organisms or cell walls in *Rag-1* knockout mice, which lack mature T and B cells, led to significant myelin breakdown early during infection, comparable to the level observed in wild-type mice. From this, they conclude that *M. leprae*–induced demyelination can occur in the absence of immune cells.

These findings, however, do not explain two major clinical observations in leprosy. First, it is well known that nerve damage in leprosy occurs particularly during (upgrading) type-1 reactions. Type-1 leprosy reactions are idiopathic episodes of strongly increased inflammation and cell-mediated immune reactivity and are often accompanied by acute inflammation of peripheral nerves. The latter complication frequently leads to extensive and irreversible nerve damage. The treatment of choice is rapid administration of immunosuppressive drugs to prevent further nerve damage (*1*).

Second, although patients with lepromatous leprosy display demyelination and nerve damage, these processes are chronic and relatively slow, despite the presence of high bacillary indices. Thus, in the absence of an adequate cellular immune response, symptomatic neurodegeneration progresses relatively slowly, despite the abundant presence of *M. leprae* organisms.

These combined clinical and epidemiological data suggest that inflammatory immune reactions play an important role in leprosy nerve damage and that the mere presence of *M. leprae* itself does not explain the full phenotype of leprosy nerve damage. Indeed, inflammatory responses seem to be needed for the complete manifestation of demyelination and associated neurological symptoms in other neurodegenerative diseases, as Rambukkana *et al.* point out. In my view, this likely applies also to leprosy: During a first and early phase of *M. leprae*–specific targeting of peripheral nerves, contact-dependent myelin breakdown takes place, and this may continue to progress further. During episodes of enhanced immunity and inflammation, acute and extensive additional nerve damage can take place, to which cytokines and immune effector cells contribute (*2*, *3*), although the precise mechanisms involved remain to be elucidated.

Thus, in my view, the human immune response plays a significant role in the full manifestation of leprosy neuritis and nerve damage. It is important to empasize this point, given its implications for the effective treatment and management of nerve damage in leprosy control.

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Response

IT IS KNOWN THAT ALMOST ALL CLINICAL features of leprosy are associated with immune responses (*1*), but we know nothing about the early events, preclinical stage, and associated pathology in nerve injury. It is impossible to explain all features of a complex spectral disease like leprosy in one paper. Our report explains one aspect of this complex pathology, the early consequence of *M. leprae* interaction with myelinating Schwann cells.

The key message of our report is that demyelination is an early step in nerve injury after the attachment of *M. leprae* and its components to myelinated Schwann cells (*2*). It certainly does not explain the immune-mediated clinical features of leprosy; rather, it is a model system to study the molecular basis for early nerve damage. In the absence of immune cells, *M. leprae* attachment to Schwann cell-axon units, the earliest interaction of the invading pathogen (*3*), results in significant demyelination. Such myelin damage could set forth the foundation to recruit immune cells in later infection. We neither concluded nor stated our finding as the major mechanism of nerve damage in leprosy. In fact, we stated that an immune response is needed for the complete manifestation of nerve damage in leprosy and other neurodegenerative diseases. Because the clinical manifestation of nerve injury, mainly due to inflammatory responses, occurs years after a slow infectious process, it is obvious that other events are occurring before the immune system comes into play. In fact, we know nothing about the early or preclinical stage of leprosy (certainly not after 72 hours postexposure, as in our study).

Thus, in early *M. leprae* infection, mechanism(s) other than immune responses are certainly involved in nerve injury. Because the Schwann cell is a privileged site for *M. leprae* that eludes surveillance by immune cells (*3*), we concluded that such non–immune-mediated mechanisms may play critical roles in nerve damage in the very early stage of the infectious process, although it may not be able to manifest clinically.

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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.

Mistaken Identity

MARTIN DELANEY'S REVIEW OF JOHN Crewdson's book *Science Fictions* ("Double jeopardy for Gallo," Books *et al.*, 31 May, p. 1615) is excellent and to the point. However, I am somewhat confused by the photograph picturing Robert Gallo and Luc Montagnier. The accompanying caption identifies Gallo at the left and Montagnier at the right. They are now good friends, but did they really exchange identities?

EDWARD DE MAEYER

The correct caption: Montagnier (left) and Gallo (right) embrace after being honored at a 2000 ceremony in Spain for identifying HIV.

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The Ups and Downs of Global Research Centers

HERE, WE PRESENT AN ANALYSIS OF THE changing performance of the largest "research centers" of the world. Of the total 2,790,179 papers listed by the Science Citation Index (SCI) for the period 1996–98, 38.3% have at least one author from the top 40 research centers. This formidable concentration pattern of research output is reinforced in 1999–2001, with 39.6% of the 2,929,977 papers associated with the world's 40 largest research centers.

Here, we define a center as a "greater

urban region" by a uniform logic where the objective was to identify units (cities and surrounding suburbs) by the way they function as daily labor markets. We combined neighboring cities where the distance between cities is less than 45 minutes by ground transport. We then determined how many papers were published by authors from each research center.

The 1999–2001 top 40 list includes 22 European and 14 North American centers, along with three Asian centers and one Australian center. Africa and South America are not represented. Japanese centers have prominent positions on the list. Tokyo-Yokohama is the research center with the world's highest number of papers published in the period studied, and Osaka-Kobe is third. London is in second place, and the top two are far ahead of the other centers on the list. The highest-scoring North American centers are the San Francisco Bay Area (4), Boston (6), New York (7), and Los Angeles (9). From Europe, Paris (5), Moscow (8)—the only representative from the former Soviet Union—and Amsterdam (10) are among the top 10 research centers. There is a considerable gap in publications between the centers in the top 10 and those in the lower ranks. It is notable that Beijing is ranked 12th; that U.S. centers show a very compact pattern, with most of the represented centers having high ranks; that Northern European centers hold higher ranks than Southern European ones; and that the United Kingdom is represented by no less than six centers in the top 40.

We compared data from 1996 to 1998 with data from 1999 to 2001 to identify "winners" and "losers." The weighted arithmetic mean change is +8.5%. Half of the cities are within a range from +6.3 to +11.1%, which is an average change. We classify nine centers as winners—an increase of 11.6% or more—and 10 cities as losers—an increase of 4.8% or less.

Large research nations with multiple centers in the top 40 are the United States with 12 centers, the United Kingdom with six, and Germany with five. Of these nations, only the United States has one winner. The traditional top research nations include seven of the 10 losing regions. To find the successes, one must look outside those nations traditionally seen as research heavyweights.

The big winner is Beijing, with a more than 60% increase in research output from 1996–98 to 1999–2001. All four Southern European research centers (Milan, Barcelona, Madrid, and Rome) on the top 40 list are winners, which shows a pattern of advancement for a large part of Southern Europe. Only one U.S. center, Baltimore, and one Canadian center, Toronto, are members of the high-growth category, which also includes Sydney.

The big losers are Moscow and St. Petersburg. Other members of this category include some larger European and North American cities with long histories as research centers, e.g., Paris, London, Washington, DC, and the capital-like city Frankfurt near the former German capital Bonn.

If the growth pattern from 1996–98 to 1999–2001 continues, a shift in the rank of major research centers can be envisaged, although the overall pattern is rather stable. Centers located in the Pacific Rim will increase in importance together with Southern European centers. The traditional heavyweight centers of Northern Europe and the United States will decrease in importance, as will Russia.

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Human Reproductive Cloning

BROCK'S THOUGHTFUL VIEWPOINT "HUMAN cloning and our sense of self" (Reflections on Self: Immunity and Beyond, 12 April, p. 314) prompts us to raise another issue that has been lost in the cacophony surrounding this controversial topic. Some claim that no legitimate scientific purpose can be served by perfecting technology to permit human reproductive cloning. Others include the preservation of endangered species among the legitimate and beneficial goals of mammalian cloning (*1*). Although it may seem difficult to imagine plausible circumstances under which our own species might become endangered, one possibility is the spontaneous origin or malicious development of a virus that is as lethal as AIDS and as contagious as chicken pox. However, with AIDS, individuals exist who are genetically resistant to the virus, no matter how many times they are exposed (*2*). In the event of a worldwide pandemic, the identification and cloning of rare genetically resistant individuals might therefore provide an effective last-ditch strategy for preventing our extinction. If safe, effective procedures for human reproductive cloning were developed, society could, if it chose, permit their use only for such emergencies, but not for other purposes (*3*). For those who consider human cloning to be intrinsically immoral (*4*), its use to prevent our extinction raises the existential question of whether the preservation of any particular moral system or code of ethics should take precedence over the preservation of the human species. One might well ask what moral system will prevail after *Homo sapiens* has become extinct? If any life-forms still exist, it is likely to be a Darwinian system. These are questions truly worthy of consideration by the Presidential Council on Bioethics or the ethical, legal, and social implications program of the Human Genome Project.

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CORRECTIONS AND CLARIFICATIONS

ASSOCIATION AFFAIRS: PRESIDENTIAL ADDRESS: "Science, sustainability, and the human prospect" by P. H. Raven (9 August, p. 954). Some text is missing at the end of page 956. The text should read, "John Browne, chief executive officer of BP-Amoco, for example, set his company on a course that will embrace alternative energy sources and energy conservation, reasoning that in the face of global warming, they must do this if they are to continue to be a profitable energy company in the future. The kinds of grassroots activities that are promoting sustainability on a local scale have become a powerful force throughout the world." The correct version is available at www.sciencemag.org/cgi/content/full/297/5583/954.

NEWS OF THE WEEK: "Senate puts the heat on science nominees" by Jeffrey Mervis (26 July, p. 493). A response by Kathie Olsen to a question from Senator John McCain (R-AZ) was misquoted. After McCain quoted from a recent administration report on climate change put out by the Environmental Protection Agency, Olsen said, "I don't have the exact numbers and everything in my head to be able to respond..." Olsen did not say she did not understand the text, as *Science* reported; it was McCain who interpreted her answer that way. The article also misrepresented President Bush's response to the EPA report. Bush had told reporters that it was "a product of the bureaucracy," a position that McCain described as Bush "basically dismissed it."