

Basic and Translational Vascular Research in China Past, Present, and Future

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In parallel with China's economic boom, the lifestyle of Chinese people has dramatically changed. China has entered the society of aging, and the risk factors, including obesity, high-salt diet, overnutrition, sedentary behaviors, lack of physical activity, and air pollution, became more prevalent. Cardiovascular diseases have become a main threat to the public health and economic burden and the leading cause of morbidity and mortality in China (Online Figure I). Here, we reviewed the history of vascular medicine, current status of research in vascular biology, medicine and funding opportunities, and challenges in future.

Vascular Medicine in China: History and Development

As early as 2000 years ago, the Chinese people proposed in the Inner Canon of Huangdi that meridians are used to transport blood, working as blood vessels. After the introduction of Western medicine to China, the research on modern vascular medicine began to emerge but developed at a slow pace. In 1934, Prof Zhengang Lin from Peking Medical University published *Cirrhosis of Cardiac Arteriosclerosis and Pathology of Syphilis and the Formation of Myocardial Infarction and Its Clinical Significance*, which are the earliest monographs on atherosclerosis from the Chinese medical community. The first conference specifically focused on cardiovascular disease was held in 1959. In 1966, Prof Yingkai Wu, a pioneer cardiologist in China, headed the first study for the prevention and control of cardiovascular disease in Shijingshan District, Beijing, China, creating the Shougang model for China's prevention and control of chronic diseases. After a decade of Cultural Revolution in the 1970s in China, the scientific researches and academic activities gradually recovered. Under the leadership of Prof Wu, the Chinese Society of Cardiology, a branch society affiliated to Chinese Medical Association was initiated in 1978. In 1982, a branch society of cardiovascular research in Chinese Association of Pathophysiology was established. Since then, dozens of societies of basic and clinical cardiovascular research were established in China.

Nowadays, China has become one of the biggest resources for multicenter and population study worldwide. Based on the data from the clinical research registration website of National Institutes of Health (<https://clinicaltrials.gov/ct2/home>), there are 17 652 registered clinical trials on vascular medicine in the world currently, of which 1060 are possessed by and located in mainland China. Among these, >85% of trials are led by China. Although it accounts for only 14.3% of that by the United States (7433), it ranks first place in the number of existing clinical studies in China. However, this is still not proportional to its huge population. The representative major findings in translational research in China are listed in the [Online Data Supplement](#).

As a treasure of traditional Chinese Medicine, Chinese herb preparations (including Simiao Huoxue Decoction and Mao Dongqing) had been successfully used for the treatment of thromboangiitis obliterans since 1963. Danshen dripping pill is a widely used Chinese medicinal product in treating coronary artery disease. It has recently finished the stage III clinical trial to treat diabetic retinopathy and expected to become the first Chinese medicine preparation approved by the US Food and Drug Administration. In addition, a range of novel compound Chinese medicine has become commercially available in other Asia-Pacific countries, including Japan, Korea, and Australia, for example, Caditonic Pills, GuanXinErHao, GuanXinShuTong, Qili Qiangxin capsule, etc. A multicenter and randomized study of the effects of Qili Qiangxin capsules in patients with chronic heart failure has caught great attention of US medical field.

Challenges of Vascular Biology Research in China

According to the Report on Cardiovascular Diseases in China (2015), cardiovascular and cerebrovascular diseases become the leading cause of death in China (Online Figure IA). China has a population of 290 million experiencing different kinds of cardiovascular and cerebrovascular diseases, including hypertension in 270 million people, stroke in 7 million people, and myocardial infarction in 2.5 million people. One hundred

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The online-only Data Supplement is available with this article at <http://circres.ahajournals.org/lookup/suppl/doi:10.1161/CIRCRESAHA.117.310839/-/DC1>.

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(*Circ Res.* 2017;121:335-337. DOI: 10.1161/CIRCRESAHA.117.310839.)

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Circulation Research is available at <http://circres.ahajournals.org>

DOI: 10.1161/CIRCRESAHA.117.310839

fifty-nine million people are admitted to hospitals annually, and the costs on hospitalization in total and per capital are increased astronomically. In the last decade, the Chinese mortality rates of cardiovascular and cerebrovascular diseases are increased to 262 per 100 000 in urban and 296 per 100 000 in rural, respectively (Online Figure IB). The high mobility rate of China's cardiovascular and cerebrovascular diseases can be mainly ascribed to the paucity of early diagnosis of vascular lesions and lack of effective control of risk factors. In addition, the prevalence of cardiovascular disease in China has their distinct characters. For example, the incidence of stroke in China is higher than that of myocardial infarction, and the mortality rate of cerebral hemorrhage is greatly higher than in the United States and other western countries. Secondly, diabetes mellitus has become a major public health problem in China. The age-standardized prevalence of total diabetes mellitus and prediabetes were 9.7% and 15.5% in population, respectively. Third, the hypertension has become a rapidly growing public health concern in China, more than half of the cardiovascular diseases are associated with hypertension. There is an urgent need to establish a national strategy for basic, translational, and clinical research in line with the Chinese population.

Opportunities and Status Quo of Vascular Biology Research in China

With the development of China's economy, funds for scientific research are also increased rapidly. The National Natural Science Foundation of China (NSFC) and the Ministry of Science and Technology of China are the main funding agencies for vascular biology research in China. From 2007 to 2016, the NSFC and Ministry of Science and Technology of China allocated \$159 million and \$25 million research funding, respectively, for the studies in vascular disease. In 2009, the Department of Health Science of NSFC was further established as professional organization that funds the basic research of medicine in China. In recent years, it accepts a total of ~50 000 grant applications annually. The main types of funded grants are classified into research-related projects and talent-oriented projects. In 2016, the number of vascular biology projects funded was 3.5× than that of 2007 (Figure [A]), with the total funding increased from \$4 million in 2007 to \$28 million in 2016 (Figure [B]). Meanwhile, the overall supporting rate elevated from 11.1% in 2007 to 27.9% in 2016 (Figure [C]).

The research on vascular biology and vascular medicine in China is developing vigorously. In the past 10 years (2006–2015), Chinese scholars have published >18 000 research articles according to Web of Science statistics, searched with blood vessels, hypertension, and atherosclerosis as keywords. This accounts for ~10% of the total number of relevant articles in the world, second only to the United States in number (Online Figure IIA). The number of articles on vascular research by Chinese scientists in 2015 was 6-fold than that in 2006 (Online Figure IIB). Moreover, China ranks the ninth place in the world with regard to the total number of annually publication citation in 10 years (Online Figure IIC), and the number of highly cited articles with top 1% citation in 2015 was >7× of that in 2006 (Online Figure IID). In 2011, the first China's National Key Laboratory for Cardiovascular Disease

was established based in Fuwai Hospital, Beijing. Moreover, there are dozens of cardiovascular key laboratories from the Ministry of Education and Ministry of Health and hundreds of cardiovascular research institutes nationwide (Online Table I). Dozens of professional societies, such as Society of Vascular Medicine, Circulation, and Atherosclerosis, were established.

Moreover, the Chinese government attaches great importance to the cultivation of young talent and strength in vascular biology and medicine research field. For example, there are at least 5 different kinds of talent funds from NSFC as shown in the [Online Data Supplement](#). Moreover, the Ministry of Education of China has initiated the Yangtze River Scholar award, also known as the Cheung Kong Scholar award in 1998 to support the most distinguished professors in universities.

In 2013, NSFC launched a special research program project on the mechanisms underlying vascular homeostasis and remodeling, with at least \$30 million to be invested during the next 8 years. This is, by far, China's largest research program on vascular diseases. This major research program encourages cross-disciplinary collaboration, and in the past 4 years, it has funded 124 scientists with a total of \$20 million, with breakthrough results achieved in the areas of vascular injury, atherosclerosis, hypertension, vascular development and aging, pulmonary vascular diseases, and other fields. Since then, total 465 research articles were published supported by this program project, including 4 articles on nature and science and 42 articles on circulation, circulation research, and other American Heart Association journals. The representative main discoveries in vascular biology supported by this project are listed in the [Online Data Supplement](#).

Prospective

Management of vascular diseases has increasingly garnered the attention by Chinese government and the public. The major unsolved questions in this field involved 2 aspects. One is the mechanism of maintenance of vascular homeostasis and injury repair in response to environmental cue. As Chinese cardiovascular researchers, we also need to explore the underlying mechanisms for those distinct characters of cardiovascular disease in China, genetically and epigenetically. With the advance and development of stem cell research, nanotechnology, material science, 3D printing, etc, some major breakthrough will be achieved in the field in the near future. The other important issue is pathogenesis, prevention, and therapy of metabolic diseases and vascular complications. For Chinese scientists, metabolic vascular diseases become more urgent problem to solve because diabetes mellitus and metabolic syndrome have become a major public health problem in China.

There is still a long way to go for China's vascular biology and vascular medical research. For example, we still lack distinguished world-renowned scientists in the vascular field. Only one national cardiovascular key laboratory has been established to date. There is still a shortage of original studies with high impact, as well as multidisciplinary joint researches. The big gap between basic research and clinical application still exists. There is no loud Chinese voice and Chinese regimens in the international academic arena.

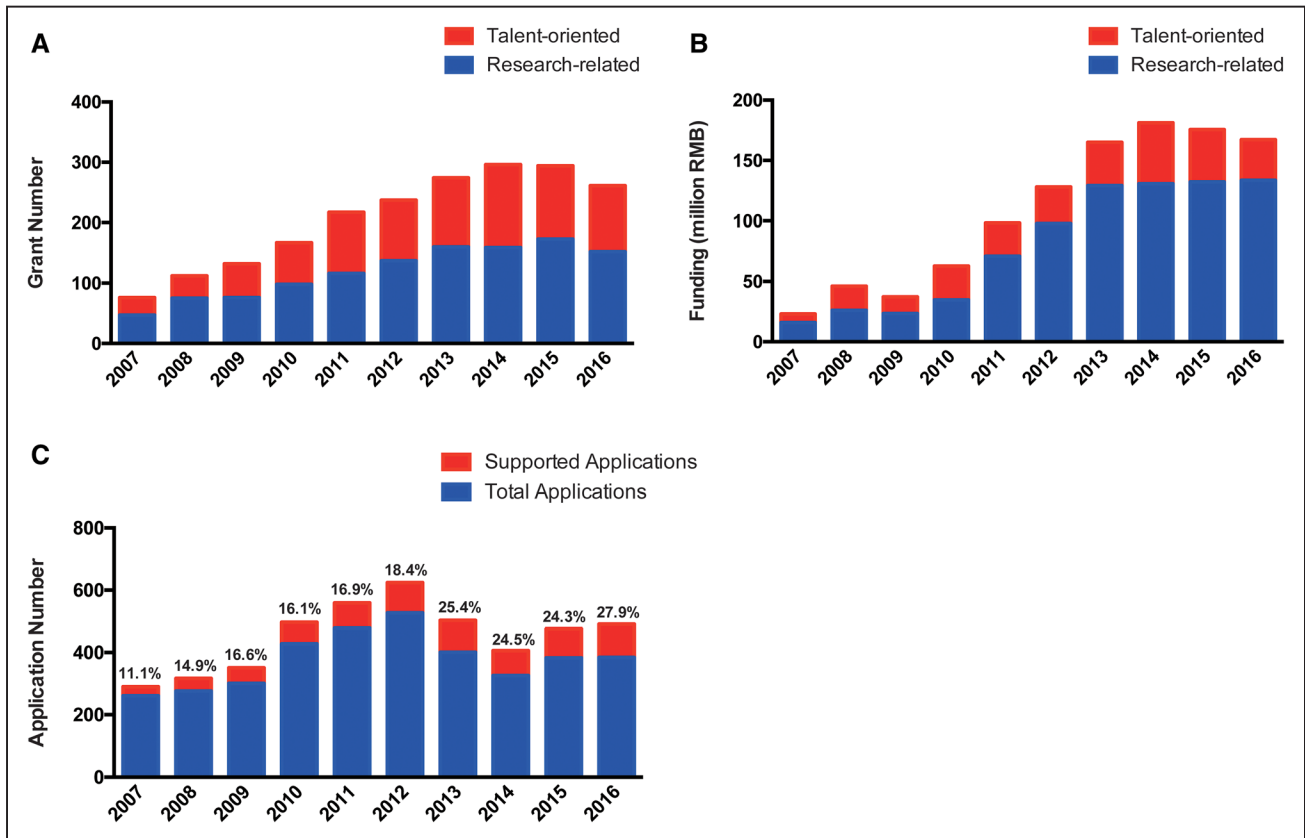


Figure. Grants from the National Natural Science Foundation of China (NSFC) for vascular biology and medicine during 2006 to 2015. **A**, The number of talent-oriented and research-related grants. **B**, The funding amounts of talent-oriented and research-related grants. **C**, The supporting rates of NSFC grants. The data were provided by NSFC. RMB indicates Renminbi.

However, we must acknowledge that there are advantages for the current Chinese cardiovascular biologists as well. China owns the largest cardiovascular patients resources and precious biological samples. During the past 20 years, many active Chinese researchers with overseas experience have returned to China under the support of governmental and institutional talent programs, such as One Hundred Talents Program initiated in 1994, and more recently, Thousand Young Talents Program launched in 2011 by the central government. In addition, the government-oriented input and encouragement of multidisciplinary collaborations are greatly increased in recent years. With the more highly motivated and talented interdisciplinary researchers are involved, the in-depth basic research on vascular biology and clinical translation will be dramatically accelerated,

thereby making great contributions to the health of Chinese people.

Acknowledgments

We thank Yuanguo Zhu from National Natural Science Foundation of China and Wenyang Yang, Yu Dong, and Jielan Ding from National Science Library, Chinese Academy of Sciences for the analysis of publications in the field of vascular research.

Sources of Funding

This research was supported by funding from the National Natural Science Foundation of China (91539203 and 81220108004).

Disclosures

None.

Circulation Research

JOURNAL OF THE AMERICAN HEART ASSOCIATION



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Circ Res. 2017;121:335-337

doi: 10.1161/CIRCRESAHA.117.310839

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 0009-7330. Online ISSN: 1524-4571

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