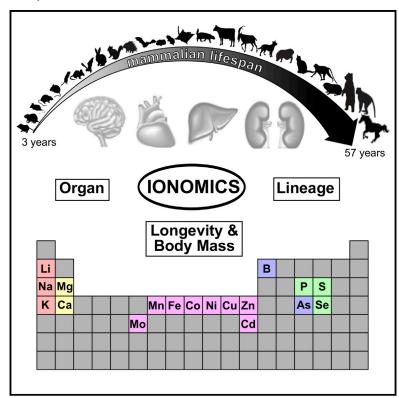
# **Cell Reports**

## **Organization of the Mammalian Ionome According to** Organ Origin, Lineage Specialization, and Longevity

#### **Graphical Abstract**



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#### In Brief

By examining the levels of 18 elements in the brain, heart, kidney, and liver of 26 mammalian species, Ma et al. report the elemental composition of mammalian organs, the common and lineage-specific patterns of element utilization, and correlation of various elements with body mass and longevity traits.

### **Highlights**

- Elements with similar biological functions share common distribution patterns
- · Organ distribution of elements correlates with expression of element-utilizing enzymes
- Liver Se levels reflect the number of selenocysteine residues in selenoprotein P
- Liver Zn and Cd levels correlate positively with species lifespan









## Organization of the Mammalian Ionome According to Organ Origin, Lineage Specialization, and Longevity

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#### **SUMMARY**

Trace elements are essential to all mammals, but their distribution and utilization across species and organs remains unclear. Here, we examined 18 elements in the brain, heart, kidney, and liver of 26 mammalian species and report the elemental composition of these organs, the patterns of utilization across the species, and their correlation with body mass and longevity. Across the organs, we observed distinct distribution patterns for abundant elements, transition metals, and toxic elements. Some elements showed lineage-specific patterns, including reduced selenium utilization in African mole rats, and positive correlation between the number of selenocysteine residues in selenoprotein P and the selenium levels in liver and kidney across mammals. Body mass was linked positively to zinc levels, whereas species lifespan correlated positively with cadmium and negatively with selenium. This study provides insights into the variation of mammalian ionome by organ physiology, lineage specialization, body mass, and longevity.

#### **INTRODUCTION**

The full set of elements used by organisms, or the ionome, supports diverse cellular functions (Eide et al., 2005; Salt et al., 2008). Transition metals alone are estimated to be required by more than one-third of enzymes (Holm et al., 1996; Waldron and Robinson, 2009). Selenium (Se) and iodine (I) are used as components of proteins or hormones. Together with manganese (Mn), iron (Fe), cobalt (Co), nickel (Ni), copper (Cu), zinc (Zn), and molybdenum (Mo), these trace elements are needed only in minute quantities but often act as important protein cofactors and active site components. Their deficiency or overload can result in severe pathological conditions (Fraga, 2005; Goldhaber, 2003).

In contrast, the metals sodium (Na), magnesium (Mg), potassium (K), calcium (Ca), as well as nonmetals phosphorus (P) and sulfur (S), are required in much larger quantities and are often called macronutrients. Some exist as free ions for establishing the electrochemical gradient across biological membranes (e.g., Na<sup>+</sup> and K<sup>+</sup>); others reside in specific subcellular compartments as signaling molecules (e.g., Ca<sup>2+</sup>). Many are constituents of macromolecules like proteins (e.g., sulfur) and nucleic acids (e.g., phosphate groups), or key structural components in bones, shells and exoskeletons (e.g., calcium phosphate minerals). Yet another group of elements, including lithium (Li), arsenic (As), and cadmium (Cd), are present in the environment and can be readily taken up by plants and animals but have no apparent biological functions. Depending on the quantity, these elements elicit different biological responses, features that underlie both their use in medical treatments when applied in moderate concentrations, and their toxicity when absorbed in excess.

Although a number of large-scale cross-species ionomics studies have been performed in plants (Ozaki et al., 2000; Watanabe et al., 2007; White et al., 2012), similar studies are lacking in mammals. In particular, the variation of element levels across organs, species, and lineages is not well understood. Since the use of these elements is likely shaped by evolution and environmental constraints, one may also be able to identify the links between the ionome and life-history traits (e.g., body mass, time to maturity, and longevity). Crucially, the nature of these questions means that one may need to look across a spectrum of organisms and organs to identify the common trends.



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