BIOGRAPHICAL SKETCH

NAME: **Xiaohui Kong, PhD**

eRA COMMONS USERNAME: **KONG.XIAOHUI**

POSITION TITLE: **Postdoctoral Fellow**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
Lanzhou University, China	B.S.	08/2010	06/2014	Biotechnology
Tsinghua University, China	Ph.D.	09/2014	01/2022	Biological Sciences,
Stanford University, Palo Alto, CA	Postdoc	04/2022	Present	Cardiology

A. Personal Statement

As a long-term goal, I would like to establish my own research group in an academic setting and further explore the countermeasures to the gene therapy for the cardiomyopathy. **I became interested in the genetics and cardiomyopathy during my Ph.D. work**. My graduate research has been dedicated to understanding the regulatory mechanism of long non-coding RNA *lncRNA-Smad7* in early development of mESCs. Transforming growth factor β (TGF-β) superfamily proteins are potent regulators of cellular development and differentiation. Under guidance of Dr. Qiaoran Xi in Tsinghua University, China, I investigate the antagonistic effects between Nodal/TGF-β and BMP signaling via *lncRNA-Smad7* which provide a framework for understanding cell fate determination in early development. My graduate study was funded by National Natural Science Foundation of China and Tsinghua-Peking Center for Life Sciences. I named 1 peer-reviewed articles as the first-listed author and 3 peer-reviewed articles as the co-author for my Ph.D. work. I provided new insight into the role of lncRNAs in regulating cross-talk between Nodal/TGF-β and BMP signaling during early development [Kong et al., NAR 2022]. During graduate study, I acquired a broad spectrum of experimental and established multiple systems to discover the mechanisms (specially differentiation system of the cardiomyocytes from mESCs, ChIP and ChIRP protocol, reporter system in vitro, ELISA and EMSA assays, and all kinds of the molecular biology.

I decide to pursue a postdoctoral training in Dr. Joseph Wu lab at Stanford University where I would like to bridge my expertise in molecular and biochemistry biology with Dr. Wu's expertise in cardiovascular research. Dr. Wu is a direct of induced pluripotent stem cell (iPSC) and a pioneer in human heart disease. The overarching goal of my postdoctoral research training is to use patient iPSC-derived cardiomyocytes as the in vitro platform for the drug screen and synergistic drug combinations again the IR (ionizing radiation) exposure. Following this strategy, we will screen the radioprotective drugs, and optimize the synergistic combinations. As I aim to do the translational research and translate the basic research to the clinical trial, I am interested in the genome editing for the pathogenetic heart diseases to benefit the therapeutic countermeasures in clinical as well. The Wu laboratory is composed of members from diverse research backgrounds such as tissue engineering, electrophysiology, computation biology which offer rich opportunities to leverage new skill sets such as multi-omics profiling, big data analysis, and stem cell biology.

Since I joined the Wu Lab, I have extended great understanding in stem cell biology and participated in multiple iPSC lines from patients suffering from genetic heart diseases (Catecholaminergic polymorphic ventricular tachycardia, dilated cardiomyopathy, and Spinal muscular atrophy) [Kong et al., Stem Cell Res 2023; Zeng et al., Stem Cell Res 2023]. Working at the Wu Lab offers unrivaled opportunity to develop and establish a unique research niche. We have the human iPSC-based in vitro cardiovascular disease modeling for CRISPR gene editing, and multi-omics profiling to screen the radioprotective drug combinations. Completion of this proposal will establish/set up/etc for a career development application. I will be incredibly enthusiastic to the translational study in my future career.

Xiaohui Kong, Nadjet Belbachir, Wenshu Zeng, Christopher D Yan, Sai Navada, Marco V Perez, Joseph C Wu[#] (2023). Generation of two induced pluripotent stem cell lines from catecholaminergic polymorphic ventricular tachycardia patients carrying RYR2 mutations. Stem Cell Res. May 12;69:103111.

Wenshu Zeng, **Xiaohui Kong**, Christina Alamana, Yu Liu, Jessica Guzman, Paul D Pang, John W Day, Joseph C Wu[#] (2023). Generation of two induced pluripotent stem cell lines from spinal muscular atrophy type 1 patients carrying no functional copies of SMN1 gene. Stem Cell Res. Apr 17;69:103095.

Wenqiang Liu, Wenshu Zeng, **Xiaohui Kong**, Min Htet, Rebecca Yu, Matthew Wheeler, John W Day, Joseph C Wu[#] (2023). Generation of two induced pluripotent stem cell lines from Duchenne muscular dystrophy patients. Stem Cell Res. Oct:72:103207.

Xiaohui Kong, Kun Yan, Pujuan Deng, Haipeng Fu, Hongyao Sun, Wenze Huang, Shuangying Jiang, Junbiao Dai, Qiangfeng Cliff Zhang, Jun-jie Gogo Liu, Qiaoran Xi[#] (2022). *LncRNA-Smad7* mediates crosstalk between Nodal/TGF-β and BMP signaling to regulate cell fate determination of pluripotent and multipotent cells. ***Nucleic Acids Research*** 50, Issue 18, Pages 10526–10543.

Haipeng Fu, Tingyu Wang, **Xiaohui Kong,** Kun Yan, Jingyi Cao, Yang Yang, Jingyi Cao, Yafei Yuan, Nan Wang, Kehkooi Kee, Zhi John Lu, Qiaoran Xi[#] (2022). A micropeptide NEMEP induced by TGF-β/Nodal signaling boosts glucose uptake in mesendoderm differentiation of embryonic stem cells. ***Nature Communications*** 13, 3984.

Ying Liu[*], Yajing Fu[*], Qian Wang, Mushan Li, Zheng Zhou, Deemah Dabbagh, Chunyan Fu, Hang Zhang, Shuo Li, Tengjiang Zhang, Jing Gong, **Xiaohui Kong**, Weiwei Zhai, Jiaming Su, Jianping Sun, Yonghong Zhang, Xiao-Fang Yu, Zhen Shao, Feng Zhou[#], Yuntao Wu[#] & Xu Tan[#] (2019). Proteomic profiling of HIV-1 infection of human CD4(+) T cells identifies PSGL-1 as an HIV restriction factor. ***Nature Microbiology*** 4(5): 813-825. (*, co-first authors [#], co-corresponding authors)

Zhimiao Lin[*], Shuo Li[*], Cheng Feng[*], Shang Yang, Huijun Wang, Danhui Ma, Jing Zhang, Mengting Gou, Dingfang Bu, Tengjiang Zhang, **Xiaohui Kong**, Xintong Wang, Ofer Sarig, Yali Ren, Lanlan Dai, Hankui Liu, Jianguo Zhang, Fei Li, Yongyan Hu, Gilly Padalon-Brauch, Dan Vodo, Feng Zhou, Ting Chen, Haiteng Deng, Eli Sprecher, Yong Yang[#] & Xu Tan[#] (2016). Stabilizing mutations of KLHL24 ubiquitin ligase cause loss of keratin 14 and human skin fragility. ***Nature Genetics*** 48, 1508–1516.

Positions and Employment

2014 - 2022	Graduate Student, Tsinghua University, China (PI: Dr. Qiaoran Xi, PhD)
2022 -	**Postdoctoral Fellow, Stanford University (PI: Joseph C. Wu, MD, PhD)**

Awards and Honors

2011	National Scholarship for Encouragement, Lanzhou University (5,000 RMB)
2012	National Scholarship for Encouragement, Lanzhou University (5,000 RMB)
2013	National Scholarship for Encouragement, Lanzhou University (5,000 RMB)
2014	Outstanding undergraduates, Lanzhou University
2021	Second-class scholarship, Tsinghua University (5,000 RMB)
2024	2-year AHA postdoctoral fellowship gran
2024	Poster Award of the 2024 Stanford-Arizona-Morehouse-UAB Cardiovascular Research Symposium

Presentations

2017	Doctoral Forum of School of life sciences in Tsinghua University, China
2018	Doctoral Forum of School of life sciences in Tsinghua University, China
2019	Doctoral Forum of School of life sciences in Tsinghua University, China
2019	FASEB (Federation of American Societies for experimental biology) conference, Florida, USA
2022	Stanford-Cornell Cardiovascular Research Symposium, Palo Alto, USA
2024	Stanford-Arizona-Morehouse-UAB Cardiovascular Research Symposium, Palo Alto, USA

Teaching and Other Experiences

2017	Teaching Assistant of Molecular Biology, Tsinghua University, China.
2018	Teaching Assistant of Molecular Biology, Tsinghua University, China.
2019	Teaching Assistant of Molecular Biology, Tsinghua University, China.
2021	Teaching Assistant of Molecular Biology, Tsinghua University, China

C. Contributions to Science

1. **Unraveling the novel mechanism in regulating cross-talk between Nodal/TGF-β and BMP signaling by lncRNAs**

   My Ph.D. study served as the foundation for my systems biology expertise involving molecular biology, biochemistry biology, and cellular biology. To investigate the novel regulators related to the early development, my study focused on the novel long non-coding RNAs (lncRNA) which were induced by TGF-β signaling and played roles in the early development. Amongst the lncRNAs, I mainly investigated the regulatory roles and mechanism of *lncRNA-Smad7* which was transcribed divergently to SMAD7. *LncRNA-Smad7* is activated by Nodal signaling in mESCs and regulates cardiomyocyte differentiation by repressing *Bmp2* expression. In addition, *lncRNA-Smad7* represses *Bmp2* expression through binding to its promoter region via its $(CA)_{12}$-repeats. These findings thus provide new insight into the role of lncRNAs in regulating cross-talk between Nodal/TGF-β and BMP signaling during early development.

   Xiaohui Kong, …, Qiaoran Xi[#] (2022). *LncRNA-Smad7* mediates crosstalk between Nodal/TGF-β and BMP signaling to regulate cell fate determination of pluripotent and multipotent cells. ***Nucleic Acids Research*.**

2. **Providing new insight into the role micropeptides during early development.**

   Further expanding on the work above, I was part of a collaborative effort involving Dr. Haipeng Fu to identify the Nodal enhanced micropeptide NEMEP which regulated glucose uptake during mesendoderm differentiation of embryonic stem cells. Here, we identified the NEMEP as a highly conserved, transmembrane micropeptide and a direct target of Nodal signaling in mesendoderm differentiation of mouse embryonic stem cells (mESCs). This work provides a clear example for the direct functional impact of altered glucose metabolism on cell fate determination through micropeptide.

   Haipeng Fu, Tingyu Wang, **Xiaohui Kong**, …, Qiaoran Xi[#] (2022). A micropeptide NEMEP induced by TGF-β/Nodal signaling boosts glucose uptake in mesendoderm differentiation of embryonic stem cells. ***Nature Communications*.**

3. **Identifying HIV restriction factor.**

   As an Ph.D. student in the first rotation year at Tsinghua University, I performed to screen the HIV (Human immunodeficiency virus) restriction factor in human primary $CD4^+$ T cells. I screened parts of over 14,000 proteins quantified in this project by isobaric tag-based mass spectrometry during HIV-1 infection of human primary CD4+T cells. As the collaborator with Dr. Ying Liu, we identified PSGL-1 (P-selectin glycoprotein ligand 1) as an HIV-1 restriction factor and a key mediator of interferon-γ's anti-HIV activity.

   Ying Liu[*], …, **Xiaohui Kong**, Feng Zhou[#], Yuntao Wu[#] & Xu Tan[#] (2019). Proteomic profiling of HIV-1 infection of human CD4(+) T cells identifies PSGL-1 as an HIV restriction factor. ***Nature Microbiology*.**

4. **Investigating a new disease-causing mechanism related to dysregulation of autoubiquitination**

   As an Ph.D. student in the first rotation year at Tsinghua University, I contributed to the preliminary identification that KLHL24 start-codon mutations cause EBS (epidermolysis bullosa simplex). This finding further identified a new disease-causing mechanism due to dysregulation of autoubiquitination and open new avenues for the treatment of related disorders.

   Zhimiao Lin[*], …, **Xiaohui Kong**, Yong Yang[#] & Xu Tan[#] (2016). Stabilizing mutations of KLHL24 ubiquitin ligase cause loss of keratin 14 and human skin fragility**.** ***Nature Genetics*.**

5. **Biorepository of patient iPSCs:** A discovery of iPSC reprogramming revolutionized the field of pharmacogenetics by providing an accessible, versatile, and adaptable platform for precision medicine. Stanford Cardiovascular Institute (SCVI) Biobank has the largest biorepository dedicated to generating human iPSCs and sharing with research community. By collaboration with Biobank, I contributed to identify the characters of multiple iPSC lines from patients with diverse cardiovascular diseases.

   Xiaohui Kong,…, Joseph C Wu# (2023). Generation of two induced pluripotent stem cell lines from catecholaminergic polymorphic ventricular tachycardia patients carrying RYR2 mutations. **Stem Cell Res**.
   Wenshu Zeng, **Xiaohui Kong**, …, Joseph C Wu# (2023). Generation of two induced pluripotent stem cell lines from spinal muscular atrophy type 1 patients carrying no functional copies of SMN1 gene. **Stem Cell Res**.
   Wenqiang Liu, Wenshu Zeng, **Xiaohui Kong**, …, Joseph C Wu# (2023). Generation of two induced pluripotent stem cell lines from Duchenne muscular dystrophy patients**. Stem Cell Res**.

Complete list of published work in Google Scholar:
https://scholar.google.com/citations?user=ANePJuMAAAAJ&hl=zh-CN

D. Score of the courses

TSINGHUA UNIVERSITY ACADEMIC TRANSCRIPT
School/Department: School of Life Science
Subject: Biology

Course Number	Course Title	Credit	Degree	Course Grade	Year-Semester
60450021	Ethics and Scientific Misconduct in Life Science Research	1	Y	97	2014-Autumn
70450083	Frontier of Biotechnology	3	Y	76	2014-Autumn
70450126	Modern Life Sciences	6	Y	87	2014-Autumn
70450233	**Modern Biological Technology**	**3**	**Y**	**94**	**2014-Autumn**
74000173	Principles of Immunology	3	Y	77	2014-Autumn
60680021	Introduction to Dialectics of Nature	1	Y	85	2015-Spring
70450173	Brain and Cognitive Science	3	Y	83	2015-Spring
90450112	Lab Rotation	2	Y	Pass	2015-Spring
90450141	Current Topics of Transcriptional Regulation	1	Y	90	2015-Spring
90680032	Chinese Marxism and Contemporary World	2	Y	88	2015-Spring
90640012	English for Doctor Candidate	2	Y	75	2016-Spring
99990041	Literature Summarizing and Presentation of Thesis	1	Y	90	2016-Autumn
99990061	Comprehensive Examination in the Major Field	1	Y	78	2016-Autumn
90450101	Graduate Student Seminar Series	1	Y	Pass	2021-Spring
99990032	Academic Activities and Symposia	2	Y	Pass	2021-Spring