ISPPG 2024

November 22-24

中国·昆明

KUNMING·CHINA

# 灵长类表型与遗传研究国际研讨会

# International Symposium on Primate Phenotype and Genetics

# 会议手册

# Conference Manual

## 会议主办 Organizer

中国科学院昆明动物研究所

Kunming Institute of Zoology, Chinese Academy of Sciences

## 会议承办 Co-organizers

遗传进化与动物模型重点实验室

Key Laboratory of Genetic Evolution & Animal Models, Chinese Academy of Sciences

模式动物表型与遗传研究国家重大科技基础设施（灵长类设施）

National Research Facility for Phenotypic and Genetic Analysis of Model Animals (Primate Facility)

国家非人灵长类实验动物资源库

National Resource Center for Non-Human Primates

## 会议资助 Funding

云南省科学技术协会

Yunnan Association for Science and Technology

# Contents

# Introduction of the International Symposium on Primate Phenotype and Genetics (ISPPG)

Non-human primates (NHPs) share significant genetic, physiological, and behavioral similarities with humans, making them ideal experimental models for biomedical research and valuable for preclinical studies in translational medicine. Investigating primate phenotype and genetics, along with systematic analysis of the mechanisms underlying disease phenotype and developmental processes, offers a robust approach to discovering the fundamental principles and biomarkers associated with human health and disease. Such research has the potential to drive transformative advancements in biomedicine and facilitate more effective translation of findings into clinical applications.

To advance research on primate phenotype and genetics in China and to strengthen communication and cooperation among researchers from various domestic and international institutions, the Kunming Institute of Zoology, Chinese Academy of Sciences, will host the International Symposium on Primate Phenotype and Genetics (ISPPG) from 22 to 24 November 2024 in Kunming, Yunnan Province, China.

We invite distinguished scholars and experts in primate phenotyping and genetic research, both domestically and internationally, to present the latest achievements and advancements in cutting-edge primate research, discuss future trends in the field, and foster interdisciplinary communication and collaboration.

## I. Themes

The symposium will primarily focus on primate genomics research, development and application of animal models for major diseases, primate model phenotype research and evaluation, and primate biomedical research and its application.

## II. Schedule

22 November 2024: Registration

23 November 2024: Opening ceremony and presentation of reports

24 November 2024: Tour of the National Research Facility for Phenotypic and Genetic Analysis of Model Animals (Primate Facility)

## III. Location

Conference venue: Baohua Road, Huahongdong, Xishan District, Kunming, Yunnan, China

Hotel address: Shengshi Qianhe Hotel, Xiaokang Avenue, Kunming Panlong District, Kunming, Yunnan, China

## IV. Organizer

Kunming Institute of Zoology, Chinese Academy of Sciences

## V. Co-organizers

Key Laboratory of Genetic Evolution & Animal Models, Chinese Academy of Sciences

National Research Facility for Phenotypic and Genetic Analysis of Model Animals (Primate Facility)

National Resource Center for Non-Human Primates

## VI. Funding

Yunnan Association For Science and Technology

## VII. Organization

Chaiman: Yonggang Yao ( 姚永刚 ) ; Executive Chaimman: Dongdong Wu ( 吴东东 )

## VIII. Expenses

Including the travel and accommodation expenses of the experts invited on the meeting, the rest of the participants are responsible for their own accommodation expenses (with access to discount rates provided by the conference service). Meals will be organized by the conference service. Buses to the conference venue are provided.

## IX. Contact Information

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| International Symposium on Primate Phenotype and Genetics | | | |
|---|---|---|---|
| **November 22 (Friday)** | | | |
| **Whole Day** | **Registration & sign-in** | | |
| **November 23 (Saturday)** | | | |
| **09:00-09:30** | **Opening Ceremony** | | |
| | **Director Address, Yonggang YAO ( 姚永刚 )**<br>Primate Phenotype and Genetic Analyses – From Basic Research to Clinical Applications | | |
| **Session 1: Primate genomics** | | | |
| **Time** | **Speaker** | **Affiliation & Presentation title** | **Moderator** |
| 09:30-09:55 | Tomas MARQUES BONET | University Pompeu Fabra<br>Global patterns of genome diversity across the primate radiation | Zhijin LIU<br>刘志瑾<br>Capital Normal University |
| 09:55-10:20 | Jeffrey ROGERS | Baylor College of Medicine<br>Genomic analysis of nonhuman primates: Applications for evolutionary and biomedical studies | |
| 10:20-10:45 | Dongdong WU<br>吴东东 | Kunming Institute of Zoology, CAS<br>Reference genomes provide insights into phenotype evolution of primates | |
| 10:45-11:00 | **Coffee Break & Group Photo** | | |
| 11:00-11:25 | Christian ROOS | German Primate Center, Leibniz Institute for Primate Research<br>Conservation Genomics of the Critically Endangered Cat Ba langur | Yong SHAO<br>邵永<br>Kunming Institute of Zoology, CAS |
| 11:25-11:50 | Yafei MAO<br>毛亚飞 | Shanghai Jiao Tong University<br>The structure, evolution, and function of structural variation in primate genomes | |
| 11:50-12:00 | **Session 1 Discussion** | | |
| 12:00-13:30 | **Lunch break** | | |

| | | | |
|---|---|---|---|
| **Session 2: Animal Models and Disease Mechanisms** | | | |
| 13:30-13:55 | Zhonghua LU<br>路中华 | University of Chinese Academy of Science<br>Development of Nonhuman Primate Models and Therapeutic Strategies for Neurodegenerative Diseases | Hui ZHAO<br>赵晖<br>Chinese University of Hong Kong<br><br>Lei SHI<br>石磊<br>Kunming Institute of Zoology, CAS |
| 13:55-14:20 | Joji TSUNADA | Chinese Institute for Brain Research, Beijing<br>Flexible Vocal Behavior and Underlying NeuralMechanisms in Marmoset Monkeys (*Callithrix jacchus*) | |
| 14:20-14:45 | Yuji NAYA | Peking University<br>Constructive process for the flexible use of long-term association memory in the primate medial temporal lobe | |
| 14:45-15:10 | Chi Kwan Vincent CHEUNG | Chinese University of Hong Kong<br>Examining Motor Modularity as a Theory of Neuromotor Control in Humans and Animal Models | |
| 15:10-15:35 | Yongchang CHEN<br>陈永昌 | Kunming University of Science and Technology<br>Establishment, Mechanistic Exploration, and Gene Therapy of Nonhuman Primate Models for Duchenne Muscular Dystrophy | |
| 15:35-15:45 | **Session 2 Discussion** | | |
| 15:35-15:50 | **Coffee Break** | | |
| **Session 3: Primate Stem Cell and Developmental Biology** | | | |
| 15:50-16:15 | Stephen DALTON | Chinese University of Hong Kong<br>Using human brown adipocytes to develop new therapies for type II diabetes | Ping ZHENG<br>郑萍<br>Kunming Institute of Zoology, CAS |
| 16:15-16:40 | Falong LU<br>陆发隆 | Institute of Genetics and Developmental Biology, CAS<br>Epigenetic regulation mediated by RNA poly(A) tails | |
| 16:40-17:05 | Lijun DING<br>丁利军 | Medical School of Nanjing University<br>MVA metabolites in granulosa cell and oocyte aneuploidy | |
| 17:05-17:15 | **Session 3 Discussion** | | |
| 17:15-17:30 | **Summary & Closing remark** | | |
| 18:30-20:00 | **Dinner** | | |
| **November 24 (Sunday)** | | | |
| 09:00-12:00 | Visit to the National Research Facility for Phenotypic and Genetic Analysis of Model Animals (Primate Facility) | | |
| 12:00-14:00 | **Lunch** | | |

# Kunming Institute of Zoology, Chinese Academy of Sciences

The Kunming Institute of Zoology (KIZ) is directly affiliated with the Chinese Academy of Sciences (CAS). Located at the head of the Indo-Burma biodiversity hotspot, KIZ is dedicated to research in the fields of biodiversity, evolution, conservation, and sustainable utilization of resources in southwestern China, Eastern Himalayas, and Southeast Asia. Furthermore, KIZ is committed to excellence in two major areas, i.e., Genetics & Evolutionary Biology, Primate Animal Models & Human Disease Mechanisms.

Since its founding in 1959, KIZ has been committed to exploring the fundamental aspects of the world we live in, with a focus on genetics and evolutionary biology, primate animal models, and human disease mechanisms. It provides a fertile environment for scientific innovation and lively interactions and offers competitive reward packages and high-quality training programs for graduate students and postdoctoral fellows.

Since the implementation of the CAS Knowledge Innovation Program, KIZ has experienced

rapid development in scientific research. Currently, KIZ contains the State Key Laboratory of Genetic Resources and Evolution, and CAS Key Laboratory of Animal Models and Human Disease Mechanisms. KIZ also established the KIZ-Chinese University of Hong Kong Joint Laboratory of Bioresources and Molecular Research in Common Diseases. Accordingly, major KIZ breakthroughs, which include the development of non-human primate models for disease and pharmaceutical research, theoretical advances in evolution and genomics, and cultivation of genetic resources of domestic animals and their wild counterparts, have had a strong emphasis on fostering innovation with profound implications for health, conservation, public education, and management of the diverse biological resources of Yunnan Province and proximate regions with rich biodiversity.

Since its establishment, KIZ has focused on the evolution, protection, and utilization of biodiversity. In accordance with the decisions and arrangements of CAS, it has concentrated on national key scientific and technological issues. Under the leadership of prominent and older generation scientists, important high-level research has been achieved, with vital contributions to national and local development. KIZ continues to undertake major scientific research tasks, including 973 major national science and technology projects, 863 national high technology research programs, Strategic Priority Research Program of CAS, and National Natural Science Foundation of China. Furthermore, KIZ has won 5 national second-place prizes for natural science, 1 second-place prize for technological inventions, and 3 scientific and technological progress awards. Ministerial and provincial level awards as well as CAS awards have been granted, and 313 patents have been authorized as of 31 December 2021.

Internationally, KIZ maintains collaborations across the globe, with numerous partnerships and connections with renowned scientific research institutions in East Asia, Southeast Asia, the Americas, Europe, and other countries. In this new era, KIZ has helped establish the “Sino-Africa Joint Research Center” and “Southeast Asia Biodiversity Research Institute” of CAS, thus furthering cooperation between Africa and Southeast Asia. KIZ is also a member of several important international networks and projects, including the International Barcode of Life, Bird Genome 10K Consortium, Dog 10K Project, and Global Ant Genomics Alliance.

# Key Laboratory of Genetic Evolution & Animal Models

In September 2023, Key Laboratory of Genetic Evolution & Animal Models was approved for construction. This laboratory will face the urgent demand for animal models, especially large animal models, for life and health research, and will rely on China's rich large animal resources, innovatively introduce the idea of evolutionary biology, and integrate cutting-edge multidisciplinary technologies to systematically analyze the formation and evolution of key animal phenotypes, including disease phenotypes, and elucidate their regulatory laws and biological mechanisms. Relying on China's abundant large animal resources, the laboratory will innovatively introduce the idea of evolutionary biology, integrate multidisciplinary cutting-edge technologies, systematically analyse the formation and evolution mechanism of key animal phenotypes, including disease phenotypes, and elucidate their regulatory laws and biological mechanisms.

On this basis, it will create major disease models of large animals (including monkeys, pigs, and dogs) represented by non-human primates, accurately fit human life patterns and disease occurrence and development processes, and achieve large-scale innovative utilization, strengthen the security of the national biopharmaceutical field, seize the opportunity for large animal research and models. Utilize the global high ground. The laboratory has three research directions, including the formation and evolution of animal phenotypes; Animal phenotype research and model creation techniques; Creation and utilization of animal models.

In 2023, the laboratory published a total of 209 SCI papers, of which 58 were published as first author or corresponding author (including co authors) in internationally renowned journals such as Science (2 papers), Cell (2 papers), Immunity, Science Advances, Cell Research, and National Science Review with a five-year impact factor ≥ 9. Obtained 27 authorized patents, including 22 invention patents; Two patents were successfully converted.

# National Research Facility for Phenotypic and Genetic Analysis of Model Animals (Primate Facility)

The National Research Facility for Phenotypic and Genetic Analysis of Model Animals (MAF) is supported by the “12th Five-Year” National Major Scientific and Technological Infrastructure Projects of China. The Kunming Institute of Zoology (KIZ) (Chinese Academy of Sciences (CAS)) in Kunming and the China Agricultural University in Beijing are the lead legal entities involved in the construction and support of facilities for non-human primates (NHPs) (*Primate Facility* in Kunming, Yunnan) and porcine animals (*Pig Facility* in Zhuozhou, Hebei), respectively.

Primates represent a strategic national resource, serving as indispensable experimental models for investigating the mechanisms underlying major diseases, facilitating vaccine and drug development, and evaluating innovative therapeutic technologies. The *National Research Facility for Phenotypic and Genetic Analysis of Model Animals (Primate Facility)* is distinguished as the most extensive and only large-scale research facility in the world carrying out primate phenotypic and genetic research at an unparalleled scale. With the capacity to accommodate the needs of 5 500 experimental primate subjects, the facility occupies a leading position worldwide regarding the availability of experimental primate resources, construction of genetically edited animal models, and precise determination of phenotypes and behaviors, leading to significant research contributions. The f*acility* plays a pivotal role in advancing national projects and strategic science and technology initiatives, leveraging its global leadership to study key phenotype mechanisms, brain functions and diseases, infectious disease mechanisms, and drug innovation.

The *Primate Facility* covers a construction area of 24 100 $m^2$ and was developed over a five-year constructive period. The facility includes four major systems: (1) Primate Production and Breeding System, (2) Primate Phenotype Analysis System, (3) Primate Genetic Analysis System, and (4) Information Processing and Intelligent Automatic Management and Control System.

The facility aims to establish world-class, large-scale, integrated research platforms for studying genetic and phenotypic patterns in NHPs at the molecular, cellular, tissue, and morphological levels, with a focus on mapping the longitudinal process from embryogenesis to adult behavior and aging. The *Primate Facility* is dedicated to collecting and analyzing phenotypic and genetic data while standardizing large-scale production and breeding of NHPs. Through its integrated system, the facility aims to ensure the consistent and precise execution of high-throughput studies on phenotypic and genetic relationships.

The *Primate Facility* is oriented towards strategic national needs and advances in cutting-edge scientific disciplines using NHP models, contributing to national R&D programs and supporting frontier research in neuroscience, disease mechanisms, and drug research and development. Focused on addressing critical issues related to human biological processes, the facility supports research in advanced fields, such as human brain function and cognition, neurological and psychiatric disorders, infectious diseases, and cardiovascular and metabolic conditions, to deepen our understanding of fundamental human biological principles, elucidate the regulatory mechanisms of life phenotypes, clarify the development pathways of major diseases, and promote the discovery of novel scientific patterns and the preclinical application of emerging technologies.

As a core platform for regional scientific and technological innovation and development, the facility is set to become an essential center of science and technology in South and Southeast Asia. Moreover, it will also play a central role in the implementation of the “Belt and Road” Science and Technology Innovation Action Plan.

Main Building of the Primate Facility

# National Resource Center for Non-Human Primates

The establishment of the National Resource Center for Non-Human Primates (NRCNHP) was approved by the Ministry of Science and Technology of the People's Republic of China and the Ministry of Finance of the People's Republic of China in June 2019, relying on the Kunming Institute of Zoology, Chinese Academy of Sciences, and jointly constructed with the Institute of Medical Biology, Chinese Academy of Medical Sciences and the Institute of Biophysics, Chinese Academy of Sciences.

The Center, which consisted of four modules germplasm resource bank, biobank, animal models of disease bank and database for non-human primates, closely focuses on national strategic needs, with the goal of "building an international leading Non-Human Primates National Resource Center" and the guiding principles of "optimization, integration, sharing and efficiency". The Center collects, integrates and optimizes non-human primates and tree shrews germplasm resources and carries out sharing services in seven aspects: resource collection and preservation, scientific and technological resource remittance, resource excavation and application, public sharing and services, research and development of common technologies and resource development, monitoring of domestic and international dynamics, and domestic and international exchanges and cooperation.

By the end of 2023, the Center now holds more than 10,000 non-human primates and tree shrews of eight species: rhesus macaque, pig-tailed monkey, crab-eating monkey, assamese monkey, cotton-eared Marmoset, rhinopithecus bieti, stump-tailed macaque, boddaert; more than 41,000 biological samples such as organs, tissues, cells, and nucleic acids; 24 animal models for diseases such as AIDS, Parkinson's disease, depression, and COVID-19 pandemic Disease; and more than 128,000 pieces of data including basic information, physiology, biochemistry, genetics, phenotyping, omics, imaging, and other data. Meanwhile, NRCNHP has established the rhesus macaque MRI database, rhesus macaque and crab-eating macaque blood biochemistry and blood routine database, and the whole genome database of tree shrew.

The Center has a high-level talent team of 73 people, including 10 comrades with senior titles, 7 comrades with vice-senior titles, 3 recipients of the National Outstanding Young Scientist Fund, 1 New Cornerstone Investigator Program researcher, 2 recipients of the Youth Thousand Talent Programme, 1 recipient of the National Ten Million Talent Project, 1 key technological talent, Chinese Academy of Sciences, and 2 technological innovation talent of Yunnan Province.

Since the establishment of the Center, it has been making efforts to carry out research on the preservation and sustainable use of strategic resources of non-human primates and tree shrews, and collecting, integrating and optimizing the germplasm resources of non-human primates and tree shrews in accordance with the decision-making and deployment of the national and Chinese Academy of Sciences (CAS). The openness-and-sharing of these resources in a scientific and orderly manner has supported the achievement of a number of high-level research results, and achieved significant social and economic benefits, and made an important contribution to the development of the country and the local community. The Center actively undertakes many major scientific research tasks, such as the National Key Research and Development Programme, the Biological Resources Programme, Chinese Academy of Sciences, and the National Natural Science Foundation.

During the 14th Five-Year Plan period, the Center will focus on the preservation, development and utilization of strategic resources of non-human primates and tree shrews, improve the quality of germplasm resources and the level of technical services, and effectively support the strategic needs of the people's health, the biomedical industry, and the research of life sciences, so as to build it into an international leading resource center.

# Speakers' Abstracts and CV

## Topic: Primate Phenotype and Genetic Analyses - From Basic Research to Clinical Applications

**Yonggang Yao（姚永刚）**

Kunming Institute of Zoology, CAS, China

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## Abstract

Non-human primates (NHPs) have many advantages over other experimental animals in advancing biomedical research, especially the modeling of neurodegenerative and infectious diseases, and in understanding human beings, given the high degree of similarity in respect to genetics, anatomy, physiology, behavior,emotion, and cognitive function. NHPs constitute irreplaceable and in many ways superior models compared with common experimental animals such as rodents. Using NHPs to clarify the mechanisms underpinning genotypes and phenotypes will undoubtedly improve our understanding of complex traits and human diseases, as well as the responses of biological processes to environmental factors. On this point, NHPs constitute the perfect living template for us humans to understand ourselves. The establishment of the National Major Scientific and Technological Infrastructure for Primate Phenotype and Genetic Research provides researchers with a comprehensive and systematic platform that supports the translation from basic research to clinical applications. The creation of such facilities not only accelerates scientific research on primates but also offers new directions for addressing some of the challenges currently faced in life sciences and medical research.

**Key words:** Non-human primate, phenotype, genotype, clinical medicine, facility

## Short CV

Dr. Yong-Gang Yao is the director general and principal investigator of the Kunming Institute of Zoology, Chinese Academy of Sciences (CAS). He obtained his bachelor's degree from Anhui Normal University in 1997 and his Ph.D. from the Kunming Institute of Zoology in 2003. He joined the School of Medicine at Johns Hopkins University as a post-doc in February 2003 and served as a visiting fellow at the National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH), in October 2004. He joined the Kunming Institute of Zoology as a principal investigator in December 2007.

Dr. Yao is involved in researching the genetic basis and molecular mechanisms underlying human diseases, with a particular focus on Alzheimer's disease. Furthermore, his team is also investigating the biology of the Chinese tree shrew, which is gaining prominence as a valuable laboratory animal. Currently, Dr. Yao is leading the establishment and construction of the National Research Facility for Phenotypic and Genetic Analysis of Model Animals (Primate Facility).

To date, Dr. Yao has published more than 300 peer-reviewed research articles and commentaries in various SCI-indexed journals, including Am J Hum Genet, PNAS, Autophagy, Alzheimers Dement, Natl Sci Rev, and Cell Discov. As of Auguest 30, 2024, his work has been cited over 11300 times (Web of Science), with an h-index of 54. He was recognized as one of the 2020-2023 ELSEVIER most-cited Chinese researchers. In addition to his research, Dr. Yao holds various editorial positions, including editor-in-chief of Zool Res and Zool Res Divers Conserv, associate editor of J Hum Genet, and editorial board member of J Genet Genomics and Mol Cell Neurobiol. He has received multiple awards, including the State Natural Science Award of China (second class) and Zhuliyuehua Award for Outstanding Teachers of the University of Chinese Academy of Sciences.

## Topic: Global patterns of genome diversity across the primate radiation

**Tomas Marques Bonet**

University Pompeu Fabra, Spain

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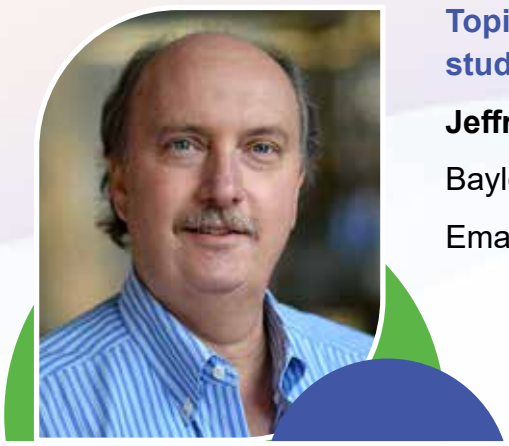
## Abstract

The Primate Sequencing and Conservation Initiative (PSCI) is an international consortium of primatologists, geneticists, and computational biologists dedicated to exploring the genomic diversity of nonhuman primates and informing conservation strategies. By leveraging whole genome sequencing at 30X coverage, PSCI has built one of the largest and most comprehensive datasets in primate genomics. We initially sequenced 809 individuals across 233 species, revealing complex patterns of genetic variation and evolutionary relationships that inform our understanding of primate diversity. These initial analyses provided critical insights into genetic diversity within species, highlighting variations that ranged widely and underscored a nuanced relationship between genetic variation and species' conservation statuses, as defined by the IUCN. Expanding this foundational work, PSCI has now continued the sequencing from wild-caught or wild-born samples, further strengthening the dataset's value for studying wild populations and their unique genetic profiles. The enriched dataset offers an unparalleled opportunity to analyze patterns of genetic diversity, phylogenetic relationships, and evolutionary history across primate species, thus advancing the conservation of these vital species through robust, data-driven insights.

## Short CV

Over the past 15 years, my study of primates has been foundational in advancing our understanding of human biology. Genomic insights from primates have significantly contributed to medical advancements and the field of evolutionary biology. In 2023, my lab achieved a major milestone by leading a Special Issue in Science, publishing the complete genomes of 50% of the world's primate species. This international effort underscored how mutations in primate genomes inform the functional consequences in humans. Additionally, in 2024, a co-led study on human noncoding genome regions was published in Nature, further enhancing our understanding of human biology. As an independent researcher, I led the first global study on great ape genome diversity, revealing the genetic distinctions between humans and apes (Prado-Martinez et al. Nature 2013; deManuel et al. Science 2016). My lab has also achieved breakthroughs, such as recovering the oldest ape genetic material and identifying unique introgression events in bonobos, which has implications for conservation and combating illegal trafficking (Welker et al. Nature 2019). In functional genomics, my team has explored molecular differences between humans and great apes, uncovering regulatory mechanisms and human-specific genomic features (Ferrandez et al. Genome Research 2022). Throughout my career, I have published over 200 peer-reviewed articles, with about a quarter appearing in high-impact journals (Nature, Cell, Science). I also hold a European patent and have secured prestigious funding, including ERC and NIH grants, and private conservation funding from Revive&Restore.

In service to the scientific community, I have held leadership roles, such as Director of the Institute of Evolutionary Biology and panelist for the European Research Council. Additionally, I founded the Cryozoo at the Barcelona Zoo, a cell bank for animal species. My mentorship includes training 23 PhD students and nine postdoctoral researchers, many of whom have advanced to prominent roles globally. Notably, I recently received the Premi Ciutat de Barcelona 2023 and I am member of the Real Academy of Sciences in Spain (2024).



## Topic: Applications for evolutionary and biomedical studies

**Jeffrey Rogers**

Baylor College of Medicine, USA

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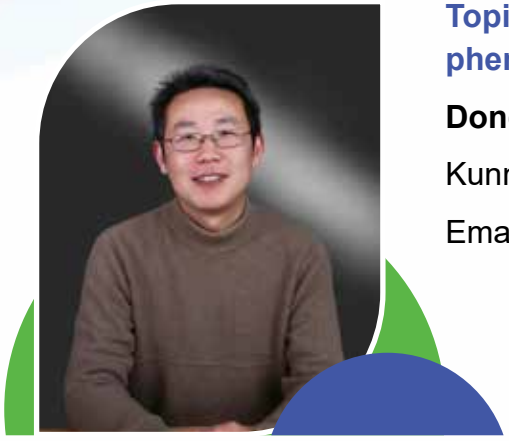
## Abstract

The recent advances in genome sequencing technologies and the associated reduction in costs have created many new opportunities for large-scale genomic analysis of nonhuman primates. In collaboration with researchers at a number of primate research centers, we have generated whole genome sequence data for hundreds of rhesus macaques, cynomolgus macaques, baboons and marmosets along with smaller datasets for chimpanzees, squirrel monkeys and other nonhuman primate species used in biomedical research. Analyses of the large amount of genetic variation within primate species has led to the discovery of functionally significant mutations and naturally occurring primate models of human genetic disease. This line of research is providing novel information about the causes and the potential treatments for human disease. In parallel, we are working with primatologists, evolutionary geneticists and computational biologists to describe and investigate genetic variation within and between natural populations of primates. This work is leading to new insights into the processes of primate evolutionary diversification, the history of primate divergence and inter-species hybridization, and the genetic basis of primate adaptation. This presentation will describe specific examples that illustrate the power of comparative primate genomics for both biomedical studies intended to advance human health and fundamental studies that increase our understanding of the remarkable biological diversity within the Order Primates.

## Short CV

Dr. Jeffrey Rogers is Associate Professor and Principal Investigator in the Human Genome Sequencing Center and Department of Molecular and Human Genetics, Baylor College of Medicine. His research is focused on the genetics and genomics of nonhuman primates. Dr. Rogers received his Bachelor's degree in Anthropology from Northwestern University and PhD in Anthropology from Yale University. Throughout his career, Dr. Rogers has made contributions to both the genetic analysis of nonhuman primate models of disease and the genetic analysis of fundamental questions in primate biology and evolution.

Dr. Rogers has published more than 200 peer-reviewed papers on a variety of topics related to primate genomics. He is currently one of the Co-Leaders of the Primate Sequencing and Conservation Initiative, a large-scale genomics project comparing whole genome sequences across more than 300 primate species. Dr. Rogers was Leader or Co-Leader for a number of projects that produced new reference genome assemblies for primate species including olive baboons, rhesus macaques, mouse lemurs, sooty mangabeys and others. His work on the genetics of rhesus macaques in US research colonies has led directly to the discovery and analysis of spontaneously occurring primate models of human genetic diseases. One long-standing research interest of Dr. Rogers is the population genetics of Papio baboons. He has collected and analyzed blood samples from wild baboons in Tanzania, Zambia and Ethiopia. With an international group of colleagues he is generating new insights into the population genetics of wild baboons and the genetic structure of baboon hybrid zones. Dr. Rogers has published numerous papers in Nature, Nature Genetics, Cell, Science, Science Advances and Molecular Psychiatry, and has an h-index of 57. He is currently a member of the editorial boards for Genome Research and the American Journal of Primatology.



## Topic:Reference genomes provide insights into phenotype evolution of primates

**Dongdong Wu （吴东东）**

Kunming Institute of Zoology, CAS, China

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### Abstract

Non-human Primates are the flagship groups of biodiversity conservation, the key to understanding human evolutionary history, and the bridge connecting basic research and clinical research. We decoded the genetic information of primates, reconstructed the tree of primate life, revealed incomplete lineage sorting and genetic introgression widely accompanying the evolutionary history of primates, and discovered new cases of hybrid speciation in primates; analyzing the evolutionary genetic basis of complex traits such as the brain, social system, and immune system in primates, gained new insights into the evolutionary mechanisms of primates, and provided new ideas for the study of related disease mechanisms; evaluating the factors related to endangering process of primates, providing scientific information and new insights for the development of conservation management.

### Short CV

Dr. Wu focuses on the origin and genetic mechanisms of complex traits in primates, especially humans, based on large-scale genomics data and multidisciplinary research; Dr. Wu has published more than 50 papers as a corresponding author or co-corresponding author in Science, Science Advances, Nature Genetics, Nature Ecology and Evolution, PNAS, Nature Communications and others.

## Topic: Conservation Genomics of the Critically Endangered Cat Ba langur

**Christian Roos**

Gene Bank of Primates and Primate Genetics Laboratory, German Primate Center – Leibniz Institute for Primate Research, Goettingen, Germany

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### Abstract

Many mammal species have declining populations, but the consequences of small population size on the genomic makeup of species remain largely unknown. We investigated the evolutionary history, genetic load and adaptive potential of the Cat Ba langur (*Trachypithecus poliocephalus*), a primate species endemic to Vietnam's famous Ha Long Bay and with less than 100 living individuals one of the most threatened primates in the world. Using high-coverage whole genome data of four wild individuals, we revealed the Cat Ba langur as sister species to its conspecifics of the northern limestone langur clade and found no evidence for extensive secondary gene flow after their initial separation. Compared to other primates and mammals, the Cat Ba langur showed low levels of genetic diversity, long runs of homozygosity, high levels of inbreeding and an excess of deleterious mutations in homozygous state. On the other hand, genetic diversity has been maintained in protein-coding genes and on the gene-rich human chromosome 19 ortholog, suggesting that the Cat Ba langur retained most of its adaptive potential. The Cat Ba langur also exhibits several unique non-synonymous variants that are related to calcium and sodium metabolism, which may have improved adaptation to high calcium intake and saltwater consumption.

**Key words:** *Trachypithecus poliocephalus*, non-human primate, conservation status, adaptation, harsh environment

### Short CV

Dr. Roos is head of the Gene Bank of Primates and leader of the Biodiversity & Evolutionary Genetics group at the German Primate Center, Leibniz Institute for Primate Research, Goettingen, Germany. He obtained his Diploma from the Technical University of Munich in 2000 and his Ph.D. in 2003, also from the Technical University of Munich. He habilitated in 2013 in Zoology at the University of Goettingen and became professor at the University of Goettingen in 2020.

Dr. Roos is mainly interested in research related to primate evolution, speciation, hybridization, diseases, adaptation, and conservation, with a particular focus on Asian primates.

To date (October 2024), Dr. Roos authored almost 300 scientific publications, including peer-reviewed research and review articles as well as books and book chapters. As of October 31,2024, his work has been cited over 15000 times (Google Scholar), with an h-index of 61. He is regional vice chair of the IUCN SSC Primate Specialist Group, East and Southeast Asia, and editorial member of various journals, including Asian Primates J, Front Zool, Genes, Zool Res and Vietn J Primatol.

## Topic: The structure, evolution, and function of structural variation in primate genomes

**Yafei Mao（毛亚飞）**

Bio-X Institutes, Shanghai Jiao Tong University, China

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### Abstract

One of the early and still unresolved grand challenges of the Human Genome Project has been reconstructing the evolutionary history of every base pair in the human reference sequence, particularly regarding structural variants (SVs). Characterizing these SVs—often linked to adaptation and human diseases—has remained difficult due to technological constraints. However, recent advances in long-read sequencing have opened new avenues for understanding the genomic organization, evolutionary origins, and functional consequences of SVs in primate genomes. In this study, we utilized complete human and nonhuman primate (NHP) genomes to identify over a million lineage-specific SVs and introduced the concept of structurally divergent regions (SDRs), which cannot be described merely as an SV. SVs and SDRs are often recurrent or fixed across primate lineages. The 631 genes associated with these regions reveal either parts of the ape genome that are no longer under selection (mean pLI = 0.133) or, more intriguingly, areas where rapid structural diversification has facilitated the emergence of new genes with positive selection signatures. Ironically, these genetic innovations frequently come with a fitness cost, as SDRs are associated with human disease susceptibility, including human-specific RGPD duplications and deletion alleles linked to Joubert syndrome. Unraveling gene innovations in these previously inaccessible and dynamic regions of primate genomes is essential for gaining insights into genetic variation and understanding human diseases within the context of primate evolution.

**Key words:** primate genomes, long-read sequencing, structural variants (SVs), structurally divergent regions (SDRs), human diseases

### Short CV

Dr. Yafei Mao is an Associate Professor and Principal Investigator at Shanghai Jiao Tong University. He received a Ph.D. in Evolutionary Genomics from the Okinawa Institute of Science and Technology and completed postdoctoral training at the University of Washington. He has broad interests in evolutionary medicine, primate evolution, and structural variation. His Lab utilizes cutting-edge experimental and computational technologies to understand the organization and dynamic regulation of the primate genome through development, diseases, and evolution. He is also a member of the editorial boards of BMC Biology and Genome Biology.

## Topic: Development of Nonhuman Primate Models and Therapeutic Strategies for Neurodegenerative Diseases

**Zhonghua Lu（路中华）**

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## Abstract

Parkinson's disease (PD) is a debilitating neurodegenerative disorder. Its symptoms are typically treated with levodopa or dopamine receptor agonists, but their action lacks specificity due to the wide distribution of dopamine receptors in the central nervous system and the periphery. Here, we report the development of a gene therapy strategy to selectively manipulate PD-affected circuitry. Application of this therapeutic approach rescues locomotion, tremor, and motor skill defects in both mouse and primate models of PD, supporting the feasibility of targeted circuit modulation tools for the treatment of PD in humans. In a second study, we have generated PSEN1 mutant cynomolgus macaques (PSEN1-ΔE9) through the genomic deletion of PSEN1 exon 9. Whole-genome sequencing and genotyping analyses of somatic cells confirmed the ΔE9 mutation at both the DNA and transcript levels, with minimal off-target effects. Fibroblasts derived from newborns exhibited signatures of familial Alzheimer's disease (AD) pathogenesis, including disrupted PSEN1 endoproteolysis, resulting in the presence of full-length PSEN1 protein and an increased beta-amyloid (Aβ)42/40 ratio. Furthermore, blood transcriptome profiling of mutant macaques revealed molecular dysregulation associated with AD.

**Keywords:** Parkinson's disease, Alzheimer's disease, disease model, circuit-targeted gene therapy, retrograde AAV

## Short CV

Dr. Zhonghua Lu, Ph. D., is a principal investigator at the Shenzhen Institute of Advanced Technology (SIAT), Chinese Academy of Sciences. Dr. Lu received his Ph.D. in neurobiology from Duke University (2007) working with Dr. Guoping Feng. He then joined Dr. Linda Buck's laboratory at The Fred Hutchinson Cancer Research Center/Howard Hughes Medical Institute for his postdoctoral training. In 2016, Dr. Lu established his own laboratory at SIAT. His group mainly focus on the development of gene therapy strategies and core technologies for brain disorders. His group also develop new animal models for brain disorders, including autism spectrum disorders, Alzheimer's disease, schizophrenia, and epilepsy. He has published more than 30 peer-reviewed papers in journals including Cell, Nature, and Cell Reports. He has also won the 2023 "Top 10 Scientific Advances in Life Sciences of China" award.

## Topic: Flexible Vocal Behavior and Underlying Neural Mechanisms in Marmoset Monkeys (*Callithrix jacchus*)

**Joji Tsunada**

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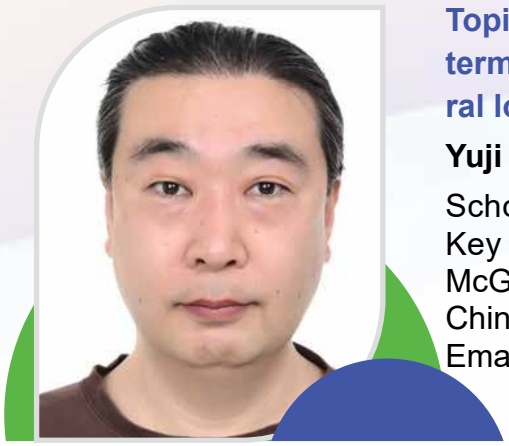
## Abstract

Vocal communication is essential for social cohesion in both humans and non-human primates. A key feature of human vocal communication, however, is our ability to flexibly modify and control our speech depending upon communicative contexts as well as environmental conditions (context-dependent vocal production). Unfortunately, many individuals with neurological or developmental disorders face difficulties in this communicative ability, resulting in significant burdens not only for patients but also for society. Understanding the neural mechanisms underlying context-dependent vocal control is crucial for addressing communication difficulties. Whereas recent progress in human and monkey neurophysiological studies has identified differential roles within the frontal cortex in vocal control, spanning planning, initiation, and articulation of vocalizations, the specific neural computations underlying context-dependent vocal control, particularly at the single neuron level, remain unknown, largely due to the lack of suitable animal models to study human-like vocal production. The marmoset monkey (*Callithrix jacchus*) offers a promising model based on its rich and diverse vocal repertoire used to convey internal states or to inform external contexts. Furthermore, marmosets demonstrate a remarkable ability to control various aspects of their vocalizations, such as call type, timing, duration, sound intensity, and acoustics. This presentation will explore the marmoset monkey's capacity for context-dependent vocal production in the laboratory setting and share our recent findings on neuronal computations in the frontal cortex that govern flexible vocal behavior, providing insights into human speech control and disorders.

**Keywords:** common marmoset, vocalizations, prefrontal cortex, neurophysiology

## Short CV

Dr. Tsunada obtained his D.V.M. (2004) and Ph.D. (2008) degrees from Hokkaido University in Japan. He then received postdoctoral training at the University of Pennsylvania, U.S.A. His postdoctoral work studied neural mechanisms of auditory perceptual decision-making and vocal production using non-human primates. After returning to Japan as a research assistant professor at Iwate University, he finally started his laboratory in 2020 at the Chinese Institute for Brain Research, Beijing (https://cibr.ac.cn/science/team/detail/43). His team studies social vocal communication using marmoset monkeys. His past research has been published in key journals of the research field, including Nature Neuroscience, Nature Communications, eLIFE, and the Journal of Neuroscience. His current work has been supported by the National Natural Science Foundation of China and the Beijing Natural Science Foundation.



## Topic: Constructive process for the flexible use of long-term association memory in the primate medial temporal lobe

**Yuji Naya**

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### Abstract

Declarative memory is our “everyday-language memory,” which allows us to describe the things that we remember. This remarkable cognitive function brings us sensory or declarative information when we recollect. On this account, declarative associations offer more flexibility than other non-declarative memory because we are able to choose future actions based on the retrieved information. Using nonhuman primates as an experimental model, we investigated how the MTL areas serve for the flexible use of the stored information in the item-location association task. The task required animals to retrieve an item’s location relative to a background image which was presented with a tilt as a context-cue. We found that the location information retrieved from an item-cue appeared first in the perirhinal cortex before the HPC. Then, the retrieved location information was fit to the context-cue in the HPC to represent a target location in the first-person perspective in the current situation. These results suggest involvements of the HPC in the flexible use of memory by combining the stored memory and incoming perception to construct goal-directed information for future actions.

**Key words:** declarative memory, allocentric space, first-person perspective, hippocampus

### Short CV

Dr. Yuji Naya is a tenured associate professor of School of Psychological and Cognitive Sciences at Peking University. After receiving a B.S. (Basic Science) and a M.S. (Molecular Cell Biology) from Tokyo University, he started his PhD training in the laboratory of Dr. Yasushi Miyashita at Tokyo University in 1993. In 1995, he obtained an assistant professor position at Tokyo University before the completion of his PhD course. In 2003, he was recognized by the Japanese Neuroscience Society with the Young Investigator Award. In the same year, he was promoted to a tenured faculty position at Tokyo University. In 2005, he moved to New York University as an associate research scientist in the laboratory of Dr. Wendy A. Suzuki. Dr. Naya joined Peking University in 2013.

Dr. Naya elucidated involvements of bidirectional signaling between the perirhinal cortex and visual area TE in object-object association memory at Tokyo University (Naya et al., PNAS, 1996; Science, 2001; JNS, 2003). Then he discovered time cells in the primate hippocampus and its integration with object signal in the perirhinal cortex at New York University (Naya and Suzuki, Science 2011; Naya et al., PNAS 2017). After he moved to Peking University in 2013, he built laboratory of primate memory system including human, macaque and marmoset as experimental models. Particularly, he focused on constructive process for scene perception and memory. Until now his group discovered the view-center background signal in the ventral visual pathway (Chen and Naya, Cerebral Cortex 2020; Li et al., 2024, Prog. Neurobiol) and neuronal operations of flexible use of context-guided memory (Yang and Naya, PLOS Biology 2020 and 2023) using monkey electrophysiology, and object-based cognitive map (Zhang and Naya, Cerebral Cortex 2020; Zhang et al.,

## Topic: Examining Motor Modularity as a Theory of Neuromotor Control in Humans and Animal Models

**Vincent C. K. Cheung（张智钧）**

School of Biomedical Sciences and Gerald Choa Neuroscience Institute, The Chinese University of Hong Kong, Hong Kong SAR, China

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### Abstract

The mammalian motor system is a distributed, ultra-complex network that comprises the sensorimotor cortices, basal ganglia, thalamic and brainstem nuclei, cerebellum, and spinal interneuronal circuits. Neuroscientists have approached the “hard problem” of understanding neural control of movement by formulating theories of motor control. For any such theory to be useful, it must facilitate the tackling of the following questions. What are the neurophysiological and developmental origins of the movement control policy in the theory? What is the neural basis of motor skill learning? And how may our neuroscientific knowledge guide development of neuro-rehabilitation for movement disorders? I argue that the theory of motor modularity – the idea that the motor system constructs movement by combining a limited number of discrete coordination modules called muscle synergies – is a viable theory of motor control. Our recent findings obtained from animal models and humans have relied on motor modularity to shed light on all questions above. Specifically, muscle synergies are encoded by spinal interneuronal populations and accessible by the motor cortex, and the plasticity of muscle synergies contributes to changes of motor patterns during motor development and motor learning. Finally, muscle synergies may serve as predictive markers and targets of intervention for personalized rehabilitation for stroke survivors.

**Keywords:** motor neuroscience; motor control; motor primitives; neuro-rehabilitation; stroke

### Short CV

A motor neuroscientist and biomedical engineer, Vincent C. K. Cheung is Associate Professor at the School of Biomedical Sciences of The Chinese University of Hong Kong (CUHK). He obtained his B. Sc. in Mathematics and Pharmacology & Therapeutics from University of British Columbia, Ph. D. in Neuroscience and Biomedical Engineering from MIT and Harvard Medical School, and then postdoctoral training from MIT’s McGovern Institute for Brain Research. Prof. Cheung’s research focuses on understanding how the central nervous system controls voluntary movement and enables learning of motor skills. He is also interested in exploring how knowledge of movement modules may be translated into a new rehabilitation strategy for stroke survivors. To answer his scientific questions, Prof. Cheung has relied on collection of neurophysiological and motion data from humans, the use of novel neural technologies in animal models, and computational analysis of complex data using machine learning techniques. Prof. Cheung’s papers have appeared in journals including *Nature Communications*, *PNAS, Journal of Neuroscience*, and *Neural Computation*. He was invited to speak for both professional conferences (e.g., Neural Control of Movement Society) and events for the general audience (e.g., TEDxCUHK). Prof. Cheung’s research is supported by the CUHK Faculty of Medicine Faculty Innovation Award, the Hong Kong Research Grants Council, and other sponsors. Recipient of the Angus MacDonald Teaching Award of MIT (2006) and Teachers of the Years Award of CUHK Medicine (2021, 2022), Prof. Cheung directs courses in neuroscience, human physiology and neuroanatomy at CUHK. He also serves as the Dean of Students of the C. W. Chu College of CUHK.

## Topic: Establishment, Mechanistic Exploration, and Gene Therapy of Nonhuman Primate Models for Duchenne Muscular Dystrophy

**Yongchang Chen（陈永昌）**

State Key Laboratory of Primate Biomedical Research, Institute of Primate Translational Medicine, Kunming University of Science and Technology, China

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### Abstract

Duchenne muscular dystrophy (DMD) is an X-linked lethal muscle-wasting disease caused by mutations in the DMD gene, resulting in abnormal function of dystrophy protein. Currently, there are no effective treatments available. The lack of ideal animal models and a thorough understanding of the molecular and cellular mechanisms during disease progression has hindered drug development. Using CRISPR/Cas9, we generate rhesus monkey model of DMD, which revealed that early muscle degeneration is primarily driven by changes in the muscle microenvironment and cellular composition, particularly involving mononuclear cells within muscle, such as immune cells, fibro-/adipogenic progenitors, and muscle stem cells. The dynamic changes in these cell fates and their functional abnormalities significantly impact early disease progression, providing crucial insights into the molecular and cellular mechanisms underlying early DMD pathogenesis. These models also offer a more accurate platform for testing our recently developed DMD treatments, including gene-level repair strategies and utrophin activation, aiding clinical translation.

**Key words:** Duchenne muscular dystrophy, gene therapy, nonhuman primate model

### Short CV

Dr. Yongchang Chen is the dean of the Faculty of Life Science and Technology and a professor at the Institute of Primate Translational Medicine at Kunming University of Science and Technology. He leads a National Natural Science Foundation of China Outstanding Youth Fund project and serves as Chief Scientist for the National Key Research and Development Program of China. Additionally, he is the Executive Director of the Chinese Society of Bioengineering and a Director of the Chinese Society of Neuroscience. Dr. Chen's research focuses on hereditary neurodevelopmental diseases, where he uses gene editing to create nonhuman primate models for Rett syndrome and Duchenne muscular dystrophy. These models accurately replicate patient genotypes and phenotypes, driving important advances in understanding and treating these conditions. He has published over 30 papers in leading journals such as *Cell* and *Cell Stem Cell*, and two of his studies have been selected among the top ten advances in Life Sciences in China, highlighting his influence on the field.

## Topic: Using human brown adipocytes to develop new therapies for type 2 diabetes

**Stephen Dalton**

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## Abstract

Most patients with type 2 diabetes (T2D) take some form of medication, but these focus on controlling hyperglycemia, using drugs that have common or overlapping mechanisms of action. These medications often have undesirable side effects and have only incremental efficacy in reducing hemoglobin A1C levels. This is often compounded by the need for dual and triple-drug therapies in conjunction with injectable insulin, and reduced efficacy over time. Insulin resistance and resulting hyperglycemia that develops in T2D is associated with increased, systemic inflammation that contributes to a broad range of clinical complications. Therefore, the efficacy of drugs that solely regulate glucose homeostasis as a mechanism of action is limited. This establishes a need to develop new approaches for the treatment of T2D.

Human brown adipose tissue (hBAT) regulates metabolic homeostasis and energy expenditure by impacting the clearance of circulating glucose and triglycerides. A second aspect of this involves the secretion of 'adipokines', lipoprotein complexes, and vesicles by BAs that impact inflammation and systemic metabolic regulation. These BA-associated functions restrict the development of T2D at the metabolic level and minimize disease complications. Animal model studies show that transplantation of BAT from healthy individuals reverses T2D and a broad range of associated complications. In humans, increased BAT activity improves insulin-sensitivity in type 2 diabetics and improves the clinical status of individuals with co-morbidities. Patients with T2D typically have limited amounts of brown adipocytes, leading to the proposal that increasing the mass of BAT depots would be a viable therapeutic strategy. A major impediment preventing the development of such a therapy has been the unavailability of a transplantable cell source. This presentation will discuss our approach to solving this challenge, using pluripotent stem cells as a technology platform.

**keywords:** stem cells, diabetes, brown adipocytes abstract- attached

## Short CV

Before joining the Chinese University of Hong Kong as Global Stem Scholar and Professor in the Faculty of Medicine, Stephen Dalton (SD) was Professor and Endowed Chair in Molecular Cell Biology at the University of Georgia where he was founding Director of the "Center for Molecular Medicine", and Georgia Cancer Coalition Distinguished Scholar. Originally from the UK, Dr. Dalton received his Ph.D. from the University of Adelaide in Australia, followed by post-doctoral research at the Imperial Cancer Research Fund in London, with Sir Richard Treisman. Following this, SD was appointed to the Roche Institute of Molecular Biology (Hoffman La Roche, New Jersey, USA), with an academic appointment at Columbia University in New York City. Since then, SD has continued research on the therapeutic use of stem cells. This includes collaborations with Johnson and Johnson (New Jersey, USA), Nestle' (Lausanne, Switzerland) and Viacyte Inc. (San Diego, USA), which was recently acquired by Vertex Pharmaceuticals. Dr. Dalton's current work focusses on developing cell-therapy and gene-editing technologies for the treatment of alpha/beta-thalassemia and diabetes.

## Topic: Epigenetic regulation mediated by RNA poly(A) tails

**Falong Lu（陆发隆）**

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## Abstract

Poly(A) tails are added to the 3'-ends of most eukaryotic mRNAs in a non-templated manner and are typically discarded in conventional transcriptome sequencing due to their homopolymeric nature, leaving their regulatory roles largely unexplored. We have developed new methods, PAIso-seq and PAIso-seq2, for accurate transcriptome-wide sequencing of poly(A) tails, leading to the unexpected discovery of extensive non-adenosine nucleotides—uridine, cytidine, and guanosine—within the body of poly(A) tails. The types, quantities, and positions of these non-A nucleotides, coupled with the lengths of the poly(A) tails, provide a vast coding capacity, indicating that poly(A) tails may encode significant RNA epigenetic regulatory information. Using the mammalian oocyte-to-embryo transition as a model, we revealed extensive dynamic changes of poly(A) tail non-A nucleotides during development. Moreover, dynamic post-transcriptional regulation through poly(A) tails is essential for successful reproduction in both oocyte maturation and early embryonic development. Collectively, we propose that poly(A) tails encode rich epigenetic regulatory information.

**Key Words:** poly(A) tail, epigenetic regulation, oocyte, embryo

## Short CV

**POSITION**

2017/05-current Investigator, Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, Beijing, China.

**TRAINING**

2012/08-2017/05 Postdoctoral research in Program in Cellular and Molecular Medicine, Boston Children's Hospital / HHMI, MA, USA. Laboratory of Dr. Yi Zhang

2012/01-2012/08 Postdoctoral research in Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill / HHMI, NC, USA. Laboratory of Dr. Yi Zhang

**EDUCATION**

2004-2011 Ph.D. in Graduate University of the Chinese Academy of Sciences, Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, Beijing, China. Laboratory of Dr. Xiaofeng Cao

2000-2004 B.S. in College of Life Science, Peking University, Beijing, China

**Research Directions**

1. Mechanisms of Epigenetic Regulation
2. Epigenetic Regulation underlying Mammalian Development
3. Application of Poly(A) Tail Epigenetic Information in mRNA-based Biotechnology

## Topic: MVA metabolites in granulosa cell and oocyte aneuploidy

**Lijun Ding（丁利军）**

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### Abstract

Exploring the mechanisms of aging-related meiotic defects and aneuploidy in oocytes is of great benefit for improving the pregnancy outcomes of aged women. Oocytes are enveloped by granulosa cells (GCs) to form follicles, which constitute the reproductive units in ovaries. GCs form a metabolic couple with oocytes for oocyte growth and maturation. Numerous studies have reported that metabolic coupling between GCs and oocytes could affect the process of oocyte meiosis resumption, spindle assembly, and chromatin arrangement.

To further clarify the metabolic coupling changes between GCs and oocytes during ovarian aging, we systematically characterized the dynamic changes in the overall transcriptomic landscapes of oocytes and GCs from young and aged mice throughout oocyte meiosis. The results revealed that the mevalonate (MVA) pathway, an essential metabolic pathway that uses acetyl-CoA to produce cholesterol and isoprenoids, was specifically highly expressed in GCs with the resumption of oocyte meiosis, and the expression of MVA pathway in GCs decreased with age. Atorvastatin- mediated inhibition of MVA metabolism in GCs decreased the first polar body extrusion rate, and increased oocyte meiotic defects and aneuploidy in young cumulus-oocyte complexes. Further studies showed that the effect of the MVA pathway on oocyte meiosis was mainly regulated by protein isoprenoylation mediated by the MVA metabolites. Importantly, upregulation of the MVA pathway in aged GCs could ameliorate the depletion of ovarian reserve, decrease oocyte meiotic defects, and improve oocyte quality.

**Keywords:** MVA pathway, GCs, oocyte aneuploidy, meiotic defects

### Short CV

Dr. Ding is a principal investigator at Nanjing Drum Tower Hospital, Nanjing University, Vice Chairman of the Reproductive Immunology Society of Jiangsu Province, and deputy Director of the Science and Technology Department of the Drum Tower Hospital. He has been committed to the clinical and basic research of reproductive and regenerative medicine for decades and achieved a series of progress on the mechanism of ovary ageing and aneuploidy in oocytes, finding of endometrial perivascular stem cells, and stem cells therapy of Asherman's syndrome and premature ovarian failure. As the first author and corresponding author, Dr. Ding has published more than 30 articles in Nature Aging, Signal Transduction And Targeted Therapy, Biomaterials, Stem Cells, Human Reprod, and other journals.

# Moderators

**Zhijin Liu（刘志瑾）**

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## Short CV

### Research Fields:

Primatology, Evolutionary and Ecological Genomics, Population Genomics

### Education:

PhD, 2002-2007, Ecology, University of Chinese Academy of Sciences, Beijing, China

Bachelor, 1998-2002, Biology, Qufu Normal University, Shandong, China

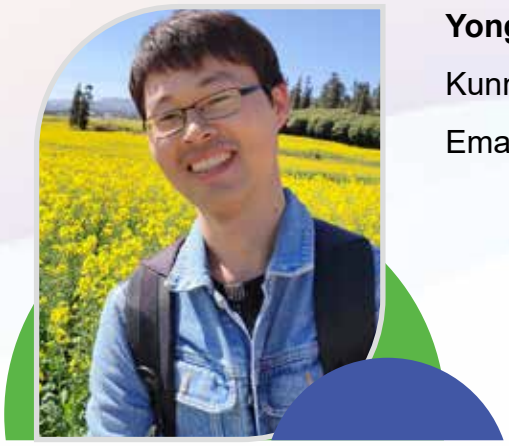
### Professional Positions:

Professor, 2024-present, College of Life Sciences, Capital Normal University, Beijing, China

Associate Professor, 2020-2023, College of Life Sciences, Capital Normal University, Beijing, China

Associate Professor, 2010-2020, Institute of Zoology, Chinese Academic of Sciences, Beijing, China

Research Assistant, 2007-2009, Institute of Zoology, Chinese Academic of Sciences, Beijing, China



**Yong Shao（邵永）**

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## Short CV

Yong Shao, Ph.D., Professor, Member of Youth Promotion Association of Chinese Academy of Sciences. He mainly does research on genome evolution and genetic mechanisms of special trait formation in primates. He has published a series of articles related to primatology in high-impact journals, such as *Science*, *Nature*, *Mol Biol Evol*. As the members of editorial Boards of BMC Genomics and Sci Rep, he has been invited to process and review many manuscripts for Innovation, Int J Biol Macromol, Zool Res and other journals.

**Hui Zhao（赵晖）**

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## Short CV

Prof. ZHAO Hui ( 趙暉 ) is working at the School of Biomedical Sciences, The Chinese University of Hong Kong. He received his Bachelor Degree and Master Degree from Shandong University. He then went to Germany, and got his Ph.D. from the University of Essen, Germany. He had his post-doctoral training at the National Institutes of Health and Child Health and Development (NICHD) before he joined The Chinese University of Hong Kong in 2008. Professor Zhao's research interests cover developmental biology and cancer biology. His laboratory studies the mechanism of neural crest differentiation, germ layer formation and cell migration, and how these multiple events affect the embryonic patterning. In the past few years, he also studied the tumorigenesis of neuroblastoma. Recently his group utilized TALEN and Cas9 nucleases to do gene targeting in Xenopus, zebrafish, and stem cells. He has published over 70 papers in high impact journals including PNAS, Development, EMBO Journal, Nucleic Acids Research and Journal of Biological Chemistry. He serves as reviewers for various magazines including PNAS, Development, and Plos Biology. His research is supported by the funds from the Ministry of Science and Technology, the National Natural Science Foundation of China and Hong Kong Research Grants Council.

**Lei Shi（石磊）**

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## Short CV

Lei Shi earned his BS from Southwest University, Chongqing, China and his PhD from the Kunming Institute of Zoology, CAS. After a first postdoc at the University of Michigan, Ann Arbor, USA and the second postdoc at Salk Institute for Biological Studies, La Jolla, USA, he worked as a Principal Investigator (Neurogenomics lab) at Kunming Institute of Zoology since 2020, His research areas include genetics, evolution, developmental neuroscience, and aging.

### Research

The central direction of Shi lab has been focused on the novel mechanisms that underlie the evolution, development and dysfunction of the human cerebral cortex.

My group — rooted in the Yunnan province, southwest of China — is experimenting with *lissencephalic* species (mice and Chinese tree shrews) and *gyrencephalic* species (primates) using state-of-the art strategies of brain evolution and development. We are tackling three challenging questions:

(1)The evolutionary genetic mechanisms of primate cortical size and folding;

(2)The molecular and cellular basis of primate cortical formation during development;

(3)What are the roles of relatively conserved genes for the evolution of primate phenotype;

Overall, through answering these questions, we believe that we can be closer to the truth about the origin of human intelligence more than ever, which will also help disclose the undiscovered mechanisms of our exceptional vulnerability to cognitive diseases like autism, Alzheimer's disease, Parkinson's et al.

**Ping Zheng（郑萍）**

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## Short CV

Ping Zheng is professor of reproductive and developmental biology in Kunming Institute of Zoology (KIZ), Chinese Academy of Sciences since 2009. She received her Ph.D in KIZ in 2001, and took the post-doc training in Temple University and National Institutes of Health in USA during 2003-2009. Following that, she established her own lab in KIZ in 2009. Her research works are focused on the germ cells and early embryonic development, using mice, tree shrew and rhesus monkeys as animal models. Her works have been published in high-profile journals including Science, Cell Stem Cell, Cell Research, Science Advances, Nature Communications et al.

# Notes

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目前公司年销售额突破了一亿元人民币。现有员工 52 人，包括多名专职维修工程师，专职技术支持人员，并拥有自己的 DEMO 实验室，展示价值超百万元的设备，并可为客户提供 DEMO 演示实验。经过全体员工多年辛勤耕耘，昆明友宁现在已经成为云南省生物学领域特别是分子生物学研究相关领域以及人工辅助生殖、产前筛查、新生儿筛查等领域相关仪器设备、试剂耗材经销的知名企业。成为诸多国际知名品牌的云南省代理商，代理的生物学、临床医学、分析仪器行内的著名品牌产品，我们的客户遍及云南全省，包括各大高校、研究院所、大中型医院、CDC 系统、动物 CDC 系统、公安系统、法医系统、农林牧业系统及生物制药业、食品企业等。

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## 主要优质产品

1. 伯乐生命科学（BIO-RAD）：生命科学产品：**核酸研究产品**（数字 pcr、荧光定量 pcr、高速梯度 pcr、核酸电泳、凝胶成像、电穿孔、基因枪）；**蛋白研究产品**（蛋白电泳系统、转印系统、化学发光、荧光成像系统、蛋白纯化系统、双向电泳系统、脉冲场电泳、悬液芯片系统等）；**细胞研究产品**（细胞计数仪、流速细胞仪、细胞成像仪）；**相关试剂耗材**（PCRmix、电泳、填料、纯化柱、抗体、塑料耗材等）。
2. 徕卡（LEICA）：**高端显微产品**（超高分辨显微成像系统、多光子显微成像系统、数字光片显微成像系统、荧光寿命显微成像系统、共聚焦显微成像系统、共聚焦光电联用显微成像系统、全场景成像系统、高分辨显微成像系统、全内反射显微成像系统、激光显微切割系统等）；**常规显微产品**（倒置显微镜、正置显微镜、体视显微镜、对应荧光显微镜等）；**常规病理相关产品**（组织包埋机、组织脱水机、样品标记、石蜡切片机、冰冻切片机、染色封片机、全自动免疫组化染色系统、高通量数字扫描系统、荧光数字扫描系统）；**电镜制样相关产品**（自动组装处理机、临界点干燥仪、镀膜仪、冷冻断裂修复仪、修块机、超薄切片机、三离子束切割抛光仪、高压冷冻仪等）。
3. 艾本德：(Eppendorf)：离心机（台式、落地式、超速式、连续流、冷冻式等）、移液器、分液器以及超低温冰箱、CO2 培养箱、摇床和细胞显微镜操作系统。耗材类包括移液器吸头、离心管、微量滴定板高性能优质产品。
4. 瑞孚迪（Revvity、原 Perkin Elmer）：产前筛查及新生儿筛查全套的检测设备及试剂耗材。
5. 宾德（BINDER）：CO2 培养箱、标准培养箱、低温培养箱、生长箱、超低温冰箱、干燥箱、烘箱、恒温恒湿箱、高低温交变实验箱、步入式恒温恒湿箱、人工气候箱、植物生长箱等。
6. 艾卡（IKA）：磁力搅拌、分散、加热板、旋转蒸发仪、生物反应器、移液器、干浴器等。
7. 爱博才思（SCIEX）：三重四极杆串联质谱仪、三重四极杆线性离子阱复合型质谱仪、高分辨串联质谱仪、毛细管电泳仪等。
8. 赛默飞（ThermoFisher）：生物工艺解决方案（培养基、血清、细胞株等）、移液器、塑料制品与相关耗材及实验设备。
9. 帝肯（TECAN）：酶标产品（全波长酶标、多功能酶标、高速洗板机、96/384 道洗板机等）、自动化工作站（质谱样本前处理工作站、NGS 建库工作站、文库制备工作站、酶免工作站、全自动核酸提取工作站、单细胞分液仪等）。
10. 因普恩（Implen）、超微量核酸蛋白测定仪（N30、N50、N60、N80、N120、NC40）。
11. 上海净信：样本研磨产品（全自动组织研磨、冷冻研磨、手持研磨、单细胞悬液制备、均质）；超声产品（超声波细胞破碎仪、DNA 核酸打断仪、非接触式 DNA 打断仪、低温超声波萃取、超声波提取仪等产品）。
12. 厦门致微：立式灭菌器、卧式灭菌器、台式灭菌器等产品。
13. 美菱生物医疗：4℃冰箱、-20℃冰箱、-40℃冰箱、-86℃冰箱、层析柜、洁净工作台、液氮罐、监控系统、智慧疫苗、冷库、定制自动化样本库等产品。
14. 上海润度：CO2 培养箱、CO2 细胞培养摇床、微生物培养摇床、高速摇床、恒温恒湿箱、超净工作台、生物安全柜、细胞培养耗材等产品。
15. 台湾海博特：植物表型影像分析设备、LED 植物生长箱、步入式人工气候房、多光谱 LED 植物光源、环境记录分析仪等产品。


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