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Life Science: Innovation and prosperity—commemorating the 60th anniversary of the Chinese Academy of Sciences

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In tandem with the birth and growth of the People's Republic of China (PRC), the Chinese Academy of Sciences (CAS) passed through six decades by the year of 2009. In the past 60 years, the CAS researchers in life sciences witnessed hardships in the early years of establishment, difficulties in the extremist period of the Cultural Revolution, efforts to revitalize research since China adopted the reform and opening-up policy, and great progress after the CAS initiated the Knowledge Innovation Program. Through the unremitting hard work and unwaveringly effort of several generations, the CAS carried forward the spirit of bravely innovating and honestly seeking truth. Up to date, the CAS has established research capabilities covering most disciplines in life sciences, accomplished large-scale scientific facilities, key laboratories, biological resource protection systems and biological information centers, and optimized organization of human resources, all significantly contributing to the improvement in conventional biology and modern life sciences. Especially after 1998, the year when the Pilot Project of the Knowledge Innovation Program was launched and the new orientation of the Academy "catering to the national strategic demands and aiming at the world science frontiers" was brought forth, the life sciences of the Academy, focusing on the construction of the national innovation system, the strategic choice of the Academy and the strategic requirements of the nation, made significant progress in such fields as public health, formulation and manufacturing of new drugs, strategic conservation and sustainable use of biological resources, modern ecological agriculture, industrial biotechnology and other fields, which significantly enhanced innovation awareness and improved innovation ability.

In the new century while we enjoy the benefits that technology has brought us, the human society is also faced with unprecedented pressure from environmental deterioration, energy shortage, farmland reduction, financial crises and worsening aging problems. The development of human society requires a new breakthrough of key technology as happened in the agricultural, industrial and information revolutions. Obviously, the revolution of bio-economy based on life sciences and biotechnology is approaching, which will offer new solutions to the increasingly urgent social, environmental, financial and economic challenges. It is not only a grand challenge entrusted to us by history, but also a treasured opportunity for new development in life science. Therefore, we must strengthen our conviction, implementing the Scientific Outlook on Development, comprehensively designing strategies, actively handling related issues, to drive the life science research in the CAS into a new phase.

1 History of CAS Life Sciences in the Past Six Decades

One month after the PRC was established, CAS was founded on November 1, 1949, indicating that the development of science and technology within China had entered a

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new era. In the past six decades, life sciences have experienced various stages of the CAS development and featured many historic breakthroughs.

1.1 Early Years after Establishment (1949 — 1956)

As same as other disciplines in the CAS, life sciences experienced the primary stage of development during the years of 1949 to 1956.

In June 1950, the CAS founded its first batch of biological research entities in Shanghai and Beijing. The Shanghai Institute of Physiology and Biochemistry was organized from the preparatory office of the Medical Institute of Academia Sinica. CAS also originated the Shanghai Institute of Experimental Biology from the parts of the Institute of Botany and the Institute of Zoology, Academia Sinica, as well as the Institute of Physiology and part of the Institute of Zoology, National Academy of Peiping. In August 1950, an entomology laboratory was built on the entomological research team of the Institute of Zoology, Academia Sinica, and the entomology laboratory of the Institute of Zoology, National Academy of Peiping. The new laboratory was later, in January 1953, expanded to the Institute of Entomology. Based on the parts of the Institute of Zoology and the Institute of Botany, Academia Sinica, the CAS Shanghai Institute of Hydrobiology was set up, which was later moved to Wuhan in 1954. Based on the Institute of Botany, National Academy of Peiping and the plant research section of the Fan Memorial Institute of Biology, the CAS Beijing Institute of Plant Taxonomy started its research. Based on the zoological research section of the Fan Memorial Institute of Biology and animal specimens inherited from the Institute of Zoology, National Academy of Peiping, a committee of animal specimens assortment was initiated, which was in April 1951 renamed as the animal specimens working committee, expanded in January 1953 into the zoological laboratory, and further expanded in May 1957 into the Institute of Zoology. In 1950, a preparatory office of the Institute of Psychology was established. By the end of 1955, the CAS owned altogether 15 independent biological research entities, which indicated that the biological research in China had entered a new historical stage and served as the foundation for systematic biological research. In 1955, the CAS initiated the Division of Biology and Geoscience, marking initial establishment of academic leadership in biological research in China, which also laid a management system for long-term development of biology and the nation.

In 1950, the mission statement of the CAS was clarified as: the CAS places serving the people as the guiding principle of scientific research, follows trends of modern sciences, learns experience from advanced international peers, performs theoretical and experimental studies, in order to catch up with the international research levels. Afterwards, CAS life science researchers considered national needs as their own research targets, consistently explored key scientific problems, took concrete practice in biological research, and made significant contributions to the nation. In 1951, mandated by the central government, the CAS for the first time dispatched scientists to carry out scientific investigation in Tibet, providing important advice to improve agriculture, forestry, husbandry and health. In 1953, CAI Xitao, a well-known botanist, introduced rubber in Yunnan, solving the shortage of rubber in new China's earliest years. At the same time, it set a new research area concerning protection and utilization of tropical plants. In 1954, the South China Institute of Botany joined the CAS and later set up the first natural reserve in China. In 1955 when the country greatly needed antibiotics, the CAS steered a national research council on antibiotics, which successfully organized in Beijing the first national working conference on antibiotics research and an international symposium on antibiotics. Soon after, research was applied to the production of antibiotics, such as penicillin and chloramphenicol, which signaled the independent development and manufacture of antibiotics in China.

1.2 Years of Development (1956 — 1966)

The CAS experienced its first period of rapid development from 1956 to 1966. As sufficient attention was paid to biological research in *the Outlines of the National 12-year Scientific Research and Technological Development*, the biological institutions in the CAS were rapidly developed, constituting a research system with most disciplines and regions. Through 1966, the number of newly established, expanded and merged institutes reached 14. In 1956, the Beijing Institute of Experimental Biology was established, which was renamed as the Institute of Biophysics in 1958. In 1956, the Wuhan Botanical Garden was founded, which was upgraded to a research institute in 1958. In 1957, the Wuhan Microbiology Laboratory was established, which was expanded to an independent research institute in 1960. In 1958, several research institutes were established, including the Sichuan Institute of Agricultural Biology, which was renamed as the Chengdu Institute of Biology in 1962, the Kunming Institute of Botany, the Institute of Microbiology, the Shanghai Institute of Physiology and the Shanghai Institute of Biochemistry. The latter two institutes were originated from the Shanghai Institute of Physiology and Biochemistry. In 1959, the Institute of Genetics and the Kunming Institute of Zoology were established, as well as the Qinghai Institute of Biology, which was renamed in 1962 as the Northwest Institute of Plateau Biology, and the Shanghai Institute of Applied Entomology. In 1961, the Xinjiang Integrated Research Institute of Water, Soil and Biological Resources was established and in 1962, the Institute of Entomology was merged into the Institute of Zoology. By the beginning of the Cultural Revolution in 1966, the CAS had total 33 biological research institutes. The establishment of the new research institutes provided more professionals, research facilities and management resources, which laid solid foundation for important scientific and technological achievements.

In 1956, the CAS initiated a 12-year program for the natural scientific research and technological development, including regionalization and natural resource investigation, protein structure and biosynthesis, and other cutting-edge research issues that had strategic, comprehensive and key bearings on national economic and social development. In the same year, the CAS organized a symposium of genetics in Qingdao, which was praised by academic circles as an example of free discussion of academic thoughts.

In this decade, the CAS and its affiliates organized more than ten large-scale scientific investigations, including the comprehensive investigation of natural resources, and investigations on Mount Qomolangma, the Heilongjiang River Basin, Xinjiang, Qinghai, Gansu, Inner Mongolia, Ningxia and tropical biological resources. In 1959, compilation of *the Flora of China* was initiated. From 1956 to 1965, Professor MA Shijun and his research team conducted a comprehensive study with respect to the occurrence, behavior, development and control strategies of locusts, which marked a breakthrough in the prevention of locust plague in both China and the world. In 1961, Prof. ZHU Xian in the Shanghai Institute of Experimental Biology and his fellow researchers successfully made the first fatherless female toad lay eggs for reproduction, which was a globally recognized advance. By the end of 1964, the Institute of Biophysics performed research on biological effects of nuclear explosions, which provided scientific basis for the prevention/treatment of human radiation injuries in possible nuclear explosions or accidents and was of great significance to radiobiology. Since 1965, led by Prof. WANG Yinglai, the scientists from the Shanghai Institute of Biochemistry, the Institute of Organic Chemistry and Department of Chemistry, Peking University, had worked for six and half years to synthesized biologically active bovine insulin, for the first time in the world. This demonstrated China's world-class standing in the field of polypeptide and protein synthesis. In addition, fundamental research on the mechanisms of morphine analgesia and photophosphorylation was also accomplished in accordance with international standards of excellence.

1.3 Years of Cultural Revolution (1966 — 1976)

During the chaotic ten-year Cultural Revolution, life science research in the CAS suffered a major setback. A large number of research institutes were closed or decentralized. Only four institutes, the Institute of Microbiology, the Institute of Genetics, the Shanghai Institute of Biochemistry and the Institute of Biophysics, were directly affiliated to the CAS. The Institute of Psychology and the biological test centers in Beijing and Shanghai were shut down. Other institutes were under control of local governments. In such a hard period, CAS life scientists unswervingly adhered to responsibilities and ethics of science. With a convinced faith and against all odds, they kept research moving forward despite all difficulties.

In 1968, with support of Vice Premier NIE Rongzhen, the research on synthesis of yeast alanine transfer RNA was launched. CAS institutes, including the Shanghai Institute of Biochemistry, the Shanghai Institute of Experimental Biology, the Shanghai Institute of Organic Chemistry and six Beijing institutes such as the Institute of Biophysics, together with Department of Biology, Peking University and the Shanghai No. 2 Biochemical Reagent Factory, started 13-year joint efforts and eventually synthesized, for the first time in the world, the RNA molecule with full biological activity. In 1971 and 1973, the Beijing Research Group of Insulin Crystal Structure, which consisted of the Institute of Biophysics, the Institute of Physics and Peking University, determined the crystal structures of porcine insulin at 2.5 Å and 1.8 Å resolutions, respectively. Later in 1984, the structure of high resolution at 1.2 Å was achieved. Dr. Dorothy Hodgkin, a world-renowned British crystallographer and the Nobel Prize Laureate, considered this structure the most accurate one of insulin. In 1970, the TONG Dizhou Laboratory, the Institute of Hydrobiology and the Yangtze River Fisheries Research Institute (in Shashi) started cooperation in breeding carp nucleus-crucian cytoplasm hybrid fish. Three years later, they successfully obtained the reproducible hybrid variety that grew fast, introducing a new method in freshwater fish breeding. In 1974, artemisinin B, artemisinin analogues and derivatives developed by the Shanghai Institute of Organic Chemistry and the Shanghai Institute of Material Medica were classified by the World Health Organization (WHO) as the most preferred drugs for severe malaria. Later in 1995, these drugs were included in *the International Pharmacopoeia*. In 1975, the Institute of Microbiology, in cooperation with the Beijing Pharmaceutical Factory and the Northeast Pharmaceutical Factory, brought forth the new technique of two-step fermentation for the production of vitamin C. This technique, whose intellectual property rights were held by Chinese researchers, brought significant economic benefits.

Also in this period, the Shanghai Institute of Biochemistry conducted research on the theory and technique of pollen transformation of higher plants, providing a new method for molecular breeding. The Institute of Genetics, the Institute of Botany and the Shanghai Institute of Plant Physiology made a series of cutting-edge scientific and technological achievements in such fields as anther, pollen and protoplast culture and plant regeneration, promoting the development of plant tissue culture and bio-engineering research in China.

1.4 Years of Rehabilitation and Revitalization (1977 — 1984)

The National Conference of Science held in 1978 brought forth the flourishing days of science development for China. Life science research in the CAS was also rejuvenated. Approved by the State Council in 1977, the CAS retrieved 18 biological research institutes. In 1978, the Shanghai Institute of Experimental Biology and the Hubei Institute of Microbiology were respectively renamed as the Shanghai Institute of Cell Biology and the Wuhan Institute of Virology. In 1977, the Institute of Psychology was restored. During this period, new institutes were also established, including the Institute of Developmental Biology in 1979, the Shanghai Brain Research Institute in 1980 and the preparatory office of the Shanghai Bio-engineering Experiment Base, which was renamed in 1983 as the Shanghai Bio-Engineering Research Center. In addition, a number of ecosystem research stations for forests, grasslands and lakes were established. The normal research system was restored.

Following adjustments of the CAS orientations, life sciences in the CAS focused on greatly strengthening applied research, actively and selectively participating in development projects, and continuously emphasizing fundamental research. In the process of the full restoration of scientific research, significant progress was achieved constantly. In 1979, Prof. CHEN Shixiang published *the Classification of Kingdoms of Organisms*, demonstrating the classification of life into three superkingdoms and six kingdoms, which made outstanding contributions to the theory of evolution. In 1979, *the Picture Index of Senior China Plant* and the *Claves Familiarum Generumque Cormophytorum Sinicorum* were published, under the auspices of the Institute of Botany, in corporation with the South China Institute of Botany, the Kunming Institute of Botany and a number of other organizations. The publication filled in the gap of systematic introduction of plants in China. In 1978, research on Chinese river dolphin was carried out jointly by the Institute of Hydrobiology, the Institute of Biophysics and the Institute of Acoustics. At the same time, important practical results were achieved in national economy related fields, such as domestication and utilization of animal and plant resources, breeding new varieties of wheat, corn, rapeseed, soybean, sweet potato and cotton, plant disease/pest control, and ecosystem conservation and management.

1.5 Years of Reform and Development (1984 — 1998)

As China deepened its Reform and Opening up policy, the CAS entered into a transformation period of research system reform. In this period, the CAS continuously explored new developing modes, continued to open up new frontiers, and cultivated young talents, so as to provide vitality to life science research.

By clarifying scientific orientations of institutes, goals and responsibilities of institute directors, and management of human resources, research directions of various institutes were better defined and an open, mobile and united research system was set up in the CAS. Since the deployment of key laboratories in the CAS in 1985, 17 biological laboratories had been established with stable support from the Academy, including the Laboratory of Molecular Enzymology in the Institute of Biophysics, the Laboratory of Reproductive Biology in the Institute of Zoology and the Laboratory of Systematic Mycology and Lichenology in the Institute of Microbiology, etc. Since the former State Planning Commission started the state key laboratory program in 1983, the Laboratory of Molecular Biology, the Laboratory of Plant Molecular Genetics, and the Laboratory of Freshwater Ecology and Biotechnology were subsequently established. In particular, the Laboratory of Molecular Biology in the Shanghai Institute of Biochemistry obtained formal approval in 1986, becoming the China's first state key laboratory. Since 1987, with financial support from the World Bank, the CAS had built up about 20 state key laboratories, including five biological ones (the Laboratory of Drug Research, the Laboratory of Plant Cell and Chromosome Engineering, the Laboratory for Integrated Management of Pest Insects and Rodents, the Laboratory of Microbial Resources, and the Laboratory of Biochemical Engineering). As national research bases, these laboratories played important roles in developing cutting-edge research, meeting national strategic demands, training talents, and performing international and domestic cooperation. At the time, aging researchers and extreme shortage of young talents became an issue. According to a survey carried out by the CAS Bureau of Life Science and Biotechnology in 1987, the average age of scientific group leaders was 55. Therefore, the CAS initiated special funding and laboratories for young scientists, including the “Max Planck Research Group” co-sponsored by the German Max Planck Society. In particular, the Hundred Talents Project, launched in 1994, has been attracting a great number of outstanding young scientists and provided a powerful impetus for the restructuring of research personnel. In addition, the Shanghai Life Science Research Center, set up in 1996, played an important role in talent training.

During this period, through disciplinary adjustment of life sciences in both micro- and macro-scales, cutting-edge research gained significant achievements. Supported by the CAS Key Research Projects and the National Scientific Foundation of China (NSFC), research projects were initiated, including gene expression and regulation in eukaryotic cells, nascent polypeptide folding, structure and function of macromolecular complexes, signal transduction, molecular genetics and development, embryonic stem cells and animal cloning, molecular mechanisms of neural plasticity and brain activity, as well as research on biodiversity, molecular phylogenesis and integrated biology. In response to the global hotspot of genome research, the Ministry of Science and Technology initiated the Rice Genome Project, in which the CAS took the leading role and established the National Center for Gene Research in Shanghai. Soon after, the human genome project, including human functional genomics and bioinformatics, was started in the CAS, which received international attention. In 1987, three projects of "Synthesis of Yeast Alanine Transfer RNA", "Quantitative Relation Between Modification of Functional Groups of Proteins and Their Biological Activity" and "the Picture Index of Senior China Plant and Claves Familiarum Generumque Cormophytorum Sinicorum" won the first prizes of the National Natural Science Award. In 1989, the CAS Natural Science Award was formally set up and four biological projects, "the Chinese Fern Families and Genera: Systematic Arrangement and Historical Origin", "*A Synopsis of the Avifauna of China* (English edition)", "Conformational Flexibility of Enzyme Active Sites", and "Information Processing in the First Synaptic Layer of Retina" were awarded first prizes.

Advances in basic research in life sciences laid a solid foundation for a rapid development of biotechnology in the CAS. In the 6th and 7th "Five-year Plan", as well as the national "863 Project", the CAS has been China's prime mover in the field of biotechnology. More than 1500 staff from over 40 CAS institutes contributed to a wide range of scientific breakthroughs in the areas of plant genetic and cell engineering, transgenic animal, vaccines and drugs of genetic engineering, monoclonal antibodies, and protein engineering.

To meet the challenge of national food security, the CAS initiated in 1986 a comprehensive project of land improvement to develop sustainable agriculture in the Yellow River-Huaihe-Haihe Plain. Cooperating with the governments of Henan and Shandong provinces，the CAS promoted the adjustment of wheat strains by large-scale demonstration of high-quality, high-yield and disease-resistant wheat. In addition, effective prediction on annual production of grain was established, providing guidance for agricultural production.

1.6 Years of Knowledge Innovation Program (1999 — the present)

The last ten years witnessed a rapid development of the CAS. The implementation of the Knowledge Innovation Program in this decade served as a favorable opportunity for breakthroughs and rapid development of various fields. In line with the concept of maintaining historical continuity while keeping abreast with the time and facing towards the future, the CAS defined its new Mission Statement "catering to the national strategic demands and aiming at the world science frontiers, efforts will be made to promote original innovation in scientific research and the innovation and integration of key technologies, so as to scale the heights of world science and technology, and make fundamental, strategic and forward-looking contributions to China's economic progress, national security and sustainable development". Following such principle and taking the favorable opportunity, CAS life scientists made a series of important original achievements, bringing the research level to international advanced standards.

In this decade, the CAS adjusted the layout of life sciences, optimizing administration, regional distribution and research priorities, to reinforce solid foundation for future development. Research clusters in Beijing, Shanghai, central/south China and west China were formed and major research areas were installed, including public health and medicine, modern agriculture, strategic biological resources, and advanced industrial biotechnology. The subsequent reform of institutes, construction of platforms and optimization of human resources have been benefiting the organization of research activities, the output of scientific achievements, and the sustainable development of innovation capability.

In 1999, the Shanghai Institutes for Biological Sciences was built up by combining eight large institutes, which embodied the concept of integrating a group of institutes concerned with life sciences to establish large-scale institutions with comprehensive and multidisciplinary advantages. In 2001, the Institute of Genetics and the Institute of Developmental Biology were integrated into the Institute of Genetics and Developmental Biology. In the next year, the Shijiazhuang Institute of Agricultural Modernization joined in as the Center for Agricultural Resources Research of the institute. In 2003, the South China Institute of Botany, the Wuhan Institute of Botany, and the Xishuangbanna Institute of Tropical Botany changed their status to botanical gardens, so that the CAS-affiliated botanical garden system was established. At the same time, new institutes representing national demands and scientific orientations were established successively. Such institutes showed great flexibility in the organizational structures, dependent on their legal status and international/domestic co-sponsors. For example, within the frame of the Shanghai Institutes for Biological Sciences, the Institute of Neuroscience, the Institute of Nutritional Sciences, the Institute of Health Sciences, the Shanghai Institute for Advanced Studies, the CAS-MPG Partner Institute for Computational Biology, and the Institut Pasteur of Shanghai were set up. Other newly established institutes include the Guangzhou Institute of Biomedicine and Health, the Beijing Institute of Genomics, the Tianjin Institute of Industrial Biotechnology, the Qingdao Institute of Bioenergy and Bioprocess Technology, and the Beijing Institute of Life Science. The establishment of these new institutes have positively affected the overall layout of life sciences and biotechnology, and vice versa, especially when adjusting research focus, seeking new growth points, and developing interdisciplinary research.

Remarkable achievements were also gained in the construction of research platforms, featuring documentation and information systems, large-scale scientific facilities, state key laboratories, national botanical garden systems and the technical support system of strategic biological resources, to reliably support the CAS research base of life sciences and the major national S&T projects. In 2002, the

Shanghai Information Center for Life Sciences was set up after the Shanghai Center of Documentation and Information joined the Shanghai Institutes for Biological Sciences. In 2007, the Southwest China Germplasm Bank of Wild Species was built and placed into operation. In 2008, the projects of protein research facilities and high-level biosafety laboratory were approved by the central government. As of 2008, the number of national key laboratories in the CAS has reached 18. In addition, 15 botanical gardens were constructed in a system of three-level administration, in which the gardens are affiliated to the Academy, to institutes, or co-sponsored by local governments.

In this period, talent training and recruitment is the core work of human resources. Over the past decade, supported by the CAS Hundred Talents Program, the National Science Foundation of China for Distinguished Young Scholars and projects like Innovative Groups, a great number of talents have been recruited to and trained in the Academy. By the end of 2008, there were totally 68 members of the Chinese Academy of Sciences and the Chinese Academy of Engineering, 119 scientists who were awarded Distinguished Young Scholars by the National Science Foundation of China and 13 innovative groups working in the field of life science and biotechnology in the CAS. Researchers below the age of 45 became the main innovative force. Such research teams, composed of elite scientists with optimal distribution in their research fields and age, are the most reliable resource to enable our innovative goals in life sciences and biotechnology.

2 Major Progress in CAS Life Sciences since the Implementation of Knowledge Innovation Program

Since the CAS Knowledge Innovation Program launched in 1999, significant achievements have been gained in life science research.

From 1999 to 2008, the CAS received 48 national awards in the field of life sciences and biotechnology, two of which were the National Supreme Award of Science and Technology of China. The two winners were Prof. LI Zhensheng (CAS member) from the Institute of Genetics and Developmental Biology and Prof. WU Zhengyi (CAS member) from the Kunming Institute of Botany. Other awards included 26 second prizes of the National Natural Science Award, 2 National Technical Invention Awards and 18 second prizes of the National Scientific and Technological Progress Award. In the past ten years, the CAS life science researchers published 15275 articles in the Science Citation Index (referred to as SCI) journals, accounting for 16.7% of the national total. Among which, 50 papers were published in *Nature*, 34 in *Science*, 11 in *Cell*, respectively accounting for 44.6%, 27.6% and 28.9% of the papers published in these journals by scientists in China. Meanwhile, the CAS conducted in-depth and fruitful research in four fields including health and medicine, strategic biological resources, modern agriculture, and modern industrial biotechnology, with key results transferred into application.

2.1 Health and Medicine

In this field, aiming at both national strategic demands and international standards, the CAS has made significant progress in such fields as genomics, protein science, mechanisms of major diseases, major emerging and infectious diseases, stem cell and regenerative medicine, reproductive and developmental biology, neuroscience, cognitive and psychological sciences, nutritional science, and new drug R&D.

In the field of human genome research, CAS scientists participated in the International Human Genome Project, accomplishing 1% of the human genome sequencing and 10% of the human genome haplotype map. Such wonderful achievements gained international recognition for genomic research in China.

In the field of protein science, developments of new techniques and methods, as well as research on protein structure and function, have made substantial progress. Crystal structures of important biological macromolecules were solved, including the mitochondrial membrane protein complex II and its substrate-bound form, spinach major light-harvesting complex, the PA subunit of RNA polymerase in influenza virus, as well as the complex of neurotrophin-3 and its receptor. Such results have not only made internationally recognized contributions to structural biology, but also benefited elucidation of disease mechanism and drug development.

Neuroscience research serves as the basis for the treatment of neurodegenerative diseases and mental-psychological disorders. The CAS made a series of important discoveries with international recognition in the field, for example, the new mechanism of neuronal migration, the mechanism underlying the preferential protein trafficking in polarized neurons, the essential role of TRPC channels in the guidance of nerve growth cones, and the functions of glial cells in information processing. These achievements have provided important theories for the prevention and treatment of neurological diseases, and for the development and rehabilitation of central nervous system.

Original and significant results were achieved in cognitive science. Through the comprehensive research on gene, brain, behavior and cognition, mystery of decision making and principles of learning and memory were systematically revealed. The concave-eared frogs were discovered as the first species of non-mammals that are able to generate and detect ultrasonic sound, which was of great significance to bionic techniques. To answer the fundamental question in cognitive science, “what are primitive units over which cognitive process operates”, the “Global-first” theory of topological perception was originally initiated and systematically developed.

Researchers in the fields of reproduction, stem cell and regenerative medicine have gained notable achievements. The discovery of an important antimicrobial peptide in the reproductive system was of great significance to the studies on infertility caused by abnormal sperm maturation, male contraception and the prevention of sexually transmitted diseases. Research on human nuclear transfer embryonic stem cells achieved breakthrough, which was officially published for the first time in the world that human somatic nucleus could be re-programmed and developed to blastocyst. In addition, rat somatic cells were reprogrammed and pluripotent stem cell lines were successfully generated.

Significant progress has been made in the mechanisms of major diseases. For example, gene mutations of heat shock transcription factor 4 were discovered in hereditary cataract. The mechanism of hereditary dentinogenesis imperfecta was discovered. The gene causing brachydactyly type A-1 disease was successfully mapped and cloned. The key molecules in receptor regulation, pain modulation and morphine tolerance were discovered, and the function of protein kinases in opioid tolerance and dependence was revealed. Many breakthroughs were gained in diabetes research, including the discovery of a nonpeptidic agonist of glucagon-like peptide I receptors, systematic illustration of the relationship between vesicle secretion and glucose regulation. In addition, the nutritional intervention on diabetes was carried out while the nutritional and genetic factors related to metabolic diseases were analyzed, providing large amount of basic data for the research on chronic metabolic diseases.

The CAS has developed about 120 drugs currently available in the market, 50 of which have been granted New Drug Certificates after the certification system was implemented in 1999. The drugs of major influence include antofloxacin hydrochloride (original fluoroquinolone antibiotic in China), salvianolate (a successful example for the modernization of Chinese traditional medicines), Guanfu base A hydrochloride (China's first anti-arrhythmic drug with independent intellectual property), recombinant straphylokinase for injection (the first straphylokinase drug in the world for the treatment of thrombosis), compound SH (an anti-AIDS drug registered in Thailand in March 2004), and schiperine (for treatment of Alzheimer's disease and currently in the international Phase III clinical trial).

Taking advantage of accumulated research and talents, the CAS has made significant contributions in major national emergencies to ensure social stability. In the prevention and control of SARS, the CAS accomplished SARS genome sequencing, developed quick diagnosis kits for detecting early-stage disease, solved the structures of SARS proteins that were important for drug development, and made progress in tracking the source of SARS virus to show that bats were the natural reservoirs. In the case of avian flu, CAS reported the first case of infection in wild migratory birds and studied its impact on the global spread of the H5N1 virus. The CAS also succeeded in developing generic drugs of "Tamiflu" and "Zanamivir" with improved synthetic procedures. Immediately after the Wenchuan earthquake, CAS staffs arrived in the stricken region to offer psychological assistance. Consequently, several China specific modes of psychological assistance in disaster areas were established and the research on post-disaster assistance made a series of accomplishments, both promoting the development of disaster psychology in China.

2.2 Strategic Biological Resources

To meet the nation's growing demand for strategic biological resources, from the 1950s, the CAS started the compilation work of *Flora of China*, *Fauna of China* and *Spore Flora of China*. Other important progress in this field includes the establishment of the national scientific botanical garden system and the research of higher fungi, *Gentianaceae* and *Orchidaceae* in southwest China.

Excellent achievements were made in the conservation and exploitation of biodiversity resources. The Institute of Hydrobiology developed ex-situ conservation at Tian'ezhou and captive breeding for Yangtze finless porpoise, which is the only successful case of ex-situ conservation for cetaceans. By the end of 2008, as one of the national large-scale scientific facilities, the Southwest China Wildlife Germplasm Bank had collected and sorted around 150 families, more than 4000 species and 22000 pieces of wild plant seeds. Cooperated with local governments, the CAS has been actively promoting the national scientific botanical garden system, which currently consists of 15 botanical gardens including the Wuhan Botanical Garden, the South China Botanical Garden, the Xishuangbanna Tropical Botanical Garden, the Lushan Botanical Garden, the Shenzhen Fairy Lake Botanical Garden and the Nanjing Botanical Garden Memorial Sun Yat-Sen, etc. While protecting rare and endangered species, the CAS also introduced many plants of economic and medicinal value, consequently benefiting the ex-situ conservation and sustainable utilization of strategic plant resources.

The compilation of *Flora of China, Fauna of China* and *Spore Flora of China* has made big progress. *Flora of China*, a masterpiece that comprehensively summarizes the systematic classification of vascular plants in China, consists of 80 volumes and 126 fascicules, covering 301 families, 3408 genera and 31142 species of plants, and containing 9,080 pictures. It is the world's longest Flora to date, with its publication accomplished in October 2004. *Fauna of China* has been published with 125 volumes including 31 volumes on vertebrates, 44 volumes on invertebrates and 50 volumes on insects. *Spore Flora of China* made a classified research on the following five categories in China: marine algae, freshwater algae, fungi, lichens and moss spores. To date, it has been published with 66 volumes, recording 249 families of spore producing plants.

In the research field of biological effects of climate change, the Institute of Botany carried out systematic research on the primary production and rain use efficiency of the arid and semiarid ecosystem in the Mongolian Plateau. The results were of great importance to assess the impact of climate change on grassland ecosystems. Researchers in the South China Botanical Garden revealed that old-growth forests could continuously accumulate carbon in soils. Scientists in the Institute of Zoology and their international collaborators discovered the correlation between locust plagues in China and climate change in the past millennium, indicating the plagues were more prone to the cooling events.

Regarding the special features of plants in southwest China, CAS scientists conducted detailed studies on *Orchidaceae* plants, higher fungi and *Gentianaceae* plants respectively. The project of Research on *Orchidaceae* Plants in China made creative achievements, with 9 books and 101 articles published. The project of Classification and New Chemicals in the Higher Fungi in Southwest China was accomplished with 12 books and 134 articles published, and a herbarium of more than 140000 cryptogamic specimens established. The project of Research on Chinese *Gentianaceae* Plants was accomplished with 2 books and 72 articles. These three projects enabled discovery of large amount of new species and utilization of important plant resources, thus all winning the second prizes of the National Natural Science Award.

2.3 Modern Agriculture

In the field of modern agriculture, the CAS have achieved fruitful results not only in such basic research areas as growth, development and environmental regulation of plant, crop genomics, and animal genetics and evolution, but also in practical demonstration of plant breeding, aquaculture and bio-pesticides, etc.

Research in rice genomics and functional genomics has stepped into the international advanced level. Through the Rice Genome Project, CAS scientists successively completed the draft sequence and whole genome fine map of rice (*indica*), and provided the intra- and inter-subspecies molecular marker maps of rice. As part of the International Rice Genome Sequencing Project, the sequence of rice (*japonica*) chromosome 4 was determined in the CAS. Facilitated by the sequencing results, the CAS conducted in-depth genetic and functional study on important rice agronomic traits. A set of genes with independent intellectual property were cloned and their functions were elaborated, including *MOC1* (for tillering control), *SKC1* (for salt tolerance), *Eui* (for elongation of uppermost internode), *GW2* (for grain weight control), *GIF1* (for grain filling), *LA1* and *PROG1* (for erect growth).

CAS researchers have been showing interests in the molecular mechanisms in higher plants. Internationally recognized breakthroughs were achieved on the mechanism of higher plant architecture, using *Arabidopsis thaliana* and rice as models. In exploring the mechanism of photosynthesis, proteins LPA1, LPA2, LPA3, DEG5, and DEG8 were successively discovered to function in the biosynthesis, assembly, degradation and regulation of chloroplast thylakoid membrane protein complexes. In addition, the high-energy intermediate in the synthesis of adenosine triphosphate was identified in photophosphorylation. Finally, it was demonstrated that low concentration of sodium bisulfite could promote photophosphorylation and thus improve the photosynthetic rate by 15%-20%. This technique has been applied to rice and wheat, in the critical production period to increase the yield by 5%-10%.

In the field of animal genetics and evolution, the CAS participated in international research projects concerning chicken genomics. The genome of British broiler, Swedish layer and Chinese Silkie chicken was sequenced and about two million genetic variations were analyzed. The whole-genome fine map of silkworm was successfully completed, representing 99.6% of the genome and predicting 14623 genes. In addition, in-depth research on the origin and genetic diversity of major Chinese domestic animals such as pig, cattle, sheep, goat, donkey, horse, dog, rabbit and chicken was carried out, revealing that southern China and surrounding areas were primary regions for domestication, and the spread of domestic animals was closely related to human migration.

In animal reproduction, the project of Experimental Embryology of Sexual and Asexual Mammal Reproduction emphasized on fertilization mechanism and micro-fertilization, receiving the second prize of National Natural Science Award. In 2002, CAS scientists cloned cattle from adult somatic cells and acquired the first surviving population, reflecting world-class animal cloning research in China.

In breeding new crops varieties, wheat breeding research has made important breakthroughs. The high-yield, disease-resistant and high-quality “Xiaoyan” series of wheat varieties were cultivated by the cross-breeding of *Elytrigia elongatum* and wheat. Xiaoyan6 has been planted in 150 million Mu (10 million hectares), with an increased yield of 0.8 billion Jin (0.4 million tons). Based on this, a new wheat variety named “Kenong199” featuring high productivity and adaptability was cultivated, and has been applied in large-scale demonstration, covering over 0.5 million Mu (about 33 thousand hectares) in Hebei, Shandong, Henan and other provinces. Furthermore, the cultivation and popularization of new fruit varieties has been successful. The “Jintao” variety of kiwifruit, which held independent intellectual property, successfully made its patent transferred worldwide in 2001. In addition, more than 20 new varieties of cold and disease resistant wine grapes such as “Jingxiu” and “Beimei” have been popularized for more than 0.7 million Mu (about 47 thousand hectares) with annual profit of about 4 billion Yuan.

In aquaculture research, CAS scientists bred and popularized a series of major aquatic products. For example, allogynogenetic silver crucian carp "Zhongke3", certificated as a new variety by the National Committee for Examination and Approval of Original Breeding and Good Breeding, raised annual value of more than one billion Yuan. "Dalian1" hybrid abalone was granted certificate of national-level new variety, with annual production of 15 thousand tons and direct profit of 3 billion Yuan. "Zhongkehong", a new variety of bay scallop, accounts for 70% of scallop production in China. In addition, the CAS initiated the farming of *Litopenaeus vannamei* in China, with annual production value of over 10 billion Yuan.

In regard to biopesticides, 4 ingredients and 9 products of insect viruses have been developed by the CAS, 8 of which acquired pesticide registration and market access. Such biopesticides totally account for annual production of 5-ton ingredients and 200-ton reagents, with application area of 30 million Mu (2 million hectares). The project of New Technology in Pest Control by Parasitoid Wasp Transmitted Virus was granted several patents, due to its safety, economy, durability and efficiency. This technique has been demonstrated in more than 0.3 million Mu (20 thousand hectares) and won the second prize of National Technology Invention Award. Progress was also made in the breeding, planting and processing of high-yield pyrethrums. In Yunnan, over 0.12 million Mu (8 thousand hectares) of pyrethrums yields 4 thousand tons of dried flowers, accounting for 30% of the world total. More than 20 pyrethrin products have been registered, ending the period of lacking natural pyrethrin pesticides in China.

Progress was also made in prewarning and control of agricultural disasters. First, CAS researchers clarified the occurrence law of rodent infestation in typical farming areas, established forecasting models, and overcame rodents' tolerance and resistance to the first generation of anticoagulant rodenticide. In addition, locust plague was studied in a wide perspective, from molecular mechanism to climate change. The results indicated that the phase change in migratory locust was related to the transcription and regulation at the genomic level, while small RNA molecules were involved in its negative feedback control. Such study would benefit the development of controlling drugs and the forecast of locust plagues.

2.4 Industrial Biotechnology

To meet the national demands for bioenergy, biomaterials and environmental biotechnology, the CAS has made active deployment in the field of biotechnology. By undertaking national research projects and strengthening market-oriented research, the CAS has contributed a lot in promoting technology transfer.

In the field of industrial biotechnology, CAS scientists have participated a great number of projects, including the 973 projects of "Cell Factories for Biorefinery" and "Extremophiles and Their Application Potentials", "The Basic Biology and the Adaptation Strategies of Extremophiles" supported by the NSFC for Creative Research Groups, the 863 key projects of "Molecular Modification and Engineering Application of Industrial Biocatalysts" and "Biorefinery Technology for Bio-based Chemicals", and the projects supported by local governments involving bioenergy, biomaterials, bio-based products and industrial enzymes. Significant progress has been gained in key technologies of biorefining, metabolic engineering, biocatalysis and biotransformation, with a number of research outcomes appraised, for example, "Xylitol Production by Bioconversion", "Steam Explosion and Mechanical Fractionation Technology for Biomass" and "Key Technologies and Materials of Biodiesel Production", and so on.

The cooperation of production, education and research sectors plays an important role in the transfer of industrial biotechnology. The CAS has established various forms of cooperation with a number of international and domestic enterprises as well as universities. For example, the Institute of Plant Physiology and Ecology of the Shanghai Institutes for Biological Sciences and the Swiss Federal Institute of Technology jointly established the Shanghai Center for Cassava Biotechnology; the Institute of Microbiology and the North China Pharmaceutical Group signed a strategic cooperation agreement; and the Shanghai Institutes for Biological Sciences and the Henan Tianguan Group Co., Ltd. agreed to jointly build a 30000-ton acetone-butanol production line.

With respect to bioenergy, research on power generation through biomass gasification was carried out. The biomass gasification was performed in a circulating fluidized bed, converting biomass wastes, such as waste wood, straw and husk, to combustible gas. After decoking and purification, the gas was sent into the gas engine to generate electricity. In addition, CAS scientists developed a comprehensive treatment for the mixed-garbage with low calorific value and high moisture content, with such advantages as utilization of low-grade heat, increased uniformity of litter, and reduced pollution emission. This technology was industrialized through cooperation and the municipal solid waste processing system, with capacity of 400-500 tons/day, has been set up.

Great progress has been made in bio-based products. To produce xylitol by bioconversion, CAS scientists cooperated with the Shandong Weilong Industry Group Co., Ltd. to conduct industrial trials, yielding xylitol of >99% purity. Such new technique and the bacterial strains used therein, holding independent intellectual property, will make it possible to replace traditional chemical methods with bioconversion in the production of xylitol. Another example was given by the 50-ton energy-efficient production line of abscisic acid, which was set up at Sichuan Longmang Fusheng Technology Co., Ltd., with the original technology from the Chengdu Institute of Biology.

In the field of environmental biotechnology, the project of "Development of Environmental Microbial Agents and Its Application in Biological Treatment of Refinery and Textile Wastewater" passed the evaluation. The efficient, economical and safe microbial reagents were successfully applied in more than ten demonstration projects, gaining significant economic, environmental and social benefits. This project also received the first prize of the Scientific and Technological Progress Award of Sichuan Province.

3 Challenges and Strategic Thinking of Life Science

(1) While a progressive modern civilization is created with the development of human society, more and more severe challenges are emerging. In regard to life science, such challenges are mainly displayed as follows. With the acceleration of population aging and the changes in social structure and lifestyles, aging-associated, chronic, emerging and infectious diseases become growing threats to human health. With the rapid progress of industrialization and urbanization, substantial food security issue is caused by both arable land reduction and growing food demand. Due to energy shortage, clean and renewable energy sources are in urgent need. Global climate change caused by human activities also added dramatic pressures on the natural and socioeconomic systems. To address these challenges, critical breakthroughs of life science and biotechnology are required in the fields of medicine, agriculture, energy and environment, so as to provide solutions for human survival and development. With benefiting human society and protecting global environment as its intrinsic responsibilities, life sciences and biotechnology have become hotspot and focus of scientific research since the second half of the last century.

(2) The continuous progress of science leaves life sciences with much more new features of the times. First of all, the era of molecular biology originating in the 1950's has been transformed into a post-genome era. With the concepts and tools of genomics, proteomics, metabolomics and bioinformatics, scientists start demonstrating life systems from a systematic and complex point of view, exploring the essence of life phenomena such as inheritance, development, death, metabolism and neural activities. This progress of epistemology and methodology will provide great impetus to life sciences not only in the theoretical breakthroughs, but also in the transformation of basic research to applied research. In such a case, the linkage and mutual promotion between basic and applied research are highly enhanced, which will raise new ideas and methods for modern biomedicine against major diseases like cancer, diabetes and neurodegeneration. In the long term, the above described impetus will have a significant impact on overall economic development and social progress.

In addition, life science in the new era is associated with the feature of interdisciplines. To solve puzzles in life sciences, it requires not only the intradisciplinary collaboration, but also the involvement of other disciplines such as physics, chemistry and information sciences. By making use of the new scientific and technological achievements in nanotechnology, information technology and space technology, it is believed that progress of life sciences and biotechnology will be achieved in the near future.

Thirdly, ethical issues have become increasingly important in life science research. In recent years, great benefits were made by rapid development of stem cell technology, animal cloning, transgenic technology and synthetic biology. In the mean time, many old and new ethical problems have been brought about. There is a concern that these technologies may have unforeseen consequences against both human beings and the natural environments. To face the social and ethical impact brought by every breakthrough in the field of life sciences, we should pay close attention, carefully respond and take necessary precautionary measures, with respect to the national security, social stability and ecological safety. At the same time, protection of research achievements should be emphasized to promote the healthy and rapid development of life sciences.

(3) To meet the challenges, we need to clearly recognize the trend of life science, and take the new demands from scientific and economic development into consideration. On the sound basis achieved during the period of Knowledge Innovation Program, we should strive to seek for new breakthroughs in life science and biotechnology, and to make great contributions to social development and scientific-technological progress. To achieve such goals, the following aspects must be emphasized at present and in the future:

(i) Looking into the future and strengthening strategic research and planning. On one hand, as a main force of national strategic development in science and technology, the CAS must take in-depth and systematic considerations in, extract key points for a leapfrog development from, and make overall developmental outlines for the fields of national strategic needs, such as ecological and high-value agriculture and biological industry, generally applicable health assurance, sustainable energy and resources, ecological and environmental conservation, and the fields of cutting-edge basic research. On the other hand, as a major advisory body to the government on science and technology related issues, the CAS should also submit consultative reports and important advice to decision makers and adjust programs in life science based on such advisory work.

(ii) Optimizing the layout of science and technology and strengthening the build-up of scientific research bases. While carefully reviewing the significant progress made in the past 12 years of the Knowledge Innovation Program, we need to set up a group of new research centers in cutting-edge areas to meet emerging demands and challenges. In addition, the strategic orientation of the affiliated institutes needs clarification to establish an integrated research layout with explicit directions and focuses. By implementing the international evaluation, some outstanding institutes will be further strengthened and eventually promoted to the international advanced level. Taking into consideration different features of life science related institutes throughout the country, we should enhance the overall scientific layout as well as regional development, deploying of research clusters in the following four regions: Beijing, Shanghai, central/south China and west China.

(iii) Building up qualified research teams of high standards. It is our focal point in the future to establish first-class groups with invigorating academic ideas and rigorous academic tradition, full of team spirit and dedication to the cause of scientific research. More attention must be paid to recruiting and training young scientists, especially those of leading potentials in fundamental areas. The CAS will provide scientists excellent working conditions with better research facilities and relaxed academic environments with more research time, promoting full play to their intelligence and talents.

(iv) Exploring and implementing new organizational mechanisms of research activities, and promoting interdisciplinary collaboration and technological integration. First of all, the existing cross-disciplinary centers will fully function, and new centers will be gradually developed to facilitate interactions between life science and other disciplines like mathematical sciences, chemistry, information science, computational science, space science, geography, and remote sensing. Second, by integrating CAS researching forces in ecological agriculture and those in emerging and infectious diseases, centers for focused research can be established accordingly. Given the complementary advantages of the eastern and western biological institutes, in their research interests, human resources, techniques and platforms, the CAS will promote their cooperation and communication in such aspects. Finally, the strategic cooperation with international key research institutions, universities, as well as enterprises will be further strengthened.

(v) Improving public research platforms and technical support systems, to promote the scientific research capability. Such research platforms shall include internationally advanced protein research facilities, high-level biosafety laboratories, biotechnological platforms for genetic engineering, stem cell and animal cloning, large-scale experimental animal centers with enriched collections of model organisms and mutants, platforms of genomic research, platforms of brain and cognitive sciences, national botanical garden systems, natural history museums, large-scale field facilities for ecological simulation, and germplasm banks.

(vi) Developing domestic cooperation and setting up an innovation alliance for bioindustrial technologies. The measures will include promoting strategic cooperation within the Yangtze River Delta and the Pearl River Delta, scheming up cooperative alliance covering bioindustry, modern agriculture and pharmaceutical industry, and encouraging technology transfer to the outstanding domestic enterprises, to promote both national and regional economic development.

Recalling the past six-decade development of the Chinese Academy of Sciences, especially the recent 12 years after the launch of the Knowledge Innovation Program, we have made great achievements in the forefront research of basic sciences and key applied technologies, the build-up of talented teams, the institutional reform and the infrastructure constructions. Looking forward to the future, we are full of confidence and hopes. We will exert persistent efforts to the national economy, social development and the progress of life sciences, for the aspirations of the times, and for the great revitalization of the Chinese nation.

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