

## REVIEW

# Cardiovascular research is thriving in China

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Cardiovascular disease has become the leading cause of death and constitutes a serious public health issue in China. Faced with the burgeoning epidemic of cardiovascular disease and the huge burden and economic losses it causes, the Chinese government has attached the utmost importance to cardiovascular research, increasing funding to support basic and clinical studies, integrating resources and recruiting outstanding talent from overseas. The continued and growing support from the government has yielded substantial changes in terms of new discoveries, scientific publications and drug research and development within the last decade. In spite of the advances in cardiovascular research, China still faces significant challenges ahead in encouraging innovation, developing the prevention-oriented health policies and strengthening international collaboration.

**LINKED ARTICLES**

This article is part of a themed section on Chinese Innovation in Cardiovascular Drug Discovery. To view the other articles in this section visit <http://dx.doi.org/10.1111/bph.2015.172.issue-23>

**Abbreviations**

CVD, cardiovascular disease; NSFC, National Natural Science Foundation of China

**Introduction**

China's rapid economic growth has been accompanied by improved living conditions and changes in lifestyle. The rising incomes, faster pace of life and increased access to processed foods have led to overconsumption of sugar, oil, dairy and meat products. Excessive urbanization and motorization has further encouraged the sedentary lifestyle and largely reduced opportunities for physical activities, resulting in a greater prevalence of overweight and obesity, hypertension, lipid disorders and diabetes. The combination of sedentary lifestyle, obesity and diabetes has fuelled the epidemic of cardiovascular disease (CVD) and the morbidity and mortality of CVD increase continuously on a scale previously unexpected. A recent epidemic study has shown that one in five Chinese adults is suffering from CVD and this number is expected to double in the coming decade; about 3.5 million Chinese die of CVD annually, which accounts for 41% of total deaths, making CVD the leading cause of death in China (Chinese National Center for Cardiovascular Diseases, 2012).

Another recent study based on a nationally representative sample of adults in China indicates that 11.6% of Chinese adults have diabetes and the prevalence of prediabetes was about 50.1% (Xu *et al.*, 2013), making containment of the epidemic of CVD even more challenging.

In light of China's large and ever-growing population, the burgeoning epidemic of CVD and huge economic burden it causes, the Chinese government has attached the utmost importance to scientific research into CVD, increasing the funding to basic and clinical studies, setting up research centres and recruiting talents from overseas. All these efforts are dedicated to curbing the CVD epidemic and improving the health of Chinese population.

**Substantial funding**

The overall investment in research and development in China in 2012 was 1029.84 billion RMB, increasing by 18.5% from 2011, ranking third in the world, according to the latest

release from National Bureau of Statistics of China (Communiqué on National Expenditures on Science and Technology in 2012, [http://www.stats.gov.cn/english/pressrelease/201309/t20130926\\_454873.html](http://www.stats.gov.cn/english/pressrelease/201309/t20130926_454873.html)). The National Natural Science Foundation of China (NSFC) is one of the major funding agencies in China providing an advanced framework for funding basic science and technology research. It has played a leading role in the development of basic research in China over the past 25 years. To answer the call for improving public health nationwide, NSFC launched a health department in 2009. The initial funding from the Department of Health Sciences of NSFC was 1.8 billion RMB and in 2013 the grant funding increased to 4.6 billion RMB with a 2.5-fold increase. In particular, research funds for experimental cardiovascular studies from NSFC increased remarkably from 23 million RMB in 2004 to 312 million RMB in 2013, totalling over one billion RMB in the last decade (Figure 1). Notably, NSFC has recently initiated a 5 year Major Research Plan with a total funding of 200 million RMB, which aims to tackle the key pathological changes of CVD, revealing the mechanisms of vascular homeostasis and remodelling.

In addition, the National High-Tech Research and Development Program ('863 Program') and National Basic Research Program of China ('973 Program') managed by the Chinese Ministry of Science and Technology are two other major funding sources of cardiovascular research. The funding on cardiovascular basic research mainly comes from NSFC and the '973 Program', while CVD-related applied research programmes, such as pharmaceutical research, are mainly funded by the '863 Program' and National Science and Technology Major Projects. In line with its 11th 5 year plan stressing the urgent need for innovation and competitive edge, the Chinese government launched a prospective and grand project of Key New Drug Innovation under National Science and Technology Major Projects in 2008 with a total of 6.5 billion RMB (US\$960 million) to accelerate domestic drug research and development. This initiative supports both academic groups and pharmaceutical companies to establish

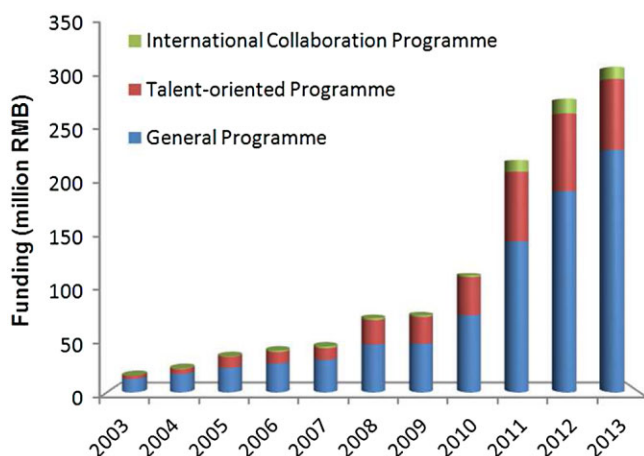
platforms for drug discovery and to develop prospective technologies for drug research and development.

## New platforms

The urgent call for CVD research and substantial financial support has greatly encouraged and enabled the setup of research centres and key laboratories at national, ministerial and provincial levels. The biggest and most comprehensive one is China's National Center for Cardiovascular Diseases which was founded in 2011 with the support from the Ministry of Science of Technology and is based in Fuwai Hospital, the hospital most renowned for the treatment of CVD in China. The centre evolved from the first state key CVD laboratory set up in 1984 with the goal of conducting research to improve the prevention and management of CVD. Based in the centre, the Chinese Ministry of Science and Technology, jointly with the Ministry of Health, set up the Technical Platform for CVD drug research and development under the Key New Drug Innovation Project. In addition to the national centre, some cardiovascular research institutes have been set up in some leading medical schools. The Institute of Molecular Medicine at Medical School of Peking University was initiated in 2005 focusing on basic and translational study of cardiovascular and metabolic diseases. These research centres are substantially funded to allow for further infrastructure development and advancing the research needs of China. Taking the National Center for Cardiovascular Diseases as an example, 63.5 million US dollars was granted to the principal investigators, from the '973 program' and the '863 program' in the last 5 years, and in the year of 2011 alone, more than 19 million US dollars was granted. These institutes also provide a good and favourable platform for investigators from many different disciplines to work together to tackle the problems and threats posed by CVD.

## Brain gain

What is essential to scientific research is high-calibre talent. Nowhere in the world has a government taken the task of tempting emigrated talents to return home as seriously as in China. The Chinese government has been the most assertive government in the world in introducing policies targeted at triggering a reverse brain-drain. Several talent programmes have been implemented in order to attract elite researchers from globally recognized universities or institutes in the world. 'One Hundred Talents Program' (also known as 'Century Program') initiated by Chinese Academy of Sciences as early as 1994 allows more independence to research institutes in head-hunting and to guarantee the support for the programme recruits on a selective basis. The subsequent 'One Thousand Talents Plan' was launched and administered by the central government of China in 2008 committed to a more authorized and stable recruiting plan. These talent programmes not only provide financial support for research projects and team construction efforts, but also require employers and related governmental departments to create more favourable policies regarding research, work evaluation



**Figure 1**

NSFC funding for cardiovascular research in China from 2003 to 2013.

and stimulus benefits. Up to 2013, more than 3000 professionals supported by the 'One Thousand Talents Plan' have returned to China, and most of them have now taken leadership positions in universities and research institutions. For example, all the principal investigators of the Institute of Molecular Medicine at Peking University were recruited from the United States and European countries. The Chair of this Institute, Professor Ruiping Xiao, and Professor He-Ping (Peace) Cheng who returned 7 years ago from the United States where they earned their tenure in NIH as senior investigators, are backed by the 'One Thousand Talents Plan'. Notably, supported by the 'One Thousand Talents Plan' and National Major Drug Development Program, the booming pharmaceutical industry has attracted and recruited 164 returnees from overseas, up to 2013, most of whom act as project leaders.

As China opens up more to the world and looks set to lead the world, international cooperation in the field of cardiovascular research has been given greater emphasis. Just as business depends on trading goods and services, science depends on exchanging ideas and data. The major funding agencies, the Ministry of Science and Technology and NSFC implement programmes open to foreign researchers in order to strongly encourage the collaboration with world-class overseas laboratories. Peking University and Massachusetts General Hospital are collaborating to advance biotechnology, research, drug discovery, education and training in the area of cardiovascular medicine. In particular, the Institute of Molecular Medicine at Peking University is collaborating with Massachusetts General Hospital to develop and characterize non-human primate (monkey) models for diabetes, obesity and CVD studies and has joint research programme with some of the leading pharmaceutical companies in the world. Two influential cardiology conferences in China, The Great Wall International Congress of Cardiology jointly with Asia Pacific Heart Congress held every year in Beijing and Shanghai-based Oriental Cardiology Conference, have attracted a growing involvement of international societies such as American Heart Association, American College of Cardiology and European Society of Cardiology.

## Where do we stand now?

China has put itself on the map with some important pioneering breakthroughs in both laboratory and clinical studies of CVD, including the discovery of superoxide flash (Wang *et al.*, 2008), role of miRNA in pathogenesis of arrhythmia (Yang *et al.*, 2007), cardiac fibrosis (Pan *et al.*, 2012) and myocardial infarction (Wang *et al.*, 2011), genetic aetiology of atrial fibrillation (Chen *et al.*, 2003), genetic and epidemiological studies of coronary artery disease and diabetes in the Chinese population (Yang *et al.*, 2010; Lu *et al.*, 2012), metabolic vascular disorders in atherogenesis, hypertension and stroke (Liu *et al.*, 2007; Yang *et al.*, 2010; Zhang *et al.*, 2012; Chen *et al.*, 2014) and translational studies on cardiovascular protection (Ma *et al.*, 2006; Lu *et al.*, 2007; 2008; Wang *et al.*, 2010; Li *et al.*, 2011; Yi *et al.*, 2012; Wu *et al.*, 2014). Notably, the role of MG53 in cardiomyocytes was first defined by Dr Ruiping Xiao, one of the most eminent figures among the high-calibre returnees. Their recent findings support the

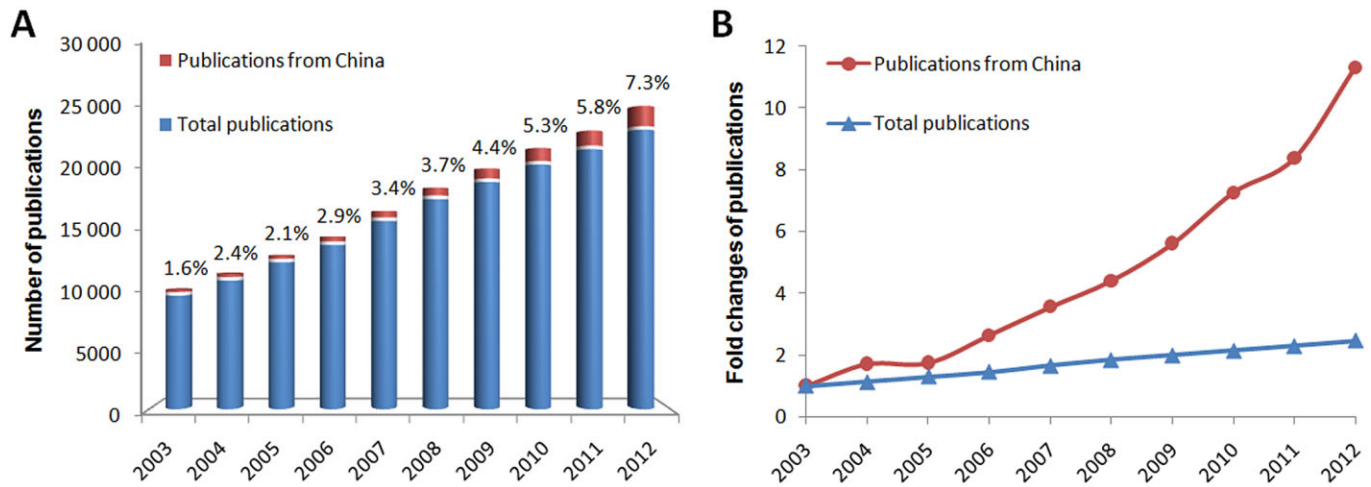
concept of targeted cell membrane repair in regenerative medicine, and recombinant MG53 protein as an attractive biological reagent for restoration of membrane repair defects in metabolic disorders and associated cardiovascular complications. (Weisleder *et al.*, 2012; Song *et al.*, 2013). Most recently, Chinese scientists have made a significant discovery about an endogenous mechanism of postnatal coronary vascular growth that provides avenues for understanding and stimulating cardiovascular regeneration following injury and disease (Tian *et al.*, 2014). This finding, published in the Science magazine, was viewed as 'a crowning achievement for deciphering coronary origins' (Burns and Burns, 2014).

China has shown rapid growth in the publications in the international journals – the most commonly used indicator of research productivity, surpassing many developed countries in recent years. Over the last decade, from 2003 to 2012, there were 163 356 publications globally that focused on cardiovascular research, of which China contributed 7092 publications (4.34%; Figure 2). The number of publications in cardiovascular research from China increased its ranking, from 15th in 2003 to 3rd in 2012.

Coupled with robust government support and the research and development activities of multinationals in China, the pharmaceutical industry in China has evolved from imitation (making only generic) to innovation, and has started to play a bigger role in global drug research and development. A totally China invented and developed chemical drug NBP (butylphthalide), prescribed for ischaemic stroke, owns independent intellectual property rights and has set a precedent that pharmaceutical intellectual property transfers from China to developed countries. In particular, traditional Chinese medicine research and development has been given considerable emphasis and has achieved a growing impact in the world. Modern molecular and metabolic technologies have been used to identify and analyse the effective components of traditional Chinese herbal medicine (Shi *et al.*, 2011). A multicentre, randomized, double-blind, parallel-group, placebo-controlled study of the effects of a traditional Chinese medicine patent drug (qili qiangxin capsule) on chronic heart failure reported that on a background of standard Western therapy for heart failure, qili treatment significantly improved cardiac function in the patients. This study may have broken the barrier for traditional Chinese medicine to be able to provide clinical evidence of efficacy (Li *et al.*, 2013; DeMaria *et al.*, 2014). Another traditional Chinese medicine Compound Danshen Dripping Pill – effective for angina and coronary heart diseases – has been approved by Food and Drug Administration of the United States for Phase III clinical trials and is being prepared for entry into American and European markets. It represents a breakthrough in the globalization of traditional Chinese medicines.

## What challenges lie ahead?

Although cardiovascular research in China is booming and remains upbeat, it has a weak foundation to build on to keep pace with the developed countries, and there is still a long way to go before it is at the forefront globally. For scientific publications, only the growth in quantity overtakes the



**Figure 2**

Number of publications originating from China in the field of cardiovascular research in the last decade (from Thomson Reuters Beijing Office).

growth in quality, and the average citation per paper from China is only 6.21, much less than the world average of 10.71. There is still a lack of world-class academic leaders, support for innovative and entrepreneur spirit, and novel and momentous findings that are crucial to the advancement of cardiovascular research. The inefficiency and bureaucracy of a government-run research evaluation system and grant administration constitute significant barriers to the development and growth of research capacity. Another major concern is that the efforts to introduce brilliant minds from abroad embarrassingly encounter policy difficulties and thus produce lower yields than expected.

As China is now playing an increasingly important political and economic role in the world, it needs to work with other countries to develop common strategies to alleviate the growing health burden from CVD. Putting CVD in a worldwide perspective offers great opportunities for collaboration between China and the United States and other countries (Bai *et al.*, 2013). China is seeking to join top-tier scientists and researchers to establish cardiovascular research centres and laboratories with a strong emphasis on translational research, integrating basic research with clinical study and pharmaceutical research and development. Key areas of CVD research that require immediate attention may include reducing CVD risks through prevention-oriented health policy and developing new therapeutic approaches for stroke and diabetic CVD that constitute a major threat to the Chinese population. All these efforts will be key moves in the battle against the threatening CVD epidemic that China now faces.

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## Author contributions

F. G. substantially contributed to the conception and design, drafting and revising the article and the final approval of the version to be submitted; R. J. S. contributed to the acquisition, analysis and interpretation of data; Y. J. revised the article critically for important intellectual content; B. F. Y. revised the article critically for important intellectual content and final approval of the version to be submitted.

## Conflict of interest

None.

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