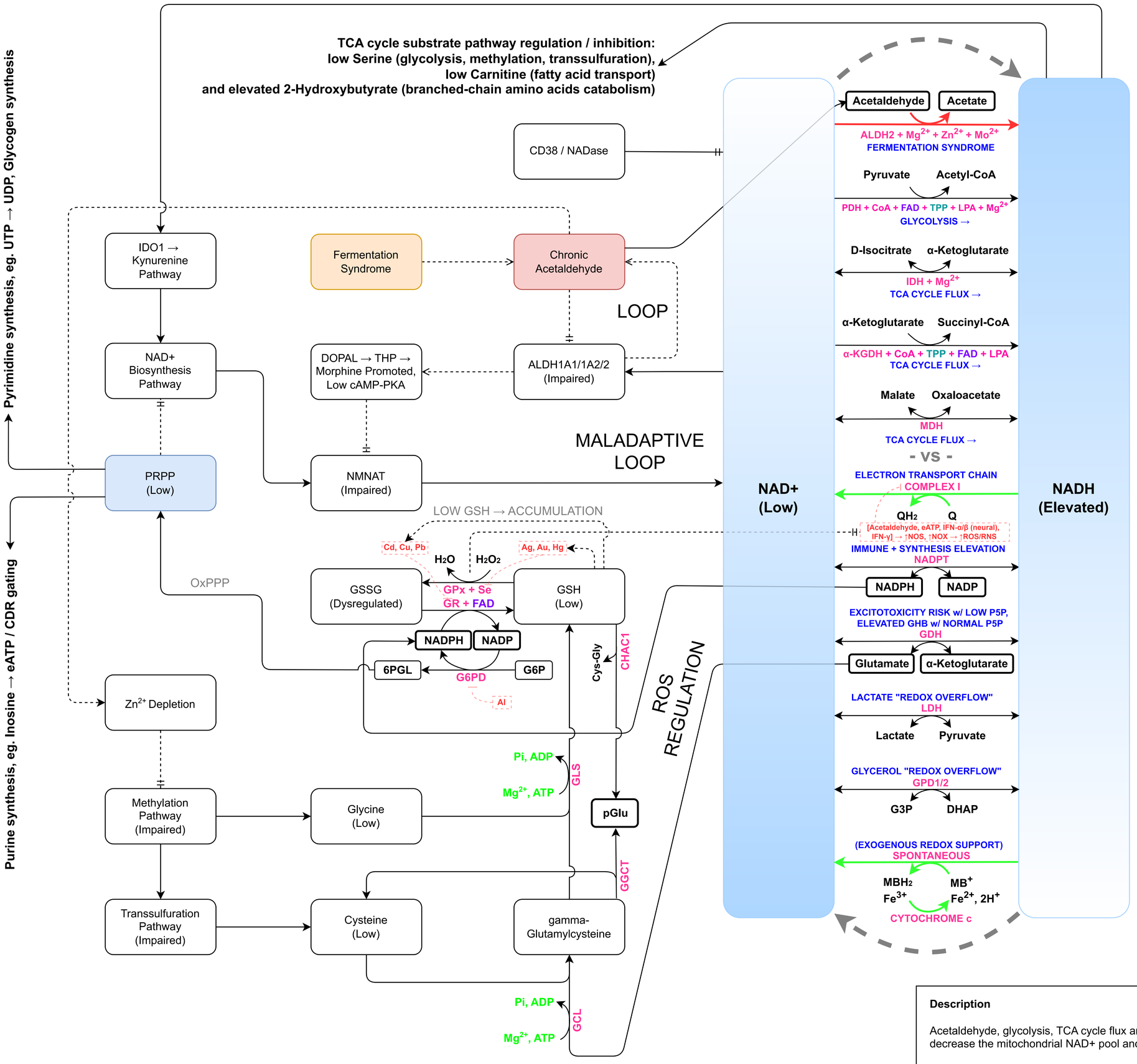

6PGL - 6-Phosphoglucono-δ-Lactone
Ag - Silver
Al - Aluminium
α-KGDH - Alpha-Ketoglutarate Dehydrogenase
ALDH - Aldehyde Dehydrogenase
ADP - Adenosine Diphosphate
ATP - Adenosine Triphosphate
Au - Gold
cAMP-PKA - Cyclic Adenosine Monophosphate - Protein Kinase A
Cd - Cadmium
CD38 - Cluster of Differentiation 38 (NAD^+ glycohydrolase)
CHAC1 - Glutathione-Specific gamma-Glutamylcyclotransferase 1
CDR - Cell Danger Response
COMPLEX I - NADH:Ubiquinone Oxidoreductase
Cys-Gly - Cysteinyl-glycine
DHAP - Dihydroxyacetone Phosphate
DOPAL - 3,4-Dihydroxyphenylacetaldehyde
eATP - Extracellular Adenosine Triphosphate
FAD - Flavin Adenine Dinucleotide
G3P - Glycerol 3-Phosphate
G6P - Glucose-6-Phosphate
G6PD - Glucose-6-Phosphate Dehydrogenase
GCL - Glutamate-Cysteine Ligase
GGCT - gamma-Glutamyl Cyclotransferases
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_2O - Water
H_2O_2 - Hydrogen Peroxide
Hg - Mercury
IDH - Isocitrate Dehydrogenase
IDO1 - Indoleamine 2,3-Dioxygenase 1
IFN - Interferon
LDH - Lactate Dehydrogenase
LPA - Lipoamide
MB^+ - Methylene Blue
MBH_2 - Leucomethylene Blue
MDH - Malate Dehydrogenase
Mo^{2+} - Molybdenum Ion
Mg^{2+} - Magnesium Ion
NAD^+ - Nicotinamide Adenine Dinucleotide (oxidised)
NADH - Nicotinamide Adenine Dinucleotide (reduced)
NADP - 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
P5P - Pyridoxal 5-Phosphate
Pb - Lead
PDH - Pyruvate Dehydrogenase
pGlu - Pyroglutamate
P_i - Inorganic Phosphate
PRPP - 5-Phosphoribosyl-1-Pyrophosphate
Q - Ubiquinone
QH_2 - Ubiquinol
ROS - Reactive Oxygen Species
RNS - Reactive Nitrogen Species
Se - Selenium
TCA - Tricitric Acid
THP - Tetrahydropapaveroline
TPP - Thiamine Pyrophosphate
UDP - Uridine Diphosphate
UTP - Uridine Triphosphate
Zn^{2+} - Zinc Ion

Connector Key:

Path →
Promoted -------->
Inhibited --------|

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]

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Description

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

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 synthesis and peroxidase, reductase activity - *unless* inhibited by low glycine and/or cysteine. Also from low Mg-ATP, Se, FAD, total NADP:NADPH pool size and/or excess heavy metals, where elevated pyroglutamate (pGlu) may also be observed.

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.