Seung-Cheol Lee, Madridge J Cancer Stud Res. 2017
http://dx.doi.org/10.18689/2640-5180.a2.002

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

Seung-Cheol Lee
Department of Radiology, School of Medicine, University of Pennsylvania USA

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 productiondecreased 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 ^{1}H 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 McGaberesearch funds.