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Natural copper isotope ratios in human blood serum as a potential biomarker for Alzheimer's disease

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Alzheimer's disease (AD) is a neurogenerative disease affecting nearly 58 million people worldwide. One of the main issues nowadays remains to diagnose the disease early enough for treatments to be intended. The search for new, early and innovative biomarkers is essential.

One of the main characteristics of AD is the accumulation of Aß-peptides forming amyloid plaques in the brain[1]. Amyloid plaques are highly concentrated in metals such as Cu, Zn and Fe[2]. Amyloid plaques are found in the brain but also in the cerebro-spinal fluid (CSF) and serum of AD patients. Previous studies have shown a significative difference in the isotope composition of Cu and Zn in the brain of AD patients[3] and of Cu in the CSF of AD patients[4].

Here, we are investigating the influence of AD on the isotope composition of Cu in human blood serum. Using the MC-ICP-MS Sapphire at IPGP, we measured the isotope compositions of 56 samples of human blood serum, both male and female (AD; n = 30, control; n = 26) from Hôpital Lariboisière and Australian Imaging, Biomarker and Lifestyle (AIBL) observational cohort. AD patients have a significatively lighter copper isotope composition compared to healthy controls (p-value = 0.02, Mann-Whitney test); respectively $\delta^{65}Cu$ = -0.27 (2sd = 0.85) and $\delta^{65}Cu$ = 0.02 (2sd = 0.67).

The same shift was measured by Moynier et al., in the brain of AD patients compared to healthy controls[3]. It suggests that Cu stable isotope ratios in the serum directly reflects the brain and could a good biomarker candidate for AD.

[1] Scheltens, Philip et al. **(**2021), *The Lancet,* 397, 1577 – 1590

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[3] Moynier et al., (2020), *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring, 12*, e12112

[4] Lahoud et al., (2024), submitted