A Tale of Two Sugars: ^{13}C NMR Study of Glucose and Fructose Metabolism in Glioblastoma Cells

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Increased dietary consumption of sugar has been implicated in a number of clinical pathologies, including obesity and other metabolic diseases. High fructose corn syrup, a sugar mixture of about 40% glucose and 60% fructose, is a ubiquitous sweetening additive in a number of drinks and food.[1] In this study, we have investigated the metabolism of these two types of sugar in glioblastoma cells, specifically the aggressive SfXL cell line. ^{13}C NMR spectroscopy was used in this study due to high specificity courtesy of the wide chemical shift dispersion of carbon-13. Glioblastoma multiforme (GBM), or cancer of the glial cells, is a highly aggressive and mostly chemoresistant form of brain cancer with very dismal chance of survival.[2] The goal of this study was to investigate the metabolism of fructose and glucose in glioblastoma, given the ubiquity of these two sugars in Western diet.

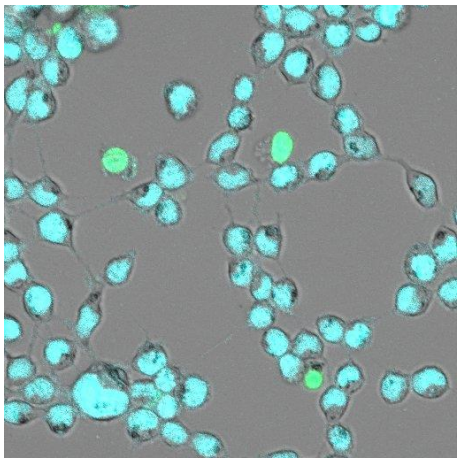

Fig. 1 Confocal image (20x) of SfXL glioblastoma cells stained with live (magenta) and dead (green) fluorescent dyes.

SfXL cells (see confocal image in Fig. 1) were cultured and propagated in 15cm petri dishes with DMEM and FBS media. The cells were incubated in 5% CO2 environment at 37 deg C. 5 mM [1-^{13}C]glucose was administered to the cultured cells with different incubation times, ranging from 10 mins. to 48 hrs. In a similar manner 5 mM [1-^{13}C]fructose (in the presence or absence of unlabeled glucose in the media) was added to cell dishes with different incubation times of the ^{13}C substrate. The cells were then harvested when the dishes were 90-95% confluent. Perchloric acid (PCA) extraction of the cells were done and neutralized with NaOH. The cell extracts were lyophilized for 2-3 days and the resulting powders were re-suspended in D_2O. 200 µL aliquots of these D_2O solutions were used for NMR measurements in a Bruker Avance III HD 600 MHz system at UT Dallas.

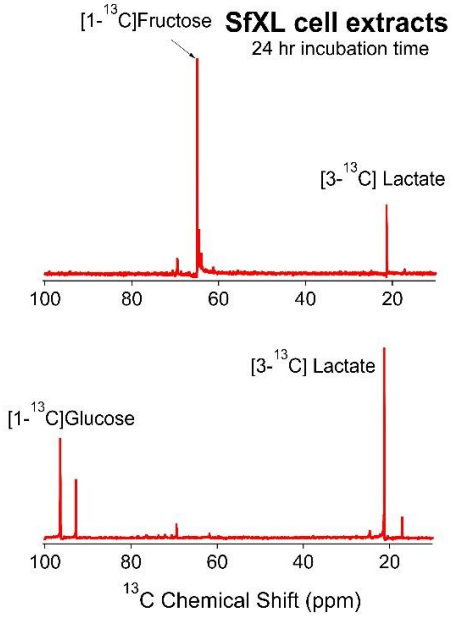

Fig. 2 Representative ^{13}C NMR spectra of cell extracts of SfXL glioblastoma cells incubated with [1-^{13}C]fructose and unlabeled glucose (top) and [1-^{13}C]glucose (bottom). These NMR data were taken at 14.1 T and 37 deg C.

The main finding of this preliminary work is that, despite the same caloric content of these two sugars, fructose and glucose metabolized quite differently in brain cancer cells. In the absence of glucose in the media, there was no indication of metabolism of [1-^{13}C]fructose in SfXL cells. In the presence of unlabeled glucose in DMEM, we have observed metabolism of [1-^{13}C]fructose into [3-^{13}C]lactate (see Fig. 2). However, lactic acid production rate from [1-^{13}C]fructose is found to relatively slower compared to lactic acid production from [1-^{13}C]glucose. Metabolic kinetics of these two sugars will be discussed, as well as results of co-administered ^{13}C-fructose and ^{13}C-glucose will be presented.

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