Research & Reviews: Journal of Pharmaceutical Analysis

Short Communication

Vol. 9, Iss. 3

2020

Mass Spectrometry Congress 2019: Swath mass spectrometry as a tool for quantitative profiling of the bone marrow plasma from alcoholic liver disease - Renu Goel - Translational Health Science and Technology Institute, India

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Alcoholic hepatitis is characterized by acute or acute-on-chronic hepatic failure and associated with a high mortality. Specific therapies should be considered for those at high risk of mortality. Model for End-Stage Liver Disease (MELD) score is a marker of disease severity and mortality in persons with chronic alcoholic liver disease. Author's aim is to find out a diagnostic biomarker for disease severity along with the MELD score which can be used as a predictor of short term mortality in persons with alcoholic hepatitis. Understanding molecular pathogenesis is pivotal in managing the disease. They employed sequential window acquisition of all theoretical mass spectra (SWATH-MS) to seek crucial proteins involved in disease progression. Bone marrow plasma is taken from chronic liver disease patient as a part of stem cells therapy clinical trial. In this study, a quantitative proteomic of bone marrow plasma with low and high MELD scores were compared with normal bone marrow plasma from non-cirrhotic portal hypertension patient whose liver function test was normal using a SWATHMS strategy. In total, 232 proteins were differentially expressed in all groups. 17 proteins are down regulated and 81 up regulated in patients with MELD score <15 with control. Moreover, 37 proteins are down regulated, 59 up regulated while comparison of MELD score >15 with control. Inhibition of coagulation, complement and intrinsic prothrombin pathways are revealed by functional analysis. Humoral immune response, immune cell trafficking and inflammation pathways are enriched under physiological system development. Proteins preliminarily discovered in this study may be associated with dysregulation bone marrow microenvironment during disease progression. To the author's knowledge, this study presents the most complete view of bone marrow plasma in low and high MELD score, identifying hundreds of differentially expressed proteins, which together form a rich resource for novel drug targets or diagnostic biomarker discovery.

SWATH MS is a method of independent data acquisition (DIA) that aims to complement traditional proteomics techniques based on mass spectrometry, such as shotgun and SRM methods. Essentially, it allows a complete and permanent recording of all fragment ions of detectable peptide precursors present in a biological sample. It thus combines the advantages of the shotgun (high speed) with those of the SRM (high reproducibility and consistency). SWATH MS is able to quantitatively analyze the matrisome in unenriched and ECM enriched tissues. SWATH MS provides more reproducible coverage of the matrisome compared to DDA MS. Quantitative analysis by SWATH MS reveals that the lung has a higher matrisomal protein content than the liver. In the DIA acquisition setup, the mass spectrometer

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cycles through the cycle time in 2-4 seconds through a set of precursor acquisition windows designed to cover 400-1200 m / z as a whole mass range easily covered by a quadrupolar mass analyzer and into which most of an

organism's tryptic peptide precursors fall. During each cycle, the mass spectrometer thus fragments all the precursors of the quadrupole isolation window (e.g. 475-500 m / z for 25 Da wide windows) and records a full and high precision ion spectrum of all the precursors selected in this isolation window.

Alcoholic liver disease is the result of overconsumption of alcohol which damages the liver, leading to fat build-up, inflammation, and scarring. It can be fatal. The disease is a major cause of chronic liver disease in Western countries. In the human body, liver is the one of the most complex organs. These include filtering toxins from the blood, storing energy, making hormones and proteins, and regulating cholesterol and blood sugar. Liver damage can affect the whole body. Once the damage begins, it can take a long time to become noticeable, as the liver is usually very efficient at regenerating and repairing itself. Often, by the time the damage is noticed, it is irreversible.

Alcoholic liver disease is the leading cause of chronic liver disease in Western countries and the third most common cause of liver transplantation. Refraining from drinking alcohol is the only way for a person to recover. Treatment options include medications, lifestyle changes, and surgery. The recommended daily limits are no more than one drink per day for women and no more than two drinks per day for men. The first signs of alcoholic liver disease are vague and affect a range of systems in the body. In addition to feeling generally unwell, the signs may include: pain in the abdomen; nausea and vomiting; diarrhea and decreased appetite. The most distinctive signs of advanced liver disease are: jaundice, or a yellow tinge of the whites of the eyes and skin; edema or swelling of the lower limbs; a buildup of fluid in the abdomen, known as ascites; fever and chills; extremely itchy skin; nails that curl excessively, known as clubbing; lose a significant amount of weight; general weakness and muscle wasting; blood in vomit and stool; bleeding and bruising more easily and reactions more sensitive to alcohol and drugs.

Once a person is diagnosed with alcoholic liver disease at any stage, it is recommended that they never start drinking again. Any conditions that have reversed will usually return once drinking is restarted. Since alcohol dependence can make it more difficult to stop drinking alcohol, it is necessary to gradually reduce alcohol consumption. Those who regularly drink more than the recommended daily alcohol limit should not stop drinking without medical assistance. Withdrawing from alcohol can be life threatening. People should seek the help of a healthcare professional to safely manage alcohol withdrawal. The recommended daily limits are no more than one drink per day for women and no more than two drinks per day for men. Cognitive behavioral therapy (CBT) and drugs called benzodiazepines can be used to relieve withdrawal symptoms in someone who is alcoholic. People with severe alcohol dependence may stay in an inpatient

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rehabilitation facility for closer monitoring. Continuous treatment may then be necessary to prevent a relapse into alcohol consumption. Medicines such as acamprosate, naltrexone, topiramate, baclofen, and disulfiram can also be used to prevent relapses.

Biography:

Renu Goel has obtained her M.Tech and PhD degree in Biotechnology from Institute of Bioinformatics, India with Prof. Akhilesh Pandey, Johns Hopkins University, Maryland. Her research group is working on identifying pathways or proteins involved in early stages of progression of diseases such as type II diabetes, liver diseases and dengue fever by using proteomics, metabolomics and bioinformatics approaches. She has also worked on draft map of human proteome published in Nature. During this period she has published around 30 research articles in high impact factor international journals. She is an Editorial Board Member for many journals.

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