ADVANCED TECHNOLOGIES IN BIOMEDICINE

BEIJING · CHINA NOVEMBER 4-5,2019

指导单位：北京市科学技术委员会

学术主办单位：Science | AAAS

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Science Asia Conference
Advanced Technologies in Biomedicine

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Conference Information

We have witnessed disruptive innovations in biotechnology in recent years. These technologies have revolutionized how we pursue scientific knowledge and transformed the diagnostic and therapeutic landscape. Therefore, we believe a high-level conference on 'advanced technologies in biomedicine' would be perfectly aligned with our editorial interest and most appropriate for Beijing' s vision on innovative and sustainable activities of research and development.

The meeting will bring together brilliant minds in the fields, including academic and industrial scientists who develop the cutting-edge technologies in biomedicine, physicians who understand the challenges and opportunities to apply these technologies in the clinics, and would help foster collaborations.

Topics include molecular technologies such as genome editing, super-resolution imaging, and single-cell omics; frontiers in stem cell research; disease modeling in animals; and gene- and cell-based therapies.

Related reports of the conference will be posted on the following WeChat accounts

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BAS 2019
北京国际学术交流季
BEIJING INTERNATIONAL ACADEMIC SEASON

Beijing International Academic Season is a series of high-end brand academic exchange activities organized by the Beijing Municipal Commission of Science and Technology with the support of the Beijing Government.

In accordance with the principle of focusing on academic research, gathering the world's top scientists and deep-level multi-angle discussion, Beijing International Academic Season will build a platform for the extensive exchange of international scientific and technological circles in the frontier areas of the foundation, and help Beijing build a globally influential science and technology innovation center.

The Beijing International Academic Season organizes high-level academic series exchange activities around the basic frontiers of quantum science, graphene, brain science, medical health, and nanotechnology.

Science | AAAS

The American Association for the Advancement of Science (AAAS) is the world's largest multidisciplinary scientific society and a leading publisher of cutting-edge research through its Science family of journals. AAAS seeks to "advance science, engineering, and innovation throughout the world for the benefit of all people", it serves individual members in more than 91 countries around the globe.

Science has long been one of the most credible and trusted sources of information for scientists around the world since its founding in 1880 with seed money from Thomas Edison. Published by the not-for-profit AAAS, Science and its growing family of journals continue to set the standard for original research and news content that scientists have come to depend on. Science is a weekly publication, with a worldwide print circulation of nearly 130,000 and over 14 million pageviews to Science online each month. Science readers are educated and engaged. Our audience is composed of some of the brightest thinkers, scholars, researchers, politicians, and students in the world.

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1 Meeting Program

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Organizers

Steve Mao

Senior Editor
Science/ AAAS

Valda Vinson

Editor (Research)
Science/ AAAS

Keynote Speakers

Yinuo Li

China Office, Bill & Melinda Gates Foundation, China

Richard A. Young

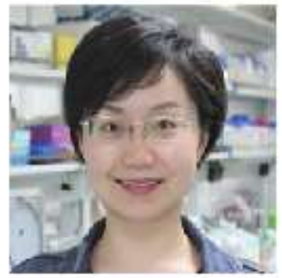
Whitehead Institute, MIT, US

Speakers

(In alphabetical order)

Juan Carlos Belmonte

Salk Institute, US



Ling-Ling Chen

Shanghai Institute of Biochemistry and Cell Biology, CAS, China

Hongkui Deng

Peking University, China

Caixia Gao

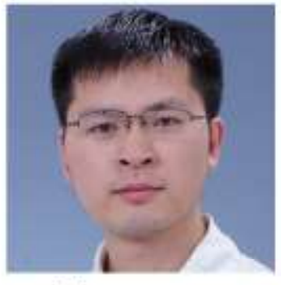
Institute of Genetics and Developmental Biology, CAS, China

Maria Jasin

Memorial Sloan Kettering Cancer Center, US

Weizhi Ji

Kunming University of Science and Technology, China



Wei Li

Institute of Zoology, CAS, China

Huck Hui Ng

Agency for Science, Technology and Research, Singapore

Osamu Nureki

The University of Tokyo, Japan

2 List of Organizers and Speakers

Speakers

(In alphabetical order)

Lei (Stanley) Qi
Stanford University, US

Fuchou Tang
Peking University, China

Hongmei Wang
Institute of Zoology, CAS, China

Xiaoliang Sunney Xie
Peking University, China

Luhan Yang
Qihan Biotech, China

3 Organizer Introduction

Steve Mao

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After graduated from Peking University, Dr. Steve Mao obtained a Ph.D. in Cell Biology from UT Southwestern Medical Center at Dallas. As a postdoctoral fellow at Cold Spring Harbor Laboratory and Harvard University, he focused his research on genome organization and single cell sequencing technologies, respectively. He worked as an Assistant, Associate, and Senior Scientific Editor in Cell for about five years before joining Science as a Senior Editor of molecular biology, biotechnology and synthetic biology. His areas of responsibility include DNA biology, RNA biology, transcription and epigenetics, nuclear and chromatin biology, ribosome biology, synthetic biology, and biotechnology development.

Organizer Introduction

Valda Vinson

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Valda Vinson is Editor (Research) at Science. She came to the United States as a Fulbright scholar and after completing a Ph.D. and post-doctoral studies, spent 2 years as a Senior Lecturer at the University of the Western Cape. She started her career in publishing when she joined the Science staff in 1999. Since then, she has handled research papers in the areas of structural biology, biochemistry, and biophysics as an Associate and Senior Editor. In 2013 Dr. Vinson became Deputy Editor, overseeing research content in the areas of cellular and molecular biology and biomedicine, and in 2018 was named Editor, Research. As Editor she works with Life Science editors to attract and select exciting research papers and reviews, while following standards that support transparency and reproducibility. She also works with others on the editorial management team on editorial policies at Science and is involved in initiatives that bring together stake-holders within the publishing industry to discuss policies.

4 Speaker Introduction and Abstract

November 4, Monday (Day 1)

Opening Remarks

Bill Moran

Science, AAAS

Bill Moran is the current publisher of Science, leading the publishing team to be responsible for the content, copyright, subscription, participation, publicity, cooperative publishing, Science career and other publishing operations of Science series.

During his 11 years of work with American Association for the Advancement of Science, Bill has always been committed to expanding the international publishing activities of the association and enhancing international cooperation. He took the lead in setting up an office in Beijing. Ten years ago, he further started the customized publishing business of Science. He also worked with the editorial team to enhance the visibility of Science and the American Association for the Advancement of Science in the scientific and technological circles of developed and developing countries. It is worth mentioning that in 2014, under the joint arrangement and promotion of Bill and the Chinese Academy of Science, Chinese Premier Li Keqiang met with Marcia McNutt, then Editor in Chief of Science Magazine.

Before joining the American Association for the Advancement of Science, Bill was Vice President of Nature America, the US division of Nature Publishing Group, and the head of new product development and journal co publishing of Informa Group.

Opening Keynote

Yinuo Li

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Yinuo Li serves as Director of China Country Office of Bill & Melinda Gates Foundation overseeing a team that works with China' s public, private, and nonprofit sectors to address key domestic and global health, development, and policy issues.

Dr. Li joined the foundation in 2015 after a career at McKinsey & Company where she was most recently a partner at the firm's Palo Alto office. Her McKinsey career began in Los Angeles, California, United States, in 2005. From 2008 to 2013, while based in McKinsey' s Beijing office, Yinuo served as co-leader of the Healthcare Practice, and leader of the Social Sector and Global Public Health Practice. Her areas of expertise included health system and reform, global health, pharmaceutical and diagnostic products, digital healthcare, and health financing. Her clients covered leading multinational and Chinese pharmaceutical and life science companies, institutional investors, trade associations, government agencies, nonprofit organizations, and academic institutions.

Dr. Li was elected a partner at McKinsey in 2011. In 2014, she moved to McKinsey' s office in Palo Alto, California, United States, where she focused on Healthcare and Social Sector Practice. She is a sought-after speaker on topics ranging from industry perspectives to strategy, organization, talent recruitment/development, and women' s leadership.

Dr. Li has a B.S. in biology from Tsinghua University in Beijing and a Ph.D. in molecular biology from UCLA.

How innovations in R&D can solve the world' s toughest heath challenges

90% of the world' s communicable disease burden is in developing countries. However, only 10% of relevant investment in worldwide R&D is for developing countries. Less than 20 of the 1,500 medicines authorized since 1975 target diseases in developing countries.

The past 50 years have seen two major waves of progress in human health and well-being, first in South America, then in Asia. Continued progress in global health will depend on our accelerating progress in sub-Saharan Africa, where, by 2050, 86% of the world' s extremely poor people will be concentrated.

Economic development may gradually improve health as well as living standards in Africa, but slowly and not inevitably. Not if infectious diseases continue to ravage the continent. Malaria, TB and HIV take enormous tolls in productivity as well as lives, hobbling Africa' s progress. By reducing these scourges, biomedical advances could greatly accelerate improvement in living standards, which would further redound to the benefit of public health—a virtuous cycle.

Building out the infrastructure of universal health care is important, though it may take several decades. Meanwhile, innovation is needed to discover and devise new interventions that can be effective in poor, tropical countries where the public health infrastructure will be incomplete for the foreseeable future

Session I Gene Editing

Maria Jasin

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Maria Jasin obtained a Ph.D. from the MIT and was a postdoctoral fellow at the University of Zürich and at Stanford University. Her lab at Memorial Sloan Kettering Cancer Center performed the first gene editing experiment, expressing a rare-cutting endonuclease to generate a DNA double-strand break (DSB) in the mammalian genome and developing genetic and molecular assays to identify DSB repair events. These experiments established a crucial role for both homologous recombination, also called homology-directed repair (HDR), and nonhomologous end-joining (NHEJ) in DSB repair: A DSB repaired by NHEJ leads to a variety of mutations in the genome, while a DSB repaired by HDR leads to a predetermined modification. With the approaches established in the lab, the breast cancer suppressors BRCA1 and BRCA2 were determined to be crucial for HDR repair, thus implicating HDR as a tumor suppression mechanism. The lab also has a major effort directed at understanding the generation and repair of programmed DSBs during meiotic progression which are essential for genome transmission. Dr. Jasin is a member of NAS, NAM, and the American Academy of Arts and Sciences. She was awarded the Basser Global Prize for BRCA Research in 2018 and the Shaw Prize in Life Science and Medicine in 2019.

Recombination mechanisms revealed through high resolution mapping of double-strand break repair events at mouse meiotic hotspots

Homologous recombination (HR) is a critical DNA repair mechanism in both mitotic and meiotic mammalian cells, in addition to being an important pathway for genome modification. In mitotic cells, it serves to repair lesions arising during DNA replication. In meiotic cells, double-strand break (DSB) formation is part of the meiotic program, such that hundreds of DSBs are introduced at a fraction of the thousands of meiotic DSB hotspots. Repair of these DSBs using the chromosome homolog is critical for successful meiotic divisions, due to the requirement for interhomog pairing and crossing over. A favored model for HR derives from 1983 from a model proposed by Szostak, Orr-Weaver, Rothstein, and Stahl for events in budding yeast. By generating high resolution meiotic recombination maps at a hotspot, including heteroduplex DNA, we reconsider this model for mammalian meiotic recombination events.

Caixia Gao

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Dr. Caixia Gao is Principal Investigator of the Institute of Genetics and Developmental Biology (IGDB), Chinese Academy of Sciences. Prior to joining IGDB in 2009, she served as Research Scientist of DLF' s biotechnology group in Denmark, where she worked in plant genetic transformation and molecular biology. She completed her Ph.D. in Plant Genetics from China Agricultural University, Beijing, and her M.Sc. and B.S. degrees in Agronomy from Gansu Agricultural University, Lanzhou. Her current research mainly focuses on developing novel technologies to achieve efficient and specific genome engineering, and applying them to study the function of genes and modify plant traits for high-quality, disease resistance and stress tolerance in crop species.

Genome editing with programmable nucleases in crop plants

Crop improvement requires the constant creation and use of new allelic variants. Conventional breeding can be limited in providing the genes and alleles required to meet the agricultural challenges. In the past decade, genome editing can accelerate plant breeding by allowing the introduction of precise and predictable modifications directly in an elite background. The most promising utilization of the CRISPR-Cas9 system can be used to generate targeted genome modifications including mutations, insertions, replacements and chromosome rearrangements. The use of CRISPR in agriculture should be considered as simply a new breeding method that can produce identical results to conventional methods in a much more predictable, faster and even cheaper manner.

Lei (Stanley) Qi

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Dr. Stanley Qi (also Lei S. Qi) is an Assistant Professor in the Department of Bioengineering and Department of Chemical and Systems Biology at Stanford University. He is a core faculty in the multidiscipline Stanford ChEM-H Institute. He obtained B.S. in Physics and Math from Tsinghua University, China, Master in Physics from UC Berkeley, and PhD in Bioengineering from UC Berkeley. During his PhD work at Berkeley, he studied synthetic biology with Adam Arkin, and was the first to explore CRISPR engineering for targeted gene editing and gene regulation with Jennifer Doudna. After PhD, he performed independent research work as a Faculty Fellow at UCSF. He joined Stanford faculty in 2014.

Dr. Qi is one of the early developers and pioneers in the CRISPR technologies. He invented the dCas9 molecule and co-invented the CRISPR interference/activation (CRISPRi/a) technology. He is also a co-inventor of the UC patent on the CRISPR gene editing technology. His work led to a series of useful CRISPR technologies, including CRISPR for gene transcription regulation, epigenetic modification, 3D genome structure organization, live-cell genome imaging, and CRISPR-based synthetic biology. He has won awards including NIH Director' s Early Independence Award, Pew Biomedical Scholar, and Alfred. P. Sloan Fellowship. His current research focuses on CRISPR based gene therapy and cell therapy to treat complex diseases.

Genome engineering and research beyond editing

Synthetic manipulation of the genome is key to understanding the genetic makeup of living organisms, which holds great promise for curing diseases. Despite significant advances of CRISPR technology for gene editing, genome engineering broadly defined, is still in an early stage. We investigated technologies that enable new capacities of engineering the genome beyond editing. To achieve the goal, we developed the nuclease-dead dCas9 system, repurposed from the bacterial Cas9 nuclease. We demonstrated its use for transcription control and epigenetic modifications of the genome and expanded the capability of genome engineering for gene position control in the 3D space of the nucleus. We showed dCas9-mediated system allows real-time live imaging of gene editing and chromosome reorganization consequences. We combined CRISPR tools with synthetic biology and developed genetic devices with multiple input-output (I/O) based on dCas9 regulators and receptor sensors or promoters. We showed cells engineered with I/O devices promote better immunotherapy towards recognition and killing of cancer cells. Novel genome engineering allows gaining unprecedented knowledge of genomics and enriches our approaches for gene therapies.

Session I Gene Editing

Osamu Nureki

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Osamu Nureki completed his education and gained a doctor of Science at the University of Tokyo (Graduate School of Science). After receiving the doctorate, he worked one year in RIKEN as a post-doc, and then worked as the assistant professor and associated professor at the University of Tokyo for 8 years. In 2003, he became the full professor at Tokyo Institute of Technology, and continued the structural studies of translational apparatus, and also started the project of membrane protein. In 2008, he moved to The University of Tokyo (Institute of Medical Sciences), and mainly worked on membrane transporters and cancer research to design anti-cancer drugs. In 2010, he finally moved back to The University of Tokyo (Graduate School of Science). His group has three main research projects. 1. Membrane channels and transporters, 2. RNA silencing and CRISPR-Cas system, and 3. Chronic inflammation. Especially, his group has pioneered high-resolution crystallography of membrane proteins using lipidic cubic phase crystallization method and microfocus beam in SPring-8 synchrotron.

Molecular mechanism of CRISPR and structure-based development of genome editing tool towards medical applications

The CRISPR-associated endonuclease Cas9 can be targeted to specific genomic loci by single guide RNAs (sgRNAs). We have solved the crystal structures of Cas9, from 5 sources (984 a.a. to 1,629 a.a.), complexed with sgRNA and its target DNA at atomic resolutions. These high-resolution structures combined with functional analyses revealed the generality and diversity of molecular mechanism of RNA-guided DNA targeting by Cas9, and uncovered the distinct mechanisms of PAM recognition. On the basis of the structures, we succeeded in changing the specificity of PAM recognition, which paves the way for rational design of new, versatile genome-editing technologies.

Session II Stem Cell

Juan Carlos Belmonte

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Juan Carlos Belmonte is a Professor in the Gene Expression Laboratory at the Salk Institute for Biological Studies since 1993. In 2004, he helped to establish the Center for Regenerative Medicine in Barcelona and was its Director between 2004 and 2014.

Dr. Belmonte graduated from the University of Valencia, Spain with a bachelor's degree in Pharmacy and Science. He then earned a master's degree in Pharmacology from the same university before moving on to complete his Ph.D. in Biochemistry and Pharmacology at the University of Bologna, Italy and the University of Valencia, Spain. He followed that with being a postdoctoral fellow in different institutions, including the European Molecular Biology Laboratory and University of California, Los Angeles (UCLA). He is a main catalyzer in one of today's most promising areas of biomedicine: regenerative medicine. His work may help to discover new molecules and specific gene/cell treatments to prevent and cure diseases affecting mankind both in the adult and embryonic stages, as well as inducing endogenous in vivo regenerative responses that may allow for tissue and organ regeneration in humans. It also may contribute to increase our knowledge of aging and aging-associated diseases, thereby leading to healthier aging and increased lifespan.

Dr. Belmonte has over 450 publications. He has also received several awards and honors over the years, a notable one was the naming of a secondary school, Instituto Enseñanza Secundaria (IES) Izpisua Belmonte, in his hometown of Hellín, Albacete, Spain. In 2018, Dr. Belmonte was named by Time Magazine as one of the 50 Most Influential People in Healthcare of 2018.

Organoids and inter-species chimeric approaches for tissue and organ generation

The primary goal of regenerative medicine is the derivation of cells, tissues and organs that are functional and safe for transplantation. In the last decade, towards this end, different approaches have been developed. Two of the most promising ones are the generation of tissue and organ specific organoids in vitro and the generation of inter-species chimeras in vivo. I will present new results from our experiments designing approaches for generating organ constructs in vitro as well as in vivo differentiation via inter-species chimeras, that when coupled to gene editing, may provide a clinical avenue for the generation of cell and tissues for transplantation.

Huck Hui Ng

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Professor Ng Huck Hui is the Deputy Executive Director of the Biomedical Research Council, under the Agency for Science, Technology and Research. Prof Ng is renowned in the fields of gene regulation and genomics and stem cells, having spent more than a decade in research to understand and uncover the intricacies of gene regulation and how they relate to cell biology. His laboratory is currently developing diagnostic and therapeutics modalities for brain and liver diseases. Prof Ng had held several administrative positions. He was the Executive Director of the Genome Institute of Singapore and the Executive Director of the A*STAR Graduate Academy. Prior to joining A*STAR, Professor Ng was a postdoctoral fellow with Harvard Medical School under the prestigious Damon Runyon-Walter Winchell Postdoctoral Fellowship. He was also the President for the Stem Cell Society Singapore, which is a major platform for educating the public on stem cell research. In 2016, Professor Ng was elected to be an Associate Member of the European Molecular Biology Organization, making him the only associate member to be based in Singapore. In recognition of his scientific contributions, Professor Ng has received numerous local and international honours and awards, including the Young Scientist Award in 2004, Singapore Youth Award in 2005, National Science Award in 2007, Junior Chamber International (JCI) The Outstanding Young Persons Singapore Awards in 2009, Singapore Youth Award (Commendation Medal) in 2010, President's Science Award (Team Award) in 2011, President' s Science Award (Team Award) in 2018 and The Public Administration Medal (Silver), National Day Awards 2019. Outside of A*STAR, Professor Ng is very active in the local universities and organizations and holds adjunct positions at the National University of Singapore (NUS) Yong Loo Lin School of Medicine, NUS Faculty of Science, Nanyang Technological University (NTU) School of Biological Sciences, and the Singapore Eye Research Institute (SERI). He also sits on the Board of Science Centre Singapore and NUS High School.

Modeling human diseases using human organoid systems

One of the greatest limitations in understanding human diseases is the lack of in vitro models that can recapitulate features and functions of human organs. The human organs are comprised of multiple cell-types forming a unique architecture. To develop new understanding of human diseases, our laboratory generates in vitro organoid systems using novel culture methodologies.

Parkinson' s disease (PD) is a progressive movement disorder, characterized by a selective loss of dopaminergic (DA) neurons in substantia nigra pars compacta (SNpc). Numerous studies of PD genetics have identified genes associated with the disease. The effects of these mutations are not fully understood due to the lack of advanced experimental in vitro systems to model the progressive manifestation of PD. To this end, our group recently established a new protocol to generate 3D human midbrain-like organoids from human pluripotent stem cells that recapitulate features of the midbrain, including the production of neuromelanin, which is concentrated in mDA neurons of SNpc and mature mDA neurons. The 3D environment therefore appears to generate the niche to support the maturation of mDA neurons. This provides a unique opportunity to experimentally model PD pathology in vitro by looking at how mutations in PD-associated genes are correlated with dysfunction of mitochondria lead to synucleinopathies/tauopathies and neuronal toxicity in DA neurons. The midbrain-like organoids provide a new avenue for the investigation of human midbrain biology and modeling of PD.

Weizhi Ji

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Prof. Weizhi Ji currently is Member of Chinese Academy of Sciences, Professor and Director of Yunnan Key Laboratory of Primate Biomedical Research/ Institute of Primate Translational Medicine, Kunming University of Science and Technology. In 1985-1987, Prof. Ji worked as a scientist in Oregon National Primate Research Center and Smithsonian Institution in US. Since 1996 till 2005, he had served as the director of Kunming Institute of Zoology, Chinese Academy of Sciences. In the meantime, from 1995 to 1997, he held visiting professor position in University of Wisconsin. In 1996, Prof. Ji was named the director of China-US Joint Primate Biology Laboratory, which was co-established by Kunming Institute of Zoology and Wisconsin Primate Research Center. Prof. Ji has been engaged in primate reproductive biology research since 1980s and he takes the lead in primate stem cell research in China. His lab reported the first gene-modified rhesus and cynomolgus monkeys via CRISPR-Cas9-mediated gene targeting in 2014 and then first showed the feasibility of generate chimeric monkeys using ESCs in 2015. His team has established human, monkey, rabbit and mouse embryonic stem cell lines and adult stem cell lines. His study found the mechanism of embryonic stem cells differentiate into neural stem cells in vivo and the integration mechanisms in vitro. Now his research focuses on generation of transgenic monkeys, stem cell self-renewal mechanisms and stem cell replacement therapy research, where he has published papers in top journals of this area, such as Cell, Cell Stem Cells, PNAS, Biology of Reproduction, and Human Reproduction.

Nonhuman primate models for human nervous diseases

As one of the most complex diseases, nervous diseases remain uncurable simply because of the lack of suitable animal models for the mechanism study. The genetic modified monkey may have a superiority as the animal model and will be advantageous to study developmental phenotypes at disease stages as nonhuman primates (NHP) is close to human in genetics. Recent advances in genome editing paved the way for the generation of NHP models for human diseases and a dozen of gene-edited monkey models resulted by a null mutation in a single gene lead to a clear phenotype which are detectable in the limited samples. Using TALEN- and CRISPR-mediated targeted base editing, and transgenic techniques, we have generated several monkey models of nervous diseases, all of which have demonstrated the similar phenotypes to the patients' that can' t be mimicked in other species of disease models. Throughout the observations on monkey models, we can reveal the disease progress that also can' t be achieved directly in patients. The disease models will provide us a tool to understand the disease mechanism and give hopes for developing new treatment for the diseases. However, the development of an efficient methods for off-targeting tests is another key concern in gene edited disease models.

Panel Discussion

Valda Vinson

Editor (Research)
Science/ AAAS

Huck Hui Ng

Agency for Science, Technology and Research, Singapore

Lei (Stanley) Qi

Stanford University, US

Luhan Yang

Qihan Biotech, China

Richard A. Young

Whitehead Institute, MIT, US

4 Speaker Introduction and Abstract

November 5, Tuesday (Day 2)

Session III Disease Modeling

Luhan Yang

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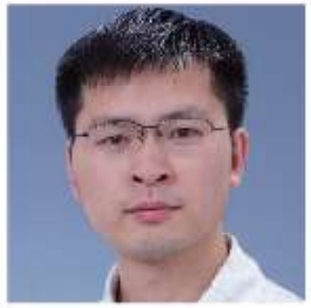
Dr. Luhan Yang is Chief Executive Officer of Qihanbio, co-founder and Chief Scientific Officer of eGenesis. Dr. Yang is currently leading the two companies to make unremitting efforts for research and development of xenotransplantation. The two companies are revolutionizing the field of transplantation with an unparalleled, multiplexed gene editing platform for the development of human-compatible organs, tissues and cells. Dr. Yang leads a world class genome engineering team harnessing the latest gene-editing techniques with the capability to solve the global organ crisis by reinvigorating the field of xenotransplantation and offering the potential to expand the applicability of transplantation into other areas such as cell therapy. She previously developed the highly programmable genome-engineering tool, CRISPR-Cas9, for use in mammalian cells, and pioneered the first isogenic human stem cell lines to model human diseases at the tissue level. She was recently honored with Richard J. Herrnstein Prize by Harvard University (2014), "30 Under 30" in Science and Healthcare by Forbes Magazine (2014), in the Bloomberg 50 (2017), named "Young Global Leader" by the World Economic Forum (2017) and was featured in "30 Under 40" by Business Insider (2017). Dr. Yang holds B.S. degrees in Biology and Psychology from Peking University and a Ph.D. in Human Biology and Translational Medicine from Harvard Medical School.

Transform xenotransplantation into clinical reality using CRISPR-Cas genome editing technologies

Xenotransplantation is a promising strategy to alleviate the shortage of organs for human transplantation. The concerns of pig-to-human immunological compatibility and the risk of cross-species transmission of porcine endogenous retroviruses (PERVs) have impeded the clinical application of this approach. Using CRISPR-Cas9, we inactivated all the PERVs in a porcine primary cell line and generated PERV-inactivated pigs via somatic cell nuclear transfer. Our study highlights the value of PERV inactivation to prevent cross-species viral transmission and demonstrated the successful production of PERV-inactivated animals to address the safety concerns in clinical xenotransplantation. Using our genome editing platform and upon the PERV-inactivation pig background, we are creating pigs with advanced immunological modifications to address immunological and functional compatibility issues.



Wei Li

Institute of Zoology, Chinese Academy of Sciences, Beijing, China

Wei Li is a principle investigator in Institute of Zoology, Chinese Academy of Sciences, and vice director of State Key Laboratory of Stem Cell and Reproductive Biology. Wei received his B.S. from Wuhan University in 2006 and Ph.D. in 2012 from Chinese Academy of Sciences. He has published more than 70 scientific papers in highly reputable journals such as Nature, Cell, Nature Biotechnology, and has received a number of awards and honors, such as International Award of the Japanese Association for Laboratory Animal Science, Outstanding Science and Technology Achievement Prize of the CAS, the Young Top-notch Talent of the "Ten thousand Talent Program". Current interests in his laboratory include: (i) development of mammalian genome engineering technologies and synthetic biology. (ii) dissection of genetic and epigenetic basis of reproduction- and regeneration-related phenotypes. (iii) clinical application of gene therapy.

Balancing embryonic development through "imbalance"

Imbalanced allelic gene expression has been widely observed and plays important roles in mammalian development and disease progress. How it is established, regulated and functioning, remains to be explored. Here by combining the haploid stem cell and genome editing technologies, we identified the imprinting-related factors necessary for crossing same-sex reproduction barriers in mammals, and then established a unisexual reproduction method for producing normally growing bimaternal mice and live bipaternal mice. We also identified the aberrantly expressed non-canonical imprinting genes in cloned mice, which can significantly increase the animal cloning efficiency up to 14% after being rescued.

Hongkui Deng

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Hongkui Deng earned his B.Sc. in Cell Biology from Wuhan University and his Ph.D. in immunology from the University of California, Los Angeles. From 1995 to 1997 he was an Aaron Diamond Postdoctoral Fellow with Dan R. Littman at the NYU School of Medicine' s Skirball Institute, where he identified major co-receptors responsible for HIV entry into cells. From 1998 to 2000, he was the director of molecular biology at Viacell Inc. working on ex vivo expansion of human hematopoietic stem cells. Hongkui Deng was awarded the prestigious Cheung Kong Scholarship in 2000 and became a professor at Peking University in 2001. Since 2013, he has been the director of the Peking University Stem Cell Research Center. Professor Deng' s research focuses on somatic cell reprogramming and lineage specific differentiation of human pluripotent stem cells. His lab also explores chemical biological approaches for manipulating cell fate and function. His group was the first to report a chemical approach to induce pluripotent stem cells. He has been awarded several awards and honors including the Tan Jiazhen Life Science Award and Wu Jieping-Paul Janssen Medical & Pharmaceutical Award. He also serves on a number of editorial boards including Cell, Cell Stem Cell, Stem Cell Report, and Cell Research. Professor Deng was elected to the ISSCR Board of Directors in 2010 and re-appointed for a second term in 2013.

Using chemical approaches to reprogram epigenome and generate desired functional cells

Cell fate manipulation is a fundamental question in biology and shows great potential for application in the development of new disease models, drug screening and cell-based therapies. In recent years, we have been developing chemical approaches completely using small molecules to direct cell-fate conversion; hence permitting the generation of diverse cell types including extended pluripotent stem cells and functional lineages such as hepatocytes and neurons. The chemical approach is a non-integrative method to modulate the epigenome and is versatile as it provides spatiotemporal orchestrations of molecular targets in a synergistic manner, which is a simple way to manipulate cell fates and favorable for clinical translations. Very recently, we have employed this approach to foster functional maturation and maintenance of differentiated cells. We have been able to produce a large amount of competent human hepatocytes in vitro. These cells highly resemble and functionally rival freshly isolated primary human hepatocytes for a series of in vitro applications including drug-metabolizing activities, toxicity prediction and modelling hepatitis B virus infection. Furthermore, to apply these cells in the treatment of acute liver failure, we have developed a novel bioartificial liver system, which exhibited high efficacy in preclinical studies using large animal models.

Session III Disease Modeling

Hongmei Wang

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Hongmei Wang, Ph.D., is a professor of Institute of Zoology, Chinese Academy of Sciences (CAS). Dr. Wang also serves as the Vice President of Innovation Academy for Stem Cell and Regeneration, CAS. Dr. Wang received her B.A. in Biology and a M.A. in Cell Biology from Beijing Normal University, a Ph.D. in Reproductive Physiology from The State Key Laboratory of Reproductive Biology, Institute of Zoology, CAS and completed her postdoctoral training in Dr. Benjamin K Tsang' s laboratory at Ottawa Health Research Institute. Dr. Wang is now a professor at the State Key Laboratory of Reproductive Biology and a recipient of "National Science Foundation for Distinguished Young Scholars" . She is working in the field of reproduction and developmental biology, where she has published over 50 peer-reviewed papers in the areas of embryo implantation, placentation and ovarian follicular development. Wang Lab is investigating the molecular mechanisms involved in placental development, particularly in the area of epithelial-mesenchymal transition, invasion/migration and syncytialization of the trophoblast lineage and placentation-related diseases, such as fetal growth restriction, pre-eclampsia and hydatidiform moles.

Deciphering the secrets of how primates are formed

Fine-tuned development of the embryo is a prerequisite for successful implantation and the born of a healthy baby. Dysregulation of embryo development may lead to adverse pregnancy outcomes, such as abortion and the born of babies with birth defects. By combining in vitro culture models for monkey and human embryos, and a well-established platform for the extraembryonic placenta research (including various trophoblast cell fusion/invasion/migration models, trophoblast stem cells, live-cell imaging, tissue clearing, high-throughput proteomics, single cell RNA-seq, etc), we spend all our efforts in trying to decipher the hidden secrets of how primate embryos are developed and what are the roles of the extraembryonic tissues in supporting the embryos at different stages of pregnancy.

Session IV Single-cell Technologies

Xiaoliang Sunney Xie

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Professor Xiaoliang Sunney Xie is an internationally renowned biophysical chemist, and the Lee Shau-kee professor of Peking University. After a career at Pacific Northwest National Laboratory, he became the first tenured professor at Harvard University among Chinese scholars who went to the US since the Reform in China. As a pioneer of single-molecule biophysical chemistry, coherent Raman scattering microscopy, and single-cell genomics, he made major contributions to the emergence of these fields. In particular, his inventions in single-cell genomics have been used in in vitro fertilization to benefit hundreds of couples in China by avoiding the transmission of monogenic diseases to their newborns. Prof. Xie was elected member of AAAS, US National Academy of Sciences, US National Academy of Medicine, and foreign member of Chinese Academy of Sciences. He also won numerous prestigious awards including NIH Director' s Pioneer Award twice, E.O. Lawrence Award by US DOE, Albany Prize in Medicine and Biomedical Research, and Qiu Shi Science and Technology Prize.

Decoding the human functional genome

When the draft of the human genome was first released in 2003, geneticist Eric Lander commented that "Human genome, bought the book, hard to read" – we simply did not have the grammar or index to understand its function.

Now we can have the human genome of a particular individual, or even a single cell from an individual, for a cost less than $1000. Each cell of an individual has essentially the same genome, yet they carry out completely different functions in each tissue. The advent of single cell genomics has allowed determination of the transcriptome, methylome and open chromosome sites of a single human cell, which allowed us to categorize cell types in unprecedented way. Primarily based on single cell analyses of heterogenous human tissues, the international project of the Human Cell Atlas (HCA) aimed to provide a catalog of human cell types.

However, beyond HCA' s cell typing, the compelling challenge is decoding the human functional genome, i.e. understanding cell functions based on the human genome. Processes such as gene expression and regulation, cell differentiation and development, are pertinent to chromatin structures, and regulatory networks, for which transcription factors (TF) are of critical importance.

In bacteria, a TF acts like a key to turn on and off the expression of a particular gene at a unique genomic locus. In contract, in eukaryotes, a TF usually similar in size, does not have a unique binding locus in the much bigger genome. There are only ~1000 TFs in humans, controlling about 20,000 genes. The specificity of gene regulation is achieved through a combinatorial binding of several TFs, which act like a keyset to turn on and off a particular gene. However, because of technical difficulties, there has been little knowledge about how these keysets are selected and organized.

Recently, my laboratory has made technical progresses in three related areas: (1) Determination of high-resolution 3D genome structures of a single diploid human cell; (2) Probing gene regulatory network by discovering correlated gene modules among which protein-protein interactions exist; (3) Genome wide mapping transcription-factor cooperative and correlated colocalization (TF3C). With these new single cell genomic data, we are now in a position to decode the human functional genome.

Session IV Single-cell Technologies

Fuchou Tang

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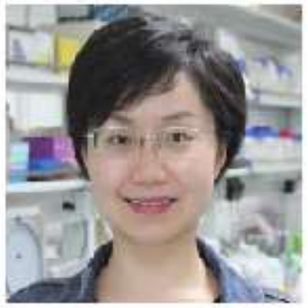
Dr. Fuchou Tang is Professor at BIOPIC, College of Life Sciences, Peking University. He is also Associate Director of Beijing Advanced Innovation Center for Genomics (ICG). He set up his own lab as a principal investigator at Peking University in 2010. Dr. Fuchou Tang' s lab focuses on the epigenetic regulation of gene expression network during human early embryonic development and germline development (Cell, 2013; Nature, 2014; Cell Stem Cell, 2014; Cell, 2015; Science, 2015; Nature, 2016; Cell Stem Cell, 2017a, 2017b, 2017c; Nature Genetics, 2018; Nature, 2018; Nature Cell Biology, 2018a, 2018b; Cell Stem Cell, 2018). Recently, his lab also worked on cellular heterogeneity of colorectal cancer (Science, 2018). His lab pioneered the single cell sequencing field and has systematically developed a serial of single cell functional genomic sequencing technologies [scRRBS (Genome Research, 2013); scMicrofluidic-seq (PNAS, 2014); SUPER-seq (Genome Biology, 2015); scTrio-seq (Cell Research, 2016); scCLEVER-seq (Cell Stem Cell, 2017b); scCOOL-seq (Cell Research, 2017); MR-seq (Science Bulletin, 2017)]. His work has been cited for more than 8,000 times. Some of his work has been selected as Top 10 scientific and technological progresses of China in the years of 2014 and 2015. He is an editorial board member of Genome Biology, and Open Biology. He has been invited to give presentations at AGBT (Advances in Genome Biology & Technology), ISSCR (International Society for Stem Cell Research), ICHG (International Congress of Human Genetics), Gordon Conference, HCA (Human Cell Atlas), etc. He organized the Cold Spring Harbor Asia conference of Frontiers in Single Cell Genomics in 2016 and 2018.

Reconstituting the transcriptome and DNA methylome landscapes of human implantation

Implantation is a milestone event during mammalian embryogenesis. Implantation failure is a considerable cause of early pregnancy loss in humans. Owing to the difficulty of obtaining human embryos early after implantation in vivo, it remains unclear how the gene regulatory network and epigenetic mechanisms control the implantation process. By combining an in vitro culture system for the development human embryos after implantation and single-cell multi-omics sequencing technologies, more than 8,000 individual cells from 65 human peri-implantation embryos were systematically analyzed. Unsupervised dimensionality reduction and clustering algorithms of the transcriptome data show stepwise implantation routes for the epiblast, primitive endoderm and trophectoderm lineages, suggesting robust preparation for the proper establishment of a mother-to-offspring connection during implantation. Female embryos showed initiation of random X chromosome inactivation based on analysis of parental allele-specific expression of X chromosome-linked genes during implantation. Notably, using single-cell triple omics sequencing analysis, the re-methylation of the genome in cells from the primitive endoderm lineage was shown to be much slower than in cells of both epiblast and trophectoderm lineages during the implantation process, which indicates that there are distinct re-establishment features in the DNA methylome of the epiblast and primitive endoderm even though both lineages are derived from the inner cell mass. Collectively, our work provides insights into the complex molecular mechanisms that regulate the implantation of human embryos, and helps to advance future efforts to understanding early embryonic development and reproductive medicine.

Session IV Single-cell Technologies



Ling-Ling Chen

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Ling-Ling Chen carried out doctoral and post-doctoral work in Biomedical Science at UConn Health, USA with Gordon G. Carmichael from 2004 and 2010. She also completed an MBA degree in Management at the UConn Business School in 2009 and was promoted to Assistant Professor in Residence at UConn in 2010. Chen moved to the Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences as an independent PI in 2011 and was promoted to Senior PI in 2017. She was selected as the Howard Hughes Medical Institute (HHMI) International Research Scholar in 2017.

Chen primarily studies long noncoding RNAs (lncRNAs), a giant class of RNA molecules that are emerging as important regulators in gene expression networks. Her group has pioneered methods for studying non-polyadenylated RNAs and discovered widespread expressed snoRNA-related lncRNAs and circular RNAs. In addition to the characterization of their unusual biogenesis pathways, her group discovered that some sno-lncRNAs are conspicuously absent from patients with Prader-Willi Syndrome and circular RNAs are involved in innate immunity regulation and related to the autoimmune disease systemic lupus erythematosus. Her group now continues efforts to elucidate the biogenesis and function of these unconventional regulatory RNAs in different cellular contexts and in relevant human diseases.

Chen serves the community as Editorial Boards of several journals: Genome Biol, Mobile DNA, RNA, RNA Biol, Transcription and Trends Genet; and as an organizer including CSHA on RNA Biology (2018/2020) the Annual Meeting of the RNA Society (2020), CSHL on Regulatory RNA (2020) and Keystone Symposium on Noncoding RNAs (2021). She is the recipient of several awards including being named as a Chinese Biological Investigators Society (CBIS) Young Investigator, an Asian-Pacific Molecular Biology Network (A-IMBN) Research Young Investigator, and the L' OREAL China for Women in Science and Young Investigator Award of CAS.

Linking circular RNA processing and function

Long noncoding RNAs (lncRNAs) are emerging as new regulators in gene expression networks and exhibit a surprising range of shapes and sizes. Many lncRNAs are transcribed by RNA polymerase II and are capped, polyadenylated, and spliced like mRNAs. By developing methods for genome-wide discovery and characterization of non-polyadenylated RNAs, we have identified several RNA species with unexpected formats. These RNAs are derived from long primary transcripts via unusual RNA processing pathways and are stabilized by different mechanisms, including capping by small nucleolar RNA (snoRNA)–protein (snoRNP) complexes at their ends or forming circular structures. We have shown that some such RNAs are involved in gene regulation and implicated in human diseases such as Prader-Willi Syndrome and the autoimmune disease systemic lupus erythematosus.

I will discuss our most recent findings on the biogenesis, function and potential application of one type of circular RNAs that is produced by pre-RNA back-splicing of exons of thousands of genes in eukaryotes.

Session IV Single-cell Technologies

Richard A. Young

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Richard Young is a Professor at the Whitehead Institute and MIT. Dr. Young studies gene regulation in health and disease. He has served as an advisor to the World Health Organization, the National Institutes of Health and numerous scientific societies and journals. Dr. Young' s honors include Membership in the National Academy of Sciences and Scientific American has recognized him as one of the top 50 leaders in science, technology and business. He has founded and advised companies in the biotechnology and pharmaceutical industry, and currently serves on the Board of Syros Pharmaceuticals, CAMP4 Therapeutics, Omega Therapeutics and Dewpoint Therapeutics. Dr. Young is also an aviator and holds a commercial pilot license. He received his PhD from Yale University.

New insights into biomolecular condensates in biology and medicine

DNA, RNA and protein are essential polymers of living cells. The physicochemical properties of polymers include condensate formation by phase separation, where entropy is overcome by the force produced by large numbers of weak interactions. Biomolecular condensates have emergent properties that help explain many conundrums long posed by biologists in various fields. I will describe our emerging understanding of phase-separated condensates in biology, discuss how they are impacting the study of disease, and explain how they may change the course of drug discovery and development.

Zhongguancun Life Science Park Development Forum in 2019

中关村生命科学园发展论坛 2019
Zhongguancun Life Science Park Development Forum in 2019

Industrial Roadshow

There will be invited industrial speakers to present their companies' R&D strength and market leading edge.
The industrial roadshow is starting from 15:00.
There are 15 minutes for each project.

Time: 15:00 on Tuesday, November 5 (day 2)

TIE国际创新走廊
Tsing- Innovation Ecosystem

Tsing-Innovation Ecosystem (TIE) was launched by Tsinghua Holdings in September,2017 as an international technological innovation and technology services platform. We sincerely welcome partners from all over the world to join us in promoting greater collaboration, cooperation, and development in the progression from technological to industrial innovation.

We are committed to:

Connecting domestic enterprises with overseas innovative technology projects for technological innovation integration and industrial upgrading

Matchmaking overseas investment opportunities and looking for potential Unicorn companies from all over the world.

Enabling governments and organizations to have extensive contacts with technological, government and business leaders worldwide.

Providing supports and services for both domestic and international companies by linking capital, market and industries.

中关村生命科学园
Zhongguancun Life Science Park

Founded in 2000, ZGC Life Science Park located between G6 and G7 expressway,on the north of Beiqing Road, Changping District,is an important part of ZGC National Independent Innovation Demonstration Zone,and is a hi-tech science park engaged in life sciences,biotechnology and biomedical research.

The park have over 500 enterprises in life science field, including Novo Nordisk,Yangtze River Pharmaceutical Group,Wantai BioPharm,Mindray, CapitalBio,BeiGene, Shenogen, Berry Genomics,etc.,and has attracted topnotch scientists such as Wang Xiaodong, Shi Yigong, Shao Feng,etc.Innovation elements such as projects,talents and enterprises are now highly concentrated. The average R&D ratio of the park is 7.19% which is higher than the national average. In fields like biopharmaceuticals, gene testing and diagnostic reagents, a batch of breakthrough technologies and achievements have been produced, which make ZGC Life Science Park the R&D center with global influence, and welcomes scientists, entrepreneurs and investors across the world.