

row cells and research to determine whether a pluripotent stem cell with therapeutic benefit exists in adults.

On July 19, Bush missed an opportunity to show support for research on cells that do have the potential to differentiate into many different kinds of tissues. His veto thwarted new prospects for advancing embryonic stem-cell research and will result in a terrible waste: tens of thousands of fertilized eggs will be destroyed without a single one being permitted to contribute to our knowledge of cell differentiation. Fortunately, research on embryonic stem cells will proceed in a number of excellent scientific centers in this country, without federal funding and, one might argue, at a pace unfettered by the federal bureaucracy. But the lack of federal support and the political climate do hinder stem-cell re-

search in the United States. A new center in Singapore, for example, has recently attracted gifted American investigators who are fed up with political restrictions on their research. Other countries — such as China, Sweden, and the United Kingdom — are also entering the field.

We really don't know what will ultimately come out of research on embryonic stem cells. It is important to play down promises to the public that the work will produce anything of clinical value in the foreseeable future. We simply don't know how an embryonic stem cell will behave in a human, and we don't know whether human marrow contains a pluripotent stem cell that can transdifferentiate. Equally important, we don't yet know whether research on embryonic stem cells will teach us how to revise the differentiation program of a tissue-specific

stem cell, thereby circumventing the need for embryonic cells. Research on stem cells will encounter many twists and turns, but it is an endeavor that is eminently worth pursuing. The delay of medical advances by theological disputes is not in the best interests of the sick and disabled.

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Bit Player or Powerhouse? China and Stem-Cell Research

Fiona Murray, Ph.D., and Debora Spar, Ph.D.

For more than a decade, China has been shocking the West. Although it is still poor and officially Communist, the world's most populous country has turned old convictions on their heads, emerging from decades of isolation to become a hive of high-tech manufacturing, a major diplomatic and military power, and one of the world's largest holders of U.S. securities. The subtitle of a recent book described the China phenomenon most succinctly when it promised, breathlessly, to explain "how the rise of the next

superpower challenges America and the world."¹

In the area of scientific research, by contrast, both fact and prediction are more ambiguous. On the one hand, Chinese authorities clearly have bold ambitions. President Hu Jintao has repeatedly stressed the importance of "scientific development" to China's continuing growth, and in January he vowed that "China over the next 15 years will join the list of innovative countries."² The natural sciences figure prominently among the government's

areas of focus, and government spending on science and technology has more than doubled since 1999. On the other hand, China remains an exceedingly poor country, with a per capita annual income of only \$1,284 in 2005; hundreds of millions of Chinese peasants lack access to even the most basic medical services. China is still governed by a staunchly Communist regime, and both its industrial infrastructure and capital markets are dominated by state-owned enterprises. These are not the kinds of con-

ditions that typically catalyze scientific advances.

Nevertheless, China's meteoric rise in other sectors raises the question of whether it could become a powerhouse in medical science as well. Indeed, *Science* and *Nature* have both reported in recent years that China's stem-cell programs hold potential, and in 2004 a delegation from Britain's Department of Trade and Industry concluded more emphatically that Chinese research in the field was already world-class. The country's laboratories, the delegation announced, "are at, or approaching, the forefront of international stem-cell research."³ Is China — like Korea, perhaps, and Singapore — poised to participate in the next round of global scientific advances? Does it have the funds? The motivation? The incentives and infrastructure to generate cutting-edge research? And in areas such as research on embryonic stem cells, for which the U.S. government currently severely restricts federal funding, could China even surpass the United States in either research or commercial development?

In December 2005, we visited China to examine whether the country had the emerging or even latent capacity to compete in the burgeoning field of stem-cell research — whether it was building the requisite intellectual capacity in this field; whether it had the necessary physical, financial, and institutional infrastructure; and whether the Chinese were pursuing innovation through different channels from those that prevail in the West. Although the evidence we collected was anecdotal, we concluded that China is in fact accumulating substan-

tial expertise in this area but does not yet have the infrastructure that scientific breakthroughs in stem-cell science are likely to require. In the future, however, the Chinese might develop new ways

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in which to fund and organize this science.

Currently, government funding of stem-cell science in China is woefully limited — more limited than the public perception would indicate and even more limited than the funding provided through several state programs in the United States. The bulk of the money comes through grants from the Ministry of Science and Technology, mostly in the form of two dedicated projects, one for basic stem-cell research and the other for applied stem-cell research. The grants are allocated centrally, and individual researchers then apply for portions of the overall allocation. Although precise figures are hard to come by, it appears that the ministry provided about 100 million yuan (roughly \$12 million) to each of the two major projects between 2000 and 2005. Local governments, particularly in Beijing and Shanghai, have put in some additional monies — perhaps as much as 100 million yuan

during this same period — in matching funds for basic research. Still, the total amount of government spending on stem-cell research since 2000 has probably been only about 300 million yuan (roughly \$38 million). In the immediate future, these figures are expected to soar: according to a report by the United Kingdom Stem Cell Initiative, China's Ministry of Science and Technology plans to devote between \$33 million and \$132 million to stem-cell research during the next 5 years.

By contrast, California alone has earmarked \$3 billion to fund stem-cell research at California institutions during the next decade, New Jersey has announced a \$380 million investment in a state stem-cell institute, and Connecticut has earmarked \$100 million for 10 years' worth of research. The British government devoted \$72.7 million of public funds to stem-cell research between 2004 and 2006. And in both the United States and Britain (as in Singapore, Israel, and other promising sites for stem-cell research), public monies are liable to be matched, at some stage, by private investment. As of June 2005, American firms focusing on stem-cell research had raised \$441 million from venture capitalists, and wealthy philanthropists may well step in with additional funds. Britain's Wellcome Trust, for example, in partnership with the U.S. Juvenile Diabetes Foundation, has already donated more than \$34 million. Such private sources are distinctly immature in China, leaving researchers particularly dependent on their limited government funding.

Similarly, the total numbers of stem-cell researchers and labora-

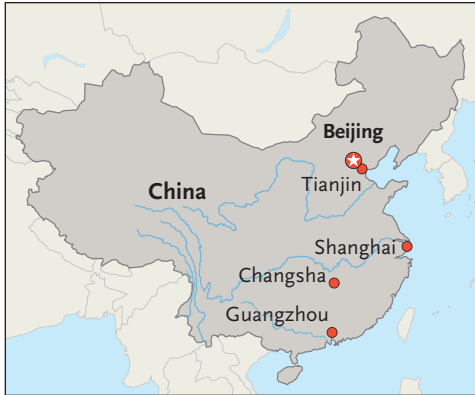
Partial List of Leading Stem-Cell Researchers in China.			
Researcher	Major Affiliation	Type of Stem Cells	Research Focus
Li Lingsong	Stem-Cell Research Center, Peking University, Beijing	Human and mouse embryonic and neural	Derivation of new human embryonic stem-cell lines and neural differentiation
Zhou Qi	Institute of Zoology, Chinese Academy of Sciences, Beijing	Rat and mouse embryonic	Animal cloning and animal nuclear transfer (monkey and mouse to rabbit, monkey, and mouse)
Sheng Hui Zhen	Center for Developmental Biology, Xinhua Hospital, Jiaotong University, Shanghai	Nuclear-transfer embryonic and human embryonic	Therapeutic cloning (nuclear transfer), transplantation of human nuclei into rabbit oocytes, and manipulation of human embryonic stem cells
Lu Guangxiu	Xiangya Medical College, Central Southern University, Changsha	Human and rabbit embryonic	Therapeutic cloning, nuclear transfer, and manipulation of human embryonic stem cells
Zhao Robert Chunhua	Chinese Academy of Medical Sciences, State Key Laboratory of Experimental Hematology, Tianjin	Human adult (bone marrow-derived) and mesenchymal	Applied research in tissue engineering (e.g., skin regeneration)
Zhu Jianhong	Huashan Hospital and Fudan University, Shanghai	Human adult and fetal neural	Clinical applications involving autologous transplantation
Huang Shaoliang	Center of Hematopoietic Stem-Cell Transplantation, Second Affiliated Hospital, Sun Yat-sen University, Guangzhou	Human (including cord blood) hematopoietic and mesenchymal	Clinical applications of stem-cell transplantation in blood disorders

tories in China remain relatively small. An estimated 300 to 400 researchers with Ph.D.s are working on all types of stem cells, and there are about seven top-notch laboratories, including Peking University's Stem-Cell Research Center and the Institute of Zoology at the Chinese Academy of Sciences, both in Beijing; Xinhua Hospital in Shanghai; and Xiangya Medical College in Changsha. Each of these laboratories boasts a top-caliber scientist: Li Lingsong at Peking University, Zhou Qi at the Institute of Zoology, Sheng Hui Zhen at Xinhua Hospital (she is also affiliated with Jiaotong University), and Lu Guangxiu at Xiangya Medical College (see table). Other institutions of note include the National Institute of Biological Sciences in Beijing, the Shanghai Institutes for Biological Sciences of the Chinese Acad-

emy of Sciences, and the Guangzhou Institute of Biomedicine and Health of the Chinese Academy of Sciences in Guangdong. The pool of lower-level researchers is limited, however, and promising students, like the leaders of their laboratories, go abroad for advanced training. At this stage, therefore, the pipeline of scientific talent in China is small.

Moreover, the collaboration among these researchers appears to be quite limited. Repeatedly, Chinese researchers report that they present their findings at international (rather than Chinese) conferences and that they aim to publish their work in English-language journals. Although these preferences are understandable in light of the status granted to Western conferences and journals, they underscore a marked tendency for Chinese scientists not to share

findings among themselves and a lack of social infrastructure for collaboration and exchange. Chinese publications that describe research on human embryonic stem cells, for example, list an average of only 1.5 institutional affiliations, as compared with an average of 2.2 institutions for all such publications worldwide. Similarly, our conversations with several leading Chinese scientists suggested that informal collaboration — the exchange of materials, sharing of results, and circulation of graduate students among laboratories — was lacking. If scientific research, especially in new and complex areas involving several disciplines, tends to progress through the interconnected findings of a broad group of investigators, then China does not seem to be building the domestic networks that one might



Chinese Centers of Stem-Cell Research.

expect to lead to breakthrough discoveries.

At this stage, therefore, China's role in stem-cell research seems marginal. Some extremely talented researchers are working in areas that may well prove to be productive, but their work hardly adds up to the scientific superpower that others have both praised and feared.

In the long run, however, China's hidden assets may well prove to be more important, particularly to the development of stem-cell technology. Most crucially, China brings to stem-cell science the same asset it has brought to industries that produce everything from athletic shoes to software: lower prices. It is simply cheaper to produce goods in China than in nearly any other country. As China develops, its wages and material costs will rise accordingly, but in sophisticated sectors such as medical research, it is liable to retain a cost advantage for quite some time. And if this advantage can be matched with exemplary technical skills, China could become a major force in the stem-cell industry, using its cost advantage to produce standardized components (such as cloned laboratory animals and

equipment for stem-cell manipulation) more efficiently than any other country.

Similarly, even if we presume that the path-breaking discoveries in the stem-cell arena will occur outside China's borders (if they occur at all), China's distinctive attitude toward the embryo, combined with its relatively lax regulatory system, could help its researchers leap the translational gap between laboratory science and medical application. Unlike their counterparts in North America and Europe, most Chinese citizens do not view the embryo as being imbued with an inherent moral value. It is not that Chinese researchers or regulators have a callous attitude toward the embryo — they don't. But stem-cell research in China is unlikely ever to be prone to the intense moral politicking that characterizes the field in the West, particularly in the United States.

Moreover, protocols for medical trials and testing are structured very differently in China. In the United States, the Food and Drug Administration wields power over this process, sharply delineating the steps that any laboratory innovation must go through before it can be considered as a medical treatment. In China, the boundaries are considerably more porous. Top researchers such as Zhu Jianhong of Fudan University in Shanghai and Huang Shaoliang of Sun Yat-sen University of Medical Sciences in Guangzhou are also elite physicians, treating hundreds of patients a year, often with techniques they have created in their own laboratories. Although such doctors are subject to the judgments of their hospitals' institutional review boards,

the constraints these institutions impose are almost certainly less onerous than those that might emerge from a distant regulatory body. As a result, Zhu and Huang have greater freedom to test treatment protocols and to move laboratory innovations rapidly into a health care setting. At the moment, the advantages of this position are minimal, since the science of stem cells is still far from being applied and since greater international collaboration might well prod Chinese scientists into conforming more closely to global standards. Ultimately, however, China's scientific fluidity could well become a factor in its technological advancement.

So for the moment, it seems, China's position in stem-cell science is similar to its position in other spheres. It is an up-and-coming player — a player with global ambitions, a burgeoning pool of talent, and specific assets that derive from its sheer size. In the future, China may be a powerhouse in the international stem-cell sector, able to leverage its talents, scale, and cost advantages to push the science out of the laboratories and into the clinics. But that future is not yet here.

An interview with Dr. Spar can be heard at www.nejm.org.

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