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^{18}O-assisted ^{31}P NMR and mass spectrometry: From phosphometabolomics to fluxomics

Evaluation of metabolomics phenotypes requires knowledge not only in metabolite levels but also their turnover rates from which metabolic fluxes and status of the whole metabolic system can be deducted. In this regard, stable isotope 18O-based metabolite tagging technology provides quantitative measurements of metabolite levels and turnover rates of many metabolites which metabolism include water as a reactant, most notably phosphometabolites, amino and organic acids. Using this technology dynamics of over 10 major metabolic and signaling pathways can be tracked simultaneously, including ATP turnover, oxidative phosphorylation, glycolysis/glycogenolysis, Krebs and urea cycles pentose phosphate pathway and phosphotransfer reactions. The 18O labeling methodology is based on the incorporation of the 18O nuclei (from H218O), into metabolite group with each act of enzymatic reaction, and subsequent distribution of 18O-labeled groups among different molecules. Using this approach major metabolites and their turnover rates can be quantified in cells and tissue samples and whole blood by 18O-assisted 31P NMR and 1H NMR spectroscopy and mass spectrometry. In this way obtained dynamic metabolomics profile appears to be sensitive indicator of energy and metabolic imbalances like the ones created by genetic deficiencies, myocardial ischemia, heart failure, aging and neurodegenerative disorders. Thus, 18O-assisted 31P NMR/mass spectrometry is a valuable tool for phosphometabolomic and fluxomic profiling of transgenic models of human diseases revealing system-wide adaptations in metabolic networks, as well as for biomarker identification in human diseases and metabolic monitoring of treatment efficacy and drug toxicity.

Biography

Petras Dzeja has completed his PhD from Kaunas Medical University, Lithuania and Postdoctoral studies from Department of Biochemistry, University of Minnesota, Minneapolis, USA. He is the Co-director of Metabolomics NMRS Core, at Mayo Clinic, Rochester, a world renown Medical Center. He has developed ^{18}O-assisted ^{31}P NMR and mass spectrometric phosphometabolomics technology and pioneered phosphotransfer network, phosphometabolomics and system bioenergetics concepts. He has published more than 80 papers in reputed journals and has been serving as a Editorial Board Member of PLOS ONE as a metabolomics expert.

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