北京未来基因诊断高精尖创新中心
Beijing Advanced Innovation Center for Genomics

北京大学生物医学前沿创新中心
Biomedical Pioneering Innovation Center

2019单细胞组学国际研讨会
Single Cell Omics Beijing 2019 Symposium

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北京未来基因诊断
高精尖创新中心(ICG)

北京大学生物医学
前沿创新中心(BIOPIC)

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Host Organization

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Beijing Advanced Innovation Center for Genomics

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Director, Beijing Advanced Innovation Center for Genomics
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Principle Investigator of Biomedical Pioneering Innovation Center (BIOPIC)
Professor of School of Life Sciences, Peking University
Investigator of Center of Life Sciences (CLS)
Winner of National Science Fund for Distinguished Young Scholars

Co-Chair

Yanyi Huang

Associate Director of Beijing Advanced Innovation Center for Genomics (ICG)
Principle Investigator of Biomedical Pioneering Innovation Center (BIOPIC)
Professor of College of Engineering, Peking University
Investigator of Center of Life Sciences (CLS)
Winner of National Science Fund for Distinguished Young Scholars

Program

Saturday, Oct. 19, 2019

Venue: Qiulin Lecture Hall, PKU, No. 5 Yiheyuan Road, Haidian District, Beijing

07:30–09:00	Registration	Venue: Qiulin Lecture Hall
09:00–09:05	Welcome Remarks	Xiaoliang Sunney Xie
Session 1	Epigenome and Genome 3D Architec-	Chair: Yanyi Huang
09:05–09:35	Decoding the Gene Regulation Network in Human Germline Cells by Single-cell Functional Genomics Approaches	Fuchou Tang
09:35–10:05	A Single Cell Framework for Multi-omic Analysis of Disease Identifies Malignant Regulatory Signatures	William Greenleaf
10:05–10:35	Decoding Functional Human Genome with Transcription Factor Colocalization (TFC) and Corelated Gene Modules (CGM)	Xiaoliang Sunney Xie
Session 2	Transcriptomics	Chair: Fuchou Tang
11:00–11:30	Spatial Genomics: In Situ Transcriptome Profiling by RNA seqFISH+	Long Cai
11:30–12:00	Health Care from the Start of Life: Applications of Single Cell Omics Sequencing	Jie Qiao
13:30–14:00	Understanding pancreatic organogenesis at single-cell level	Cheng-Ran Xu
14:00–14:30	A Human Cell Landscape for Cell Type Identification at the Single-Cell Level	Guoji Guo
Session 3	Genomic Variations	Chair: Xiaoliang Sunney Xie
14:30–15:00	Single Cell Approaches in Studying Genome Instability in Aging and Cancer	Jan Vijg
15:00–15:30	Whole-Genome Detection of Dynamic DNA Damage in Single Human Cells	Chenghang Zong
16:00–16:30	Characterization of Primary Sequences and 3D Structures of Single-cell Genomes	Dong Xing
Session 4	Applications to Immunology	Chair: Zemin Zhang
16:30–17:00	Decoding the Developing Human Immune System	Muzlifah Haniffa
17:00–17:30	Single Cell Analysis of Paediatric-onset Colitis and Inflammatory Bowel Disease Reveals Common Pathogenesis and A Novel Treatment	Fan Bai

Program

Sunday, Oct. 20, 2019

Venue: Qiulin Lecture Hall, PKU, No. 5 Yiheyuan Road, Haidian District, Beijing

Session 5	Technology Developments	Chair: Fuchou Tang
09:00–09:30	Highly Accurate DNA Sequencing: Error Correction Code and Beyond	Yanyi Huang
09:30–10:00	Identifying and Rationally Modulating Cellular Drivers of Enhanced and Diminished Immunity	Alex K. Shalek
10:00–10:30	Technology Development for Single-cell RNA-seq	Jianbin Wang
Session 6	Applications to Cancer	Chair: Yanyi Huang
11:00–11:30	Application of Novel Single Cell Bioinformatics Methods in Cancer Immunology	Zemin Zhang
11:30–12:00	Single-cell Transcriptomics Profiling of Esophageal Squamous Cell Carcinoma	Chen Wu
Session 7	Applications to Neuroscience	Chair: Zemin Zhang
13:30–14:00	Spatial and Temporal Regulation of Human Cortex Development Revealed by Single-cell RNA-Seq Analysis	Xiaoqun Wang
14:00–14:30	Integration of Single Cell and Spatially Resolved Methods in the Study of Neurodegenerative Disease Mechanisms	Silas Maniatis
Session 8	Bioinformatics	Chair: Zemin Zhang
14:30–15:00	On the Information Content and Representation of Human Cells	Xuegong Zhang
15:00–15:30	Cell BLAST and Beyond	Ge Gao
Session 9	Proteomics	Chair: Sunney Xie
16:00–16:30	High-throughput Single-cell Proteomics Quantifies the Emergence of Macrophage Heterogeneity	Nikolai Slavov
16:30–17:00	Single Cell Proteomic Analysis Using PASEF	Catherine CL Wong
17:00–17:30	Probing Principles in Gene Regulation and Cell Fate Specification Using Single-cell ChIP-seq	Aibin He

Speakers

Xiaoliang Sunney Xie

TITLE: Transcription Factor Colocalization: The Key to Decode Functional Human Genome

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.

ABSTRACT:

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.” 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.

However, beyond cell typing, the compelling challenge is decoding the human functional genome, i.e. understanding cell functions. 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 of transcription factor colocalization (TFC). With these new single cell genomic data, we are now in a position to decode the human functional genome.

Fuchou Tang

TITLE: Decoding the Gene Regulation Network in Human Germline Cells by Single-cell Functional Genomics Approaches

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; Nature, 2019). 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); 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 year of 2014 and Top 10 scientific and technological progresses of China in the year of 2015. He is editorial board members of Genome Biology, & 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.

ABSTRACT:

Human germline cells are crucial for maintenance of the species. However, the developmental trajectories and heterogeneity of human germline cells remain largely unknown. We performed single-cell RNA-seq and DNA methylome sequencing analyses of human germline cells in female and male human embryos spanning several critical developmental stages. We found that female fetal germ cells (FGCs) undergo four distinct sequential phases characterized by mitosis, retinoic acid signaling, meiotic prophase, and oogenesis. Male FGCs develop through stages of migration, mitosis, and cell-cycle arrest. Individual embryos of both sexes simultaneously contain several subpopulations, highlighting the asynchronous and heterogeneous nature of FGC development. Moreover, we observed reciprocal signaling interactions between FGCs and their gonadal niche cells, including activation of the bone morphogenic protein (BMP) and Notch signaling pathways. Our work provides key insights into the crucial features of human germline cells during their highly ordered mitotic, meiotic, and gametogenetic processes in vivo.

William Greenleaf

TITLE: A Single Cell Framework for Multi-omic Analysis of Disease Identifies Malignant Regulatory Signatures

William Greenleaf is an Associate Professor in the Genetics Department at Stanford University School of Medicine, with a courtesy appointment in the Applied Physics Department. He is a member of Bio-X, the Biophysics Program, the Biomedical Informatics Program, and the Cancer Center. He received an A.B. in physics from Harvard University (summa cum laude) in 2002, and received a Gates Fellowship to study computer science for one year in Trinity College, Cambridge, UK (with distinction). After this experience abroad, he returned to Stanford to carry out his Ph.D. in Applied Physics in the laboratory of Steven Block, where he investigated, at the single molecule level, the chemo-mechanics of RNA polymerase and the folding of RNA transcripts. He conducted postdoctoral work in the laboratory of X. Sunney Xie in the Chemistry and Chemical Biology Department at Harvard University, where he was awarded a Damon Runyon Cancer Research Foundation Fellowship, and developed new fluorescence-based high-throughput sequencing methodologies. He moved to Stanford as an Assistant Professor in November 2011. Since beginning his lab, he has been named a Rita Allen Foundation Young Scholar, an Ellison Foundation Young Scholar in Aging (declined), a Baxter Foundation Scholar, and a Chan-Zuckerberg Investigator. His highly interdisciplinary research links molecular biology, computer science, bioengineering, and genomics a to understand how the physical state of the human genome controls gene regulation and biological state. Efforts in his lab are split between building new tools to leverage the power of high-throughput sequencing and cutting-edge microscopies, and bringing these new technologies to bear against basic biological questions of genomic and epigenomic variation. His long-term goal is to unlock an understanding of the physical “regulome” — i.e. the factors that control how the genetic information is read into biological instructions — profoundly impacting our understanding of how cells maintain, or fail to maintain, their state in health and disease.

ABSTRACT:

Much of the gene regulatory potential of a cell is encoded within the nucleoproteinstructure of chromatin. We have developed diverse methods to probe this chromatin architecture, including at the fundamental unit of biological organization – the single cell. In order to identify the molecular determinants of human diseases, such as cancer, that arise from a diverse range of tissue, it is necessary to accurately distinguish normal and pathogenic cellular programs.

We have developed a novel approach for single-cell multi-omic deconvolution of healthy and pathological molecular signatures within phenotypically heterogeneous malignant cells.By first creating immunophenotypic, transcriptomic and epigenetic single-cell maps of hematopoietic development from healthy peripheral blood and bone marrow mononuclear cells, we identify cancer-specific transcriptional and chromatin signatures from single cells in a cohort of mixed phenotype acute leukemia (MPAL) clinical samples. Our results reveal widespread heterogeneity in the pathogenetic gene regulatory and expression programs across patients, yet relatively consistent changes within patients even across malignant cells occupying diverse portions of the hematopoietic lineage. An integrative analysis of transcriptomic and epigenetic maps identifies 91,601 putative gene-regulatory interactions and classifies a number of transcription factors that regulate leukemia specific genes, providing a template for integrative, multi-omic analysis for the interpretation of pathogenic molecular signatures in the context of developmental origin.

Long Cai

TITLE: Spatial Genomics: in Situ Tanscriptome Profiling by RNA SeqFISH+

Long Cai is a Professor of Biology and Biological Engineering at Caltech. His lab pioneered the field of spatial genomics by developing a method that allows the simultaneous imaging of over 10,000 genes in single cells within their native spatial context. This technology has opened a new way to directly visualize the genome in situ with microscopy, with many applications in neuroscience, stem cell biology, developmental biology and precision medicine. For this work, Dr. Cai has received the NIH New Innovator Award, Transformative Award, Paul G. Allen Frontiers Foundation Distinguished Investigator Award. Dr. Cai received his AB/AM in Physics and Chemistry at Harvard College, under the supervision of Dudley Herschbach, and his PhD in Chemistry at Harvard with Sunney Xie. He trained as a Beckman Institute Postdoctoral Fellow with Michael Elowitz at Caltech.

ABSTRACT:

Imaging the transcriptome in situ with high accuracy has been a major challenge in single cell biology,particularly hindered by the limits of optical resolution and the density of transcripts in single cells. We developed seqFISH+, that can image the mRNAs for 10,000 genes in single cells with high accuracy and sub-diffraction-limit resolution, in the mouse brain cortex, subventricular zone, and the olfactory bulb, using a standard confocalmicroscope. The transcriptome level profiling of seqFISH+ allows unbiased identification of cell classes and their spatial organization in tissues. In addition, seqFISH+ reveals subcellular mRNA localization patterns in cells and ligand-receptor pairs across neighboring cells. This technology demonstrates the ability to generate spatial cell atlases and to perform discovery-driven studies of biological processes in situ.

Jie Qiao

TITLE: Health Care from the Start of Life: Applications of Single Cell Omics Sequencing

Jie Qiao, is Academician of Chinese academy of engineering, President and Chief Physician of Peking University Third Hospital, Director of the National Clinical Research Center on Obstetrics and Gynecology (OBYGN) Disease, Expert Advisory Committee Member of the Healthy China Initiative, President of China Women Doctors Association, Chair for the Reproductive Medical Society of Chinese Medical Doctor Association, Chief editor of《Human Reproduction Update (Chinese version)》and Special Consultant《NEJM Medical frontier》.

Her reproductive research focus on the molecular mechanism of human gametogenesis and embryo development, infertility causes and clinical treatments, the protection and preservation of female fertility as well as developing new pre-implantation diagnosis methods. Qiao has led the team to achieve a number of technical and theoretical breakthroughs in the systematic study of human embryonic development and team made many landmark contributions to the development of reproductive medicine. From 2016, about 600,000 outpatients visited Peking University Third Hospital ART Center every year. Up to now, she has published more than 200 SCI papers as the first or corresponding author, including Science, Cell, JAMA, Nature, Lancet, Nature Genetics etc, providing new insights into the mechanism of epigenetic regulation during embryonic development and bringing hope to a great number of infertile patients in China.

ABSTRACT:

China has a large population and increasing prevalence of infertility and birth defects. Growing number of infertility families are under great mental and economic pressure. Besides, it brings great difficulties to the quality and structure optimization of the national population. China has closely followed the development trend of the world and quickly achieved a series of the leading level achievements in the field of Assisted Reproductive Technology (ART). However, ART also facing the development bottleneck, such as low success rate, high incidence of failed fertilization and other issues. The lack of knowledge on embryo development mechanism limits the improve of ART in the clinic.

Embryo development depends on a highly unusual cellular context in which to execute such a critical succession of cell divisions. Errors during this process could cause failed fertilization and development arrest. In recent years, the rapid development of single-cell sequencing technology has provided great help to basic research and clinical issues. With the help of single-cell sequencing technology, we are now able to dissect different molecular layers in single cells, such as genome, transcriptome, DNA methylation, chromatin accessibility, etc., which are very crucial for revealing the secret of human gamete and embryo development.

In the basis of mechanism research, we have promoted the clinical application of array-based and NGS-based technology in preimplantation genetic testing (PGT), such as SNP array and MARSALA. MARSALA-PGT enables simultaneous diagnosis of single gene mutation, chromosomal abnormalities and linkage analysis. Until now, over 500 families with single genetic disorders have entered the MARSALA-PGT process and 100 healthy babies have been born.

Cheng-Ran Xu

TITLE: Understanding pancreatic organogenesis at single-cell level

The generation of terminally differentiated cell lineages during organogenesis requires multiple, coordinated cell fate choice steps. However, this process has not been clearly delineated, especially in complex solid organs, such as the pancreas. We performed single-cell RNA sequencing in pancreatic cells sorted from multiple genetic reporter mouse strains at various embryonic stages. Using this approach, we defined the distinct road maps for dorsal and ventral pancreatic progenitor specification. Our study also deciphered the developmental trajectories and regulatory strategies of the exocrine and endocrine pancreatic lineages as well as intermediate progenitor populations along the developmental pathways. Furthermore, we demonstrated that repressing the activity of the ERK pathway is essential for the induction of islet lineage differentiation. Our studies provide key insights into the regulatory mechanisms of cell fate choice and stepwise cell fate commitment and can be used as a resource to guide the induction of functional islet lineage cells from stem cells in vitro.

Dr. Cheng-Ran Xu received his bachelor degree from Fudan University and Ph.D. degree from Peking University. He did postdoctoral research at University of Pennsylvania with Dr. Ken Zaret. Since 2013, he has been a Principal Investigator of the School of Life Sciences of Peking University and Peking-Tsinghua Center for Life Sciences. His studies focused on the cell differentiation pathways and regulatory mechanisms of liver and pancreas development.

Guoji Guo

TITLE: A Human Cell Landscape for Cell Type Identification at the Single-Cell Level

Dr. Guoji Guo is the deputy director of Center for Stem Cell and Regenerative Medicine at Zhejiang University School of Medicine. He is also the deputy chair of Stem Cell Society at Zhejiang University. He obtained his Ph.D at National University of Singapore in 2005, and then moved to Harvard Medical School for postdoc training. In 2014, he was recruited and directly tenured at Zhejiang University. In 2017, he was awarded the National Science Fund for Excellent Young Scholars. Dr. Guoji Guo is interested in developing new single cell analysis technologies and applying these technologies to study stem cell self-renewal.

ABSTRACT:

The transcriptome of a cell represents its unique cell type identity. However, a systematic single-cell atlas has not been achieved for human beings. We used single-cell RNA sequencing to determine the cell type composition of all major human organs and construct a basic scheme for the human cell landscape (HCL). We reveal a single-cell hierarchy for many tissues that have not been well characterized previously. We present a “single-cell HCL analysis’’ pipeline that helps to define human cell types and exemplify its utility in stem cell biology. Finally, we perform single-cell comparative analysis of the human and mouse cell landscapes to reveal the conserved genetic networks in the mammalian system.

Jan Vijg

TITLE: Single Cell Approaches in Studying Genome Instability in Aging and Cancer

Jan Vijg, Ph.D., is Professor and Chairman of the Department of Genetics at the Albert Einstein College of Medicine in New York since July, 2008. He received his Ph.D. at the University of Leiden, The Netherlands, in 1987. From 1990 to 1993 he was founder and Scientific Director of Ingeny B.V., a Dutch Biotechnology company. In 1993 he moved to Boston, to take up a position as Associate Professor of Medicine at Harvard Medical School. In 1998 he accepted an offer from the University of Texas Health Science Center in San Antonio, Texas, to become a Professor in the Department of Physiology. From 2006 to 2008 he was a Professor at the Buck Institute for Age Research in Novato, California. With his research team he was the first to develop transgenic mouse models for studying mutagenesis in vivo (in 1989) and has used these models ever since in studying the relationship between damage to the genome and aging. He has published over 200 scientific articles and two books, and is inventor or co-inventor on 8 patents.

ABSTRACT:

As in most other animal species human life span is limited by the process of aging, the nature of which is still incompletely understood. While aging is multifactorial and differs between species, it is conceivable that ultimately life span in most species is limited by intrinsic cellular decay due to the natural imperfection of molecular, cellular and physiological transactions. The rate of these processes may differ from species to species, as well as among individuals of the same species, depending on the proficiency of molecular maintenance programs. An example is genome maintenance. Heritable deficiencies in genome maintenance lead to segmental progeroid syndromes, such as Werner's Syndrome. Such genetic defects could increase steady-state levels of DNA damage, which in turn would interfere with transcription, cause adverse cellular responses, such as apoptosis and cellular senescence, and lead to more DNA mutations. All three end points have been shown to increase over the life-time in various organs and tissues of multiple species. Using recently developed single-cell approaches my laboratory has been working on the quantitative analysis of somatic mutations as a possible cause of aging. I will present recent data on single-cell whole genome sequencing of primary human cells as a function of age and in relation to cancer susceptibility and DNA repair defects.

Chenghang Zong

TITLE: Whole-Genome Detection of Dynamic DNA Damage in Single Human Cells

I pursued my Ph.D. in theoretical chemistry and biophysics at UC-San Diego under the guidance of Dr. Peter Wolynes. My research focused on molecular dynamics simulation of proteins and the non-equilibrium dynamics of various biological processes, including dynamics equilibrium of filament growth/decay, phosphorylation, and gene regulation. In Dr. Ido Golding's lab at University of Illinois, I began the experimental research in characterizing the stability in gene regulation by smFISH method. As a postdoc in Dr. Sunney Xie's lab at Harvard University, I worked on whole genome sequencing of single human cells and led the development of a new single cell amplification method that allows single cell whole genome sequencing with significantly improved uniformity.

The research of my laboratory at Baylor College of Medicine lies in the interface between novel single cell technologies and quantitative biology. We pursue the development of new quantitative and high-throughput methods for characterizing genomic and transcriptional variations at single cell resolution. My team have developed a highly sensitive single-cell RNA-seq method (MATQ-seq). In the single cell genome analysis, my team have developed a new single-cell whole genome amplification method: Linearly Produced Semiamplicon based Split Amplification Reaction (LPSSAR). In LPSSAR, with linear preamplification chemistry and split amplification reactions, we are able to effectively filter out the vast majority of amplification errors, which lead to the whole genome detection of DNA damage associated variants (DAVs). We have successfully applied this new method to characterize the genome maintenance in the ageing process as well as the disease systems including cancer and neurodegeneration.

ABSTRACT:

Spontaneous DNA damage frequently occurs in all cells. With DNA damage being quickly detected and repaired, the cell reaches an equilibrium state in the maintenance of its genome. Detecting transient DNA damage at whole-genome scale in single cells is essential to understand the stability of the genome and the state of cell stress at single cell resolution. Here we report a single-cell whole genome amplification method – Linearly Produced Semiamplicon based Split Amplification Reaction (LPSSAR) that enables the whole-genome detection of DNA damage associated variants (DAVs). By profiling the levels of DNA damage in single human cortical neurons, we observed a clear ageing effect on DNA damage: the increase of DNA damage along with age. Furthermore, by distinguishing the de novo mutations from the widely existing DAVs in single cells, we are able to achieve a reliable estimation of de novo mutations.

In contrast to the increased level of DNA damage, the level of the de novo mutations is nearly unchanged along the age, indicating that from the perspective of somatic mutations, the genome of final differentiated neurons is stable. These results promote us to redefine the DNA damage based ageing theory as dynamic DNA damage ageing theory in which we hypothesize that the driving force of ageing is the increased loads of dynamic DNA damage along with age.

Dong Xing

TITLE: Characterization of Primary Sequences and 3D Structures of Single-cell Genomes

Dr. Dong Xing received his Ph.D. at Peking University in 2012 and completed his postdoc training with Prof. Xiaoliang Sunney Xie at Harvard University. Dr. Xing's research is in the field of single-cell genomics. Together with colleagues, he developed single-cell genomic analysis methods including LIANTI, META-CS and Dip-C. Dr. Xing joined Peking University as an assistant professor in 2019.

ABSTRACT:

We present a survey of single-cell genomes in terms of both DNA sequence variations and chromatin 3D organizations. First, we developed a whole-genome amplification (WGA) method, Linear Amplification via Transposon Insertion (LIANTI), which combines Tn5 transposition and T7 in vitro transcription for single-cell genomic analyses. LIANTI enabled digitized CNV detection with kilobase resolution. This allowed direct observation of0 the stochastic firing of DNA replication origins, which differs from cell to cell. Second, detection of single-cell SNVs suffers from false positives (FPs) due to intracellular single-stranded DNA damage and the process of WGA. We developed a new single-cell WGA method termed multiplexed end-tagging amplification of complementary strands (META-CS), which significantly reduced FPs by virtue of DNA complementarity. With META-CS, we determined SNV frequencies along the genome in differentiated single human blood cells, and identified cell type dependent mutational patterns for major types of lymphocyte. Third, we developed a chromatin conformation capture method, termed Dip-C, that can detect more chromatin contacts and impute the two chromosome haplotypes. We reconstrued the genome structures of single diploid human and mouse cells with high spatial resolution. We discovered that the two alleles of imprinted loci and the two X chromosomes were structurally different, and cells of different types displayed statistically distinct genome structures.

Muzlifah Haniffa

TITLE: Decoding the Developing Human Immune System

Muzlifah Haniffa is a Wellcome Trust Senior Research Fellow, Lister Institute Research Fellow and Consultant Dermatologist based in Newcastle University. She graduated from medical school in Cardiff and trained as a junior doctor in Cambridge. She received her dermatology specialist training in Newcastle. She was awarded an Action Medical Research Training Fellowship and a Wellcome Trust Clinical Intermediate Fellowship. Her research programme aims to understand the functional organisation of the developing and adult human immune system in health and disease.

ABSTRACT:

Muzlifah has used functional genomics, comparative biology and more recently single cell RNA sequencing to study human mononuclear phagocytes. In this seminar, she will discuss the power and utility of single cell RNA sequencing to understand the functional organisation of the developing human immune system.

Fan Bai

TITLE: Single Cell Analysis of Paediatric-onset Colitis and Inflammatory Bowel Disease Reveals Common Pathogenesis and a Novel Treatment

Dr. Fan Bai was born in 1981. He received BSc (Physics) from Peking University in 2003 and DPhil (Biophysics) from University of Oxford in 2008. After three years postdoctoral training at University of Oxford and Osaka University, he returned to China in 2011 and lead his own research team. Dr. Fan Bai is pioneering the application of single cell sequencing in biomedical research. Dr. Bai and co-workers published the world's first whole genome sequencing of individual circulating tumor cells collected from cancer patients' peripheral blood (PNAS,2013; Genome Research,2017;

Clinical Cancer Research,2019) and received broad media coverage. Recently, Dr. Bai's team investigated multiple tumor lesions in patients with Hepatocellular Carcinoma, revealing remarkable intra-tumor heterogeneity and the genetic feature of intra-liver metastases (Gastroenterology,2016; Cancer Cell,2019). By combining single-bacterium fluorescent imaging and sequencing, Dr. Bai's team has revealed the mechanism underlying bacterial antibiotic persistence (Molecular Cell,2016; Molecular Cell,2019; received editorial comments from Nature).

ABSTRACT:

Paediatric-onset colitis and inflammatory bowel disease (IBD) have significant impacts on the growth of infants and children, but the etiopathogenesis underlying disease subtypes remains incompletely understood. Here, we report single-cell clustering, immune phenotyping, and risk gene analysis for children with undifferentiated colitis, Crohn's disease and ulcerative colitis. We demonstrated disease-specific characteristics as well as common pathogenesis underpinned by an impaired cAMP-response pathway. Our comprehensive analysis of colonic mucosae in children with colitis and IBD has uncovered common pathogenesis and a novel treatment.

Yanyi Huang

TITLE: Highly Accurate DNA Sequencing: Error Correction Code and Beyond

Professor Yanyi Huang received his BS (Chemistry) and ScD (Inorganic Chemistry) degrees from Peking University in 1997 and 2002, respectively. He then conducted his postdoc research at Caltech (Applied Physics, 2002-2005), and at Stanford (Bioengineering, 2005-2006). He started his independent career at Peking University in 2006 as a Principal Investigator and then promoted to Associate Professor in 2009, and Professor in 2013. He is Principal Investigator and Associate Director in Beijing Advanced Innovation Center for Genomics (ICG), Professor of Materials Science and Engineering, Principal Investigator in Biomedical Pioneering Innovation Center (BIOPIC), Principal Investigator in Peking-Tsinghua Center for Life Sciences, Adjunct Professor of Analytical Chemistry, and Cooperative Principal Investigator of Chinese Institute for Brain Research, Beijing.

Professor Huang has published over 150 papers. He has received National Natural Science Award, 2nd Rank, in 2003, the National Excellent Doctoral Thesis Award in 2004, the Fok Ying Tung Education Foundation Young Investigator Award in 2010, The NSFC Award for Excellent Young Scholars in 2012, and the NSFC Award for Distinguished Young Scientist in 2015. He became Fellow of Royal Society of Chemistry in 2014. He has been actively serving the community including sitting on the Advisory Board of Lab on a Chip, the Editorial Board of Biomicrofluidics, and Science China Life Sciences, and the Features Panel of Analytical Chemistry.

ABSTRACT:

The high-throughput sequencing technology sequences massive DNA molecules parallelly to increase the data amount. While the throughput is mostly determined by the chip design, we propose that the information efficiency, the information entropy produced per sequencing cycle, is a more essential feature of the sequencing technology. Guided by this new concept, we proposed the DNA bit sequencing based on a dual-base flowgram that is compatible with any single-nucleotide addition chemistry and was previously used in the highly accurate error-correction code sequencing technology. The information efficiency of bit sequencing is 2 bit/cycle, which is equal to that of the prevailing reversible terminator technology. By utilizing this high information efficiency, we were able to encode the sequencing signal into bit sequences and map them precisely onto the reference genome. To perform a high-throughput bit sequencing, we manufactured a complete sequencer consisting of the fluidic and imaging system, sequencing chips with millions of microwells and the signal processing software. When applied to copy number variation detection, noninvasive prenatal testing and gene-expression profiling, bit sequencing showed high consistency with other commercial high-throughput sequencers yet faster turn-over speed.

Alex K. Shalek

TITLE: Identifying and Rationally Modulating Cellular Drivers of Enhanced and Diminished Immunity

Alex K. Shalek is currently the Pfizer-Laubach Career Development Associate Professor at MIT, as well as a Core Member of the Institute for Medical Engineering and Science (IMES), an Associate Professor of Chemistry, and an Extramural Member of The Koch Institute for Integrative Cancer Research. He is also an Institute Member of the Broad Institute, an Associate Member of the Ragon Institute, an Assistant in Immunology at MGH, and an Instructor in Health Sciences and Technology at HMS. His research is directed towards the development and application of new technologies that facilitate understanding of how cells collectively perform systems-level functions in healthy and diseased states. Dr. Shalek received his bachelor's degree summa cum laude from Columbia University and his Ph.D. from Harvard University in chemical physics under the guidance of Hongkun Park, and performed postdoctoral training under Hongkun Park and Aviv Regev (Broad/MIT). To date, his interdisciplinary research has focused on realizing and utilizing nanoscale manipulation and measurement technologies to examine how small components (molecules, cells) drive systems of vast complexity (cellular responses, population behaviors).

ABSTRACT:

Immune homeostasis requires constant collaboration between a diverse and dynamic set of cell types. Within our immune tissues, distinct cellular subsets must work together to defend against pathogenic threats, maintain tolerance, and establish memory. While surveying multiple healthy individuals enables exploration of potential ensemble immune solutions, contrasts against outliers of health and disease can reveal deviations that underscore diagnostic,therapeutic, and prophylactic features of enhanced function or dysfunction. Here, I will discuss how we can leverage single-cell genomic approaches – and, in particular, single-cell RNA-Seq – to explore the extensive functional diversity among immune cells within and across individuals, and uncover, from the bottom-up, distinct cell types and states associated with improved or impaired immunity. Moreover, I will discuss emerging experimental and computational strategies for altering ensemble cellular responses through targeted intra- or extracellular induction or suppression of these preferred or unwanted types and states, respectively.

Jianbin Wang

TITLE: Single-cell Transcriptomic Analysis Deciphers Cell Transition States in Multistep of Esophageal Cancer Development

Jianbin Wang is an assistant professor of life sciences at Tsinghua University in Beijing. Jianbin obtained his PhD and postdoctoral training at Stanford 2008-2015. Jianbin's technology-oriented lab focuses on the development of molecular biotechnologies. With the ability to perform high-throughput precise measurement, the lab aims to answer some molecular and cellular genetic questions from basic research and clinical fields. Some of the specific research areas include 1) new methods for nucleic acid and protein analysis; 2) molecular genetics of human and pathogen; 3) cellular genetics of normal and diseased tissue. The lab also collaborates in a broader area to help solve technique problems related to molecular measurement.

ABSTRACT:

Transcriptome profiling by RNA sequencing (RNA-seq) has been widely used to study cellular status. Though multiple ultra-high-throughput single-cell RNA-seq systems have acquired attention, their capabilities in accelerating biological research have not been fully explored. We have modified the standard single-cell RNA-seq protocol to extend its applications in various scenarios. Furthermore, we developed a new whole transcriptome amplification method based on the bacterial transposase Tn5. A convenient and versatile RNA-seq library preparation method is compatible with a wide range of input materials from nanogram of total RNA down to single cells. Our single-cell RNA-seq results demonstrated higher reproducibility and GC uniformity than prevailing methods.

Zemin Zhang

TITLE: Application of Novel Single Cell Bioinformatics Methods in Cancer Immunology

Dr. Zemin Zhang is a Professor of Peking University and a principal investigator at BIOPIC, and Beijing Advanced Innovation Center for Genomics. Dr. Zhang obtained his BS from Nankai University, PhD from Penn State University and postdoctoral trainings at UCSF. Dr. Zhang spent >16 years at Genentech/Roche, leading the cancer genomics and bioinformatics group to discover anticancer targets and biomarkers using genomic and computational technologies. He has pioneered multiple research directions in computational cancer biology and cancer genomics including the first ever whole genome tumor sequencing. He is also an inventor for >60 issued patents, and has directly contributed to the initial finding of the molecular targets of multiple cancer therapeutic agents in clinical trials. His lab currently focuses on understanding the interplay between immune and cancer cells using both large-scale cancer genomics data and the cutting-edge single cell sequencing technologies. He is a CUSBEA Scholar as well as Cheung Kong Scholar.

ABSTRACT:

Recent advances in single cell RNA sequencing have far-reaching potentials to discover and understand cell types, providing insights into organ composition, tumor microenvironment, cell lineage and fundamental cell properties. However, the complexity of the data present bioinformatics challenges to fully unleashing the power of scRNA-seq data. Here, we developed multiple tools for cell clustering, identification, visualization, lineage tracking, spatial organization, and integration, and then applied these tools to the scRNA-seq data we generated for multiple sets of tumor-infiltrating immune cells. We revealed novel cell types, tumor-specific immune cell properties, cell-cell interactions, and dynamic properties of cancer-related immune cells, and we further illustrate how such properties might be functionally related to cancer biology and immunotherapies.

Chen Wu

TITLE: Single-cell Transcriptomics Profiling of Esophageal Squamous Cell Carcinoma

Dr. Chen Wu received her M.D from China Medical University and Ph.D. from Peking Union Medical College. Her lab has focused the research interests on cancer genetics and genomics. Through comprehensive landscape profiling based on cancer multi-omics data, her work has revealed susceptibility and driver genes and risk factors in esophageal cancer. Dr. Wu has conducted the world's largest genetic and genomic landscape of driver genes and susceptible genes and elucidated their functions to identify therapeutic targets for esophageal squamous cell cancer in Chinese populations. Aiming at translating research into precision prevention and treatment, her achievements have significantly improved the understanding of carcinogenesis of esophageal cancer in China. The total citation of her 103 publications is 4,651.

ABSTRACT:

Esophageal squamous cell carcinoma (ESCC) is prevalent among certain populations and exhibits poor prognosis without specific markers for early detection. Two key questions still need resolving: 1) the initiation and development of ESCC are still poorly understood, and 2) the heterogeneity in tumor ecosystems consisting diverse mechanisms of cancer-associated risks. Here, we performed single-cell transcriptomic profiling to understand how ESCC initiates against normal aging process and examine the cellular interplays in tumor and microenvironment. We construct a single-cell developmental atlas based on a mouse model over six ESCC development stages. Based on transcriptomic profiles, we identify detailed transition signatures depicting landmarks along malignancy progression. Our comprehensive single-cell transcriptomic profiling on 234,094 cells from 60 ESCC patients reveals of 8 epithelial transcriptional programs, 44 immune and 16 non-immune stromal cell subtypes. Association analysis has enabled robust interpretation of consequences to lifestyle risks of smoking and drinking, and genomic alterations in TP53 and NOTCH1. We develop a patient stratification strategy that can significantly improve patient survival prediction. Our work deepens our understanding of ESCC initiation and ecosystems suggesting these molecules as useful markers for early ESCC detection, monitoring, and potential therapy.

Xiaoqun Wang

TITLE: Spatial and Temporal Regulation of Human Cortex Development Revealed by Single-cell RNA-Seq Analysis

2012-present Professor, Institute of Biophysics, Chinese Academy of Sciences ,2009—2012 Assistant Professor (Research), UCSF, University of California, at San Francisco .Dr.Xiaoqun Wang is interested in the function and regulation of neural stem cells in the mammalian brains. More specifically we are working on 1) Neural stem cell subtypes; 2) Niches and neural differentiation of neural stem cell; 3) Modeling human brain developmental diseases with pluripotent stem cells and in animal models; 4)Cellular mechanism regulating neuronal stem cell fate and circuits formation during the development of cerebral cortex; 5)Molecular regulations of nervous system diseases, including lisencephaly, microcephaly, autism, depression and neurodegenerative diseases.

ABSTRACT:

The human brain contains billions of neurons that were originally generated from neuroepithelial cells. The cerebral cortex can be divided into the following lobes: the frontal lobe (FL), parietal lobe (PL), occipital lobe (OL) and temporal lobe (TL), with each showing specialized functions in sensory and motor control and having specific projections to different targets of the nervous system. Our previous study revealed the developmental process of the human prefrontal cortex, which is the most uniquely expanded region of the human nervous system5. However, spatial and temporal regulation of different brain region at single-cell resolution at a serial of embryonic time points has not yet been performed systemically. We identified 29 cell sub-clusters, which showed different proportions in each region and the pons showed especially high percentage of astrocytes. Embryonic neurons were not as diverse as adult neurons, although they possessed important features of their destinies in adults. Neuron development was unsynchronized in the cerebral cortex, as dorsal regions appeared to be more mature than ventral regions at this stage. Region-specific genes were comprehensively identified in each neuronal sub-cluster, and a large proportion of these genes were neural disease related. Our results present a systematic landscape of the regionalized gene expression and neuron maturation of the human cerebral cortex.

Silas Maniatis

TITLE: Integration of Single Cell and Spatially Resolved Methods in the Study of Neurodegenerative Disease Mechanisms

Silas Maniatis received his PhD in Biochemistry from Harvard University. During his doctoral work, he utilized automated olfactory avoidance behavioral training systems and high throughput sequencing to study how memory formation in drosophila is regulated via small RNAs. This work spanned multiple disciplines, including instrument design and construction, drosophila genetics, molecular, and computational biology. Prior to his doctoral work, Silas was a member of Richard Axel's lab at Columbia University Medical Center. In the Axel lab, Silas utilized imaging and behavioral methods to identify the molecular and cellular underpinnings of sexual dimorphism in the mouse brain. Silas' research career also includes work in startup and established biotech companies. At Genetics Institute, Silas built and operated robotic systems for high-throughput small molecule drug discovery screens. Silas was also a founding employee of Acceleron Pharma, where he helped establish the company's research facilities and technological platform. His work at Acceleron Pharma included the construction of expression systems and cell lines now producing Luspatercept and several related molecules. At NYGC, Silas' work is focused on understanding how intercellular interactions contribute to neurodegeneration. Given the intrinsic relationship between the physical arrangement of cells in the CNS and CNS function, methods that deliver data with spatial resolution are highly desirable for such studies. Accordingly, Silas' work focusses on development and application of spatially resolved methods to studies of ALS and related dementias.

ABSTRACT:

Paralysis in the neurodegenerative disease amyotrophic lateral sclerosis (ALS) results from denervation of skeletal muscle as a consequence of motor neuron loss. Interactions between motor neurons, microglia and astrocytes in the spinal cord contribute to this loss, but the spatiotemporal ordering of molecular events that drive neurodegeneration is poorly understood. Given the functional importance of the physical arrangement of cells in the CNS, spatially resolved methods for studying gene expression could provide fundamental insights into the molecular and cellular pathologies in neurodegenerative diseases.

We have used spatial transcriptomics to study gene expression in the spinal cords of an ALS mouse model during disease progression, and in postmortem spinal cord tissue from ALS patients. By integrating spatial transcriptomic analyses with single cell RNAseq data and imaging-based methods, we identified spatiotemporally distinct subpopulations of distinct cell types. We also resolved pathway dynamics amongst multi-cell type ensembles detected at various spinal cord locations and disease states. ALS driven pathway activities shared across mouse models and postmortem patient tissue revealed the role of autophagy in non-cell-autonomous mechanisms that drive ALS pathology. Analysis of ALS mice in which autophagy was genetically ablated in motor neurons revealed glial ensembles that differentially respond to autophagy dependent signaling from neurons.

Solid phase capture, imaging, and dissociation based multi-omic technologies are rapidly developing, and the capabilities that these technologies provide can be combined to generate a comprehensive, spatiotemporal, multi-scale, dataset incorporting resolution, replication, and biological perturbation. Our studies demonstrate the utility of such technological combinations, and provide a framework for in depth studies of the neurodegenerative disease mechanisms.

Xuegong Zhang

TITLE: On the Information Content and Representation of Human Cells

Xuegong Zhang earned his BS degree in Industrial Automation in 1989 and Ph.D. degree in Pattern Recognition and Intelligent Systems in 1994, both from Tsinghua University. He joined the faculty of Tsinghua University in 1994, where he is now a Professor of Pattern Recognition and Bioinformatics in the Department of Automation, and an Adjunct Professor of the School of Life Sciences and also the School of Medicine. Dr. Zhang worked at Harvard School of Public Health as a visiting scientist on computational biology in 2001-2002, and had been a visiting scholar in the MCB program at USC in 2007. He is the Director of the Bioinformatics Division, Beijing National Research Institute for Information Science and Technology (BNRIST). His research interests include machine learning, informatics methods for single-cell sequencing data, Human Cell Atlas, and the analyses of multi-modal big healthcare data. Dr. Zhang is the Executive Editor-in-Chief of Quantitative Biology, and was elected to the Board of Directors of ISCB (International School of Computational Biology) in 2019.

ABSTRACT:

The human genome is the basic script of the story of human life, and cells are the basic venue where the stories take place. Studying the omics characteristics of single cells is a key to understanding the whole story of life. The Human Cell Atlas and several other community efforts are setting the great goal of systematically profiling molecular features of all types of cells of human or model organisms, which will be a giant step in describing and understanding the system of life. Single-cell omics technologies bring massive but noisy observations on multiple molecular features of thousands to millions of dimensions for each single cell. And such observations can be done on thousands of cells in one experiment.

With the quick accumulation of single-cell data, cells are becoming data entities in the super-high dimensional space, and the dimensionality is still increasing as new technologies emerge. Understanding the information content underlying the noisy high-dimensional data is a key challenge in fully understand the cells. We have been making efforts to address this challenge from statistical and algorithmic views in recent years. This talk will share example results of our recent and on-going work on developing models and methods for predicting the number of expressed genes based on the observed incomplete data, finding the embedding space of high-dimensional gene expression, and coding gene expression profiles with sparse binary vectors for efficient atlas mapping.

Ge Gao

TITLE: Cell BLAST and Beyond

As biology turns increasingly into a data-rich science, the massive amount of data generated by high-throughput technologies present both new opportunities and serious challenges. As a bioinformatician, Dr. Ge Gao is interested in developing novel computational technologies to analyze, integrate and visualize high-throughput biological data effectively and efficiently, with applications to decipher and understand the function and evolution of gene regulatory systems.

Since 2011, when he was first recruited as a Principal Investigator (tenure-track) by Peking University, Dr. Gao has developed twelve online bioinformatic software tools and databases for efficient analyses of large-scale omics data. These tools and databases have had over 600 million hits from users worldwide, demonstrating their global significance and impact. His research has led to 15 peer-reviewed papers with him as (co-)corresponding or first author, of which several have been highlighted by Essential Science Indicators (ESI), Faculty of 1000, InCoB'16 as well as journals. In the coming years, Dr. Gao will continue his efforts to develop novel bioinformatics technologies for the analysis of Peta-scale data, and apply these powerful computational tools to profile and model regulatory networks at single-cell resolution. Furthermore, as an integral part of BIOPIC, the Gao lab will continue contributing to the overall success of BIOPIC through collaborations and education.

ABSTRACT:

An effective and efficient cell-querying method is critical for integrating existing scRNA-seq data and annotating new data. Based on a novel adversarial-enhanced neural network generative model, Cell BLAST is an accurate and robust cell querying method for real-world scRNA-seq cell query and annotation with an interactive Web portal available at http://cblast.gao-lab.org. Moreover, the model's generative nature enables the adaptively "learning" the regulatory network from massive data directly, which further sheds lights into several interesting applications.

Nikolai Slavov

TITLE: High-throughput Single-cell Proteomics Quantifies the Emergence of Macrophage Heterogeneity

Nikolai Slavov received BS from MIT in 2004 and then pursued doctoral research in the Botstein laboratory at Princeton University, aiming to understand how cells coordinate their growth, gene expression, and metabolism. As a postdoc in the van Oudenaarden laboratory at MIT, Dr. Slavov characterized trade-offs of aerobic glycolysis (also known as Warburg effect). During a brief stint as a fellow at Harvard university, Dr. Slavov obtained direct evidence for differential stoichiometry among core ribosomal proteins, suggesting that specialized ribosomes regulate protein synthesis. The Slavov laboratory at Northeastern University pioneered methods for high-throughput quantification of proteins and used them to quantify thousands of proteins in differentiating cells. These data have allowed us to begin characterizing post-transcriptional regulation in single cells at systems level, identify cell lineages, classify cancer cells, and discover macrophage polarization in the absence of polarizing cytokines.

ABSTRACT:

The fate and physiology of individual cells are controlled by networks of proteins. Yet, our ability to quantitatively analyze protein networks in single cells has remained limited. To overcome this barrier, we developed SCoPE2. It integrates concepts from Single-Cell ProtEomics by Mass Spectrometry (SCoPE-MS) with automated and miniaturized sample preparation, substantially lowering cost and hands-on time. SCoPE2 uses data-driven analytics to optimize instrument parameters for sampling more ion copies per protein, thus supporting quantification with improved count statistics. These advances enabled us to analyze the emergence of cellular heterogeneity as homogeneous monocytes differentiated into macrophage-like cells in the absence of polarizing cytokines. We used SCoPE2 to quantify over 2,000 proteins in 356 single monocytes and macrophages in about 85 hours of instrument time, and the quantified proteins allowed us to discern single cells by cell type. Furthermore, the data uncovered a continuous gradient of proteome states for the macrophage-like cells, suggesting that macrophage heterogeneity may emerge even in the absence of polarizing cytokines. Our methodology lays the foundation for quantitative analysis of protein networks at single-cell resolution.

Catherine C.L. Wong

TITLE: Single Cell Proteomic Analysis Using PASEF

Dr. Catherine C.L. Wong is Director of Center for Precision Medicine Multi-omics Research (CPMMR), and Principal Investigator of Peking University-Tsinghua University Center for Life Sciences (CLS). She has been dedicated to the development of mass spectrometry technology and the methodological application of proteomics in basic and clinical research. Currently, the single-cell proteomics technology developed by her team maintains a leading position in the aspect of the identified protein number. Besides, Professor Wong has developed many innovative methods for identification of post-translational modification of various difficult proteins. Among them, the first direct identification of arginylation substrates and the accurate specific modified sites, has successfully filled up the blank and opened up the whole research field of arginylation. Up to present, she has published 73 SCI papers, including Science, Nature Communications, PNAS and so on.

ABSTRACT:

Single cell proteomic analysis provides crucial information on cellular heterogeneity in biological systems. Herein, we describe a nanoliter-scale oil-air-droplet (OAD) chip for achieving multistep complex sample pretreatment and injection for single cell proteomic analysis in the shotgun mode. By using miniaturized stationary droplet microreaction and manipulation techniques, our system allows all sample pretreatment and injection procedures to be performed in a nanoliter-scale droplet with minimum sample loss and a high sample injection e□ciency (>99%), thus substantially increasing the analytical sensitivity for single cell samples. We applied the present system in the proteomic analysis of 100 ± 10, 50 ± 5, 10, and 1 A549 cell(s), and protein IDs of 1360, 612, 192, and 51 were identified, respectively. The OAD chip-based system was further applied in single human oocyte analysis.

Aibin He

TITLE: Probing Principles in Gene Regulation and Cell Fate Specification Using Single-cell ChIP-seq

Dr. Aibin He received his Ph.D. degree at Peking Union Medical College, and did his postdoc training with Dr. William T. Pu at Harvard Medical School and Boston Children's Hospital. Dr. He started his own independent research at Institute of Molecular Medicine and Center for Life Sciences, Peking University in 2014. His lab is enthusiastic in developing novel technologies in single-cell omics and live imaging at large scales to understanding of genome regulation and cell lineage decisions in development, organ regeneration and disease. Fascinated by precisely controlled cardiac progenitor cells (CPCs) differentiation and allocation during heart development, we mainly focus on understanding of cellular origins and fates, and epigenetic mechanisms of cardiogenesis and heart regeneration. Particularly, our research directions include but are not limited to the following two aims: Aim 1 is to probe epigenetic underpinnings of CPCs specification and fate choice determination at single-cell level. To this end, we will combine single-cell transcriptomic profiling with in-house developed new single-cell epigenomic techniques to define the key intermediate lineages specific enhancers and master transcription factors centered regulatory network. Aim 2 is to reconstruct digital cell lineage roadmap of early heart development and regeneration through custom digital scanned light-sheet microscopy. The goal of this aim is to map holistic heart cells' behaviors, including proliferation, specification, and allocation during differentiation to form distinct parts of the heart. The multi-disciplinary knowledge from developmental biology, epigenetics, bioinformatics, optical microscopy and mathematical modeling will be harnessed to tackle these above questions.

ABSTRACT:

Divergent cell lineages from the common tissue progenitor/precursor cells during development and disease are tightly controlled by dynamic gene regulation. In particular, chromatin states, such as various histone modifications and selective transcription factor binding on cis-regulatory DNA elements, play an instructive role in shaping gene regulation and corresponding cell lineage choices. Despite recent great advances in single-cell transcriptomics, single-cell DNA methylation and chromatin accessibility,

single-cell measures of genome-wide DNA-protein interactions and implications in our understanding of epigenomic heterogeneities underlying cellular state and function far lag behind. In this talk, I will present our two recently developed single-cell ChIP-seq technologies, sc-itChIP and CoBATCH, and demonstrate how these can be harnessed to study basic principles in cellular states and regulation in cell culture and in vivo endothelial cell lineage development across 10 mouse organs. In addition, I will show how single-cell ChIP-seq can be integrated with scRNA-seq to decipher high-resolution regulatory landscape of cell fate transition. We envision that the single-cell ChIP-seq approach can provide novel insights into a broad spectrum of biological processes, including cell identity definition by multi-dimension chromatin modifications, principles in binding kinetics and regulatory outcomes of transcription factors, epigenetic landscapes in physiological and pathological processes, and so on.

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