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


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## INTRODUCTION

- Deuterium ($^2H$) is the heavy stable non-radiating isotope of hydrogen ($^1H$) that carries one extra neutron in the atomic nucleus. Therefore deuterium's atomic mass is ~ twice of that of $^1H$.
- Hydrogen atoms of water participate in virtually all ion exchange and substrate ←→ product transport reactions through the cell membrane and hydrogen also acts as the reducing equivalent in energy producing as well as reductive macromolecule 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 decelerates 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 know.

## 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 $NADP^+$ 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.
- Deuteration of DNA with adjacent nuclear membrane structures is an important epigenetic event directly involved in driving oncogenesis to alter gene expression, replication and growth.

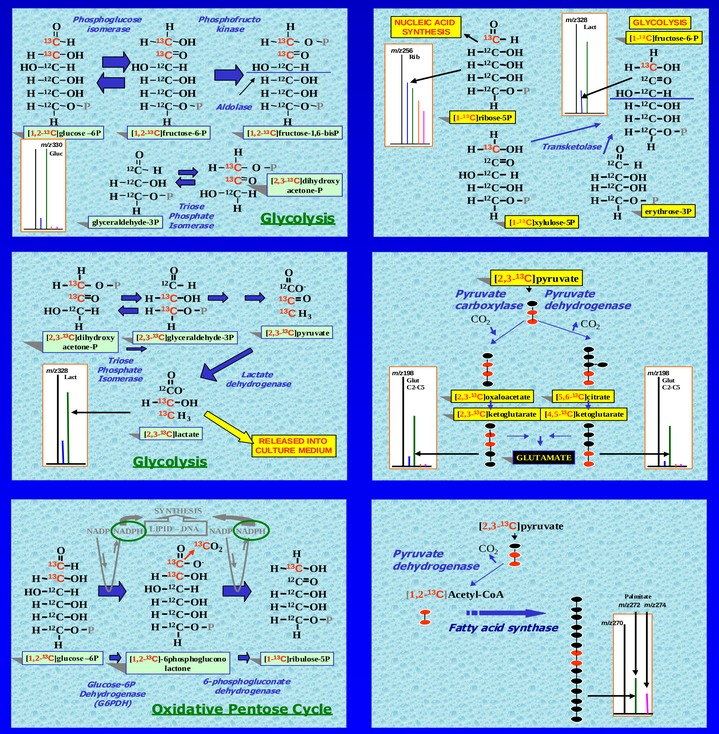
## AIM

- To determine metabolic flux-modifying effects of deuterium depleted water (DDW: 100, 50 and 25 ppm) as compared to normal deuterium-containing water (150 ppm) on [1,2-$^{13}C_2$]-D-glucose metabolism in cultured pancreatic (MIA-PaCa), lung (H-441) and breast (MCF-7) ductal carcinoma cells.

## METHODS

After 72 hours of incubation with the [1,2-$^{13}C_2$]-D-glucose tracer in DDW we analyzed its uptake and contributions to lactate production, glycolysis, RNA ribose, glycogen, cholesterol and long chain fatty acid synthesis as well as TCA cycle glutamate and $^{13}CO_2$ release using GC/MS.

## $^{13}C$ LABELED GLUCOSE INTERMEDIARY METABOLISM - MACROMOLECULE SYNTHESIS




## RESULTS & CONCLUSIONS

Metabolic profiles of tumor cells after 72 hours of DDW treatment

**Figure 1**

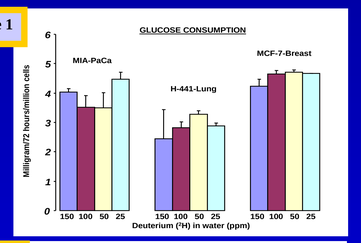



**Figure 4**

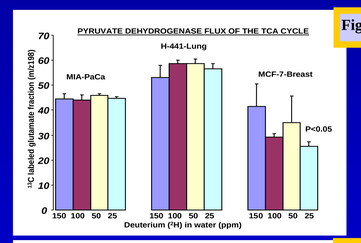



**Figure 2**

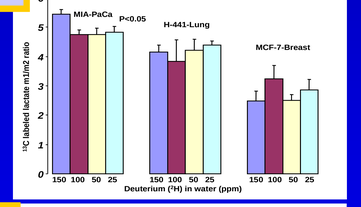



**Figure 5**

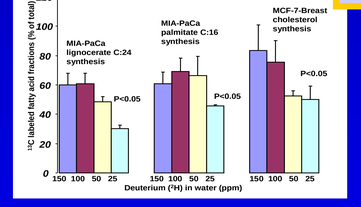
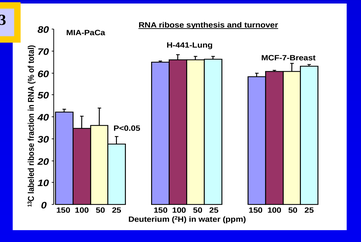



**Figure 3**




- Deuterium depleted water (DDW) did not significantly alter glucose uptake, oxidation and glycogen synthesis in any of the cell lines (Figure 1).
- Pentose cycle flux relative to glycolysis decreased in MIA-PaCa cells (Figure 2).
- RNA ribose synthesis and turnover also decreased in Mia-PaCa cells after 25 ppm treatment (Figure 3).
- TCA cycle substrate flux decreased in MCF-7 breast tumor cells (Figure 4).
- Lignocerate (C:24) and palmitate syntheses 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 sterol and fatty acid precursor synthesis, which likely affects the rate of divisions and cellular proliferation via the regulation of reductive synthesis and new membrane formation.
- Deuterium depletion in cytoplasmic water may control cancer formation similarly as low deuterium containing mitochondrial matrix metabolic water use for reductive synthesis, which is the natural intracellular deuterium depleting mechanism to control epigenetic DNA deuteration 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.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LITERATURE: *In Vivo*. 2000, 14(3): 437-9.; *FEBS Lett.* 1993, 317(1-2): 1-4.



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