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Response

OUR REPORT AND A SECOND PAPER (*1*) establish that the absence of SCD-1 reduces adiposity in two forms of rodent obesity and in lean animals. Although this effect is attributable to an increased rate of energy expenditure, the underlying cellular mechanism(s) and the full complement of tissues that contribute to this increased energy expenditure are as yet unknown. Thus, the extent to which these effects are the result of altered metabolism and/or signaling in the brain, or elsewhere, awaits further experimentation. However, Laviano *et al.* should note that C75, an inhibitor of fatty acid synthase [first described by Loftus *et al.* (*2*)], has recently been shown to increase peripheral energy expenditure by disinhibiting CPT1 (*2*, *3*). This result is thus consistent with the possibility that SCD-1 deficiency may increase energy expenditure by reducing the intracellular levels of malonyl CoA in peripheral tissues. Alternative mechanisms are also possible. It should also be noted that SCD-1–deficient animals are leaner than controls, despite the fact that these animals are hyperphagic (perhaps, as Laviano *et al.* speculate, secondary to reduced levels of malonyl CoA in the hypothalamus).

The potential use of an SCD-1 inhibitor as a human therapeutic awaits a more complete understanding of the mechanism underlying the effects of SCD-1 deficiency and, more importantly, a clear indication that the inhibition of this enzyme is both safe and efficacious. It is certainly possible that the increased energy expenditure associated with SCD-1 deficiency could lead to unwanted clinical sequelae related to increased levels of reactive oxygen species [a theoretical possibility noted in The Rockefeller University's news release about our report (*4*)] or any number of other possible unforeseen effects. Whether such effects prove to be similar to those associated with uncouplers of oxidative phosphorylation such as dinotrophenol awaits the results of careful preclinical studies and, if such agents prove safe in animals, safety trials in humans.

Whether the entire obese population, or a substantial subset of obese subjects, should be managed using pharmacologic agents versus lifestyle changes is a major public health issue. Our view is that in an environment where major surgery is often used to treat human obesity, there is a role for safe and effective drug treatment. Such treatments would be indicated in cases where weight loss is known to improve health. In our estimation, it is premature to predict whether drugs that alter neural signaling or those that act by a different mechanism altogether will prove safe and effective.

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Chemical Emissions: An Ongoing Issue

IN THE SPECIAL ISSUE ON GREEN CHEMISTRY (2 Aug.), the Viewpoint authors emphasize the importance of minimizing risk by reducing hazards from industrial chemicals ("Practical approaches to green solvents," J. M. DeSimone, p. 799; "Biodegradable polymers for the environment," R. A. Gross and B. Kalra, p. 803; "Green chemistry: Science and politics of change," M. Poliakoff *et al.*, p. 807). They illustrate this point with some data from the 2000 Toxics Release Inventory, compiled by the U.S. Environmental Protection Agency (TRI, available at www.epa.gov/tri). A closer examination of the TRI reveals the extent of the emissions problem.

The year 2000 reports document the release of 7.1 billion pounds (3.2 billion kg) of toxicants, of which 26.8% was released into the air. Those "original" industries that have reported their emissions since the first TRI was published in 1987 were the worst offenders. In this group, releases into the air accounted for 48.8%, or 11.1 billion pounds (5.01 billion kg), of on-site and off-site releases. These figures are dwarfed by the total of 37.89 billion pounds (17.19 billion kg) of toxic waste that was reported as "managed"—a TRI term that includes recycling, waste treatment, energy recovery, and other techniques. Again, the original industries posed the greatest problem, accounting for 31.68 billion pounds (14.37 billion kg) of managed waste, up by 34% from the 1999 total. Thus, managed and re-

leased wastes total approximately 45 billion pounds (20.4 billion kg) in the United States, or just over 160 pounds (72.6 kg) per person per year, and are increasing. Because not all industries are required to report data to the TRI, these figures underestimate the total toxic waste problem by a substantial amount.

Unfortunately, we know little about the impact of these ubiquitous wastes on human health. There are few data available that document exposure and still fewer data about the impact of these exposures on health. To fill these important gaps in knowledge and reduce risk, it is important to support health monitoring and tracking efforts and to use governmental programs to provide incentives to move toward greener chemistry. Better health and a better environment are sure to follow.

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Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 6 months or issues of general interest. They can be submitted by e-mail (science_letters@aaas.org), the Web (www.letter2science.org), or regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

Response

WE APPRECIATE LOCKWOOD'S COMMENTS AND feel that there are a number of points that are important to add. We believe that it is not appropriate to include managed wastes in a metric for emissions. The chemical industry deserves credit and encouragement for the part that it has played in introducing innovative methodologies to recycle, treat, and recover by-products and energy from what were once off-site emissions. These efforts form a firm foundation for the next generation of improvements, which include green chemistry.

It is also difficult to compare raw TRI data, because over the years, the U.S. Environmental Protection Agency has made numerous changes to the rules for collecting data, such as expanding the list of reportable chemicals, lowering the reportable threshold, and changing the definition of what must be reported. Indeed, the American Chemistry Council calculates a 65% reduction in TRI emissions during the past 12 years when these factors have been taken into account.

What is clear is that there is a significant opportunity for further improvement in achieving sustainable manufacturing and sustainable growth in an economically profitable manner. In our view, the most promising approach to these issues is green chemistry. Although it is important to understand fully the nature of our environmental problems (toxicity and exposure), we feel that it is at least as important for all members of the chemical community to engage in the ongoing discovery of the solutions to these problems. We need to remove the obstacles to implementation so that the accomplishments made thus far can be built upon for even greater environmental and economic benefit. Unrelenting effort must continue (and must be led by the industry) to reduce risk, improve our knowledge, and seek incentives to accelerate the move toward green chemistry.

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