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Magnetic resonance metabolic analysis provides targets for suitable drugs and biomarkers for prognosis to targeted signaling inhibitors on cancer

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We are exploring metabolic information obtainable from nuclear magnetic resonance (NMR) and mass spectrometry (MS) to correlate cellular and tumor response to targeted signaling inhibitors. ^{13}C NMR and MS of mantle cell lymphoma cells after incubation with ^{13}C -labeled glucose or glutamine provided isotope enrichment of several key metabolites. The enrichment information was converted to metabolic fluxes including glycolysis, pentose phosphate pathway, TCA cycle, glutaminolysis and *de novo* fatty acids synthesis, by using a novel bonded cumomer metabolic flux analysis. The alteration in metabolic fluxes following signaling inhibitors correlated with changes in associated gene expression as analyzed from RNA sequencing data. There was a four-fold decrease in glycolysis in RL cells vs a two-fold decrease in Jeko cells after same amount of ibrutinib, a Bruton tyrosine kinase inhibitor. Also, there was a two-fold decrease in glutaminolysis in RL cells while no change in Jeko cells. *De novo* fatty acids production decreased by two-fold in RL cells vs no change in Jeko cells. The results suggest metabolic targets of additional drugs for ibrutinib-resistant Jeko cells. The glucose uptake decreased similarly in both RL and Jeko cells after ibrutinib while there was a two-fold difference in lactate production change between RL and Jeko cells. This result suggests lactate as a promising marker of the tumor response to this signaling inhibitor. It is particularly significant because FDG-PET has been failing to distinguish responding patients from non-responding patients at interim scans during treatment. We have developed a novel ^1H magnetic resonance spectroscopy (MRS) lactate imaging technique for cancer patients and pursuing its application to detecting response to signaling inhibitor therapy in lymphoma patients.

Biography:

Dr. Lee is a research assistant professor of the department of radiology, University of Philadelphia. He obtained PhD from department of physics, KAIST, Korea and had postdoc training in *in vivo* NMR of cells and tumors from Korea Basic Science Institute and University of Pennsylvania. His research focus is NMR/MRI based metabolic investigation of cancer in cells, animal models and human patients for the purpose of detecting early therapeutic response to novel targeted drugs. He is a recipient of ACS-IRG, ITMAT and McGahey research funds.