

Determination of copper poisoning in Wilson's disease and other metal dysbalances using laser ablation inductively coupled plasma spectrometry (LA-ICP-MS)

R. Weiskirchen

Institute of Molecular Pathobiochemistry, Experimental Gene Therapy and Clinical Chemistry, RWTH University Hospital Aachen, Germany

Wilson's disease (WD) is an autosomal recessive disorder occurring in about 1 in 30,000 people due to mutations in the Wilson disease (*ATP7B*) gene. Affected persons build up extensive copper accumulates in the body. The main accumulation and storage sites of copper are liver and brain. We have previously introduced novel LA-ICP-MS techniques for quantitative imaging of various metals in tissue obtained from experimental WD models or clinical samples from WD patients (Boaru *et al.*, *J Cell Mol Med* 2015;19:806-14; Weiskirchen and Uerlings, *Cell Mol Med: OA* 2015;1:3). These innovative metal imaging techniques have extended the repertoire of analytical possibilities in WD diagnosis. Here optimized and extended these studies and show that the accumulation of copper in the brain of *Atp7b* null mice is majorly found in special regions, while hepatic copper is distributed uniformly within the liver. Gene therapy in *Atp7b* null mice with an AAV8 vector expressing a codon-optimized version of the *Atp7B* gene directed under control of the α 1 antitrypsin promoter resulted in a massive reduction of hepatic and cerebral copper as assessed by LA-ICP-MS (Moreno *et al.*, *J Hepatol*, in press; Uerlings *et al.*, submitted). These data highlight the fact that LA-ICP-MS technology is one of the most powerful and sensitive techniques allowing simultaneous imaging and quantification of various trace metals with good sensitivity in experimental WD models. The applicability of the LA-ICP-MS technology in the diagnosis of WD, other metal-associated disorders, or potential future applications in experimental research and clinical daily routine will be discussed.