An hour’s drive from Kunming in southwestern China, past red clay embankments and sprawling forests, lies an unusual zoo. Inside the gated compound is a quiet, idyllic campus; a series of grey, cement animal houses stack up on the lush hillside, each with a clear plastic roof to let in the light. This is the Yunnan Key Laboratory of Primate Biomedical Research, and its inhabitants are some 1,500 monkeys, all bred for research.

The serenity of the facility belies the bustle of activity within. Since it opened in 2011, this place has quickly become a Mecca for cutting-edge primate research, producing valuable disease models and China is positioning itself as a world leader in primate research.

BY DAVID CYRANOSKI
Administration, the number of businesses breeding macaques for laboratory use rose from 10 to 34 between 2004 and 2013, and the quota of animals that those companies could sell in China or overseas jumped from 9,868 to 35,385 over that time. Farm populations of marmosets, another popular research animal, are also on the rise.

Most monkeys are shipped to pharmaceutical companies or researchers elsewhere in the world, but the growing appreciation among scientists of monkey models has prompted investment by local governments and private companies in dedicated research colonies. The country’s 2011 five-year plan singled out primate disease models as a national goal; the science ministry followed up by pumping 25 million yuan (US$3.9 million) into the endeavour in 2014.

Scientists visiting China are generally pleased with the care given to animals in these facilities, most of which have, or are trying to get, the gold-standard recognition of animal care — accreditation by AAALAC International.

Ji’s Yunnan Key Laboratory is the most active primate facility, but others are giving it a run for its money. The new monkey facility at the Kunming Institute of Zoology was funded as part of the national development scheme for big science equipment that includes telescopes and supercomputers. The money will help the institute to double its colony of 2,500 cynomolgus monkeys (Macaca fascicularis) and rhesus macaques.

Zhao Xudong, who runs the primate-research facility, says that the plan is to “set it up like a hospital, with separate departments for surgery, genetics and imaging”, and a conveyor belt to move monkeys between departments. There will be systems for measuring body temperature, heart rate and other physiological data, all to analyse the characteristics, or ‘phenotypes’, of animals, many of which will have had genes altered. “We are calling it the ‘genotype versus phenotype analyser’,” says Zhao. It will take ten years to finish, but he hopes to begin building this year and to start research within three. Other facilities, although smaller, are also expanding and diversifying.

The Institute of Neuroscience in Shanghai plans to increase its population of 600 Old World monkeys to 800 next year and expand its 300-strong marmoset colony.

A QUESTION OF COST

Outside China, the numbers are heading in the opposite direction. Harvard Medical School closed its affiliated primate facility in May 2015 for ‘strategic’ reasons. Last December, the US National Institutes of Health decided to phase out non-human-primate experiments at one of its labs and subsequently announced that it would review all non-human-primate research that it funds. In Europe, researchers say, the climate is also growing colder for such research.

Costs are a major disincentive. In 2008, Li Xiao-Jiang, a geneticist at the Erasmus Medical Centre in Rotterdam, said that it cost $6,000 to buy a monkey in the United States, and $20 per day to keep it, whereas the corresponding figures in China are $1,000 and $5 per day. “Because the cost is higher, you have to write a bigger grant, and then the bar will be higher when they judge it,” says Li. Funding agencies “really do not encourage large-animal research”.

For Li, the solution was simple: go to China. He now has a joint position at the Institute of Genetics and Developmental Biology in Beijing, where he has access to around 3,000 cynomolgus monkeys at a farm in Guangzhou and some 400 rhesus monkeys at the Chinese Academy of Medical Sciences’ monkey facility in Beijing. He has churned out a series of publications on monkeys with modified versions of the genes involved in Duchenne muscular dystrophy and Parkinson’s disease.

Neuroscientist Anna Wang Roe says that red tape drove her to leave China. Roe’s team at Vanderbilt University in Nashville, Tennessee, is

“CHINA WILL BECOME THE PLACE WHERE ALL THERAPEUTIC STRATEGIES HAVE TO BE VALIDATED.”
attempting to work out how modules in the brain are connected, and the human disorder. Some incessantly suck their thumbs. “I’ve never seen that in a monkey before — never so constant,” says Ji.

Among the range of other disease models in Ji’s menagerie are monkey versions of cardiovascular disease, which he is working on in collaboration with the Karolinska Institute. And last year, Ji made the world’s first chimeric monkeys using embryonic stem cells, an advance that could make the production of genetically modified animals even easier. The question now is whether these genetically modified monkeys will propel understanding of human brain function and dysfunction to a higher level. “You can’t just knock out one gene and be sure you’ll have human-like disease phenotype,” says Ji.

Researchers see an opportunity to understand human evolution as well as disease. Su Bing, a geneticist at the Kunming Institute of Zoology, is working with Ji to engineer monkeys that carry the human version of a gene called Srgap2, which is thought to endow the human brain with processing power by allowing the growth of connections between neurons. Su also plans to use CRISPR–Cas9 to introduce human versions of Mcph1, a gene related to brain size, and the human Foxp2 gene, which is thought to give humans unique language ability. “I don’t think the monkey will all of a sudden start speaking, but will have some behavioural change,” predicts Su.

INTERNATIONAL DIVIDE

Although the opportunities are great, there are still obstacles for scientists who choose to locate their animal research in China. Trying to keep a foot in two places can be challenging, says Grégoire Courtine, a spinal-cord-injury researcher based at the Swiss Federal Institute of Technology in Lausanne, who travels almost monthly to China to pursue his monkey research at Motac. He has even flown to Beijing, done a couple of operations on his experimental monkeys, then returned that night. “I’m 40 years old, I have energy in my body. But you need to really will it,” he says.

Another downside, says Li, is that policies can change suddenly in China. “There is uncertainty. That makes us hesitate to commit,” says Li, who has retained his post at Emory University. And the immunity that China’s primate researchers have had to animal-rights activism could start to erode, warns Deborah Cao, who researches law at Griffith University in Brisbane, Australia, and last year published a book on the use of animals in China. People are starting to use Chinese social-media sites to voice outrage at the abuse of animals, Cao says.

China has competition in its bid to dominate primate research, too. Japan has launched its own brain project focused on the marmoset as a model: the animal reaches sexual maturity in a year and a half, less than half the time it takes a macaque. Some research facilities in China are now building marmoset research colonies — but Japan is considered to be several years ahead.

And some researchers want to ensure that such work continues outside Asia. Courtine says that he’s “fighting to keep alive” a monkey-research programme he has in Fribourg, Switzerland, because he thinks it’s important to have a division of labour. “Research that requires quantity, I’ll do in China. I would like to do sophisticated work in Fribourg,” he says.

Back at his primate centre in Yunnan, Ji is sure that such work is already taking place. His dream, he says is “to have an animal like a tool” for biomedical discovery. He knows there is a lot of competition in this field, especially in China. But he feels confident: “The field is wide, and there are many, many projects we can do.”

David Cyranoski writes for Nature from Shanghai, China.

CORRECTION
The News Feature ‘Monkey Kingdom’ (Nature 532, 300–302; 2016) wrongly affiliated Erwan Bezard with INSERM — he is actually director of the Institute of Neurodegenerative Diseases at the University of Bordeaux. It also referred to Liping Zhang instead of Liping Wang.