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Hyperpolarized ^{13}C Metabolic Imaging: A New Way to Look at Cancer

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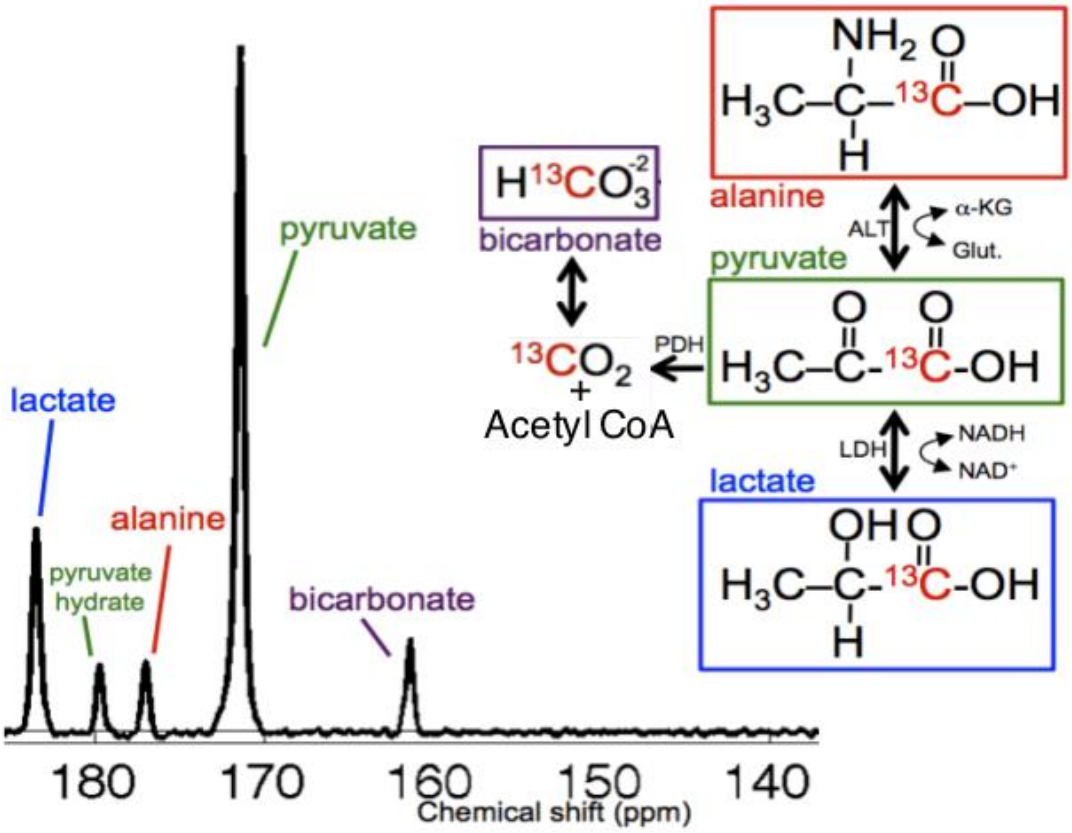
With a growing interest into cancer metabolic reprogramming, new research targets local metabolic activity to improve our ability to characterize the disease. For example, one of the hallmarks of cancer is the so-called Warburg effect, i.e., the fact that tumor cells preferentially use glycolysis to generate energy at the expense of the more efficient pathway of oxidative phosphorylation, even in the presence of oxygen. Therefore, imaging techniques that inform about the metabolic phenotype of a tumor would present an important tool for cancer diagnosis, treatment monitoring, and prediction of response to therapy.

The relatively recent development of hyperpolarized ^{13}C metabolic imaging provides unprecedented opportunities for real-time observation of in vivo metabolic pathways critical to the identification and evaluation of cancer. This magnetic resonance imaging (MRI)−based method relies on a process called dissolution "dynamic nuclear polarization" (DNP) that amplifies the MRI signal of a compound by multiple orders of magnitude. This is a complex process that involves mixing with an electron donor and microwave irradiation at very low temperatures (about 1 Kelvin) in a strong magnetic field (3 to 5 Tesla). Most of the natural abundance carbon is MRI-invisible (^{12}C, almost 99%). Therefore, compounds are used that are specifically enriched (to over 99%) in ^{13}C, which is also a stable, i.e., non-radioactive, isotope, but MRI-visible. These ^{13}C-labeled compounds behave like their "normal" ^{12}C counterparts in biochemical and enzymatic reactions. After subjecting the ^{13}C-compound to the DNP process, the frozen compound is dissolved by a hot liquid and converted into an injectable solution while maintaining the high level of polarization. However, after dissolution the signal amplification starts to decay with a time constant on the order of tens of seconds, depending on the respective compound. This leads to a short duration of only 1-2 minutes where the signal is high enough to be observed in the MRI scanner. Therefore, after removal of the electron donor, the hyperpolarized substrate solution has to be quickly transferred and injected into the patient already lying in the MRI scanner. Injected compounds and metabolic products can then be differentiated based on their specific MRI signature (see Figure). This property makes it such a powerful modality and an advantage over radionuclide-based imaging techniques such as positron emission tomography (PET) or single-photon emission computed tomography (SPECT).

The most widely used compound is [1-^{13}C]pyruvate, which sits at the junction of the key pathways of aerobic and anaerobic metabolism. It can be used to assess energy metabolism within normal and tumor tissue, highlighting critical changes during disease. Besides application in cancer, hyperpolarized ^{13}C metabolic imaging is currently being investigated in other pathologies such as cardiovascular disease, liver disease, and traumatic brain injury.

Figure: Pyruvate metabolism and in vivo ^{13}C spectrum from a rat heart following the injection of hyperpolarized [1-^{13}C]pyruvate. Pyruvate and its metabolic products, [1-^{13}C]lactate, [1-^{13}C]alanine, and ^{13}C-bicarbonate, are easily visualized. A small fraction of the [1-^{13}C]pyruvate is in equilibrium with metabolically inactive [1-^{13}C]pyruvate hydrate.



For Further Reading:

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