Isotopic signatures of biometals: from the whole body to sub-cellular fractions

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Isotopic signatures of biometals are currently of interest as novel or complementary tools for diagnosis/prognosis of diseases and for achieving a better understanding of metal metabolism [1,2]. While the serum Cu isotopic signature has been shown to be valuable for diagnosis and prognosis of liver diseases [1], serum Fe isotope ratio variations are suitable for monitoring Fe overload/deficiency diseases [1]. The exact processes underlying *in vivo* isotope fractionation are not well understood, but *in vitro* and *in vivo* studies using cell cultures and murine models, repectively, are providing deeper insight into the isotope fractionation observed in human biofluids. Isotopic signatures of Mg and Cu have been addressed in human serum for a diagnostic perspective and in biofluids and organs of murine models and in *in vitro* studies using cell cultures (Cu) for unraveling the factors contributing to a deviating isotopic signature. Patients suffering from type 1 diabetes (T1D) showed a light Mg isotopic signature compared to that of the reference population, potentially associated to the administered insulin or inherent biological traits of T1D. Cu isotope fractionation was statistically meaningful at the onset and during progression of cholestatic liver disease and non-alcoholic fatty liver disease. Also, alcoholic liver disease leads to an altered Cu isotopic signature in human serum and in compound-specific serum fractions. The severity of the ^{65}Cu depletion in the labile serum fraction of alcoholic cirrhosis patients seems to be affected by the extent of the labile Cu deregulation. Also in a neurological context, Cu isotopic analysis of neuron-like cells revealed that neuronal differentiation affects the Cu isotopic signature accompanying Cu uptake, but this effect does not seem to be associated with the mitochondrial Cu pathway.

References

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