Indeed, a recent study shows that FOXO transcription factors are acetylated, and that deacetylation promotes cell cycle arrest and quiescence over programmed cell death. (*8*). Modifiers of TCF, FOXO, or β-catenin that can shift the balance of their interactions to favor quiescence would have potential implications for cancer therapy. It is also curious that despite epidemiological evidence indicating that antioxidants lower cancer risk, these new findings suggest that activating the oxidative stress response might promote quiescence and thereby antagonize cancerous cell proliferation. Thus, the oxidative stress response may not only promote cell survival and longevity, but also may prove useful in the development of cancer therapies.

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PLANETARY SCIENCE

The Interior of Mars

Yingwei Fei and Constance Bertka

The planetary core is the engine of a planet: It drives convection of the mantle, shapes the planet's surface, and—if the core contains convective molten metal that creates a dynamo—generates a global magnetic field. Based on its mean density and the bulk chemistry of terrestrial planets, Mars is believed to have a dense metallic core and a silicate mantle. However, because no seismic data exist for Mars, the density profile of its interior and the depth of the core-mantle boundary are not known precisely, and it remains unclear whether the martian core is solid or liquid.

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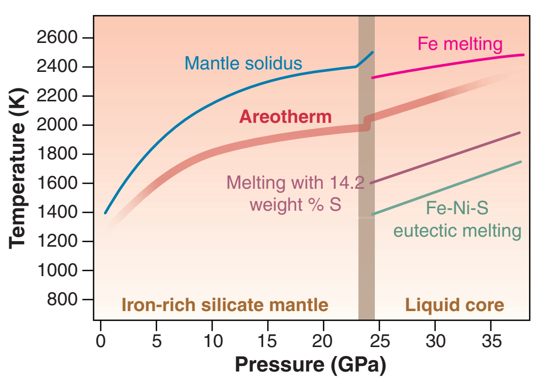
For the past decade, space missions to Mars have provided important constraints on the physics and chemistry of its interior, although these missions were primarily designed to map and understand surface or near-surface features of the planet. From a combined analysis of Mars Global Surveyor tracking data and Mars Pathfinder and Viking Lander range and Doppler data, the planet's moment of inertia—an important geophysical parameter for understanding the planet's internal density distribution—has been determined at high precision (*1*, *2*). Topography and gravity data collected by Mars Global Surveyor have constrained the global average thickness of the martian crust to between 30 and 80 km (*3*, *4*).

Models that combine these data with a range of possible core compositions allow the boundaries for mantle density to be defined. The results indicate that the martian mantle is more iron-rich than that of Earth (*5*, *6*). Interpretations of the chemistry and mineralogy of martian meteorites (*7*) and of the basaltic rocks at the landing sites of the Mars Exploration Rover Mission (*8*), although model dependent, are consistent with this conclusion.

Several lines of independent evidence suggest that the martian core has been liquid throughout its history. The first line of evidence comes from the discovery of strongly magnetized ancient crust by Mars Global Surveyor (*9*, *10*). The magnetization was acquired more than 4 billion years ago, implying a short-lived (~0.5 billion years) early martian core dynamo (*11*). Such a core dynamo may be driven either by compositional convection (which is set in motion by a composition gradient) in a liquid outer core due to solidification of an inner core, or by thermal convection in a fully liquid core due to high heat flux out of the core (*11*).



Evidence for a liquid core. Melting curves of putative martian mantle and core materials are compared with the estimated temperature profile (areotherm) for the martian interior. The martian mantle is expected to be solid, because its temperature is lower than the mantle solidus (the temperature at which melting begins). The minimum melting temperature in the Fe-Ni-S system (the eutectic melting temperature) at martian core pressures is also shown. Given an estimated core temperature of 2000 K, Mars has an entirely liquid core for a model core composition with 14.2 weight % sulfur.

Thermal evolution models of the martian core indicate that core solidification would have generated a long-lived (>1 billion years) dynamo (*12*). This scenario is not consistent with the observed martian magnetic field history. The short-lived early martian dynamo may have been caused by an initially superheated core after rapid core formation (*12*) or by mantle processes such as overturning of a chemically or mineralogically distinct layer (*13*), resulting in an increased heat flux out of the core. These models require a liquid core to initiate a dynamo. Evidence for a subsequent short-lived (<0.4 billion years) martian core dynamo around 3.75 billion years ago (*14*) would further strengthen the case for a liquid core, because it is difficult to produce a short-lived dynamo with multiple episodes if the core starts to solidify. The second line of evidence for a liquid martian core comes from measurements of the solar tidal deformation of Mars, obtained by analyzing Mars Global Surveyor radio tracking data (*2*). The measurements indicate that at least the outer part of the core is liquid and are also consistent with an entirely liquid core.

High-pressure experimental melting data for martian core materials at martian core pressures provide the third line of evidence for a liquid martian core (see the figure). At core pressures, the iron-nickel-sulfur system begins to melt at such a low temperature (~1400 K) that any amount of sulfur in the core would lead to at least a liquid outer core for any reasonable thermal model (*15*, *16*). Given an estimated present-day core temperature of 2000 K (*12*) and a model core composition containing 14.2 weight % sulfur, the martian core is most certainly liquid (see the figure).

The size of the martian core is the least-constrained physical parameter of the planet, but it has important implications for the chemical compositions of the core and the mantle. Space missions with multiple landers equipped

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with seismometers are required to precisely determine the size of the core. Such missions would also provide fundamental information on the structure and density profile of the martian interior, which is critical for understanding both the formation and evolution of Mars. This understanding is essential for providing a general context to explore the formation and evolution of terrestrial planets, including our own.

Previous and ongoing missions are providing a wealth of information about the martian surface and the role that water may have played throughout the history of the planet. However, the forces that have shaped the planet's surface are driven in large part by the evolution of its interior. A comprehensive understanding of the planet's history requires a greater understanding of its interior. A mission that focuses on the martian interior is overdue.

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DEVELOPMENTAL BIOLOGY

Ignoratio Elenchi: Red Herrings in Stem Cell Research

Peter J. Quesenberry, Gerri Dooner, Mark Dooner, Mehrdad Abedi

According to recent reports, cells from bone marrow can incorporate into other tissues and take on the identity of the resident cells. This has been shown in vivo for liver, heart, brain, skin, lung, pancreas, and the gut. One dramatic report even showed reversal of fatal liver failure in mouse by bone marrow cells derived from purified stem cells (*1*). These reports have generated a lively, and at times divisive, debate. Overriding the discussion is a general perception that the published work is not reproducible. As stated in a recent review received by us: "It would be nice to know why and how highly competent scientists can repeatedly come up with completely contradictory results."

Some researchers in the field have developed specific criteria that, they argue, should be met before work on this problem can be accepted (*2–4*). Far from resolving the issues, these criteria have acted as diversions from the proper goals of this research. In essence, they present an argument that purports to prove one thing, but instead proves a different conclusion not at issue. This logical fallacy is known as ignoratio elenchi ("ignoring the issue"). Its most common form is the red herring. These criteria include a demonstration of the robustness of the phenomenon, of the clonal nature of the stem cells, and of definite determinations that the bone marrow cells have not fused with the target tissue cells.

There is no absolute way to assess "robustness." Nevertheless, quite high proportions of cells derived from bone marrow have been documented in lung (*5*), liver (*1*), and skeletal muscle (*6*). But tissues with less marrow-to-target cell conversion, namely the brain and heart, have been highlighted in the controversy. In fact, a wide variety of results have been reported in different tissues. For instance, the percentage of marrow-derived cells for skeletal muscle has varied from 0.2 to 12.5%; for lung, from 1 to 35%; and for liver, from none to 30 to 50%. The bone marrow cell type or host treatment differed among these reports. Injury, an important trigger of stem cell incorporation, ranged from none to radiation, to radiation plus exercise, bleomycin, cardiotoxin, or genetic injury. Human granulocyte colony-stimulating factor treatment was used in a few studies. The exact identity of the bone marrow cells also varied widely, from whole bone marrow, various subsets of bone marrow populations, cells recovered after transplantation, to cells from umbilical cord blood. Some studies were in mouse, some in human. The negative results (showing no marrow cell incorporation) have been mainly in cardiac and neural tissues, in which cell plasticity is less robust, although not nonexistent. With such diversity of experimental models, only one study has actually exactly duplicated another. Several papers have been touted as failing to reproduce plasticity results (*7*, *8*). But, in fact, even the authors of "Little Evidence for Plasticity of Adult Hematopoietic Stem Cells" (*7*) commented (*9*) that "our data are not directly comparable to those of Krause *et al.* (*5*) and do not implicitly refute their observations." Abedi and colleagues (*6*) have now established that there are at least eight variables that determine whether marrow cells differentiate into skeletal muscle: injury, cell type, timing of engraftment, chimerism with radiation, route of administration, number of cells administered, the functional state of the cells, and stem cell mobilization after engraftment. A single exception in which experimental details were replicated is the work of Murry *et al.* (*10*) on cardiac reconstitution. These authors attempted to reproduce previously reported studies but obtained different results. The discrepancy remains unexplained. Thus, there have been a large number of studies published with varied and provocative results, but in fact there have been virtually no attempts to precisely reproduce the work of others.

FACTORS INFLUENCING CELL PLASTICITY

- Injury*
- Cell type
- Timing of engraftment
- Chimerism with radiation
- Route of administration
- Number of cells administered
- Functional state of cells
- Stem cell mobilization after engraftment

*Most important

The second, often cited criterion is that the donor cells should all be derived from a single clone. This appears to be based on two misperceptions: that transdifferentiation (a change from one differentiated cell type to another) is the only valid route to clinical utility, and that defined bone marrow stem cell populations are homogeneous. Transdifferentiation has not been established in any system, and most investigators do not think that this process accounts for stem cell plasticity. Rather, directed differentiation from minor stem cell populations appears more likely. In addition, most stem cell populations that are defined as purified by their ability to renew hematopoiesis in vivo are quite heterogeneous when other criteria are

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