



# **LISTS OF 25 SDU LABS**

**Office of Research Management and International Affairs  
Cheeloo College of Medicine  
Shandong University**



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## Brief Lists of 24 SDU Labs

No.	Lab Name	Director(s)	Research Areas
1	Key Laboratory of Cardiovascular Remodeling and Function Research	Yun Zhang	The mechanisms, detection techniques and intervention strategies of cardiovascular remodeling, such as atherosclerosis, hypertension, abdominal aortic aneurysm, diabetic cardiomyopathy, adipose tissue affecting cardiovascular disease etc.
2	Institute of Women, Children and Reproductive Health, Shandong University	Zijiang Chen	The maintenance and promotion of reproductive health through basic research, clinical practice, and technological innovation. identifying causative genes of reproductive disorders and elucidating the corresponding pathogenesis, and resolving controversies and promoting conceptual changes over infertility treatment. technological innovation in embryo culture and genetic testing to reduce the risks of birth defects
3	Lab of Kidney Disease Pathogenesis and Intervention Strategies Research	Fan Yi	The role of local immune responses, metabolic homeostasis regulation, and epigenetic modifications in renal diseases
4	Immunity and Liver Disease	Chunhong Ma	Liver immune microenvironment regulation and developing intervention strategy, the liver inflammation induced by viral infection, metabolism and other environmental factors and its malignant transformation mechanism
5	Lab of Receptor Biology and Pharmacology	Jinpeng Sun	Microenvironment pharmacology, GPCR decoupling, ligand discovery, cellular mechanisms of functional diversity, the development of preferential drugs
6	Medical and Pharmaceutical Basic Research Innovation Center of Emergency and Critical Care Medicine, China's Ministry of Education	Yuguo Chen	Acute chest pain as the main cause of critical cardiovascular diseases, cardiac arrest and cardiopulmonary resuscitation, acute organ injury and protection, research and development of innovative medicines and intelligent emergency equipment, medical big data and artificial intelligence, and basic research on zero-magnetism medicine

7	Shandong Key Laboratory of Immunohematology, Qilu Hospital, Shandong University	Jun Peng	Pathogenesis and of primary immune thrombocytopenia (ITP) , and myelodysplastic syndromes (MDS) , and differentiation of hematopoietic stem cells
8	Tomographic Anatomy Research Centre, Department of Anatomy and Neurobiology, School of Basic Medical Sciences, Qilu Medical College, Shandong University, China	Shuwei Liu	The digital human body, digital brain mapping and foetal brain development ( Digitised adult brain atlas; Digitising the Fetal Brain Atlas ); Tomographic Anatomy and Neurodevelopment ; Neuroimaging ; computational medicine ; brain science ; imaging of neuropsychiatric disorders ; pathogenesis of neurodevelopmental and related diseases
9	NHC Key Laboratory of Health Economics and Policy Research (Shandong University)	Qiang Sun	Economic evaluation of pharmacoconomics and medical security policies, management and support for pharmaceuticals and consumables, tuberculosis control and rational use of anti-tuberculosis drugs, etc.
10	Neurosurgery Laboratory at Qilu Hospital of Shandong University	Xingang Li	The mechanism of neuroimmune regulation in the occurrence and glioma development and its possible intervention targets, the molecular mechanism of cerebrovascular functional remodeling and possible intervention approaches, as well as research on the molecular pathology of neuromuscular diseases and degenerative diseases
11	Drug Design and Chemical Biology Research	Hao Fang	Structure-based drug design, synthesis, and chemical biology research; Computer-aided drug design and virtual screening; Development of novel methods for peptide synthesis; Design and application of biocompatible materials
12	Shandong University-BOP Oral Joint Microbiome Laboratory	Qiang Feng	Oral microbiome and oral/systemic health, mining the human microbiome/transcriptome/single cell/ spatiotemporal omics data from oral and systemic diseases in the dry lab, the mechanisms between key oral pathogen and relative diseases in the wet lab
13	Tissue Engineering and Regeneration Laboratory	Baojin Ma	Multi-layer bioactive biomaterials, tissue engineering, and nanomedicine
14	Environmental health laboratory	Xuewen Li	Antibiotics and the spread of ARB in the environment, antibiotic resistance control strategies in animal husbandry areas, the sustainable development of intensive vegetable areas from the perspective of antibiotic residue and antibiotic resistant bacterial prevention and control

15	Institute of Biotherapy for Hematological Malignancies of Shandong University	Chengyun Zheng	Regulation of stem cell (iPSC and MSC) differentiation and bio-safety evaluation of in vitro manipulated stem cells; Development and functional evaluation of stem cell-based renal tissue regeneration
16	Visualization and Light-Controlled Regulation Guided Drug Research	Minyong Li	Visualization of Biological Activity; Molecular Probe Development; Rational Drug Design and Medicinal Chemistry; Discovery and Identification of Drug Targets and Binding Sites; Development of Novel Organic Synthesis Methods
17	Center for Gene and Immunotherapy	Dongqi Tang	Exploring synthetic immunotherapy strategies to engineer immune cells; investigating the application of CRISPR gene editing technology in gene therapy, and developing gene drugs; developing functional protein drugs for treating metabolic diseases like diabetes; exploring the role of organoid technology in drug screening, tissue and organ reconstruction, and developing methods for evaluating tumor-related drugs and screening new drugs
18	Endocrinology and Metabolism Lab of the Second Hospital of Shandong University	Shihong Chen	Diabetic peripheral neuropathy and diabetic encephalopathy, the pathogenesis, early diagnostic markers, clinical translation of therapeutic drugs and functional imaging of neurological complications of diabetes mellitus
19	Interventional Oncology Institute of Shandong University	Yuliang Li	The molecular mechanism of Iodine-125 radioactive seeds in cancers; The molecular mechanism of traditional Chinese medicine for gallstones
20	JDY-Lab	Duyin Jiang	The role of fetal dermal mesenchymal stem cells in skin tissue repair, regeneration and anti-aging; basic research and application of tissue engineering materials and (denatured) acellular dermal matrix in burn wound repair; the study of the biological activity of keloid fibroblasts inhibited by mesenchymal stem cells; the hierarchical management, diagnosis and treatment of acute and chronic wounds and specialized training

21	Kidney Multidisciplinary Innovation Lab	Gang liu	To investigate the pathogenesis of common kidney diseases of CKD; To identify the risk factors, immune-inflammatory mechanism and genetic background in developing and progression of diabetic kidney disease(DKD); To develop prevention and stem cell treatment strategies of CKD
22	Translational medical Laboratory for neurodegenerative diseases	Jianzhong Bi	Epidemiology and molecular genetics of neurodegenerative diseases; Study on pathogenesis and early biomarkers of neurodegenerative diseases(e.g., dementia/Parkinson disease); Research and development of innovative treatments for neurodegenerative diseases
23	Liu Ping Research Lab	Qinghai Wang	Basic and clinical research of vascular remodeling for many years, especially in the research of peripheral vascular membrane, identifying promising novel targeted therapies for treating atherosclerosis and vascular remodeling
24	The 3D printing Dental Medicine Research Center of Shandong University	Qingguo Lai; Bin Zou	3D ceramic printing-based regeneration and repair of large bone defects and the 3D bioprinting-based organ reconstruction
25	NHC Key Laboratory of Otorhinolaryngology	Jinpeng Sun	Engaged in the study of microenvironment pharmacology, in which he systematically dissected the mechanism of membrane receptors sensing microenvironment and regulating physiological functions, and developed the modulating strategies targeting these receptors



## **Key Laboratory of Cardiovascular Remodeling and Function Research, Shandong University — Karolinska Institutet Collaborative Laboratory for Cardiovascular Research**

### **Establishment and Development:**

Founded in 1959, the Department of Cardiology of Qilu (Cheeloo) Hospital is one of the earliest cardiovascular disciplines in China and serves as a comprehensive platform for clinical practice, teaching, research and training. This department consists of outpatient clinics, three inpatient wards, a critical care unit (CCU), an echocardiographic laboratory, an electrocardiographic laboratory, four cardiac catheterization laboratories, and a branch department at Qingdao Campus. The scientific research is based on the National Key Laboratory for Innovation and Transformation of Luobing Theory, the Key Laboratory of Cardiovascular Remodeling and Function Research of the MOE and the NHC and Shandong University — Karolinska Institutet Collaborative Laboratory for Cardiovascular Research. The department has undertaken more than 300 national and provincial research projects and published more than 1,400 papers in high-impact international journals. The laboratory covers an area of 10,000 square meters, with more than 800 pieces of equipment, the total value of all equipment is more than \$20 million.



### **Team Members:**

The director of the laboratory is Professor Yun Zhang, a member of the Chinese Academy of Engineering, FACC, FESC, Hon. FASE. Our team is composed of the leading experts in their fields, young and passionate researchers. Many of them

undertake the excellent scientist fund or basic scientific fund from the government.

### **Research Areas:**

The Key Laboratory of Cardiovascular Remodeling and Function Research features research on the mechanisms, detection techniques and intervention strategies of cardiovascular remodeling, such as atherosclerosis, hypertension, abdominal aortic aneurysm, diabetic cardiomyopathy, adipose tissue affecting cardiovascular disease etc.

### **Research Achievements:**

In the field of basic research, this department was the first to establish a series of animal models of atherosclerotic vulnerable plaque, discovered multiple novel genes and mechanisms underlying the development and progression of vulnerable plaque and ventricular remodeling, developed new biomarkers and imaging techniques for detecting vulnerable plaque and ventricular remodeling, and revealed a series of new therapeutic targets for the early intervention of atherosclerosis and heart failure. In the field of clinical research, the department led the world-renowned EMINCA and CAPITAL studies, participated in over 30 international and national multi-center clinical trials, led or participated in the preparation of more than 20 Chinese and foreign clinical treatment guidelines.

### **Main Publications:**

10 selected publications

1. STABILITY Investigators. Darapladib for preventing ischemic events in stable coronary heart disease. *N Engl J Med.* 2014 May 1;370(18):1702-11. doi: 10.1056/NEJMoa1315878. Epub 2014 Mar 30. PMID: 24678955.
2. HEAAL Investigators. Effects of high-dose versus low-dose losartan on clinical outcomes in patients with heart failure (HEAAL study): a randomised, double-blind trial. *Lancet.* 2009 Nov 28;374(9704):1840-8. doi: 10.1016/S0140-6736(09)61913-9. Epub 2009 Nov 16. Erratum in: *Lancet.* 2009 Dec 5;374(9705):1888. PMID: 19922995.
3. AleCardio Investigators. Effect of aleglitazar on cardiovascular outcomes after acute coronary syndrome in patients with type 2 diabetes mellitus: the AleCardio randomized clinical trial. *JAMA.* 2014 Apr 16;311(15):1515-25. doi: 10.1001/jama.2014.3321. PMID: 24682069.
4. Wang S, Zhang C, Zhang M, Liang B, Zhu H, Lee J, Viollet B, Xia L, Zhang Y, Zou MH. Activation of AMP-activated protein kinase  $\alpha 2$  by nicotine instigates formation of abdominal aortic aneurysms in mice in vivo. *Nat Med.* 2012 Jun;18(6):902-10. doi: 10.1038/nm.2711. PMID: 22561688; PMCID: PMC3559018.
5. Chen ZY, Jing D, Bath KG, Ieraci A, Khan T, Siao CJ, Herrera DG, Toth M, Yang C, McEwen BS, Hempstead BL, Lee FS. Genetic variant BDNF (Val66Met) polymorphism alters anxiety-related behavior. *Science.* 2006 Oct 6;314(5796):140-3. doi: 10.1126/science.1129663. PMID: 17023662; PMCID:



PMC1880880.

6. Zhao M, Veeranki SP, Magnussen CG, Xi B. Recommended physical activity and all cause and cause specific mortality in US adults: prospective cohort study. *BMJ*. 2020 Jul 1;370:m2031. doi: 10.1136/bmj.m2031. PMID: 32611588; PMCID: PMC7328465.
7. Jiang F, Yang J, Zhang Y, Dong M, Wang S, Zhang Q, Liu FF, Zhang K, Zhang C. Angiotensin-converting enzyme 2 and angiotensin 1-7: novel therapeutic targets. *Nat Rev Cardiol*. 2014 Jul;11(7):413-26. doi: 10.1038/nrcardio.2014.59. Epub 2014 Apr 29. PMID: 24776703; PMCID: PMC7097196.
8. Dong M, Yang X, Lim S, Cao Z, Honek J, Lu H, Zhang C, Seki T, Hosaka K, Wahlberg E, Yang J, Zhang L, Länne T, Sun B, Li X, Liu Y, Zhang Y, Cao Y. Cold exposure promotes atherosclerotic plaque growth and instability via UCP1-dependent lipolysis. *Cell Metab*. 2013 Jul 2;18(1):118-29. doi: 10.1016/j.cmet.2013.06.003. PMID: 23823482; PMCID: PMC3701322.
9. Liu B, Zhang M, Chu H, Zhang H, Wu H, Song G, Wang P, Zhao K, Hou J, Wang X, Zhang L, Gao C. The ubiquitin E3 ligase TRIM31 promotes aggregation and activation of the signaling adaptor MAVS through Lys63-linked polyubiquitination. *Nat Immunol*. 2017 Feb;18(2):214-224. doi: 10.1038/ni.3641. Epub 2016 Dec 19. PMID: 27992402.
10. Zhang M, Sui W, Cheng C, Xue F, Tian Z, Cheng J, Zhang J, Zhang T, Zhang J, Wang W, Xiong W, Hao P, Ma J, Xu X, Wang S, Sun S, Zhang M, Zhang Y, Zhang C. Erythropoietin promotes abdominal aortic aneurysms in mice through angiogenesis and inflammatory infiltration. *Sci Transl Med*. 2021 Jul 21;13(603):eaaz4959. doi: 10.1126/scitranslmed.aaz4959. PMID: 34290056.

### **Facilities & Resources:**

Our state-of-the-art facilities and cutting-edge technology enable us to conduct research that is both rigorous and innovative. The laboratory covers an area of 10,000 square meters, with more than 800 pieces of equipment, the total value of all equipment is more than \$20 million. The laboratory consists of animal laboratory, cytology laboratory, gene laboratory, protein laboratory, pathology laboratory, confocal laser microscopy laboratory, flow cytometry laboratory, genetics laboratory, immunology laboratory, biomechanics and computational biology laboratory, small animal ultrasound and CT imaging platform, small animal cardiac function room, etc. The laboratory space and equipment conditions can meet the requirements of most experiments.





### **Collaborations & Partnerships:**

We believe in the power of collaboration. That's why we have forged partnerships with Professor Yihai Cao, one of the most famous scientists from KI in the field of angiogenesis, metabolism, tumor and cardiovascular disease to further advance our research. We also collaborate with Professor Qingbo Xu, Xinliang Ma and Xingli Wang from UK and USA in the field of cardiology for many years.

### **Recreational Activities:**

Academic seminars are held regularly to help improve the communication between researchers.

### **Other Features:**

Our lab also performs the research on traditional Chinese medicine. We have done a lot of work in the scientific research of traditional Chinese medicine and published many articles in SCI journals.

### **Contact:**

For more information or inquiries, please contact us at [swl@email.sdu.edu.cn](mailto:swl@email.sdu.edu.cn) or visit our website at <https://xxgcg.sdu.edu.cn/>

## **Institute of Women, Children and Reproductive Health, Shandong University**

### **Establishment and Development:**

Our institute was established by Prof. Zi-Jiang Chen in 1987, with an independent clinical and translational base, i.e. Center for Reproductive Medicine, Shandong University. It is one of the earliest to carry out research and application of assisted reproductive technology (ART) in China, and fulfilled the world's first gamete intrauterine transfer in 1992. It is the first batch of doctoral and master's degree programs and post-doctoral stations approved by the State Council. Over the years, it has achieved significant milestones in Reproductive Medicine. It was qualified to conduct in-vitro fertilization (IVF) in 2003, and has since grown to one of the leading IVF centers with over 500,000 patients coming each year. It established the Key Laboratory of Reproductive Endocrinology under the Ministry of Education in 2010, National Research Center for Assisted Reproductive Technology and Reproductive Genetics in 2011, Joint Reproductive Genetics Laboratory with Chinese University of Hong Kong in 2013, further solidifying its position as a leading institution in the field. It was selected as one of the top 100 hospitals in China in 2019 and ranking the second in the reproductive medicine specialty in 2021. In 2023, the center was reorganized and established the State Key Laboratory of Reproductive Medicine and Offspring Health, the Institute of Women, Children and Reproductive Health, Shandong University, and the Suzhou Collaborative Innovation Center for Reproductive Medicine, Shandong University.

### **Team Members:**

Led by Prof. Zi-Jiang Chen, the academician of the Chinese Academy of Sciences, our institute has more than 50 full-time researchers in reproductive medicine, including 14 doctoral supervisors and 26 master's supervisors. Now it hosts 5 chief scientists of the National Key Research and Development Program of China, 1 awarded the National Science Foundation for Distinguished Young Scholar of China, 2 distinguished professors of the "Changjiang Scholars Award Program" of the Ministry of Education, and 1 leading talent of the National Special Support Program for High-level Talents. Furthermore, we have 1 Young Experts of the "Changjiang Scholars Award Program" of the Ministry of Education, 4 young talents of the National Special Support Program for High-level Talents, 1 special expert of Taishan Scholars of Shandong Province, and 14 young experts of Taishan Scholars of Shandong Province.

### **Research Areas:**

Our institute specializes in the maintenance and promotion of reproductive health through basic research, clinical practice, and technological innovation. We are dedicated in identifying causative genes of reproductive disorders and elucidating the corresponding pathogenesis, and resolving controversies and promoting conceptual changes over infertility treatment. We are also actively engaged in technological innovation in embryo culture and genetic testing to reduce the risks of birth defects.

### **Research Achievements:**

Our institute dedicates to clinical and basic research on reproductive medicine and offspring health.

1) We have depicted the translational map of the human oocyte-to-embryo transition, and the chromatin accessibility and 3D structural maps of human early embryo development, to uncover the intricate molecular regulatory mechanisms during human embryogenesis (Science, 2022; Nature, 2019; Cell, 2018).

2) We have established large biobanks and specialized disease cohorts for multiple reproductive disorders, such as premature ovarian insufficiency (POI), polycystic ovary syndrome (PCOS). By whole-exome-sequencing and genome-wide association studies, we portraited the genetic landscape underlying POI and identified novel susceptible genes/loci for PCOS (Nat Med, 2023; NEJM, 2019; Nat Genet, 2011&2012).

3) We have finished a series of multi-center randomized controlled clinical trials (RCT) to provide first-level evidences and guidance for the efficacy and safety of strategies in ART. We proposed that the freeze-only strategy favors the high responders in increasing their live birth rate (NEJM, 2016) while for normal responders the conventional fresh embryo transfer strategy presents with similar pregnancy outcomes (NEJM, 2018). In contrast to fresh single blastocyst transfer, frozen single blastocyst transfer increased live birth rates and significantly reduced multiple pregnancy rates (The Lancet, 2019). We also clarified the scope of application of preimplantation genetic testing for aneuploidy and (NEJM, 2021), and revealed that among women with recurrent implantation failure, treatment with prednisone cannot improve the live birth rate compared with placebo (JAMA, 2023).

Our work significantly contributes to advancing knowledge in reproductive medicine and advocates for the standardization of the diagnosis and treatment of reproductive endocrine diseases. The work in Science has been included in the China's TOP10 breakthroughs in life science in 2022. Robert L. Barbieri, the Chairman Emeritus of Obstetrics and Gynecology and Reproductive Biology, Brigham and Women's Hospital said "China has become the world's leader in clinical trials of fertility treatment".

### **Main Publications:**

1. Yan J#, Qin Y#, Zhao H#, Sun Y#, Gong F#, Li R#, Sun X#, Ling X#, Li H#, Hao C, Tan J, Yang J, Zhu Y, Liu F, Chen D, Wei D, Lu J, Ni T, Zhou W, Wu K, Gao Y, Shi Y, Lu Y, Zhang T, Wu W, Ma X, Ma H, Fu J, Zhang J, Meng Q, Zhang H, Legro RS, Chen ZJ\*. Live Birth with or without Preimplantation Genetic Testing for Aneuploidy. **N Engl J Med.** 2021;385(22):2047-2058.
2. Qin Y#, Zhang F, Chen ZJ\*. BRCA2 in Ovarian Development and Function. **N Engl J Med.** 2019;380(11):1086.
3. Shi Y#, Sun Y#, Hao C#, Zhang H#, Wei D#, Zhang Y#, Zhu Y, Deng X, Qi X, Li H, Ma X, Ren H, Wang Y, Zhang D, Wang B, Liu F, Wu Q, Wang Z, Bai H, Li Y, Zhou Y,



- Sun M, Liu H, Li J, Zhang L, Chen X, Zhang S, Sun X, Legro RS, Chen ZJ\*. Transfer of Fresh versus Frozen Embryos in Ovulatory Women. **N Engl J Med**. 2018;378(2):126-136.
4. Chen ZJ#, Shi Y, Sun Y, Zhang B, Liang X, Cao Y, Yang J, Liu J, Wei D, Weng N, Tian L, Hao C, Yang D, Zhou F, Shi J, Xu Y, Li J, Yan J, Qin Y, Zhao H, Zhang H, Legro RS\*. Fresh versus Frozen Embryos for Infertility in the Polycystic Ovary Syndrome. **N Engl J Med**. 2016;375(6):523-33.
5. Wei D#, Liu JY#, Sun Y#, Shi Y#, Zhang B#, Liu JQ, Tan J, Liang X, Cao Y, Wang Z, Qin Y, Zhao H, Zhou Y, Ren H, Hao G, Ling X, Zhao J, Zhang Y, Qi X, Zhang L, Deng X, Chen X, Zhu Y, Wang X, Tian LF, Lv Q, Ma X, Zhang H, Legro RS, Chen ZJ\*. Frozen versus fresh single blastocyst transfer in ovulatory women: a multicentre, randomised controlled trial. **Lancet**. 2019;393(10178):1310-1318.
6. Sun Y\*#, Cui L#, Lu Y#, Tan J#, Dong X#, Ni T#, Yan J, Guan Y, Hao G, Liu JY, Zhang B, Wei D, Hong Y, He Y, Qi J, Xu B, Lu J, Zhang Q, Zhao S, Ji X, Du X, Zhang J, Liu J, Wang J, Huang Y, Huang D, Du Y, Vankelecom H, Zhang H, Chen ZJ\*. Prednisone vs Placebo and Live Birth in Patients With Recurrent Implantation Failure Undergoing In Vitro Fertilization: A Randomized Clinical Trial. **JAMA**. 2023;329(17):1460-1468.
7. Chen X#, Ke Y#, Wu K#, Zhao H#, Sun Y, Gao L, Liu Z, Zhang J, Tao W, Hou Z, Liu H, Liu J\*, Chen ZJ\*. Key role for CTCF in establishing chromatin structure in human embryos. **Nature**. 2019;576(7786):306-310.
8. Zou Z#, Zhang C#, Wang Q#, Hou Z#, Xiong Z, Kong F, Wang Q, Song J, Liu B, Liu B, Wang L, Lai F, Fan Q, Tao W, Zhao S, Ma X, Li M, Wu K, Zhao H\*, Chen ZJ\*, Xie W\*. Translatome and transcriptome co-profiling reveals a role of TPRXs in human zygotic genome activation. **Science**. 2022;378(6615):abo7923.
9. Gao L#, Wu K, Liu Z, Yao X, Yuan S, Tao W, Yi L, Yu G, Hou Z, Fan D, Tian Y, Liu J\*, Chen ZJ\*, Liu J\*. Chromatin Accessibility Landscape in Human Early Embryos and Its Association with Evolution. **Cell**. 2018;173(1):248-259.
10. Ke H#, Tang S#, Guo T#, Hou D, Jiao X, Li S, Luo W, Xu B, Zhao S, Li G, Zhang X, Xu S, Wang L, Wu Y, Wang J, Zhang F\*, Qin Y\*, Jin L\*, Chen ZJ\*. Landscape of pathogenic mutations in premature ovarian insufficiency. **Nat Med**. 2023;29(2):483-492.

### **Facilities & Resources:**

Our state-of-the-art facilities and cutting-edge technology enable us to conduct research that is both rigorous and innovative. We have a comprehensive suite of specialized laboratories with advanced instrumentation, including high-resolution microscopy systems, microinjection operating systems, flow cytometry-based cell analysis and sorting platforms, and molecular biology platforms. We have established

large biobanks (2,800,000 samples), specialized disease cohorts (50,000 cases) for multiple reproductive disorders (POI, PCOS, EPL, etc.), and ARTKID cohorts (20,000 parent–offspring trios, follow-up to adolescence), to enable elucidating the mechanisms involved in reproductive disorders and evaluating the offspring health of ART.

**Collaborations & Partnerships:**

We believe in the power of collaboration. That's why we have forged partnerships with international institutes, including Harvard Medical School, National Institutes of Health, Yale University School of Public Health, Baylor College of Medicine, Penn State College of Medicine, and University of British Columbia, and national institutes including but not limited to The Chinese University of Hong Kong, Tsinghua University, University of Chinese Academy of Sciences, Shanghai Jiao Tong University, Nanjing Medical University, and Chinese Academy of Sciences (Kunming Institute of Zoology) to further advance our research.

**Recreational Activities:**

We pulsate with diverse activities and thrive on a collaborative and supportive team culture. From weekly journal clubs to high-level lectures, there's always something happening. We host guest lectures by renowned experts to present cutting-edge research findings, and encourage lively discussions and knowledge-sharing. Our philosophy is "Enjoyable work, healthy life—a harmonious blend of productivity and well-being." Currently, our center offers a variety of leisure pursuits tailored to student's interests and hobbies, including basketball, football match, yoga sessions, professional development workshops and more. We also organize dinners for festivals, when we come together, share our thoughts, and celebrate achievements. Our team bonds over shared goals and a passion for reproductive health.

**Other Features:**

N/A

**Contact:**

For more information or inquiries, please contact us at [conghongbin@sduivf.com](mailto:conghongbin@sduivf.com) or visit our website at <http://www.sduivf.sdu.edu.cn>.

## Lab of Kidney Disease Pathogenesis and Intervention Strategies Research

### **Establishment and Development:**

Kidney diseases pose a significant health threat to the public. It has been reported that CKD affects more than 10% of the general population worldwide. One of the major challenges in the treatment of CKD is the restoration of kidney function and structure, which involves intricate systemic processes and requires the utilization of various approaches, including the discovery of new drugs, stem cell therapy, and the application of organoids. Therefore, developing new therapies for CKD depends on interdisciplinary collaboration and cutting-edge technology. Our lab takes multidisciplinary approaches to perform comprehensive and multi-dimensional research on kidney diseases and has made significant breakthroughs in elucidating the pathophysiology of kidney injury, analyzing protein structures, identifying targets, synthesizing potential drugs, and culturing diverse organoids. We have published over 150 papers in high-level peer-reviewed journals such as Cell Metabolism, Nature Communications, Kidney International, and JASN. We aim to integrate multiple research approaches to discover risk populations, target genes, molecular mechanisms, and innovative interventions for Kidney diseases.

### **Team Members:**

Our team is composed of three doctoral supervisors including Dr. Fan Yi, Dr. Tang Wei, Dr. Yusheng Xie. Prof. Yi is the leader of Science Fund for Creative Research Groups of the National Natural Science Foundation of China, winner of the National Science Fund for Distinguished Young Scholars. Dr. Yi's research interests are focused on investigating kidney diseases pathophysiology, especially the kidney regional immunity and epigenetic regulation mechanism. Dr. Yi has published more than 120 articles, with 8327 citations and an H-index of 49. The published manuscripts have garnered considerable interest and acclaim within the international scholarly community. The manuscript published in Cell Metabolism was distinguished as the cover article and was accompanied by an editorial commentary. Furthermore, the study published on Nature Communications received commendation from F1000. Three articles published on the Kidney International were honored with special editorial commentaries.

Dr. Tang's research interest focuses on regulation DNA damage and repairment in kidney disease. The goal is to explore the novel strategies for acute kidney injuries. Dr. Tang has published several high-level papers such as Science, Molecular Therapy.

Dr. Xie is mainly engaged in the investigation of chemical tools for recognition and intervention of the epigenetic regulation. His discovery led to the development of a Sirt2 drug screening platform and the pursuit of targeted drug discovery. Furthermore, Dr. Xie underscored the critical role of innovative chemical biology tools in the fundamental theoretical exploration of post-translational modification (PTM)-related protein machinery, as well as in the translational application of strategic interventions.

### **Research Areas:**

Our research emphasizes the role of local immune responses, metabolic homeostasis

regulation, and epigenetic modifications in renal diseases. The study systematically elucidates the impact of various immunity-related and metabolism-related molecules on kidney diseases. Moreover, the research conducts systematic studies on the functions of novel GPCRs in renal damage, especially in renal aging, providing a significant theoretical and experimental foundation for identifying new drug targets and developing preventive and therapeutic strategies for kidney diseases.

### **Research Achievements:**

Our research team is dedicated to unraveling kidney disease mechanisms, emphasizing local immune regulation, epigenetic regulation mechanisms, and GPCR signaling. These studies aim to identify new drug targets and provide theoretical and experimental foundations for the prevention and treatment of kidney diseases. We were the first to clarify the involvement of pattern recognition receptors like NOD2 in podocyte damage and insulin resistance, potentially triggering kidney-specific immune responses and podocyte injury (*Kidney international 2013, Hypertension 2013*). This research was highlighted in *Kidney International* with editorial commentary. Further studies showed that JAML exacerbates podocyte damage by disrupting lipid metabolism, with these findings featured on the cover of *Cell Metabolism*. The team's exploration of kidney-specific immune responses, particularly the function of resident memory T cells, has opened new therapeutic avenues for kidney diseases. (*Molecular Therapy 2020, Kidney international 2017*). Using cryo-electron microscopy, We've detailed the roles of specific GPCR subtypes in kidney injury, uncovering changes in adhesion-class GPCR receptors and steroid hormone patterns during kidney repair processes. The related results were published in *Nature Chemical Biology and JASN*, providing insights for GPCR-targeted drug development in kidney diseases.

Notably, we also conduct series research on epigenetic modification mechanism in kidney disease. We identified HDAC4 and Sirt6 as the key enzymes involved in kidney diseases and participated podocyte injury in diabetic nephropathy and hypertension-induced kidney damage. Related results have published *Kidney International* and *Nature Communications*, featured by F1000 recommendation. Related results also have published in *Circulation Research*, which was selected as the cover article and honored by editorial commentary.

### **Main Publications:**

Selected publications in last 5 years (\*represents the corresponding authors).

1. Fu Y#, Sun Y#, Wang M, Hou YF, Huang W, Zhou D, Wang ZY, Yang ST, Tang W, Zhen JH, Li YJ, Wang XJ, Liu M, Zhang Y, Wang B, Liu GY, Yu X, Sun J, Zhang C, and Yi F\*. Elevation of JAML Promotes Diabetic Kidney Disease by Modulating Podocyte Lipid Metabolism. *Cell Metabolism*, 2020; 32(6):1052-1062. **(Cover paper, this article was honored by an editorial commentary, Citations: 75).**
2. Guo J, Wang Z, Wu J, Liu M, Li M, Sun Y, Huang W, Li Y, Zhang Y, Tang W, Li X, Zhang, C, Hong F, Li N, Nie J, and Yi F\*. Endothelial SIRT6 Is Vital to Prevent Hypertension and Associated Cardiorenal Injury Through Targeting Nkx3.2-GATA5

Signaling. *Circulation Research*, 2019;124(10):1448-1461. (Cover paper, this article was highlighted in “In this issue” and was honored by an editorial commentary, Citations: 106).

3. Liu M, Liang K, Zhen J, Zhou M, Wang X, Wang Z, Wei X, Zhang Y, Sun Y, Zhou Z, Su H, Zhang C, Li N, Gao C, Peng J, and Yi F\*. Sirt6 deficiency exacerbates podocyte injury and proteinuria through targeting Notch signaling. *Nature Communications*, 2017;8(1):413. (F1000 recommendation, Citations: 230).

4. Lin H#, Xiao P#, Bu RQ#, Guo SC#, Yang Z#, Yuan DP#, Zhu ZL, Zhang CX, He QT, Zhang C, Ping YQ, Zhao RJ, Ma CS, Liu CH, Zhang XN, Jiang D, Huang SH, Xi YT, Zhang DL, Xue CY, Yang BS, Li JY, Lin HC, Zeng XH, Zhao H, Xu WM, Yi F\*, Liu ZM\*, Sun JP\*, Yu, X\*. Structures of the ADGRG2–Gs complex in apo and ligand-bound forms. *Nature Chemical Biology*. 2022;18(11):1196-1203.

5. Zhan P, Zhang Y, Shi, WC, Liu XH, Qiao Z, Wang ZY, Wang XJ, Wu JC, Tang W, Sun Y, Zhang Y, Zhen JH, Shang J, Liu M\*, Yi F\*. Myeloid-derived growth factor deficiency exacerbates mitotic catastrophe of podocytes in glomerular disease. *Kidney international*, 2022;102(3):546-559. (This article was highlighted in “In this issue”).

6. Zhang Y, Yang Y, Yang F, Liu X, Zhan P, Wu J, Wang X, Wang Z, Tang W, Sun Y, Zhang Y, Xu Q, Shang J, Zhen J, Liu M, Yi F\*. HDAC9-mediated epithelial cell cycle arrest in G2/M contributes to kidney fibrosis in male mice. *Nat Commun*. 2023 May 25;14(1):3007.

7. Huang W, Wang BO, Hou YF, Fu Y, Cui SJ, Zhu JH, Zhan XY, Li RK, Tang W, Wu JC, Wang ZY, Wang M, Wang XJ, Zhang Y, Liu M, Xie YS, Sun Y, Yi F\*. JAML promotes acute kidney injury mainly through a macrophage-dependent mechanism. *JCI Insight*. 2022 Jun 16;7(14):e158571.

8. Li L, Tang W, Zhang Y, Jia M, Wang L, Li Q, Han Q, Peng X, Xie Y, Wu J, Wang Z, Zhen J, Wang X, Liu M, Sun Y, Zhang C, Yi F\*. Targeting tissue-resident memory CD8+ T cells in the kidney is a potential therapeutic strategy to ameliorate podocyte injury and glomerulosclerosis. *Mol Ther*. 2022 Aug 3;30(8):2746-2759

9. Xie Y, Du S, Liu Z, Liu M, Xu Z, Wang X, Kee JX, Yi F\*, Sun H, Yao SQ. Chemical Biology Tools for Protein Lysine Acylation. *Angew Chem Int Ed Engl*. 2022 May 16;61(21):e202200303.

10. Jia M, Li L, Chen R, Du J, Qiao Z, Zhou D, Liu M, Wang X, Wu J, Xie Y, Sun Y, Zhang Y, Wang Z, Zhang T, Hu H, Sun J, Tang W, Yi F\*. Targeting RNA oxidation by ISG20-mediated degradation is a potential therapeutic strategy for acute kidney injury. *Mol Therapy*. 2023 Oct 4;31(10):3034-3051.

11. Zuo FW, Liu ZY, Wang MW, Du JY, Ding PZ, Zhang HR, Tang W, Sun Y, Wang XJ, Zhang Y, Xie YS, Wu JC, Liu M, Wang ZY, Yi F\*. CCDC92 promotes podocyte injury by regulating PA28 $\alpha$ /ABCA1/cholesterol efflux axis in type 2 diabetic mice. *Acta Pharmacol Sin*. 2024 Jan

12. Wu JC, Wang XJ, Zhu JH, Huang XY, Liu M, Qiao Z, Zhang Y, Sun Y, Wang ZY, Zhan P, Zhang T, Hu HL, Liu H, Tang W, Yi F\*. GPR97 deficiency ameliorates renal interstitial fibrosis in mouse hypertensive nephropathy. *Acta Pharmacol Sin*. 2023



Jun;44(6):1206-1216.

13. Zuo F, Wang Y, Xu X, Ding R, Tang W, Sun Y, Wang X, Zhang Y, Wu J, Xie Y, Liu M, Wang Z, Yi F\*. CCDC92 deficiency ameliorates podocyte lipotoxicity in diabetic kidney disease. *Metabolism*. 2024 Jan;150:155724

14. Liu M, Zhang Y, Zhan P, Sun W, Dong C, Liu X, Yang Y, Wang X, Xie Y, Gao C, Hu H, Shi B, Wang Z, Guo C, Yi F\*. Histone deacetylase 9 exacerbates podocyte injury in hyperhomocysteinemia through epigenetic repression of Klotho. *Pharmacol Res*. 2023 Dec;198:107009.

15. 16. Su Z, Li Y, Lv H, Cui X, Liu M, Wang Z, Zhang Y, Zhen J, Tang W, Wang X, Yi F\*. CLEC14A protects against podocyte injury in mice with adriamycin nephropathy. *FASEB J*. 2021 Jul;35(7):e21711.

16. Cui X, Shi E, Li J, Li Y, Qiao Z, Wang Z, Liu M, Tang W, Sun Y, Zhang Y, Xie Y, Zhen J, Wang X, Yi F\*. GPR87 promotes renal tubulointerstitial fibrosis by accelerating glycolysis and mitochondrial injury. *Free Radic Biol Med*. 2022 Aug 20;189:58-70.

### **Facilities & Resources:**

Our team is supported by the Key Laboratory for Experimental Teratology of Ministry of Education, Shandong Key Laboratory of Infection and Immunity. We boast multi-color fluorescence flow cytometry, real-time quantitative PCR instrument, laser confocal microscope, single crystal X-ray diffractometer, small animal micro CT imaging analysis system, fluorescence microscope, laser confocal microscope, laser confocal high content imaging analysis system, scanning electron microscope, transmission electron microscope, two-photon microscope, atomic force microscope, live cell workstation, panoramic tissue multispectral imaging and quantitative analysis system, biacore biomolecular interaction analysis system, mass spectrometry instrument, single crystal X-ray diffractometer, 400 MHz fully digital superconducting nuclear magnetic resonance spectrometer, cryo-electron microscopy, Seahorse Cell Energy Analysis System XFe96, small animal Metabolism System, small animal nuclear magnetic resonance Imaging instrument, SPF grade IVC mouse feeding system and other related facilities. In addition, several national key laboratories and open laboratories available in our university. Generally, our team is equipped with many large equipments and basic instruments required for performing above studies.

### **Recreational Activities:**

There are many types of outdoor and indoor activities in our university. We have modern gymnasium, concert hall and various social groups such as badminton, basketball, running. Our university often holds interesting sports, sets up several sports and entertainment and competitions suitable for all teachers and students to participate, strengthens the physical exercise, and improves the physical health. In addition, variety show is regularly held in Baotu Spring Campus to inherit the fine tradition of Qilu Medicine of the century-old "Broad Wisdom and Truth-seeking". Many types of professional development workshops are held to communicate with famous researchers in different fields.

**Other Features:**

Totally, there are more than 30 master and doctoral graduates in our team. In our lab, joint lab meeting is held each week. Journal club is organized by graduates actively to learn the latest references. We usually hold a spring outing every year.

**Contact:**

For more information or inquiries, please contact us at [wangxiaojie@sdu.edu.cn](mailto:wangxiaojie@sdu.edu.cn) or visit our website at [https://www.en.bms.sdu.edu.cn/Departments/Department\\_of\\_Pharmacology.htm](https://www.en.bms.sdu.edu.cn/Departments/Department_of_Pharmacology.htm).

## Immunity and Liver Disease

### **Establishment and Development:**

Immunity and Liver disease was born from a shared vision and passion for the liver immune microenvironment in both physiological and pathological conditions. Considering the huge burden of liver diseases and the significant roles of immune disorders, our founders decided to establish a laboratory dedicated to identify the novel immune subsets and key regulators responsible for liver immune homeostasis and relate diseases, to illustrate the molecular mechanism and regulatory network, to develop new strategies for multiple liver diseases. The journey of Immunity and Liver disease began with the same research interests and long term close cooperation focusing on liver immunology. With a small but dedicated team, we set out to establish a research laboratory that would be recognized for its excellence and impact. Since its inception, Immunity and liver disease has gone through a remarkable journey of growth and development. We have expanded our team to include five professors, two associate professors, three postdoctors and one research assistant. Our research has evolved to address the cell interaction, metabolic and functional homeostasis of liver immune microenvironment (such as macrophages, NK cells, T cells) in both physiological and pathological conditions to investigate the important immune regulatory molecules in liver homeostasis and chronic liver diseases, to reveal the crosstalk among liver, gut, fat and other tissues and its effect in whole body homeostasis, to develop novel intervention strategies for related liver diseases. Additionally, we have carried out valuable collaborations and partnerships with Dr. Brett T Spear in University of Kentucky, Dr. Kazuya Yamagata in University of Tokyo and Dr. Nailin Li in Karolinska Institute to further enhance our research capabilities.

### **Team Members:**

Our team is composed of four doctoral supervisors. Dr. Chunhong Ma received her Ph.D degree in Immunology from Shandong University in 2002. Dr. Ma is the winner of the National Science Fund for Distinguished Young Scholars, National special support program for high-level personnel recruitment. Dr. Ma's interests are focused on investigating immune microenvironment and gene regulation in liver diseases. She has strong interests in exploring the action of important immune mediators such as Tim-3 and ZHX2 in innate and adaptive immunity, and identifying novel strategies to improve antitumor immunity.

Dr. Xiaohong Liang's research interest focuses on regulation of cancer immune microenvironment. The goal is to explore the novel strategies of tumor immunotherapy. Much of the focus is on how innate immune cells, including macrophages and NK cells, is manipulated in tumor microenvironment and involves in tumor development.

Dr. Lifen Gao is mainly engaged in the investigation of macrophage, CAR-T, metabolic related diseases and tumor immunity, and is committed to exploring the regulatory mechanism of macrophage homeostasis in related diseases, developing novel CAR-T cells for liver cancer.

Dr. Xuetian Yue's major research interest is the response of tumors to nutrient stress, including glucose, glutamine and lipids. Together, we dedicate to explore the mechanism maintaining liver immune homeostasis and related diseases and develop new intervention strategies.

### **Research Areas:**

Immunity and liver disease focuses on investigating liver immune microenvironment regulation and developing intervention strategy, systematically exploring the liver inflammation induced by viral infection, metabolism and other environmental factors and its malignant transformation mechanism. We are especially interested in the cell interaction among macrophages, NK cells, T cells and hepatocytes, as well as immune metabolism and immunosenescence in liver homeostasis and related diseases.

### **Research Achievements:**

We have made significant contributions in delineating immune microenvironment and their interaction network during HBV infection, metabolic liver diseases and the malignant transformation of non-resolving liver inflammation. Some research work have been published in *J Hepatol*, *Cell Mol Immunol*, *Gastroenterology*, etc. These studies revealed an important mechanism of NK dysfunction, macrophage polarization, identified the key role of Tim-3, ZHX2 and Tipe1 in chronic viral infection mediating non-resolving inflammation and liver cancer pathogenesis, opening up a new field for HCC diagnosis and intervention. Recently, we focused on liver immune microenvironment regulation and intervention strategy research. We systematically explored the liver inflammation induced by viral infection, metabolism and other environmental factors and its malignant transformation mechanism. We identified the crucial roles of several important checkpoints including Tim-3, ZHX2, Siglec-9, Tipe1, Tim-4 in regulating T cells, NK cells, macrophages or hepatocytes, which provides new targets and strategies for liver cancer and virus infection (*Sci Transl Med.* 2023, *J Exp Med.* 2021, *J Hepatol.* 2024, *Cancer Res.* 2023, *Cell Death Differ.* 2023, *Cell Rep.* 2022, *Nat Commun.* 2023, etc.). We documented the regulatory mechanisms of nutrient deprivation and metabolic reprogramming in driving liver cancer progression and inducing exhaustion of hepatic NK cells (*Redox biol.*2023, *Hepatology* 2023, *Cell Rep.* 2023, *Nat Commun.* 2023, *Mol Ther.* 2022). In addition, we elucidated the potential target for HBV related liver disease and multiple human coronaviruses (*Signal Transduct Target Ther.* 2023, *Signal Transduct Target Ther.* 2021, *Cell Mol Gastroenterol Hepatol.* 2022, *Adv Sci (Weinh).* 2022, *Cell Mol Immunol.* 2021).

### **Main Publications:**

Selected publications in last 5 years (\*represents the corresponding authors).

1. Xiao R, Tian Y, Zhang J, Li N, Qi M, Liu L, Wang J, Li Z, Zhang J, Zhao F, Wang T, Tan S, Li C, Wu Z, Yu M, Jiang X, Zhan P, Gao L, Han B, Liu X, **Liang X\***, **Ma C\***. Increased Siglec-9/Siglec-9L interactions on NK cells predict poor HCC prognosis and present a targetable checkpoint for immunotherapy. *J Hepatol.*

2024 Feb 7:S0168-8278(24)00106-5.

2. Zhang Y, Fan Y, Hu H, Zhang X, Wang Z, Wu Z, Wang L, Yu X, Song X, Xiang P, Zhang X, Wang T, Tan S, Li C, Gao L, Liang X, Li S, Li N, **Yue X\***, **Ma C\***. ZHX2 emerges as a negative regulator of mitochondrial oxidative phosphorylation during acute liver injury. *Nat Commun.* 2023 Nov 18;14(1):7527.
3. Ma S, Tian Y, Peng J, Chen C, Peng X, Zhao F, Li Z, Li M, Zhao F, Sheng X, Zong R, Li Y, Zhang J, Yu M, Zhu Q, Tian X, Li Y, Neckenig MR, Liu H, Zhan P, Yue X, Wu Z, Gao L, Liang X, **Liu X\***, **Li C\***, **Ma C\***. Identification of a small-molecule Tim-3 inhibitor to potentiate T cell-mediated antitumor immunotherapy in preclinical mouse models. *Sci Transl Med.* 2023 Nov 15;15(722):eadg6752.
4. Tan S, Wang Z, Li N, Guo X, Zhang Y, Ma H, Peng X, Zhao Y, Li C, Gao L, Li T, **Liang X\***, **Ma C\***. Transcription factor Zhx2 is a checkpoint that programs macrophage polarization and antitumor response. *Cell Death Differ.* 2023 Sep;30(9):2104-2119.
5. Kong Y, Wu M, Wan X, Sun M, Zhang Y, Wu Z, Li C, Liang X, Gao L, Ma C, **Yue X\***. Lipophagy-mediated cholesterol synthesis inhibition is required for the survival of hepatocellular carcinoma under glutamine deprivation. *Redox Biol.* 2023 Jul;63:102732.
6. Tian P, Yang W, Guo X, Wang T, Tan S, Sun R, Xiao R, Wang Y, Jiao D, Xu Y, Wei Y, Wu Z, Li C, Gao L, **Ma C\***, **Liang X\***. Early life gut microbiota sustains liver-resident natural killer cells maturation via the butyrate-IL-18 axis. *Nat Commun.* 2023 Mar 27;14(1):1710.
7. Wang Y, Wang Y, Ding L, Ren X, Wang B, Wang L, Zhao S, Yue X, Wu Z, Li C, Liang X, Ma C, **Gao L\***. Tim-4 reprograms cholesterol metabolism to suppress antiviral innate immunity by disturbing the Insig1-SCAP interaction in macrophages. *Cell Rep.* 2022 Nov 29;41(9):111738.
8. Guo X, Tan S, Wang T, Sun R, Li S, Tian P, Li M, Wang Y, Zhang Y, Yan Y, Dong Z, Yan L, Yue X, Wu Z, Li C, Yamagata K, Gao L, Ma C, **Li T\***, **Liang X\***. NAD<sup>+</sup> salvage governs mitochondrial metabolism, invigorating natural killer cell antitumor immunity. *Hepatology.* 2023 Aug 1;78(2):468-485.
9. Cheng Y, Bai F, Ren X, Sun R, Guo X, Liu W, Wang B, Yang Y, Zhang X, Xu Y, Li C, Yang X, Gao L, Ma C, **Li X\***, **Liang X\***. Phosphoinositide-Binding Protein TIPE1 Promotes Alternative Activation of Macrophages and Tumor Progression via PIP3/Akt/TGF $\beta$  Axis. *Cancer Res.* 2022 Apr 15;82(8):1603-1616.
10. Tan S, Guo X, Li M, Wang T, Wang Z, Li C, Wu Z, Li N, Gao L, Liang X, **Ma C\***. Transcription factor Zhx2 restricts NK cell maturation and suppresses their antitumor immunity. *J Exp Med.* 2021 Sep 6;218(9):e20210009.



11. Sun Y, Teng Y, Wang L, Zhang Z, Chen C, Wang Y, Zhang X, Xiang P, Song X, Lu J, Li N, Gao L, Liang X, Xia Y, **Wu Z\***, **Ma C\***. LINC01431 Promotes Histone H4R3 Methylation to Impede HBV Covalently Closed Circular DNA Transcription by Stabilizing PRMT1. *Adv Sci (Weinh)*. 2022 May;9(16):e2103135.
12. Wang L, Sun Y, Song X, Wang Z, Zhang Y, Zhao Y, Peng X, Zhang X, Li C, Gao C, Li N, Gao L, Liang X, **Wu Z\***, **Ma C\***. Hepatitis B virus evades immune recognition via RNA adenosine deaminase ADAR1-mediated viral RNA editing in hepatocytes. *Cell Mol Immunol*. 2021 Aug;18(8):1871-1882.

### **Facilities & Resources:**

Our state-of-the-art facilities and cutting-edge technology enable us to conduct research that is both rigorous and innovative. Our team is supported by the Key Laboratory for Experimental Teratology of Ministry of Education, Shandong Key Laboratory of Infection and Immunity. We boast multi-color fluorescence flow cytometry, real-time quantitative PCR instrument, laser confocal microscope, single crystal X-ray diffractometer, small animal micro CT imaging analysis system, fluorescence microscope, laser confocal microscope, laser confocal high content imaging analysis system, scanning electron microscope, transmission electron microscope, two-photon microscope, atomic force microscope, live cell workstation, panoramic tissue multispectral imaging and quantitative analysis system, biacore biomolecular interaction analysis system, mass spectrometry instrument, single crystal X-ray diffractometer, 400 MHz fully digital superconducting nuclear magnetic resonance spectrometer, cryo-electron microscopy, Seahorse Cell Energy Analysis System XFe96, small animal Metabolism System, small animal nuclear magnetic resonance Imaging instrument, SPF grade IVC mouse feeding system and other related facilities. In addition, several national key laboratories and open laboratories available in our university. Generally, our team is equipped with many large equipments and basic instruments required for performing above studies.

### **Collaborations & Partnerships:**

We believe in the power of collaboration. That's why we have carried out collaborations with Dr. Brett T Spear from University of Kentucky, Dr. Kazuya Yamagata from University of Tokyo, Dr. Nailin Li from Karolinska Institute, Dr. Zhigang Tian from University of Science and Technology of China, Prof. Youhai Chen from Shenzhen University of Technology, Prof. Jianwei Wang from Chinese Academy of Medical Sciences and Peking Union Medical College, Dr. Jinming Yu from Shandong First Medical University, etc. In addition, we have established stable cooperative relations with professors of different disciplines in Shandong University including Hong Liu and Yuanhua Sang (State Key Laboratory of Crystal Materials), Xinyong Liu and Minyong Li (Key Laboratory of Chemical Biology of Ministry of Education), Jiwei Cui (School of Chemistry and Chemical Engineering) to further advance our research.

**Recreational Activities:**

There are many types of outdoor and indoor activities in our university. We have modern gymnasium, concert hall and various social groups such as badminton, basketball, running. Our university often holds interesting sports, sets up a number of sports and entertainment and competitions suitable for all teachers and students to participate, strengthens the physical exercise, and improves the physical health. In addition, variety show is regularly held in Baotu Spring Campus to inherit the fine tradition of Qilu Medicine of the century-old "Broad Wisdom and Truth-seeking". Many types of professional development workshops are held to communicate with famous researchers in different fields.

**Other Features:**

Totally, there are more than 60 master and doctoral graduates in our team. In our lab, joint lab meeting is held each week. Journal club is organized by graduates actively to learn the latest references. Christmas symposium is regularly held during Christmas to talk about the achievements and projects. In order to better relax, we usually hold a spring outing or autumn outing every year. We go hiking and skiing together.

**Contact:**

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## Lab of Receptor Biology and Pharmacology

### Research Direction:

Our research is dedicated to the study of receptor biology and pharmacology.

### Establishment and Development:

Jinpeng Sun, the lab founder, engaged in the GPCR study during his postdoctoral research in the lab of Prof. Robert J Lefkowitz (2012 Nobel Laureate in Chemistry, the founder of the GPCR research area) at Duke University.

### Education

1998	B.Sc.	University of Science and Technology of China (USTC).
2001	M.S.	University of Science and Technology of China (USTC).
2007	PhD.	Albert Einstein College of Medicine, Bronx, New York. (USA)

### Postdoctoral Training

2007-2011                      Research Associate.

Advisor: Robert Lefkowitz, James B. Duke Professor of Medicine and Biochemistry and Investigator, Howard Hughes Medical Institute (2012 Nobel Prize)

In February 2011, Dr sun returned to China, and was hired a full-time job at Shandong University, and work as professor and PhD supervisor. Since then, Prof. Sun established the lab of Membrane Receptor and Drug Target with international cultural atmosphere. In 2021, Prof Sun was appointed as executive vice president of the Advanced Medical Research Institute. In 2018, Prof Sun was awarded [the National Science Fund for Distinguished Young Scholars in Pharmacology](#). And since December 2023, Prof Sun took up the position of the executive vice president of Cheeloo College of Medicine, Shandong University.

Sun lab has been conducting research on membrane receptors and drug targets for more than a decade. We have carried out in-depth studies centering on [GPCR de-orphanization in sensory system](#), [GPCR ligand discovery and recognition mechanism](#); [GPCR functional diversity and development of functional biased drugs](#), and achieved a series of original results. (1) We have revealed the coding mechanism of GPCRs for olfactory, itch and force sensation, and explained the basic process of these life activities at the molecular level. (2) We have clarified the molecular mechanism of fatty acid and peptide hormone recognition by GPCR, and developed lead drugs for the treatment of diabetes, obesity, atopic dermatitis, and schizophrenia by targeting these GPCR receptors. (3) We have put forward a series of working models of the GPCR-arrestin signal pathway, and carried out a series of biased drug discovery and development according to these models. The working models of bias signal include: the "flute model" of GPCR receptor phospho-patterns, the theory of polyproline rich region dockine sites and allosteric regulation, and the mechanism of receptor core-induced and ligand-dependent conformational changes in

arrestin.function. These models provide a theoretical explanation for the diversity of receptor function selectivity and a theoretical basis for the design of biased drugs. (4) We have discovered the membrane receptors of glucocorticoids, progesterone and other steroid hormones, providing important theoretical support for the function and pharmacological effects of non-nuclear receptors of steroid hormones, which filled the gaps of steroid hormone receptor theory in textbooks.

In recent years, Prof Sun has published more than 80 articles in Nature (7 articles), Science, Cell (2 articles), Cell Metab, Nat Chem Biol (3 articles), Nat Metab and other well-known journals as corresponding author, and has been invited to give presentations in international and domestic academic conferences. Our researches have imposed profound impact in GPCR area. Prof Sun has been awarded the New Cornerstone Investigator Program (2023), the National Science Fund for Distinguished Young Scholars (2018), C.C.TAN (JIA-ZHEN TAN) Life Science Award (2022), The Second Prize of Chinese Medical Science Prize (2022), and the Third Session of National Award for Excellence in Innovation (2023). Currently, Prof Sun is presiding a number of funds such as National key research and development program, Key Program and General Program; of National Natural Science Foundation of China, Key Program of Beijing Municipal Natural Science Foundation.

#### **Team Members:**

Our team comprises top experts in the field, including 6 professors, among whom are:



Sun Jinping, Professor, Doctoral Supervisor and Vice Dean of Cheeloo College of Medicine, Shandong University, Dean of the School of Advanced Medical Research at Shandong University, Recipient of the National Science Fund for Distinguished Young Scholars, New Cornerston Investigator, Recipient of 15th Tan Life Science Innovation Award in 2022.



Yang Fan, Professor, Doctoral Supervisor, Recipient of the National Science Fund for Excellent Young Scholars, Shandong Province Science Fund for Distinguished Young Scholars, and Second Prize of the Chinese Medical Science and Technology Award



Xiao Peng, Professor, Doctoral Supervisor, Recipient of the National Science Fund for Excellent Young Scholars, Shandong Province Science Fund for Excellent Young Scholars, Youth Taishan scholar and Second Prize of the Chinese Medical Science and Technology Award.



Zhang pengju, Professor, Doctoral Supervisor.



Guo lulu, Professor, Doctoral Supervisor, supported by Young Elite Scientists Sponsorship Program. Young Expert of Shandong Taishan Scholar Program. Qilu Young Scholar of Shandong University.

Additionally, our team includes a group of young and passionate researchers, consisting of 7 post-doctoral fellows and nearly 50 graduate students. They tirelessly work together on research related to membrane receptor GPCR.





### **Research Areas:**

The lab of Sun has long been focused on microenvironment pharmacology, engaging in research on GPCR decoupling, ligand discovery, cellular mechanisms of functional diversity, and the development of preferential drugs. We have discovered multiple endogenous ligands of GPCR, developed the pharmacological theory of arrestin-mediated GPCR biased signaling transduction, and established a series of biased intervention strategies.

### **Research Achievements:**

We have made significant contributions in microenvironment pharmacology, membrane receptor G protein coupled receptor (GPCR) for a long time. We have systematically studied the mechanism of GPCR sensing microenvironment and regulating physiological function, analyzed the molecular mechanism of GPCR sensing itch, smell, force and carbon-carbon double bond, discovered the recognition of steroid hormone membrane receptor subfamily, and realized the identification of many important GPCR endogenous ligands. We have explored receptors for auditory and vestibular sensations and identified a subfamily of membrane receptors that recognize steroids. Additionally, we have developed a systematic ligand-receptor screening method, identifying over 20 important GPCRs, including endogenous ligands for multiple drug target receptors involved in metabolism, such as the insulin peptide ligand for the olfactory receptor OLF1R109 in pancreatic islets, and fatty acid ligands for GPR120 and GPR132, providing intervention strategies for metabolic diseases. A series of working models of GPCR preference are also proposed, including the flute model of GPCR signal transduction and the theory of proline terminal separation, which lays a theoretical foundation for the development of GPCR preference ligands. we have published more than 80 articles in Nature (×7), Science (×1, cover article), Cell (×2, 1 cover articles), Nature Metabolism (×1), Cell Metabolism (×1), Nat Chem Biol (×3), Cell Research (×2), PNAS (×6), Nat Commun (×7) and so on. Recently, our research on the molecular mechanisms of olfactory perception was successfully selected as one of China's Top 10 Scientific Advances in 2023.

### **Main Publications:**

1. Shang P, Rong NK, Jiang JJ, Cheng J, Zhang MH, Kang DW, Qi L, Guo LL, Yang GM, Liu Q, Zhou ZZ, Li XB, Zhu KK, Meng QB, Han X, Yan WQ, Kong YL, Yang LJ, Wang XH, Lei DP, Feng X, Liu XY, Yu X, Wang Y#, Li Q#, Shao ZH#, Yang F#, Sun JP#. **Structural and signaling mechanism of TAAR1 enabled preferential agonist design.** Cell. (IF 64.5)2023
2. Xu Z, Guo L, Yu JJ, Shen SY, Wu C, Zhang WF, Zhao C, Deng Y, Tian XW, Feng YY, Hou HL, Su LT, Wang HS, Guo S, Wang HL, Wang KX, Chen PP, Zhao J, Zhang XY, Yong XH, Cheng L, Liu LX, Yang SY, Yang F, Wang XH, Yu X#, Xu YF#, Sun JP#, Yan W#, Shao ZH#. **Ligand recognition and G-protein coupling of trace amine receptor TAAR1.** Nature. (IF 64.8) 2023
3. Guo L, Cheng J, Lian S, Liu Q, Lu Y, Zheng Y, Zhu K, Zhang M, Kong Y, Zhang C, Rong N, Zhuang Y, Fang G, Jiang J, Zhang T, Han X, Liu Z, Xia M, Liu S, Zhang L, Liberles SD, Yu X, Xu Y#, Yang F#, Li Q#, Sun JP#. **Structural basis**

- of amine odorant perception by a mammal olfactory receptor.** *Nature.* (IF 64.8) 2023 Jun;618(7963):193-200.
4. Mao C, Xiao P, Tao XN, Qin J, He QT, Zhang C, Guo SC, Du YQ, Chen LN, Shen DD, Yang ZS, Zhang HQ, Huang SM, He YH, Cheng J, Zhong YN, Shang P, Chen J, Zhang DL, Wang QL, Liu MX, Li GY, Guo Y, Xu HE, Wang C, Zhang C, Feng S#, Yu X#, Zhang Y#, Sun JP#. **Unsaturated bond recognition leads to biased signal in a fatty acid receptor.** *Science.* (IF 56.9) 2023 Apr 7;380(6640):eadd6220.
  5. Ping YQ, Xiao P, Yang F, Zhao RJ, Guo SC, Yan X, Wu X, Zhao FH, Zhou FL, Xi YT, Yin WH, He FD, Zhang DL, Zhu ZL, Jiang Y, Torsten Schöneberg, Ines Liebscher#, Xu H. Eric#, Sun JP#. **Structural basis for the tethered peptide activation of adhesion GPCRs.** *Nature.* (IF 64.8) . 2022. 2022 Apr;604(7907):763-770.
  6. Yang F, Guo L, Li Y, Wang G, Wang J, Zhang C, Fang GX, Chen X, Liu L, Yan X, Liu Q, Qu C, Xu Y, Xiao P, Zhu Z, Li Z, Zhou J, Yu X, Gao N#, Sun JP#. **Structure, function and pharmacology of human itch receptor complexes.** *Nature.* (IF 64.8) 2021 Dec;600(7887):164-169.
  7. Ping YQ, Mao C, Xiao P, Zhao RJ, Jiang Y, Yang Z, An WT, Shen DD, Yang F, Zhang H, Qu C, Shen Q, Tian C, Li ZJ, Li S, Wang GY, Tao X, Wen X, Zhong YN, Yang J, Yi F, Yu X, Xu HE#, Zhang Y#, Sun JP#. **Structures of the glucocorticoid-bound adhesion receptor GPR97-Go complex.** *Nature.* (IF 64.8) 2021 Jan;589(7843):620-626.
  8. Xiao P, Guo S, Wen X, He QT, Lin H, Huang SM, Gou L, Zhang C, Yang Z, Zhong YN, Yang CC, Li Y, Gong Z, Tao XN, Yang ZS, Lu Y, Li SL, He JY, Wang C, Zhang L#, Kong L#, Sun JP#, Yu X#. **Tethered peptide activation mechanism of the adhesion GPCRs ADGRG2 and ADGRG4.** *Nature.* (IF 64.8) 2022 Apr;604(7907):771-778.
  9. Yang F, Mao C, Guo L, Lin J, Ming Q, Xiao P, Wu X, Shen Q, Guo S, Shen DD, Lu R, Zhang L, Huang S, Ping Y, Zhang C, Ma C, Zhang K, Liang X, Shen Y, Nan F, Yi F, Luca VC, Zhou J, Jiang C, Sun JP#, Xie X#, Yu X#, Zhang Y#. **Structural basis of GPBAR activation and bile acid recognition.** *Nature.* (IF 64.8) 2020 Nov;587(7834):499-504.
  10. Xiao P, Yan W, Gou L, Zhong YN, Kong L, Wu C, Wen X, Yuan Y, Cao S, Qu C, Yang X, Yang CC, Xia A, Hu Z, Zhang Q, He YH, Zhang DL, Zhang C, Hou GH, Liu H, Zhu L, Fu P, Yang S, Rosenbaum DM, Sun JP#, Du Y#, Zhang L#, Yu X#, Shao Z#. **Ligand recognition and allosteric regulation of DRD1-Gs signaling complexes.** *Cell.* (IF 64.5) 2021 Feb 18;184(4):943-956.e18.
  11. Yan Z, Wang JY, Yang F, Zhu KK, Wang PG, Guan Y, Ning SL, Lu Y, Li Y, Zhang C, Zheng Y, Zhou SH, Wang XW, Wang MW, Xiao P, Yi F, Zhang C, Zhang PJ, Xu F, Liu BH, Zhang H, Yu X #, Gao N#, Sun JP#. **Cryo-EM structure of the X-linked acrogigantism-related orphan GPR101-Gs complex enabled identification of ligands with rejuvenating potential.** *Nat Chem Biol.* (IF 14.8) 2023 accept.
  12. Lin H, Xiao P, Bu RQ, Guo S, Yang Z, Yuan D, Zhu ZL, Zhang CX, He QT, Zhang C, Ping YQ, Zhao RJ, Ma CS, Liu CH, Zhang XN, Jiang D, Huang S, Xi YT, Zhang DL, Xue CY, Yang BS, Li JY, Lin HC, Zeng XH, Zhao H, Xu WM, Yi F#, Liu Z#, Sun JP#, Yu X#. **Structures of the ADGRG2-Gs complex in apo and ligand-bound forms.** *Nat Chem Biol.* (IF 14.8) 2022 Nov;18(11):1196-1203.

13. Yang F, Xiao P, Qu CX, Liu Q, Wang LY, Liu ZX, He QT, Liu C, Xu JY, Li RR, Li MJ, Li Q, Guo XZ, Yang ZY, He DF, Yi F, Ruan K, Shen YM, Yu X, Sun JP#, Wang JY#. Allosteric mechanisms underlie GPCR signaling to SH3-domain proteins through arrestin. (IF 14.8) *Nat Chem Biol* 2018 Sep;14(9):876-886.
14. Cheng J, Yang Z, Ge XY, Gao MX, Meng R, Xu X, Zhang YQ, Li RZ, Lin JY, Tian ZM, Wang J, Ning SL, Xu YF, Yang F, Gu JK, Sun JP#, Yu X#. Autonomous sensing of the insulin peptide by an olfactory G protein-coupled receptor modulates glucose metabolism. *Cell Metab.* (IF 29.0) 2022 Feb 1;34(2):240-255.
15. Wang JL, Dou XD, Cheng j, Gao MX, Xu GF, Ding W, Ding JH, Li y, Wang SH, Ji ZW, Zhao XY, Huo TY, Zhang CF, Liu YM, Sha XY, Gao JR, Zhang WH, Hao Y, Zhang C, Sun JP#, Jiao N# and Yu X#. Functional screening and rational design of compounds targeting GPR132 to treat diabetes. *Nat Metab.* (IF 20.1) 2023 accept.
16. Chen Y, Mao C, Gu R, Zhao R, Li W, Ma Z, Jia Y, Yu F, Luo J, Fu Y, Sun J#, Kong W#. Nidogen-2 is a Novel Endogenous Ligand of LGR4 to Inhibit Vascular Calcification. *Circ Res.* (IF 20.1) 2022 Dec 2;131(12):1037-1054.
17. An W, Lin H, Ma L, Zhang C, Zheng Y, Cheng Q, Ma C, Wu X, Zhang Z, Zhong Y, Wang M, He D, Yang Z, Du L, Feng S, Wang C, Yang F, Xiao P#, Zhang P#, Yu X#, Sun JP#. Progesterone activates GPR126 to promote breast cancer development via the Gi pathway. *Proc Natl Acad Sci USA.* (IF 11.1) . 2022 Apr 12;119(15):e2117004119.
18. Huang SM, Xiong MY, Liu L, Mu J, Wang MW, Jia YL, Cai K, Tie L, Zhang C, Cao S, Wen X, Wang JL, Guo SC, Li Y, Qu CX, He QT, Cai BY, Xue C, Gan S, Xie Y, Cong X, Yang Z, Kong W, Li S, Li Z, Xiao P, Yang F, Yu X, Guan YF, Zhang X#, Liu Z#, Yang BX#, Du Y#, Sun JP#. Single hormone or synthetic agonist induces Gs/Gi coupling selectivity of EP receptors via distinct binding modes and propagating paths. *Proc Natl Acad Sci U S A.* (IF 11.1) 2023 Jul 25;120(30):e2216329120.
19. Wang MW, Yang Z, Chen X, Zhou SH, Huang GL, Sun JN, Jiang H, Xu WM#, Lin HC#, Yu X#, Sun JP#. Activation of PTH1R alleviates epididymitis and orchitis through Gq and  $\beta$ -arrestin-1 pathways. *Proc Natl Acad Sci U S A.* (IF 11.1) 2021 Nov 9;118(45):e2107363118.
20. Qu CX, Park JY, Yun MW, He QT, Yang F, Kin K, Han D, Li R, T.M.Iverson, V.V.Gurevich, Sun JP#, Chung KY#. Scaffolding mechanism of arrestin-2 in the cRaf/MEK1/ERK signaling cascade. *Proc Natl Acad Sci U S A.* (IF 11.1) 2021 Sep 14;118(37):e2026491118.
21. Ma L, Yang F, Wu X, Mao C, Guo L, Miao T, Zang SK, Jiang X, Shen DD, Wei T, Zhou H, Wei Q, Li S, Shu Q, Feng S, Jiang C, Chu B, Du L#, Sun JP#, Yu X#, Zhang Y#, Zhang P#. Structural basis and molecular mechanism of biased GPBAR signaling in regulating NSCLC cell growth via YAP activity. *Proc Natl Acad Sci U S A.* (IF 11.1) 2022 Jul 19;119(29):e2117054119.
22. Fu Y, Huang Y, Yang Z, Chen Y, Zheng J, Mao C, Li Z, Liu Z, Yu B, Li T, Wang M, Xu C, Zhou Y, Zhao G, Jia Y, Guo W, Jia X, Zhang T, Li L, Liu Z, Guo S, Ma M, Zhang H, Liu B, Du J, Wang W, Tang C, Gao P, Xu Q, Wang X, Liu J, Sun JP#, Kong W#. Cartilage oligomeric matrix protein is an endogenous  $\beta$ -arrestin-2-selective allosteric modulator of AT1 receptor counteracting vascular injury. *Cell Res.* (IF 20.396) 2021 Jul;31(7):773-790.
23. Wang HM, Xu YF, Ning SL, Yang DX, Li Y, Du YJ, Yang F, Zhang Y, Liang N, Yao W, Zhang LL, Gu LC, Gao CJ, Pang Q, Chen YX, Xiao KH, Yu X#, Sun JP#.

- The catalytic region and PEST domain of PTPN18 distinctly regulate the HER2 phosphorylation and ubiquitination barcodes. *Cell Research*. (IF 20.396) 2014 Sep;24(9):1067-90.
24. Guo L, Zhang Y, Fang G, Tie L, Zhuang Y, Xue C, Liu Q, Zhang M, Zhu K, You C, Xu P, Yuan Q, Zhang C, Liu L, Rong N, Peng S, Liu Y, Wang C, Luo X, Lv Z, Kang D, Yu X, Zhang C, Jiang Y, Dong X, Zhou J#, Liu Z#, Yang F#, Eric Xu H#, Sun JP#. Ligand recognition and G protein coupling of the human itch receptor MRGPRX1. *Nat Commun*. (IF 16.6) 2023 Aug 17;14(1):5004.
  25. He QT, Xiao P, Huang SM, Jia YL, Zhu ZL, Lin JY, Yang F, Tao XN, Zhao RJ, Gao FY, Niu XG, Xiao KH, Wang J#, Jin C#, Sun JP#, Yu X#. Structural studies of phosphorylation-dependent interactions between the V2R receptor and arrestin-2. *Nat Commun*. (IF 13.691). 2021 Apr 22;12(1):2396.
  26. Liu Q, He QT, Lyu X, Yang F, Zhu ZL, Xiao P, Yang Z, Zhang F, Yang ZY, Wang XY, Sun P, Wang QW, Qu CX, Gong Z, Lin JY, Xu Z, Song SL, Huang SM, Guo SC, Han MJ, Zhu KK, Chen X, Kahsai AW, Xiao KH, Kong W, Li FH, Ruan K, Li ZJ, Yu X, Niu XG, Jin CW, Wang J#, Sun JP#. DeSiphering receptor core-induced and ligand-dependent conformational changes in arrestin via genetic encoded trimethylsilyl 1H-NMR probe. *Nat Commun*. (IF 13.691) 2020 Sep 25;11(1):4857.
  27. Li T, Yu B, Liu Z, Li J, Ma M, Wang Y, Zhu M, Yin H, Wang X, Fu Y, Yu F, Wang X, Fang X, Sun JP#, Kong W#. Homocysteine directly interacts and activates the angiotensin II type I receptor to aggravate vascular injury. *Nat Commun*. (IF 13.691) 2018 Jan 2;9(1):11.
  28. Liu CH, Gong Z, Liang ZL, Liu ZX, Yang F, Sun YJ, Ma ML, Wang YJ, Xiao KH, Zhou Z, Yu X#, Sun JP#. Arrestin biased GPCR agonism induces acute catecholamine secretion through TRPC3 coupling. *Nat Commun*. (IF 13.691) 2017 Feb 9;8:14335.
  29. Yang F, Yu X, Liu C, Qu CX, Gong Z, Liu HD, Li FH, Wang HM, He DF, Yi F, Song C, Tian CL, Xiao KH, Wang JY#, Sun JP#. Phospho-selective mechanisms of arrestin conformations and functions revealed by unnatural amino acid incorporation and 19F-NMR. *Nat Commun*. (IF 13.691) 2015 Sep 8;6:8202.
  30. Lu S#, He X, Yang Z, Chai Z, Zhou S, Wang J, Rehman AU, Ni D, Pu J, Sun JP#, Zhang J#. Activation pathway of a G protein-coupled receptor uncovers conformational intermediates as targets for allosteric drug design. *Nat Commun*. (IF 13.691) 2021 Aug 5;12(1):4721.
  31. Dong JH, Wang YJ, Cui M, Wang XJ, Zheng WS, Ma ML, He DF, Hu QX, Zhang DL, Ning SL, Liu CH, Wang C, Wang Y, Li XY, Lin A, Kahsai A, Cahill III T, Chen ZY, Yu X, Sun JP#. Adaptive activation of a stress response pathway improves learning and memory through Gs and  $\beta$ -arrestin-1 regulated lactate metabolism. *Biol Psychiatry*. (IF 12.069) 2017 Apr 15;81(8):654-670.
  32. Qu CX, Mao CY, Xiao P, Shen QY, Zhong YN, Yang F, Shen DD, Tao XN, Zhang HB, Yan X, Zhao RJ, He JY, Guan Y, Zhang C, Hou GH, Zhang PJ, Hou GG, Li ZJ, Yu X, Chai RJ#, Guan YF, Sun JP#, Zhang Y#. Ligand recognition, unconventional activation and G protein coupling of the prostaglandin E2 receptor 2 (EP2). *Science Advances* (IF 13.116) 2021 Apr 2;7(14):eabf1268.
  33. Guan Y, Du HB, Yang Z, Wang YZ, Ren R, Liu WW, Zhang C, Zhang JH, An WT, Li NN, Zeng XX, Li J, Sun YX, Wang YF, Yang F, Yang J, Xiong W, Yu X, Chai RJ, Tu XM#, Sun JP#, Xu ZG#. Deafness-Associated ADGRV1 Mutation Impairs USH2A Stability through Improper Phosphorylation of WHRN and WDSUB1 Recruitment. *Adv Sci (Weinh)*. (IF 15.1) 2023 Jun;10(16):e2205993.

34. Lin JY, Cheng J, Du YQ, Pan W, Zhang Z, Wang J, An J, Yang F, Xu YF, Lin H, An WT, Wang J, Yang Z, Chai RJ, Sha XY, Hu H.L#, Sun JP#, Yu X#. In vitro expansion of pancreatic islet clusters facilitated by hormones and chemicals. Cell Discov. (IF 10.56) 2020 Apr 7;6:20.

### Facilities & Resources:

Our laboratory has excellent basic scientific research conditions, with flow analysis center, molecular imaging/behavioral center, multi-factor detection center, cryo-electron microscope structure characterization center, medical biology high performance computing center and other platforms. Here you can perform colorful flow cytometry, 3D optical imaging analysis of live animals, behavioral video analysis, ultra-high resolution multi-mode ultrasonic photoacoustic imaging of small animals, cell energy metabolism analysis and high-resolution mass spectrometry analysis. Our laboratory is proficient in plasmid construction, cell culture, virus packaging, protein expression and purification. GPCR downstream effector recruitment and detection or second messenger detection technology were established well. Single particle cryo-electron microscope structure analysis, cryo-electron microscope data calculation and model building, molecular dynamics simulation and other technologies are also available in our lab.



**Collaborations & Partnerships:**

Our laboratory is fortunate to have established long-term good cooperative relations with many top laboratories at home and abroad. Our cooperative partners include Professor Gao Ning's team from Peking University, Professor Zhang Yan's team from Zhejiang University, Professor Xu Huaqiang's team from Shanghai Institute of Pharmacology, Chinese Academy of Sciences, Professor Shao Zhenhua's team from Sichuan University, Germany Professor Ines Liebscher team of Schonheimer Institute, Professor Zhang Lei team of Xi 'an Jiaotong University, Professor Yi Fan team of Shandong University, Professor Kong Wei team of Peking University, Professor Liu Zhijie team of Shanghai University of Science and Technology, Professor Chai Renjie team of Southeast University. This also provides a stable scientific research background for the advancement of our subject research.

**Recreational Activities:**

There are many sports venues in our university, including professional football and basketball courts. Moreover, our campus is adjacent to Quancheng Park and Baotu Spring, where our lab mates often go to relax and unwind. Every week, our lab organizes a football match. During traditional festivals such as New Year's Day and Dragon Boat Festival, our laboratory holds a series of activities to celebrate these occasions. Regular group meetings are organized in our laboratory, during which teachers summarize and analyze the recent achievements of students, provide them with professional and meticulous guidance, plan their future development directions, and offer insights into their employment and learning.

**Other Features:**

We have unique GPCR-ligand pairing technique, GPCR force-sensing screening platform, GPCR signal transduction technology which are the characteristics of our lab.

Teamwork and kindness are part of our lab culture. At the same time, we also emphasize that only by loving life can we do scientific research well.

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## **Medical and Pharmaceutical Basic Research Innovation Center of Emergency and Critical Care Medicine, China's Ministry of Education, Shandong Provincial Engineering Research Center for Emergency Medicine**

### **Establishment and Development:**

The Medical and Pharmaceutical Basic Research Innovation Center of Emergency and Critical Care Medicine, the China's Ministry of Education and Shandong Provincial Engineering Research Center for Emergency Medicine was born from a shared vision and passion for acute chest pain as the main cause of critical cardiovascular diseases, cardiac arrest and cardiopulmonary resuscitation, acute organ injury and protection, research and development of innovative medicines and intelligent emergency equipment, medical big data and artificial intelligence, and basic research on zero magnetic medicine. Recognizing the need for that cardiovascular diseases are an important group of acute high-risk cardiogenic chest pain, which is the "number one killer" of patients, our founders decided to establish a laboratory dedicated to research on the mechanism and translational research of acute and critical cardiovascular disease , protect important organ function and severe infection and sepsis. The journey of our lab began with the Institute of Emergency and Critical Care Medicine of Shandong University based on the discipline of Emergency Medicine, established by Prof. Yuguo Chen. With a small but dedicated team, we set out to establish a research laboratory that would be recognized for its excellence and impact. Since its inception, our lab has gone through a remarkable journey of growth and development. We have created a key technology system for rapid, stratified and precise treatment of acute cardiogenic chest pain, which serves the realization of the major strategic goal of "Healthy China 2030". We have expanded our team to include 4 doctoral supervisors and 9 Master's supervisors who are engaged in emergency medicine, cardiology and basic medicine. Additionally, we have forged valuable collaborations and partnerships with Academician Yihai Cao, Academician Jiancheng Fang and Academician Yun Zhang.

### **Team Members:**

Our team is composed of 1 Taishan Scholar Climbing Program Expert, 1 National Nature Science Fund for Distinguished Young Scholars, 1 National Ten Thousand Talent Program for Young Top-notch Talents, 1 winner of China Youth Science and Technology Award, 2 chief scientists of national major projects, 2 Outstanding Contribution Experts of the National Health Commission, 11 Taishan Scholar Youth Experts, 1 Qilu Young Scholar, and 4 Qilu Health and Wellness Outstanding Young Talent of Shandong Province. Our team has undertaken more than 50 national, ministerial, and provincial projects, including 4 national key R&D projects, 1 National Special Investigation on Basic Scientific and Technological Resources, 1 National Nature Science Foundation Outstanding Youth Science Fund Project, and 1 National Natural Science Foundation key project. Yuguo Chen , the leader of Emergency Department, is the fellow of the American Society of Cardiology (FACC), the American Society of Cardiovascular Angiography and Intervention (FSCAI), the



European Society of Cardiology (FESC) and the Hong Kong College of Emergency Medicine. He is the chairman of the 9th Emergency Medicine Branch of the Chinese Medical Association. Together, they work tirelessly to acute chest pain as the main cause of critical cardiovascular diseases, cardiac arrest and cardiopulmonary resuscitation, acute organ injury and protection, research and development of innovative medicines and intelligent emergency equipment, medical big data and artificial intelligence, and basic research on zero magnetic medicine.

### **Research Areas:**

The Medical and Pharmaceutical Basic Research Innovation Center of Emergency and Critical Care Medicine, the China's Ministry of Education and Shandong Provincial Engineering Research Center for Emergency Medicine specializes in acute chest pain as the main cause of critical cardiovascular diseases, cardiac arrest and cardiopulmonary resuscitation, acute organ injury and protection, research and development of innovative medicines and intelligent emergency equipment, medical big data and artificial intelligence, and basic research on zero-magnetism medicine.

### **Research Achievements:**

We have made significant contributions in emergency and severe diseases involving basic research, clinical research, and medical-engineering research. Our team has undertaken more than 50 national, ministerial, and provincial projects, including 4 national key R&D projects, 1 National Special Investigation on Basic Scientific and Technological Resources, 1 National Nature Science Foundation Outstanding Youth Science Fund Project, and 1 National Natural Science Foundation key project. We have published over 200 SCI papers, including *Circulation*, *Eur Heart J*, *JAMA*, *JAMA Cardiol*, and *Nature Communication*, edited or co-edited over 10 textbooks including national planned textbooks of Emergency Medicine, chaired the formulation of more than 10 national and international guidelines or consensus, obtained over 20 national patents. The team have received over 10 provincial and ministerial-level science and technology awards, including the first prize of the Chinese Medical Science and Technology Award and the first prize of the Shandong Province Science and Technology Progress Award.

### **Main Publications:**

1. Zhai X, Cao S, Wang J, Qiao B, Liu X, Hua R, Zhao M, Sun S, Han Y, Wu S, Pang J, Yuan Q, Wang B, Xu F, Wei S, Chen Y. Carbonylation of Runx2 at K176 by 4-Hydroxynonenal Accelerates Vascular Calcification. *Circulation*. 2024 Feb 13.
2. Yang K, Ren J, Li X, Wang Z, Xue L, Cui S, Sang W, Xu T, Zhang J, Yu J, Liu Z, Shang H, Pang J, Huang X, Chen Y, Xu F. Prevention of aortic dissection and aneurysm via an ALDH2-mediated switch in vascular smooth muscle cell phenotype. *Eur Heart J*. 2020 Jul 7;41(26):2442-2453.
3. Yang K, Cui S, Wang J, Xu T, Du H, Yue H, Ye H, Guo J, Zhang J, Li P, Guo Y, Pan C, Pang J, Wang J, Yu X, Zhang C, Liu Z, Chen Y, Xu F. Early Progression of

- Abdominal Aortic Aneurysm is Decelerated by Improved Endothelial Barrier Function via ALDH2-LIN28B-ELK3 Signaling. *Adv Sci (Weinh)*. 2023 Nov;10(32):e2302231.
4. Liu L, Pang J, Qin D, Li R, Zou D, Chi K, Wu W, Rui H, Yu H, Zhu W, Liu K, Wu X, Wang J, Xu P, Song X, Cao Y, Wang J, Xu F, Xue L, Chen Y. Deubiquitinase OTUD5 as a Novel Protector against 4-HNE-Triggered Ferroptosis in Myocardial Ischemia/Reperfusion Injury. *Adv Sci (Weinh)*. 2023 Oct;10(28):e2301852.
  5. Liu H, Yin H, Wang Z, Yuan Q, Xu F, Chen Y, Li C. Rho A/ROCK1 signaling-mediated metabolic reprogramming of valvular interstitial cells toward Warburg effect accelerates aortic valve calcification via AMPK/RUNX2 axis. *Cell Death Dis*. 2023 Feb 11;14(2):108.
  6. Zhang J, Guo Y, Zhao X, Pang J, Pan C, Wang J, Wei S, Yu X, Zhang C, Chen Y, Yin H, Xu F. The role of aldehyde dehydrogenase 2 in cardiovascular disease. *Nat Rev Cardiol*. 2023 Jul;20(7):495-509.
  7. Zheng J, Lv C, Zheng W, Zhang G, Tan H, Ma Y, Zhu Y, Li C, Han X, Yan S, Pan C, Zhang J, Hou Y, Wang C, Bian Y, Liu R, Cheng K, Ma J, Zheng Z, Song R, Wang M, Gu J, McNally B, Ong MEH, Chen Y, Xu F; BASIC-OHCA Coordinators and Investigators. Incidence, process of care, and outcomes of out-of-hospital cardiac arrest in China: a prospective study of the BASIC-OHCA registry. *Lancet Public Health*. 2023 Dec;8(12):e923-e932.
  8. Pan C, Xu C, Zheng J, Song R, Lv C, Zhang G, Tan H, Ma Y, Zhu Y, Han X, Li C, Yan S, Zheng W, Wang C, Zhang J, Bian Y, Ma J, Cheng K, Liu R, Hou Y, Chen Q, Zhao X, McNally B, Chen R, Kan H, Meng X, Chen Y, Xu F. Fine and coarse particulate air pollution and out-of-hospital cardiac arrest onset: a nationwide case-crossover study in China. *J Hazard Mater*. 2023 Sep 5;457:131829.
  9. Wang H, Zhao S, Wang S, Zheng Y, Wang S, Chen H, Pang J, Ma J, Yang X, Chen Y. Global magnitude of encephalitis burden and its evolving pattern over the past 30 years. *J Infect*. 2022 Jun;84(6):777-787.
  10. Pang J, Xu F, Aondio G, Li Y, Fumagalli A, Lu M, Valmadre G, Wei J, Bian Y, Canesi M, Damiani G, Zhang Y, Yu D, Chen J, Ji X, Sui W, Wang B, Wu S, Kovacs A, Revera M, Wang H, Jing X, Zhang Y, Chen Y, Cao Y. Efficacy and tolerability of bevacizumab in patients with severe Covid-19. *Nat Commun*. 2021 Feb 5;12(1):814.

### **Facilities & Resources:**

Our state-of-the-art facilities and cutting-edge technology enable us to conduct research that is both rigorous and innovative. We have over 200 pieces of equipment, including 25 valued at more than 500,000 yuan, with a total original value of over 30 million yuan. We focus on our main research direction and have built ten central featured platforms including cardiovascular featured research, microscopic characterization, flow sorting, immunohistochemistry, cell biology, molecular biology experimental, energy metabolism platform, drug synthesis, zero magnetic medicine basic research, and physiology analysis. Based on the platform, we have gradually

established the following technology systems, including cell biology, molecular biology, morphology, flow cytometry, animal model construction and translational research-related technologies. In addition, we have an emergency and critical biobank platform, covering an area of more than 1000 m<sup>2</sup>.

#### **Collaborations & Partnerships:**

We believe in the power of collaboration. That's why we have forged partnerships with leading universities such as Karolinska Medical College, Harvard Medical School, the University of Wyoming and the University of Michigan. To further advance our research. Our lab is active in international scientific and technological exchange activities, and participated in a number of large-scale international academic conferences every year supported by Shandong Branch of Emergency Medicine, providing an academic exchange platform for global professionals. We also invited experts from the United States, Austria and other countries and regions through the short-term overseas expert project to conduct nearly 30 lectures.

#### **Recreational Activities:**

The laboratory has a pleasant environment, featuring a tea break room and a rest area. Additionally, there are multiple meeting rooms equipped with conference systems for efficient and professional meetings. Our lab also organizes team-building activities to enhance the friendship among lab members. E.g. social gatherings, sports and fitness activities, cultural events, festivals and celebrations, professional development workshops.

#### **Other Features:**

Cardiovascular characteristic platform is an important research base for basic and translational medicine of cardiovascular diseases. With the goal of translational medicine and the orientation of clinical problems, we will solve major problems such as early warning and prediction of cardiovascular diseases, disease treatment and drug intervention.

The nanomedicine Research platform is committed to building a technology research and transformation platform for the prevention, diagnosis and treatment of major diseases such as cardiovascular and cerebrovascular diseases, inflammation and infection.

Zero magnetic medical basic research platform mainly focuses on the basic research of zero magnetic medicine, provides technical support and experimental basis related to zero magnetic medicine.

#### **Contact:**

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## **Shandong Key Laboratory of Immunohematology, Qilu Hospital, Shandong University**

### **Establishment and Development:**

The Hematology Department of Qilu Hospital of Shandong University was founded in 1959 by Professor Maohong Zhang. The Hematology Department of Qilu Hospital of Shandong University is a national clinical key specialty, one of the first doctoral programs and post-doctoral stations in China, the innovation studio of leading scientific and technological talents in Shandong Province, and the Clinical Medical Research Center of Hematology System Diseases in Shandong Province. It is a branch of the Institute of Hematology, Chinese Academy of Medical Sciences and the National Clinical Medical Research Center for Blood System Diseases, Peking University People's Hospital. The Hematology Laboratory under the Hematology Department of Shandong University Qilu Hospital is the third-level key laboratory of the State Administration of Traditional Chinese Medicine, the key discipline and key laboratory of Shandong Province during the "Eleventh Five-Year Plan" strengthening construction, and the provincial key Laboratory of Blood Immunology of Shandong Province. The establishment of cell morphology room, central laboratory, cell culture room, molecular biology laboratory, flow cytometry room and stem cell room to provide assistance for the diagnosis, assessment and differential diagnosis of hematological diseases in the whole hospital. At present, it can perform fusion gene quantitative analysis, chromosome analysis, FISH detection, immune typing, MAIPA, platelet function detection and many other leading laboratory tests in China.

### **Team Members:**

Our team is composed of leading experts in their fields, young and passionate researchers, and support staff dedicated to excellence. Together, they work tirelessly to explore various aspects of hematology.

Professor Jun Peng, Chief Physician, Professor, Ph.D./M.D. Advisor, Vice President of Qilu Hospital of Shandong University, Director of the Department of Hematology. He has published 14 papers in Blood as the corresponding/ co-corresponding author. As a principal investigator, he has undertaken nine national and ministerial levels research projects, such as the National Natural Science Foundation of China and the sub-project of the National Program on Key Basic Research Project of China (973 Program) of the Ministry of Science and Technology. Professor Peng is a member of the thrombosis and hemostasis group of the Chinese Society of Hematology, and the Professional Committee of Experimental Hematology, Chinese Society of Pathophysiology. He serves as the editorial board member of Thrombosis Journal, Thrombosis Research, Journal of Clinical Hematology and Chinese Journal of Hematology.

Shuqian Xu, Ph.D./M.D. Advisor, Taishan Scholar Young Expert, Researcher, Chief Physician, Master Tutor, Deputy Director of Red Cell Disease Department of Hematology. In recent years, she has published papers in Nature Genetics, Blood, Genes and Diseases and other journals.

Prof. Daoxin Ma majors in the field of hematology, specializing in molecular diagnostics, disease stratification, and personalized treatment of hematologic diseases. Holding a Doctor of Medicine degree, he advanced his expertise with postdoctoral research at the prestigious Karolinska Institute in Sweden. Now, he excels as a Chief Technician and doctoral supervisor, deeply involved in the clinical diagnosis and foundational research of blood diseases.

Miao Xu, she was named a Young Taishan Scholar of Shandong Province, a Qilu Young Scholar of Shandong University, appointed as a research fellow and doctoral supervisor at Shandong University in the same year, and began her standardized training as a resident doctor, continuing her basic and clinical research on platelet-related diseases.

### **Research Areas:**

Jun Peng specializes in pathogenesis and of primary immune thrombocytopenia (ITP), and myelodysplastic syndromes (MDS), and differentiation of hematopoietic stem cells.

Shuqian Xu specializes in myelodysplastic syndromes (MDS) and gene therapy for hereditary diseases. She is committed to the applied research and exploration of thalassemia gene therapy, and uses CRISPR therapy technology to efficiently edit pathogenic targets, providing new ideas for the treatment of thalassemia.

Daoxin Ma focuses on the role of the bone marrow immune microenvironment in Acute Myeloid Leukemia (AML), specifically investigating immune imbalance and its impact on disease progression, drug resistance, and relapse, along with novel signaling pathways. Additionally, his studies include the role of gut microbiota and its metabolic products in AML, exploring how these factors affect disease development.

Miao Xu primary focus lies in unraveling the intricate mechanisms underpinning platelet-related diseases, including immune thrombocytopenia (ITP), disseminated intravascular coagulation (DIC), and thrombosis.

### **Research Achievements:**

The Department of Hematology has 6 sub-specialties, including hemostasis and thrombosis, leukemia disease, hematopoietic stem cell transplantation, lymphocyte disease, plasma cell disease and red blood cell disease, which have strong academic influence in China. Among them, the research on primary immune thrombocytopenia has reached the international leading level, and the research on leukemia has reached the international and domestic leading level.

In the diagnosis and research of primary immune thrombocytopenia, the Department of Hematology established the theory of ITP immune intolerance, proposed the concept of "first-line combined therapy" for the first time, and took the lead in the RCT study of recombinant human TPO for the treatment of pregnancy complicated with ITP, solving the worldwide problem of no medicine for pregnancy complicated with ITP. ITP patient diagnosis and treatment data management system was established. At the same time, a series of determination tests on the pathogenesis of ITP have been established and promoted in 26 medical institutions in China, and more

than 6,000 patients have applied ITP. The Department of Hematology led the development of the Chinese expert consensus on the diagnosis and treatment of adult primary immune thrombocytopenia in 2009, 2011, 2012, 2016, 2023, and the treatment guidelines for primary immune thrombocytopenia in 2018 and 2020.

In the diagnosis and research of leukemia, the Department of Hematology has conducted systematic and in-depth research from the three levels of basic medicine, translational medicine and clinical medicine to promote early warning, early diagnosis, early treatment and improve prognosis of leukemia. We have established a big data platform related to acute myeloid leukemia, a follow-up system of leukemia sample bank, a BCR-ABL(P210) detection and evaluation system for chronic myeloid leukemia (CML), and a flow cytometry MRD detection platform for leukemia, etc., improving the basic and clinical research system for leukemia, and fully revealing new mechanisms of leukemia pathogenesis and drug resistance. It has promoted the development of intelligent diagnosis and treatment technology for leukemia. The Department of Hematology led the development of expert consensus on the prevention and treatment of novel coronavirus infection in patients with inert B-cell non-Hodgkin lymphoma, and the Chinese expert Consensus on the detection and clinical interpretation of minimal residual disease in chronic lymphocytic leukemia (2023 edition).

#### **Main Publications:**

1. Liu Y#, Zuo X#, Chen P#, Hu X, Sheng Z, Liu A, Liu Q, Leng S, Zhang X, Li X, Wang L, Feng Q, Li C, Hou M, Chu C, Ma S\*, Wang S\*, Peng J\*. Deciphering transcriptome alterations in bone marrow hematopoiesis at single-cell resolution in immune thrombocytopenia. *Signal Transduct Target Ther.* 2022 Oct 7;7(1):347. doi: 10.1038/s41392-022-01167-9.
2. Hou Y#\*, Xie J#, Wang S#, Li D, Wang L, Wang H, Ni X, Leng S, Li G, Hou M, Peng J\*. Glucocorticoid receptor modulates myeloid-derived suppressor cell function via mitochondrial metabolism in immune thrombocytopenia. *Cell Mol Immunol.* 2022 Jul;19(7):764-776. doi: 10.1038/s41423-022-00859-0. Epub 2022 Apr 12.
3. Zhao H#, Ma Y#, Li D, Sun T, Li L, Li P, Liu X, Zhou H, Hou Y, Liu Y, Han P, Zhao Y, Jing F, Peng J\*, Hou M\*. Low-dose chidamide restores immune tolerance in ITP in mice and humans. *Blood.* 2019 Feb 14;133(7):730-742. doi: 10.1182/blood-2018-05-847624.
4. Wang R, Yang X, Liu J, Zhong F, Zhang C, Chen Y, et al. Gut microbiota regulates acute myeloid leukaemia via alteration of intestinal barrier function mediated by butyrate. *Nat Commun.* 2022 May 9;13(1):2522.
5. Yang X, Liu J, Liu W, Wu H, Wei Y, Guo X, et al. circFAM193B interaction with PRMT6 regulates AML leukemia stem cells chemoresistance through altering the oxidative metabolism and lipid peroxidation. *Leukemia.* 2024 Feb 29;
6. Liu N, Xu S, Yao Q, Zhu Q, Kai Y, Hsu JY, Sakon P, Pinello L, Yuan GC, Bauer DE, Orkin SH. Transcription factor competition at the  $\gamma$ -globin promoters controls hemoglobin switching. *Nat Genet.* 2021 Apr;53(4):511-520. doi: 10.1038/s41588-021-00798-y. Epub 2021 Mar 1. Erratum in: *Nat Genet.* 2021 Mar

17.; PMID: 33649594; PMCID: PMC8038971.

7. Xu S, Luk K, Yao Q, Shen AH, Zeng J, Wu Y, Luo HY, Brendel C, Pinello L, Chui DHK, Wolfe SA, Bauer DE. Editing aberrant splice sites efficiently restores  $\beta$ -globin expression in  $\beta$ -thalassemia. *Blood*. 2019 May 23;133(21):2255-2262. doi: 10.1182/blood-2019-01-895094. Epub 2019 Jan 31. PMID: 30704988; PMCID: PMC6533605.

8. Pengcheng Xu; Yajing Zhao; Tianshu Yu; Yafei Yu; Xiaofei Ni; Haoyi Wang; Lu Sun; Panpan Han; Lingjun Wang; Tao Sun; Xinguang Liu; Hai Zhou; Jun Peng; Ming Hou; Yu Hou\*; Miao Xu\*; Atorvastatin restores imbalance of cluster of differentiation 4 (CD4) + T cells in immune thrombocytopenia in vivo and in vitro, *British Journal of Haematology*, 2021

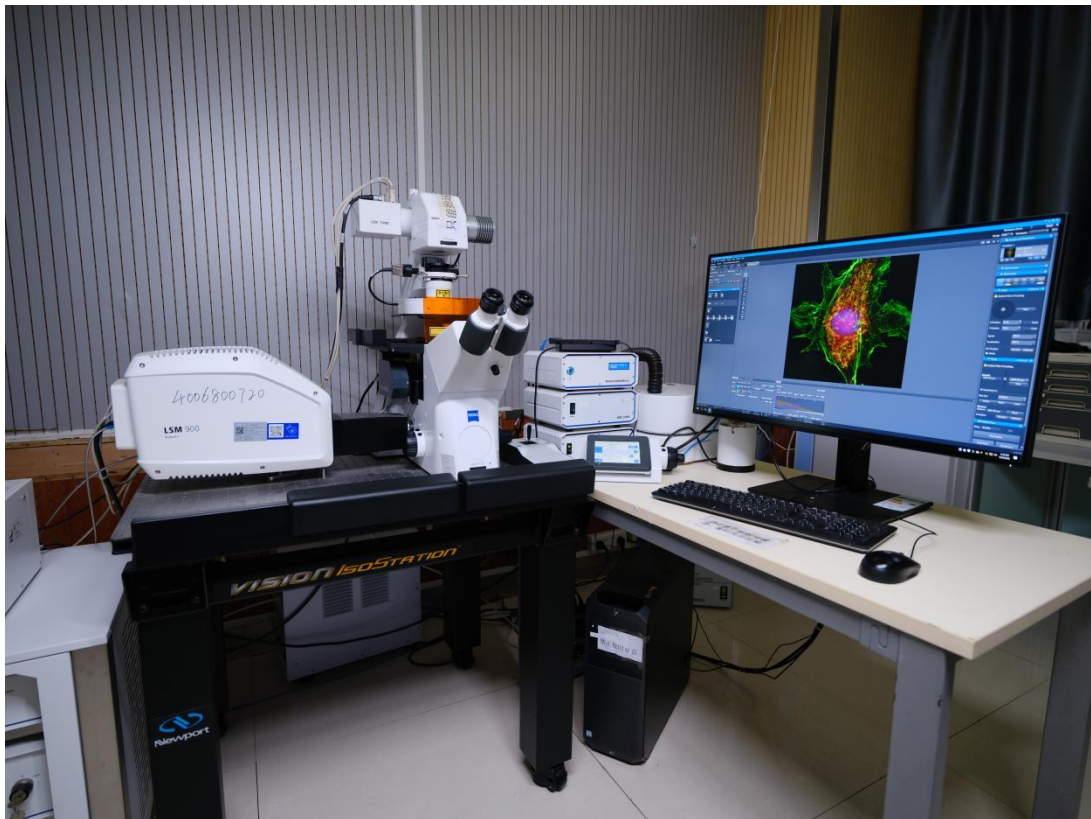
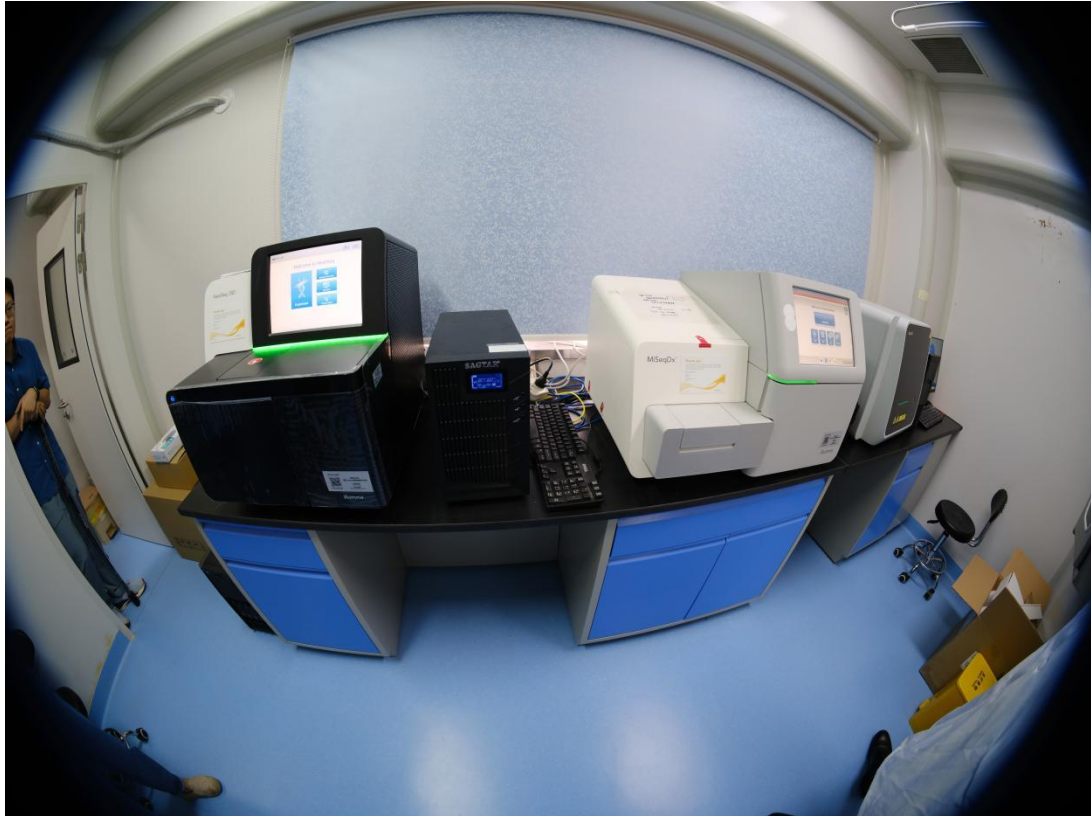
9. Jing Qin; Qiang Liu; Anli Liu; Shaoqiu Leng; Shuwen Wang; Chaoyang Li; Ji Ma; Jun Peng; Miao Xu\*; Empagliflozin modulates CD4+ T cell differentiation via metabolic reprogramming in immune thrombocytopenia, *British Journal of Haematology*, 2022, 198(4): 765-775.

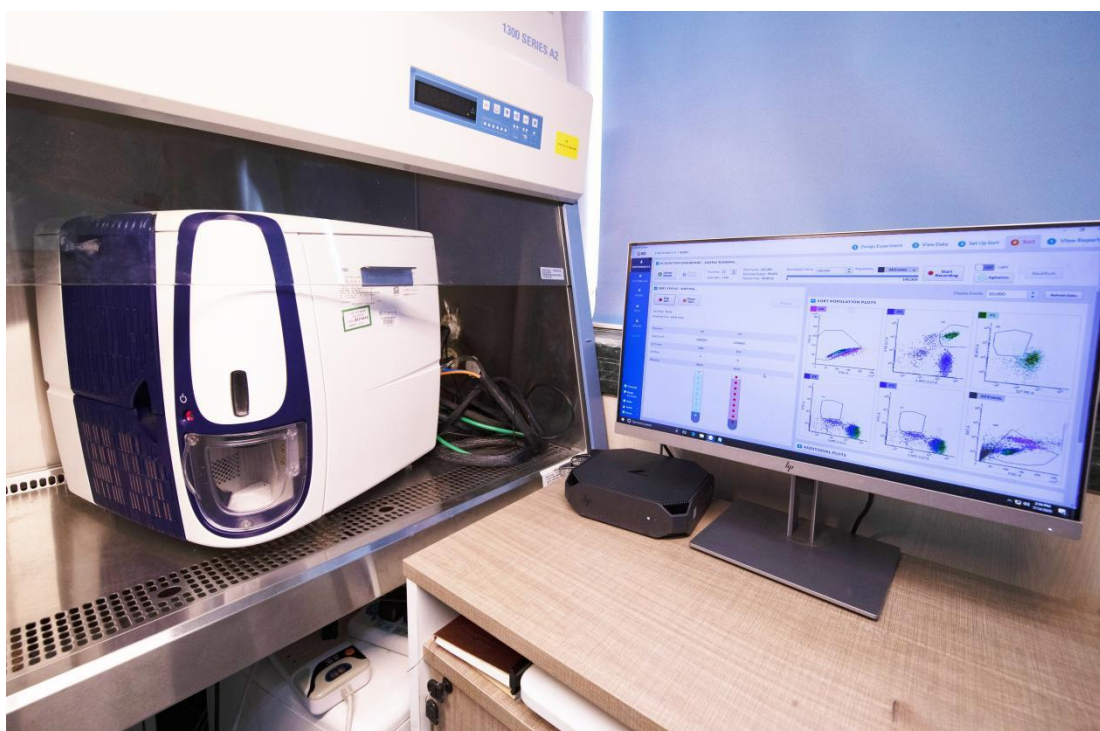
10. Yun Wang; Lei Sheng; Fengjiao Han; Qiuyu Guo; Zihan Zhang; Yu Hou; Qi Feng; Hai Zhou; Xuebin Ji; Jun Peng; Ming Hou\*; Miao Xu\*; Efficacy and safety of treatments in newly diagnosed adult primary immune thrombocytopenia: A systematic review and network meta-analysis, *eClinicalMedicine*, -02-, 56: 2023, 101777.

#### **Facilities & Resources:**

Our laboratory has established cell morphology room, central laboratory, cell culture room, molecular biology laboratory, flow cytometry room and stem cell room to provide assistance for the diagnosis, assessment and differential diagnosis of hematological diseases in the whole hospital. At present, it can perform fusion gene quantitative analysis, chromosome analysis, FISH detection, immune typing, MAIPA, platelet function detection and many other leading laboratory tests in China. The Department of hematology has a variety of characteristic diagnosis and treatment techniques, such as chimeric antigen receptor T cell immunotherapy, autologous and allogeneic hematopoietic stem cell transplantation, stem cell apheresis, anti-platelet membrane glycoprotein autoantibody detection, fluorescence in situ hybridization, platelet aggregation function detection, leukemia fusion gene detection.







### **Collaborations & Partnerships:**

We believe in the power of collaboration. That's why we have forged partnerships with Karolinska Institutet, Lund University, Comptons University of Madrid, University of Toronto, Tianjin Blood Research Institute, Peking University People's Hospital to further advance our research.

Our research group has already established long-term cooperative relationships with University of Toronto in Canada, and Lund University in Sweden. Both University of Toronto and the John Semple group at Lund University are at the international forefront of research in the field of ITP, with extensive experience in constructing ITP mouse models and conducting related animal experiments.

### **Recreational Activities:**

Aside from their profound contributions to medical research, they have rich personal interests. Such as Prof. Ma Daoxin, he avidly reads a diverse range of books, spanning from the latest scientific studies to works in literature and history, finding both inspiration and relaxation in this pursuit. Additionally, running is a cherished hobby for him. It serves not just as physical exercise but also as a means for stress relief and contemplation. Miao Xu's passions extend beyond the laboratory to the vibrant world of performing arts and music.

### **Other Features:**

Special research areas in the hematology Department include primary immune thrombocytopenia and acute leukemia. Among them, the ITP pathogenesis, specific diagnosis and targeted intervention strategies are at the international and domestic advanced level, and the biological behavior abnormalities, drug resistance and

intervention reversal of leukemia are at the domestic advanced level.

**Contact:**

For more information or inquiries, please visit our website at <https://www.qiluhospital.com/list-328-1.html> .

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**Tomographic Anatomy Research Centre, Department of Anatomy and  
Neurobiology, School of Basic Medical Sciences, Shandong University, China**

**Establishment and Development:**

The team led by the applicant has been committed to neuroimaging research and embryonic brain development research for a long time, and has undertaken 20 projects of the National Natural Science Foundation of China and provincial and ministerial-level projects, and has published more than 300 papers in journals such as Cerebral Cortex, NeuroImage and Human Brain Mapping, etc. (of which more than 70 papers have been indexed by SCI). He has edited 34 academic books, including "Functional Neuroimaging" and "Clinical Central Nervous Anatomy", and translated the world's most famous anatomical work, "Gesellschaft für Anatomie" (41st edition). In 2018, he won the second prize of Shandong Province Science and Technology Award for the project of "Creation and Promotion of Chinese Digital Standard Brain Atlas". In the past 5 years, he has undertaken 3 projects of the National Natural Science Foundation of China (NSFC), and is currently working on the project of "Pre-natal Development and Visualisation of Structural Brain Network Groups" (No.31771328), which constructs the structural brain networks and brain atlas of the foetus from the mid-pregnancy to the birth, and compares the attributes of the structural network of the brain of the foetus and the newborn, to reveal the mechanism of foetal development. The results have been published in NeuroImage, Frontiers in Neuroscience and other journals.

**Team Members:**

1. Shuwei Liu is currently a professor at Shandong University, deputy director of the Institute of Brain and Brain-like Science at Shandong University, and director of the Digital Human Research Institute at Shandong University. His research interests include tomographic anatomy, computational neuroscience, neurodevelopment and pathogenesis of neuropsychiatric disorders.
2. Yuchun Tang: Tomographic anatomy, neuroimaging, computational neuroscience
3. Lei Feng: tomographic anatomy and neurodevelopmental research.
4. Wenjuan Zhou: pathogenesis of neurodevelopmental and related diseases
5. Haiwei Meng: imaging in Parkinson's disease and neurodevelopmental areas
6. Feifei Xu: Fetal brain structural and functional imaging studie
7. Fengxia Wu: the treatment and mechanism of Parkinson's disease
8. Zhen Liu: Neuropathy and Pain

**Research Areas:**

The digital human body, digital brain mapping and foetal brain development (Digitised adult brain atlas; Digitising the Fetal Brain Atlas); Tomographic Anatomy and Neurodevelopment; Neuroimaging; computational medicine; brain science; imaging of neuropsychiatric disorders; pathogenesis of neurodevelopmental and related diseases

### **Research Achievements:**

- (1) 2018.01-2021.12 Pre-natal development and visualisation of structural brain network groups, NSFC, 600,000 RMB
- (2) 2016.01-2019.12 Early Morphogenesis of Cortical Folding in the Brain, National Natural Science Foundation of China, 650,000 Yuan
- (3) 2014.01-2017.12 Imaging genetics of attention networks, National Natural Science Foundation of China, 700,000 RMB
- (4) 2011.01-2013.12 Sexual dimorphism in prenatal development of the cerebral cortex, National Natural Science Foundation of China, 330,000 Yuan
- (5) 2019.01-2022.12 Application and Industrialisation of Digital Human Research Results in Clinical Surgical Planning, Major Science and Technology Innovation Project of Shandong Province, 2 million yuan
- (6) 2017.01-2019.12 4D Digital Brain Mapping Visualisation System for Chinese People, Shandong Key R&D Programme, 2 million RMB
- (7) 2015.01-2017.12 R&D and Demonstration of High-Precision Digital Human Information Technology, Shandong Province Major Science and Technology Special Project, 2 million yuan.
- (8) National Natural Science Foundation of China (NSFC) upper-level project, 31872802, Probabilistic mapping of white matter fibre connectivity in the brainstem, 2019/01-2022/12, 600,000 RMB, first place
- (9) National Natural Science Foundation of China Young Science Fund Project, 81301280, Amphoteric Heteromorphism of White Matter in the Chinese Brain and Its Relationship with Cognitive Function, 2014/01-2016/12, 230,000 RMB, first place
- (10) Effects of silencing  $\alpha$ -synuclein on Parkinson's disease mice and its mechanism. Shandong Provincial Natural Science Foundation Youth Fund

### **Main Publications:**

- (1) Tian Mimi, Xu Feifei, Xia Qing, Tang Yuchun, Zhang Zhonghe, Lin Xiangtao, Meng Haiwei, Feng Lei, Liu Shuwei\*. Morphological development of the human fetal striatum during the second trimester. *Cerebral Cortex*. 2022, 00:1-11.
- (2) Wang Wenjun, Yu Qiaowen, Liang Wenjia, Xu Feifei, Li Zhuoran, Tang Yuchun\*, Liu Shuwei\*. Altered Cortical Microstructure in Preterm Infants at Term-equivalent Age Relative to Term-born Neonates. *Cerebral Cortex*, 2022, 1-12.
- (3) Liang Wenjia, Yu Qiaowen, Wang Wenjun, Thijs Dhollander, Emmaneul Suluba, Li Zhuoran, Xu Feifei, Hu Yang, Tang Yuchun\*, Liu Shuwei\*. A comparative study of the superior longitudinal fasciculus subdivision between neonates and young adults. *Brain Structure and Function*, 2022.
- (4) Wang Yu, Xu Feifei, Zhou Wenjuan, Hou Lanwei, Tang Yuchun, Liu Shuwei\*. Morphological and hemispheric and sex differences of the anterior ascending ramus and the horizontal ascending ramus of the lateral sulcus. *Brain Structure and Function*. 2022.
- (5) Zhao Xiaotian, Liang Wenjia, Wang Wenjun, Liu Hailan, Zhang Xiaolei, Liu Chengxin, Zhu Caiting, Cui Baoxia, Tang Yuchun\*, Liu Shuwei\*. Changes in and asymmetry of the proteome in the human fetal frontal lobe during early

development. *Communications Biology*, 2022. 5:1031.

(6) Tang Yuchun, Zhao Lu, Lou Yunxia, Shi Yonggang, Fang Rui, Lin Xiangtao, Liu Shuwei, Arthur Toga. Brain structure differences between Chinese and Caucasian cohorts: A comprehensive morphometry study. *Human Brain Mapping*, 2018, 39: 2147-2155.

(7) Tang Yuchun, Sun Wei, Arthur Toga, Ringman JM, Shi Yonggang. A probabilistic atlas of human brainstem pathways based on connectome imaging data. *Neuroimage*, 2018, 169: 227~239.

(8) Ge X, Shi Y, Li J, Zhang Z, Lin X, Zhan J, Ge H, Xu J, Yu Q, Leng Y, Teng G, Feng L, Meng H, Tang Y, Zang F, Toga AW, Liu S\*. Development of the human fetal hippocampal formation during early second trimester. *Neuroimage*. 2015; 119:33-43.

(9) Feng L, Meng H, Wu F, Cheng B, He X, Wang X, Li Z, Liu S. Olfactory ensheathing cells conditioned medium prevented apoptosis induced by 6-OHDA in PC12 cells through modulation of intrinsic apoptotic pathways. *Int J Dev Neurosci*. 2008 May-Jun; 26(3-4):323-9.

(10) Wu F, Poon WS, Lu G, Wang A, Meng H, Feng L, Li Z, Liu S. Alpha-synuclein knockdown attenuates MPP+ induced mitochondrial dysfunction of SH-SY5Y cells. *Brain Res*. 2009; 1292: 173-9.

#### **Facilities & Resources:**

The main equipment includes SKC500 CNC milling machine, HN051 CNC sawing machine, Olympus BX63 fluorescence microscope system, SGI high-performance image workstations from Silicon Graphics of the United States, HP servers, and 50 high-performance computers from DELL of the United States.

#### **Collaborations & Partnerships:**

##### **International Conferences**

June 2011 Padua, Italy 11th European Congress of Clinical Anatomy

September 2009 Istanbul, Turkey 10th European Congress of Clinical Anatomy

May 2008 Tehran, Iran 5th Asia Pacific International Congress of Anatomists

December 2007 Qingdao, China First International Symposium on Tomographic Anatomy

##### **Recent National Conferences**

Nov 2011 Jinan Symposium on Tomographic Anatomy

April 2011, Qingdao The 6th National Symposium on Anatomy and Clinic (Head and Neck)

October 2010 Workshop on Archaeology of Human Bones, Jinan, China

August 2009 Yantai, China 2009 Annual Meeting of the Chinese Anatomical Society

April 2005 Workshop on Human Cross-Section Data Acquisition and Image Processing, Jinan, China

#### **Recreational Activities:**

Academic afternoon teas are held weekly, We don't just talk about academics, we talk



about our life events. Some of the fun activities are held such as talk about the Ethics of Experiments (Declaration of Helsinki) together. Going to tourist attractions in Jinan is also a frequent event. the students and teachers play basketball and football together every week. Occasionally, we go to watch football matches on live. When new students arrive and graduates are sent off, we have a dinner and a chat half a year.

**Other Features:**

The feature of the lab is that the researchers and students of enrolment are not limited to medical students, and the intersection of medical and engineering research is the hallmark of our lab. Only through cross-collaboration of different disciplines can we continue to innovate.

**Contact:**

tyc@sdu.edu.cn



## **NHC Key Laboratory of Health Economics and Policy Research, Shandong University**

### **Establishment and Development:**

The NHC (National Health Commission) Key Laboratory of Health Economics and Policy Research (Shandong University) (“the Laboratory”) was established in 2000, and is the only national key laboratory in China on health economics and policy research. In 2002, underpinned by the Laboratory, the Centre for Health Management and Policy Research (Shandong University) was founded. In 2015, the Shandong University - Karolinska Institutet Global Health Research Collaborative Centre was established. On September 1, 2016, the Centre was successfully selected as a pilot entity for the Key New Think-tank in Shandong Province, being the only industry think-tank in the field of health research.

As a research institution with significant influence both domestically and internationally in the fields of health economics, health management, and policy research, the Laboratory's mission is to conduct high-level, interdisciplinary academic research, cultivate high-end health management talents, provide policy advice for health system reform and development, and serve the health of the people. The Centre for Health Management and Policy Research (Shandong University)/the Laboratory is also a teaching entity, with over 30 staff and 160 graduate students currently.

### **Team Members:**

The PI, Prof Qiang Sun has been collaborating with Prof Cecilia Stålsby Lundborg from KI. Together, they work tirelessly on research related to improving antibiotic use and antimicrobial resistance (AMR) governance. The team currently has 2 full-time doctoral supervisors and over 10 young and passionate researchers and support staff.

### **Research Areas:**

The NHC Key Laboratory of Health Economics and Policy Research specializes in research on economic evaluation of pharmacoconomics and medical security policies, management and support for pharmaceuticals and consumables, tuberculosis control and rational use of anti-tuberculosis drugs, etc.

### **Research Achievements:**

In recent years, the team has been leading many scientific research projects, including projects of National Natural Science Foundation of China, the China Medical Board of the United States, the Natural Science Foundation of Shandong Province, and the National Health Commission of China. Team members have published over 100 journal articles in top journals such as Lancet Global Health, Plos Medicine, Health Affairs, BMC, Vaccines, and Quality of Life Research. The collaboration with KI focuses on research and graduate training on the globally hot topic of antibiotic resistance. Together, they have jointly applied for two general projects funded by the National Natural Science Foundation of China (NSFC) and published over 20 articles on SCI journals.

**Main Publications:**

10 selected publications

1. Overuse of antibiotics for the common cold – attitudes and behaviors among doctors in rural areas of Shandong Province, China
2. Study protocol for One Health data collections, analyses and intervention of the Sino-Swedish integrated multisectoral partnership for antibiotic resistance containment (IMPACT)
3. Antibiotic use in people and pigs: a One Health survey of rural residents' knowledge, attitudes and practices in Shandong province, China
4. Antibiotic consumption in Shandong Province, China: an analysis of provincial pharmaceutical centralized bidding procurement data at public healthcare institutions, 2012–16
5. Long-term outcomes of an educational intervention to reduce antibiotic prescribing for childhood upper respiratory tract infections in rural China: Follow-up of a cluster-randomised controlled trial
6. The impacts of diagnosis-intervention packet payment on the providers' behavior of inpatient care—evidence from a national pilot city in China
7. Interventions to optimize the use of antibiotics in China: A scoping review of evidence from humans, animals, and the environment from a One Health perspective
8. The impacts of the National Medication Price-Negotiated Policy on the financial burden of cancer patients in Shandong province, China: An interrupted time series analysis
9. Antibiotic use in township hospitals during the COVID-19 pandemic in Shandong, China
10. Socioeconomic Factors Contributing to Antibiotic Resistance in China: A Panel Data Analysis

**Facilities & Resources:**

Since the inclusion as a pilot entity for the Key New Think-tank in Shandong Province in 2016 and now an official member, the Centre for Health Management and Policy Research (Shandong University)/the Laboratory has make the utmost of the platform. Many policy briefs have been selected for inclusion in Shandong University's Think Tank Express and submitted to the Ministry of Education and other central government departments. Through this channel, we get our voices heard and the Laboratory has significantly stabilized and upgraded its domestic influence on the health policy research areas.

**Collaborations & Partnerships:**

We have established partnership relationships with multiple top universities at home and abroad, including Peking University, Fudan University, KI, Sheffield University, University of Toronto, and other institutes to further advance our research.

**Recreational Activities:**

Regular social gatherings, and sports activities are held within the team. New year gala, concerts, festive activities, and graduation celebrations are organized on campus, which have a strong Chinese cultural feature.

**Other Features:**

Health Economics and Policy Forum is held every other week to provide a pleasant and encouraging environment for staff and students of the Laboratory to learn and discuss hot topics in the areas. Distinguished speakers from all over the world are invited to present lectures on the research frontiers in the health fields.

**Contact:**

For more information or inquiries, please contact us at [qiangs@sdu.edu.cn](mailto:qiangs@sdu.edu.cn) or visit our website at <https://chmp.sdu.edu.cn/>

## Neurosurgery Laboratory at Qilu Hospital of Shandong University

### **Establishment and Development:**

Neurosurgery Laboratory at Qilu Hospital of Shandong University was born from a shared vision and passion for developing prevention and treatment methods for neurological diseases. Recognizing the need for understanding of the pathogenesis of neurological diseases, our founders decided to establish a laboratory dedicated to study the pathogenesis of neurological diseases and interpret the brain's functions to provide new theories, new methods, and new technologies for clinical research. The journey of Neurosurgery Laboratory at Qilu Hospital of Shandong University began with research on glioma. With a small but dedicated team, we set out to establish a research laboratory that would be recognized for its excellence and impact. Since its inception, Neurosurgery Laboratory at Qilu Hospital of Shandong University has undergone a remarkable growth and development journey. We have expanded our team to include 11 provincial-level or above talents, one of which is National Top-notch Young Professional. Our research has evolved to address research on brain and brain-inspired science focuses on "brain interpretation, brain protection, brain simulation, brain control and reconstruction". Additionally, we have forged valuable collaborations and partnerships with neurosurgery centers in six countries, including the United States, Norway, and Australia, to enhance our research capabilities further. We established the "China-Norway Brain Research Center" with the University of Bergen in 2015. We invited more than ten world-leading experts in the field of neuroscience from both China and abroad, including Nobel Prize winner Professor Edvard Moser, "Norwegian King's Prize" winner Prof. Rolf Bjerkvig, as well as academicians of the Chinese Academy of Sciences Zhou Liangfu and Zhao Jizong, as guest or honorary professors.

### **Team Members:**

Our team is composed of four Taishan Scholars of Shandong Province and 7 Young Experts of Taishan Scholars of Shandong Province, one of which is a National Top-notch Young Professional, four research assistants, three technicians, thirteen post doctors, and over 100 registered undergraduates, masters and PhD students. Together, they work tirelessly to study the mechanism, prevention and treatment of neurological diseases.

**Research Areas:**

Neurosurgery Laboratory at Qilu Hospital of Shandong University specializes in the mechanism of neuroimmune regulation in the occurrence and glioma development and its possible intervention targets, the molecular mechanism of cerebrovascular functional remodeling and possible intervention approaches, as well as research on the molecular pathology of neuromuscular diseases and degenerative diseases.

**Research Achievements:**

We have made significant contributions in interpretation of mechanisms and development of diagnostic and treatment methods for neurological diseases. We have undertaken over 50 National Natural Science Foundation projects and more than 50 major projects at the provincial and ministerial levels, with annual research funding exceeding 10 million yuan.

We have received more than 80 awards, including the second and third prizes of the National Science and Technology Progress Award nominated by the Ministry of Education; the first, second, and third prizes of the Shandong Province Science and Technology Progress Award; the Chinese Medical Science and Technology Award, and the Top Ten Scientific and Technological Achievements of Shandong Province. We have published around 50 SCI-index papers annually, with an average impact factor exceeding 5, and participated in formulating industry standards, domestic consensus, and domestic guidelines. We have been granted 29 patents approved in the past five years, 4 of which have been translated into clinics.

**Main Publications:**

10 selected publications

1. Wenhan W, Keyi L, Bowei X, et al. Piezotronic effect for in situ electrostimulation of neural stem cell therapy for nerve injury[J]. *Nano Energy*, 2024, 120: 109181-.
2. Rigg E, Wang J, Xue Z, et al. Inhibition of extracellular vesicle-derived miR-146a-5p decreases progression of melanoma brain metastasis via Notch pathway dysregulation in astrocytes[J]. *J Extracell Vesicles*, 2023, 12(10): e12363.
3. Sun Y, Mu G, Zhang X, et al. Metabolic Modulation of Histone Acetylation Mediated by HMGCL Activates the FOXM1/ $\beta$ -catenin Pathway in Glioblastoma[J]. *Neuro Oncol*, 2023.
4. Wang W, Duan J, Ma W, et al. Trimanganese Tetroxide Nanozyme protects Cartilage against Degeneration by Reducing Oxidative Stress in Osteoarthritis[J]. *Adv Sci (Weinh)*, 2023, 10(17): e2205859.
5. Zide W, Huimin G, Yuqi Z, et al. Lymph node-inspired immunoregulatory hydrogel with siRNA delivery property for postoperative glioblastoma treatment[J]. *Chemical Engineering Journal*, 2023, 476.
6. Pan Z, Zhao R, Li B, et al. EWSR1-induced circNEIL3 promotes glioma progression and exosome-mediated macrophage immunosuppressive polarization via stabilizing IGF2BP3[J]. *Mol Cancer*, 2022, 21(1): 16.
7. Li B, Chen X, Qiu W, et al. Synchronous Disintegration of Ferroptosis Defense Axis via Engineered Exosome-Conjugated Magnetic Nanoparticles for Glioblastoma Therapy[J]. *Adv Sci (Weinh)*, 2022, 9(17): e2105451.
8. Ji J, Ding K, Luo T, et al. TRIM22 activates NF- $\kappa$ B signaling in glioblastoma by accelerating the degradation of I $\kappa$ B $\alpha$ [J]. *Cell Death Differ*, 2021, 28(1): 367-381.
9. Han M, Wang S, Yang N, et al. Therapeutic implications of altered cholesterol homeostasis mediated by loss of CYP46A1 in human glioblastoma[J]. *EMBO Mol Med*, 2020, 12(1): e10924.
10. Wang J, Qi Q, Zhou W, et al. Inhibition of glioma growth by flavokawain B is mediated through endoplasmic reticulum stress induced autophagy[J]. *Autophagy*, 2018, 14(11): 2007-2022.

### **Facilities & Resources:**

Our state-of-the-art facilities and cutting-edge technology enable us to conduct rigorous and innovative research. We boast Leica laser scanning focus microscope, BD flow cytometer, IVIS Spectrum small animal live imaging system, biomolecule interaction detection system, live cell dynamic imaging and analysis system, depth Learning server, cryo-serial image acquisition system, EEG/event-related potential analysis systems and ultracentrifuges, etc.







### **Collaborations & Partnerships:**

We believe in the power of collaboration. That's why we have forged partnerships with Theodore Berger and Dong Song from University of Southern California; Rolf Bjerkvig, Frits Thorsen, Hrvoje Miletic, et al from University of Bergen; Thomas Daubon from University of Bordeaux; Barbara Klink from National Genetic Center of Luxembourg; Xiuying Wang from University of Sydney; Xinmin Li from University of Alberta to further advance our research.

### **Recreational Activities:**

Birthday celebrations, year-end gatherings, mountain climbing and other outdoor activities, Teachers' Day celebrations, Mid-Autumn Festival, Spring Festival and other traditional festival celebrations

### **Other Features:**

The scientific research team of the laboratory is composed of outstanding scholars from different disciplinary backgrounds. Together, we are committed to innovative research in brain function reconstruction. The laboratory has advanced scientific research equipment and instruments, providing good experimental conditions for researchers. At the same time, the laboratory actively cooperates and exchanges with well-known scientific research institutions and enterprises locally and abroad, continuously introduces advanced scientific research results and technologies, and promotes the continuous improvement of the laboratory's scientific research level and innovation capabilities.

### **Contact:**

For more information or inquiries, please contact us at mailto: [hb@sdu.edu.cn](mailto:hb@sdu.edu.cn) or visit our website at [www.brain.sdu.edu.cn](http://www.brain.sdu.edu.cn).

## Drug Design and Chemical Biology Research

### Establishment and Development:

Our laboratory initially focused on medicinal chemistry research, with a specific emphasis on drug design, synthesis, and biological evaluation targeting epigenetic drug targets such as HDAC and the anti-apoptotic protein Bcl-2. Over the past decades, we have integrated computer-aided drug design techniques into our research, such as virtual screening, which assists us in rapidly identifying bioactive lead compounds. In recent years, we have expanded our research to new targets, such as protein tyrosine phosphatase. Additionally, we have conducted chemical biology studies to gain a deeper understanding of the biological functions of target proteins.

### Team Members:

Our research team consists of senior medicinal chemists, as well as young researchers specializing in computer-aided drug design, peptide chemistry, biomaterials, and other related research areas.

### Research Areas:

1. Structure-based drug design, synthesis, and chemical biology research.
2. Computer-aided drug design and virtual screening.
3. Development of novel methods for peptide synthesis.
4. Design and application of biocompatible materials.

### Research Achievements:

We have made significant contributions in the field of HDAC inhibitors. Through the structure optimization of lead compounds, we have successfully identified selective HDAC inhibitors. Moreover, we have also designed dual-target inhibitors of proteasome/HDAC that have demonstrated excellent anti-tumor activity against bortezomib-resistant multiple myeloma. Additionally, our designed HDAC-Bax dual-functional compounds have shown improved anti-tumor potency against solid tumors by more effectively activating apoptosis. Most recently, we have developed DNA-targeted HDAC inhibitors and SHP2/HDAC dual-target inhibitors, which exert anti-tumor effects through a dual mechanism involving cytotoxicity and tumor immune activation.

### Main Publications:

1. Chen C, Li X, Zhao H, Liu M, Du J, Zhang J, Yang X, Hou X\*, **Fang H\***. Discovery of DNA-Targeting HDAC Inhibitors with Potent Antitumor Efficacy In Vivo That Trigger Antitumor Immunity. *J. Med. Chem.* 2022, 65(4):3667-3683.
2. Liu M, Gao S, Liang T, Qiu X, Yang X, **Fang H\***, Hou X\*. Discovery of Novel Src Homology-2 Domain-Containing Phosphatase 2 and Histone Deacetylase Dual Inhibitors with Potent Antitumor Efficacy and Enhanced Antitumor Immunity. *J. Med. Chem.* 2022, 65(18):12200-12218.

3. Liu M, Gao S, Elhassan RM, Hou X\*,**Fang H\***. Strategies to overcome drug resistance using SHP2 inhibitors. *Acta Pharm. Sin. B.*2021, 11(12):3908-3924.
4. Elhassan RM, Hou X\*,**Fang H\***. Recent advances in the development of allosteric protein tyrosine phosphatase inhibitors for drug discovery. *Med. Res. Rev.*2022, 42(3):1064-1110.
5. Liang T, Zhou Y, Elhassan RM, Hou X, Yang X, **Fang H\***. HDAC-Bax Multiple Ligands Enhance Bax-Dependent Apoptosis in HeLa Cells. *J. Med. Chem.*, 2020, 63(20):12083-12099.
6. Zhou Y, Liu X, Xue J, Liu L, Liang T, Li W, Yang X, Hou X, **Fang H\***. Discovery of Peptide Boronate Derivatives as Histone Deacetylase and Proteasome Dual Inhibitors for Overcoming Bortezomib Resistance of Multiple Myeloma. *J. Med. Chem.*,2020, 63, 4701-4715.
7. Liang T, Xue J, Yao Z, Ye Y, Yang X, Hou X, Fang H. Design, synthesis and biological evaluation of 3, 4-disubstituted-imidazolidine-2, 5-dione derivatives as HDAC6 selective inhibitors.*Eur. J. Med. Chem.*, 2021, 221, 113526.
8. Hou X, Sun J-P, Ge L, Liang X, Li K, Zhang Y, **Fang H\***. Inhibition of Striatal-enriched Protein Tyrosine Phosphatase by Targeting Computationally Revealed Cryptic Pockets. *Eur. J. Med. Chem.*,2020, 190, 112131.
9. Liu L, Liu R, Yang X, Hou X\*, **Fang H\***. Design, synthesis and biological evaluation of tyrosine derivatives as Mcl-1 inhibitors. *Eur. J. Med. Chem.*2020, 191, 112142.
10. Liang T, Hou X, Zhou Y, Yang X, **Fang H\***. Design, Synthesis, and Biological Evaluation of 2,4-Imidazolidinedione Derivatives as HDAC6 Isoform-Selective Inhibitors. *ACS Med. Chem. Lett.*2019, 10, 1122-1127.

### Facilities & Resources:

Our state-of-the-art facilities and cutting-edge technology enable us to conduct research that is both rigorous and innovative. In addition to the equipment available at the Shandong University Public Instrument Platform, our research group also has 2 rapid preparative liquid chromatography systems, a polarimeter, a freeze dryer, a high-speed centrifuge, an enzyme marker, and other equipment.



**Collaborations & Partnerships:**

Our collaborators include Professor Yingkai Zhang from New York University and Professor Weiping Tang from the University of Wisconsin-Madison.

**Recreational Activities:**

Jinan City is a famous historical and cultural city in China. Our research group utilizes spare time to organize team activities such as hiking and mountain climbing.

**Other Features:**

The distinctive feature of our research group is the deep integration of medicinal chemistry and computer-aided drug design, enabling accurate and rapid discovery of lead compounds and rational structure optimization, significantly enhancing research efficiency.

**Contact:**

For more information or inquiries, please contact us at [haofangcn@sdu.edu.cn](mailto:haofangcn@sdu.edu.cn)

## Shandong University-BOP Oral Joint Microbiome Laboratory

### **Establishment and Development:**

Shandong University-BOP Oral Joint Microbiome Laboratory was born from a vision and passion for oral microecology and human systemic health. Recognizing the need to clarify the relationship between oral pathogen with multiple oral and/or systemic diseases, prof. Feng Qiang decided to establish a laboratory dedicated to decode the characteristics of oral microbiome and the pathogenesis of key oral pathogen with multi-disciplinary knowledge. Our laboratory began with the department of human microbiome school and hospital of stomatology, Shandong University. With a giant team of interdisciplinary knowledge background, we established a research laboratory that would be recognized for its excellence and impact in the field of human microbiome. Since its inception, our laboratory has gone through a remarkable journey of growth and development, and our team members have received multiple founding supports from the National government and Shandong Province.

### **Team Members:**

Our team consists of 1 leading scientist and 4 top experts from their respective fields, young and passionate professional researchers, and 4 staffs who are committed to provide excellence technology support. Together, they worked enthusiastically to decode the relationship between oral pathogens and oral/systemic diseases.

### **Research Areas:**

Our laboratory focus in the field of oral microbiome and oral/systemic health. Our team is skilled at mining the human microbiome/transcriptome/single cell/spatiotemporal omics data from oral and systemic diseases in the dry lab, and study the mechanisms between key oral pathogen and relative diseases in the wet lab. Firstly, the microbiome data were analyzed and mined to identify the key pathogenic microbes. Then, the animal model was used to simulate the pathogenic mechanism and analyze the pathology of key oral microbes. Also, the molecular mechanism of the key microbes were studied by using multiple different kind of cell models and molecular technologies. By now, we have elucidated the multiple pathogenic mechanisms of oral pathogen and oral/ systemic diseases of the molecular mechanism of pathogen adhesion, invasion and interacted with host cells to regulate gene expression, and decoding the key virulence effector proteins of oral pathogenic microbes on intracellular signaling pathways.

### **Research Achievements:**

We have made several significant contributions on the characteristics of human microbiome and their pathogenic mechanisms, stem cell isolation and directed differentiation, and research on the resistance mechanisms of tumor-targeted drugs. Our research results have clarified the mechanism by which *Fusobacterium nucleatum* (*F. nucleatum*) invaded gingival tissue and interfered with the biological activity of oral cells. We also found that *F. nucleatum* significantly reduced the

proliferation and osteogenic differentiation ability of stem cells by promoting cell migration and the release of related chemokines and cytokines. By studying the distribution and role of microorganisms in the tumor microenvironment, we found that *F. nucleatum* infection weakened the efficacy of immunotherapy by increasing Lgals9-positive mast cells.

### **Main Publications:**

- [1] Ma C, Yang C, Peng A, Sun T, Ji X, Mi J, Wei L, Shen S, Feng Q. Pan-cancer spatially resolved single-cell analysis reveals the crosstalk between cancer-associated fibroblasts and tumor microenvironment. *Mol Cancer*. 2023 Oct 13;22(1):170.
- [2] Lai Y, Mi J, Feng Q. Fusobacterium nucleatum and Malignant Tumors of the Digestive Tract: A Mechanistic Overview. *Bioengineering (Basel)*. 2022 Jun 28;9(7):285.
- [3] Wang Y, Wang L, Sun T, Shen S, Li Z, Ma X, Gu X, Zhang X, Peng A, Xu X, Feng Q. Study of the inflammatory activating process in the early stage of Fusobacterium nucleatum infected PDLSCs. *Int J Oral Sci*. 2023 Feb 8;15(1):8.
- [4] Shen S, Sun T, Ding X, Gu X, Wang Y, Ma X, Li Z, Gao H, Ge S, Feng Q. The exoprotein Gbp of Fusobacterium nucleatum promotes THP-1 cell lipid deposition by binding to CypA and activating PI3K-AKT/MAPK/NF- $\kappa$ B pathways. *J Adv Res*. 2023 Apr 24: S2090-1232(23)00113-3.
- [5] Mi J, Wang S, Liu P, Liu C, Zhuang D, Leng X, Zhang Q, Bai F, Feng Q, Wu X. CUL4B Upregulates RUNX2 to Promote the Osteogenic Differentiation of Human Periodontal Ligament Stem Cells by Epigenetically Repressing the Expression of miR-320c and miR-372/373-3p. *Front Cell Dev Biol*. 2022 Jun 16;10:921663.
- [6] Gao H, Sun T, Yang F, Yuan J, Yang M, Kang W, Tang D, Zhang J, Feng Q. The Pathogenic Effects of Fusobacterium nucleatum on the Proliferation, Osteogenic Differentiation, and Transcriptome of Osteoblasts. *Front Cell Dev Biol*. 2020 Sep 11; 8:807.
- [7] Kang W, Jia Z, Tang D, Zhao X, Shi J, Jia Q, He K, Feng Q. Time-Course Transcriptome Analysis for Drug Repositioning in Fusobacterium nucleatum-Infected Human Gingival Fibroblasts. *Front Cell Dev Biol*. 2019 Sep 20; 7:204.
- [8] Kang W, Ji X, Zhang X, Tang D, Feng Q. Persistent Exposure to Fusobacterium nucleatum Triggers Chemokine/Cytokine Release and Inhibits the Proliferation and Osteogenic Differentiation Capabilities of Human Gingiva-Derived Mesenchymal Stem Cells. *Front Cell Infect Microbiol*. 2019 Dec 17; 9:429.
- [9] Hou Q, Pucci F, Pan F, Xue F, Rooman M, Feng Q. Using metagenomic data to boost protein structure prediction and discovery. *Comput Struct Biotechnol J*. 2022 Jan 3; 20:434-442.
- [10] Feng Q, Lan X, Ji X, Li M, Liu S, Xiong J, Yu Y, Liu Z, Xu Z, He L, Chen Y, Dong H, Chen P, Chen B, He K, Li Y. Time series analysis of microbiome and metabolome at multiple body sites in steady long-term isolation confinement. *Gut*. 2021 Jul;70(7):1409-1412.

### **Facilities & Resources:**

Our state-of-the-art facilities and cutting-edge technology enable us to conduct research that is both rigorous and innovative. We have built a large computing platform, developed and installed a series of bioinformatics software under Linux, analysis tools such as SOAP, R Language, Qiime2.0, MOCAT, Cytoscape, and developed a variety of bioinformatics analysis methods. In the research of the pathogenic mechanism of oral pathogenic microbiome we have established many kinds of microbiome infection animal and cell models, it can be used to carry out a series of high-precision analyses such as microscopic image tracking, microbial toxic protein function analysis, pathogenic microbiome evolution analysis and comparative genomics analysis, protein structure simulation, protein-protein, protein-small molecule, toxic protein-host receptor interaction analysis, and pathogenic microbiome infection host research, etc.

**Collaborations & Partnerships:**

We believe in the power of collaboration. We have forged partnerships with Chinese University of Hong Kong, Copenhagen University, and Shanghai Jiaotong University School of Medicine to further advance our research.

**Contact:**

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## **Tissue Engineering and Regeneration Laboratory, School of Stomatology, Shandong University**

### **Establishment and Development:**

Tissue Engineering and Regeneration Laboratory was born from a shared vision and passion for the treatment of oral diseases and the promotion of regeneration of oral tissues. Recognizing the importance of biomaterials for the treatment of oral disease, our founder is dedicated to constructing engineered multi-layered active materials, for oral tissue regeneration and inflammation treatment by regulating signaling pathways and cell fate. After receiving his Ph.D. in 2019 from Shandong University, our principal investigator Baojin Ma worked as a postdoctoral fellow in Prof. Alberto Bianco's group at the CNRS in Strasbourg (France) during 2019-2021. In February 2021, he joined the School of Stomatology, at Shandong University and started Tissue Engineering and Regeneration Laboratory (new). After three years of vigorous development, our lab has become a team of over twenty and possesses more than 200 square meters of area. Dr. Ma was selected as the "Qilu Young Scholars" of Shandong University and "Taishan Young Scholars" of Shandong Province and served as the leader of the Youth Innovation Team in Shandong Province's higher education institutions. Additionally, we have forged valuable collaborations and partnerships with the State Key Laboratory of Crystal Materials of Shandong University and CNRS at Strasbourg University to further enhance our research capabilities.

### **Team Members:**

Our team is composed of one associate researcher, three post-doctors, three experimental technique workers, three doctors, and five masters. Together, they work tirelessly to design and synthesize multifunction biomaterials for nanomedicine and tissue repair.

### **Research Areas:**

Tissue Engineering and Regeneration Laboratory specializes in the fields of multi-layer bioactive biomaterials, tissue engineering, and nanomedicine.

### **Research Achievements:**

Our Lab is committed to achieving efficient tissue repair and inflammation treatment through structural regulation and functional design of materials, contributing to the development of oral medicine. Our achievements have been published on *Nat. Rev. Mater.*, *Adv. Funct. Mater.*, *J. Am. Chem. Soc.*, *J. Dent. Res.*, *ACS Nano*, *Adv. Sci.*, *Small* and other international high-level journals.

### **Main Publications:**

- [1] B. Ma, A. Bianco, *Nature Reviews Materials* 2023, 8, 403.
- [2] L. Shang, Y. Yan, Z. Li, H. Liu, S. Ge, B. Ma, *Advanced Science* 2024, 11, 2306528.
- [3] S. Liu, L. Zhang, Z. Li, F. Gao, Q. Zhang, A. Bianco, H. Liu, S. Ge, B. Ma,

- Advanced Functional Materials* 2024, 34, 2306534.
- [4] Y. Xiao, Z. Li, A. Bianco, B. Ma, *Advanced Functional Materials* 2023, 33, 2209291.
- [5] M. Liu, J. Shao, Y. Zhao, B. Ma, S. Ge, *Journal of Dental Research* 2023, 102, 555.
- [6] Z. Liu, Y. Yu, W. Kang, F. Chen, F. Yan, B. Ma, S. Ge, *Composites Part B: Engineering* 2022, 244, 110186.
- [7] C. Lv, W. Kang, S. Liu, P. Yang, Y. Nishina, S. Ge, A. Bianco, B. Ma, *ACS nano* 2022, 16, 11428.
- [8] B. Ma, C. Martín, R. Kurapati, A. Bianco, *Chemical Society Reviews* 2020, 49, 6224.
- [9] B. Ma, S. Wang, F. Liu, S. Zhang, J. Duan, Z. Li, Y. Kong, Y. Sang, H. Liu, W. Bu, *Journal of the American Chemical Society* 2019, 141, 849.
- [10] S. Wang, Y. Zhao, S. Yao, Z. Wang, Z. Zhang, K. Wen, B. Ma, L. Li, *Small* 2024 2309328.

### **Facilities & Resources:**

Our state-of-the-art facilities and cutting-edge technology enable us to conduct research that is both rigorous and innovative. We boast more than 200 square meters of experimental area, a laboratory animal room, and a cell laboratory. Our lab also equips more than 28 precise instruments such as a rheometer, lyophilizer, freezing microtome, and fluorescence microscope.

### **Collaborations & Partnerships:**

We believe in the power of collaboration. Our Lab has close cooperation with Prof. Alberto Bianco, who is a Fellow of the European Academy of Science and Academia Europaea, who in 2019 obtained the CNRS Silver Medal and since 2011 has been the Editor of the journal Carbon. Meanwhile, we also cooperate with Prof. Hong Liu, who is a professor at Shandong University and was awarded Distinguished Young Scholar by the National Natural Science Foundation of China. Prof. Liu has published more than 400 papers with a total citation of over 36000 and H-index of 86. In 2022, as Editor-in-Chief, he launched a new journal, *BMEMat*.

### **Recreational Activities:**

We often have dinner parties and go camping outdoors in the spring and fall. Snacks and drinks are available in the laboratory seating area

### **Contact:**

For more information or inquiries, please contact us at [baojinma@sdu.edu.cn](mailto:baojinma@sdu.edu.cn).

## Environmental Health Laboratory

### **Establishment and Development:**

Environmental health laboratory was born from a shared vision and passion for environmental pollution and human health. Recognizing the need for antibiotic pollution and antibiotic-resistant bacteria, our founders decided to establish a laboratory dedicated to prevent and control the antibiotic-resistant bacteria. The journey of our team began with the research on environment and human health and we have been engaged in research on antibiotics and the spread of ARB in the environment since 2009 and we have led more than 20 projects, including the National Natural Science Foundation Program of China. With a small but dedicated team, we set out to establish a research laboratory that would be recognized for its excellence and impact. Since its inception, our team has gone through a remarkable journey of growth and development. We have expanded our team to include multiple doctoral and master's students who are proficient in laboratory related skills. Our research has focuses on the research on the transmission characteristics and diffusion patterns of antibiotics and antibiotic-resistant bacteria/genes. Additionally, we have forged valuable collaborations and partnerships with Peking University, China CDC, Oxford University in the UK, Uppsala University in Sweden, Karolinska School of Medicine to further enhance our research capabilities.

### **Team Members:**

Our team is composed of professors, associate professors, and lecturers who have been engaged in research on antibiotic-resistant bacteria for a long time and more than 10 doctoral and master's students who are proficient in experimental skills related to antibiotic resistant bacteria such as screening of antibiotic-resistant bacteria, identification of strains, phenotype analysis, plasmid transformation and conjugation transfer experiments, SHIME model experiments and proficient in using statistical analysis tools such as SAS, SPSS, and R,. Together, they work tirelessly to the fields of aquaculture environment, planting environment, and hospital environment, conducting research on the transmission characteristics and diffusion patterns of antibiotics and antibiotic-resistant bacteria/genes, comprehensively analyzing the development laws and transmission drivers of bacterial resistance, and providing theoretical basis and technical support for the prevention and control of bacterial resistance in agricultural and medical environments. we have been engaged in research on antibiotics and the spread of ARB in the environment since 2009 and we have led more than 20 projects, including the National Natural Science Foundation Program of China. In 2016, the first "One Health" research queue for antibiotic-resistant bacteria in China was established in Yi'shui, Shandong Province, China. It provides long-term real-time tracking of the evolution of bacterial resistance and provides a more reliable theoretical basis for the field of bacterial resistance evolution and prevention and control

### **Research Areas:**

specializes in research on antibiotics and the spread of ARB in the environment since 2009. Based on the "One Health" concept, we have implemented antibiotic resistance control strategies in animal husbandry areas, ensuring the sustainable development of intensive vegetable areas from the perspective of antibiotic residue and antibiotic resistant bacterial prevention and control. We have conducted traceability analysis and prevention technologies for antibiotic resistant bacterial infections in hospitals, focusing on antibiotic reduction and antibiotic resistant bacterial transmission prevention and control technologies.

### **Research Achievements:**

We have made significant contributions in establishing the first "One Health" research queue for antibiotic-resistant bacteria in Yishui in 2016, Shandong Province, China. The evolution of bacterial resistance was tracked in real-time for a long time. In 2018, the first designated hospital in our province built a resource library of drug-resistant bacterial strains for daily infections. More than 10000 serious threat drug-resistant strains, including animal and clinical sources of *Escherichia coli*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*, have been preserved. In recent years, our team has published international journal papers such as *Water Research*, *Science of The Total Environment*, and *Environmental Pollution* in the fields of aquaculture environment, planting environment, and hospital environment. Multiple papers have been selected as highly cited papers in ESI (top 1%). Through conducting research on the transmission characteristics and diffusion patterns of antibiotics and resistant bacteria/resistant genes, we comprehensively analyze the development patterns and driving forces of bacterial resistance, Provide theoretical basis and technical support for the prevention and control of bacterial resistance in agricultural and medical environments.

### **Main Publications:**

1. Zou H, Zhou Z, Berglund B, Zheng B, Meng M, Zhao L, Zhang H, Wang Z, Wu T, Li Q, Li X. Persistent transmission of carbapenem-resistant, hypervirulent *Klebsiella pneumoniae* between a hospital and urban aquatic environments. *Water Res.* 2023 Aug 15;242:120263. doi: 10.1016/j.watres.2023.120263. Epub 2023 Jun 22. PMID: 37390655.
2. Zou H, Han J, Zhao L, Wang D, Guan Y, Wu T, Hou X, Han H, Li X. The shared NDM-positive strains in the hospital and connecting aquatic environments. *Sci Total Environ.* 2023 Feb 20;860:160404. doi: 10.1016/j.scitotenv.2022.160404. Epub 2022 Nov 22. PMID: 36427732.
3. Wang D, Berglund B, Li Q, Shanguan X, Li J, Liu F, Yao F, Li X. Transmission of clones of carbapenem-resistant *Escherichia coli* between a hospital and an urban wastewater treatment plant. *Environ Pollut.* 2023 Nov 1;336:122455. doi: 10.1016/j.envpol.2023.122455. Epub 2023 Aug 24. PMID: 37633440.
4. Li Q, Zou H, Wang D, Zhao L, Meng M, Wang Z, Wu T, Wang S, Li X. Tracking spatio-temporal distribution and transmission of antibiotic resistance in aquatic environments by using ESBL-producing *Escherichia coli* as an indicator. *J Environ*

Manage. 2023 Oct 15;344:118534. doi: 10.1016/j.jenvman.2023.118534. Epub 2023 Jun 30. PMID: 37393874.

5. Gu C, Li X, Zou H, Zhao L, Meng C, Yang C, Hui Zhang, Berglund B. Clonal and plasmid-mediated dissemination of environmental carbapenem-resistant Enterobacteriaceae in large animal breeding areas in northern China. *Environ Pollut.* 2022 Mar 15;297:118800. doi: 10.1016/j.envpol.2022.118800. Epub 2022 Jan 7. PMID: 35007671.

6. Hanna N, Sun P, Sun Q, Li X, Yang X, Ji X, Zou H, Ottoson J, Nilsson LE, Berglund B, Dyar OJ, Tamhankar AJ, Stålsby Lundborg C. Presence of antibiotic residues in various environmental compartments of Shandong province in eastern China: Its potential for resistance development and ecological and human risk. *Environ Int.* 2018 May;114:131-142. doi: 10.1016/j.envint.2018.02.003. Epub 2018 Mar 2. PMID: 29501851.

7. Ji X, Zheng B, Berglund B, Zou H, Sun Q, Chi X, Ottoson J, Li X, Lundborg CS, Nilsson LE. Dissemination of extended-spectrum  $\beta$ -lactamase-producing *Escherichia coli* carrying *mcr-1* among multiple environmental sources in rural China and associated risk to human health. *Environ Pollut.* 2019 Aug;251:619-627. doi: 10.1016/j.envpol.2019.05.002. Epub 2019 May 7. PMID: 31108295.

8. Zou H, Berglund B, Xu H, Chi X, Zhao Q, Zhou Z, Xia H, Li X, Zheng B. Genetic characterization and virulence of a carbapenem-resistant *Raoultella ornithinolytica* isolated from well water carrying a novel megaplasmid containing *bla*NDM-1. *Environ Pollut.* 2020 May;260:114041. doi: 10.1016/j.envpol.2020.114041. Epub 2020 Jan 22. PMID: 32006889.

9. Sun P, Bi Z, Nilsson M, Zheng B, Berglund B, Stålsby Lundborg C, Börjesson S, Li X, Chen B, Yin H, Nilsson LE. Occurrence of *bla*KPC-2, *bla*CTX-M, and *mcr-1* in Enterobacteriaceae from Well Water in Rural China. *Antimicrob Agents Chemother.* 2017 Mar 24;61(4):e02569-16. doi: 10.1128/AAC.02569-16. PMID: 28115344; PMCID: PMC5365680.

10. Zhao Q, Berglund B, Zou H, Zhou Z, Xia H, Zhao L, Nilsson LE, Li X. Dissemination of *bla*NDM-5 via *IncX3* plasmids in carbapenem-resistant Enterobacteriaceae among humans and in the environment in an intensive vegetable cultivation area in eastern China. *Environ Pollut.* 2021 Jan 2;273:116370. doi: 10.1016/j.envpol.2020.116370. Epub ahead of print. PMID: 33460870.

### **Facilities & Resources:**

Our state-of-the-art facilities and cutting-edge technology enable us to conduct research that is both rigorous and innovative. The Analysis and Testing Center of Shandong University is an open unit for analysis, testing, and quality evaluation, which has been certified by the National Bureau of Technical Supervision and approved by the Ministry of Health. It has numerous experts with high professional level and supporting instruments such as SHIME simulation equipment required for research projects. The State Key Laboratory of Microbiology Technology of Shandong University has built many research platforms for bacteriology, infection microecology, genomics, bioinformatics, proteomics, etc. It is a research support system with

international standards, and has the instruments and equipment required for genomics and proteomics research. All of the above provide comprehensive and scientific support and guarantee conditions for future research plans.

**Collaborations & Partnerships:**

We believe in the power of collaboration. That's why we have forged partnerships with Peking University, Zhejiang University, Chinese Academy of Sciences, China Center for Disease Control and Prevention, as well as Oxford University, Uppsala University, Sweden and Karolinska Medical College to further advance our research.

**Recreational Activities:**

We will hold academic seminars every week, record 10000 steps of exercise check-in every day, gathering of team members during holidays, organizing mountaineering activities, regularly go to various places for sampling and learning, and participating in various academic conferences.

**Other Features:**

The team conducts research on the transmission characteristics and diffusion patterns of antibiotics and antibiotic-resistant bacteria/genes, comprehensively analyzing the development patterns and transmission drivers of bacterial resistance. In 2016, the first One Health research queue for antibiotic-resistant bacteria was established in China, and in 2018, the first designated hospital in our province established a resource library of antibiotic-resistant bacterial strains for daily infections of drug-resistant pathogenic bacteria.

**Contact:**

For more information or inquiries, please contact us by visiting our website at <https://faculty.sdu.edu.cn/lixuewen/en/index.htm> or mailing to: [lxw@sdu.edu.cn](mailto:lxw@sdu.edu.cn).

## **Institute of Biotherapy for Hematological Malignancies of Shandong University; Shandong University-Karolinska Institutet Collaborative Laboratory for Stem Cell Research**

### **Establishment and Development:**

Shandong University-Karolinska Institutet Collaborative Laboratory for Stem Cell Research was born from a shared vision and passion for tumor immunotherapy, stem cells, and regenerative medicine study. Recognizing the need for in-depth cooperation with famous scholars of KI in the field of stem cells, our founders decided to establish a laboratory dedicated to stem cell research. The collaboration started in 2005 when prof. Chengyun Zheng was recruited from KI by Shandong University, and was a natural continuation of his 8 years' research education and training at KI. The earlier collaborations were mainly in studies of cancer biology and immunology, as well as inherent hematological disorders, such as familial hemophagocytic lymphohistiocytosis (FHL). Institute of Biotherapy for Hematological Malignancies of Shandong University was established in 2010. Subsequently in 2014, under the promotion of prof. Zheng Chengyun, Shandong University-Karolinska Institutet Collaborative Laboratory for Stem Cell Research was established. With dramatic developments in stem cell research, especially in the fields of inducible pluripotent stem cells (iPSCs) and mesenchymal stem cells (MSCs), the collaboration team has gradually shifted their research collaborations in stem cell therapies. Additionally, we have forged valuable collaborations and partnerships with prof. Qi Zhou (Academician of Chinese Academy of Sciences, State Key Laboratory of Stem Cell, Chinese Academy of Sciences) and Qing Yi (internationally famous multiple myeloma immunology expert, Director of Center for Hematologic Malignancy Research Institute, Houston Methodist) to further enhance our research capabilities in immunotherapy for hematological tumors.

### **Team Members:**

Our team is composed of 2 leading experts in their fields, 13 young and passionate researchers, and 2 support staff dedicated to excellence.

Prof. Chengyun Zheng, PhD of Hematology in Karolinska Institute, Sweden, Director of the team, PhD supervisor of Shandong University, dedicated to immunotherapy and stem cell basic and clinical application research.

Prof. Dawei Xu, Director of Hematology Laboratory in Karolinska Institutet.

Prof. Yang Jiang, PhD of Immunology in Shandong University, Associate professor of Shandong University, dedicated to immunotherapy and stem cell research.

Prof. Dexiao Kong, PhD of Hematology in Shandong University, Deputy Director of Hematology Department, dedicated to immunomodulatory therapy of aplastic anemia and hematological malignancies.

In 2012, the team became a post-doctoral mobile station, cultivating 4 postdocs, 27 doctoral students and 34 master students. Together, they work tirelessly to immunotherapy of hematologic neoplasm and stem cell basic and clinical application research.



### **Research Areas:**

Shandong University-Karolinska Institutet Collaborative Laboratory for Stem Cell Research specializes in developing a curative approach for inherited immune defects by transplantation of autologous hematopoietic stem cells (HSC) derived from iPSC or MSC after correction of disease gene mutations. The collaborations also work on stem cell-based 3-D renal tissue regeneration, aiming to develop future stem cell-based cell therapies for kidney failure. Hence, the research directions are:

- 1) Regulation of stem cell (iPSC and MSC) differentiation and bio-safety evaluation of in vitro manipulated stem cells.
- 2) Development and functional evaluation of stem cell-based renal tissue regeneration.

### **Research Achievements:**

Under the guidance of relevant national policies and regulations, autologous and allogeneic hematopoietic stem cell transplantation was started in 2004. To achieve better therapeutic effect, since May 2009, we formulated the working system and process for the application of MSCs, published clinical trial of MSCs treatment on the NCBI website, and conducted basic and clinical studies based on MSCs. We found that MSCs has achieved good therapeutic effects in diabetes mellitus, ankylosing spondylitis, pulmonary interstitial fibrosis and severe pneumonia.

In the past five years, our team has published more than 20 SCI papers, with a total funding of 5 million yuan, authorized 5 national invention patents and 2 clinical trials. In 2023, we won the second prize of Science and Technology Progress of Shandong Province.

### **Main Publications:**

1. Hui Li, Dexiao Kong, Yi Zhao, Xia Liu, Fang Xiao, Xiaoyan Li, Jianting Hu, Yingjie Chen, Shengli Li, Baozhu Wang, Yuan Chen, Yang Jiang, Xiaoli Liu, Xiumei Fen, Yanan Guo, Xiaoli Feng, Jing Ren, Fang Wang, Ying Han, William Donelan, Lijun Yang, Dawei Xu, Dongqi Tang, **Chengyun Zheng**. Irisin protected hemopoietic stem cells and improved outcome of severe bone marrow failure. *Biomed Pharmacother.* 2023;169:115863.
2. Jing Ren, Xiumei Feng, Yanan Guo, Dexiao Kong, Yongjing Wang, Juan Xiao, Wen Jiang, Xiaoli Feng, Xiaoli Liu, Ai Li, Congcong Sun, Mingming He, Bingen Li, Juandong Wang, Yang Jiang, **Chengyun Zheng**. GSK-3 $\beta$ / $\beta$ -catenin pathway plays crucial roles in the regulation of NK cell cytotoxicity against myeloma cells. *FASEB J.* 2023;37(3):e22821.
3. Liyuan Liu, Haixia Liu, Xiaowen Huang, Xiaoli Liu, **Chengyun Zheng**. A High-Throughput and Uniform Amplification Method for Cell Spheroids. *Micromachines (Basel).* 2022;13(10):1645.
4. Wen Jiang, Fanglin Li, Yang Jiang, Shengli Li, Xiaoli Liu, Yaqi Xu, Bingen Li, Xiaoli Feng and **Chengyun Zheng**. Tim-3 Blockade Elicits Potent Anti-Multiple Myeloma Immunity of Natural Killer Cells. *Front Oncol.* 2022;12:739976.

5. Xiaoli Liu, Huichao Lin, Jiaao Song, Taiyi Zhang, Xiaoying Wang, Xiaowen Huang, **Chengyun Zheng**. A Novel SimpleDrop Chip for 3D Spheroid Formation and Anti-Cancer Drug Assay. *Micromachines (Basel)*. 2021;12(6):681.
6. Li R, **Zheng C**, Wang Q, Bi E, Yang M, Hou J, Fu W, Yi Q, Qian J. Identification of an immunogenic DKK1 long peptide for immunotherapy of human multiple myeloma. *Haematologica*. 2021;106(3):838-846. **(Co-corresponding author)**
7. Yang Jiang, Shuo Li, Qian Zhou, Shenghou Liu, Xiaoli Liu, Juan Xiao, Wen Jiang, Yaqi Xu, Dexiao Kong, Fang Wang, Fengtao Wei, **Chengyun Zheng**. PDCD4 Negatively Regulated Osteogenic Differentiation and Bone Defect Repair of Mesenchymal Stem Cells Through GSK-3 $\beta$ / $\beta$ -Catenin Pathway. *Stem Cells Dev*. 2021;30(16):806-815.
8. Yaqi Xu, Xiaoli Feng, Qian Zhou, Wen Jiang, Yibo Dai, Yang Jiang, Xiaoli Liu, Shuo Li, Yongjing Wang, Fang Wang, Ai Li, and **Chengyun Zheng**. Novel Small Molecular Compound AE-848 Potently Induces Human Multiple Myeloma Cell Apoptosis by Modulating the NF- $\kappa$ B and PI3K/Akt/mTOR Signaling Pathways. *Onco Targets Ther*. 2020; 13: 13063–13075.
9. Xu Y, Zhou Q, Feng X, Dai Y, Jiang Y, Jiang W, Liu X, Xing X, Wang Y, Ni Y, **Zheng C**. Disulfiram/copper markedly induced myeloma cell apoptosis through activation of JNK and intrinsic and extrinsic apoptosis pathways. *Biomed Pharmacother*. 2020;126:110048.
10. Xiaoyan Zhou, Xiaoli Liu, Li Liu, Chao Han, Zhaohong Xie, Xiangtian Liu, Yingying Xu, Fan Li, Jianzhong Bi, **Chengyun Zheng**. Transplantation of IFN- $\gamma$  Primed hUCMSCs Significantly Improved Outcomes of Experimental Autoimmune Encephalomyelitis in a Mouse Model. *Neurochem Res*. 2020;45(7):1510-1517.

#### **Facilities & Resources:**

Our state-of-the-art facilities and cutting-edge technology enable us to conduct research that is both rigorous and innovative. Our team relies on Institute of Biotherapy for Hematological Malignancies of Shandong University, Institute of Medical Sciences in the Second Hospital of Shandong University and the Animal Laboratory. We have independent ventilation, thousand level clean GMP laboratory and SPF animal experimental center, which have reached the national clean standard. We have complete and advanced instruments, such as flow cytometer, fluorescence confocal microscope, fluorescence quantitative PCR instrument, American Abbott drug concentration detector, ultrasonic fragmentation, low temperature high-speed centrifuge, horizontal and vertical electrophoresis imaging and observation system, immunoenzyme linked immunosorbent assay, CO<sub>2</sub> cell incubator, ultra-clean working table, biological safety cabinet, -80°C refrigerator, inverted microscope, fluorescence microscope and cell culture and frozen storage facilities, automatic blood coagulator, freezing microtome, paraffin microtome, automatic tissue dehydrator, small animal living imaging and other advanced instruments and equipments, which meeting the need for the facilities and sites for conducting scientific research.

**Collaborations & Partnerships:**

We believe in the power of collaboration. At present, our team has performed high-quality visits and academic exchanges for more than 10 times, several members have gone to KI to strengthen cooperation and exchange, and Professor Anders Hemstem, Professor Nailin Li, and Professor Magnus Nordenskjold have also visited the Second Hospital of Shandong University for academic lectures and subject cooperation. We have performed academic discussions with Professor Dawei Xu of KI every year, and have sent many visiting scholars to KI for exchange and study.

Moreover, our laboratory and the Institute of Zoology in the Chinese Academy of Sciences established a special clinical research base of strategic stem cell and regenerative medicine research of the Chinese Academy of Sciences. At present, our laboratory has sent several researchers to the Institute of Zoology in the Chinese Academy of Sciences to learn new technologies. And our laboratory also conducted a wide range of academic exchanges and subject cooperation with Beijing Xuanwu hospital, Qilu hospital, Shandong provincial hospital, Shandong University of Chinese medicine and other high level academic and medical unit.

**Recreational Activities:**

In 2018, the Second Hospital of Shandong University has successfully obtained the right to hold the 8th Chinese Annual Conference of Stem Cell. With the theme of "The research and transformation of stem cells--the new Era", 6 academicians, nearly 100 top scholars and experts, more than 2000 researchers of stem cells across China, gathered together to talk about the frontier.

Take this opportunity, Prof. Yibiao Wang and Chengyun Zheng established The Stem Cell Association of Shandong Provincial and held the first annual meeting. Then, academic conferences are held every year, and the association is gradually developed to have fifth professional committee, promoting the development of stem cells in our province and even the whole country.

**Other Features:**

Our team is characterized by cell immunotherapy, and the clinical research of stem cells and immune cells, and has a certain influence in the whole country. Our outstanding advantages are as follows: 1) NK cell functional regulation, CAR-T / CAR-NK immune cells for hematological malignancies (B cell tumors, multiple myeloma, leukemia); 2) various types of hematopoietic stem cell transplantation for hematological tumors, bone marrow failure disease or genetic immune deficiency disease; 3) treatment and prevention of MSCs for GVHD and related complications; 4) treatment of MSCs for severe infection and bone marrow failure.

**Contact:**

For more information or inquiries, please contact us at [sdeyzcy@email.sdu.edu.cn](mailto:sdeyzcy@email.sdu.edu.cn)

## Visualization and Light-Controlled Regulation Guided Drug Research

### **Establishment and Development:**

The "Visualization and Light-Controlled Regulation Guided Drug Research" innovation team at the School of Pharmaceutical Sciences, Shandong University, relies on the Key Laboratory of Chemical Biology of Natural Products of the Ministry of Education and the State Key Discipline of Medicinal Chemistry for support. Our team focuses on addressing the challenges posed by major diseases such as malignant tumors and neurodegenerative disorders in terms of their occurrence, development, and clinical treatment. Our core objective revolves around the development of precise drugs and diagnostic probes. Anchored in drug and probe design (including pharmaceutical design and chemical biology), chemical synthesis (synthetic medicinal chemistry), and biological characterization (analytical chemistry, pharmacology, and imaging), our aim is to innovate drug and probe development and practical applications. The team conducts extensive and in-depth fundamental research aimed at the development and practical application of innovative drugs and probes, aiming to contribute significantly to the field.

### **Team Members:**

Our team is composed of leading experts in their respective fields, each with extensive experience and a track record of excellence. This elite group includes 5 professors and 1 associate professor, all of whom have honed their expertise through years of study and work both domestically and overseas. Dedicated to pushing the boundaries of drug research and innovation, our team is committed to tackling the most pressing challenges in pharmaceutical science. Through collaboration, creativity, and a relentless pursuit of excellence, we aim to drive forward the field of drug research and bring about meaningful advancements in medicine.

### **Research Areas:**

1. **Visualization of Biological Activity:** Research focuses on developing various types of probes for visualizing biological processes, including fluorescent probes, bioluminescent probes, chemiluminescent probes, and visual prodrugs.
2. **Molecular Probe Development:** This area explores orthogonal reactions in biology, light-controlled and photoaffinity reactions, as well as novel strategies and technologies for targeted protein degradation.
3. **Rational Drug Design and Medicinal Chemistry:** Research delves into rational drug design and medicinal chemistry targeting ion channels, GPCRs (G-protein-coupled receptors), Cys-loop receptors, autophagy, and protein-protein interactions.
4. **Discovery and Identification of Drug Targets and Binding Sites:** Efforts are made to discover and identify drug targets and binding sites, enhancing the understanding of drug-target interactions.
5. **Development of Novel Organic Synthesis Methods:** This research direction focuses on the development of new methods in organic synthesis, paving the

way for synthesizing novel drug candidates and molecular probes.

### **Research Achievements:**

We have made significant contributions to the field of drug research and innovation. Through our pioneering work in visualizing biological activity, developing molecular probes, and designing targeted therapies, we have advanced our understanding of disease mechanisms and facilitated the development of novel treatment strategies.

### **Main Publications:**

1. Yang X, Ma G, Zheng S, Qin X, Li X, Du L, Wang Y, Zhou Y, Li MY\*. Optical control of CRAC channels using photoswitchable azopyrazoles. *J. Am. Chem. Soc.* 2020, 142, 9460-70. 2.
2. Dong G, Ye X, Wang S, Li W, Cai R, Du L, Shi X, Li MY\*. Au-24 as a Potential Thioredoxin Reductase Inhibitor in Hepatocellular Carcinoma Cells. *Pharmacol. Res.* 2022, 177,106113
3. Yang X, Li M, Qin X, Tan S, Du L, Ma C, Li MY\*. Photophosphatidylserine guides natural killer cells photoimmunotherapy via Tim-3. *J. Am. Chem. Soc.* 2022, 144, 3863-3874.
4. Liang D, Yu C, Ma Z, Yang X, Li Z, Dong X, Qin X, Du L, Li MY\*. Identification of anthelmintic parbendazole as a therapeutic molecule for HNSCC through connectivity map-based drug repositioning. *Acta Pharm. Sin. B.* 2022, 12, 2429-42.
5. Sun Y, Gao Y, Tang C, Dong G, Zhao P, Peng D, Wang T, Du L, Li MY\*. Multiple rapid-responsive probes towards hypochlorite detection based on dioxetane luminophore derivatives. *J. Pharm. Anal.* 2022, 12, 446-52.
6. Ye X, Wang C, Zhang S, Tang Q, Wojtas L, Li MY\*, Shi X. Chiral Hemilabile P,N-Ligand-Assisted Gold Redox Catalysis for Enantioselective Alkene Aminoarylation. *Chem.-Eur. J.* 2022, 28, e202201018.
7. Zuo Z, Kang T, Hu S, Su W, Gan Y, Miao Z, Zhao H, Feng P, Ke B, Li MY\*. A Bioluminescent Probe for Detecting Norepinephrine in Vivo. *Anal. Chem.* 2022, 94, 6441-6445.
8. Li W, Ma Z, Chen J, Dong G, Du L, Li MY\*. Discovery of Environment-Sensitive Fluorescent Ligands of  $\beta$ -Adrenergic Receptors for Cell Imaging and NanoBRET Assay. *Anal. Chem.* 2022, 94, 7021-7028.
9. Li X, Li MY\*. The application of zebrafish patient-derived xenograft tumor models in the development of antitumor agents. *Med. Res. Rev.* 2023, 43, 212-236.
10. Li Z, Ma S, Zhang L, Zhang S, Ma Z, Du L, Li MY\*. Targeted protein degradation induced by HEMTACs based on HSP90. *J. Med. Chem.* 2023, 66, 1, 733–751

### **Facilities & Resources:**

Our laboratory boasts state-of-the-art facilities and resources essential for cutting-edge drug discovery and development. Equipped with advanced chemical synthesis laboratories, computational modeling tools, and molecular biology facilities,

we enable comprehensive research spanning from initial compound design to preclinical evaluation. Additionally, our capabilities encompass cell culture facilities, biochemical assay platforms, and animal research facilities compliant with ethical regulations. Advanced imaging and microscopy systems further enhance our ability to visualize molecular interactions and cellular processes. With collaborative spaces fostering interdisciplinary interactions, our team is poised to drive innovation and translate research findings into tangible therapeutic solutions, ultimately advancing healthcare and improving patient outcomes.

**Collaborations & Partnerships:**

We have forged partnerships with leading universities, research institutions, and industry partners to further advance our research.

**Recreational Activities:**

During leisure time, our team enjoys a variety of recreational activities to foster camaraderie and relaxation.

**Other Features:**

N/A

**Contact:**

For more information or inquiries, please contact us at [mli@sdu.edu.cn](mailto:mli@sdu.edu.cn) or visit our website at <https://www.pharm.sdu.edu.cn/info/1058/13354.htm>

## Center for Gene and Immunotherapy

### **Establishment and Development:**

Center for Gene and Immunotherapy was established in 2016, with a Cell Engineering Laboratory and an Organoid Laboratory, aiming to integrate advanced gene engineering technology, cell engineering technology, and medicine to explore and develop new treatment methods for diseases such as cancer and genetic disorders, promoting human health. The founder of the laboratory, Professor Tang Dongqi, serves as the director of the Gene and Immunotherapy Center at the Second Hospital of Shandong University, as well as a professor, doctoral supervisor, Taishan Scholar overseas expert, and chairman of the Regenerative Medicine Branch of the Shandong Medical Association. Under his leadership and after years of effort, the team has grown from a small group of individuals to a large research group of over twenty members today, with members publishing over thirty high-quality papers in SCI-indexed journals such as *Diabetes and Blood*. The laboratory team undertakes important projects funded by the National Natural Science Foundation, provincial-level natural science funds, and has published research findings in high-level journals like *PNAS* and *Nature Communications*. Additionally, the laboratory actively explores interdisciplinary collaboration, establishing partnerships with various laboratories and research institutions to continuously expand research areas and enhance research innovation.

### **Team Members:**

**Tang Dongqi:** Director of the Gene and Immunotherapy Laboratory at the Second Hospital of Shandong University, Professor at Shandong University, Ph.D. supervisor, Taishan Scholar overseas expert, and Chairman of the Regenerative Medicine Branch of the Shandong Medical Association.

**Zhang Wen:** Associate Researcher, young Taishan Scholar expert, Ph.D. from Shandong University. He is primarily dedicated to developing precise, effective, and controllable CAR-T, CAR-NK, TCR-T, and other tumor immunocellular and stem cell drugs. He has published over ten papers in SCI-indexed journals and has received funding from national-level projects.

**Liu Jiang:** Assistant Researcher, Ph.D. from Shandong University. His main research direction is the modification of immune cells to kill tumor cells using gene engineering technology. He has published multiple papers in SCI-indexed journals and holds several invention patents.

**Zhu Guidong:** Postdoctoral fellow, mainly exploring the role of organoids in drug screening, tissue, and organ reconstruction.

**Pei Guojing:** Postdoctoral fellow, focusing on the application of nanocarriers in the field of immune cell therapy.

**Guo Linpei,:** Postdoctoral fellow, primarily exploring the application of adenovirus in plasmid construction and immune cell therapy.

**Wang Zhaoqi.:** Postdoctoral fellow, dedicated to developing different gene therapy vectors and exploring their role in cellular therapy.



Additionally, the team includes 2 Ph.D. students, 3 research assistants, and over ten project collaborators who work together with researchers and postdoctoral fellows to advance research in the aforementioned directions. This diverse team collaboration is committed to driving innovation and development in the fields of gene engineering and immunotherapy.

### **Research Areas:**

The Gene and Immunotherapy Center houses the Cell Engineering Laboratory and Organoid Laboratory, aiming to integrate advanced gene engineering technology, cell engineering technology, and medicine to explore and develop novel therapeutic methods for diseases such as cancer and genetic disorders, promoting human health. The main research directions include: exploring synthetic immunotherapy strategies to engineer immune cells; investigating the application of CRISPR gene editing technology in gene therapy, and developing gene drugs; developing functional protein drugs for treating metabolic diseases like diabetes; exploring the role of organoid technology in drug screening, tissue and organ reconstruction, and developing methods for evaluating tumor-related drugs and screening new drugs.

### **Research Achievements:**

Under the collective efforts of Professor Tang Dongqi and all the research staff in the laboratory, the team has published articles in high-impact journals such as PNAS and Nature Communications. They have also secured funding for several national-level general projects and major projects in Shandong Province, including:

1. Shandong Province Major Science and Technology Innovation Project - Research on Key Technologies, Product Development, and Clinical Program of CAR-T/TCR-T/CAR-NK Cells (Project Number: 2021CXGC011101), Jan 2022 - Dec 2024, 12.14 million RMB, Principal Investigator.
2. National Natural Science Foundation of China General Project - "Discovery of Secreted FNDC5 (s-Irisin) and Molecular Mechanism of GLP-1 Regulation of *fnDC5* Gene" (Project Number: 81970743), Jan 2020 - Dec 2023, 550,000 RMB, Principal Investigator.
3. Shandong Province Major Science and Technology Innovation Project - "New Technology of Precise Cancer Medical Treatment Based on CAR-T Cells and Micro-Nano Chips" (Project Number: 2018YFJH0503), Jul 2018 - Dec 2020, 1.1 million RMB, Principal Investigator.
4. Shandong Province Key Industry Key Technology Project - "Construction and Clinical Application of Next-Generation CAR-T Cells" (Project Number: 2016CYJS01A04), Jan 2016 - Dec 2018, 1.5 million RMB, Principal Investigator.
5. National Natural Science Foundation of China General Project - "Effects and Mechanism of Irisin on Atherosclerotic Plaque Formation and Vascular Remodeling" (Project Number: 81570407), Jan 2016-Dec 2019, 550,000 RMB, Principal Investigator.

### **Main Publications:**

1. Tang DQ, Lu S, Sun YP, Rodrigues E, Chou W, Yang C, Cao LZ, Chang LJ, Yang LJ. Reprogramming liver-stem WB cells into functional insulin-producing cells by persistent expression of Pdx1- and Pdx1-VP16 mediated by lentiviral vectors. *Lab Invest.* 2006 Jan;86(1):83-93. doi: 10.1038/labinvest.3700368. PMID: 16294197; PMCID: PMC3417286.
2. Yuan Zhang, Rui Li, Yan Meng, Shiwu Li, William Donelan, Yan Zhao, Lei Qi, Mingxiang Zhang, Xingli Wang, Taixing Cui, Li-Jun Yang, and Dongqi Tang. Irisin Stimulates Browning of White Adipocytes through Mitogen-Activated Protein Kinase p38 MAP Kinase and ERK MAP Kinase Signaling. *Diabetes.* 2014 Feb;63(2):514-25.
3. Zhang Y, Li S, Donelan W, Xie C, Wang H, Wu Q, Purich DL, Reeves WH, Tang D, Yang LJ. Angiopoietin-like protein 8 (betatrophin) is a stress-response protein that down-regulates expression of adipocyte triglyceride lipase. *Biochim Biophys Acta.* 2015 Nov 11. pii: S1388-1981(15)00199-7. doi: 10.1016/j.bbali.2015.11.003.
4. Yuzhu Zhang, Haibo Song, Yuan Zhang, Fei Wu, Qian Mu, Miao Jiang, Fang Wang, Wen Zhang, Liang Li, Lei Shao, Shiwu Li, Lijun Yang, Mingxiang Zhang, Qi Wu, and Dongqi Tang. Irisin Inhibits Atherosclerosis by Promoting Endothelial Proliferation Through microRNA126 - 5p. *J Am Heart Assoc.* 2016 Sep; 5(9): e004031.
5. Zhang W, Zhang M, Gao C, Zhang Y, Ge Y, Guo S, Guo X, Zhou Z, Liu Q, Zhang Y, Ma C, Tao F, Xu P. Coupling between D-3-phosphoglycerate dehydrogenase and D-2-hydroxyglutarate dehydrogenase drives bacterial L-serine synthesis. *Proc Natl Acad Sci U S A.* 2017, 114(36): E7574-E7582.
6. Manman Zhang, Chao Gao, Xiaoting Guo, Shiting Guo, Zhaoqi Kang, Dan Xiao, Jinxin Yan, Fei Tao, Wen Zhang, Wenyue Dong, Pan Liu, Chen Yang, Cuiqing Ma & Ping Xu. Increased glutarate production by blocking the glutaryl-CoA dehydrogenation pathway and a catabolic pathway involving L-2-hydroxyglutarate. *Nature Communications* 2018, 9(1):2114
7. Fangjun Li, Mu Yang, Yunhe Li, Mingqiang Zhang, Wenjuan Wang, Dongfeng Yuan and Dongqi Tang. An improved clear cell renal cell carcinoma stage prediction model based on gene sets. *BMC Bioinformatics* (2020) 21:232.
8. Li Hui, Donelan William, Wang Fang et al. GLP-1 Induces the Expression of FNDC5 Derivatives That Execute Lipolytic Actions. *Front Cell Dev Biol.* 2021, 9: 777026.
9. Sun J, Zhang W, Zhao Y, Liu J, Wang F, Han Y, Jiang M, Li S, Tang D. Conditional control of chimeric antigen receptor T-cell activity through a destabilizing domain switch and its chemical ligand. *Cytotherapy.* 2021 Dec;23(12):1085-1096. doi: 10.1016/j.jcyt.2021.07.014. Epub 2021 Sep 28. PMID: 34593327.
10. Zhang W, Yang M, Wang G, Ou S, Hu J, Liu J, Lei Y, Kang Z, Wang F, Liu J, Ma C, Wang C, Gao C, Tang D. A biosensor for D-2-hydroxyglutarate in frozen sections and intraoperative assessment of IDH mutation status. *Biosens Bioelectron.* 2024 Mar 1;247:115921. doi: 10.1016/j.bios.2023.115921. Epub 2023 Dec 12. PMID: 38104390.

### **Facilities & Resources:**

Our cutting-edge facilities and resources drive our team to explore forefront scientific inquiries, execute precise experiments, and advance immunotherapy, genetics, and molecular biology. Key equipment includes:

Cell Culture Facility: Equipped with biosafety cabinets, CO<sub>2</sub> incubators, and cell culture hoods for maintaining various cell lines.

Molecular Biology Lab: Fully equipped with PCR machines, gel documentation systems and electrophoresis equipment for genetic and molecular analysis.

Flow Cytometry Facility: Featuring high-end flow cytometers for cell analysis, cell sorting, and immunophenotyping studies.

Microscopy Suite: Includes fluorescence microscopes, confocal microscopes, and electron microscopes for cellular imaging and analysis.

Animal Facility: Maintained according to ethical standards for conducting in vivo studies, housing various animal models for preclinical research.

Genomics and Proteomics Center: Equipped with next-generation sequencing platforms, mass spectrometers, and bioinformatics tools for genomic and proteomic analysis.

Chemistry Lab: Supporting chemical synthesis, compound screening, and drug development studies with a range of analytical instruments and synthetic equipment.

### **Collaborations & Partnerships:**

We have established close partnerships with multiple laboratories and research institutions. Through interdisciplinary team collaboration, we have brought together talents from different fields to collectively explore and develop new treatment methods for diseases such as cancer and genetic disorders. For example, we have established deep interdisciplinary collaboration with the Materials and Engineering School of Shandong University, aiming to address the challenges in gene and drug delivery by developing novel nanocarriers to advance this field. Additionally, we have collaborated with multiple research teams from Shandong University, Qilu University of Technology, and Jinan University to apply for major technological innovation projects in Shandong Province, with the goal of addressing the current challenges faced by CAR-T cell therapy. In terms of external collaborations, we have formed close partnerships with research institutes and biotech companies across various regions, engaging in collaborative projects spanning areas such as organoid research and cell engineering.

### **Recreational Activities:**

The laboratory not only provides a variety of recreational activities for us to relax and unwind after scientific research, but also holds regular team dinners and organizes two outdoor group outings each year. We prioritize the health of research personnel by hosting various forms of sports competitions regularly, offering everyone excellent exercise opportunities. Additionally, we encourage participation in academic lectures and skills training to enhance professional development.

**Other Features:**

Our laboratory has a professional team and advanced facilities and resources, providing a solid foundation for researchers to conduct high-quality experiments. Our team has rich research experience, enabling us to offer professional theoretical guidance and experimental support to team members. Meanwhile, our collaborations with various research institutions and universities provide members with a broader platform for development. It is worth mentioning that our director, Tang Dongqi, also serves as the executive editor of the "Current Urology" journal.

**Contact:**

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## **Endocrinology and Metabolism Lab of the Second Hospital of Shandong University**

### **Establishment and Development:**

Endocrinology and Metabolism Lab of the Second Hospital of Shandong University was born from a shared vision and passion for diabetic neuropathy. Recognizing the need to understand the mechanisms and therapeutic targets of diabetic neuropathy, our founders decided to establish a laboratory dedicated to explore the mechanisms of Lipin1 in diabetic neuropathy. We set out to establish a research laboratory that would stand out for its excellence and impact. We have published a number of articles and won some honors in recent years. Since its inception, Endocrinology Research Group of the Second Hospital of Shandong University has gone through a remarkable journey of growth and development. Our study direction has been developed into investigating the pathogenesis, diagnostic markers and therapeutic targets of diabetic peripheral neuropathy, diabetic encephalopathy and depression with diabetes. Additionally, we have established valuable collaborations and partnerships with the Department of Physiology, the Department of Anatomy and Neurobiology, the Department of Biostatistics, and the School of Control Science and Data of Shandong University to further enhance our research capabilities.

### **Team Members:**

Our lab is located in the Second Hospital of Shandong University, Shandong, China. We are broadly interested in a wide range of topics related to endocrinology and metabolism, neuroscience, epidemiology, informatics and biomedical engineering. Our team is composed of 3 professors, 2 postdoctors, 6 doctors and 12 masters. Professor Shihong Chen and Professor Xianghua Zhuang have been engaged in the clinical and basic research of diabetic peripheral neuropathy and diabetic encephalopathy for a long time, and have accumulated lots of experience in clinical treatment and pathogenesis research. Professor Shuyan Yu is committed to the study of the nervous system, using viral tracing, genetic engineering, pharmacology, electrophysiology and behavioral methods to explore the pathogenesis and experimental treatment of psychiatric diseases.

Our lab has abundant scientific research experience, mighty innovation ability, it is a solidarity and passionate team. Team members have clear tasks and responsibilities. Our team has established a form of team cooperation with complementary advantages and formed a good team atmosphere.

### **Research Areas:**

Endocrinology and Metabolism Lab specializes in diabetic peripheral neuropathy and diabetic encephalopathy. Our lab explores the pathogenesis, early diagnostic markers, clinical translation of therapeutic drugs and functional imaging of neurological complications of diabetes mellitus.

### **Research Achievements:**

Endocrinology and Metabolism Lab explored the mechanism of diabetic peripheral neuropathy and diabetic encephalopathy from different perspectives such as phospholipid metabolism, inflammatory response, mitochondrial function, adult hippocampal neurogenesis and so on. Focusing on clinical needs, we also found different markers and established diagnostic system for early monitoring and treatment of diabetic neuropathy. We have made significant contributions in *Nature communications*, *Redox Biology*, *Journal of Neuroinflammation*, *International Immunopharmacology et al.* Three professors in our lab have hosted 10 National Natural Science Foundation projects and a number of provincial projects. The research achievements of our group won the second prize of Shandong Province Science and Technology Progress Award.

### **Main Publications:**

- [1] Yinliang Zhang; Chunyuan Du; Wei Wang; Wei Qiao; Yuhui Li; Yujie Zhang; Sufang Sheng; Xuenan Zhou; Lei Zhang; Heng Fan; Ying Yu; Yong Chen; Yunfei Liao; Shihong Chen; Yongsheng Chang; Glucocorticoids increase adiposity by stimulating Krüppel-like factor 9 expression in macrophages, *Nature communications*, 2024, 15(1): 1190.
- [2] Xiaolin Han; Shan Huang; Ziyun Zhuang; Xiaochen Zhang; Min Xie; Nengjun Lou; Mengyu Hua; Xianghua Zhuang; Shuyan Yu; Shihong Chen; Phosphatidate phosphatase Lipin1 involves in diabetic encephalopathy pathogenesis via regulating synaptic mitochondrial dynamics, *Redox Biology*, 2024, 69(102996).
- [3] Changmin Wang; Ye Li; Yuhang Yi; Guiyu Liu; Ruoqing Guo; Liyan Wang; Tian Lan; Wenjing Wang; Xiao Chen; Shihong Chen; Shu Yan Yu; Hippocampal microRNA-26a-3p deficit contributes to neuroinflammation and behavioral disorders via p38 MAPK signaling pathway in rats, *Journal of Neuroinflammation*, 2022, 19(1): 283.
- [4] Tian Lan; Ye Li; Cuiqin Fan; Liyan Wang; Wenjing Wang; Shihong Chen; Shu Yan Yu; MicroRNA-204-5p reduction in rat hippocampus contributes to stress-induced pathology via targeting RGS12 signaling pathway, *Journal of Neuroinflammation*, 2021, 18(1): 243.
- [5] Xiaochen Zhang; Shan Huang; Ziyun Zhuang; Xiaolin Han; Min Xie; Shuyan Yu; Mengyu Hua; Zhonghao Liang; Chao Meng; Ling Yin; Xianghua Zhuang; Shihong Chen; Lipin2 ameliorates diabetic encephalopathy via suppressing JNK/ERK-mediated NLRP3 inflammasome overactivation, *International Immunopharmacology*, 2023, 118: 109930.
- [6] Wang Wenjing., Wang Lihong., Wang Liyan., Li Ye., Lan Tian., Wang Changmin., Chen Xiao., Chen Shihong., Yu Shuyan.(2023). Ginsenoside-Rg1 synergized with voluntary running exercise protects against glial activation and dysregulation of neuronal plasticity in depression. *Food Funct*, 14(15), 7222-7239.
- [7] Wang Meijian., Xie Min., Yu Shuyan., Shang Pan., Zhang Cong., Han Xiaolin., Fan Cuiqin., Chen Li., Zhuang Xianghua., Chen Shihong.(2021). Lipin1 Alleviates Autophagy Disorder in Sciatic Nerve and Improves Diabetic Peripheral Neuropathy. *Mol Neurobiol*, 58(11), 6049-6061.

- [8] Wang Meijian., Hou Xinguo., Hu Wenchao., Chen Li., Chen Shihong.(2019). Serum lipid and lipoprotein levels of middle-aged and elderly Chinese men and women in Shandong Province. *Lipids Health Dis*, 18(1), 58.
- [9] Zheng Guanlin., Li Haizhen., Zhang Tie., Yang Libo., Yao Shutong., Chen Shihong., Zheng Maochuan., Zhao Qin., Tian Hua.(2018). Irisin protects macrophages from oxidized low density lipoprotein-induced apoptosis by inhibiting the endoplasmic reticulum stress pathway. *Saudi J Biol Sci*, 25(5), 849-857.
- [10] Shang Pan., Zheng Fengjie., Han Feng., Song Yuwen., Pan Zhe., Yu Shuyan., Zhuang Xianghua., Chen Shihong.(2020). Lipin1 mediates cognitive impairment in fld mice via PKD-ERK pathway. *Biochem Biophys Res Commun*, 525(2), 286-291.
- 10 selected publications

### **Facilities & Resources:**

The clinical research is based on the platform of Shandong Provincial priority clinical specialty and National Standardized Metabolic Disease Management Center. The basic research is based on the Basic Research Institute of the Second Hospital of Shandong University, the Key Laboratory of Basic and Clinical Mental Diseases of Shandong Province, and the Key Laboratory of Translational Medicine of Neurodegenerative Diseases in universities of Shandong Province.

Our state-of-the-art facilities and cutting-edge technology enable us to conduct research that is both rigorous and innovative. We boast Metabolic cage, behavioral tests, Transmission electron microscopy, inverted confocal microscope, et al.

### **Collaborations & Partnerships:**

We believe in the power of collaboration. That's why we have forged partnerships with Tianjin Medical University, Qilu Hospital of Shandong University, the Department of Physiology, the Department of Anatomy and Neurobiology, the Department of Biostatistics, and the School of Control Science and Data of Shandong University to further advance our research.

### **Recreational Activities:**

Our team is a solidarity and relaxed group, and there is a friend-like relationship between professors and students. We often dine together, and also hold a party during the Spring Festival. We often organize some recreational activities, such as climbing mountains with team members, running, and Murder Mystery Game and Escape Rooms.

### **Other Features:**

Our lab group is growing rapidly and we welcome all forms of communication and cooperation. All you can see is the road under your feet, and you already have the distant oasis in your mind.

### **Contact:**

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## **Interventional Oncology Institute of Shandong University, The Interventional Medicine and Minimally Invasive Oncology Department, the Second Hospital of Shandong University**

### **Establishment and Development:**

The Interventional Medicine and Minimally Invasive Oncology Department of the Second Hospital of Shandong University was established in 2002. It has now formed a specialty with its own characteristics and academic style, and has a high reputation both domestically and internationally. It has made outstanding contributions to the development of interventional radiology in the province. In 2013, it was approved to establish the Interventional Oncology Institute at Shandong University. In 2013 and 2017, it obtained the authority to confer master's and doctoral degrees, respectively. The department is the chairman unit of the Comprehensive Interventional Medicine Branch of Shandong Medical Association and the chairman unit of the Comprehensive Interventional Physicians Branch of Shandong Medical Association.

The Interventional Medicine and Minimally Invasive Oncology Department is at the international advanced level and domestic leading level in the field of iodine-125 radioactive seed implantation for the treatment of malignant tumors and gallstones. In China, we have earlier carried out iodine-125 radioactive seed implantation for pancreatic cancer/liver cancer/lung cancer, and accumulated rich clinical experience. In 2019, we will become one of the first six "tumor radioactive seed implantation technology training bases" of the Chinese Medical Doctor Association. We have taken the lead in carrying out percutaneous transhepatic papillary balloon dilation for the treatment of common bile duct stones nationwide, and have conducted multiple multicenter studies.

### **Team Members:**

There are a total of 13 medical, teaching, and research personnel, including 2 chief physicians and 2 deputy chief physicians. Among them, 85% are young and middle-aged people under the age of 45, and 77% are doctoral and master's degree holders. We have one doctoral supervisor and one master's supervisor.

Professor Yuliang Li (lyl.pro@sdu.edu.cn), the leader of the discipline and doctoral supervisor, has multiple stable research directions and has trained 8 doctoral students and 10 master's students.

Professor Bin Liu (gordon0221@sdu.edu.cn), the vice leader of the discipline and master supervisor, has multiple stable research directions and has trained 5 master's students.

### **Research Areas:**

1. The molecular mechanism of Iodine-125 radioactive seeds in cancers.
2. The molecular mechanism of traditional Chinese medicine for gallstones.

### **Main Publications:**

1. Liu B, Ma J, Li S, Li C, Qi H, Nian D, Yin C, Zhu J, Wang C, Jia Y, Jiang T, Lu J, Wang L, Shen D, Hou X, Li D, Zhang Z, Du F, Wu H, Yu T, Li Y. Percutaneous Transhepatic Papillary Balloon Dilation versus Endoscopic Retrograde Cholangiopancreatography for Common Bile Duct Stones: A Multicenter Prospective Study. *Radiology*. 2021 Aug;300(2):470-478. DOI: 10.1148/radiol.2021201115.
2. Li D, Wang W, Liu B, et al. Characterization of circSEC11A as a novel regulator of Iodine-125 radioactive seed-induced anticancer effects in hepatocellular carcinoma via targeting ZHX2/GADD34 axis[J]. *Cell Death Discovery*, 2023, 9(1). DOI:10.1038/s41420-023-01593-w.
3. Chao Chen, Wei Wang, Zhe Yu, Shilin Tian, Yuliang Li, Yongzheng Wang. Combination of computed tomography-guided iodine-125 brachytherapy and bronchial arterial chemoembolization for locally advanced stage III non-small cell lung cancer after failure of concurrent chemoradiotherapy. *Lung Cancer*. 2020 Jun 20;146:290-296. doi: 10.1016/j.lungcan.2020.06.010.
4. Chen C, Wang W, Wang WJ, Wang YZ, Yu Z, Li YL. Locally advanced pancreatic carcinoma with jaundice: the benefit of a sequential treatment with stenting followed by CT-guided 125 I seeds implantation. *Eur Radiol*. 2021 Sep;31(9):6500-6510. doi: 10.1007/s00330-021-07764-6.
5. Gao H, Wang WJ, Lv XY, Lu G\*, Li YL\*. Mechanism of Co(III)-catalyzed annulation of N-chlorobenzamide with styrene and origin of cyclopentadienyl ligand-controlled enantioselectivity. *Org. Chem. Front.*, 2023,10, 1643-1650.
6. Wei Wang, Shi-Lin Tian, Hui Wang, Chun-Chun Shao, Yong-Zheng Wang, Yu-Liang Li. Association of Hepatitis B Virus DNA Level and Follow-up Interval with Hepatocellular Carcinoma Recurrence. *JAMA Netw Open*. 2020 Apr 1;3(4): e203707.
7. Lei Guo, Jiali Sun, Changjun Wang, Yang Wang, Ya Wang, Dong Li, Yuliang Li. Epirubicin Enhances the Anti-Cancer Effects of Radioactive 125I Seeds in Hepatocellular Carcinoma via Downregulation of the JAK/STAT1 Pathway. *Front Oncol*. 2022; 12 *Front Oncol*. doi: 10.3389/fonc.2022.854023
8. Rong, JH, Li, D, Li, YL. Lobaplatin Enhances Radioactive 125I Seed-Induced Apoptosis and Anti-Proliferative Effect in Non-Small Cell Lung Cancer by Suppressing the AKT/mTOR Pathway. *Onco Targets Ther*. 2021; 14 *Onco Targets Ther*. doi: 10.2147/OTT.S288012
9. Li, D, Wang, WJ, Wang, YZ, et al. Lobaplatin promotes 125I-induced apoptosis and inhibition of proliferation in hepatocellular carcinoma by upregulating PERK-eIF2 $\alpha$ -ATF4-CHOP pathway. *Cell Death Dis*. 2019; 10 *Cell Death Dis*. doi: 10.1038/s41419-019-1918-1
10. He, GH, Xing, DJ, Jin, D, et al. Scutellarin improves the radiosensitivity of non-small cell lung cancer cells to iodine-125 seeds via downregulating the AKT/mTOR pathway. *THORAC CANCER*. 2021; 12 *THORAC CANCER*. doi: 10.1111/1759-7714.14077.

#### **Facilities & Resources:**

Our lab has molecular biology experimental platform, cell biology experimental platform, immunology and histopathology experimental platform, microscopic

characterization platform, electrophysiology platform, SPF level experimental animal platform, evidence-based medicine platform, biomedical sample library, etc. Covering an area of over 6000 square meters, it has the foundation and high-end equipment for studying the structure and function of biological macromolecules, cell morphology and function, animal model construction and experimentation, as well as clinical sample storage, processing and analysis. It includes flux nucleic acid extraction, automatic cutting system, protein purification preparation system, analytical and sorting flow cytometry analyzer, laser confocal microscope, multispectral scanning microscope, laser micro cutting system, digital PCR instrument, fluorescence quantitative PCR instrument, tissue automatic embedding machine, automatic dehydration machine, paraffin and frozen sectioning machine, patch clamp system, calcium ion imaging system, nanoparticle tracking analyzer, IVIS Spectrum CT small animal live optical imaging system, as well as large precision instruments such as darkroom and cold room, as fluorescence quantitative PCR instrument. Facilities such as laboratory, stem cell culture room, clinical sample library, etc.

#### **Collaborations & Partnerships:**

We believe in the power of collaboration.

1. Wei Wang, Advanced Medical Research Institute, Shandong University.
2. Xiangbo Meng, Advanced Medical Research Institute, Shandong University.
3. Zhaojian Liu, Advanced Medical Research Institute, Shandong University.
4. Gang Lu, School of Chemistry and Chemical Engineering, Shandong University.
6. Shujun Fu, School of Mathematics, Shandong University

#### **Contact:**

For more information or inquiries, please contact Bin Liu at [gordon0221@sdu.edu.cn](mailto:gordon0221@sdu.edu.cn)

## JDY-Lab

### **Establishment and Development:**

JDY-Lab was born from a shared vision and passion for burn wound repair and skin-tissue engineering. Recognizing the need for scarless healing of patients, our founders decided to establish a laboratory dedicated to apply the laboratory research results of mesenchymal stem cells ( fetal dermal mesenchymal stem cells ) and acellular dermal matrix to clinical practice. The journey of JDY-Lab began with the founder of Professor Duyin Jiang was employed by Shandong University in 2007. With a small but dedicated team, we set out to establish a research laboratory that would be recognized for its excellence and impact. Since its inception, JDY-Lab has gone through a remarkable journey of growth and development. We have discovered the involvement of sex hormones and tumor suppressor genes RB and P53 mutations in the keloid formation, and was the first to carry out basic and clinical application research on one-step composite transplantation of allogeneic/xenoacellular acellular dermal matrix(ADM) in China and abroad. At present, our research has evolved to 1) fetal dermal mesenchymal stem cells for the treatment of wounds and anti-skin aging ; 2) Study on the mechanism of aging wound inflammation; 3) Study on the mechanism of keloid; 4) The application of growth factors and ADM in wound treatment.. Additionally, we have forged valuable collaborations and partnerships with collaborators in Ji'nan University to further enhance our research capabilities.

### **Team Members:**

Our team is composed of leading experts in their fields, young and passionate researchers, and support staff dedicated to excellence. Together, they work tirelessly to contribute to the wound healing and anti-aging.

#### **Principal Investigator**

Duyin Jiang (姜笃银), Ph.D., M.D.  
Chief Physician, Professor, Doctoral Supervisor  
86-15153169399  
Jdybs2@vip.163.com

Research:

Professor Jiang focuses on the basic research and application of tissue engineering materials and (denatured) acellular dermal matrix in wound repair.

#### **Staff**

Jie Zhao (赵洁), Ph.D., M.D.  
Deputy Chief Physician  
86-17660083669  
[4220458387@qq.com](mailto:4220458387@qq.com)

Research:

Basic research and clinical application of wound and burn repair.

Trainee

At present, we have 1 postdoctoral student, 7 doctoral students and 6 master's Student.

Together with the leading experts, these young researchers work hard to achieve the better wound healing.

### **Research Areas:**

JDY-Lab specializes in burn wound repair and skin-tissue engineering. The research directions of the department are: (1) the role of fetal dermal mesenchymal stem cells in skin tissue repair, regeneration and anti-aging; (2) basic research and application of tissue engineering materials and (denatured) acellular dermal matrix in burn wound repair; (3) the study of the biological activity of keloid fibroblasts inhibited by mesenchymal stem cells; (4) the hierarchical management, diagnosis and treatment of acute and chronic wounds and specialized training.

### **Research Achievements:**

We have made significant contributions in chronic wound repair and skin tissue research. We found the relationship between the characteristics of abnormal proliferation and differentiation of epithelial cells and different outcomes of wound (burn) repair in human skin. After that, we find and apart a new mesenchymal stem cell, we called it “fetal dermal mesenchymal stem cell(FDMSC)”. Around this mesenchymal cell, we had performed many researches, and during this period, we prepared a thermal-hydrolyzed protein and a acellular dermal matrix. And we found out these bio-materials have promising usage in many areas. During these years, we have gained 11 invention patents and 3 utility model patents.

### **Main Publications:**

- (1) Xiaoyang Wang; Jie Zhao; Xiaochuan Wang; Jingjuan Zhang; Yi Wang; Xinyue Wang; Shanshan Jia; Nian Shi; Meiqi Lu; Hongxia Su; Jixun Zhang; Duyin Jiang; Bacterial cellulose membrane combined with BMSCs promotes wound healing by activating the notch signaling pathway, *Frontiers in Surgery*, 2023, 9
- (2)Xiao Wang; Ya Jiao; Yi Pan; Longxiao Zhang; Hongmin Gong; Yongjun Qi; Maoying Wang; Huiping Gong; Mingju Shao; Xinglei Wang; Duyin Jiang; Fetal Dermal Mesenchymal Stem Cell-Derived Exosomes Accelerate Cutaneous Wound Healing by Activating Notch Signaling, *Stem Cells International*, 2019, 2019: 1-11
- (3)Qi Yongjun; Dong Zhengxue; Chu Hongzhen; Zhao Qi; Wang Xiao; Jiao Ya; Gong Hongmin; Pan Yi; Jiang Duyin; Denatured acellular dermal matrix seeded with bone marrow mesenchymal stem cells for wound healing in mice, *Burns*, 2019, 45(7): 1685-1694
- (4)Shengsheng Pan; Siyu Gong; Jingjuan Zhang; Shanshan Jia; Maoying Wang; Yi Pan; Xiao Wang; Duyin Jiang; Anti-aging effects of fetal dermal mesenchymal stem cells in a D-galactose-induced aging model of adult dermal fibroblasts, *In Vitro Cellular & Developmental Biology - Animal*, 2021, 57(8): 795-807
- (5)Yi Pan; Xiao Wang; Xinglei Wang; Fei Shan; Maoying Wang; Jixun Zhang; Jingjuan Zhang; Shanshan Jia; Ya Jiao; Yongjun Qi; Hongmin Gong; Duyin Jiang; Protective Effect of Conditioned Media of Human Fetal Dermal Mesenchymal Stem Cells Can Inhibit Burn-induced Microvascular Hyperpermeability, *Journal of*

Burn Care & Research, 2021, 16(1)

(6) Ji-xun Zhang; Chuan Li; Yao-nan Li; Zheng-xue Dong; Dao-jing Qiu; Du-yin Jiang ; Growth of early or midterm human foetal skin in a burn model: establishment of the model, morphological and histological observations., Biomedical Research, 2017.02, 28(6): 2504-2514

(7) Chao Wang; Ji-xun Zhang; Zhenzhong Liu ; Stool Management Followed by Surgical Debridement and Surgical Closure Combined With Negative Pressure Wound Therapy in the Treatment of Posterior Trunk Pressure Injury: A Retrospective Descriptive Study, Wound management & prevention, 2022, 68(4): 26-33

(8) Chao Wang; Ji-xun Zhang; Zhenzhong Liu ; Vacuum - assisted closure therapy combined with bi - pectoral muscle flap for the treatment of deep sternal wound infections, International Wound Journal, 2019, 17(2): 332-338

(9) Ya Jia; Xiao Wang; Ji-xun Zhang; Yongjun Qi; Hongmin Gong; Duyin Jiang ; Inhibiting function of human fetal dermal mesenchymal stem cells on bioactivities of keloid fibroblasts, Stem Cell Research & Therapy, 2017.07, 8(1): 170-178

(10) Xinyue Wang, Jie Zhao, Ya Jiao, Xinglei Wang, Duyin Jiang. Upper gastrointestinal foreign bodies in adults: A systematic review. Am J Emerg Med, 50(2021):136-141.

#### **Facilities & Resources:**

Our state-of-the-art facilities and cutting-edge technology enable us to conduct research that is both rigorous and innovative. The research group is located in the Basic Medical Research Institute of the hospital, which has five major research institutions including the Central Laboratory, Experimental Animal Center, Evidence Based Medicine Center, Gene and Immunotherapy Center, and Translational Medicine Research Center. The laboratory covers an area of more than 6000 square meters and has molecular biology experimental platform, cell biology experimental platform, immunology and histopathology experimental platform, microscopic characterization platform, electrophysiology platform, and SPF level experimental animal platform. Various experimental platforms such as evidence-based medicine platform and biomedical sample library are equipped with basic and high-end instruments and equipment for studying the structure and function of biomolecules, cell morphology and function, construction and experimentation of animal models, and storage, processing, and analysis of clinical samples.

#### **Collaborations & Partnerships:**

We believe in the power of collaboration. That's why we have forged partnerships with professor Guo Rui, from the MOE Key Laboratory of Tumor Molecular Biology in Ji'nan university. And industry partners, like Shandong Huaying Biotechnology Co., Ltd, to further advance our research.

#### **Recreational Activities:**

Our research group has a variety of team building activities, spending traditional holidays together and having monthly gatherings. We focus on emotional connections

between team members. Activities such as mountain climbing and hiking are also frequently held, since Professor Jiang believes that his students should "civilize their spirit and savage their physique".

**Contact:**

For more information or inquiries, please contact us at [Jdybs2@163.vip.com](mailto:Jdybs2@163.vip.com) or visit our website at <http://www.qlyxgrad.sdu.edu.cn/jsxx/delcxy/jdy.htm>



## **Kidney Multidisciplinary Innovation Lab**

### **Establishment and Development:**

Kidney Multidisciplinary Innovation Lab was born from a shared vision and passion for renal pathophysiology and immune-inflammatory pathogenesis of kidney diseases. Recognizing the need for cutting edge academic research in CKD epidemiology, genetic background, renal pathophysiology, immune-inflammatory pathogenesis and evidence-based treatment of kidney diseases with international reputation, our founders decided to establish a laboratory dedicated to develop novel therapeutic strategies for kidney injury. The journey of Kidney Multidisciplinary Innovation Lab began with the department of nephrology in the Second Hospital of Shandong university that established in the 1990s by the founder Professor Guang-ju Guan. The nephrology department of the Second Hospital of Shandong University is the first key clinical specialty of the Ministry of Health in Shandong Province. With a dedicated team, we established Renal Institute of Shandong University in 2011. Under the leadership of Prof. Gang liu, the institute has been developing substantially. It has been crowned as Kidney Multidisciplinary Innovation Lab.

### **Team Members:**

Our team has been keeping fast pace of stable and steady development; we have 21 nephrologists and physician-scientists, 13 master's graduate students and doctoral students. Among the nephrologists and physician-scientists, there are 3 full professors and 7 associated professors. Four have been awarded grants form Natural Science Foundation of China (NSFC); 2 has been awarded grants form the Science Foundation of Shandong province; 3 have been ranked as new talents pioneers of the Second Hospital of Shandong University. Our renal program has been recognized as a young, passionate and dynamic one.

### **Research Areas:**

Based on multidisciplinary technological platform and the database of clinical kidney biopsy , our lab has been focusing on three main directions of scientific research:

1. To investigate the pathogenesis of common kidney diseases of CKD
2. To identify the risk factors, immune-inflammatory mechanism and genetic background in developing and progression of diabetic kidney disease(DKD);
3. To develop prevention and stem cell treatment strategies of CKD.

### **Research Achievements:**

We have made significant contributions in elucidating the potential immune-inflammatory mechanism of mesenchymal stem cells ameliorate diabetic glomerular fibrosis, the cellular and molecular mechanism in preventing diabetic kidney disease and investigate the pathogenesis of common kidney diseases of CKD.

### **Main Publications:**

- [1] Wang Y, Liu J, Wang H, Lv S, Liu Q, Li S, Yang X, **Liu G\***. Mesenchymal stem cell-derived exosomes ameliorate diabetic kidney disease through the NLRP3 signaling pathway. *Stem Cells*. 2023 Jan 22;sxad010. doi: 10.1093/stmcls/sxad010. Epub ahead of print. PMID: 36682034.
- [2] Wang Y, Liu J, Zhang Q, Wang W, Liu Q, Liu S, Song Y, Wang X, Zhang Y, Li S, Yang X, Lv S, **Liu G\***. Human umbilical cord mesenchymal stem cells attenuate podocyte injury under high glucose via TLR2 and TLR4 signaling. *Diabetes Res Clin Pract*. 2021 Mar;173:108702. doi: 10.1016/j.diabres.2021.108702. Epub 2021 Feb 18. PMID: 33609619.
- [3] Song Y, Lv S, Wang F, Liu X, Cheng J, Liu S, Wang X, Chen W, Guan G, **Liu G\***, Peng C\*. Overexpression of BMP-7 reverses TGF- $\beta$ 1-induced epithelial-mesenchymal transition by attenuating the Wnt3/ $\beta$ -catenin and TGF- $\beta$ 1/Smad2/3 signaling pathways in HK-2 cells. *Mol Med Rep*. 2020 Feb;21(2):833-841. doi: 10.3892/mmr.2019.10875. Epub 2019 Dec 10. PMID: 31974602; PMCID: PMC6947920.
- [4] Song Y, Peng C, Lv S, Cheng J, Liu S, Wen Q, Guan G, **Liu G\***. Adipose-derived stem cells ameliorate renal interstitial fibrosis through inhibition of EMT and inflammatory response via TGF- $\beta$ 1 signaling pathway. *Int Immunopharmacol*. 2017 Mar;44:115-122. doi: 10.1016/j.intimp.2017.01.008. Epub 2017 Jan 13. PMID: 28092863.
- [5] Wang XL, Wu LY, Zhao L, Sun LN, Liu HY, **Liu G\***, Guan GJ\*. SIRT1 activator ameliorates the renal tubular injury induced by hyperglycemia in vivo and in vitro via inhibiting apoptosis. *Biomed Pharmacother*. 2016 Oct;83:41-50. doi: 10.1016/j.biopha.2016.06.009. Epub 2016 Jun 21. PMID: 27470548.

### **Facilities & Resources:**

The laboratory is based on the Institute of Kidney Disease of Shandong University and the Second Hospital of Shandong University. The laboratory has 4 experimental platforms: molecular biology experimental platform, cell biology experimental platform, immunology and histopathology experimental platform, protein electrophoresis platform, 1 biological sample bank, 6 public laboratories: Microscope room, flow cytometry room, precision instrument room, purification laboratory, virus room, centrifuge room. With automatic enzyme marker, fluorescent real-time quantitative PCR Instrument, microfluorescence imaging system, confocal microscope, digital microtome scanner, automatic dewatering machine, tissue encapsulation machine, pathological microtome, frozen microtome, high-speed and low temperature centrifuge, ultra-fast centrifuge, magnetic stirrer, protein electrophoresis tank, electrophoresis machine, cell constant temperature incubator, ultra-clean table, tissue shredder and various refrigerators can meet the various instruments and equipment required for the completion of the project . With the support of School of Pharmacy, Shandong University and Department of Pathology, Shandong University, this project can complete important experiments such as quantitative analysis of tissue metabolites by liquid chromatography tandem mass

spectrometry (LC-MS/MS), whole genome DNA methylation sequencing and electron microscope examination. The working conditions required for the experimental topics are fully met. We also have our database of clinical kidney biopsy for researchers.

**Collaborations & Partnerships:**

We believe in the power of collaboration. We established the Kidney Multidisciplinary Innovation Branch of Shandong Medical Association in 2021, which include the disciplines of renal internal medicine, blood purification, peritoneal dialysis, kidney transplantation, kidney pathology, pediatric nephrology, and basic renal medicine of major medical and teaching/research institutions in Shandong Province.

**Contact:**

For more information or inquiries, please contact us

PI of Kidney Multidisciplinary Innovation Lab

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Website: <http://www.sdey.net>

## Translational Medical Laboratory for Neurodegenerative Diseases

### **Establishment and Development:**

Translational medical Laboratory for neurodegenerative diseases was born from a shared vision and passion for neurodegenerative diseases, relying on Shandong University and located in the Second Hospital of Shandong University, was approved as the Key Laboratory of the Twelfth Five-Year Plan University of Shandong Province in 2011. Recognizing the gap between clinical research with basic scientific study, our founders decided to establish a laboratory dedicated to construct a clinical database of dementia. The journey of our lab began with the initial funding of National Program on Key Basic Research Project (973 Program). With a small but dedicated team, we set out to establish a research laboratory that would be recognized for its excellence and impact. Since its inception, our lab has gone through a remarkable journey of growth and development. Additionally, we have forged valuable collaborations and partnerships to further enhance our research capabilities.

### **Team Members:**

Our team is composed of 48 researchers, 3 doctoral supervisors and 5 master supervisors, forming a high level of stable academic team. Together, they work tirelessly to study on pathogenesis and early biomarkers of neurodegenerative diseases.

Current Director: Jianzhong Bi

### **Research Areas:**

1. Epidemiology and molecular genetics of neurodegenerative diseases;
2. Study on pathogenesis and early biomarkers of neurodegenerative diseases(e.g., dementia/Parkinson disease);
3. Research and development of innovative treatments for neurodegenerative diseases.

### **Research Achievements:**

We have made significant contributions in the pathogenesis, translational medicine and epidemiological research of neurodegenerative disease (e.g., Alzheimer's disease).

1) We discovered a new mechanism involved autophagy, mitochondrial dysfunction and epigenetic factors in the pathogenesis of AD, and small chemical molecules 3BDO and D609 were screened, which can improve the cognitive function of AD animal models. It was found that melatonin can play a neuroprotective role in AD by promoting mitochondrial synthesis and improving mitochondrial function. Biological macromolecules G-CSF and self-assembled AKVAV polypeptide nanofibers were found to improve the cognitive function of AD animal models by anti-inflammatory and reducing A $\beta$  deposition, which provides a new idea for the clinical treatment of AD.

2) A lot of work has been done from the induction of endogenous stem cell proliferation and differentiation by biomacromolecules to the direct or indirect intervention of exogenous mesenchymal in AD animal models, and the mechanism of

stem cell therapy for AD has been deeply discussed. It was found that both endogenous stem cells and exogenous mesenchymal stem cells can improve cognitive impairment in AD animal models, including promoting neurovascular regeneration, reducing A $\beta$  deposition and inhibiting inflammatory response.

3) Professor Bi led the team to focus on the pre-dementia stage of AD, namely the SCD and MCI stages, and conduct prospective studies using baseline investigation, cohort study, molecular epidemiology and trial epidemiology to find new influencing factors of the pre-dementia stage of AD and biomarkers that can be used for the diagnosis of the pre-dementia stage of AD. Research cohorts and bio-database for pre-dementia and Alzheimer's disease has been established.

### **Main Publications:**

(1) Xu Y, Meng Y, Wang P, Sun L, Xu S. Teaching NeuroImage: Seizures as the Initial Symptom of Relapsing Polychondritis. *Neurology*. 2022 Feb 8;98(6):e677-e678.

(2) Cao X, Chen Y, Sang X, et al. Impact prediction of translocation of the mitochondrial outer membrane 70 as biomarker in Alzheimer's disease. *Front Aging Neurosci*. 2022;14:1013943. Published 2022 Nov 2.

(3) Sheng N, Wang YQ, Wang CF, et al. AGR2-induced cholesterol synthesis drives lovastatin resistance that is overcome by combination therapy with allicin. *Acta Pharmacol Sin*. 2022;43(11):2905-2916.

(4) Xu L, Wang W, Song W. A combination of metformin and insulin improve cardiovascular and cerebrovascular risk factors in individuals with type 1 diabetes mellitus. *Diabetes Res Clin Pract*. 2022;191:110073.

(5) Xu Y, Meng Y, Wang P, Sun L, Xu S. Teaching NeuroImage: Seizures as the Initial Symptom of Relapsing Polychondritis. *Neurology*. 2022;98(6):e677-e678.

(6) Ling X, Wang T, Han C, et al. IFN- $\gamma$ -Primed hUCMSCs Significantly Reduced Inflammation via the Foxp3/ROR- $\gamma$ t/STAT3 Signaling Pathway in an Animal Model of Multiple Sclerosis. *Front Immunol*. 2022;13:835345. Published 2022 Mar 1.

(7) Yin Y, Xie Z, Chen D, et al. Integrated investigation of DNA methylation, gene expression and immune cell population revealed immune cell infiltration associated with atherosclerotic plaque formation. *BMC Med Genomics*. 2022;15(1):108. Published 2022 May 9.

(8) Jin S, Zhang C, Zhang Y, Jia G, Zhang M, Xu M. Differential value of intima thickness in ischaemic stroke due to large-artery atherosclerosis and small-vessel occlusion. *J Cell Mol Med*. 2021 Oct;25(19):9427-9433.

(9) Zhou S, Yu X, Wang M, Meng Y, Song D, Yang H, Wang D, Bi J, Xu S. Long Non-coding RNAs in Pathogenesis of Neurodegenerative Diseases. *Front Cell Dev Biol*. 2021 Aug 30;9:719247.

(10) Li Q, Chen J, Liang F, Zhang J, Qu W, Huang X, Cheng X, Zhao X, Yang Z, Xu S, Li X. RYBP modulates embryonic neurogenesis involving the Notch signaling pathway in a PRC1-independent pattern. *Stem Cell Reports*. 2021 Dec 14;16(12):2988-3004.

**Facilities & Resources:**

Our state-of-the-art facilities and cutting-edge technology enable us to conduct research that is both rigorous and innovative. We boast advanced large-scale instruments and equipment, including PET/MR, high-throughput second-generation sequencer, pyrophosphate sequencer, liquid chip analyzer, sorting flow cytometer, small animal live imaging, gait analysis system, OCT tester, PCR fluorescence quantitative analyzer, laser confocal microscope, two-color infrared laser imaging system, MRI scanner, etc. Moreover, the hospital opened the central laboratory and scientific research technology platform equipped with a variety of large-scale advanced instruments to the laboratory, which provided perfect hardware conditions for the laboratory to carry out scientific research projects.

**Collaborations & Partnerships:**

We believe in the power of collaboration. That's why we have forged partnerships with Karolinska institution to further advance our research. We look for cooperation in epidemiology (e.g., risk and protective factors, distribution, time trends, and determinants) , brain aging and dysfunction (e.g., cognitive decline, dementia, and functional dependence), screening biomarkers of dementia and functional disability.

**Recreational Activities:**

Routine social gatherings, sports and fitness activities, cultural events, festivals and celebrations, professional development workshops, and so on.

**Other Features:**

Our laboratory is an interesting, inclusive, harmonious, and warm team. Welcome to join us.

**Contact:**

For more information or inquiries, please contact us at email: xie\_zhaohong@sdu.edu.cn.

## Liu Ping Research Lab

### **Establishment and Development:**

Liu Ping Research Lab has a good foundation in the research of peripheral vascular tissue lesions, atherosclerosis and vascular remodeling. The project leader has been engaged in basic and clinical research of vascular remodeling for many years, especially in the research of peripheral vascular membrane, identifying promising novel targeted therapies for treating atherosclerosis and vascular remodeling. Transcription factors are key controllers of gene expression. We have investigated whether Smad, mitogen-activated protein kinase (MAPK), and integrin signaling pathways cross-talk to enhance adventitial fibroblast (AF) bioactivity, which was activated by transforming growth factor (TGF)-beta1 and inhibited by Gax. Our findings indicate that cross-talk among Smad, MAPK, and integrin signaling pathways may account mainly for the mechanism of AF functions. Gax is a promising therapeutic gene for dissecting the signaling pathways controlling AF bioactivities. With a small but dedicated team, we set out to establish a research laboratory that would be recognized for its excellence and impact. Since its inception, our lab has gone through a remarkable journey of growth and development. We have also identified that adventitial inflammation induces vascular remodeling via the interactions of multiple inflammatory cytokines and local Gax gene transfer in vivo can significantly inhibit these interactions and thereby attenuate local inflammation and vascular remodeling. Additionally, we have forged valuable collaborations and partnerships with Jiwei Cui and Fengming Liu, et.al to further enhance our research capabilities.

### **Team Members:**

Our team is composed of Principal Investigator (PI), Research Director, Project Coordinator or Research Associate, Research Assistant and a number of students affiliated to Shandong University, Qilu Medical College. Together, they work tirelessly to their objectives and research areas as below.

<b>ID</b>	<b>Name</b>	<b>Gender</b>	<b>Title</b>	<b>Education Background</b>	<b>Main Objectives</b>
1	Qinghai Wang	Male	deputy chief physician	Ph.D	Intravascular Ultrasound Imaging
2	Peng Wang	Male	research assistant	Ph.D	Communicating with other teams, et.al.
3	Xiangyu Xu	Male	research assistant	Ph.D	Guiding of whole lab
4	Huiling Chen	Female	resident physician	Master	Cell culturing
5	Shuaiyong Zhang	Male	doctoral candidates	Master	Gene editing and intervention



6	Peiqing Tian	Male	postgraduates	Bachelor	Proteomics
7	Liyun Xing	Female	postgraduates	Bachelor	Bioinformatics
8	Qi Jin	Male	postgraduates	Bachelor	Animal Model
9	Xiao Li	Female	postgraduates	Bachelor	ncRNA technology

### Research Areas:

1. Gax gene interferes with chemerin mediated perivascular adipocyte proliferation and differentiation (81170274). National Natural Science Foundation Project 2012-2015.
2. Study on the mechanism of MEOX2 signaling axis targeting mediated by perivascular preadipocyte derived exosomes to regulate perivascular fibroblast function and vascular remodeling. National Natural Science Foundation Project 2022-2025
3. The role of gap connexin 43 in the onset and progression of ventricular fibrillation (30871039). National Natural Science Foundation Project 2009-2011.
4. Effect of Gax gene on the proliferation of perivascular adipocytes (2009ZRB019BS). Shandong Province Nature Fund Project
5. Study on the mechanism of FSP1 regulation of vascular outer membrane fibroblast function mediated by mutual dialogue between RAGE, Wnt and STAT signaling pathways (2015GSF121008). Key Research and Development Program of Shandong Province
6. Study on the synergistic targeting of LncRNA UCA1 and miR-373 to regulate PI3K-Akt-mTOR-Stat3 signaling pathway mediating the function of vascular outer membrane fibroblasts (GG201703080074). Shandong Province Nature Fund Project
7. Study on the mechanism of vascular remodeling mediated by GXYLT2-AP-Notch signaling axle-mediated dialogue between perivascular adipocytes and extravascular fibroblasts (ZR2020MH041). Shandong Province Nature Fund Project
8. Study on the mechanism of Copb1/miR-721/Gax/PHF20L1 signaling axis targeted by exosomes to regulate perivascular adipocytes and vascular remodeling. Jinan Science and Technology Bureau, 2021-2024
9. Clinical study on the role of midsection atrial natriuretic peptide precursor (MR-proANP) in diagnosis and prediction of heart failure (201602153). Jinan Science and Technology Bureau, Under research
10. Study on the mechanism of MEOX2 signaling axis targeting peripheral vascular tissue cells and vascular remodeling. Shenzhen Science and Technology Innovation Commission, In research.

### Research Achievements:

With regard to basic research, our team leader has been engaged in mechanisms of vascular remodeling for many years, especially in the study of the vascular adventitia. The main work includes: (1) Revealing for the positive and negative regulators of vascular adventitial fibroblasts (AF) affecting vascular remodeling first time: The study found that the interaction of three signaling pathways - Smad, MAPK, and Integrin - determines the biological activity of AF. TGF- $\beta$ 1 enhances interactions among these pathways, eventually influencing the function of AF; however, specific growth inhibition homologous genes (Gax) inhibit pathways described as before. This study was published as the cover story in *ATVB*, the prestigious journal of the American College of Cardiology (AHA) (2008 SCI Impact Factor 7.4) [Liu P, et al. *ATVB*,2008, 28:725-731.] (2) The inhibitory effect of Gax gene overexpression on proliferative vascular remodeling in the vascular adventitia was reported for the first time: This team applied adenovirus carrying Gax to locally transfect the vascular adventitia in vivo, and found that Ad-Gax transfection could inhibit the proliferation and migration of vascular cells, induce vascular cell apoptosis and reduce the expression of inflammatory factors. Ad-Gax transfection significantly reduced the thickness of the vascular wall at the lesion site and inhibited negative vascular remodeling in vivo. The study has been published in *Atherosclerosis*, the leading European journal [Liu P, et al. *Atherosclerosis*, 2010;212(2):398-405.]

#### **Main Publications:**

1. Wang J, Tan JS, Hua L, Sheng Q, Huang X, Liu P. Genetic predisposition of both waist circumference and hip circumference increased the risk of venous thromboembolism [published online ahead of print, 2022 Nov 16]. *ThrombHaemost.* 2022;10.1055/a-1980-8852. doi:10.1055/a-1980-8852.
2. Wang J, Huang X, Fu C, Sheng Q, Liu P. Association between triglyceride glucose index, coronary artery calcification and multivessel coronary disease in Chinese patients with acute coronary syndrome. *Cardiovasc Diabetol.* 2022 Sep 16;21(1):187.
3. Huang X, Fu C, Liu W, Liang Y, Li P, Liu Z, Sheng Q, Liu P. Chemerin-induced angiogenesis and adipogenesis in 3 T3-L1 preadipocytes is mediated by lncRNA Meg3 through regulating Dickkopf-3 by sponging miR-217. *Toxicol Appl Pharmacol.* 2019;385:114815.
4. Cai Hua Fu, MD, Ping Liu,MD,PhD, Pei Lun Li,MD,Wen Hui Liu,MD. FSP1 promotes the biofunctions of adventitial fibroblast through the crosstalk among RAGE, JAK2/STAT3 and Wnt3a/ $\beta$ -catenin signaling pathways. *J Cell Mol Med.* 2019;23(11):7246-7260.
5. Jiang Y, Liu P, Jiao W, Meng J, Feng J. Gax suppresses chemerin/CMKLR1-induced preadipocyte biofunctions through the inhibition of Akt/mTOR and ERK signaling pathways. *J Cell Physiol.* 2018;233(1):572-586.
6. Liu P, Jiang Y, Meng J. Relationship between serum uric acid, metabolic syndrome and resting heart rate in Chinese elderly. *Obes Res Clin Pract.* 2016;10(2):159-168.
7. Liu P, Kong F, Wang J, Lu Q, Xu H, Qi T, Meng J. Involvement of IGF-1 and

- MEOX2 in PI3K/Akt1/2 and ERK1/2 pathways mediated proliferation and differentiation of perivascular adipocytes. *Exp Cell Res.* 2015;331(1):82-96.
8. Liu P, Feng J, Kong F, Lu Q, Xu H, Meng J, Jiang Y. Gax inhibits perivascular preadipocyte biofunction mediated by IGF-1 induced FAK/Pyk2 and ERK2 cooperative pathways. *Cell Signal.* 2014;26(12):3036-3045.
  9. Liu P, Zhang C, Zhao YX, Feng JB, Liu CX, Chen WQ, Yao GH, Zhang M, Wang XL, Zhang Y. Gax gene transfer inhibits vascular remodeling induced by adventitial inflammation in rabbits. *Atherosclerosis.* 2010;212(2):398-405.
  10. Liu P, Zhang C, Feng JB, Zhao YX, Wang XP, Yang JM, Zhang MX, Wang XL, Zhang Y. Cross talk among Smad, MAPK, and integrin signaling pathways enhances adventitial fibroblast functions activated by transforming growth factor-beta1 and inhibited by Gax. *ArteriosclerThrombVasc Biol.* 2008;28(4):725-731.

### Facilities & Resources:

Our state-of-the-art facilities and cutting-edge technology enable us to conduct research that is both rigorous and innovative. Our medical experimental center includes molecular biology experiment platform, cell biology experiment platform, immunology and histopathology experiment platform, microscopic characterization platform, electrophysiology platform, SPF experimental animal platform, evidence-based medicine platform, biomedical sample bank, etc. Covering an area of more than 6,000 square meters, it has basic and high-end instruments and equipment for the study of the structure and function of biological macromolecules, cell morphology and function, the construction and experiment of animal models, and the storage, processing and analysis of clinical samples, with a total value of more than 73.15 million yuan, including 13 equipment with more than 1 million yuan. Including the sorting high-end flow cytometry analyzer, Beckman high-end flow cytometry, laser scanning confocal microscopy, multispectral scanning microscopy, laser microdissection, IVIS Spectrum CT small animal live optical imaging system, digital PCR, cell energy metabolism system, 2D image-guided biological irradiation system, mouse magnetic resonance body fat detector, pyrophosphate sequence analyzer, confocal microRaman spectrometer, automatic single-cell transcription analyzer and digital pathological section scanner, etc.

### Collaborations & Partnerships:

We believe in the power of collaboration. That's why we have forged partnerships with our partners to further advance our research.

Leading universities	Research institutions	Industry partners
Shandong University	Biocolloids and Biointerfaces Lab of Shandong University	Jiwei Cui
Shandong University	Department of Microbiology and Immunology, Shandong University	Fengming Liu

### Recreational Activities:

In the Teachers' Day, we were all happy to send warm thoughts of love and regards to our loving teachers. We've drawn inspiration from Ping Liu, a professor of Cardiology at Shandong University who grew interested in doing more to connect students with their passions and creative energies.

“We need to be cranking out innovators, problem solvers, and creative thinkers, people that aren't afraid to take risks, people that don't want to just regurgitate answers, and people that are finding their passions in life.” He said once.



### Other Features:

1. Expectation of breakthrough solutions  
Our lab pursues disruptive innovations and are called to “imagine the impossible” (LIL). Rather than settling for incremental improvements, our mission is typically to deliver “breakthrough solutions” and create places “where today’s moonshots become tomorrow’s breakthroughs”.
2. Targeted collaboration  
While labs’ typically impose a problem focus, we draw on collaborative technologies and dynamics to generate solutions. iLabs, for example, claims that it

is based on “cross-sector collaborations that bring people together,” and eLab “focuses on collaborative innovation.” This approach presumes that all participants, regardless of institutional power differences, should treat one another as equal partners.

3. Focus on experimentation

Labs like to stress that they “create space for experimentation through facilitated processes”. We encourage team partners to “try things out on a small scale, take risks, prototype, test and accept failure as part of progress”, re-inventing their own methods and approaches as they go along.

**Contact:**

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## The 3D printing Dental Medicine Research Center of Shandong University

### **Establishment and Development:**

The 3D printing Dental Medicine Research Center of Shandong University was born from a shared vision and passion for the basic research and clinical transformation of 3D printing technology in stomatology. Recognizing the need for transforming from traditional dental treatment into digital precision treatment, our founders decided to establish a laboratory dedicated to promote the transformation and application of 3D printing technology in the field of stomatology. The journey of the 3D printing Dental Medicine Research Center of Shandong University began with the demand of personalized treatment in stomatology. With a small but dedicated team, we set out to establish a research laboratory that would be recognized for its excellence and impact. Since its inception, the 3D printing Dental Medicine Research Center of Shandong University has gone through a remarkable journey of growth and development. We have expanded our team to include more than 50 members committed to the research and development of 3D printing in stomatology. Our research has evolved to address the fabrication of complex surgical guide, an accurate reconstruction of the jaw, orbital floor and ears. Additionally, we have forged valuable collaborations and partnerships with Shanghai Jiao Tong University, Peking University, and University of Hong Kong to further enhance our research capabilities.

### **Team Members:**

Our team is composed of professor Qingguo Lai, the leading experts in oral and maxillofacial surgery and plastic surgery, professor Bin Zou, the leading experts in 3D printing technology, efficient precision machining technology, robot processing technology. Young and passionate researchers including Hongyu Xing, the doctor of engineering specialized in research on 3D printing of ceramics and polymer materials, as well as Hongyu Zhao, the doctor of medicine major in the research of bone repair and regeneration and other support staffs dedicated to excellence. Additionally, we also engaged professor Zhiyuan Zhang, the member of the Chinese Academy of Engineering, Kaili Lin, from Shanghai JiaoTong University as an academic advisory board. Together, they work tirelessly to hammer at the 3D ceramic printing-based regeneration and repair of large bone defects and the 3D bioprinting-based organ reconstruction.

### **Research Areas:**

The 3D printing Dental Medicine Research Center of Shandong University specializes in the 3D ceramic printing-based regeneration and repair of large bone defects and the 3D bioprinting-based organ reconstruction.

### **Research Achievements:**

We have made significant contributions in the model surgical assisted accurate reconstruction of craniomaxillofacial as well as the head and neck defects, 3D printed implants heling facial precision plastic surgery and development of HA paste system

suitable for SLA-3D printing.

### **Main Publications:**

1. Hongyu Zhao; Hongyu Xing; Yixuan Zhao; Qinghua Chen; Bin Zou; Qingguo Lai; Additive manufacturing of graphene oxide/hydroxyapatite bioceramic scaffolds with reinforced osteoinductivity based on digital light processing technology, *Materials & Design*, 2022, 223:111231-111231
2. Chiyang Zhong; Yixuan Zhao; Hongyu Xing; Runqi Xue; Tianxiang Song; Xiaopeng Tang; Kaiwen Zhu; Yanwei Deng; Qingguo Lai Q ; Assembly of 3D-printed Ti scaffold and free vascularized fibula using a customized Ti plate for the reconstruction of mandibular defects, *Bio-Design and Manufacturing*, 2022, 5(2): 424-429
3. Hongyu Zhao; Hongyu Xing; Tianxiang Song; Xiaopeng Tang; Kaiwen Zhu; Yanwei Deng; Yun Zhao; Weihua Liu; Runqi Xue; Qingguo Lai. Mechanical properties, microstructure, and bioactivity of  $\beta$ -Si<sub>3</sub>N<sub>4</sub>/HA composite ceramics for bone reconstruction, *Ceramics International*, 2021, 47(24): 34225-34234
4. Qinghua Chen; Bin Zou; Yang Wang; Kaiwen Zhu; Yanwei Deng; Chuanzhen Huang; Qingguo Lai. 3D printing and osteogenesis of loofah-like hydroxyapatite bone scaffolds, *Ceramics International*, 2021, 47(14): 20352-20361
5. Qinghua Chen; Bin Zou; Yang Wang; Runqi Xue; Hongyu Xing; Xiangsong Fu; Chuanzhen Huang; Peng Yao; Qingguo Lai. A study on biosafety of HAP ceramic prepared by SLA-3D printing technology directly, *Journal of the Mechanical Behavior of Biomedical Materials*, 2019, 98: 327-335
6. Peng Guo, Bin Zou\*, Chuanzhen Huang, Huabing Gao, Study on microstructure, mechanical properties and machinability of efficiently additive manufactured AISI 316L stainless steel by high-power direct laser deposition, *Journal of Materials Processing Technology* 2017, 240: 12-22
7. Peng Wang, Bin Zou\*, Hongchuan Xiao, Shouling Ding, Chuanzhen Huang. Effects of printing parameters of fused deposition modeling on mechanical properties, surface quality, and microstructure of PEEK. *Journal of Materials Processing Tech.* 271 (2019) 62-74.
8. Shouling Ding, Bin Zou\*, Peng Wang, Hongjian Ding. Effects of nozzle temperature and building orientation on mechanical properties and microstructure of PEEK and PEI printed by 3D-FDM. *Polymer Testing.* 78 (2019) 105948.
9. Hongyu Xing, Bin Zou\*, Shasha Li, Xiangsong Fu. Study on surface quality, precision and mechanical properties of 3D printed ZrO<sub>2</sub> ceramic components by laser scanning stereolithography. *Ceramics International.* 43 (2017) 16340-16347.
10. Peng Wang, Bin Zou\*, Shouling Ding, Lei Li, Chuanzhen Huang. Effects of FDM-3D printing parameters on mechanical properties and microstructure of CF/PEEK and GF/PEEK. *Chinese Journal of Aeronautics.* 34 (2021) 236–246.

### **Facilities & Resources:**

Our state-of-the-art facilities and cutting-edge technology enable us to conduct research that is both rigorous and innovative. We boast dual nozzle 3D printer and 3D

bioprinters.

**Collaborations & Partnerships:**

We believe in the power of collaboration. That's why we have forged partnerships with Shanghai Jiao Tong University, Peking University, and University of Hong Kong to further advance our research.

**Recreational Activities:**

The atmosphere in the research group is harmonious. In leisure time, the research group camped, skied and climbed mountains together. Research members often participate in academic exchange meetings.

**Other Features:**

The laboratory focuses on the clinical difficulties in the accurate repair of composite tissue defects in the head and neck area of the five facial features, optimizes the additive material system of biological materials such as titanium metal, bioceramics and polymers, and develops bionic tissue engineering scaffolds to realize the reconstruction of complex living tissues and organs. Strive to break through the bottleneck of regeneration and repair of composite tissue and organ defects in the head and neck region of the five senses and complete the clinical transformation and application of related medical products.

**Contact:**

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## NHC Key Laboratory of Otorhinolaryngology

### **Establishment and Development:**

Auditory, Nasopharyngeal and Throat (ENT) are important senses of the human body. The mechanism of different sensation generation and the development of new drugs targeting sensory receptors have great significance. NHC Key Laboratory of Otorhinolaryngology was established in 1989, relying on the Department of Otorhinolaryngology of Qilu Hospital, Shandong University. The Department of Otorhinolaryngology of Qilu Hospital is one of the birthplaces and foundations of otorhinolaryngology in China, and it has been the first in China to carry out total laryngectomy, endolaryngectomy, laryngeal grafting, laryngeal reconstruction, etc. In terms of basic research, we have revealed the coding mechanism of G protein coupled receptors (GPCRs) for olfactory and force sensation, and explained the basic process of these life activities at the molecular level. We have carried out in-depth studies centering on GPCR deorphanization in sensory system, GPCR ligand discovery and recognition mechanism; GPCR functional diversity and development of functional biased drugs, and achieved a series of original results. Moreover, we have explored in depth the biomarkers and pathogenic mechanisms of head and neck tumors, and strengthened interdisciplinary collaboration to promote early intervention and treatment of head and neck tumors. In recent years, we have published more than 80 articles in Nature (7 articles), Science, Cell (2 articles), Cell Metab, Nat Chem Biol (3 articles), Nat Metab and other well-known journals as corresponding author.

### **Team Members:**

Our team is composed of four doctoral supervisors including Prof. Jinpeng Sun, Prof. Dapeng Lei, Dr. Xin Feng and Dr. Yan Yuan. Prof. Sun is the Vice Dean of Cheeloo College of Medicine, Shandong University, Dean of the School of Advanced Medical Research at Shandong University, Recipient of the National Science Fund for Distinguished Young Scholars, New Cornerston Investigator, Recipient of 15th Tan Life Science Innovation Award in 2022. Prof. Sun has published more than 80 articles in Nature (7 articles), Science, Cell (2 articles), Cell Metab, Nat Chem Biol (3 articles), Nat Metab and other well-known journals as corresponding author, and has been invited to give presentations in international and domestic academic conferences. Our researches have imposed profound impact in GPCR area. Prof Sun has been awarded the New Cornerstone Investigator Program (2023), the National Science Fund for Distinguished Young Scholars (2018), C.C.TAN (JIA-ZHEN TAN) Life Science Award (2022), The Second Prize of Chinese Medical Science Prize (2022), and the Third Session of National Award for Excellence in Innovation (2023). Currently, Prof Sun is presiding a number of funds such as National key research and development program, Key Program and General Program; of National Natural Science Foundation of China, Key Program of Beijing Municipal Natural Science Foundation.

Professor Lei, serving as the Chief Physician, Professor, and Doctoral Supervisor,

currently holds the position of Director of the Department of Otolaryngology Head and Neck Surgery at Qilu Hospital of Shandong University. Additionally, he serves as the Deputy Director of the Key Laboratory of Otolaryngology Head and Neck Surgery of the National Health Commission, a member of the Ear, Nose, and Throat Head and Neck Surgery Branch of the Chinese Medical Association, and the Deputy Leader of the Head and Neck Group of the China Medical Association. Professor Lei has led seven National Natural Science Foundation projects and received six provincial and ministerial-level awards. He has authored or co-authored over 40 papers in SCI and domestic core journals, including being the lead author of the first "Expert Consensus on Surgical and Comprehensive Treatment of Hypopharyngeal Cancer" and "Expert Consensus on Pharyngolaryngeal Endoscopic Examination" in China, and has participated in the formulation of multiple expert consensuses.

Dr. Xin Feng is a Professor in the Department of Otorhinolaryngology, Qilu hospital of Shandong University. He received his M.D degree from Shandong University and completed post-doctoral training at the Asthma and Allergic Diseases Center at the University of Virginia in the U.S. Currently, he serves as the principal investigator for the National Natural Science Foundation of China, the Shandong Provincial Key Research and Development Program, and the Natural Science Foundation of Shandong Province. His research interests include the pathogenesis of nasal polyps, chronic rhinosinusitis, and allergic rhinitis, as well as the relationship between the rhinologic diseases and asthma.

Dr. Yan Yuan had been a distinguished faculty member at the University of Pennsylvania and joined Shandong University last year. He has been engaged in research in the fields of virology and oncology with significant achievements and contributions to the fields of virology and oncology. He is widely recognized as a foremost expert in viral oncology.

#### **Research Areas:**

NHC Key Laboratory of Otorhinolaryngology has long been engaged in the study of microenvironment pharmacology, in which he systematically dissected the mechanism of membrane receptors sensing microenvironment and regulating physiological functions, and developed the modulating strategies targeting these receptors. In head and neck squamous cell carcinoma pathogenesis and intervention strategy area, we explore the molecular biomarkers and pathogenesis of head and neck tumors, providing a theoretical basis for the diagnosis, intervention, and treatment of tumors. In particular, through the Kaposi's sarcoma and osteosarcoma platforms, our laboratory is dedicated to investigating the viral etiology of human sarcomas and the molecular mechanisms underlying virus-mediated transformation of mesenchymal stem cells leads to human sarcomas. In addition, our team has investigated the mechanisms of human airway inflammatory diseases, including chronic rhinitis (CRS), allergic rhinitis (AR), rhinoviruses, and asthma. The focus is on elucidating the intricate cellular interactions among diverse immune cell

populations, as well as immune metabolism in maintaining nasal mucosal homeostasis.

### **Research Achievements:**

We have made significant contributions in microenvironment pharmacology, membrane receptor GPCR for a long time. We have systematically studied the mechanism of GPCR sensing microenvironment and regulating physiological function, analyzed the molecular mechanism of GPCR sensing itch, smell and force, and realized the identification of many important GPCR endogenous ligands. We have explored receptors for auditory and vestibular sensations and identified a subfamily of membrane receptors that recognize steroids.

We are the first in China to apply radiomics, multidimensional deep learning, pathomics, and hyperspectral analysis for the classification, diagnosis, and prognosis assessment of malignant tumors of the pharynx and larynx. We have developed a multimodal non-invasive assessment model for early evaluation of pharyngeal and laryngeal tumors, significantly enhancing the accuracy of diagnosis and assessment. We have comprehensively elucidated the oncogenic mechanism of KSHV regulation through solubilization of DNA replication and assembly of viral DNA replication complexes.

We identified the importance of targeting eosinophil-derived LTB4 in asthma therapeutic strategies and the presence of compensatory mechanisms that aid in viral clearance in patients with allergic airway diseases. We identified novel biomarkers and pathways associated with unified airway disease, eosinophilic inflammation, and the comorbidity of CRS, nasal polyps, and asthma. In addition, our sinus segmentation and recurrence prediction in patients with CRS provides a noninvasive tool for personalized preoperative treatment recommendations based on recurrence risk, which is a significant advance.

We have published more than 80 articles in Nature (×7), Science (×1, cover article), Cell (×2, 1 cover articles), Nature Metabolism (×1), Cell Metabolism (×1), Nat Chem Biol (×3), Cell Research (×2), PNAS (×6), Nat Commun (×7) and so on. Recently, our research on the molecular mechanisms of olfactory perception was successfully selected as one of China's Top 10 Scientific Advances in 2023.

### **Main Publications:**

Selected publications in last 5 years (\*represents the corresponding authors).

1. Shang P, Rong NK, Jiang JJ, Cheng J, Zhang MH, Kang DW, Qi L, Guo LL, Yang GM, Liu Q, Zhou ZZ, Li XB, Zhu KK, Meng QB, Han X, Yan WQ, Kong YL, Yang LJ, Wang XH, Lei DP, Feng X, Liu XY, Yu X, Wang Y\*, Li Q\*, Shao ZH\*, Yang F\*, Sun JP\*. Structural and signaling mechanism of TAAR1 enabled preferential agonist design. Cell. 2023
2. Xu Z, Guo L, Yu JJ, Shen SY, Wu C, Zhang WF, Zhao C, Deng Y, Tian XW, Feng

YY, Hou HL, Su LT, Wang HS, Guo S, Wang HL, Wang KX, Chen PP, Zhao J, Zhang XY, Yong XH, Cheng L, Liu LX, Yang SY, Yang F, Wang XH, Yu X\*, Xu YF\*, Sun JP\*, Yan W\*, Shao ZH\*. Ligand recognition and G-protein coupling of trace amine receptor TAAR1. *Nature*. 2023

3. Guo L, Cheng J, Lian S, Liu Q, Lu Y, Zheng Y, Zhu K, Zhang M, Kong Y, Zhang C, Rong N, Zhuang Y, Fang G, Jiang J, Zhang T, Han X, Liu Z, Xia M, Liu S, Zhang L, Liberles SD, Yu X, Xu Y\*, Yang F\*, Li Q\*, Sun JP\*. Structural basis of amine odorant perception by a mammal olfactory receptor. *Nature*. 2023 Jun;618(7963):193-200.

4. Mao C, Xiao P, Tao XN, Qin J, He QT, Zhang C, Guo SC, Du YQ, Chen LN, Shen DD, Yang ZS, Zhang HQ, Huang SM, He YH, Cheng J, Zhong YN, Shang P, Chen J, Zhang DL, Wang QL, Liu MX, Li GY, Guo Y, Xu HE, Wang C, Zhang C, Feng S\*, Yu X\*, Zhang Y\*, Sun JP\*. Unsaturated bond recognition leads to biased signal in a fatty acid receptor. *Science*. 2023 Apr 7;380(6640): eadd 6220.

5. Ping YQ, Xiao P, Yang F, Zhao RJ, Guo SC, Yan X, Wu X, Zhao FH, Zhou FL, Xi YT, Yin WH, He FD, Zhang DL, Zhu ZL, Jiang Y, Torsten Schöneberg, Ines Liebscher\*, Xu H. Eric\*, Sun JP\*. Structural basis for the tethered peptide activation of adhesion GPCRs. *Nature*. 2022. 2022 Apr;604(7907):763-770.

6. Yang F, Guo L, Li Y, Wang G, Wang J, Zhang C, Fang GX, Chen X, Liu L, Yan X, Liu Q, Qu C, Xu Y, Xiao P, Zhu Z, Li Z, Zhou J, Yu X, Gao N\*, Sun JP\*. Structure, function and pharmacology of human itch receptor complexes. *Nature*. 2021 Dec;600(7887):164-169.

7. Ping YQ, Mao C, Xiao P, Zhao RJ, Jiang Y, Yang Z, An WT, Shen DD, Yang F, Zhang H, Qu C, Shen Q, Tian C, Li ZJ, Li S, Wang GY, Tao X, Wen X, Zhong YN, Yang J, Yi F, Yu X, Xu HE\*, Zhang Y\*, Sun JP\*. Structures of the glucocorticoid-bound adhesion receptor GPR97-Go complex. *Nature*. 2021 Jan;589(7843):620-626.

8. Xiao P, Guo S, Wen X, He QT, Lin H, Huang SM, Gou L, Zhang C, Yang Z, Zhong YN, Yang CC, Li Y, Gong Z, Tao XN, Yang ZS, Lu Y, Li SL, He JY, Wang C, Zhang L\*, Kong L\*, Sun JP\*, Yu X\*. Tethered peptide activation mechanism of the adhesion GPCRs ADGRG2 and ADGRG4. *Nature*. 2022 Apr;604(7907):771-778.

9. Yang F, Mao C, Guo L, Lin J, Ming Q, Xiao P, Wu X, Shen Q, Guo S, Shen DD, Lu R, Zhang L, Huang S, Ping Y, Zhang C, Ma C, Zhang K, Liang X, Shen Y, Nan F, Yi F, Luca VC, Zhou J, Jiang C, Sun JP\*, Xie X\*, Yu X\*, Zhang Y\*. Structural basis of GPBAR activation and bile acid recognition. *Nature*. 2020 Nov;587(7834):499-504.

10. Xiao P, Yan W, Gou L, Zhong YN, Kong L, Wu C, Wen X, Yuan Y, Cao S, Qu C, Yang X, Yang CC, Xia A, Hu Z, Zhang Q, He YH, Zhang DL, Zhang C, Hou GH, Liu H, Zhu L, Fu P, Yang S, Rosenbaum DM, Sun JP\*, Du Y\*, Zhang L\*, Yu X\*, Shao Z\*. Ligand recognition and allosteric regulation of DRD1-Gs signaling complexes. *Cell*. 2021 Feb 18;184(4):943-956.e18.

11. Yan Z, Wang JY, Yang F, Zhu KK, Wang PG, Guan Y, Ning SL, Lu Y, Li Y, Zhang C, Zheng Y, Zhou SH, Wang XW, Wang MW, Xiao P, Yi F, Zhang C, Zhang PJ, Xu F, Liu BH, Zhang H, Yu X\*, Gao N\*, Sun JP\*. Cryo-EM structure of the X-linked acrogigantism-related orphan GPR101-Gs complex enabled identification of ligands

- with rejuvenating potential. *Nat Chem Biol.* 2023 accept.
12. Lin H, Xiao P, Bu RQ, Guo S, Yang Z, Yuan D, Zhu ZL, Zhang CX, He QT, Zhang C, Ping YQ, Zhao RJ, Ma CS, Liu CH, Zhang XN, Jiang D, Huang S, Xi YT, Zhang DL, Xue CY, Yang BS, Li JY, Lin HC, Zeng XH, Zhao H, Xu WM, Yi F\*, Liu Z\*, Sun JP\*, Yu X\*. Structures of the ADGRG2-Gs complex in apo and ligand-bound forms. *Nat Chem Biol.* 2022 Nov;18(11):1196-1203.
13. Cheng J, Yang Z, Ge XY, Gao MX, Meng R, Xu X, Zhang YQ, Li RZ, Lin JY, Tian ZM, Wang J, Ning SL, Xu YF, Yang F, Gu JK, Sun JP\*, Yu X\*. Autonomous sensing of the insulin peptide by an olfactory G protein-coupled receptor modulates glucose metabolism. *Cell Metab.* 2022 Feb 1;34(2):240-255.
14. Wang JL, Dou XD, Cheng j, Gao MX, Xu GF, Ding W, Ding JH, Li y, Wang SH, Ji ZW, Zhao XY, Huo TY, Zhang CF, Liu YM, Sha XY, Gao JR, Zhang WH, Hao Y, Zhang C, Sun JP\*, Jiao N\* and Yu X\*. Functional screening and rational design of compounds targeting GPR132 to treat diabetes. *Nat Metab.* 2023 accept.
15. Chen Y, Mao C, Gu R, Zhao R, Li W, Ma Z, Jia Y, Yu F, Luo J, Fu Y, Sun J\*, Kong W\*. Nidogen-2 is a Novel Endogenous Ligand of LGR4 to Inhibit Vascular Calcification. *Circ Res.* 2022 Dec 2;131(12):1037-1054.
16. An W, Lin H, Ma L, Zhang C, Zheng Y, Cheng Q, Ma C, Wu X, Zhang Z, Zhong Y, Wang M, He D, Yang Z, Du L, Feng S, Wang C, Yang F, Xiao P\*, Zhang P\*, Yu X\*, Sun JP\*. Progesterone activates GPR126 to promote breast cancer development via the Gi pathway. *Proc Natl Acad Sci USA.* 2022 Apr 12;119(15):e2117004119.
17. Huang SM, Xiong MY, Liu L, Mu J, Wang MW, Jia YL, Cai K, Tie L, Zhang C, Cao S, Wen X, Wang JL, Guo SC, Li Y, Qu CX, He QT, Cai BY, Xue C, Gan S, Xie Y, Cong X, Yang Z, Kong W, Li S, Li Z, Xiao P, Yang F, Yu X, Guan YF, Zhang X\*, Liu Z\*, Yang BX\*, Du Y\*, Sun JP\*. Single hormone or synthetic agonist induces Gs/Gi coupling selectivity of EP receptors via distinct binding modes and propagating paths. *Proc Natl Acad Sci USA.* 2023 Jul 25;120(30):e2216329120.
18. Wang MW, Yang Z, Chen X, Zhou SH, Huang GL, Sun JN, Jiang H, Xu WM\*, Lin HC\*, Yu X\*, Sun JP\*. Activation of PTH1R alleviates epididymitis and orchitis through Gq and  $\beta$ -arrestin-1 pathways. *Proc Natl Acad Sci USA.* 2021 Nov 9;118(45):e2107363118.
19. Qu CX, Park JY, Yun MW, He QT, Yang F, Kin K, Han D, Li R, T.M.Iverson, V.V.Gurevich, Sun JP\*, Chung KY\*. Scaffolding mechanism of arrestin-2 in the cRaf/MEK1/ERK signaling cascade. *Proc Natl Acad Sci USA.* 2021 Sep 14;118(37):e2026491118.
20. Ma L, Yang F, Wu X, Mao C, Guo L, Miao T, Zang SK, Jiang X, Shen DD, Wei T, Zhou H, Wei Q, Li S, Shu Q, Feng S, Jiang C, Chu B, Du L\*, Sun JP\*, Yu X\*, Zhang Y\*, Zhang P\*. Structural basis and molecular mechanism of biased GPBAR signaling in regulating NSCLC cell growth via YAP activity. *Proc Natl Acad Sci USA.* 2022 Jul 19;119(29): e2117054119.
21. Fu Y, Huang Y, Yang Z, Chen Y, Zheng J, Mao C, Li Z, Liu Z, Yu B, Li T, Wang M, Xu C, Zhou Y, Zhao G, Jia Y, Guo W, Jia X, Zhang T, Li L, Liu Z, Guo S, Ma M, Zhang H, Liu B, Du J, Wang W, Tang C, Gao P, Xu Q, Wang X, Liu J, Sun JP\*, Kong W\*. Cartilage oligomeric matrix protein is an endogenous  $\beta$ -arrestin-2-selective

- allosteric modulator of AT1 receptor counteracting vascular injury. *Cell Res.* 2021 Jul;31(7):773-790.
22. Wang HM, Xu YF, Ning SL, Yang DX, Li Y, Du YJ, Yang F, Zhang Y, Liang N, Yao W, Zhang LL, Gu LC, Gao CJ, Pang Q, Chen YX, Xiao KH, Yu X\*, Sun JP\*. The catalytic region and PEST domain of PTPN18 distinctly regulate the HER2 phosphorylation and ubiquitination barcodes. *Cell Research.* 2014 Sep;24(9):1067-90.
23. Guo L, Zhang Y, Fang G, Tie L, Zhuang Y, Xue C, Liu Q, Zhang M, Zhu K, You C, Xu P, Yuan Q, Zhang C, Liu L, Rong N, Peng S, Liu Y, Wang C, Luo X, Lv Z, Kang D, Yu X, Zhang C, Jiang Y, Dong X, Zhou J\*, Liu Z\*, Yang F\*, Eric Xu H\*, Sun JP\*. Ligand recognition and G protein coupling of the human itch receptor MRGPRX1. *Nat Commun.* 2023 Aug 17;14(1):5004.
24. He QT, Xiao P, Huang SM, Jia YL, Zhu ZL, Lin JY, Yang F, Tao XN, Zhao RJ, Gao FY, Niu XG, Xiao KH, Wang J\*, Jin C\*, Sun JP\*, Yu X\*. Structural studies of phosphorylation-dependent interactions between the V2R receptor and arrestin-2. *Nat Commun.* 2021 Apr 22;12(1):2396.
25. Liu Q, He QT, Lyu X, Yang F, Zhu ZL, Xiao P, Yang Z, Zhang F, Yang ZY, Wang XY, Sun P, Wang QW, Qu CX, Gong Z, Lin JY, Xu Z, Song SL, Huang SM, Guo SC, Han MJ, Zhu KK, Chen X, Kahsai AW, Xiao KH, Kong W, Li FH, Ruan K, Li ZJ, Yu X, Niu XG, Jin CW, Wang J\*, Sun JP\*. DeSiphering receptor core-induced and ligand-dependent conformational changes in arrestin via genetic encoded trimethylsilyl 1H-NMR probe. *Nat Commun.* 2020 Sep 25;11(1):4857.
26. Qu CX, Mao CY, Xiao P, Shen QY, Zhong YN, Yang F, Shen DD, Tao XN, Zhang HB, Yan X, Zhao RJ, He JY, Guan Y, Zhang C, Hou GH, Zhang PJ, Hou GG, Li ZJ, Yu X, Chai RJ\*, Guan YF, Sun JP\*, Zhang Y\*. Ligand recognition, unconventional activation and G protein coupling of the prostaglandin E2 receptor 2 (EP2). *Science Advances.* 2021 Apr 2;7(14):eabf1268.
27. Guan Y, Du HB, Yang Z, Wang YZ, Ren R, Liu WW, Zhang C, Zhang JH, An WT, Li NN, Zeng XX, Li J, Sun YX, Wang YF, Yang F, Yang J, Xiong W, Yu X, Chai RJ, Tu XM\*, Sun JP\*, Xu ZG\*. Deafness-Associated ADGRV1 Mutation Impairs USH2A Stability through Improper Phosphorylation of WHRN and WDSUB1 Recruitment. *Adv Sci (Weinh).* 2023 Jun;10(16):e2205993.
28. Lin JY, Cheng J, Du YQ, Pan W, Zhang Z, Wang J, An J, Yang F, Xu YF, Lin H, An WT, Wang J, Yang Z, Chai RJ, Sha XY, Hu H.L\*, Sun JP\*, Yu X\*. In vitro expansion of pancreatic islet clusters facilitated by hormones and chemicals. *Cell Discov.* 2020 Apr 7;6:20.
29. Wang, W., H. Liang, Z. Zhang, C. Xu, D. Wei, W. Li, Y. Qian, L. Zhang, J\*. Liu\*, and D. Lei\*, Comparing three-dimensional and two-dimensional deep-learning, radiomics, and fusion models for predicting occult lymph node metastasis in laryngeal squamous cell carcinoma based on CT imaging: a multicentre, retrospective, diagnostic study. *E Clinical Medicine.* 2024. 67: p. 102385.
30. Zhao, X., W. Li, J. Zhang, S. Tian, Y. Zhou, X. Xu, H. Hu, D. Lei\*, and F. Wu\*, Radiomics analysis of CT imaging improves preoperative prediction of cervical lymph node metastasis in laryngeal squamous cell carcinoma. *Eur Radiol.* 2023. 33(2): p. 1121-1131.

31. Wu, K, F. Chang, W. Li, D. Wei, S. Cao, Y. Xie, C. Li, and D. Lei\*, Preliminary study based on methylation and transcriptome gene sequencing of lncRNAs and immune infiltration in hypopharyngeal carcinoma. *Front Oncol.* 2023. 13: p. 1117622.
32. Wang, W., Z. Zhang, W. Li, D. Wei, J. Xu, Y. Qian, S. Cao, and D. Lei\*, Characterization of the immune cell function landscape in head and neck squamous carcinoma to assist in prognosis prediction and immunotherapy. *Aging (Albany NY).* 2023. 15(21): p. 12588-12617.
33. Wang, S., B. Luo, B. Bai, Q. Wang, H. Chen, X. Tan, Z. Tang, S. Shen, H. Zhou, Z. You, G. Zhou, and D. Lei\*, 3D Printed Chondrogenic Functionalized PGS Bioactive Scaffold for Cartilage Regeneration. *Adv Healthc Mater.* 2023. 12(27): p. e2301006.
34. Li, C., R. Guan, W. Li, D. Wei, S. Cao, C. Xu, F. Chang, P. Wang, L. Chen, and D. Lei\*, Single-cell RNA sequencing reveals tumor immune microenvironment in human hypopharyngeal squamous cell carcinoma and lymphatic metastasis. *Front Immunol.* 2023. 14: p. 1168191.
35. Jia, W., S. Chen, R. Wei, X. Yang, M. Zhang, Y. Qian, H. Liu\*, and D. Lei\*, CYP4F12 is a potential biomarker and inhibits cell migration of head and neck squamous cell carcinoma via EMT pathway. *Sci Rep.* 2023. 13(1): p. 10956.
36. Li, C., S. Chen, W. Jia, W. Li, D. Wei, S. Cao, Y. Qian, R. Guan, H. Liu\*, and D. Lei\*, Identify metabolism-related genes IDO1, ALDH2, NCOA2, SLC7A5, SLC3A2, LDHB, and HPRT1 as potential prognostic markers and correlate with immune infiltrates in head and neck squamous cell carcinoma. *Front Immunol.* 2022. 13: p. 955614.
37. Wang, J., X. Cai, L. Zhang, and D. Lei\*, Linc01513 inhibits the malignant potential of Nasopharyngeal carcinoma by binding to PTBP1. *J Cancer,* 2021. 12(24): p. 7380-7389.
38. Li, W., D. Wei, Y. Qian, S. Cao, D. Liu, D. Lei\*, and X. Pan\*, A novel surgical approach for hypopharyngeal carcinoma resection via the paraglottic space. *BMC Surg.* 2021. 21(1): p. 230.
39. Li, W., D. Wei, A. Wushouer, S. Cao, T. Zhao, D. Yu, and D. Lei\*, Discovery and Validation of a CT-Based Radiomic Signature for Preoperative Prediction of Early Recurrence in Hypopharyngeal Carcinoma. *Biomed Res Int.* 2020. 2020: p. 4340521.
40. Duan C, Yu X, Feng X\*, Shi L, Wang D. Expression Profiles of Matrix Metalloproteinases and Their Inhibitors in Nasal Polyps. *J Inflamm Res.* 2024 Jan 3;17:29-39.
41. He S, Chen W, Wang X, Xie X, Liu F, Ma X, Li X, Li A, Feng X\*. Deep learning radiomics-based preoperative prediction of recurrence in chronic rhinosinusitis. *iScience.* 2023 Mar 30;26(4):106527.
42. Wang M, Gong L, Luo Y, He S, Zhang X, Xie X, Li X, Feng X\*. Transcriptomic analysis of asthma and allergic rhinitis reveals CST1 as a biomarker of unified airways. *Front Immunol.* 2023 Jan 17;14:1048195.
43. Chen W, He S, Xie X, Yang X, Duan C, Ye P, Li X, Lawrence MG, Borish L, Feng X\*. Over-expression of CRTH2 indicates eosinophilic inflammation and poor prognosis in recurrent nasal polyps. *Front Immunol.* 2022 Nov 18;13:1046426.
44. Wang M, Tang S, Yang X, Xie X, Luo Y, He S, Li X, Feng X\*. Identification of

key genes and pathways in chronic rhinosinusitis with nasal polyps and asthma comorbidity using bioinformatics approaches. *Front Immunol.* 2022 Aug 17;13:941547.

45.Feng X#, Lawrence MG, Payne SC, Mattos J, Etter E, Negri JA, Murphy D, Kennedy JL, Steinke JW, Borish L. Lower viral loads in subjects with rhinovirus-challenged allergy despite reduced innate immunity. *Ann Allergy Asthma Immunol.* 2022 Apr;128(4):414-422.e2.

46.Pal K#, Feng X#, Steinke JW, Burdick MD, Shim YM, Sung SS, Teague WG, Borish L. Leukotriene A4 Hydrolase Activation and Leukotriene B4 Production by Eosinophils in Severe Asthma. *Am J Respir Cell Mol Biol.* 2019 Apr;60(4):413-419.

47.Xu X, Zhu N, Zheng J, Peng Y, Zeng M-S, Deng K, Duan C, Yuan Y\*. EBV abortive lytic cycle promotes nasopharyngeal carcinoma progression through recruiting monocytes and regulating their directed differentiation. *PLoS Pathog.* 2024 20(1): e1011934.

48.Lu, Z., Zhang, X., Zhu, N. Wang, Y., Yuan, Y.\* and Zeng, M.S.\* Neuropilin 1 is a mesenchymal stem cell receptor for Kaposi's sarcoma-associated herpesvirus through TGFBR1/2-mediated macropinocytosis. *Science Adv.* 2023.9, eadg1778.

49.Chen, W., Ding, Y., Liu, D., Lu, Z., Wang, Y., and Yuan, Y\*. Kaposi Sarcoma-associated Herpesvirus vFLIP Promotes MEndT to Generate Hybrid M/E State for Tumorigenesis. *PLoS Pathog.* 2021; 17:e1009600.

50.Ding, Y., Chen, W., Lu, Z., Wang, Y., and Yuan, Y. Kaposi's Sarcoma-associated Herpesvirus Promotes Mesenchymal-to- Endothelial Transition by Resolving the Bivalent Chromatin of PROX1 Gene. *PLoS Pathog.* 2021; 17:e1009847.

51.Chen, Q, Chen, J., Li, Y., Liu, D., Zeng, Y., Yunus, A., Tian, Z., Yang, Y., Lu, J., Song, X., and Yuan. Y. Kaposi's Sarcoma Herpesvirus Is Associated with Osteosarcoma in Xinjiang Populations. *Proc. Natl. Acad. Sci.* 2021; USA 118(10): e2016653118.

### **Facilities & Resources:**

Our state-of-the-art facilities and cutting-edge technologies enable us to conduct rigorous and innovative research. The team operates within the National Key Laboratory of Otolaryngology Head and Neck Surgery at Qilu Hospital of Shandong University, which spans a total construction area of 1500 square meters. The laboratory is equipped with research platforms including flow analysis center, molecular imaging/behavioral center, multi-factor detection center, cryo-electron microscope structure characterization center, medical biology high performance computing center and other platforms. We have essential equipment such as Millipore water purification system, laser confocal microscopy system, Lionheart FX automated live cell imaging and analysis system, Licor dual-channel infrared laser imaging system, Roche 480II fluorescence quantitative PCR instrument, FACSCalibur flow cytometer, Beckman floor-standing refrigerated high-speed and ultra-high-speed centrifuges, Thermo Varioskan multi-functional microplate reader, and other instruments. Additionally, the laboratory is equipped with automated pathology and histology research equipment including Leica cryostat and paraffin microtome, fully



automated immunostainer, dehydrator, and other automated pathology and histology research equipment. Our laboratory is proficient in plasmid construction, cell culture, virus packaging, protein expression and purification. GPCR downstream effector recruitment and detection or second messenger detection technology were established well. Single particle cryo-electron microscope structure analysis, cryo-electron microscope data calculation and model building, molecular dynamics simulation and other technologies are also available in our lab. Overall, these devices fully meet the equipment requirements of our project.

#### **Recreational Activities:**

Our laboratory is fortunate to have established long-term good cooperative relations with many top laboratories at home and abroad. Our cooperative partners include Professor Gao Ning's team from Peking University, Professor Zhang Yan's team from Zhejiang University, Professor Xu Huaqiang's team from Shanghai Institute of Pharmacology, Chinese Academy of Sciences, Professor Shao Zhenhua's team from Sichuan University, Germany Professor Ines Liebscher team of Schonheimer Institute, Professor Zhang Lei team of Xi 'an Jiaotong University, Professor Yi Fan team of Shandong University, Professor Kong Wei team of Peking University, Professor Liu Zhijie team of Shanghai University of Science and Technology, Professor Chai Renjie team of Southeast University. This also provides a stable scientific research background for the advancement of our subject research.

#### **Other Features:**

We have unique GPCR-ligand pairing technique, GPCR force-sensing screening platform, GPCR signal transduction technology which are the characteristics of our lab. Teamwork and kindness are part of our lab culture. At the same time, we also emphasize that only by loving life can we do scientific research well. There are many sports venues in our university, including professional football and basketball courts. Moreover, our campus is adjacent to Quancheng Park and Baotu Spring, where our lab mates often go to relax and unwind. Every week, our lab organizes a football match. Regular group meetings are organized in our laboratory, during which teachers summarize and analyze the recent achievements of students, provide them with professional and meticulous guidance, plan their future development directions, and offer insights into their employment and learning.

#### **Contact:**

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