

Copper stable isotope redistribution is regulated by gut bacteria in the gastrointestinal tract of mice

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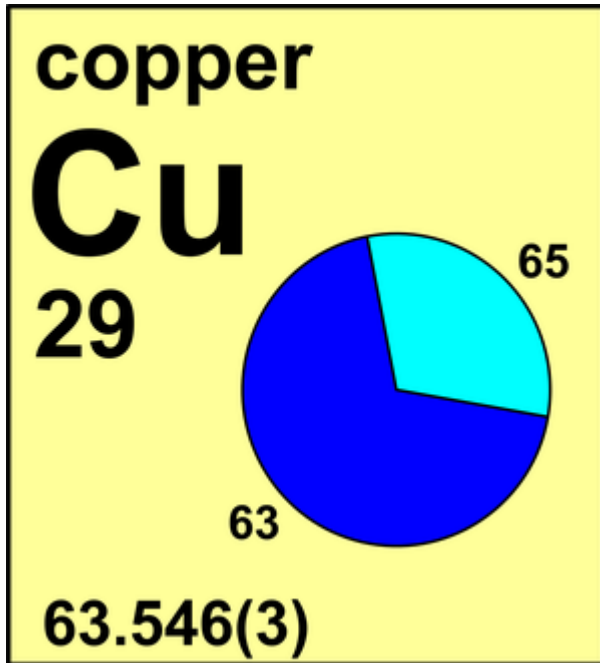
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Why study stable isotope composition?

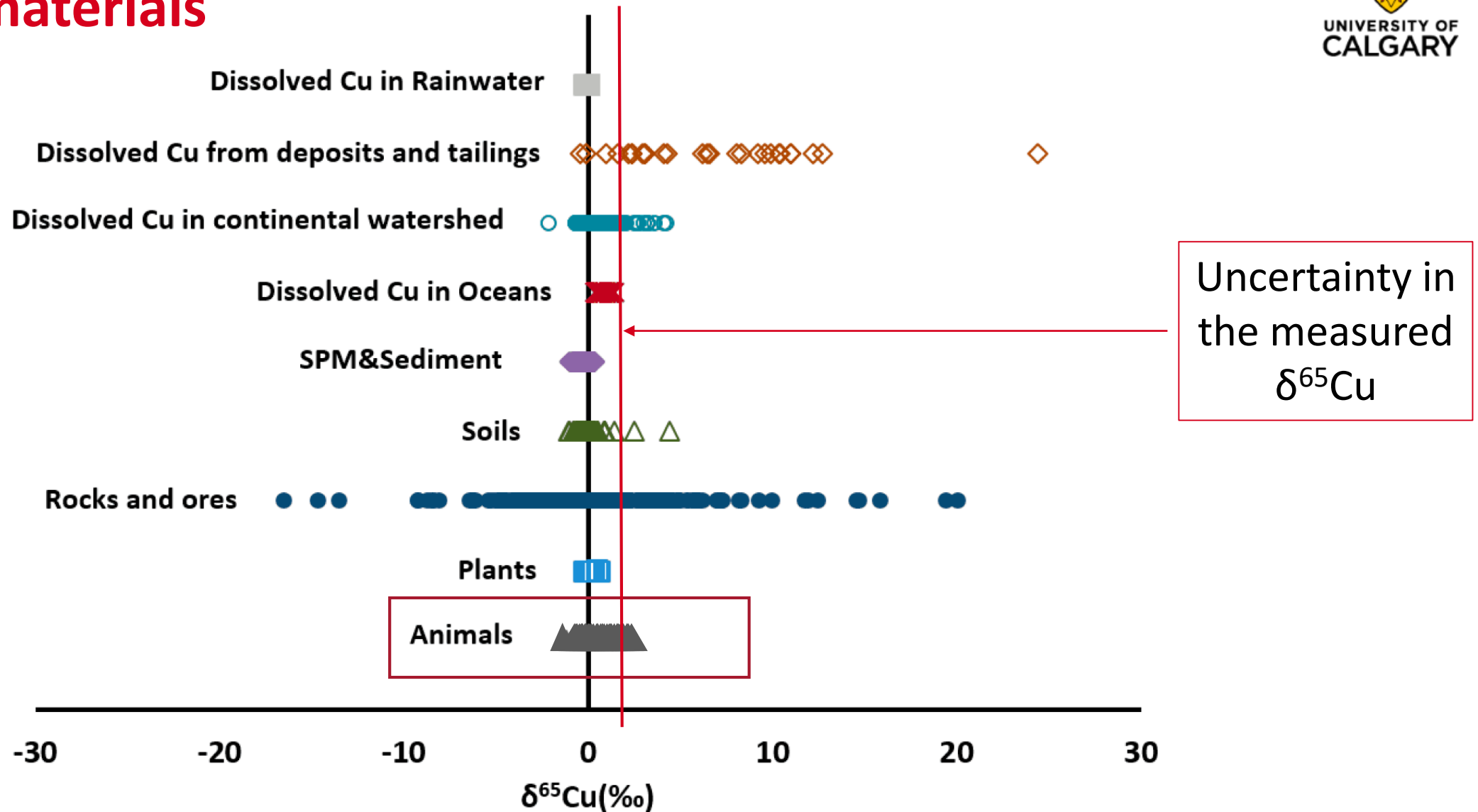


Source: <http://www.ciaaw.org/copper.html>

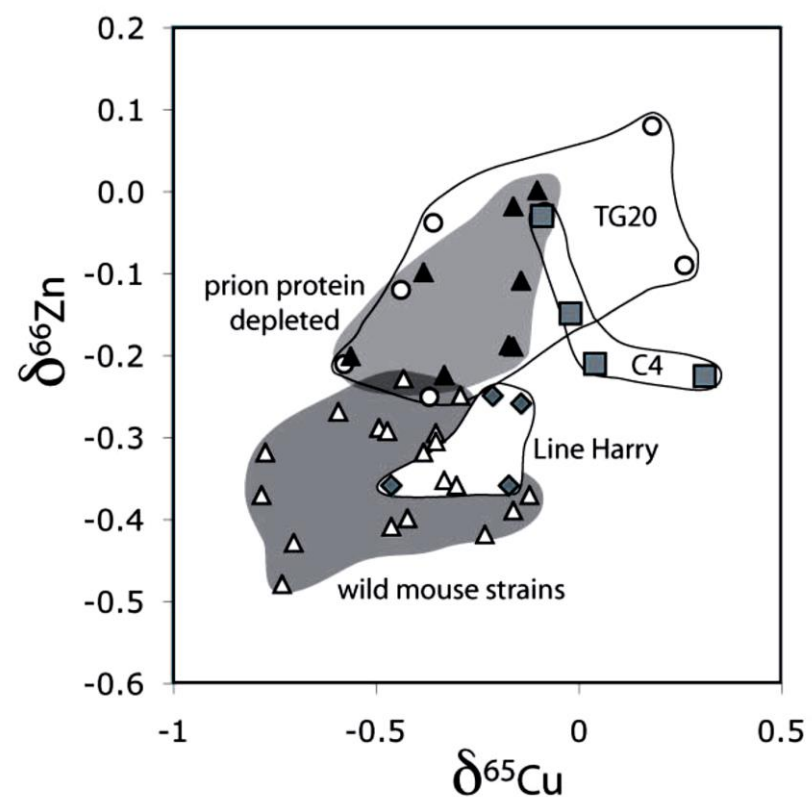
- Stable isotope composition varies in nature
- Can provide insights into the source and history of an element in a system

$$\delta^{65}\text{Cu} (\text{‰}) = \left(\frac{R_{\text{Sample}}}{R_{\text{Std}}} - 1 \right) * 1000$$

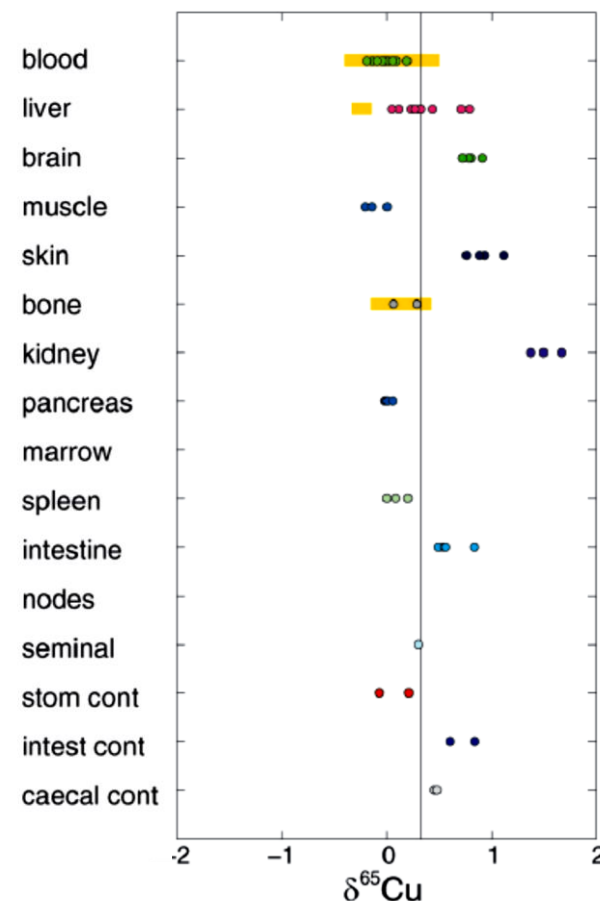
The observed variations in copper isotopic composition in natural materials



Copper isotopic composition to study metabolism

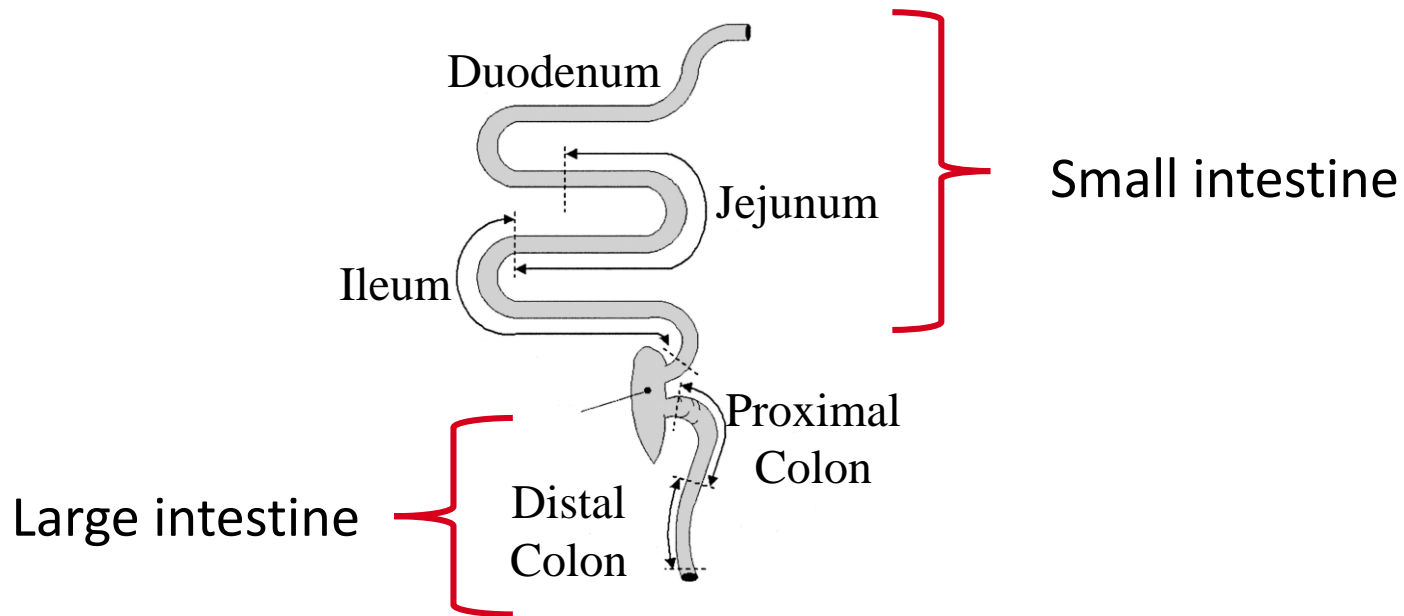


Source: Buchl et al, Geo. Chem. Trans. 2008 vol 9, p 11



Source: Balter et al, Metallomics, 2013 vol 5, p 1470

Investigate the influence of the gut microbiota on copper isotopic distribution

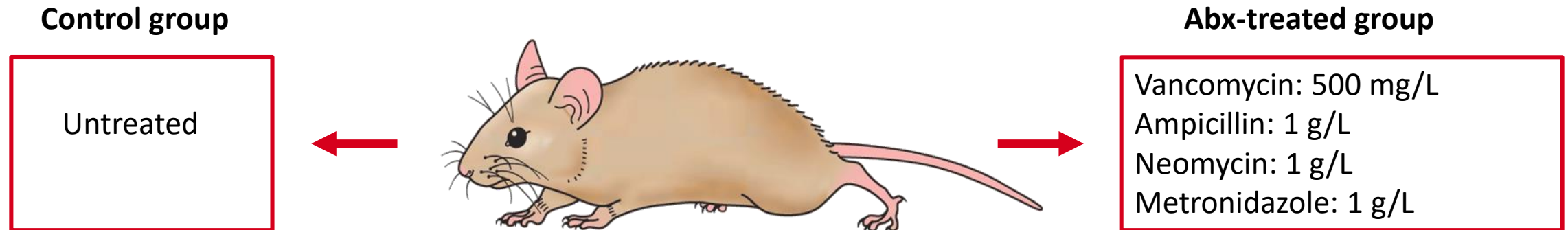


Advantages of investigating the intestines:

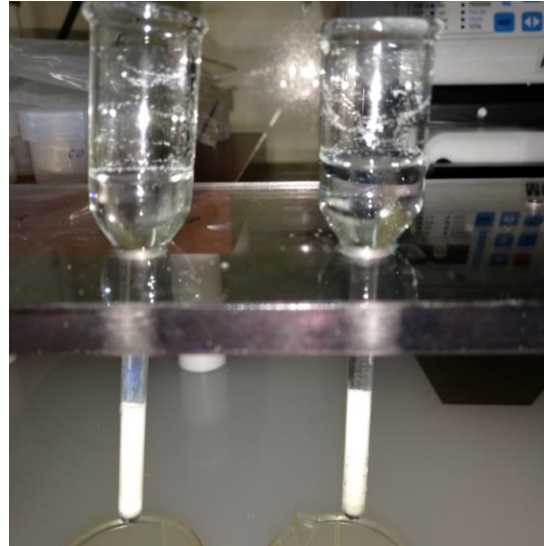
- First major interaction of dietary copper with the body
- Flow is unidirectional

The gut microbiome – “the forgotten organ”

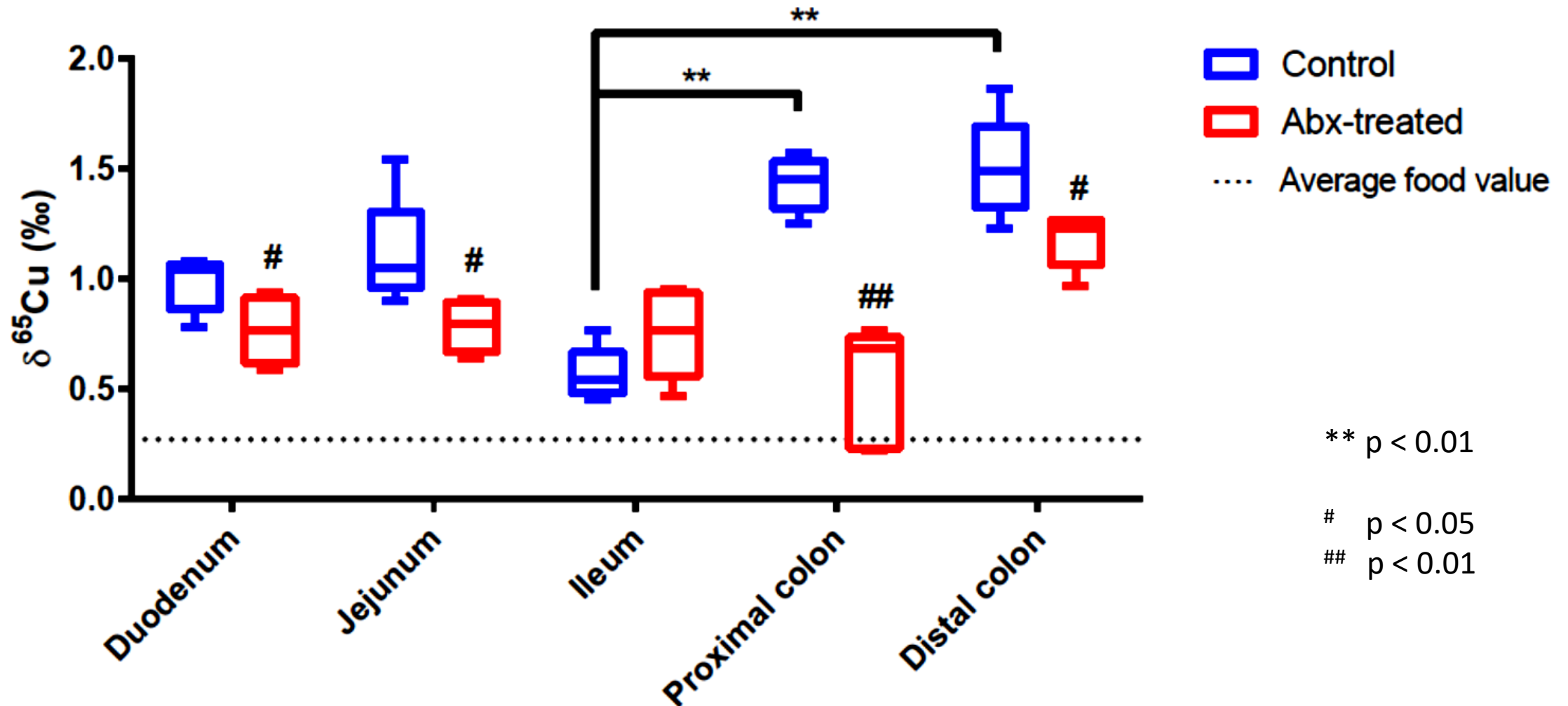
- Important role in nutrient metabolism and intestinal barrier function
- Bacterial dysbiosis is associated with many disorders/diseases
 - Eg. Obesity, diabetes, Alzheimer’s disease



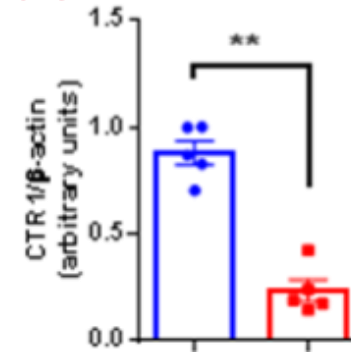
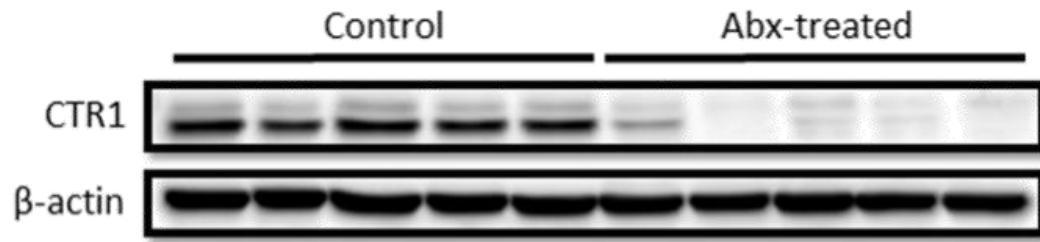
Measurement of Cu isotope amount ratios



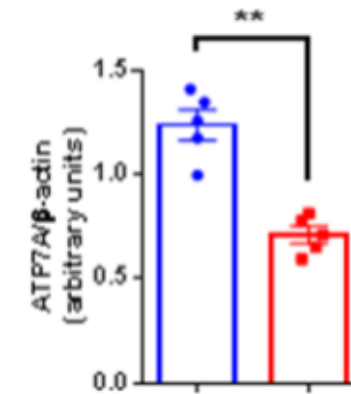
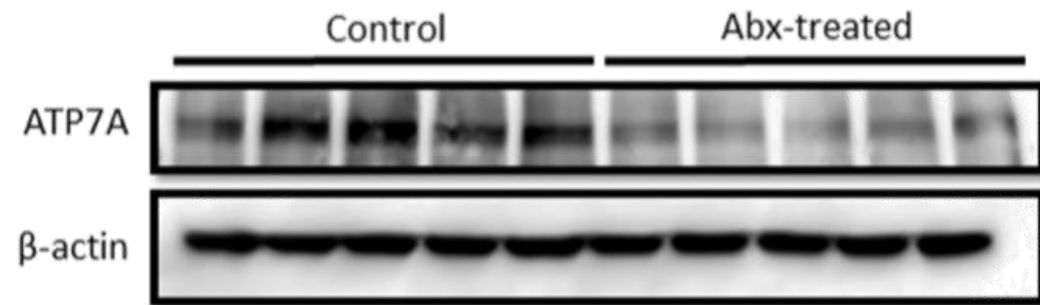
Antibiotic treatment alters the Cu isotopic distribution in the intestines of wild type mice.



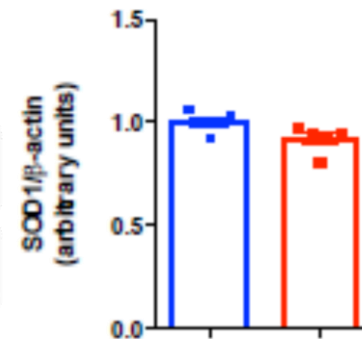
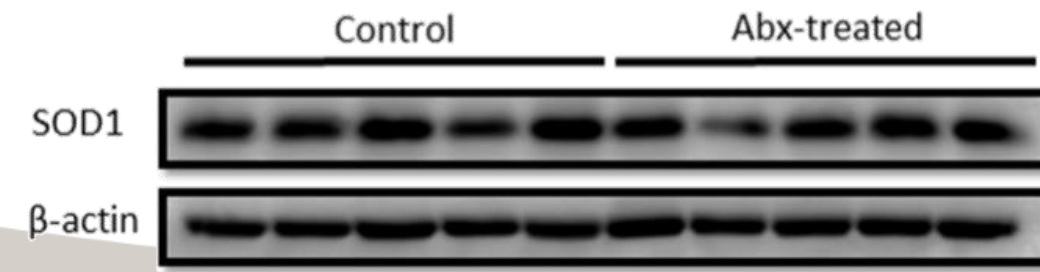
The expression levels of major copper transporters are reduced in antibiotic-treated mice



Control
Abx-treated

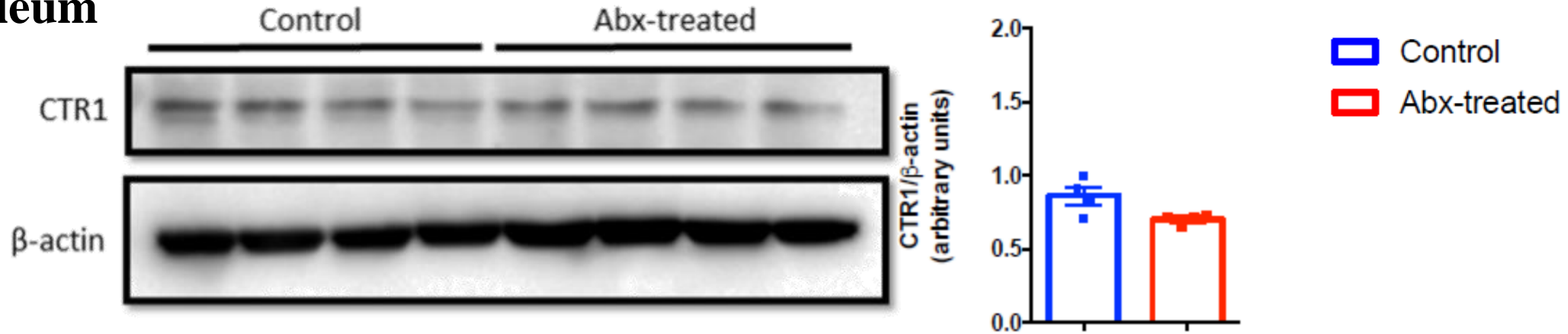


CTR1 → Copper import
ATP7A → Export protein
SOD1 → Antioxidant enzyme



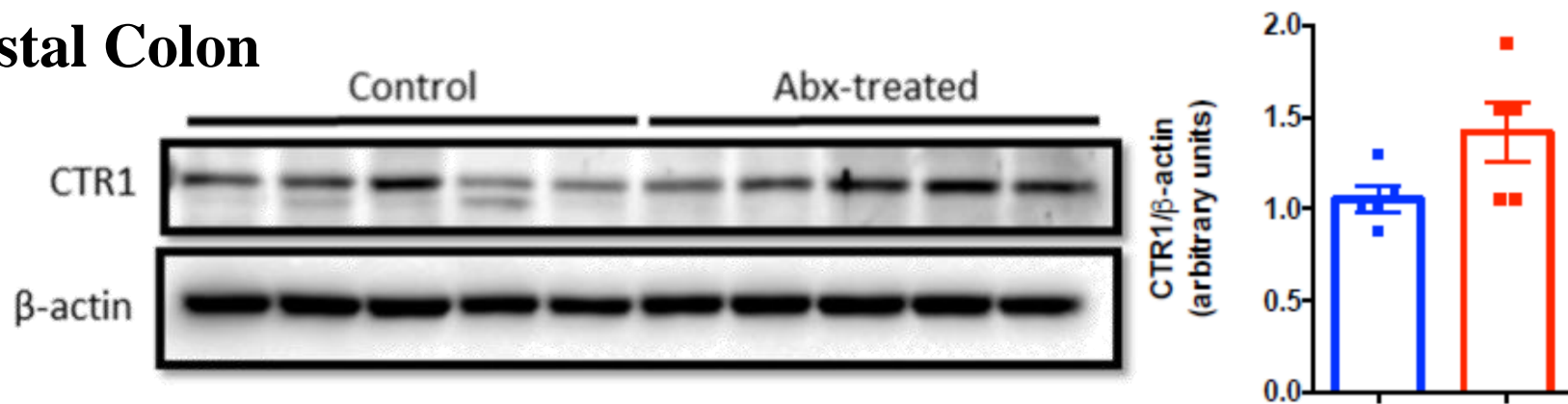
CTR1 is not altered in the ileum or distal colon of antibiotic-treated mice

Ileum



CTR1 \rightarrow Copper import

Distal Colon



Summary

- Copper stable isotope analysis is a sensitive technique to detect changes in copper metabolism.
- Produced the first detailed characterization of copper isotope distribution in the intestines of mice.
- Provided the first *in vivo* evidence that antibiotic-treatment alters copper handling in the intestines of wild type mice.