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Comparison of targeted and untargeted Stable Isotope Resolved Metabolomics (SIRM)

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Recently ^{13}C-labeled tracers have been incorporated into metabolomic studies to complement the conventional ^{1}H NMR-based metabolomic studies that result in concentration profiles of metabolites. These Stable Isotope Resolved Metabolomics (SIRM) studies produce comprehensive metabolic data that unequivocally quantifies whether the metabolite concentrations changes discovered in conventional metabolomic studies are due to increased or decreased pathway production. Cell culture is an ideal biosystem to apply this relatively new methodology because all major substrates in the central compartment (i.e., media) and tissue can be quantified, and thus accounting for all input and output to the biosystem. Cultured hepatocytes prove especially useful in demonstrating the effectiveness of untargeted SIRM because their normal function is to create glucose under fasted conditions, and thus consumption rates for glucose are often ambiguous based on concentration data alone since the carbon source could be a multitude of compounds found in the media. The comparison of rat and human cultured hepatocytes will be discussed using several ^{13}C-labeled substrates added to the media, in order to elucidate the metabolome of these two species' liver cells in 2D culture (Winnike et al., 2011). A strategy for targeted metabolomics will be described using a human cell model for resistance chronic myelogenous leukemia, the Myl and Myl-R cell lines. In this approach, an initial conventional ^{1}H NMR-based metabolomic analysis of Myl and Myl-R cells revealed that creatine is 7-fold higher in the resistant cell-line, MylR (Dewar et al., 2010). Glycine is a substrate for creatine, and therefore, 2-^{13}C-glycine was used in a targeted SIRM study to elucidate the mechanism of increased creatine in the Myl-R, and propose a potential mechanism of chemoresistance.

Biography

Jeff Macdonald's research is focused on metabolism and the liver is the primary organ performing this function. Magnetic resonance spectroscopy (MRS) is the most powerful, non-invasively biochemical imaging modality to monitor metabolism. In 2002, he founded what is now the Hamner-UNC Metabolomic Core Facility. A broad spectrum of mammalian tissue has been studies by conventional 1H NMR-based metabolomics with a focus on incorporating stable isotopes for targeted and untargeted flux analysis that complements the concentration data. In 2006, he started his comparative metabolism research effort, shifting from vertebrate to marine invertebrates and co-found the Marine MRI facility at the NCSU Center for Marine Science and Technology at Morehead City, NC.