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LETTERS

edited by Jennifer Sills

China's Rapid Urbanization

BETWEEN 1980 AND 2012, CHINA'S URBANIZATION INCREASED FROM 19.4 TO 52.6% (*1*). Unfortunately, China's urbanization has developed far ahead of its economic growth. As a consequence, China's urban economic advantages are being offset by the perennial urban curses of overcrowding, air and water pollution, environmental degradation, contagious disease, and crime (*2*, *3*).

China's rapid urbanization has also resulted in a severe labor shortage in its rural communities. By 2012, 262 million people had migrated to urban areas. The majority of the rural-to-urban migrants are men, who seek higher wages in cities but leave their children, spouses, and aging parents in the villages. The number of rural children left behind increased from 22 million in 2004 to 58 million in 2010, and the women and aging parents left behind have reached more than 47 million and 40 million, respectively (*4*, *5*). These three groups now account for more than 22% of China's total rural population. This has created societal unrest and psychological development problems for children left behind (*4*, *5*).

The labor shortage in China's rural areas has led to increased uncultivated land and hastened significant changes to traditional agricultural practices, such as reduced tillage, burning of agricultural straw on site, and overuse of chemical fertilizers and pesticides. Overused chemicals have in turn caused widespread water, soil, and air pollution, soil and farmland degradation, and biodiversity loss (*6*). Of the 16,928 species that are threatened with extinction worldwide, almost 800 are in China; 25% of China's species are endangered, and 233 vertebrate animal species are facing extinction (*7*). Biodiversity loss has been shown to lead to increased human, animal, and plant diseases. The soaring rate of cancer in cities and the 200 "cancer villages" in China reflect the damage done to the health of its people (*8*).

China is seeking and implementing innovative solutions that balance economic growth and sustainable development. During the 2012 National People's Congress, the concept of "eco-civilization" was proposed. A year later, creating a green and sustainable urbanization and building an eco-civilization were the key subjects of the 2013 Global Eco-Forum (*9*). To achieve these ambitious goals, China must refrain from forced urbanization (*10*) and develop new policies and incentives to retain sufficient workers for its rural communities. By addressing these challenges, China will improve food safety and security, reduce dependency on chemical fertilizers and pesticides, improve air and water quality, and help to protect wild plant and animal populations. At the same time, China needs to address the urban issues of reducing air pollution and providing clean water, safe neighborhoods, and efficient infrastructure—the basics of city living (*11*).

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Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the past 3 months or matters of general interest. Letters are not acknowledged upon receipt. Whether published in full or in part, Letters are subject to editing for clarity and space. Letters submitted, published, or posted elsewhere, in print or online, will be disqualified. To submit a Letter, go to www.submit2science.org.

Gain-of-Function Research: Unproven Technique

THE LETTER "GAIN-OF-FUNCTION EXPERIments on H7N9" (R. A. M. Fouchier *et al.*, 9 August, p. 612; published online 7 August) is based on unproven assumptions from previous H5N1 studies and on less-than-critical examination of the basic biology of influenza viruses (*1*). Furthermore, there is no scientific basis for the claim that gain-of-function (GOF) research on H7N9 may lead to development of more effective vaccines. There is a need to advance influenza vaccine development, but GOF experiments are

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Ultrafine for extra strength
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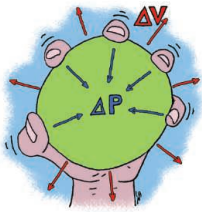

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unlikely to provide the required insights.

Influenza vaccines have been manufactured for many decades based on the isolation of a virus with a specific pandemic potential or seasonal prevalence. These isolates need to be propagated in eggs or, more recently, in cell cultures. Once obtained in sufficient quantities, vaccines are prepared either by inactivating the whole virus particle or isolating a particular fragment. Recently, a vaccine was produced by cloning viral hemagglutinin (*2*). It has so far been necessary to produce a new vaccine to protect against every influenza virus suspected of pandemic or seasonal threat, irrespective of the structure of viral hemagglutinin or detected mutations in its amino acid sequence.

Fundamental scientific studies have previously established that influenza viruses have high error rates in their viral polymerase and variation in their propensity to infect many avian and mammalian species. Furthermore, evolutionary pressures result in multiple reassortment and mutational events that follow no clear pathway and are impossible to predict or associate with a specific outcome in any population (*3*). Aside from its biosecurity and biosafety risks, GOF research is not based on scientific grounds, but rather on highly speculative assertions. Experience to date with H7N9 viruses in regard to neuraminidase inhibitor activity or the presence of certain hemagglutinin motifs are not novel findings (*4*). The previous GOF studies on H5N1 contributed little to the development of new vaccines or therapeutic measures. The current proposal is based on self-serving advocacy rather than a scientific determination.

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Gain-of-Function Research: Unknown Risks

WE WERE ASTONISHED BY THE RECENT LETTER by R. A. M. Fouchier *et al.* ("Gain-of-function experiments on H7N9," 9 August, p. 612; published online 7 August) and the simultaneous publication in *Nature* (*1*). We find it odd that an H7N9 influenza A research manifesto signed by a number of flu virologists should be aired so prominently, coming as it does from a distinguished but unrepresentative group. The Letters were disavowed within 24 hours by opinions from two influential Chinese influenza scientists (*2*, *3*). Publishing research manifestos is de rigueur for projects that require setting up colossal infrastructure, such as the hunt for the Higgs boson. However, the proposed agenda for H7N9 research is obvious to any experienced infectious disease researcher. Indeed, H7N9 in the Fouchier *et al.* Letter could be replaced by MERS-coronavirus or any newly discovered virus that poses a perceived threat.

More egregiously, Fouchier *et al.* try to make the point that gain-of-function (GOF) experiments are now a standard part of a virology research agenda. This astonishing assertion is simply not true. There are some very strong arguments to the contrary; for example, avian influenza GOF experiments cannot prove their point because the deliberate infection of humans is impossible. They can infer and suggest, but no more. Apart from the implausibility of predicting what nature might turn up (*4*, *5*), inferences are of limited value to a health minister. Solid data are what counts. Questions have been raised about the statistical robustness of the findings from the key H5N1 GOF studies given the small numbers of animals used (*6*).

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Even though there are substantial risks involved in GOF research, surprisingly, no independent risk-benefit assessment has been undertaken, which is deeply troubling given the magnitude of the risk—a man-made flu pandemic. Given that scientists still have not reached a consensus regarding GOF research, the benefits cannot be currently quantified. By contrast, the risks are real and can and should be quantified. A compelling argument can be made that GOF work should be frozen until we have a comprehensive risk assessment.

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CORRECTIONS AND CLARIFICATIONS

Editors' Choice: "Beating fluorescent background" by P. Szuromi (13 September, p. 1153). The luminescent lifetime of the nanoparticles is 5 to 13 μs, not 5 to 13 ms. The HTML and PDF versions online have been corrected.

News & Analysis: "Researchers wary as DOE bids to build sixth U.S. climate model" by E. Kintisch (13 September, p. 1160). The article stated that the Department of Energy provides $6.2 million this year for the Community Earth System Model (CESM). To clarify, the $6.2 million supports the National Center for Atmospheric Research but does not represent the Department of Energy's total support for CESM. The HTML and PDF versions online have been corrected.

Reports: "Positive feedback between PU.1 and the cell cycle controls myeloid differentiation" by H. Y. Kueh *et al.* (9 August, p. 670; published online 18 July 2013). The second author's name was misspelled. It should be Ameya Champhekar. The HTML and PDF versions online have been corrected.

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