High precision isotopic analysis of Cu in a murine model with induced-liver cirrhosis

Marta Costas-Rodríguez[1], Lindsey Devisscher[2], Hans Van Vlierberghe[2] and Frank Vanhaecke[1*]

[1] Ghent University, Department of Analytical Chemistry, Krijgslaan 281 – S12, 9000 Ghent, Belgium
[2] Ghent University Hospital, Department of Gastroenterology and Hepatology, De Pintelaan 185-1K12IE, BE-9000 Ghent, Belgium

Contact: frank.vanhaecke@ugent.be

Abstract

High-precision isotopic analysis of Cu is providing valuable clinical information on liver diseases, such as end-stage liver disease (ESLD) and hepatocellular cancer [1-2]. The Cu isotopic composition in serum is substantially lighter in liver cirrhosis patients and a link between the severity of the disease and the δ^{65}Cu value, a finding that could be useful in the context of prioritization of liver transplants, was observed. In a follow-up study of ESLD patients after liver transplantation, a generalized normalization of the Cu isotopic composition towards the reference value was found for patients that recover normal liver function [3].

In this work, Cu isotopic composition was studied in a murine model with induced-liver cirrhosis to reveal the role of Cu in liver disease and identify the factors governing the δ^{65}Cu values. Liver cirrhosis was induced in mice via common bile duct ligation. Isotopic analysis was performed using multi-collector ICP-mass spectrometry in serum and livers of cirrhotic mice and in a healthy age-matched population. Significant Cu isotopic variations were observed between the cirrhotic mice and the reference population, both in serum and liver. These differences were about 1‰. A good correlation was observed between the serum and the bilirubin level, indicative of the degree of the disease. These results evidence that impaired bile excretion and hepatocellular dysfunction is accompanied by Cu isotope fractionation towards the light isotope.

[1] M Costas-Rodríguez, Y Anoshkina, S Lauwens, H Van Vlierberghe, J Delanghe, F Vanhaecke, Metallomics, 2015, 7, 491-498

[2] V Balter, A Nogueira da Costa, V Paky Bondanese, K Jaouen, A Lamboux, S Sangrajrang, N Vincent, F Fourel, P Télouk, M Gigou, C Lécuyer, P Srivatanakul, C Bréchot, F Albarède, P Hainaut, Proc Natl Acad Sci USA., 2015, 112, 982-985

[3] S Lauwens, M Costas-Rodríguez, H Van Vlierberghe, Frank Vanhaecke, Sci Rep, 2016 (Submitted)