Metabolic protonation of matrix water entails deuterium depletion for mitochondrial health via Eigen and Zundel type hydronium complex formation: medical implications

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Hydronium is the aqueous cation (H_3O^+) produced by the protonation of bulk water (H_2O) and it is the positive ion present when protons (positively charged hydrogen ions; H^+) are added to surrounding water molecules [1]. The mitochondrial matrix is such highly protonated compartment from food deriving excess protons, especially at ATPase proton discharge sites, that it must first form hydronium cations to transiently anchor in and physically alter as many as four surrounding metabolic water shells [2]. Although it has previously been shown that positively charged excess hydrogen ions readily transform bulk metabolic water to hydronium-based Eigen- (H_3O^+) and Zundel-type ($H_5O_2^+$) cation complexes, the vastly altered proton solvation, tunneling and mobility patterns of the highly-structured matrix water shell have not yet been interpreted in connection with the morphology and function of mitochondria found in mammalian cells. Such interpretations are timely because several studies found two to four hydronium-solving water layers that differ from bulk water [3-6] due to the almost doubled values for hydrogen bond enthalpies (strengths) at protonated sites. The Eigen- and Zundel-type structuring of matrix water provides new insights into the fundamental physical force behind continuous proton harvesting and oxygen consumption during metabolic water formation with its rapid recycling from less protonated solvation shells by mitochondrial hydratases of the tricarboxylic acid cycle. While molecular-dynamics simulations have successfully been applied to determine hydrogen-bond strengths in bulk (liquid) water for the past, more recent simulations performed for protonated water open new doorways to medical interpretations of mitochondrial proton harvesting, water producing, structuring and recycling functions, where apparently only structured water layers are present, as revealed by inelastic incoherent neutron scattering studies [2]. Proton tunneling and mobility patterns in hydrogen-bonding water solvation shells are greatly limited by both hydronium and deuteron substitutions [5, 6]. Therefore, as these cations readily alter the viscosity and structure of interfacial hydration shells their critical influence on mitochondrial ATP synthesis; hence on cellular health, needs thorough additional investigations [7]. For example, the linear correlation of hydrogen bond strengths with lengths suggests that the enthalpy (strength) of an Eigen type hydrogen bond is 18.4 kJ/mol [6], as compared with only 10.6 kJ/mol in bulk water, which are based on Raman measurements [8, 9]. This talk discusses proton mobility in matrix water that is intimately connected with the surrounding hydrogen bonding pattern with emphasis on the excessive kinetic isotope effects of deuterium substitutions [5] in structured hydrogen bonding water shells with broad translational and medical implications.

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