The new Silk Road

Kenneth Chien and Luther Chien look to the past to inspire biomedical research of the future.

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Benefits of cultural exchange: Ming dynasty ceramics used pigments from the Middle East.

Hope lies in dreams, in imagination and in the courage of those who dare to make dreams into reality.
Jonas Salk

For over 2,000 years, China has been at the heart of Asian society and culture. From painting to porcelain, calligraphy to cuisine, it has been a dominant force in the Far East. Now, China is poised to assume a major role in science and technology, particularly in human biology and molecular medicine.

The Chinese government's dream is for their country to become a global hub for biomedical research. But, as Jonas Salk noted, the fulfilment of such a dream requires more than knowledge itself; it needs imagination and courage.

This is an ambitious goal, but the timing is right. An alarming increase in the levels of cancer and cardiovascular diseases in China have made biomedical research a top priority, and timely investment from the government is creating an infrastructure that will appeal to expatriate scientists.

Arabic influence

Perhaps the most challenging step for Chinese scientists is to become familiar with new discoveries throughout the world. In the past couple of centuries, China has been largely isolated from the latest developments in Western science. But this has not always been the case.

The blue and white porcelain of the Ming dynasty in the fourteenth and fifteenth centuries is widely acknowledged to be the pinnacle of human achievement in ceramics.

Before the Ming period, Chinese ceramics were dull and lifeless. This art was transformed by the discovery that cobalt-blue pigment could produce a brightness and intensity of blue that has never been duplicated.

But this success needed the crucially important Silk Road. The pigment arrived in China from the Middle East by the Silk Road, a trail established by merchants during the period when the Mongols ruled China in the thirteenth century. This was the major route for cultural exchange between the two regions. The importance of this exchange can be seen in several of the motifs, shapes and designs (some with Arabic characters, specifically made for the Muslim market) on the most prized ceramics in the Istanbul and Tehran palaces.

Could such profitable cultural exchange happen again? We think so. In this era of molecular medicine, we see the 'new Silk Road' as the sharing of information between Chinese biomedical institutes and those of the United States and other Western nations. This exchange would open up many opportunities, which, like the old Silk Road, would be of benefit to both sides.

One attraction for researchers is the sheer number of people with cardiovascular disease in China — it is predicted that it will affect over 100 million people in the coming years. Coupled with the relatively low cost of hospitalization, China is ideal for clinical studies of novel therapeutic and diagnostic approaches.

Proper controls

Another advantage to the West, though clearly a disadvantage to China, is that standard clinical cardiovascular care in China does not include the routine use of expensive devices and drugs because of their high cost. A true placebo group to act as a control in drug trials is difficult to find in the West, because of the routine prescription of many drugs, but in China a 'clean' group could be easily found. Pilot clinical studies, while not sufficient to justify formal US Food and Drug Administration approval, could provide the impetus for further clinical testing in Western nations. In exchange for this information, it would be important to ensure overseas investment in China's health-care system.

Unravelling the mechanistic basis of diseases that arise from multiple, independent

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genetic and environmental variables will require international and interdisciplinary teams of doctors and scientists.

International training programmes should be designed in China to develop a new generation of Chinese graduates, who will serve as a route for the exchange of technology and ideas between different subject areas. The recent establishment of a series of new institutes in China, such as the National Institute of Biological Sciences in Beijing[1], the new biomedical institute in Guangzhou[2], and the new Institute of Molecular Medicine China at Beijing University could provide an infrastructure for such training programmes.

Other attractions

The burgeoning Chinese space programme could also form the basis for a new era of biomedical engineering. A clear precedent is evident from the number of spin-offs from the US National Aeronautics and Space Administration (NASA) programme. This interdisciplinary approach would capitalize on the strengths of Chinese institutions in engineering, physics, chemistry and mathematics.

China could be attractive to the West because of its expertise in non-human primate research, an area that is currently hampered by cost and ethical issues in Western nations. The availability of established primate colonies should give China a strong position in the ongoing non-human primate genome project.

Mouse models of human disease have led to the identification of many genes and pathways that may be linked to disease. But the usefulness of mouse models is limited because of the great differences in neural and cardiovascular physiology between mice and humans. Translating these experimental observations to studies in humans will be difficult without first having supporting evidence from large-animal models, preferably non-human primates.

Exploiting the minor difference in genomic sequence between chimpanzees and humans could be a major niche for China.

Exploiting the less-than-1% difference in genomic sequence between such primate species and humans could be a major niche for China. Non-human primate studies are currently only performed in a handful of US centres and are rapidly vanishing in the European community, as witnessed by the lack of support for a Cambridge University primate-research facility[3]. Partnerships between China's research centres and biotechnology and chemistry companies should lead to cost-effective primate-based data on drug safety that would be difficult to obtain in the United States or Europe.

Guangzhou's newly constructed research institute could be a beacon of interdisciplinary research.

The other main area of opportunity is a product of China's isolation. Chinese communities away from the main industrial centres may hold the key to the genetic risk factors and biomarkers that make the population prone to common diseases.

The recent discovery by Yi-Han Chen and colleagues of a gene for a rare form of familial atrial fibrillation, a disease that is associated with a high risk for stroke and cardiovascular morbidity, shows the value of studying genes from clinically well-defined Chinese patient populations[4]. Identifying the causes of other diseases will require state-of-the-art clinical phenotyping, and the development of regional networks of referring physicians that are coordinated by a single centre with world-class expertise in human genetics.

All these projects require investment, and China could use its growing market for clinical drugs as leverage to attract support from a consortium of large pharmaceutical, biotechnology and asset-management funds. Large drug companies are already beginning to establish sites in China, particularly in Shanghai. This trend is driven not only by cost-effectiveness, but also by China's strength in chemical research.

Western pharmaceutical and biotechnology firms that are allowed to tap into the growing clinical market in China should be required to provide a minimal level of support for national biomedical training and research initiatives. The establishment of international business standards to translate these molecular-medicine initiatives into reality could lay the foundation for a strong Chinese effort in drug discovery and biotechnology. To accomplish this objective, China will need to train business professionals to have direct experience in multiple aspects of biotechnology, ranging from intellectual property management to financing.

Family history

Much of this could be achieved through building biomedical links between China and the West. During the past century, a number of Chinese families have moved back and forth between China and the United States, thereby maintaining close ties between China and the West. Our ancestor Qian Zeng Qi, a provost of Beiyang University, had the foresight to send all his sons for education abroad. It was Qian's dream that his sons would eventually return to China and bring Western scientific and business precepts to mainstream Chinese society.

Today, there are many highly trained Chinese in virtually every area of science, technology and business in the United States, and the conditions are ideal for their return to China.

Capitalizing on this human Silk Road and moving towards globalization will be key if China is to enter the front ranks of molecular medicine. Encouraging close collaboration between overseas and Chinese biomedical scientists should lead to China rapidly becoming a centre for the growing global network of molecular medicine. Perhaps an ancient Chinese parable aptly sums up this philosophy: "If you do not venture into the tiger's den, how can you capture the tiger's cub?" ■

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1. Cyranoski, D. *Nature* **420,** 257 (2002).
2. Cyranoski, D. *Nature* **425,** 333 (2003).
3. *Nature* **427,** 471 (2004).
4. Chen, Y. H. *et al. Science* **299,** 251–254, (2003).