The expression levels of cellular prion protein affect copper isotopic shifts in the organs of mice

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It is known that copper isotopic fractionations can occur in biological systems due to cellular assimilation, electron transfer processes, and protein formation. Recently, Buchl *et al* [1] reported that differences in the isotopic composition of brain tissues of transgenic mice were based on the expression of the cellular prion protein (PrP^c), a naturally occurring copper binding protein of importance in neurodegenerative disorders (eg. Alzheimer's disease).

In this study, we targeted specific organs where isotopic fractionation of copper could be affected by variations in PrP^c expression. The strains of mice include wild type (WT, n=4), PrP^c overexpressors (Tga20, n=4), prion knockout (*Prnp*-/-, n=3), and mice that had a mutation in the five copper binding sites (His->Ala) in the N-terminus of PrP^c (Cu-del, n=5). Copper isotopic composition ($\delta^{65}Cu$) of the intestinal tract, kidneys, liver, red blood cells, serum, and different functional regions of the brain were measured. Our results show that the isotopic shift between the food and the colon is significantly larger (ANOVA 0.023, $p<0.05$) in *Prnp*-/- and Cu-del mice compared to WT. In the brain, less of an isotopic shift is observed between the serum and the hippocampus (ave. 0.55 ‰), cerebral cortex (ave. 0.37 ‰), and brainstem (ave. 0.48 ‰) in *Prnp*-/- mice compared to Cu-del mice. Our results demonstrate that altered gene expression, in this case *Prnp*-/- and Cu-del, can affect the distribution of copper isotopes in the organs and bodily fluids of mice.

[1] Büchl, Hawkesworth, Ragnarsdottir, and Brown (2008), *Geochemical Transactions* **9**, 11-17.