Research collaboration between Germany and China

The Road to Wuhan

China is not just an economic powerhouse but is also becoming a global player in science, research and, particularly, in biotechnology. To establish good relations with Beijing European nations, including Germany, are investing in research collaborations, in hope of guaranteeing a piece of the pie in the future.

A young researcher is sitting in front of an antiquated computer. Is he doing a maths? Or is he noting down his latest results? Somewhere in between. He is chatting with someone on QQ, a very popular Chinese chat program. But whether he is discussing a scientific problem with a colleague or making an appointment for the evening will remain a secret. The Chinese characters are too difficult to read.

Next to him, three women are doing an experiment in a laboratory. One of the students is pipetting a liquid; the others are standing behind her, watching her mindfully. In contrast to the rest of China, this lab is nearly empty. Yang Dongliang, Director of the Department of Infectious Diseases, Wuhan, explains, “It’s lunch time.” Unlike the German habit of not resting until at least part of the work is done, Chinese pupils, students and workers take a break every day from 12 to 2 pm. Only a few people stay in the labs or return earlier to their work.

1986: Jump-start into 21st century’s biotechnology

When visiting Wuhan, the capital of Hubei province, located in eastern China, one quickly becomes aware of the financial opportunities this country has. Cities look modern, people are wearing the latest fashions and everyone seems to lust after even more wealth. China’s development is due to its financial situation: It has got the highest capital surplus of all the world’s countries. To maintain its economic growth and to solve essential problems in public health and nutrition, however, China has to invest in research and technology – and in biotechnology, of course, too.

In China, modern times in the biotechnology industry started in 1986. The government’s “863 plan”, a programme dedicated to fund applied research in strategic areas, was established to modernise the then fragile and socialistic economy and to improve the Chinese living standard. In many ways, the 863 programme is very similar to the German government’s “bioregio initiative” of 1995 that soon resulted in 400 new biotech companies.

Back to China’s jump-start into biotechnology, 24 years ago. Since that time, the socialist (in name at least) country has pumped billions of capitalistic dollars into biotech and medical engineering start-ups throughout the country. Now, in November 2010, almost 700 biotech companies (70% of them in the medical field), more than 13,000 medical engineering companies and almost 7,200 pharmaceutical companies are in operation between Hong Kong, Beijing and Shanghai.

However, most of these companies are unknown minor shops with a handful of employees. And even the biggest Chinese pharmaceutical group, the local market leader Shanghai Pharmaceutical Group (SPGC), reaches a turnover (€2 billion in 2008) that is only a trickle of that of Pfizer (around €50 billion), GSK (€35 billion), Novartis (€35 billion) and Co.

On the other hand, China was once the only developing country to contribute to the Human Genome Project in the 1990s. Government officials also willingly affirm that Chinese biotechnology is undergoing a qualitative change, from “follow-and-copy” towards using its own knowhow, own research and own development. In addition, the commercialisation of research results is not only allowed but explicitly desired by government.

Seeking for international partners

To further speed up development, the Chinese government is seeking foreign partners and opportunities for collaboration. And the question is how, not whether, Europe cooperates with the Chinese, says Stefan Hase-Bergen, Director of the German Academic Exchange Service (DAAD). Hase-Bergen is sure that, “in the future, China will play an important role in the world’s economy. It will be a competitor but also a partner”. Research collaborations maintain the good relationship between
Germany and China, as well as ensuring that China will keep a piece of the cake for Germany if too many countries become interested.

Urgent need for scientific knowhow

A far-reaching Sino-German cooperation on science and technology started as early as 1978, resulting in several hundred collaboration projects between German and Chinese higher educational institutions. This is, according to the German Federal Ministry of Research and Education (BMBF), the largest number of such cooperations between Germany and an Asian country.

One of the latest projects is affiliated to the Tongji Medical College (TMC) in Wuhan, the most populous city in central China with over 6 million residents, and the University of Duisburg-Essen. And visiting TMC’s Immunology Department makes it obvious that Chinese researchers don’t need equipment. They already work with state-of-the-art instruments and reagents. What they need badly, however, is scientific know-how. Meanwhile, the best Chinese students very often choose to major in biology and medicine. However, apart from a few disciplines, such as genomics and agriculture, especially in modern plant biotechnology, overall basic research in China is mostly weak.

Let’s go back to Yang Dongliang and his Department of Infectious Diseases. Director Yang took just a short break today, because he showed us his laboratories and talked about his work. He is one of the most famous immunologists in China, with a particular interest in viral hepatitis diseases. One year ago Yang started a research collaboration called “Mutual interaction of viruses with cells of the immune system: from fundamental research to immunotherapy and vaccination” with the German University of Duisburg and Essen.

“We are working on virus diseases such as hepatitis and HIV,” Yang explains. “Our goal is to invent new therapies and vaccines against these infectious diseases.” His German colleague Michael Roggendorf, Director of the Department of Virology at the University Hospital in Essen, adds via e-mail, “Our researchers analyse the molecular and cellular interactions between viruses which cause a chronic infection and cells of the human immune system. As soon as these mechanisms are understood, we might be able to eliminate the viruses.”

Widespread hepatitis but no HCV vaccine available

According to the Robert-Koch-Institut, the central federal institution which is responsible for disease control and prevention in Germany, infection with the hepatitis B virus (HBV) and hepatitis C virus (HCV) is widespread throughout the world. Up to 500 million people carry one of these viruses. The situation in most European countries is basically under control thanks to vaccination against HBV. However, liver cancer, which develops in patients who were infected a few decades ago, is a major problem. In Germany, for example, about 500,000 people suffer from HBV (less than 0.5% of the population), while in Eastern Europe between 2 and 7% of the population is chronically infected.

Worldwide, there are already several HBV vaccines on the market, such as Engerix (approved for SmithKline Beecham in 1989), HBVAXPRO (Sanofi-Pasteur, 2001) and Infanrix (GSK, 2000). However, there’s no working vaccine for hepatitis C available so far, while some are under development (also see M. P. Manns et al. in Nature Reviews Drug Discovery (2007) 6, 991: “The way forward in HCV treatment — finding the right path”). The situation in China and Africa is alarming, “About ten percent of the Chinese are infected with HBV and two percent with HCV,” virus researcher Heiner Wedemeyer estimates. If he’s right, more than 130 million people are infected.

Wedemeyer is working at the Medizinische Hochschule Hannover. He is also Secretary General of the European Associa-
tion for the study of the liver (EASL). “Research co-operation between Germany and China are very important. The HBV is very grave in this country, causing one of the most frequently death causes, liver cancer.” It’s logical that the Chinese government is interested in fighting widespread diseases like hepatitis, to unburden the country’s health care system in further decades. Only with a working system can their economy continue its vigorous advancement.

Contributions from each country

In the Transregional Collaborative Research Center (TRR60), managed by Roggendorf and Yang, more than 50 researchers work on 18 topics to do with the HIV and hepatitis virus. “All the projects are going on very good,” Yang asserts reassuringly, in the manner of a skilful PR agency, “we’re only at the beginning, but we already got a few results.” At a first scientific workshop, held in June 2010, some groups presented these results. In June, for example, Zhu Wenbo and colleagues published findings on the nucleocapsid-protein of HCV in Clinical and Vaccine Immunology, delivering an explanation for why infected people often experience persistent hepatitis C, which leads to cirrhosis or liver cancer.

The whole interdisciplinary joint research project is sponsored by the German Research Foundation (DFG) with €5.5 million for its German partners. The Ministry of Science and Technology (MOST) in Beijing contributes an additional €8.2 million for the Chinese researchers.

“Application” is the miracle word

There are no private foundations in China. Thus, researchers depend completely on the government to support their projects. In contrast to Germany, funding is paid only for equipment and travelling, but not for employees. “There is a high competition between the research groups,” says Armin Krawisch, Director of the Sino-German Centre for Research Promotion (CDZ). The centre was founded in 2000 and is a joint venture between the DFG and the National Natural Science Foundation of China (NSFC). Krawisch has opened in 2000 and is a joint venture between the DFG and the National Natural Science Foundation of China (NSFC). Krawisch has lived in Beijing since 2007 and knows the Chinese research system.

“In Europe we have rather good living conditions. So we don't face such big [economic and social] challenges as China does, which enables us to invest more in basic research. In China, the government still undertakes big efforts to improve living conditions, which is why there is a major interest in applied research to solve these problems.” Therefore, application, or rather applied research, is the miracle word.

The statistics for 2006, published by MOST, also underline the fact that basic research is not very common. However, the MOST figures are not well composed. There is data from different countries and years, so that a comparison between the Chinese system and others is actually impossible. But one thing is obvious: In contrast to other countries, China invests lots of money in development research. Only 5 percent of the whole research budget of €300 billion goes to basic research, while nearly 17 percent is spent on applied research. The remaining 78 percent – more than €230 billion – is invested in experimental development (of new or further developed materials, products or devices).

In France, for comparison, the research budget of €350 billion was equally distributed in 2005.

This concept is an advantage for the Chinese economy, as you can sell development research whereas you just have to pay for basic research. It’s easier to get the know-how from foreign partners. At least for the present.

TRR60 is the most promoted project between Tongji Medical College and Germany ever. The two nations have a longstanding relationship, thanks to the German physician Erich Paulun who founded a medical school in Shanghai in 1907. Later, it became one of the most famous Chinese institutions, Tongji University. In the 1950s, the medical department moved from Shanghai to Wuhan and merged with the Medical College of Wuhan University. Nowadays, Tongji Medical College belongs to Huazhong University of Science and Technology.

Tradition as the key – and secret text books in the library

And right there, some students told us the story of the secret text books: At Tongji’s library, old German medical books stand on the bookshelf. They deal with medical basics such as anatomy, internal medicine, surgery and chemical analysis. Unfortunately, the books are locked in a conference room and almost nobody knows about them. Even Yang was surprised to hear of their existence.

Back in history again. After the re-opening of China in the 1980s, many collaborations with German partner universities started, and today, there’s a lot of exchange. Students from all over the world, especially Germany, do internships at Huazhong University’s hospital. And every year, more than 600 Huazhong students and medical graduates travel to a partner university in order to continue their studies or to do a PhD.

One of these students is Ding Honghui. Today he is also working at the Department of Immunology and Professor Yang is his advisor. “About four years ago, Ding had three months train-
Such traditions and relationships are not only important in China – they are priceless. If Erich Paulun had been French or British, there might have been no chance for the Germans to establish research collaborations with the TMC. “Germany enjoys a good reputation among the Chinese population,” says Armin Krawisch, “they like our values, especially our reliability and quality awareness.”

Under the great dragon’s thumb?

Several times, European collaboration partners have complained about one-sided collaborations with Chinese researchers. “Still, the Chinese partners gain more profit if you just have a look at the numbers of exchange employees,” Hase-Bergen confirms. “In terms of money, the situation is equal and we try to establish programmes which are supported by the Chinese government with 50 percent.”

Espionage is another problem. There are some complaints about overly curious post-docs in German labs which lead to reservations against Chinese researchers. The requirements for joint-ventures made by the government don’t reduce these resentments, as the foreign partner is always forced to present his background knowledge.

In contrast to this, the collaboration between the Immunology Departments in Wuhan and Essen seems to sound the bell for new times. The German partner Roggendorf considers the collaboration a win-win-situation. “It’s an honour to work with such talented young Chinese researchers. We can achieve results to invent new treating methods very quickly.”

Some questions can only be answered in China

Yang adds, “Of course we could do the research both on our own. Here in Wuhan we have the same modern equipment as laboratories in Germany. For example immunofluorescent microscopes, PCR machines, flow cytometry analysers, ELISA readers, ELISpot reader, HPLC, spectrophotometers, centrifuges with high and ultra-speed, DNA sequencers, phosphoimage and gel image systems. But now we can share the information and the work is done faster thanks to the experienced team.” That means that with the help of their German partners, the Chinese can save time and concentrate on developing new drugs.

Shared basic information is no problem for German scientists. There are other reasons for them to work together with China, es-

The Government’s Strategical Constant

- By 2010, the sales of Chinese biotech products are expected to be €62 billion.
- The growth of the biotech industry in China is seen as strategic by the central government and is included in China’s core economic development plans, e.g. the 11th Five-Year Plan (2006-2010).
- At universities, there are over 200 biotechnological research centres, mainly centered around Beijing and Shanghai.
- About 200 foreign biotech companies have subsidiaries and/or joint ventures (for example, with publicly-funded research centres) in China, such as Genzyme, Roche, Monsanto, Bio-rad, Agilent, Invitrogen, Novozymes, Promega, ...
- Personal relationships are highly important for the success of establishing a presence and of operating in China. In the entry phase, finding a good Chinese partner or hiring a good Chinese manager is almost a prerequisite for foreign companies.
- There are almost 700 (other sources say 1,800) Chinese biotech companies. Most important companies are driven by the government, such as China National Biotec Group, Hualan Biological Engineer-
pecially in medical research. Only in China can specific patient data be found. Wedemeyer, from EASL stresses that, “Some scientific questions can be answered only in China. For example you can find the genotype B and C of virus Hepatitis B in China whereas in Germany the genotypes A and D are common. Furthermore we can establish huge cohort studies to examine for example, the influence of genetic factors.”

In addition, the Germans can only accept the terms of the collaboration. There are plenty of other countries who would like to work with China.

**Minimising cultural differences**

Someone is knocking at the door of Director Yang’s bureau. There are some patients waiting to see him. He excuses himself for a minute, “These people come from a small village, some hours away. I want to treat them because they have serious viral hepatitis and I have to explain how to take the medicine.”

In the meantime questions arise about the cultural differences between European and Chinese researchers. What is Yang’s opinion? “Generally there are no significant differences in research,” he says after his return. He himself has been working in Germany for several years, so that he could adjust the work in his laboratory to European standards if the need arises. “In order to minimise the cultural differences, we have to work together and support the exchange of personal,” stresses Wedemeyer. Furthermore, the concept of the project envisages that individual research groups consist either of Germans or of Chinese. So the cultural discrepancy has no impact on daily routine.

The academic researchers from Essen will benefit from a successful project. After building up collaboration structures, it’s easier for them to plan new projects. As the German and Chinese governments are interested in a long-term relationship, they explicitly fund these kinds of project. Funding for TRR60 from the DFG and NSFC may be renewed for another four or even eight years. So Yang will again be preoccupied with preparing applications and won’t have much time to carry out research. As in Western countries, a director of a scientific department has many burdensome bureaucratic duties. Apart from teaching students and treating patients, he mostly does administrative paperwork.

**Hard to get a foot into the door**

The scientific findings are also important for Germany. As there are many different genotypes of viral hepatitis, it is important to determine whether vaccination prevents infection with all of them. “The vaccination should act against all genotypes,” says virologist Wedemeyer. He has mentioned before that German patients are usually infected with the genotypes A and D. Other genotypes, like B and C, can be found in China. A research collaboration is the only way to get information about this specific patient pool. Furthermore, there are so many people in China that immunologists can work with big random samples, which improves the statistical findings. And a new therapy or vaccination might be found more quickly.

The financial long-term effect of collaborations like this still remains uncertain. At the moment, they seem lucrative not only because of their scientific findings but because of their future economic opportunities. “China is the market of the future concerning hepatitis virus infections,” Wedemeyer adds. “Pharmaceutical companies are definitely interested in producing meds for China.”

But is there any chance of German (or other) companies selling vaccines or therapeutics in China? A glance into any Chinese pharmacy is telling. Most of the medication is made in China. In 1994, the Chinese government established a new licensing system, which discriminates against imported medication. Foreign companies are not allowed to sell their pharmaceuticals independently. Nowadays pharmaceutical companies worldwide only run joint ventures in China. The economic advantages for Germany, however, are questionable. These joint ventures might create new jobs for Chinese workers, but not for Germans, if they start producing new medicine. The invention and commercialisation of new medications won’t support the German economy but the Chinese.

**Cultivating personal relationships**

Nevertheless, there is another reason why the German government invests money in shared basic information: Their good relationship with China. Germany enjoys a positive reputation among the Chinese people and their government. Thus, it has an advantage in international competition with other nations like the USA, whose relationship with China is tense. The German government shares newly discovered basic information willingly in order to keep relations warm and as an investment in the future. Soon, China will have improved its economic and global position. When that time comes, old friendships might be rewarded.  

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