

## **Isotopes of Disease**

**Francis Albarède, Ecole Normale Supérieure de Lyon, FRANCE**

Metal isotope compositions in organs and body fluids provide an enormous source of untapped information relevant to normal and pathological conditions. Strong patterns of isotope fractionation are observed in some organs such as the liver and the kidney, and in blood components as well. To a large extent, these patterns reflect the binding of metals with different amino acids, variable redox states and electronegativity. Ab initio calculations indicate that heavy isotopes tend to bind to O-rich ligands (hydroxide, carbonate, phosphate), whereas light isotopes are positively fractionated by S-bonds. Formation of blood cells (erythropoiesis) takes place with very large and coupled Cu-Fe isotope fractionation, the disruption of which clearly signal pathological, and in general, abnormal conditions. The recent years have seen the emphasis being laid on genetic diseases, such as Fe in hemochromatosis and Cu in Wilson disease, and neurodegenerative pathologies such as the Alzheimer disease for Zn. Now that preliminary groundwork on metal isotopic variability in the human body is being laid, the opportunity of using some isotopes as biomarkers has never been stronger. Particularly promising are the isotopes of Cu, the concentrations of which are known to vary in multiple forms of cancer, and of Zn, which is making a forceful entry as a biomarker of prostate cancer in the wake of PSA discredit. A number of new results on clinical cases of colon and breast cancer will be presented. The enormous challenge of using isotopes to quantitatively assess the parameters of metal homeostasis at the cellular level in relation with gene expression and regulation will clearly engage the upcoming generation of isotope geochemists, biochemists, and health scientists.



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## **How modern mass spectrometry is driving cosmochemical discoveries**

**Audrey Bouvier, University of Western Ontario, CANADA**

Recent advances in mass spectrometry techniques result in improved sensitivity, precision, and spatial resolution. The application of these new methods to the analysis of planetary materials is playing a major role in shaping our understanding of processes at the origin of the Solar System. I will present some of the most recent discoveries in isotope cosmochemistry and show how we can use stable and radiogenic isotope abundances in

planetary materials to unravel processes and their timescales such as those that formed and brought key elements into the solar nebula, planetary formation, and impact events in the inner Solar System. For example, by measuring the Pb isotopic composition of meteoritic objects, we can decipher planetary accretion and differentiation processes that took place more than four and a half billion years ago with a sub-million year resolution. We can detect isotopic anomalies in primitive materials that tell us about the stellar environment of the solar nebula. And as we examine new kinds of planetary objects we are learning more and more about the diversity of planetesimals and questioning why and how such diversity developed, what role they played in the conditions for life to emerge and evolve on Earth, and what the chances are to have the same conditions met in other stellar systems that we observe.



*Audrey Bouvier is Assistant Professor in isotope geochemistry and cosmochemistry, Canada Research Chair in planetary materials, and member of the Centre for Planetary Science and Exploration at University of Western Ontario. She received her PhD from the Ecole Normale Supérieure de Lyon in 2005. Her current research interests include the geochemical and isotopic records of planetary materials to understand the origin and distribution of isotopes in the solar nebula, the timescales of planetary accretion and differentiation in the early Solar System, and the composition of the building blocks of planets and their impact history. She is the recipient of the 2013 Nier Prize of the Meteoritical Society, which recognizes outstanding research in meteoritics and closely allied fields by young scientists.*

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## **Unraveling Earth Formation**

**Richard Carlson, Carnegie Institution of Washington, USA**

Our understanding of the steps involved in Earth formation have been transformed by a combination of astronomical observations, theoretical modeling, and drastically improved chemical and isotopic measurement techniques applied to rocks dating from the first few hundred million years of Solar System history. Extreme isotope compositions in small grains condensed from exploding stars and injected into our Solar System just before planet formation began testify to a compositional heterogeneity in the nebula that may have been inherited by the terrestrial planets. Among the advances on this subject is recognition that the growth of planetary embryos occurred quite quickly, so Earth likely formed not by the gentle accumulation of small, asteroidal-size, objects, but by violent collisions between larger, already chemically differentiated, planetary embryos. The last of these violent collisions is responsible for forming Earth's Moon. Surprisingly, after this violent birth, Earth quickly recovered so that by 4.3 billion years ago Earth was forming crustal rocks through processes similar to those still occurring today, and Earth's surface had cooled to the point where there was liquid water, likely lakes or oceans, already present.



*Richard Carlson obtained his PhD in earth science at the Scripps Institution of Oceanography. He joined the scientific staff of the Carnegie Institution of Washington's Department of Terrestrial Magnetism in 1981. His specialty is the field of trace element and isotope geochemistry and geochronology with research interests that include: timescales and mechanisms of crust formation and mantle differentiation on the terrestrial planets; nucleosynthetic isotope variability in early solar system materials, origin of large-volume volcanism; characteristics of the sub-continental mantle and its role in continent formation and preservation; and techniques for high precision chemical and isotope analysis. He is President of the Geochemical Society, a Fellow of the Geochemical Society, American Academy of Arts & Sciences, and the American Geophysical Union, and recipient of the 2008 Bowen Award (AGU) and the 2013 Day Medal (GSA).*

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## **Reconstructing past rainfall using U isotopes in soils, lakes and cave formations**

**Kate Maher, Stanford University, USA**

The intermittent presence of large Pleistocene lakes in the southwestern interior of North America, a region that is now a semi-arid desert, suggests repeated oscillations between profoundly different climatic conditions. However, the origin of these shifts is still unresolved due to apparent inconsistencies in the hydrologic cycle as portrayed by existing climate proxy data. To directly quantify past rainfall and net infiltration, which in turn provide constraints on atmospheric circulation, we have developed new methods that use reactive transport approaches combined with age-corrected uranium isotopic variations in soils, lakes and speleothem (cave deposits). Soil and speleothem records show that both winter rainfall and infiltration increased substantially prior to the Last Glacial Maximum (LGM), suggesting an earlier Last Precipitation Maximum (LPM). Lake records, combined with climate model analysis further indicate that the LGM was not as rainy as previously thought and that Holocene mega-droughts may have been related to a long-term shift in moisture source. Collectively, we find that seasonal insolation is a key long-term driver for both precipitation and surface water variability in the region.



*Kate Maher is an Assistant Professor at Stanford University in the Department of Geological and Environmental Sciences. Maher received her PhD in Earth and Planetary Sciences from U.C. Berkeley in 2005. Prior to joining Stanford in 2007, she was a Mendenhall Postdoctoral Fellow with U.S. Geological Survey in Menlo Park, CA. Maher's research focuses on the rates of chemical reactions that occur at Earth's surface and subsurface. In order to quantify the rates of chemical reactions and to determine how these rates are coupled to changes in hydrologic, chemical and biological parameters, she uses a combination of geochemical tools including isotopic tracers and geochemical reactive transport modeling.*