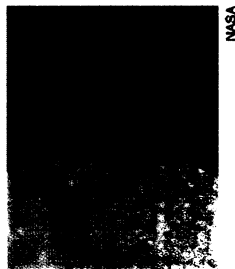


LETTERS

"The search should begin . . ."

Astronomers derive "surprising implications" from the controversial proposal that house-sized, icy objects are continually colliding with Earth (right, does dark spot reveal a "snowball"'s impact with the atmosphere?). Researchers debate whether data from "a new genetic technique" (with possible implications for the treatment of sickle cell anemia) are "a major breakthrough" or the result of an "artifact." And a 1996 finding about environmental estrogens is withdrawn.



"Snowballs" from Space?

If "snowballs" the size of houses are hitting Earth's atmosphere (Research News, 30 May, p. 1333), it would have surprising implications, not only for the origin of the oceans, but for the entire solar system. Planets are good brooms, and the lifetime of small objects in comet-like orbits is much shorter than the lifetime of the solar system (1, 2). If snowballs are hitting Earth, they must come from outside the planetary orbits. One plausible source for such material is the Kuiper Belt, a region outside the orbit of Neptune populated by cometary objects. The Kuiper Belt is thought to be the origin of most of the short-period comets (3). The apparently high density of snowballs near Earth could be used to estimate the amount of mass in the Kuiper Belt, if we were to assume that it provides the parent population.

From a simple geometrical model, encounters with roughly 20 snowballs per minute, with an average mass of about 30 tons, suggest a local mass density of about 10^{-17} grams per cubic centimeter. Adopting a simple model of the Kuiper Belt with an opening angle of 10 degrees out to a radius of 50 astronomical units (4), and assuming a uniform density of material (as given by the density near Earth), yields a mass resulting from snowballs in the Kuiper Belt on the order of a tenth of the mass of Earth. But we know that the density of objects in the Kuiper Belt must be higher than the local density of similar objects by at least a factor of 100, on the basis of the number and size of the known short-period comets and the number and size of objects found in the Kuiper Belt itself. The impact of so many snowballs on Earth would imply a mass on the order of 10 Earth masses, or more, of Kuiper Belt objects within 50 astronomical units, greatly exceeding the mass of only 0.06 to 0.25 Earth masses

inferred from observations (4). Such snowballs would have implications as well for the size distribution of the Kuiper Belt objects (5).

If the source of the snowballs were further afield, perhaps the Oort Cloud or even the interstellar medium, then even larger masses would be required to explain their claimed density in the inner solar system. If the snowballs were coming from interstellar space, their mass would exceed the estimated "missing mass" in the universe.

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References

1. L. Dones, H. F. Levison, M. Duncan, in *Completing the Inventory of the Solar System*, T. W. Rettig and J. M. Hahn, Eds. (Conference Series, Astronomical Society of the Pacific, San Francisco, CA, 1996), vol. 107, pp. 223-244.
2. H. F. Levison and M. J. Duncan, *Icarus* **108**, 18 (1994).
3. H. F. Levison, in (1), pp. 173-191.
4. J. Luu and D. Jewitt, in (1), pp. 245-254.
5. D. R. Davis and P. Farinella, *Icarus* **125**, 50 (1997).

The Purpose of Glycolysis

In the 11 April Research News article "What makes brain neurons run?" by Marcia Barinaga (p. 196), neurophysiologist Marcus Raichle argues (as phrased by Barinaga) that "nobody doubts that glucose consumption rises as much as blood flow in activated brain areas, and that oxygen use—by anyone's measure—lags behind. And that . . . argues strongly that there must be anaerobic metabolism of glucose in

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active brain areas." But James Pritchard and Robert Shulman were unable to explain this increase in anaerobic glucose breakdown by an increase in lactate.

The main purpose of glycolysis is to provide pyruvate for the trichloroacetic acid (TCA) cycle, not to make adenosine 5'-triphosphate. The glycolytic production of pyruvate reduces the cytosol by increasing the ratio of NADH [a reduced form of NAD⁺ (nicotinamide adenine dinucleotide)] to NAD⁺. Thus, glycolysis cannot continue without "something" returning the cytosolic redox potential to normal.

Two distinct pathways exist for normalizing the cytosolic redox potential. The first is the malate-aspartate and glycerophosphate shuttles. These are used almost exclusively during low-to-medium rates of TCA cycling. During high rates of respiration, it is thermodynamically unfavorable for these reducing-equivalent-carrying TCA-cycle intermediates to leave the mitochondria. During these high rates of respiration, the shuttles cannot increase their contribution to cytosolic redox stability, and the cytosolic pyruvate-lactate reaction begins producing net lactate.

Pierre Magistretti interprets Raichle's argument (oxygen use lags behind glucose consumption and blood flow) as "astroglia

metabolize the excess glucose to lactate, which they then pass on to neurons as an energy source." This does not explain the problem of low oxygen use (as Peter Fox points out), because this lactate shunt would require the same amount of oxygen as if the neurons oxidized the glucose themselves.

So, where does this lactate go? If we remember that lactate is formed mainly to oxidize the cytosol of highly metabolically active cells, then we can narrow our search. I think the search should begin with the real metabolic markers of nonaerobic glucose use, including lactate, pyruvate, and alanine. Because the lactate-pyruvate reaction occurs in red cells, both lactate and pyruvate should be considered equivalent and calculated collectively. Alanine should be measured because of the importance of the cytidine 5'-triphosphate cytosolic reaction in fueling the malate-aspartate shuttle; alanine production also increases like crazy during metabolic acidosis.

Raichle's last question (as phrased by Barinaga) is, "what need [is] the excess blood flow . . . serving if it's not answering a call for oxygen"? Blood flow probably increases in response to the decrease in pH or the increase in carbon dioxide caused by glycolysis. Thus, the products of the in-

crease in glycolytic metabolic acidosis cause an increase in glucose presentation to the cell—a beautiful example of control mechanisms regulating cytosolic redox potential.

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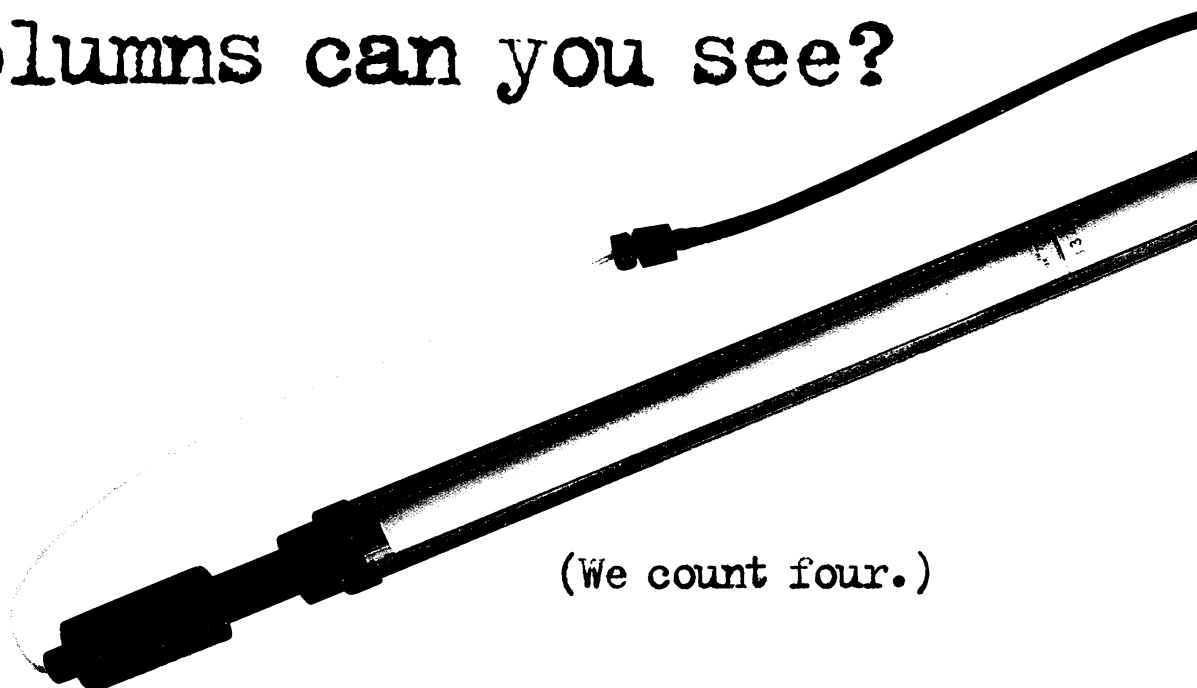


Sickle Cell Anemia Research and a Recombinant DNA Technique

The development of any new technology that could increase the frequency of homologous recombination by three to six orders of magnitude over that seen in normal mammalian cells would represent a major breakthrough. The report by Cole-Strauss *et al.* (6 Sept. 1996, p. 1386), in which an RNA-DNA hybrid oligonucleotide carrying the wild-type β^A sequence was used to correct 50 to 80% of B cells that carry a mutant β^S -globin locus, therefore gained much attention from the scientific community.

The possibility that this unexpected result could be a consequence of a potential artifact was previously raised in a letter by Thomas and Cappechi (7 Mar., p. 1404). Careful examination of the data presented

How many
gel filtration
columns can you see?



(We count four.)