Iron isotopic compositions of wild types and hemochromatosis murine models

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The iron isotopic compositions of blood and tissues are significantly depleted in heavy isotopes relative to diet by about 1 to 3 ‰ in humans [1], mice, and sheep [2]. It has been suggested that Fe isotopic compositions in the body are modulated by intestinal absorption of dietary iron. Studying the bodily isotopic fractionation of iron might therefore shed new lights on intestinal metabolism dysregulations caused by iron disorders.

Genetic hemochromatosis (GH) is a disease related to the homozygous p.*Cys282Thyr* mutation in the *HFE* gene and characterized by iron overload in tissues. This mutation blunts the induction of hepcidin expression in response of iron excess. The subsequent Fe accumulations in organs, especially in liver, pancreas and heart may result in complications such as cirrhosis, liver cancer, diabetes and heart [3, 4]. Two studies showed that Fe isotopic composition of GH patients blood is enriched in heavy isotopes relative to healthy controls by about 0.4 to 0.6 ‰ [5, 6].

To our knowledge, the Fe isotopic compositions of tissues implied in GH, have not been measured yet. In this work, we analyzed the Fe concentrations and isotopic compositions of liver, spleen and RBC of wild-types (BALB/c, DBA/2 and AKR) mice as well as in C57BL/6 *Hfe-/-* mice compared to C57BL/6 littermates control. Our data shows that fractionation of Fe isotopes in organs of wild types mice is specific of a given strain. We discuss the organs Fe concentrations and isotopic compositions of the *Hfe*-/- mice and compare the observed distributions with wild types mice using mass balance approaches.

(1)Walczyk and von Blanckenburg (2002), *Science* 295, 5562, 2065-2066. (2)Balter et al. (2013), *Metallomics* 5, 1470-1482. (3)Brissot and Loréal (2016), *Journal of hepatology* 64, 505-515. (4)Brissot et al. (2018), *Nature Reviews Disease primer*s 4, 18016. (5)Stenberg et al. (2005), *Journal of trace Elements in Medecine and Biology* 19, 55-60. (6)Krayenbuehl et al. (2005), *Blood* 105, 3812-3816.