Deuterium Magnetic Resonance Can Detect Cancer Metabolism by Measuring the Formation of Deuterated Water

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Cancer is typically diagnosed and evaluated using positron emission tomography with radiolabeled fluorodeoxyglucose, or [^{18}F]FDG-PET. The use of radioactive isotopes prevents its serial use in staging cancer progression or in the pediatric population. *Magnetic resonance imaging (MRI) is not often recognized as a metabolically-sensitive technique, but with the addition of stable isotopes, like deuterium, the chemical selectivity of MR allows for quantitative assessment of metabolic flux, important for distinguishing cancerous cells from normal cells to understand cancer progression*.

Researchers cultured cells in media containing [$^2H_7$]glucose to compare metabolism in healthy liver hepatocytes to metabolism in a hepato-carcinoma cell line (HUH-7). Figure 1 (top) shows the metabolic pathways in glycolysis that produce deuterated water (HDO). Using ^{1}H (bottom-left) and ^{2}H (bottom-right) NMR spectroscopy, researchers monitored the production of deuterated lactate and HDO from the glucose. *The signal from natural abundance HDO is observed at the beginning of the experiment with the signal increasing as deuterated glucose is consumed*.

Metabolism can be assessed by imaging the highest intensity peak in the spectrum, offering an optimal signal-to-noise ratio. This initial data suggests that HDO production could therefore be used as a surrogate for glucose uptake, which is the metric measured in FDG-PET diagnoses of cancer. *The difference is that MRI achieves this measurement without exposing the patient to radioactive isotopes*.

Facilities/Instrumentation: MagLab's AMRIS Facility: 14.1T NMR with a high sensitivity 1.7mm cryoprobe and Avance Neo Console.

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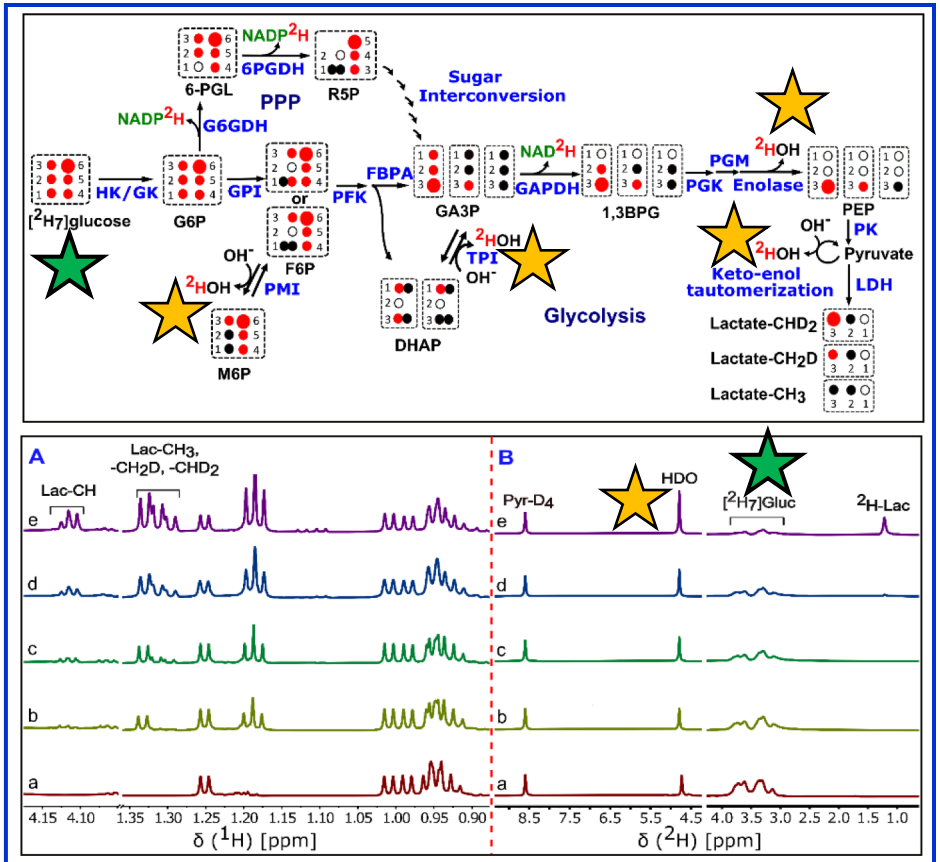

Figure 1. (top) *Metabolism pathways of [$^2H_7$]glucose (green stars), with red dots marking the presence of ^{2}H, and larger dots indicating two ^{2}H atoms. Note that HDO (gold stars) can be produced at multiple steps in the glycolytic pathway. (**bottom, left**) ^{1}H NMR spectra showing the production of deuterated lactate as detected in the ^{1}H spectrum; (**bottom, right**) ^{2}H NMR spectrum showing glucose consumption (green star), resulting in HDO production (gold star).*