

## Isotopic metallomics of aging mice

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The metallome, including metal concentrations and isotopic compositions, is suspected to be variable during lifetime having thus the potential for capturing some specificities of ageing. The way and extent the metallome is related to deregulations linked to ageing is however poorly understood. Here, we have measured a suite of trace element concentrations as well as Cu and Zn isotope compositions in organs (liver, muscle, kidney, brain and heart) at different time points (6, 16 and 24 months) of ageing mice. The mice were also characterized by phenomics, metabolomics and transcriptomics analysis. We show that changes in Cu concentration and isotope composition in the body are correlated to ageing. These chemical variations are associated with cellular pathways involving lipids metabolism, among others pathways, and result in subsequent observed phenotypes. Altogether, the results show that the Cu isotope composition is potentially a new relevant biomarker that recapitulates the metabolic activity at a given time point during lifetime.