucleotide Adenylyltransferase  
**NOS** - Nitric Oxide Synthase  
**NOX** - NADPH Oxidase  
**OxPPP** - Oxidative Pentose Phosphate Pathway  
**Pb** - Lead  
**P5P** - Pyridoxal 5-Phosphate  
**PDH** - Pyruvate Dehydrogenase  
**Pi** - Inorganic Phosphate  
**PRPP** - 5-Phosphoribosyl-1-Pyrophosphate  
**Q** - Ubiquinone  
**QH<sub>2</sub>** - Ubiquinol  
**ROS** - Reactive Oxygen Species  
**RNS** - Reactive Nitrogen Species  
**Se** - Selenium  
**TCA** - Tricaric Acid  
**THP** - Tetrahydropapaveroline  
**TPP** - Thiamine Pyrophosphate  
**UDP** - Uridine Diphosphate  
**UTP** - Uridine Triphosphate  
**Zn<sup>2+</sup>** - Zinc Ion

Low Serine (glycolysis, methylation), low Carnitine (fatty acid transport) and elevated 2-Hydroxybutyrate (branched-chain amino acids catabolism), orchestrating TCA cycle substrate pathway regulation / inhibition



**Figure 14. Pathway Diagram:** A simplified overview of mitochondrial NAD+: NADH deficiency.  
**ME/CFS: Correcting Chronic Mitochondrial Dysfunction**  
 Author: Joshua Leisk ©2026, <https://bornfree.life> [DRAFT / INCOMPLETE - may contain errors]