(not without degradation) the crash-landing of the Genesis instrument. Planetary and solar scientists are awaiting new information on the isotopic abundances of other elements collected by Genesis foils. Because solar isotopic signatures have been inferred only indirectly from abundance data in meteorites, these new solar reference data are in great demand for proper interpretations of observations on planets and in meteorites. They may help to fill some of the gaps in our understanding of how objects in the solar system formed and evolved.

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GEOCHEMISTRY

A New Twist for Mercury

Carl Lamborg

In some light-driven reactions, mercury's reactivity depends on its isotopic mass in unexpected ways, possibly allowing this element to be tracked in the environment.

According to the biogeochemist William Fitzgerald, studying mercury is like being "on the trail of a silvery comet whose path is full of surprising twists and turns" (*1*). This volatile and mutable element has offered up yet another twist, as reported by Bergquist and Blum on page 417 of this issue (*2*).

Based on kinetic effects, heavier isotopes should be less reactive in proportion to the square root of the mass of the atom or molecule involved in the reaction. Yet, Bergquist and Blum found that ^{199}Hg and ^{201}Hg did not conform to this mass-dependent behavior (see the figure). Previously, such "mass-independent fractionation" (MIF) had only been documented for oxygen and sulfur during photochemical reactions involving ultraviolet radiation (*3*).

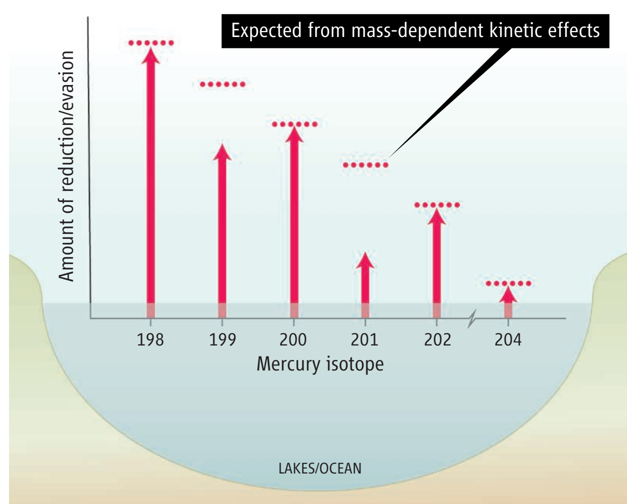
This finding offers a potentially powerful new tool for understanding the cycling of mercury in the environment. Because of its unusual volatility in the elemental state, mercury is easily exchanged between water and air and between land and air, resulting in global dispersion through the atmosphere (*4*). The process starts with the reduction of Hg^{2+} to Hg^0 vapor by biotic or abiotic reactions, resulting in supersaturation in surface waters of lakes and the ocean or high concentrations in soil interstices. The volatile Hg^0 then spends a few months to a few years in the atmosphere (*5*). Oxidation by various radical species leads to the formation of the much less volatile Hg^{2+}, which is rapidly removed from the air, closing this loop in the overall mercury cycle.

These fluxes, particularly from water to air, are difficult to measure directly. The findings of Bergquist and Blum could change that, because the initial Hg^{2+} reduction step may be largely driven by ultraviolet radiation, imprinting an MIF signal on the mercury isotope distribution. The authors also found a MIF signal in the light-driven demethylation of monomethylmercury (MeHg), the form of mercury that accumulates in biota. Thus, the magnitude of MIF signals in mercury isotope distributions in natural samples should be related to the impact of Hg^{2+} and MeHg photoreduction, because the product (Hg^0) escapes the system by water-to-air exchange. Bergquist and Blum offer an initial example: Using their laboratory-determined fractionation factor, they suggest that the MIF signal in fish can be used as a record of the amount of mercury lost from a lake or the ocean as a result of photoreduction and water-air exchange.

This report of MIF of mercury isotopes is not the first for an environmental sample, nor should it have been unexpected in hindsight. As the authors point out, ultraviolet radiation has previously been used to separate mercury isotopes under laboratory- and production-scale conditions, as part of nuclear weapons research. Jackson *et al.* previously reported MIF signals in aquatic animals and sediments from lakes (*6*). However, these are difficult measurements to make, requiring dedicated instruments and scrupulous attention to fractionation effects that arise during the analysis. Thus, results suggesting MIF from complex natural media are liable to be met with skepticism. Bergquist and Blum obtained their data during controlled laboratory experiments and for natural samples, lending enormous credibility to the finding.

Bergquist and Blum find not only mass-independent, but also mass-dependent fractionation. They and their colleagues (*7*) have documented mass-dependent fractionation in both photochemical and biological reduction of Hg^{2+}. This form of fractionation could also be very useful in tracking the biogeochemical cycling of mercury and may, in conjunction with MIF measurements, allow the impact of bacterial reduction on natural samples to be isolated and studied.

These reports are part of rapidly evolving research into heavy-element isotope fractionation made possible by advances in ultrahigh-precision isotope ratio mass spectrometry (*8*, *9*). For mercury, these studies suggest that fractionation abounds and is a fairly substantial signal. This could



Not dependent on mass. During photoreduction of Hg^{2+} and MeHg in natural waters and the subsequent water-to-air exchange of Hg^0, heavier isotopes are expected to react more slowly and to become more enriched in solution (dotted line). Bergquist and Blum show that even-numbered mercury isotopes follow this pattern, but odd-numbered isotopes instead exhibit mass-independent fractionation.

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be enormously useful for tracking the various biogeochemical transformations in the mercury cycle. However, fractionation could be so prevalent that the signals we wish to capture are obliterated as mercury winds its way through its various environmental incarnations.

Much work remains to be done before the mass-dependent and mass-independent signals can be interpreted fully. For example, detection limitations forced Bergquist and Blum to conduct their experiments at ratios of mercury to chromophoric dissolved organic matter that were orders of magnitude higher than in natural waters. But these are surmountable problems, leading to the next twist in the trail of an irresistible geochemical mystery.

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MOLECULAR BIOLOGY

Unlocking Cell Fate

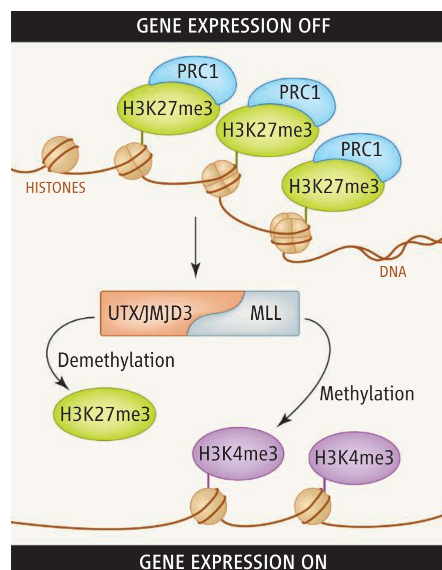
Ashley G. Rivenbark and Brian D. Strahl

Histone demethylation is associated with the activation of genes that control cellular development, differentiation, and the determination of cell fate.

Control of cell fate is a complex and poorly understood process. It is largely directed by the epigenetic regulation of gene expression—changes in gene function without changing the underlying DNA sequence. Epigenetic regulation is mediated partly through altering chromatin, the DNA and protein constituents of chromosomes. Two papers in this issue, by Chang *et al.* on page 444 (*1*) and Lee *et al.* on page 447 (*2*), advance our understanding of how epigenetic changes control cell fate and organismal development through the removal of histone methylation, a chemical modification of specific chromatin-associated proteins.

DNA is packaged within the cell's nucleus through its interaction with histone proteins (H2A, H2B, H3, and H4), which forms chromosomal regions that are either permissive or repressive for gene expression. Methylation of histones controls transcription by allowing chromosomal regions to toggle between "on" and "off" states. Moreover, this modification is reversible.

Homeotic (*Hox*) genes are fundamental in controlling embryonic development and stem cell renewal. In most differentiated cells, *Hox* genes are repressed by Polycomb group (PcG) proteins such as EZH2 (Enhancer of Zeste Homolog 2) methyltransferase, which trimethylates histone H3 at lysine 27 (H3K27me3). According to Lee *et al.*, a decrease in this specific modification during cell differentiation (*3*) is due to UTX, a demethylase specific for H3K27me3. UTX belongs to a family of enzymes that uses a Jumonji C (JmjC) domain to catalyze demethylation on lysines (*4*). Another H3K27me3 demethylase, Jumonji domain–containing 3 (JMJD3), has also recently been identified (*5*–*7*).



A genetic reprogramming "switch." UTX and JMJD3 demethylate histone H3 (H3K27me3). They also associate with the MLL complex, which methylates histone H3 (H3K4me3). This coordinated removal and addition of distinct methylation marks define an epigenetic "switch" for regulating genes that control development and cell fate.

H3K27 di- and trimethylation typically localize to the promoter region of developmentally regulated genes like the *Hox* gene clusters. Polycomb repressive complex 1 (PRC1), which contains histone H2A monoubiquitylating activity, is recruited to *Hox* genes to mediate their repression (*8*). Now, Chang *et al.*, Lee *et al.*, and the other new reports (*5*–*7*) show that the enzymes UTX and JMJD3 are recruited to *Hox* promoters, remove H3K27me3, and reverse this repression. Although UTX and JMJD3 appear to function in different contexts, and their individual or combined roles are not yet clear, their ability to control development is conclusive. For example, targeted inhibition of UTX in zebrafish and its counterpart in nematode results in posterior and gonad developmental defects, respectively (*5*, *7*). Differentiation of bone marrow progenitor cells upon cytokine stimulation is also disrupted in the absence of JMJD3 (*6*). Thus, H3K27me3 is a crucial mark in deciding cell fate.

Are there distinct roles for UTX and JMJD3 in early embryogenesis and/or in late differentiation? Both enzymes target H3K27me3, but UTX is constitutively expressed, whereas JMJD3 expression is induced in response to extracellular cues. Also, Lee *et al.* find that UTX is recruited to *Hox* genes in differentiating cells, implying that it may survey H3K27me3 globally and selectively remove H3K27me3 when given the correct developmental cues. Determining the roles of these enzymes, and other possible H3K27 demethylases, in developmental transcription cascades is a important next step.

Is removal of H3K27me3 alone enough to change cell identity or fate? The answer appears to be no. Several of the UTX/JMJD3 studies also found that loss of H3K27me3 was followed by another epigenetic change—trimethylation of histone H3 at lysine 4 (H3K4me3), which is linked to active gene transcription. Remarkably, UTX and JMJD3 are components of the MLL (Mixed Lineage Leukemia) protein complex that methylates H3K4, indicating that removal of H3K27me3

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