

if any are genes, so referring to 100,000 human genes as potential drug targets, as Bruce Agnew does in his News article ("When Pharma merges, R&D is the dowry," 17 Mar., p. 1952), is to focus attention in the wrong place.

With little attention being paid to metabolism with regard to drug discovery, it is not surprising that, as J. Drews points out in his Review ("Drug discovery: A historical perspective," 17 Mar., p. 1960), few leads and development compounds, if any, can be credited to the new drug discovery paradigm, which relies on the economy of numbers afforded by the advances in genomic science and related technologies. Nor is it surprising that genetic validation of targets can be misleading, as J. Rosamond and A. Allsop mention in their Review ("Harnessing the power of the genome in the search for new antibiotics," 17 Mar., p. 1973). An uncritical assault on the thousands of new targets revealed by the Human Genome Project might prove to be just trial and error in new clothes.

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2. R. Eistenthal and A. Cornish-Bowden, *J. Biol. Chem.* 273, 5500 (1998).

#### Response

Metabolic analysis is by no means forgotten, as implied by Cárdenas and Cornish-Bowden. What is often called target validation must eventually include this type of analysis. As I discussed in my Review, the functional role of a particular target must be understood. Structural genomics, the systematic study of the three-dimensional structure of all proteins, will be helpful in this regard (1, 2), as will traditional biochemistry and pathophysiology. Contrary to Agnew's reference in his News article to 100,000 genes in the human genome as potential drug targets, my colleagues and I have estimated, using genetic and biochemical data, the number of potential drug targets to be in the range of 5000 to 10,000 proteins, a figure that has since been broadly cited in the literature related to drug discovery (3).

Many drugs, such as antibiotics, have been around for several decades, and many were found empirically. This, however, does not invalidate approaches that target the molecular mechanism of action of new drugs. Without exception, antibiotics elicit their effects by modifying a single molecular target in a highly specific way. Finally, there are many ways to select potential drug targets from the ~100,000 human gene products. Genetic and bio-

chemical tools as well as the methods of developmental biology are at our disposal. There does not have to be an "uncritical assault" on thousands of new drug targets, as Cárdenas and Cornish-Bowden imply.

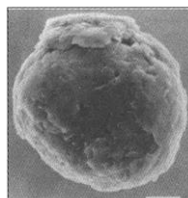
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1. S. K. Burley et al., *Nature Genet.* 23, 151 (1999).
2. P. F. Lindley, *Acta Crystallogr. D* 55, 1654 (1999).
3. J. Drews, in *Human Disease—From Genetic Causes to Biochemical Effects*, J. Drews and S. Ryser, Eds. (Blackwell, Berlin, 1997), p. 7.

### Planetary Solids Older than Earth



**A presolar grain of graphite (~4  $\mu$ m across).**

David Stevenson in his Pathways of Discovery Essay "Planetary science: A space odyssey" (11 Feb., p. 997) surveys the role that planetary science has played and is playing in the evolution of the world views held by modern humankind, but he does not include one new window of wide philosophic interest that is so stunning as to contribute to the immense sweep of his canvas.

Pieces of small planets fall to the ground (meteorites) containing within them small, solid particles that are themselves older than Earth and older than our entire planetary system. These presolar solids (mostly SiC and graphite) floated amid the interstellar dust and gas that collapsed with the solar cloud in the event that gave birth to our solar system, and they were incorporated intact into the surface debris of the small planets from which meteorites arise (1). They are recognized by laboratory experiments to contain bulk isotopic compositions (2) of C, Si, Mg, Ti, N, and O and heavy trace elements that are wildly different from the mean composition shared by all of our planetary bodies.

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Presolar solids came from long ago and far away, and they contain precise new information on the origin of the elements of which our solar system would later be born. Humankind thereby holds in its hands and studies in its laboratories solid samples that substantially predate the birth of our planetary system, but it is, ironically, our planetary system that delivers them to Earth. Stones from a time before there was an Earth, they speak not only of other systems in our universe but of times before our world existed. Their very existence shattered the belief that



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studying objects of such antiquity on Earth is impossible.

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#### References

1. For general information, see the following Web sites: [www.ciw.edu/lrn/](http://www.ciw.edu/lrn/) and [www.soest.hawaii.edu/PSRdiscoveries/July97/Stardust.html](http://www.soest.hawaii.edu/PSRdiscoveries/July97/Stardust.html)
2. *Astrophysical Implications of the Laboratory Study of Presolar Materials* (AIP Conference Proceedings no. 402), St. Louis, MO, 31 October to 2 November 1996; T. J. Bernatowicz and E. Zinner, Eds. (AIP, New York, 1997).

#### Response

When I wrote the Essay, I feared a reaction of this kind because of something I might omit, either through lack of space or oversight. Although I mentioned the importance of meteoritics in the development of our current understanding of the solar system, I did not talk about the preservation of small particles that predate solar system formation, and Clayton is right to remind us of this important, remarkable, and undisputed development. His comments are appreciated.

**David J. Stevenson**

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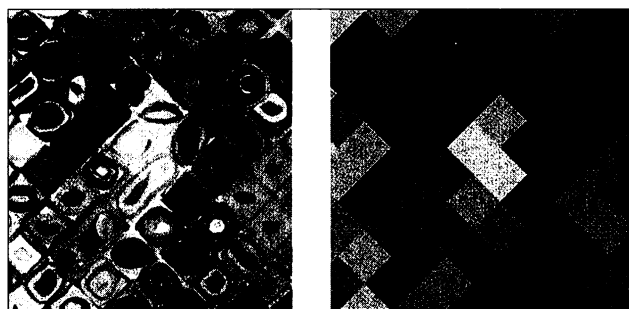
#### CORRECTIONS AND CLARIFICATIONS

**Perspectives:** (*Science's Compass*, 21 Apr.). The Perspective enhanced online for this issue was "Marking time for a kingdom" by M. W. Young (p. 451), not the Perspective by C. K. Ober.

**Table of Contents:** (14 Apr., p. 221). A word was omitted from the caption accompanying the photo of an infant in the *Compass* section. The caption should have read, "Kore wa nan desu ka?"

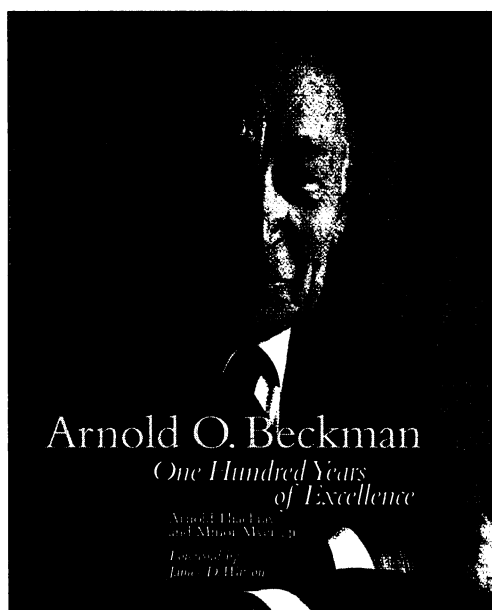
**News Focus:** "'Faster, cheaper, better' on trial" by Andrew Lawler (7 Apr., p. 32). The costs of some NASA missions were incorrectly stated. Not including the launch vehicle, the Pathfinder mission cost \$199 million and the Mars Global Surveyor cost \$148 million. The Mars 1998 missions, without launchers, cost \$193 million. Also, Donna Shirley managed the Pathfinder Sojourner rover team, not the Pathfinder project.

**Letter:** Response by Denis G. Pelli and Melanie Palomares to "Close encounters: Details veto depth from shadows" (31 Mar., p. 2425): The figure of the details of Chuck Close's portrait *Bill II* (1991) did not print correctly. The proper figure appears at right.



CREDIT: PHOTO, BILL JACOBSON, COURTESY OF PACEWILDENSTEIN

**Books et al.:** "Views of the final frontier" by J. M. Pasachoff (24 Mar., p. 2167). The Very Large Telescope in Chile belongs to the European Southern Observatory, not to the European Space Agency.



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