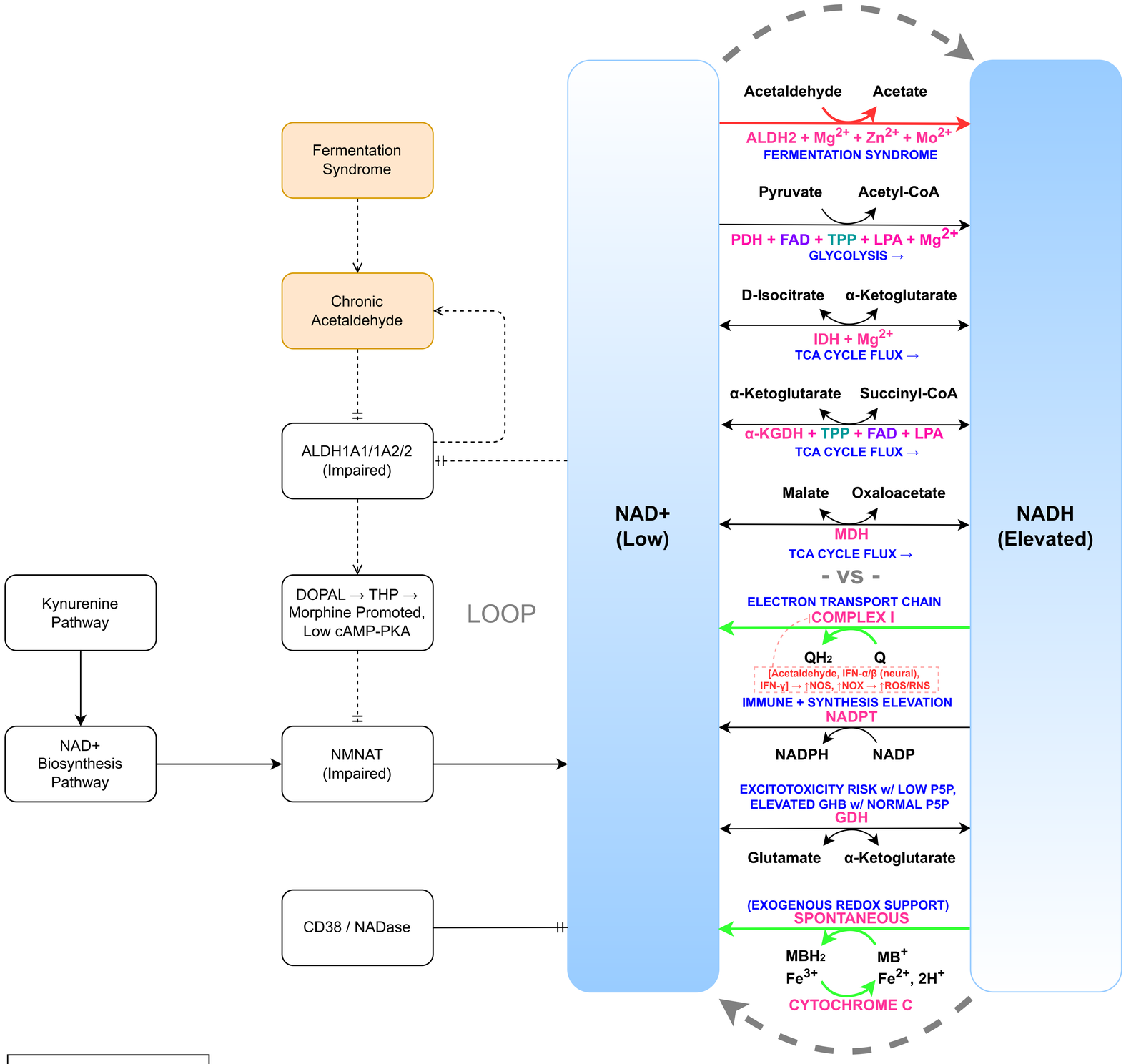

Description

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 this NAD+:NADH redox, however is inhibited by reactive oxygen and nitrogen species, primarily generated by uncoupled NOS and NOX activity - promoted by interferon signalling cascades and acetaldehyde directly.

Where Complex I is inhibited, GDH and NADPT activity is increased by the NADH pool elevation, further increasing glutamate and the NADPH pool, driving downstream activities.

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.

α-KGDH - Alpha-Ketoglutarate Dehydrogenase
ALDH - Aldehyde Dehydrogenase
cAMP-PKA - Cyclic Adenosine Monophosphate - Protein Kinase A
CD38 - Cluster of Differentiation 38 (NAD^+ glycohydrolase)
COMPLEX I - NADH:Ubiquinone Oxidoreductase
DOPAL - 3,4-Dihydroxyphenylacetaldehyde
FAD - Flavin Adenine Dinucleotide
GDH - Glutamate Dehydrogenase
GHB - gamma-Hydroxybutyrate
IDH - Isocitrate Dehydrogenase
IFN - Interferon
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
PDH - Pyruvate Dehydrogenase
P5P - Pyridoxal 5-Phosphate
Q - Ubiquinone
QH_2 - Ubiquinol
ROS - Reactive Oxygen Species
RNS - Reactive Nitrogen Species
TCA - Tricitric Acid
THP - Tetrahydropapaveroline
TPP - Thiamine Pyrophosphate
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

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