Applied Microbiology and Biotechnology (2021) 105:3971–3985
https://doi.org/10.1007/s00253-021-11317-8

MINI-REVIEW

Biotech in China 2021, at the beginning of the 14th five-year period ("145")

Rolf D. Schmid[1] · Xin Xiong[2]

Received: 21 February 2021 / Revised: 13 April 2021 / Accepted: 21 April 2021 / Published online: 3 May 2021

Abstract

As China assumes a more and more dominant role in global science, this mini-review attempts to provide a bird's eye view on how the bio-digital revolution impacts China's biosciences and bioindustry. Triggered by top-down political programs and the buildup of an impressive infrastructure in science, information technology, and education, China's biomedical and MedTech industries prosper. Plant and animal breeding programs transform agriculture and food supply as much as the Internet of things, and synthetic biology offers new opportunities for the manufacturing of specialty chemicals within the Chinese version of a "bioeconomy." It is already becoming apparent that the new five-year period "145" (2021–2025) will further emphasize emission control, bioenvironmental protection, and more supply of biomass-derived energy. This review identifies key drivers in China's government, industry, and academia behind these developments and details many access points for deeper studies.

Key points

- *Biotechnology in China*
- *Biomedical technology*
- *New five-year period*

Keywords China's industrial biotechnology · Synthetic biology · Medical biotechnology · Plant breeding · Fermented food · Emission control

Introduction and megatrends

On December 31, 2020, China's 13th five-year period ("135") has ended. Achievements during this period and plans for the 14th five-year period "145" (2021–2025) are gradually being published. Among many other advances, China has now become a major player in global science and technology. As of the end of 2019, the nation spent 2.2 trillion CN¥ (Chinese yuan) equivalent to 280 billion € (CNBS-Chinese National Bureau of Statistics 2020a, b), or 2.2% of its gross domestic product (GDP), on science and technology (S&T), the second largest expenditures after the USA. About 100 million Chinese work in S&T-related fields, 50% of them hold an academic degree, and more than 40 million youngsters leaving school each year continue high school training, half of them in science, agronomy, or medicine. Out of nearly 6.6 million young Chinese who studied abroad since 1978, mostly in North America, Europe, or Japan, over 4.23 million or 86% have chosen to return home and now hold positions in academia or industry (MOE-Ministry of Education of China (2020)-1 2019, MOE- Ministry of Education of China (2020)-2 2019). As a result, the output of scientific papers from China, according to the Nature Index, is now at about 20% of the world, and 25% in bioscience and medicine (Nature Index 2020). By impact, publications from institutes of the Chinese Academy of Sciences and from some Chinese universities have climbed to the top 50 in the world. In 2019, China accounted for some 22% of all international patent applications, more than the USA (Gurry 2020).

An extended version of this review is in print and due to appear as a book in June 2021; see Rolf Schmid and Xin Xiong, *Biotech in China – innovation, politics and economics*, ISBN 9789814877534. Updates on current biotech innovations in China can be found under the website of both authors under www.window-to-china.de.

✉ Rolf D. Schmid
rolf.d.schmid@bio4business.eu

[1] Bio4Business, Jagdweg 3, D-70569 Stuttgart, Germany

[2] NMI Natural and Medical Sciences Institute, University of Tuebingen, Markwiesenstr. 55, D-72770 Reutlingen, Germany

The foundation for these developments lies in the firm belief of Chinese leadership that S&T is indispensable to modernize a populous and large nation that 50 years ago was still widely underdeveloped. The results are impressive. In 2020, China has built a 155,000-km highway net (Chen 2020) for its 365 million cars (Liu 2020), 39,000 km of high-speed railway, and, even more important, the satellite network Beidou ("North Star") based on some 30 communication satellites which network mainland China and start to extend to other parts of the world. As the global number 2 in fast computers, and with one of the best 4G/5G networks in the world, modern information technology (IT) applications such as education, the Internet of things (IoT), or cloud-based services strive and provide an excellent base for the use of "big data" in biotech as well. However, many tasks remain: the fight against rural exodus and poverty, enhanced productivity in agriculture, improvements of the health system throughout a very unevenly inhabited nation, and urgent changes in energy supply — mostly coal — which not only are at the heart of China's severe air pollution but also engage a sizable number of its workers.

Regional considerations

China ranks number 4 among the world's largest nations, with roughly the size of the USA or Canada. Its 4 municipalities (Beijing, Tianjin, Shanghai, and Chongqing), 5 autonomous administrative regions, and 23 provinces represent quite different levels of population and economic wealth. China's master plan for a more even economic development of the country calls for 4 major hubs, which radiate into the neighboring provinces (Fig. 1). In 2020, these 4 hubs hosted 53% of the Chinese population and generated 63% of China's GDP (CNBS 2020–2023). Most of China's biomedical and biotechnology research and development (R&D) is located there, in 169 national and over 1000 provincial high-tech zones which host the majority of S&T personnel in industry. By the end of 2019, the national High-Tech Zone achieved a GDP of 12 trillion CN¥, equivalent to 1.55 trillion €, accounting for 12.3% of the national GDP (Wen 2020; MOST 2019).

As to academic R&D, most high-level universities among the nation's 2668 universities and colleges are located along the Pacific Rim, from Dalian to Hong Kong. Some of these universities have now started to establish teaching and research affiliations inland, such as the Jiaotong Universities in Xi'an and Chengdu. The other major organization in R&D, the Chinese Academy of Sciences (CAS), has established its 12 branch affiliations across the whole country, including 104 research institutions, some 1000 stations and sites, and over 60,000 employees (CAS 2020). The CAS and its 2 elite universities, the University of Science and Technology of China (USTC) in Hebei and the University of Chinese Academy of Sciences (UCAS) in Beijing, rank on positions 1, 11, and 13 of the global Nature Index 2020.

Health-related developments

In 2018, the average life expectancy at birth in China was 77.9 years for women and 75.0 years for men (World Health Organization (WHO) 2020). About 180 million Chinese or 13% of the population were older than 65 years (CER 2020). It is estimated that this number will rise to 329 million or 23.6% by 2050. As a consequence of an aging society, the 5 leading causes of death in 2017 were stroke, ischemic heart disease, lung cancer, chronic obstructive pulmonary diseases, and liver cancer. Lifestyle diseases are also on the rise. Thus, China counted 116 million diabetics (Statista 2019) in 2019 and over 2.8 million deaths from cancer in 2018 (Cao et al. 2020). The public healthcare system is centrally organized with about 33,000 hospitals in the cities, community health centers in the regions, and about 3 million registered doctors, supported by over a million "migrant doctors" and health workers in the countryside, increasingly connected via a 4G/5G network and "Internet hospitals." Public healthcare insurance now covers 1.35 billion or 96.4% of all Chinese, at least to some extent.

The industry

At the end of 2018, China counted 4441 pharmaceutical manufacturers; however, over 70% of these companies had annual sales of less than 100 million CN¥, equivalent to 13 million €. Chinese companies lead the world market as suppliers of active pharmaceutical ingredients (API), vaccines, and antibiotics. In 2018, the size of the pharmaceutical market was about 2.1 trillion CN¥, equivalent to 270 billion €. Twelve percent came from biologics, with a share of 39% for vaccines, 16% for recombinant insulins, 15% of blood products (mostly human serum albumen), and only 11% from therapeutic antibodies (most antibiotics are considered chemical drugs and do not fall into this category). Generally speaking, highly innovative drugs still originate from international companies, and Chinese manufacturers excel in generics and traditional Chinese medicine (TCM). However, innovation is strongly supported by the government through tax breaks, government purchase regulations, and infrastructures such as science parks. Table 1 provides a shortlist of biopharmaceutical companies in China and typical biopharmaceutical products.

Medicinal plants and traditional Chinese medicine

About 30% of all drugs sold in China are TCM products, as their use is deeply rooted in Chinese culture and their prescription strongly supported by the government. Thus, primary

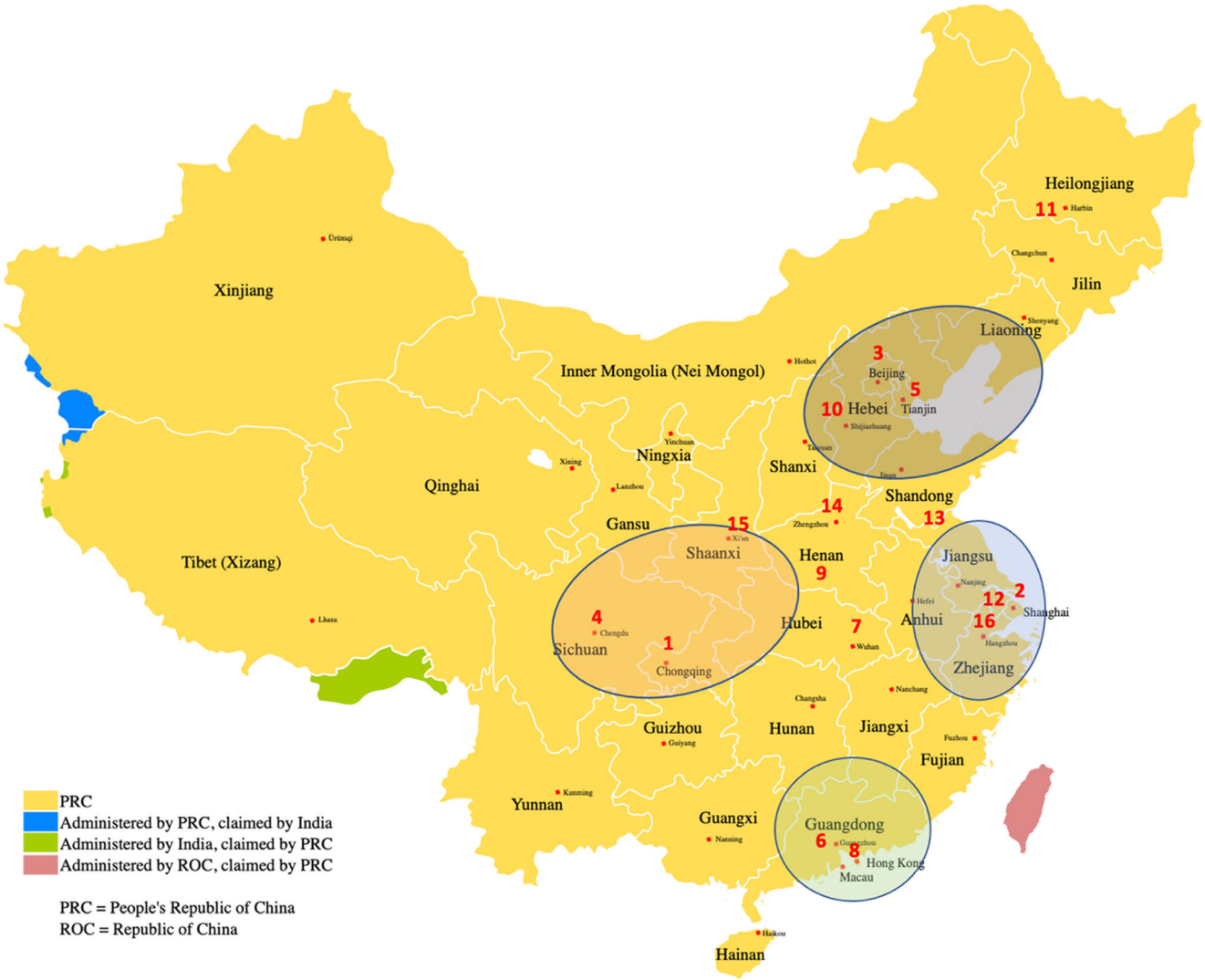

Fig. 1 Map of China and four biobusiness clusters (map from *Wikimedia China administrative*, ASDFGH). As of 2020, China had 16 megacities with over 10 million inhabitants. These were, ranked by population (number is also position on map), (1) Chongqing, (2) Shanghai, (3) Beijing, (4) Chengdu, (5) Tianjin, (6) Guangzhou, (7) Wuhan, (8) Shenzhen, (9) Nanyang, (10) Shijiazhuang, (11) Harbin, (12) Suzhou, (13) Linyi, (14) Zhengzhou, (15) Xi'an, and (16) Hangzhou. Much of China's pharmaceutical research and industry is located in 4 biobusiness clusters shown here as bubbles: the northeastern cluster (Liaoning, Hebei, Beijing, Tianjin, and Shandong), the eastern cluster (Jiangsu, Zhejiang and Shanghai), the southern cluster (Guangdong and Hong Kong), and the western cluster (Sichuan, Shaanxi, Hubei and Chongqing). In these 4 clusters lived 53% of the Chinese population and generated 63% of China's GDP

schools and high schools provide obligatory lectures on TCM for all students. In 2018, 2350 manufacturers of TCM created sales in excess of 900 billion CN¥, equivalent to 117 billion €. Registered raw materials for TCM numbered some 12,800, of which over 11,100 were from plants. Among 12,000 documented medicinal plants, nearly 7300 came from Sichuan Province in Central China, dubbed "China's pharmacy." TCM-Related research was recently stimulated by the Nobel Prize for Medicine in 2015 to TU Youyou (Famous Scientist 2018). Her discovery of artemisinine as a malaria drug, in 1972, was based on information from historic textbooks on TCM and modern methods of isolation and characterization of active ingredients.

The MedTech industry

By the end of 2018, some 17,000 manufacturers of MedTech products were certified in China. Table 2 provides a shortlist of leading companies and their products. There were 52 listed manufacturers of in vitro diagnostics (IVD), with sales of about 60 billion CN¥ equivalent to 7.8 billion €, of which 80% were spent for test kits. The rise of a well-educated middle-class population with more disposable income, an aging society, and technological developments such as cloud computing, rapid data transmission, and second-generation sequencing all contribute to a wider use of IVD in hospitals and at home. An international success story is BGI's non-invasive

Table 1 A shortlist of Chinese pharmaceutical and biopharmaceutical companies

Company name	Type	STN	Sales 2019 (million CN¥; million €)	R&D 2019 (million CN¥; million €)	Biopharmaceutical products (examples)
Jiangsu Hengrui[a] 恒瑞医药	P	SHA:600276	23,289; 3015	3896; 504	PD-1 monoclonal antibodies
Shanghai Fosun Pharma[b] 上海复星医药	P	SHA: 600196	28,585; 3701	3463; 448	Rituximab, H1N1 vaccine
Qilu Pharmaceutical[c] 齐鲁制药	S	–	25,100; 3250	1600; 207	Bevacizumab monoclonal antibody
Zhejiang Hisun[d] 海正药业	P	SHA: 600267	11,072; 1433	814; 105	Insulin, adalimumab
Chongqing Zhifei[e] 重庆智飞生物	P	SHE:300122	10,600; 1327	259; 34	Hib vaccine, HPV vaccine, 23-valent pneumococcal polysaccharide vaccine, etc.
Salubris Pharmaceuticals[f] 信立泰药业	P	SHE: 002294	4,470; 579	763; 99	Recombinant human parathyroid hormone
Walvax Biotechnology[g] 云南沃森生物技术	P	SHE: 300142	1121; 145	65; 8.4	23-Valent pneumococcal polysaccharide vaccine, etc.
InnoventBio[h] 信达生物	P	HKG:1801	1048; 140	1294; 168	PD-1 monoclonal antibody, 20 biomedical drugs in approval procedure or preclinical studies

S state-owned company, *P* private company, *STN* stock trading number

[a] https://www.hrs.com.cn

[b] https://www.fosunpharma.com

[c] http://m.qilu-pharma.com

[d] http://www.hisunpharm.com

[e] http://www.zhifeishengwu.com

[f] http://www.walvax.com

[g] https://www.walvax.com

[h] http://innoventbio.com/#/

prenatal diagnosis test for genetic screening, based on fetal DNA collected from maternal blood. BGI's NIFTY test offers screening for Down's syndrome, trisomy 13 and 18, and other genetic effects and is now available not only in China but also in many countries around the world (BGI 2017).

Genome sequencing, gene banks, and personalized medicine

Among over 200 sequencing companies in China, the two major players are the BGI in Shenzhen and GENEWIZ in Suzhou. A third large center, National Health Medical Big Data Center in Nanjing, is presently under construction. BGI has published a study on the whole genomes of some 141,000 Chinese women, based on their NIFTY tests (BGI 2018), and a "Chinese genome map" was built on the basis of 597 healthy individuals from most areas of China (Du et al. 2019) — stimulated by the fact that in Western human genome programs the Chinese population is underrepresented. These efforts are meant to facilitate genetic testing and personalized medicine and include "gene banks" such as the National Gene Bank in Shenzhen, co-financed by BGI (Fig. 2), and the Biobank in Shanghai's Zhangjiang Business Park.

Cell-based medicine and animal models for disease and brain research

Supported by a 2015 master plan of the MOST, cell and stem cell technologies are important areas of R&D in China (Hu et al. 2018). Major cell depositories are the Global Cord Blood Cooperation (GCBC), which stores cord blood of babies as a resource for stem cells later in their life, and Beike Biotechnology located in Taizhou's China Medical City which is a key player in the National Stem Cell Industrialization Programme.

Other aspects of cell technology are organ replacement and xenotransplantation. According to the China Medical Association, 4733 human livers, 10,793 kidneys, 446 hearts, and 299 lungs were transplanted in 2017 in 178 licensed hospitals (Shi et al. 2020). Chinese research on xenotransplantation of porcine cells or whole pancreas is also high. Cells and organs are provided by transgenic pigs producing human

Table 2 A shortlist of Chinese biomedical and IVD companies

Company name	Type	STN	Sales 2019 (million CN¥; million €)	Major products
Mindray Medical Devices[a] 迈瑞医疗	P	SHE: 300760	16,500; 2136	Ultrasound devices, patient monitoring, IVD
Dian Diagnostics Group[b] 迪安诊断	P	SHE: 300244	8500; 1100	Diagnostics, molecular diagnostics
LePu Medical technology[c] 乐普医疗	S+P	SHE: 300003	7800; 1010	Cardiovascular implants, stents
Yuwell Medical[d] 鱼跃医疗	P	SHE: 002223	4600; 596	Oxygen concentrator, breath care, blood pressure monitoring
Blue Sail Medical[e] 蓝帆医疗	P	SHE: 002382	3500; 453	Health care products and stents
Medical System Biotechnology[f] 美康生物	P	SHE: 300439	3300; 427	Biological IVD kits
Maccura Biotechnology[g] 迈克生物	P	SHE: 300463	3200; 414	IVD, PCR
BGI Group[h] 华大基因	P	SHE: 300676	2800; 363	IVD, e.g., for neonatal testing, tumor diagnostics
Shanghai Kehua Bioengineering[i] 科华生物	S	SHE: 002022	2400; 311	IVD
Shanghai Tofflon[a] 东富龙	S	SHE: 300171	2300; 298	Injectables and packaging

S state-owned company, *P* private company, *STN* stock trading number

[a] http://www.mindray.com

[b] http://www.dazd.cn

[c] http://www.lepumedical.com

[d] http://www.yuwell.com

[e] http://www.bluesail.cn

[f] http://www.nb-medicalsystem.com

[g] https://www.maccura.com

[h] https://www.genomics.cn

[i] https://www.skhb.com/cn/

[j] http://www.tofflon.com

insulin and reared in a pathogen-free environment (Wang et al. 2019). Pigs are also being developed as animal models of human diseases (Wu 2018), and isogenic cats and dogs are bred from mature parental oocytes by somatic cell nuclear transfer followed by embryo transfer in a commercial setting (Sinogene 2020). The National Resource Center for Mutant Mice at Nanjing University hosts over 3500 strains (NRCMM 2020). China's vantage point, however, are Macaque monkeys for which a long-read genome map is available and which are bred in over 24 facilities throughout China (Cyranoski 2018). Within the China Brain Project, started in 2017, a group of institutes such as Peking and Tsinghua University, the CAS Institute of Neurosciences in Shanghai, and the Academy of Military Medical Sciences will use this resource and focus on brain science and brain-like intelligence technology (Shi et al. 2019).

Fig. 2 National Gene Bank in Shenzhen. Photo credits: CNGB website

Telemedicine and Internet hospitals

Medical digital records in Chinese hospitals add up to some 800 million people from 8 billion patient appointments every year. Internet-based medical services have begun to curb unnecessary visits to doctors, and 38,000 hospitals can already be reached via the Internet for patient inquiries or consultations among doctors. The Internet, augmented reality, and fast data communication open new opportunities for sensor-based telemedicine based on portable instruments, for evidence-based diagnoses using image analysis, and for a robot-based support for initial patient interviews and preliminary therapy, including the use of TCM (Sun et al. 2020).

COVID-19 pandemic

Following the SARS-COV-1 epidemic in 2002, a much more aggressive coronavirus, SARS-COV-19, originated in Wuhan in late 2019. As this review is written, there are over 150 million confirmed cases and over 2 million victims on all continents. China counted some 80,000 infected people, of which some 5000 died. However, based on strict social distancing and the obligatory use of a "personal health code" on everybody's cellular phone, China now seems to be under control of this outbreak. PCR-Based assays are done at levels of several 100,000 per day per provincial center. In addition, several vaccines were developed in record time. The leading supplier has successfully passed clinical studies of phase III in 12 countries and is now offering its vaccine, based on an attenuated COVID-19 strain. Fourteen more vaccines, including some based on mRNA, are under phase II or III studies. The first vaccine based on inactivated corona viruses, developed by the Beijing Institute of Biological products (SinoPharm Biotechnology), has gotten conditional approval for emergency use by National Medical Products Administration (NMPA) on Dec. 31, 2020 (People's Daily 2020), and the government claims that over 22 million people have been vaccinated as of January 26, 2021 (Yi 2021). Production of this vaccine is said to rise to over 2 billion doses in 2021.

Industrial biotechnology

Over the past decades, China has become a leading global producer of fermentation products such as ethanol, amino acids, citric, malic and lactic acid, vitamins, industrial enzymes, and biopolymers. Apart from servicing large national markets, a sizable amount of these products is exported, and manufacturers, which often number in the dozens, suffer from overcapacities. Usually, only a few companies control these markets, and they apply R&D strategies not only to improve strains but also to reduce raw material cost and the environmental load of their processes.

Amino acids

Chinese companies lead the world in the production of bulk amino acids such as L-glutamate, L-lysine, L-threonine, and L-tryptophane. Table 3 provides a survey on the leading companies and their products.

Hydroxy acids

The estimated production of citric acid in China in 2019 was 1.37 million t. Among about 100 manufacturers, the top 4, Ensign World, Luxin Jinhe, Tiantian Citric Acid, and Cofco, account for over 90% of production. L-Malic acid is manufactured by Changmao Biochemical Engineering at an annual scale of about 5000 t through the enzymatic addition of water to fumaric acid using immobilized cells of *Escherichia coli* (Tanabe process).

Vitamin C

China has a long tradition in manufacturing vitamin C (ascorbic acid). Originally following the chemo-fermentative procedure developed by Tadeus Reichstein at Hoffmann-La Roche, researchers at the CAS Institute of Microbiology later changed to a two-step fermentation where glucose is first transformed into 2-keto-L-gulonic acid by microbial cells followed by chemical transformation, which was transferred to Hoffmann-La Roche in 1985, becoming the first large technology export from the People's Republic of China (Yang and Xu 2016). In 2018, China produced 60,000 t of vitamin C, of which 70% was exported.

Ethanol

Out of 108 billion L of fuel ethanol produced globally in 2018, China produced 2.89 million t or about 4%. Current domestic gasoline consumption stands at about 130 million t. As China targets 10% ethanol addition to gasoline by 2020 (E10), the demand for fuel ethanol would be about 13 million t, more than fourfold the amount produced (Zhang 2019). As of 2006, production by the four leading companies, shown in Table 4, had reached 1.24 million t, mostly from aged grain as a carbon source. Then, corn and wheat prices rose sharply and a discussion on their use for "eat or drive" developed. As a consequence, the National Development and Reform Commission (NDRC) stopped the approval of using corn and wheat and encouraged companies to produce fuel ethanol from non-food resources such as cassava, sweet potato, sweet sorghum, straw, or woody residues. Subsidies for projects of this kind were up to 1200 CN¥ equivalent to 155 €/t of ethanol.

Table 3 Leading Chinese manufacturers of amino acids and hydroxy acids

Product	Company name, location	Type	STN	Estimated production (2019)
Amino acids	Fufeng[a], Shandong	P	HK: 0546	1.1 million t glu, starch sweetener 650,000 t, 176,000 t thr, 200,000 Lys
	Meihua[b], Hebei	P	SHA: 600873	758,799 t glu, 9399 t medical aa, 1,795,794 t animal feed aa.
	Eppen[c], Ningxia	P	–	300,000 t, 660,000 t lys (2018)
	Global Biochem Technology Group[d]	P	HK: 00809	186,000 t lys, thr, corn sweetener 299,000 t
Citric acid	Ensign World[e]	P	–	600,000 t (2018)
	Luxin Jinhe[f]	P	–	360,000 t (2018)
	Tiantian Citric Acid[g]	P	–	300,000 t (2018)
	Cofco[h]	S	SHE: 000930	340,000 t (2018)
Malic acid	Changmao Biochemical Engineering[i]	P	–	5000 t (2018)

glu L-glutamic acid or monosodium glutamate, *lys* L-lysine, *thr* L-threonine, *trp* L-tryptophane, *P* private company, *S* state-owned company, *STN* stock exchange number

[a] http://www.fufeng-group.com

[b] http://www.meihuagrp.com

[c] http://www.eppen.com.cn

[d] http://www.globalbiochem.com/html/index.php

[e] http://www.ensignworld.com

[f] http://www.rzbc.com

[g] http://www.ttca.com.cn

[h] http://www.cofco.com/cn/BrandProduct/COFCOBiochemical/

[i] http://www.cmbec.com/home/index.asp

Recently, these developments were frozen due to new priorities for mobile energy relating to methanol from coal, electromobility, and, most recently, development of hydrogen-fueled trucks and cars.

Following a new concept of bioethanol production from syngas, proposed in 2012 by LanzaTech, there are presently several steel companies such as Baosteel, Beijing Shougang, and Capital Steel which have built pilot plants exploring this process in practice. Capital Steel operates an effluent-to-ethanol plant with an annual capacity of 46,000 t of ethanol (LanzaTech 2018).

Industrial enzymes

The use of technical enzymes in China differs from uses in Western countries: enzymes for starch degradation, for the brewing industry, and for dairies are widely used. The most important, however, are enzymes such as cellulases, laccases, and phytases for animal feed. In 2018, 80,000 t of enzymes were used for this purpose with a value of over 2 billion CN¥ equivalent to 260 million €, over 80% of the total production (CHYXX 2019). Major enzyme producers are listed in Table 5.

Biopolymers

In 2019, the estimated production of biodegradable polymers such as PLA or PBS was at 520,000 t and rose to 1 million t in 2020. Estimates for 2025 are 4–5 million t (Jin 2021). China leads also in the global production of some biopolymers, e.g., xanthan and sodium alginate.

Academic R&D and technology transfer

Innovative processes for industry are often initiated by academic institutions which explore new technologies, introduce new methods, and transfer them to industry through licensing, transfer of staff, or the foundation of start-up companies. The development of new industrial processes for the manufacture of a wide range of fine chemicals by fermentation or in plants is presently at a dynamic stage due to novel tools in synthetic biology, metabolic engineering, and robot-assisted high-throughput analysis of candidate production strains ("smart cells"). Dozens of academic groups throughout China have embarked on such technologies, with a focus on new enzymes, new host organisms, or high-yield conversion of natural substrates. IT infrastructure and access to service providers, e.g., for genome sequencing, are excellent in China.

Table 4 Major bioethanol producers in China (2018)

Company	Type	Capacity (t/year)	Carbon source**
Henan Tianguan[a]	S	700,000	Wheat, corn, manihot
Jilin Fuel Ethanol[b]	S	600,000	Corn
Cofco (Anhui)[c]	S	400,000	Corn, manihot
Cofco (Zhaodong)	S	400,000	Corn
Guangxi Cofco Biomass Energy	S	200,000	Manihot

Source: https://www.niumoney.com/news/notice_132426.html, http://baogao.chinabaogao.com/huaxuechangpin/515429515429.html

S state-owned

**Currently 87% of the raw material source is corn; 11% is cassava (manihot) or sugar cane, and only 2% is cellulose, and fed-batch fermentation using *Saccharomyces cerevisiae* is the standard process. As corn supply is limited, E10 targets may not be reached in 2020

[a] http://www.tianguan.com.cn/english/

[b] http://www.cnpc.com.cn/en/

[b] http://www.cofcotech.com

Table 7 provides a shortlist of leading universities and institutes in this field and a selection of targets.

Technology transfer to companies is a key element of the "Made-in-China 2025" plan and is supported by a wide range of political and financial measures (Table 6). As shown in Fig. 3, many technology transfer opportunities can be related to biobusiness.

Biotechnology in agriculture

In 2000, 70% of China's population still worked in agriculture, and even in 2014, 45% of all Chinese lived in rural areas. They make China the world's largest producer of rice, contributing about 30% to global production, and of other important crops such as corn, wheat, millet, sorghum, barley, potatoes and sweet potatoes, soybean, rapeseed, and sugarcane. China produced 17.3 million t of peanuts in 2018, being on top in the world. Most of the nuts are used to produce peanut oil, the Chinese cooking equivalent of olive oil in Western countries. Other large crops are tea, tobacco, and cotton. Classical breeding of cultivars has been done for many decades, and a most relevant example was the breeding of hybrid rice through crossbreeding of a wild rice species with a male-sterile strain. Starting from the 1970s, such work by Yuan Longpin and colleagues at Hunan Agricultural University led to a high-yield hybrid cultivar which helped farmers nearly quadruple China's rice production compared to 1950. Yuan's team recently has bred an alkaline- and salt-resistant rice variety which apparently provides good harvests on hitherto unfertile soils (Guo 2021). Research on transgenic crops is well established in China, and 90% of all cotton plants are insect-resistant Bt cotton. Transgenic papaya and poplars have also been planted. However, the Ministry of Agriculture, responsible for regulations on the release of environmental crops, so far has generally hesitated to license transgenic crops for food use — a consequence of consumers' concerns which ignited from the "Golden rice controversy" in 2014 when transgenic rice which had been engineered to produce vitamin A was given to schoolchildren without thorough information of the parents. It remains to be seen if the acquisition of Switzerland-based Syngenta by state-owned giant ChemChina in 2018 will change this situation (Table 7).

China accounts for nearly half of global pork production, and fish farmers contribute over 60% to the global production of fish from aquaculture. Following centuries of traditional breeding, genomic breeding of these and other farm animals is a hotspot of Chinese R&D. A shortlist of major institutes involved in the genomic breeding of plants and farm animals is provided in Table 8.

Examples are transgenic Yellow River carps (Luo et al. 2018), engineered at the CAS Institute of Hydrobiology for a triploid expression of the fish's growth hormone leading to a nearly twofold faster growth, and the goat Yangang, created by somatic cloning at Northwest A&F University (Zhi 2016).

Improving technology

Compared to industrialized nations, the productivity of Chinese farms is still low. Extensive programs are underway to improve this situation, using China's satellite and IT networks, e.g., for the survey of fields by drones, for driverless agricultural machines, or for enhancing marketing and transportation of agricultural goods. Vertical farming and agricultural IoT are also progressing (Sananbio 2020). Education and urbanization are other policies for absorbing those farmers who have lost their jobs due to technical progress, to reduce rural exodus and to provide better jobs for migrant workers.

Table 5 Shortlist of enzyme producers in China

Company name and location	Type	STN
Novozymes China, plants in Tianjin, Shenyang, and Taicang[a]	F	
Dupont-Genencor China, Wuxi plant[b]	F	
AB Enzymes China, Shanghai[c]	F	
DSM Yixing Jiecheng-Engineering[d], Jiangsu 宜兴杰成	P, F	
Sunson Industry Group[e], Beijing北京夏盛	P	–
Sino Enzymes[f], Gansu Province白银赛诺	P	–
Vland Biotech[g], Qingdao 蔚蓝生物	P	SHA: 603739
Longda BioProducts[h], Shandong 隆大生物	P	–
Boli Bioproducts, Jiangsu 江苏博立生物制品	P	–
Yiduoli[i] VTR-Biotec, Guandong 溢多利	P	SHE: 300381
Xinhuayang[j], Hubei 新华扬	P	–
Challenge Group[k], Beijing 挑战集团	S	–

P private company, *S* state-owned company, *F* foreign-owned company, *STN* stock exchange number

[a] https://www.novozymes.com/en

[b] http://biosciences.dupont.com/contact/locations/

[c] https://www.abenzymes.com/en/global-locations/

[d] http://www.jch.com.cn/pages/p2.html

[e] http://www.chinaenzymes.com/index.html

[f] http://www.sinoenzymes.com

[g] http://www.vlandgroup.com/en/about.aspx?BaseInfoCateId=99&CateId=99

[h] http://www.longda-enzyme.com/producten.html

[i] http://www.yiduoli.com/?lang=en

[j] http://www.sunhy.cn

[k] http://www.challenge.com.cn

Table 6 Measures to facilitate tech transfer from academic R&D

Measure	Target group
Public researchers may start own company[a]	Academia
Public researchers may keep up to 70% of profits from the transfer of their patents[b]	Academia
The technology trading center CTEX-TT offers technology transfer to industry through 67 local, 17 professional, and 3 international channels[c]	Academia and industry
20 state venture capital funds in 2019 held a capital of 3059 billion CN¥ (equivalent to 394 billion €)[d]. In addition, there are about 14,000 private VC funds[e]	Academia and industry
Both government and industry continuously promote the foundation of cooperative innovation platforms around emerging technologies	Industry
Industry can deduct 75% of R&D expenditures from tax, manufacturing industry 100%[f]	Industry
Central and local governments have established 169 national and over 1000 provincial high-tech zones, which in 2020 hosted 225,000 high-tech enterprises[g]	Industry

[a] http://politics.people.com.cn/n1/2020/0121/c1001-31557607.html

[b] http://scitech.people.com.cn/n1/2020/0618/c1007-31751490.html

[c] https://gyjy.ctex.cn

[d] https://www.sciping.com/28310.html

[e] http://qccdata.qichacha.com/ReportData/PDF/9155aeb68025bd7a11acb72591a3fff5.pdf

[f] http://www.gov.cn/zhengce/2021-03/25/content_5595705.htm

[g] http://www.gov.cn/xinwen/2020-10/21/content_5553081.htm

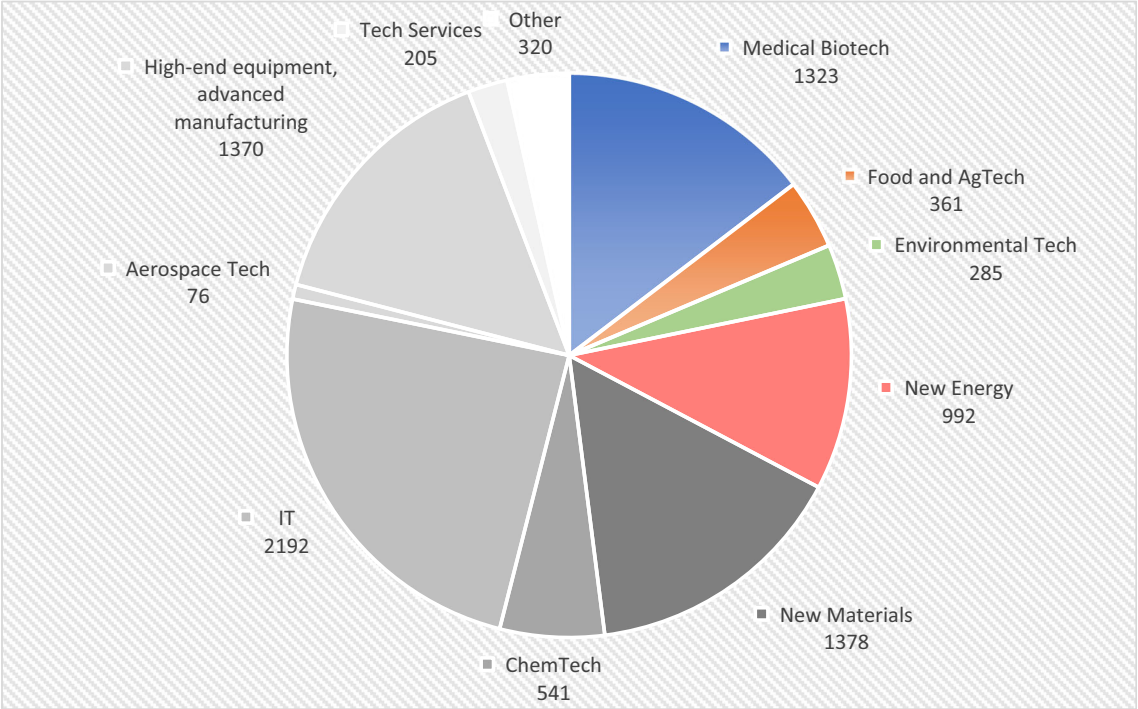

Fig. 3 Snapshot of tech transfer opportunities offered by China Technology Exchange CTEX as of April 11, 2021. Drawn after data from https://gyjy.ctex.cn. Offers arrive from over 170 universities and R&D institutions in China and abroad. The annual tech trade volume is claimed to exceed 34 billion CN¥ (equivalent to 4.4 billion €)

Biotech in food

Though most Han Chinese are lactose-intolerant, small cups of milk are usually tolerated, and milk consumption recently has soared. Though China's cowherds numbered a respectable 10 million in 2018 (Mu 2020), and the number of dairies counted about 300 (controlled by a few foreign and some national companies), 20 out of 50 million t of milk consumed had to be imported, in particular infant milk and infant milk products (Chang 2019) — a lingering consequence of consumers' mistrust after the "melamine scandal" in 2008 when melamine was blended into baby milk powder leading to 12 dead and 54,000 hospitalized babies. Yoghurts and probiotic drinks do not contain lactose and have become very popular in China. Yoghurt production in 2016 was 6.3 million t, with 5 major producers, and 60 registered probiotics, mostly powders and capsules, from 43 manufacturers.

Fermented food and drinks have an ancient tradition in China. Fermented soybean paste, soy sauce, vinegar, rice wine, other liquors, and grape wine are all important industries (Jin et al. 2017). China is the top beer producer in the world, with 38.1 billion L in 2018 (Wen 2018), twice as much as that of the USA. Table 9 offers a short list of producers and products of fermented food and drinks. A leading institution in this field is the schools of food technology and biotechnology at Jiangnan University in Wuxi, Jiangsu Province (see Table 6).

Environmental biotechnology

Similar to other nations, China has suffered from air, water, and soil pollution on its way to rapid industrialization. Over the past decade, the government has initiated more and more rigorous rules to counteract these developments.

Air pollution

Apart from desert dust and emissions due to construction, car exhausts, industry emissions, household heating, and the burning of straw are the major sources of air pollution and high levels of greenhouse gases. Since 2012, air quality is monitored by a real-time air quality network which in 2019 was based on 1499 stations in 367 cities (AQI-Map 2019). Within the "Air Pollution Prevention and Control Plan" issued in 2015, measures which have some bearing on biotech are:

- The interdiction to burn straw, providing, in theory, 700 million t of this agricultural biomass as a carbon source for fermentation,
- The use of biogas as an energy source, and
- The greening of deserts and planting of trees

In 2018, 58% of China's energy mix was still based on coal. The combined use of hydropower, nuclear, and solar energy, and wind power is expected to help reduce this figure

Table 7 Shortlist of Chinese academic groups active in industrial strain and enzyme development

Group	Location	Targets
CAS Institute of Industrial Biotechnology[a]	Tianjin	Improvement of industrial strains and enzymes
CAS Qingdao Institute of BioEnergy and Bioprocess Technology[b]	Qingdao	Lignocellulose substrates, algae biotechnology, biogas technology
CAS Dalian Institute of Chemical Physics[c]	Dalian	Bioenergy-related studies
CAS Shanghai Institutes of Biochemistry and Cell Biology[d], Institute of Plant Physiology[e]; Shanghai Institute of Organic Chemistry[f]; Huzhou Center for Biosynthetic Innovation[g]	Shanghai	SIBCB, SIOC: new industrial strain development and process engineering
		Huzhou Center for Biosynthetic Innovation: tech transfer to industry
East China University of Science and Technology[h]	Shanghai	Strain development, bioprocess engineering
Nanjing Tech University[i]	Nanjing	Strain development, bioprocess engineering
Jiangnan University[j]	Wuxi	Strain development, bioprocess engineering
Beijing University of Chemical Technology[k]	Beijing	Process engineering, synthetic biology

[a] http://english.tib.cas.cn
[b] http://english.qibebt.cas.cn
[c] http://english.dicp.cas.cn
[d] http://www.sibcb.ac.cn
[e] http://www.sippe.ac.cn
[f] http://english.sioc.cas.cn
[g] http://www.hzhr.com/Web/Company/20530.html
[h] https://www2.ecust.edu.cn/_t41/main.htm
[i] http://www.njtech.edu.cn
[j] http://english.jiangnan.edu.cn
[k] https://english.buct.edu.cn

to 50% by 2030. Though biomass contributes only a few percent to this figure, energy from biomass is already used in over 40 million rural households, 85% in the form of small household biogas digesters (Felizeter et al. 2017). In addition, gasified straw is seen as a major source of future heating systems in the countryside.

Some 30% of China's surface are either deserts or covered by sand and stones — a continuing source of dust pollution. With the "Grain for Green" program initiated in 1999, China has paid 124 million farmers in 25 provinces to plant trees on silting ground (Yang 2019), with a target figure of billions of trees until 2050. Genomic breeding of poplar, birch, eucalypt, or larch is actively pursued, e.g., by the Chinese Academy of Agricultural Sciences, but as of 2017, only 542 ha of transgenic poplars was planted (ISAAA 2021).

Water pollution

A 2016 survey of water samples from some 12,000 official monitoring sites across China revealed that only 35% of all probes provided water of good quality, and 13% of contained water is unsuited for any further use (Webber 2017). The 2015 "Water Pollution Prevention and Control Action Plan" therefore demands, among other goals, that by 2020, 95% of all urban centralized drinking water facilities should produce drinking water of at least class III quality.

Biotech contributes to clean waters mainly through biological sewage treatment plants. Since 1984, the number of such plants has grown to nearly 2300 — trickling filters in smaller communities and activated sludge plants such as the Gaobeidian Water Reclamation Plant in Beijing which has a treatment capacity of 1 million m^3/day. It is claimed, however, that many of these plants do not clean at a desirable ratio, and the sewer systems leading to these plants may still be incomplete (QU et al. 2019).

Algal blooms in China's lakes, largely caused by emissions from agriculture, and marine pollution along China's 18,000-km coastline, caused by seaweed farming and pollution, lead to frequent "green tides" in places lake Qingdao (Wang et al. 2015).

Table 8 Shortlist of academic institutes involved in research on molecular breeding in China

Institute	Topics
National Key Laboratory of Crop Genetic Improvement (Wuhan, Hubei Province)[a]	Functional genomic studies of agronomic traits, rice, corn, rape, cotton, wheat, soybeans, etc.
CAS Institute of Genetics and Developmental Biology (Beijing)[b]	National Key Lab of Plant Genomics, the National Key Lab of Plant Cell and Chromosome Engineering, the National Key Lab of Molecular and Developmental Biology, and the Hebei Key Lab of Water-Saving Agriculture
China National Seed Group, National Key Laboratory of Crops Genetic Breeding (Wuhan, Hubei Province)[c]	Corn breeding
Institute of Crop Sciences, Chinese Academy of Agricultural Sciences (Beijing)[d]	Multi-resistant wheat, corn and soybean breeding
National Key Laboratory of Plant Molecular Genetics, CAS Shanghai Institute of Plant Physiology and Ecology (Shanghai)[e]	Plant molecular genetics and functional genomics, plant molecular physiology and plant development, molecular mechanisms of plant-environment interaction
Northwest A&F University (Yangling, Shaanxi Province)[6f]	Plant breeding, plant protection in dry areas
Jilin Agricultural University, (Changchun, Jilin Province)[7g]	Grain industrial technology, wheat and corn breeding, soybean
Laboratory of Molecular Breeding, South China Agricultural University, (Guangzhou, Guangdong Province)[h]	Hybrid rice
State Key Laboratory of Crop Genetics & Germplasm enhancement, Nanjing Agricultural University (Nanjing, Jiangsu Province)[i]	Wheat, soybean genetics, germplasm enhancements
Chengdu Agricultural University (Chengdu, Sichuan Province)[j]	State Key Laboratory of Crop Genetic Resources Discovery and Utilization in Southwest China (under construction)

[a] https://croplab.hzau.edu.cn/sysgk.htm
[b] http://english.genetics.cas.cn
[c] http://www.chinaseeds.com.cn
[d] http://ics.caas.cn/en/
[e] http://www.nlpmg.ac.cn/en_index.php
[f] http://www.nlpmg.ac.cn/en_index.php
[g] https://jlaueng.jlau.edu.cn
[h] https://nxy.scau.edu.cn/534/list.htm
[i] http://slab.njau.edu.cn/English/Academic_Committee.htm
[j] https://www.sicau.edu.cn/kxyj/kypt.htm

Soil pollution

Due to rapid industrialization, coal firing, and increase of traffic, China's urban soils are polluted in many places. Soil remediation is under study but presently not yet carried out at a larger scale (Zhang and Chen 2017).

Greenhouse gases

China, with 19% of the global population, accounts for 27% of global greenhouse gas emissions. Having signed the 2015 Paris Agreement on Climate Change, China has vowed to peak CO_2 emissions by 2030 and become carbon-neutral by 2060 at the latest (Zheng et al. 2020). Pertinent measures such as investments in non-fossil energies and planting of trees are high on the political agenda, more and more stringent control of emissions from space, and new research centers, e.g., the Shandong Energy Institute (He 2020).

Biodiversity

Extending over many climate zones, China has a rich biodiversity. In 1994, the country joined the UN Convention on Biological Diversity (Cartagena Protocol) and started to implement rules and regulations for eco-environmental protection. In 2019, the CAS published an online catalogue of

Table 9 Fermented food and drink in China

Type of food or drink	Estimated amount produced	Remarks
Soybean paste (douchi and jiang)	915,000 t (2019)	34 companies
Soy sauce	10 million t (2018)	Mixed cultures of *A. oryzae* and lactobacilli
Vinegar	5 million (2018)	>6000 companies, from grains by mixed culture of molds
Yoghurt	9.6 million t (2018)	~50 companies, top 3 share 91% of the market
White liquor (40 – 55% alcohol), baijiu	7.9 billion L (2019)	Sales volume for companies with over 20 Mio. CN¥ turnover
Rice wine (14 – 17% alcohol), huangjiu	3.5 billion L(2019)	
Beer	38 billion L (2019)	27–28 L/capita, import 730 million L
Grapewine	450 million L (2019)[13]	China is among the top 10 global producers and importers

Compounded data from various statistical resources and market surveys

China's biological resources, containing 7 million records (Chen 2019). Since 2017, 11 National Parks covering some 200,000 km^2 are under mandatory and rigorous protection.

Expectations for the 14th five-year period "145" relating to biotech

Based on the great advances on S&T including biotech-related R&D in China during the "135" period, all evidence points to a continuation or even acceleration in most fields which were discussed in this article.

- Government expenditure on R&D will rise beyond the present 2.4% of GDP, industrial R&D will be even stronger supported by tax exemptions, and more money will be spent on fundamental R&D in academia,
- R&D infrastructure will be further expanded, and we will see more national research centers like the CAS National Center for Protein Science which opened in 2015 in Shanghai (http://www.ncpss.org),
- Medical care will be further improved, taking advantage of big data, Internet-based services, and financial stimuli for not only innovative drugs and equipment, but also stringent cost control of generic drugs and instrumentation (GTAI 2021),
- Genomic medicine, IT-based diagnostic services, and cell technology will be a focus of not only the next developments, but also the stimulation of TCM,
- Brain-related R&D will be strongly stimulated, based on China's unique resource of macaque and rhesus monkeys,
- Research on agricultural biotech, targeting crops, trees, husbandry, fish, and algae, will be further expanded; however, translation to food products may still be hampered in view of consumers' concerns,
- IT-Based cultivation, harvesting, processing, and marketing of agricultural goods will strongly increase,
- Industrial biotech will see a continuing trend towards less wasteful processes, and support for programs related to a cyclic economy or bioeconomy will increase, taking advantage on China's huge resources of waste products such as straw or food waste,
- Measures to ensure cleaner air, water, marine environments, and, eventually, soil will remain high-priority targets, leading to the construction of more sewers, sewage plants, and biogas reactors in the countryside,
- Finally, China will continue to export its technologies to the less industrialized countries, for instance through the belt-and-road program (Belt and Road Initiative (BRI)), and by these means will make an important contribution to the technical empowerment of hitherto less developed nations.

Author contribution RDS searched pertinent information in PubMed as well as other Western databases and wrote the article; XX contributed through the analysis of Chinese databases and blogs. Both the authors read and approved the manuscript.

Funding X. Xiong acknowledges partial support of this study by grant "6D-BioBone" (ProjectNr.: FKZ 13GW0400C), German Federal Ministry of Education and Research (BMBF).

Declarations This article does not contain any studies with human participants or animals performed by any of the authors.

Conflict of interest The authors declare no competing interests.

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