With insufficient NAD+ / elevated NADH and / or insufficiency of Mg2+ / Zn2+ / K+ / Cl-, HSD3B1,2 reactions have decreased activity.

Low activity / NADPH insufficiency downregulates the entire pathway, reverses HSD17B1,2,3,4 and AKR1C2,3,4. Exercise / resistance training promotes IFN-gamma. IFN-gamma promotes NADPH elevation.

Cortisol:cortisone senses low NAD+:elevated NADH, with elevated NADPH:low NADP. Cortisol release is triggered by limbic system response and/or low phosphatidylserine - sensing [low glucose / glycogen, low NAD+:elevated NADH | low P5P].
Cortisol promotes catabolic pathways and inhibits IFN-gamma, glycogen synthase, negatively regulating the IFN-gamma alterations.

The primary sex hormone (PSH) senses elevated NAD+:low NADH, with elevated NADPH:low NADP.

PSH inhibits cortisol, promoting IFN-gamma and glycogen synthase. PSH promotes anaplerosis to the TCA cycle at α-KG and promotes creatine synthesis via AGAT. Creatine promotes GLUT4 and glucose uptake.

These combined alterations increase flux through the TCA cycle, eventually converting nitrogen metabolites such as glutamate and glutamine into glycogen, enhancing glycogen storage and IFN-gamma activity.

Dietary input and exertion insufficiency dysregulates hormones, glycogen levels and IFN-gamma activity.

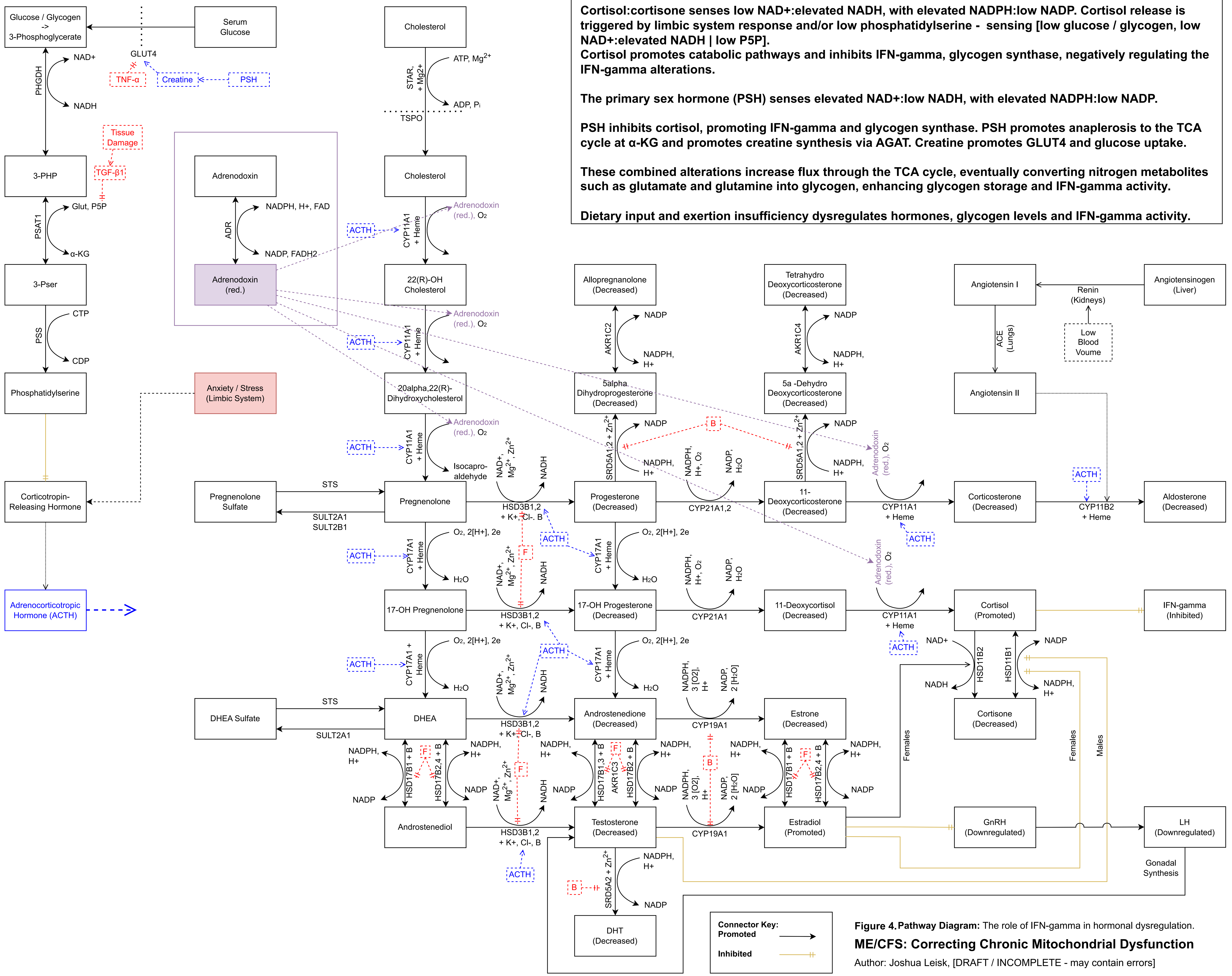

Figure 4. Pathway Diagram: The role of IFN-gamma in hormonal dysregulation.

ME/CFS: Correcting Chronic Mitochondrial Dysfunction

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