Copper Isotope Metallomics and Amyotrophic Lateral Sclerosis

T. Gabriel Enge*[†1], Anthony Dosseto[‡1], Heath Ecroyd[2], and Dianne Jolley[3]

[1]Univ. Wollongong (UOW) – Northfields Avenue, School of Earth and Environmental Sciences, 2522 NSW, Australia
[2]Illawarra Health and Medical Research Institute (IHMRI) – Northfields Avenue, School of Biological Sciences, University of Wollongong, NSW, Australia
[3]Univ. Wollongong (UOW) – Northfields Avenue, School of Chemistry, 2522 NSW, Australia

Abstract

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease in which motor-neurons undergo progressive degeneration. Evidence indicates that ALS is a protein misfolding disorder [1]. Some forms of familial ALS are due to mutations in the Cu,Zn-superoxide dismutase 1 (SOD1) protein, causing it to misfold and accumulate into deposits within the cells. A reason why these mutations destabilise SOD1 could be that binding of Cu by SOD1 may become defective [2].

An early diagnostic biomarker for ALS is essential in developing future potential treatment options, since the pathology develops well before symptoms do. Our work uses a transgenic mouse model of ALS to evaluate whether changes to Cu metabolic pathways and metal concentrations in specific tissues are associated with the onset and progression of ALS and could be used as a biomarker of disease. We have collected tissue samples from transgenic mice (n=18) at key points during disease progression (30, 60, 90 and 120 days) as well as healthy controls (n=18) and measured the Cu isotope composition (δ65Cu) and Cu, Zn, Ni, Co and Fe concentrations in brain, spinal cord, whole blood and muscle tissue (quadriceps femoris).

Our results demonstrate that Cu, Fe and Zn concentrations in muscle tissue of ALS mice are significantly higher than in healthy mice. This is also the case for Cu in spinal cord. While there is no difference in Cu concentration in blood between these two groups, preliminary results for Cu isotopes suggest differences in the isotopic composition of blood between ALS and healthy mice, warranting assessment if blood could be used as an early disease-biomarker. We will present additional results, which should shed light on the links between Cu isotope metallomics and ALS disease progression.

Broom, et al. (2014) Essays Biochem 56, 149-65. [2] Hayward, et al. (2002) J. Biol Chem 227, 15923-31.

---

*Speaker
†Corresponding author: tge571@uowmail.edu.au
‡Corresponding author: tonyd@uow.edu.au