DEUTERIUM DEPLETED WATER ALTERS GLUCOSE-DERIVED FATTY ACID AND CHOLESTEROL SYNTHESIS OF TUMOR CELLS

L.G. Boros1,2, A. Kochevarov1, I. Szigeti1, S.T. Lee1, G. Jancso3, Gy. Jáklí3, G. Somlyai4
1SIDMAP, LLC; 2UCLA School of Medicine, Los Angeles, CA, USA; 3Central Research Institute for Physics, Atomic Energy Research Branch; 4HYD Ltd., Budapest, Hungary

INTRODUCTION

- Deuterium (HD) is the heavy stable non-radiating isotope of hydrogen (H) that carries one extra neutron in the atomic nucleus. Therefore, deuteron's atomic mass is twice that of H.
- Hydrogen atoms of water participate in virtually all ion exchange and substrate transport reactions through the cell membrane and hydrogen also acts as the reducing equivalent in energy producing as well as reductive macromolecular synthesis reactions in all living cells. Deuterium is also involved in epigenetic events (changes in gene activity that are not caused by changes in the DNA sequence).
- Deuterium depletion of water in cell culture media or body fluids temporarily decreases cell growth in vitro and induces tumor regression in vivo.
- The exact mechanism and the effects of deuterium depletion on mammalian cell intermediary metabolism are not fully known.

HYPOTHESES

- Deuterium incorporation from common water into DNA increases its fragility thus accelerates mutations, aging and cancer.
- Deuterium affects the kinetics of reductive synthesis and the generation of NADPH thus altering membrane fatty acid and cholesterol synthesis.
- Deuterium alters tricarboxylic acid cycle and intermediary metabolism by altering carbon flow and the rate of product synthesis and energy production.
- Deuterization of DNA with adjacent nuclear membrane structures is an important epigenetic event directly involved in driving oncogenesis to alter gene suppression, replication and growth.

AIM

- To determine metabolic flux-modifying effects of deuterium-depleted water (DDW) in 100, 50 and 25 ppm as compared to normal deuterium-containing water (150 ppm) on [2,3-13C]-glucose metabolism in cultured mammalian MIA-PaCa-2 (H-441) and breast (MCF-7) ductal carcinoma cells.

METHODS

- After 72 hours of incubation with the [2,3-13C]-D-glucose tracer in DDW we analyzed its uptake and contributions to lactate production, glycolytic RNA, ribose, glycogen, cholesterol and long chain fatty acid synthesis as well as TCA cycle glutamate and 13CO2 release using GCMS.

RESULTS & CONCLUSIONS

- Metabolic profiles of tumor cells after 72 hours of 100% DDW treatment

- Deuterium-depleted water (DDW) did not significantly alter glucose uptake, oxidation and glycolytic synthesis in any of the cell lines (Figure 1).
- Pyruvate cycle flux relative to glycolysis decreased in MIA-PaCa cells (Figure 2).
- RNA glucose synthesis and turnover also decreased in MIA-PaCa cells after 25 ppm treatment (Figure 3).
- TCA cycle substrates flux decreased in MCF-7 breast tumor cells (Figure 4).
- Lignocerate (C24) and palmitate synthesis were decreased in MIA-PaCa cells and cholesterol synthesis was decreased in MCF-7 breast tumor cells (Figure 5).

- Based on this data decreased deuterium to hydrogen ratios regulate stored and fatty acid precursor synthesis, which likely affects the rate of division and cellular proliferation via the regulation of reductive synthesis and new membrane formation.
- Deuterium depletion in cytoplasmic water may control cancer formation similarly by decreasing intracellular matrix metabolic water use for reductive synthesis, which is the natural intracellular deuterium depletion mechanism to control epigenetic DNA methylation as the time requiring event during oncogenesis for mammalian cells.
- Deuterium depletion in water and food may have a well-defined role in cancer prevention and to improve public health.