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## Copper stable isotope redistribution is regulated by gut bacteria in the gastrointestinal tract of mice (G)

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Stable isotope abundances vary in nature due to differences in zero-point energies of the binding site of a molecule upon isotopic substitution. This causes isotopes of an element to participate in reactions with different rates resulting in a redistribution of the isotopes in a system. Although the range in relative isotopic abundance of copper in natural materials is narrow, < 1.0%, current measurement techniques allow for quantification of changes as small as 0.01%. Recent attention is focussing on the redistribution of copper isotopes in biological systems.

The present study investigated the influence of gut bacteria on the redistribution of stable copper isotopes in the gastrointestinal tract of mice. Trillions of bacteria reside in our gastrointestinal tract and play an important role in energy homeostasis, protection against pathogens, nutrient metabolism, host immunity and intestinal barrier function. Here we compared the isotopic redistribution of copper isotopes in mice with gut bacteria significantly impacted by antibiotic consumption. A significant difference, ~0.1%, in copper isotope abundances was measured in the proximal colons of the gastrointestinal tracts of antibiotic-treated mice, indicating a drastic change in copper processing in this region when bacteria were eliminated. In order to investigate the mechanism of these changes we examined copper transporters in the epithelium as they have been shown to modulate the extent of isotopic redistribution<sup>1</sup>. Both CTR1, responsible for copper import, and ATP7A, responsible for copper efflux, were significantly down-regulated in antibiotic-treated mice. Down-regulation of these proteins in intestinal epithelial cells is associated with increased extracellular copper<sup>2,3</sup> and suggest that gut bacteria are influencing the amount of bioavailable copper to cells. These results highlight the relationship between gut bacteria and copper, both identified as having an important role in health.

References:

- 1 Cadiou, J., et al. (2017) Scientific reports 7, p. 44533.
- 2 Petris, M. J., et al. (2003) Journal of Biological Chemistry 278, p. 9639
- 3 Chun, H., et al. (2017) Scientific reports 7, p. 12001.

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