Biological Nanomechanics: ATP Synthesis and Deuterium Depletion

At ~1 deuterium/6600 protons natural abundance the ATP synthase protein nanomotor may break down in every few seconds without effective deuterium depleting biochemical processes through glycolysis and the TCA cycle. This talk explains how deuterons damage mitochondrial ATP synthase nano-mechanics by severely compromising proton on-off loading onto the Asp61 C-protein residue of the FO rapidly (9000/min) rotating nano-motor subunit. This is based on the ~1500 proton/second transfer velocity of the rotating protein. Alike, there are deuterium-induced isotope effects caused by its low dissociation constant from asparagine and its high mass to co-regulate the TCA cycle by malate dehydrogenase during oxaloacetate formation. This is because in malate dehydrogenase there are also Asp168 and several arginine residues that participate in proton binding, stabilization and transfer reactions. The inherent complexities of glycolysis and the TCA cycle is explained by their primary role in deuterium depletion, as well as multiple exchanges with metabolic water in the cytoplasm coming from the mitochondrial matrix. In simple terms glycolysis acts as a metabolic "dryer" to rip off all extracellular and extramitochondrial deuterium and hydrogen atoms from glucose, while the TCA cycle acts as a metabolic "washer" by adding hydrogen atoms back from low deuterium metabolic matrix water to specific carbons to be oxidized in the TCA cycle. Therefore, natural ketogenic substrate oxidation via deuterium depleted matrix water production becomes a critical resource for mitochondrial health. On the other hand, the Warburg effect and serine oxidation with glycine cleavage (SOGC) are deuterium loading alternative energy producing pathways and are the result of excessive deuteronation of the mitochondrial matrix and intermembrane space. In conclusion, excessive deuterium loading is involved in isotopic breakdowns of ATP synthase, malate dehydrogenase and thus TCA cycle nanomechanics, which require mitochondrial repairs with important adaptive changes in cellular metabolism. These may produce the Warburg effect for lactate efflux due to insufficient pyruvic acid oxidation, even in the presence of oxygen at intolerable deuterium levels in diseased mammalian cells. The talk offers mechanisms how deuterium becomes an oncoisotope and how global warming, for example, may be a contributor to increased cancer incidence worldwide due to limited deuterium fractionation during water cycling in Nature.

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