UoE Single Award PhD program available projects

(updated on 10th November 2023, continuing update)

【1】
Project title: Treatment of autoimmune disease by targeting PP2A

Supervisor: Linrong Lu

Project introduction:
Protein phosphatase 2A (PP2A) expression is a serine/threonine phosphatase involved in many different cellular processes. Our previous study has revealed its critical role in promoting Th17 differentiation. Our ongoing project also found out that the upregulated expression in Tfh cells is closely related to the production of autoantibodies in lupus patients. This project aims to study whether we can use PP2A inhibitors to prevent or treat autoimmune diseases. We will apply the treatment to different autoimmune disease models and assess the therapeutic effects using bioinformatics and omic tools.

【2】
Project title: The cellular mechanism of skin wound repair

Supervisor: Suhong Xu

Project introduction:
The skin wound repair and regeneration is one of the most important problems in clinics and biomedicine. However, how the skin repair itself after injury is largely unknown. Particularly, it is unclear which specific cellular type involved in rapid proliferation and how early wound signal initiates the underlying cell fate transition. We will use single cell RNA sequencing to identify the key cellular type and their underlying molecular mechanism.

【3】
Project title: The molecular and cellular mechanism of scar formation after injury

Supervisor: Suhong Xu

Project introduction:
The scar formation after injury cause many burdens in human. The main components in scar structure are the collagens. However, it is unclear how collagen secretion and assembly after skin damage. This project aims to identify the molecular mechanism of collagen secretion, assembly using C. elegans epidermis as a model system. We will

use the EMS screen, and drug screen to identify the key components of collagen synthesis, secretion, and assembly.

【4】

Project title: Dynamic changes and regulatory functions of proteasomes in mammalian spermatogenesis.

Supervisor: Qianting Zhang

Project introduction:

We investigate on the dynamics of proteasomes and subsequent protein degradation events in meiosis and spermiogenesis, to answer the questions of functions and regulations of protein homeostasis in mammalian gametogenesis. We will focus on clarifying the composition, subcellular localization and substrate specificity of the proteasome during spermatogenesis. By combining genetically-modified mouse models and state-of-the-art technologies, we are able to reveal roles of proteasomes in the level of functional, physiological, cellular, biochemical and molecular. Previously, we have proposed there are at least three kinds of proteasomal degradation events during spermatogenesis. First, a group of proteins related to meiotic recombination (TEX11, SPATA22, PSMA7, etc.) are degraded by the classic PSMA7-associated 26S proteasomes. Second, other factors such as RAD51 and RPA1 are degraded by PSMA8-associated proteasomes at late meiotic prophase I. The third one is the replacement of histones by protamine during spermiogenesis, dependent on PA200-capped proteasomes. In this project, we will systematically investigate the role of proteasomes in mammalian reproduction from multiple perspectives, clarify their dynamic changes and regulatory functions during spermatogenesis, and explore PSMA8 and PSMA7 at the molecular level. In terms of the reasons for differences in subcellular localization and specificity of degradation substrates, summarize the proteasome degradation events related to mammalian spermatogenesis, and map the ubiquitination proteasome degradation events during spermatogenesis.

【5】

Project title: Molecular mechanism of MZIP2-interacting protein in regulating DNA homologous recombination

Supervisor: Qianting Zhang

Project introduction:

We identified two novel mammalian genes comprising a complex MZIP2-SPO16 mediating meiotic homologous recombination (HR), synapsis as well as crossover formation. We will continually focus on the roles of the complex in diverse biological processes such as DNA repair, genome instability and tumorigenesis, with particular

emphasis on how the scaffold protein MZIP2 function in cohort with other HR-related proteins. By investigating the molecular mechanism of DNA double strand break repair pathway in tumor cells, we will gain further understanding of the pathological significance of DNA instability in cancer progress. HeLa or U2OS cell lines stably expressing exogeneous MZIP2 by lenti-viral system are going to be generated and subjected to Immunoprecipitation-Mass Spectrometry (IP-MS). If we successfully identify new MZIP2-interacting factors, we can further explore the effect of these factors and the molecular mechanism of MZIP2 in DNA double strand break repair in tumor cells.

【7】

Project title: CRISPR interference screening of cellular mechanosensing mechanisms during cell division

Supervisor: Chew Ting Gang

Project introduction:

Cells sense and respond to mechanical forces and generate appropriate biochemical responses to direct cellular processes. In response to mechanical stresses such as compression, mechanosensitive proteins accumulate at the stress site and recruit downstream associated proteins to transduce the signals. Failure to trigger appropriate cellular mechanosensing results in pathological conditions including cell overgrowth, genome instability, cell invasion which are hallmarks of cancer. We developed a cell compression assay and identified several key proteins involved in cellular contractility that display mechanosensitive accumulation during mitosis. The student will investigate how the mechanosensitive accumulation of these protein is regulated during mitosis. To this end, a small-scale focused group CRISPR interference screening will be employed to identify factors that regulate the mechanosensitive accumulation during mitosis.

【8】

Project title: Understanding of cellular responses to compressive stress derived from tumor growth in vivo

Supervisor: Chew Ting Gang

Project introduction:

Cells grow and divide in a crowded and mechanically confined tissue microenvironment. During tumorigenesis, over-proliferation and cellular growth of tumors generate solid stress that significantly compresses the tumor interior cells and the surrounding cells, which has impacted their cellular metabolism, growth and division. Compressive stresses in tumors cause cell division defects, genome instability

and fuel the epithelial-mesenchymal transition and cancer cell migration. Previous findings in our lab showed that compressive stresses destabilize the cell cortex when cells are dividing. The dividing cells respond to the cell cortex instability by activating a mechanotransduction pathway to sustain cellular contraction to complete cell division in the presence of compressive stresses. Failure of cells to respond to the compressive stress has resulted in cytokinesis failure, which pre-condition the cells to tumorigenesis. In this study, the student will test if a similar cellular mechanoresponse could be observed in vivo. Using the fruifly cancer model with oncogenic Ras cell clones, we could study the impact of compressive stress on cells actively dividing inside the tumor or surrounding the tumor. The fruitfly cancer model is well-established and has high conservation of the cancer signaling pathways as in human cancer. The student will combine cancer genetics, cell biology and live-cell imaging to understand the cellular mechanoresponse to compressive stresses derived from the tumor growth. This study will pave the wave to the understanding of the mechanobiology of tumorigenesis. The student will be co-supervised by Prof. Wanzhong Ge from Zhejiang University who has expertise in using fruitfly as a model system to study tissue homeostasis.

【9】

Project title: Mechanistic understanding of cellular response to cortical instability during cell division

Supervisor: Chew Ting Gang

Project introduction:

Cells divide in a crowded tissue environment particularly in the tumor overgrowth condition experience high compressive solid stress, which induces mechanical instability of the cell cortex (cortical instability) during cytokinesis. Our lab has previously induced the cortical instability chemically during cell division by perturbing the mitotic cell cortex dynamics. We found that cortical instability in dividing cells depends on a stress-activated protein kinase to avoid failure of cytokinesis, which is harmful to cells. In this project, the student will aim to understand how does the protein kinase regulates cytokinesis in response to cortical instability induced by compression. The student will use CRISPRi to knock down the kinase and address whether the absence of the kinase would result in cytokinesis failure when cells experience cortical instability. In addition to chemical perturbation of the cell cortex, the student will mechanically compress the mitotic cells defective in the kinase function and test the requirement of the kinase in regulating cortical stability. The student will also make phosphorylation mutants of a downstream substrate of the kinase. These constructs will be expressed in the kinase knockdown cells to address their regulatory roles in cortical instability during cell division.

【10】
Project title: High volume computational acquisition and analysis of cell morphology

Supervisor: Chew Ting Gang

Project introduction:
Mammalian cells become spherical to provide an ideal cell geometry feasible for mitosis and cytokinesis. Maintaining a proper cell morphology is particularly important when cells are dividing in a physically constraint tissue environment. Failure of which results in chromosome segregation errors and cytokinesis defects that contribute to genome instability. Fluorescence confocal microscopy is an useful tool to acquire cell morphology information given its ability to image cells in a volumetric way. However, ever decreasing costs and increasing imaging capabilities yields an immense data volume that poses a fundamental challenge: how to screen and process data that overwhelm the capacity for comprehensive human supervision in the analysis workflow? Fortunately, increasing computational capabilities coupled with advancements in data science and machine learning driven by similar challenges facing scientists and engineers across numerous disciplines have produced a maturing set of computational frameworks and processing schemes to meet high-volume, unsupervised data processing demands. In this project, the student will work closely with experts in biomedical science (Prof. Ting Gang Chew, ZJE) and image processing (Prof. Mark D. Butala, ZJUI) to employ and tailor community developed computer vision and machine learning frameworks to quantitatively analyze cellular morphological parameters.

【11】
Project title: Cellular behaviors in response to the nano-topographical surface during cell division

Supervisor: Chew Ting Gang

Project introduction:
Cells sense and respond to the the surrounding environment with complex mechanical and geometrical properties. How cells interpret these physical cues and trigger an appropriate response during their life cycle of growth, division and aging is important for cellular health but remain largely unclear. Here, we will study how cellular contractility during cell division is tuned according to the surfaces with a nano-scale topography instead of a conventional smooth surface in cell culture. The student will use the high resolution live-cell fluorescence microscopy to study the fast response of proteins involved in cellular contraction and mechanical sensing to the surface nanotopography during cell division. Mammary epithelial cells stably expressing various fluorescence-based reporters will be used to visualize the relevant molecular activities. Pharmacological inhibition of key players in cell division will be performed

to illuminate the molecular control of cellular response to nanotopography during cell division. This study will generate insights on how the physical topography from the environment could influence cellular contractility during cell division.

【12】
Project title: Design of Stimuli-Responsive Silk–Elastin-Like Protein Hydrogels for Tissue Regeneration

Supervisor: Wenwen Huang

Project introduction:
'Smart' stimuli-responsive materials, which are sensitive to environmental triggers or biological signals, are appealing platforms for the development of regenerative medicine. However, most smart materials are synthetic polymers that are not biocompatible and biodegradable, limiting their use in biomedical related field. Our previous studies suggested that silk-elastin-like proteins are biocompatible and can be rationally designed to response to multiple environmental stimuli such as temperature, pH, and certain biological signals. Moreover, we fabricated thermo-responsive shape-changing hydrogels with tunable mechanical properties using physical and enzymatical crosslinking methods. Therefore, in current study, we propose to use a synergistic approach that integrates genetic engineering, processing and tissue engineering to fabricate new thermo-responsive injectable hydrogels. By changing the crosslinking conditions, a new set of SELP hydrogels with tunable physicochemical properties will be generated for the encapsulation and controlled differentiation of MSC. We expect current study will (1) provide new insight into the design rules of thermo-responsive injectable biomaterials for the encapsulation and lineage-specific differentiation of stem cells, and (2) elucidate the role of biomaterial extracellular microenvironment in stem cell fate regulation.

【13】
Project title: Recombinant Protein Nanogels for Multimodality Cancer Therapy

Supervisor: Wenwen Huang

Project introduction:
Multimodality therapy is one of the most promising treatment options for tumors. There is an unmet need to develop new controlled delivery carriers to improve the efficacy of multimodality therapy. In current study, synthetic biology approach and multi-scale modeling will be used to de novo design new recombinant protein carriers. Thermo-responsive silk-elastin-like proteins (SELPs) with LCST in the range of 40-45 ºC will be encoded with cancer targeting peptide and photothermal agent binding peptide. Then, the functionalized SELPs will self-assemble into nanogels and be loaded

with photothermal agents, chemotherapeutics and immune checkpoint inhibitors. The drug release profiles will be optimized by adjusting the silk-to-elastin ratio, protein concentration and crosslinking density of SELPs. We expect these novel SELP nanogels will serve as multifunctional controlled delivery carriers that can promote the synergy of photothermal therapy, immunotherapy and chemotherapy.

【14】
Project title: Tunable design and optimization of protein-based artificial muscle

Supervisor: Wenwen Huang

Project introduction:
Artificial muscle is defined as a new class of stimuli-responsive materials or devices that can reversibly generate actuation in response to an external stimulus. In recent years, artificial muscles have shown great potential in the field of soft robotics, automated rehabilitation device, smart textile, and deep-sea exploration. Numerous studies have been focused on improving the design and fabrication methods of stimuli-responsive materials for artificial muscles with capabilities similar to, or even beyond, natural muscles. However, the rapid design and low-cost fabrication of artificial muscles remain extremely challenging. With the development of interdisciplinary approach that integrates synthetic biology, material chemistry, multi-scale simulation and mechanical engineering, recombinant proteins can be designed de novo and chemically modified to possess specific stimuli-responsive features. This combinatory approach provides a new path towards the next-generation artificial muscles. This proposed project, which is build upon our expertise in protein-based materials, aims to construct new stimuli-responsive proteins using bottom-up approach, following the sequence-structure-function relationships of natural proteins. In addition, this project aims to further tune the stimuli-responsive properties of recombinant protein hydrogels using a synergistic approach that integrates chemical modification and multi-scale simulation. Moreover, this project aims to optimize the topology of the actuation layers for the fabrication of artificial muscles that can perform pre-programed tasks. In summary, this project will provide new insights to establish efficient and low-carbon production methods for protein-based materials, improve the design and modification methods of stimuli-responsive materials, and expand the application of protein-based artificial muscle in the field of robotics.

【15】
Project title: Development of deep learning based algorithm for computational immunology

Supervisor: Wanlu Liu

Project introduction:
The human adaptive immune system is a branch of the immune system that is responsible for specific antigen recognition and clearance. Through interacting with specific antigens, the adaptive immune system is activated and can store long-term immunological memories for targeted antigens. Long-term immunological memory with high antigen-specificity can therefore generate a more robust response during subsequent exposure to the antigens (2). Adaptive immune response activation requires antigen recognition by receptors expressed on T or B cells, known as T cell receptors (TCRs) or B cell receptors (BCRs), respectively. T cells and the T-cell receptor (TCR) repertoire play pivotal roles in immune response and immunotherapy. TCR sequencing (TCR-Seq) technology has enabled accurate profiling TCR repertoire and currently a large number of TCR-Seq data are available in public. With the development of single cell immune profiling techniques, vast data were generated from single cell RNA-seq and TCR/BCR-seq. However, how to data mine those multi-model single cell immune profiling data is a challenging task. In this project, we will develop deep learning based computational algorithm to better understand adaptive immune response in autoimmune disease.

【16】
Project title: Mechanism of nuclear receptor COUP-TFII in colorectal carcinogenesis

Supervisor: Xin Xie

Project introduction:
Colorectal cancer (CRC), with high incidences of recurrence and metastasis, is one of the most common malignant tumors in China. Through bioinformatic analysis and transgenic animals, our preliminary data clearly indicated an involvement of nuclear receptor COUP-TFII in Wnt-induced colorectal carcinogenesis. Currently, we are utilizing 3D organoid and single cell sequencing to dissect the underlying mechanism by which COUP-TFII controls bowel cancer development.

【17】
Project title: Development of high throughput screening to identify cancer driver genes

Supervisor: Xin Xie

Project introduction:
Refined cancer models are critical to bridge cell line, animal research and human studies. Recently, stem cell-derived organoid, which contains tissue-specific cell types and self-organizes through spatially lineage differentiation, has opened new avenues for cancer study. Here, we plan to establish an organotypic colon cancer model using

human tissues to recapitulate in vivo colon cancer progression. This ex vivo culture system will be useful to screen genes that cooperate with APC mutation in driving colorectal cancer invasion.

【18】
Project title: Establishing proximity labelling system to decipher protein-protein interaction

Supervisor: Xin Xie

Project introduction:
Protein-protein interaction (PPI) is an important mechanism defining gene function. BioID, an unbiased proximity-dependent biotinylation technique, has become an important tool for mapping of PPIs under physiological and pathological conditions. COUP-TFII is an orphan nuclear receptor that plays key roles in development and diseases. Here, we plan to generate a proximal labeling system to define COUP-TFII interactomes that mediate COUP-TFII action.

【19】
Project title: 3D osteochondral culture to model osteoarthritis pathogenesis

Supervisor: Xin Xie

Project introduction:
Osteoarthritis (OA), an age-related musculoskeletal disorder, affects more than half of the global population over 65. The prevalence in conjunction with limited knowledge of OA pathogenesis highlight the need for better disease modeling. As such, we propose to establish a three-dimensional (3D) osteochondral microtissue to mimic the human osteochondral junction in vitro, which will be useful to dissect OA pathogenesis and to test potential OA drugs.

【20】
Project title: Deciphering molecular signaling in cell-cell fusion

Supervisor: Xin Xie

Project introduction:
Cell-cell fusion is an essential process for organ development and sexual reproduction. The fusion of singly nucleated myoblast into multinucleated myotubes is the best-studied model to examine the fusion events both in vitro and in vivo. Our previous data have demonstrated the central roles of nuclear receptor COUP-TFII in myoblast

fusion. We would like to employ in vitro models and genomic approaches to uncover molecular targets impacted by COUP-TFII and to identify new regulators controlling cell fusion.

【21】
Project title: Identifying new factors driving early-onset osteoarthritis

Supervisor: Xin Xie

Project introduction:
Osteoarthritis (OA), an age-related musculoskeletal disorder, affects more than half of the global population over 65. As such, we have applied whole-genome approach to sequence samples from human patients and identify genetic risk factors for early-onset osteoarthritis. Currently, we are investigating the function of those candidate genes.

【22】
Project title: Investigation of lung squamous cell carcinoma development using AI+ Multi-omics

Supervisor: Jian Liu

Project introduction:
Lung squamous cell carcinomas (LUSC s) comprise about 25–30% of all lung cancers, which are the leading cause of cancer-related death in China and worldwide. However, LUSC development mechanisms are poorly understood, preventing the development of targeted therapies of LUSCs. We have developed an advanced website to visualize the comprehensively molecular profiles of lung cancer and other types of cancer based on our current version of the website of CancerOmics3D (http://www.canceromics3d.net/), which was underdeveloped by my lab. Besides the integration of the results with the related published datasets, such as ChIP-Seq, ATAC-Seq, RNA-Seq, Methylation sequence, Single-cell Sequence, and so on, the advanced website will integrate more functional applications, such as machine learning in predicting chromatin loops and the gene signatures in clinical diagnosis and prognosis.

【23】
Project title: Uncovering the molecular mechanisms for m6A reader EEMR1 in regulating the pluripotent states of human embryonic stem cells

Supervisor: Di Chen

Project introduction:
m6A is the most abundant epigenetic modification in mRNAs. The m6A machinery has been discovered to play key roles in regulating human embryonic stem cells (hESCs). Disruption of the m6A writer machine leads to the impaired the differentiation capacity of hESCs. However, the mechanisms through which m6A regulates hESCs remain largely unknown. In this project, we aim to decode the epigenetic information stored in m6A by investigating the key m6A reader ESC essential m6A reader 1 (EEMR1) in hESCs. Our lab has identified EEMR1 as an essential gene regulating the pluripotent states in hESCs. Knockout of EEMR1 in primed hESCs leads to the up-regulation of naïve state genes as well as down-regulation of primed state genes, two fundamental states of pluripotency. This observation indicates that m6A may regulate the pluripotent states of hESCs directly. Given that EEMR1 is an m6A reader that binds to m6A modified mRNAs, the functional effects should be determined by not only the m6A reader itself, but also the protein complex which is recruited to the m6A modified mRNAs by m6A reader. Based on these, we plan to: 1. Capture the mRNAs bound by EEMR1 in naïve and primed hESCs. 2. Map the m6A modified mRNAs in naïve and primed hESCs. 3. Identify the interacting proteins of EEMR1 by TurboID. 4. Verify the key functions of EEMR1-interacting proteins by small-scale CRISPR/Cas9 screen. 5. Uncover the molecular function of EEMR1 in regulating hESCs through reading and translating epigenetic information coded in m6A.

【24】
Project title: Characterization of m6A profiles and potential regulatory functions during human germ cell development

Supervisor: Di Chen

Project introduction:
m6A represents the most abundant modification in mRNAs. m6A has been reported to play crucial roles in different biological processes. However, whether and how m6A modification is involved in human primordial germ cell development remains to be determined. The limited number of human primordial germ cells (hPGCs) both in vivo and in vitro renders the application of classical m6A-RIP-seq to characterize the m6A profiles in hPGC development. We have established an in vitro induction system to recapitulate the development of hPGC-like cells (hPGCLCs) from human embryonic stem cells (hESCs) via intermediate incipient mesoderm like cells (iMeLCs). In this project, we aim to apply our recent-developed technique REB-seq to characterize the m6A profiles in hESCs, iMeLCs, and hPGCLCs. REB-seq is designed to identify m6A-modified mRNAs using low number of cells, and potentially using single cell. Combining the analysis of bulk-RNA-seq, single cell-RNA-seq, ATAC-seq, ChIP-seq, and REB-seq in hESCs, iMeLCs, and hPGCLCs, we plan to uncover the potential regulatory functions of m6A modifications during hPGCLC development. Lab website: www.chenlab2019.com

【25】

Project title: The potential role of long non-coding RNAs during human germ cell development

Supervisor: Di Chen

Project introduction:

Germ cells are the only carriers of genetic and epigenetic information from parents to children. In order to study the development of human germ cells, we have established an in vitro induction system to recapitulate the specification and development of human primordial germ cells (hPGCs). In this system, human embryonic stem cells (hESCs) are induced into incipient mesoderm cells (iMeLCs) first, followed by 3D culture to induce hPGC-like cells (hPGCLCs). We have performed bulk-RNA-seq, single cell-RNA-seq, ATAC-seq, WGBS-seq, and ChIP-seq of H3K27ac. Based on these genomic resources, we have characterized the transcriptional regulation of germ cell fate specification. However, the analysis of long non-coding RNAs during hPGCLC development is still lacking. In this project, we aim to analyze the expression of long non-coding RNAs in hESC, iMeLCs, and hPGCLCs, and predict the possible critical long non-coding RNAs for germ cell development by genomic analysis using the above mentioned high-throughput sequencing data. We will verify the functions of long non-coding RNAs by CRISPR/Cas9-based knock out analysis. Collectively, we plan to uncover the potential roles of long non-coding RNAs during the development of human germ cells by genomics and bioinformatic analysis. Lab website: www.chenlab2019.com

【26】

Project title: Cross-species immuno-phenotyping reeals insights into bat immunity

Supervisor: Aaron Irving

Project introduction:

Across the mammal kingdom there is a large conservation of immune cell types and immune gene expression. However, some species-specific differences in gene expression confer slightly altered functional differences in the functional capacity of immune cells. Through cross-species comparisons of genomes, relative expression and functional validation, we will gather insight into what shapes the bat immune system and how this information may reveals clues to appropriate regulation of the human immune responses to dangerous virus infections.

【27】

Project title: Investigating the role of p21 positive senescent cells in muscle aging and sarcopenia

Supervisor: Junfeng Ji

Project introduction:
Mounting studies have recently demonstrated that senescent cells play a very important role in a variety of age-associated diseases. Elimination of p16 positive senescent cells alleviates various age-associated diseases in mice. However, due to the heterogeneity of senescent cells, the role of p21 positive senescent cells in muscle aging and sarcopenia remains unknown. Our preliminary results showed that expression of p21 is upregulated in the aged mouse and human muscle tissue. This project aims to use mouse genetics and multiomics approach to unravel the mechanisms by which p21 positive senescent cells contribute to muscle aging and sarcopenia. This study will provide important insight into understanding the onset and progression of sarcopenia and developing therapeutic interventions.

【28】
Project title: Neuron circuits that control feeding behavior and energy balance

Supervisor: Weiwei Qiu

Project introduction:
Obesity as an epidemic is increasingly threatening our lives. Yet, there's a lack of understanding of how energy balance is controlled. The brain precisely controls energy intake (e.g. food intake), however, how the brain senses and integrates gut information and further controls food intake is largely unknown. In this project, we will functionally investigate hindbrain neurons that regulate food intake and how they potentially communicate with gut information in the control of food intake and in response to various physiological conditions. Taking advantage of the transgenic mouse models, the project will lead to understanding mechanistic insights of brainstem neurocircuitries that control feeding behavior, which would help elucidate obesity and benefit pharmaceutics strategies to deal with obesity in the future. Previous results are published as first authors in Cell Metabolism, Nature Metabolism etc. For more information please contact weiweiqiu@intl.zju.edu.cn and https://person.zju.edu.cn/en/QiuWeiLab

【29】
Project title: Biomedical application of natural microalgae-based multifunctional delivery system

Supervisor: Min Zhou

Project introduction:
Recently, our team explored the biomedical application of microalgae drug delivery system and investigated their functions, such as oxygenation, photodynamic effect, fluorescent characteristic, and drug loading capacity. And we primarily identified the great potential of microalgae in oral drug delivery. On this basis, we aim to evaluate the oral delivery functions of different kinds of microalgae and extend their application to more diseases. We hope to establish a series of effective oral drug delivery systems based on the understanding of the microalgae's inherent properties and the therapeutic targets for diseases.

【30】
Project title: Translational study of biomedical material based on microalgae

Supervisor: Min Zhou

Project introduction: Microalgae are a class of single-celled photosynthetic organisms with many varieties and abundant nutrients, which are important biological resources for food, bioenergy, and health care. Many microalgae and extracts have great potential in biomedical applications. Compared with synthetic biomedical materials, microalgae have advantages in renewability, production cost, biocompatibility, and functional diversity. Therefore, we hope to further evaluate the therapeutic effects and explore the mechanisms of microalgae-based material or derivatives. After that, we would carry out translational research on effective candidates and expect to get preparations/products with biomedical value.

【31】
Project title: Ga-based antibacterial agents for pneumonia treatment

Supervisor: Min Zhou

Project introduction: Recently, the abuse of antibiotics made bacteria acquire a significantly increasing drug resistance due to genetic mutation. Meanwhile, the development of new antibiotics is becoming increasingly difficult. Thus, there is a great demand for new antimicrobial agents and new antimicrobial routes. Among noble antibacterial agents, gallium ion can substitute the iron ion in target molecules just like 'Trojan horse'. It will further disturb the function of ferritin and thus affect the metabolism of bacteria. Our ongoing project has proved in vitro the antibacterial properties of Ga-based agents. This project aims to study whether these agents can show ideal effects in the treatment of pneumonia caused by drug-resistant Gram-negative bacteria. We will establish a mice pneumonia model and evaluate the treatment effect by bacterial clearance analysis and histomorphology analysis.

【32】
Project title: Wound microenvironment-responsive agents for diabetic wound healing

Supervisor: Min Zhou

Project introduction: Chronic wounds are one of the major complications associated with diabetes, which represent a huge burden for both affected individuals and the entire healthcare system. Diabetic patients have declined the ability to metabolize glucose resulting in hyperglycemic conditions which further prolong the wound healing process. Glucose oxidase (GOX) is an endogenous oxidoreductase that can specially catalyze glucose oxidation into gluconic acid and hydrogen peroxide with the assistance of oxygen. GOX is expected to reduce local glucose concentration in diabetic wounds through catalytic reactions and improve the therapeutic effect of antibiotics. Previously, we have designed GOX and AZM dual-functionalized hollow mesoporous silica nanoparticles that possess antibacterial effects and local glucose reduction simultaneously to facilitate bacteria-infected diabetic wound healing. In this project, we will structure more GOX-based nanoparticles for diabetic wound healing. We will combine Glucose oxidase with gas therapy or other catalysts to enhance the treatment effect. Particular antibacterial efficiency will be assessed in the diabetic wound healing model.

【33】
Project title: Computational analysis for dynamical progression of lung cancer

Supervisor: Zhaoyuan Fang

Project introduction:
This is a pure bioinformatics project. If you have wet experiment background, you may also apply for it, since we also need to do some cell culture experiments.

【34】
Project title: Lung cancer cell transdifferentiation using small molecules or drugs

Supervisor: Zhaoyuan Fang

【35】
Project title: The role of histone H3K36 methylation in mammary gland development and breast cancer

Supervisor: Chaochen Wang

Project introduction:
H3K36 methylation plays an important role in epigenetic regulation. In mammalian cells, H3K36 methylation is catalized by specific histone methyltransferases, including SETD1, NSD2 and NSD3. However, the roles of H3K36 methylation and individual methyltransferases in mammary gland development and breast cancer are not elucidated. This project aim for answering this question by leveraging genetically enigeered mouse models and multi-omics methods.

【36】
Project title: The role of histone H3K4 in mammary stem cell fate transition and breast cancer.

Supervisor: Chaochen Wang

Project introduction:
It has been well documented that H3K4 methylation controls gene transcription and is further invovled in cell fate determination. In addtion, mutations in the methyltransferases catalyzing H3K4 methylation are found in different types of cancers in patients. However, the role of H3K4 methylation in mammary stem cell fate determination and that in breast cancer initiation is not clear. In this project, we aim for dissecting the function of H3K4 methylation by leveraging orgnoid culture, genetic mouse models and multi-omics methods, such as single-cell transcriptomics, epigenomics and metabolomics.

【37】
Project title: The role of downstream of Calcium signaling in cell membrane repair

Supervisor: Suhong Xu

Project introduction:
The plasma membrane is a fundamental component for cell survival, as it shields against various forms of damage caused by mechanical injuries, viral invasions, bacterial infections, and immune T-cell killing of cancer cells. Interestingly, even during normal physiological events like muscle contraction and locomotion, the membrane is subject to sublytic damage, which has been found to be beneficial by activating paracrine signaling to shape the surrounding tissue environment. However, the exact molecular mechanism behind this phenomenon remains elusive. We previously found that wounding triggers immediate Calcium response, which coordinates and activates many repair machinery to facilitate membrane repair (Xu and Chisholm, Current Biology 2011, Meng et al., Dev Cell 2020, Wang et al., Dev Cell 2022). Building on this knowledge, we have discovered new Calcium targets that play crucial roles in membrane damage response and repair. Our latest project aims to uncover the intricate functions of these proteins in the membrane repair process and to further

explore the molecular mechanisms behind their response to wounding. Join us in this exciting journey of uncovering the secrets of the plasma membrane and its remarkable ability to heal itself!

【38】
Project title: The molecular mechanism of rapid RNA transcription after membrane damage

Supervisor: Suhong Xu

Project introduction:
The essence of molecular biology lies in the decoding of genetic information from DNA to RNA to protein, also known as the central dogma. However, when cells face wounds, a transcriptional-dependent response is required for the essential task of membrane repair. The exciting part is that we're still in the dark about how DNA responds to such injuries and how it initiates transcription. But wait, there's good news! Our team has devised a signal amplifier method that combines the MS2 and Suntag system. This cutting-edge technique lets us image endogenous RNA (Hu et al., eLife 2023), enabling us to observe the rapid transcription of RNA after membrane damage under confocal microscopy. This breakthrough has already led us to identify a significant number of transcribed genes (Fu et al., Nature Communications 2020; Meng et al., Dev Cell 2020), and with the RNA imaging technique, we can now explore the molecular mechanisms of RNA transcription and translocation. These critical steps are key to decoding the central dogma, and our project aims to identify the crucial regulators of immediate RNA transcription and translocation.So, come along on this scientific adventure with us as we delve into the unknown and uncover the secrets behind one of the most essential biological processes in nature. Together, we'll shine a light on the mysteries of DNA transcription and pave the way for groundbreaking scientific discoveries!

【39】
Project title: Adaptive evolution of bat antiviral ISGs

Supervisor: Aaron Irving

Project introduction:
There is an ongoing interest into the evolution of genes involved in antiviral immunity. Using a mix of wetlab and dry lab techniques we will interrogate newly synthesized bat genomes and evaluate if any known antiviral genes or other immuno-regulatory genes have undergone specici evolution in different branches of the bat phylogenetic trees. This will be coupled to experimental validation of altered immune function, antiviral efficacy and novel immuno-regulatory functions.

【40】
Project title: Multi-omic single-cell analysis of the pathological mechanisms and therapeutic targets of tendinopathies

Supervisor: Xiao Chen

Project introduction:
Tendinopathy is one of the most common degenerative soft tissue diseases. Specific molecular markers and pathological mechanisms of tendinopathy are poorly understood, severely hampering our diagnosis and treatment of tendinopathy. Our previous study has shown the critical role of macrophages and tenocytes in promoting the progression of tendinopathy. In this project, we will combine single-cell transcriptomic, epigenomic and spatial technologies with transgenic mice and tendon injury models to further investigate the critical cell subsets and their microenvironmental cues that regulate tendinopathy and to identify feasible therapeutic targets to advance precision treatment of tendinopathies.

【41】
Project title: Epidemiology of Neisseria gonorrhoeae antibiotic resistance and development of alternative therapies

Supervisor: Stijn van der Veen

Project introduction:
Neisseria gonorrhoeae is a multidrug-resistant bacterial pathogen for which ceftriaxone is currently the only remaining recommended first-line therapy. However, over the past decade, ceftriaxone susceptibility has gradual declined and in recent years the high-level ceftriaxone-resistant FC428 clone has emerged and disseminated globally. This gonococcal clone is now highly abundant in China, complicating ceftriaxone-based therapies. Therefore, development of alternative antimicrobial treatment options is essential to ensure effective treatment remains available. In this project, several strategies will be employed to identify and test alternative antigonococcal compounds, including (1) screening alternative clinically approved antibiotics that have never been used for treatment of *N. gonorrhoeae*; (2) screening or repurposing of clinically approved non-antimicrobial compounds; and (3) identification of novel antimicrobial compounds derived from natural products or traditional Chinese medicines. These compounds will be identified through screening of compound libraries and extracts of natural products. Specific compounds will be tested through a variety of methods for antimicrobial activity in vitro and in vivo in a mouse infection model. Finally, the specific molecular targets of these compounds will be identified, which will allow for further compound optimization.

【42】
Project title: Interactions between *Neisseria gonorrhoeae* and autophagy during

epithelial cell invasion and transcytosis

Supervisor: Stijn van der Veen

Project introduction:
Neisseria gonorrhoeae is an obligate human bacterial pathogen that predominantly infects the mucosal epithelium of the human urogenital tract. Infection of the mucosal epithelia results in invasion of epithelial cells and subsequent trafficking into subepithelial tissues. Intracellular bacteria are targeted by autophagy, which is an intracellular maintenance mechanism that recycles or degrades macromolecules and damaged organelles through a process involving the formation of double-membrane phagophores that engulf the target substrate and subsequently fuse with lysosomes for degradation. Our previous research has shown that intracellular *N. gonorrhoeae* is also targeted by autophagy, but a subpopulation is able to escape autophagy-mediated killing, resulting in survival and subsequent exocytosis of epithelial cells. In this project, the detailed mechanisms involved in *N. gonorrhoeae*-autophagy interactions in epithelial cells will be characterized.

【43】
Project title: Identification and testing of antigens for development of *Neisseria gonorrhoeae* vaccines and immunotherapeutics

Supervisor: Stijn van der Veen

Project introduction:
Neisseria gonorrhoeae has developed resistance against all previously and currently used antimicrobial therapies. Immune-based therapies, either in the form of vaccines or antibodies, are commonly recognized as a major attribute to our future ability to prevent and control this infectious disease. While therapeutic antibodies provide a direct effective way to selectively target bacteria for killing by complement activity or opsonophagocytosis, vaccines are generally considered the most efficient way to provide long-term protection against an infection. However, vaccine development against *N. gonorrhoeae* is complicated due to the lack of clear correlates of protection and the high rates of phase and antigenic variation, with the result that there is currently no gonococcal vaccine available or even in clinical trials. Our research recently identified MtrE and its largest surface loop (Loop2) as the most highly conserved gonococcal surface antigens. In this project, MtrE and the Loop2 peptide will be optimized as vaccine antigens based on different peptide display or modification strategies and adjuvant selection. Furthermore, the Loop2 peptide will used to develop monoclonal antibodies.

【44】
Project title: Impact of *Neisseria gonorrhoeae* outer membrane vesicles (OMVs) on

intracellular survival and exocytosis of epithelial cells

Supervisor: Stijn van der Veen

Project introduction:
Release of outer membrane vesicles (OMVs) is a highly conserved process that occurs naturally in all living stages of Gram-negative bacteria. Increasing evidence indicates that bacterial pathogenic species generally release more OMVs that are rich in virulence factors than their non-pathogenic counterparts. The bacterial pathogen *Neisseria gonorrhoeae* also secretes OMVs. It has previously been shown that *N. gonorrhoeae* OMVs induce NF-κB immune responses in a NOD1 dependent manner and for macrophages it has been shown that *N. gonorrhoeae* OMVs induced apoptosis in a PorB-dependent manner. In this study, the impact of gonococcal OMV secretion on epithelial cell invasion, intracellular survival and exocytosis will be investigated and the mechanistic details involved will be determined.

【45】
Project title: Spatial Transcriptome Analysis of human lung squamous cell carcinoma to Reveal the Mechanism of Its Development

Supervisor: Jian Liu

Project introduction:
Lung cancer is the leading cause of cancer death worldwide, and lung squamous cell carcinoma (LUSC) accounts for approximately 30% of lung cancer patients. So far, no molecularly targeted therapy has been developed to treat LUSC. Therefore, investigation of the mechanisms of LUSC development will promote the development of personalized treatment of LUSC. Here, we aim to conduct the spatial transcriptome analysis of human lung squamous cell carcinoma samples with different mutations or clinical treatment. And then, we will integrate the results with the related published datasets, such as ChIP-Seq, ATAC-Seq, RNA-Seq, Methylation sequence, HiC, and so on, to provide a comprehensive analysis of the molecular profile of human LUSC. The results will be further integrated into the website of LungCancer3D (http://canceromics3d.net/), which is underdeveloped by my lab. Furthermore, the in vitro and in vivo functional analysis, including cell culture, genetic mouse models, and PDX models, will be conducted to dissect the LUSC developing mechanisms. And the related drugs will be applied to the models to identify the druggable targets for LUSC. In summary, by taking advantage of the integration of multiple LUSC molecular profiles, followed by the functional investigations, our findings will promote molecularly targeted therapy of LUSC.

【46】
Project title: 3D Genome Analysis of human lung squamous cell carcinoma to Reveal the Mechanism of Its Development

Supervisor: Jian Liu

Project introduction:
Lung cancer is the leading cause of cancer death worldwide, and lung squamous cell carcinoma (LUSC) accounts for approximately 30% of lung cancer patients. So far, no molecularly targeted therapy has been developed to treat LUSC. Therefore, investigation of the mechanisms of LUSC development will promote the development of personalized treatment of LUSC. Here, we aim to conduct the HiC (a high‐throughput chromosome conformation capture technique) analysis of human lung squamous cell carcinoma cells or samples to reveal the profiles of chromosome architectures. And then, we will integrate the results with the related published datasets, such as ChIP-Seq, ATAC-Seq, RNA-Seq, Methylation sequence, Single-cell Sequence, and so on, to provide a comprehensive analysis of the molecular profile of human LUSC. The results will be further integrated into the website of LungCancer3D (http://canceromics3d.net/), which is underdeveloped by my lab. Furthermore, the in vitro and in vivo functional analysis, including cell culture, genetic mouse models, and PDX models, will be conducted to dissect the LUSC developing mechanisms. And the related drugs will be applied to the models to identify the druggable targets for LUSC. In summary, by taking advantage of the integration of multiple LUSC molecular profiles, followed by the functional investigations, our findings will promote molecularly targeted therapy of LUSC.

【47】
Project title: Screen the FDA-approved Cancer Drugs to Specifically Target Human Lung Squamous Cell Carcinoma

Supervisor: Jian Liu

Project introduction:
Lung cancer is the leading cause of cancer death worldwide, and lung squamous cell carcinoma (LUSC) accounts for approximately 30% of lung cancer patients. So far, no molecularly targeted therapy has been developed to treat LUSC. Therefore, investigation of the mechanisms of LUSC development will promote the development of personalized treatment of LUSC. Here, we aim to analyze 388 FDA-approved cancer drugs to specifically target human lung squamous cell carcinoma with or without combinational chemotherapy or immunotherapy in LUSC cells and mouse models. The effective drugs in killing LUSC cells will be examined how it inhibits LUSC development. Moreover, the mechanistic findings will be further validated in human LUSC samples. The promising strategies in targeting LUSC will be applied in clinical trials following the ethics and agreements of LUSC patients. In summary, this project aims to discover the application of old drugs in treating LUSC patients.

【48】

Project title: Develop a Web-based Application Supported by Comprehensive Database and Advanced Computational Method for Lung Cancer Diagnosis and Prediction

Supervisor: Jian Liu

Project introduction:

Lung cancer is the leading cause of cancer-related deaths globally. Understanding the mechanisms underlying the development of lung cancer is critical to developing personalized treatments for this disease. Our goal is to create a web-based application for lung cancer diagnosis and prediction. This application will be the enhanced version of LungCancer3D website (https://www.lungcancer3D.org/ or http://118.195.129.119/lungcancer3d/), which is under developed by my lab. This web tool will be supported by our comprehensive database of lung cancer and advanced machine learning method developed by our lab. It will perform diagnosis and make prediction of lung cancer based on multi-omics data submitted by users. The strategies include genes, genomic regions, pathway, and gene regulatory network. In summary, this web-based application has the potential to significantly impact clinical diagnosis and the development of molecularly targeted therapies for lung squamous cell carcinoma (LUSC).

【49】

Project title: Construct a Comprehensive Database of the Risk Factors associated with Lung Cancer by Data Mining

Supervisor: Jian Liu

Project introduction:

Lung cancer is the leading cause of cancer death worldwide. Understanding the mechanisms underlying the development of lung cancer is critical to developing personalized treatments for this disease. Our goal is to onstruct a comprehensive database of the risk factors associated with lung cancer. This database will be a major component of the website of LungCancer3D (https://www.lungcancer3D.org/ or http://118.195.129.119/lungcancer3d/), which is under developed by my lab. In addition to manually collecting and curating publicly available multi-omics datasets related to lung cancer, such as ChIP-Seq, ATAC-Seq, RNA-Seq, mutation, single-cell sequence, we will also integrate unpublished data generated from my lab, which includes mouse model, cell culture, organoid, and clinical data. By utilizing advanced data mining techniques, we aim to identify risk factors associated with lung cancer, which include genes, genomic regions, pathways, and gene regulatory networks. Our findings have the potential to significantly impact clinical diagnosis and the development of molecularly targeted therapies for lung squamous cell carcinoma (LUSC).

【50】
Project title: Develop an Advanced Computational Method with AI to Integrate Multi-Omics Data of Lung cancer

Supervisor: Jian Liu

Project introduction:
Lung cancer is the leading cause of cancer-related deaths globally. Understanding the mechanisms underlying the development of lung cancer is critical to developing personalized treatments for this disease. Our goal is to develop a novel method to integrate multi-omics data and identify the molecular profile of lung cancer. The outcome produced by this integrate method will be presented in the website of LungCancer3D (https://www.lungcancer3D.org/ or http://118.195.129.119/lungcancer3d/), which is under developed by my lab. This advanced computational method will be built upon artificial intelligence, machine learning, and neural networks. The integration strategies include genes, genomic regions, pathway, and gene regulatory network. Furthermore, the comprehensive multi-omics database of lung cancer developed by our lab will be utilized to develop, validate, and refine the method. In summary, this advanced integration method has the potential to significantly impact clinical diagnosis and the development of molecularly targeted therapies for lung squamous cell carcinoma (LUSC).

【51】
Project title: Application of Base Editing in Identification of Driver Mutations of Lung Squamous Cell Carcinoma

Supervisor: Jian Liu

Project introduction:
Lung cancer is the leading cause of cancer death worldwide, and lung squamous cell carcinoma (LUSC) accounts for approximately 30% of lung cancer patients. So far, no molecularly targeted therapy has been developed to treat LUSC. Therefore, investigation of the mechanisms of LUSC development will promote the development of personalized treatment of LUSC. Here, we aim to conduct base editing in LUSC cells to investigate the oncogenic roles of these genetic mutations identified in human LUSC. And then we will generate the genetic mouse models to examine if the mutations validated in vitro could drive LUSC development and to reveal the related mechanisms, followed by the drug treatments targeting on these mechanistical molecules. In summary, the identified driver mutations of LUSC will aid in developing molecularly targeted therapy for LUSC.

【52】
Project title: Single-cell Sequence of Mouse lung squamous cell carcinoma to Reveal

the Mechanism of Its Development

Supervisor: Jian Liu

Project introduction:
Lung cancer is the leading cause of cancer death worldwide, and lung squamous cell carcinoma (LUSC) accounts for approximately 30% of lung cancer patients. So far, no molecularly targeted therapy has been developed to treat LUSC. Therefore, investigation of the mechanisms of LUSC development will promote the development of personalized treatment of LUSC. Here, we aim to conduct a single-cell sequence of mouse LUSC driven by Lkb1 loss in mouse lung epithelial cells and the pre-stage of LUSC. This will characterize the developing path of mouse LUSC from different types of lung epithelial cells. We will further integrate these data with our mouse LUSC datasets, including ChIP-Seq, ATAC-Seq, RNA-Seq, HiC, and so on. And then compare with the related human LUSC molecular profiles using our website of LungCancer3D (http://canceromics3d.net/), which is underdeveloped by my lab. Furthermore, the in vitro and in vivo functional analysis, including cell culture, genetic mouse models, and PDX models, will be conducted to dissect the LUSC developing mechanisms. And the related drugs will be applied to the models to identify the druggable targets for LUSC. In summary, by taking advantage of the integration of multiple LUSC molecular profiles, followed by the functional investigations, our findings will promote molecularly targeted therapy of LUSC.

【53】
Project title: Multi-omics Investigation on the Roles of Dysregulated Microenvironment in Pre-tumor and Tumor Stage during Cancer Development

Supervisor: Jian Liu

Project introduction:
(General background)Cancer is a heterogeneous disease, meaning it varies from person to person in terms of its genetic and molecular characteristics. By analyzing multiple omics data, including genomics, transcriptomics, proteomics, metabolomics, and epigenomics, we can obtain a comprehensive profile of the dysregulated microenvironment in an individual's tumor. This information can help in tailoring treatment plans based on the unique characteristics of the tumor and the surrounding microenvironment. Personalized medicine allows for more targeted therapies, resulting in improved treatment outcomes and reduced side effects.(Aims)Understanding tumor-host interactions: Tumors do not develop in isolation but interact closely with their surrounding microenvironment, including immune cells, stromal cells, blood vessels, and extracellular matrix components. Dysregulation of these interactions can promote tumor growth, invasion, and metastasis. Multi-omics approaches enable us to dissect the intricate molecular networks and signaling pathways involved in tumor-host interactions. By studying

these interactions, we can identify key players and targets that can be exploited for therapeutic purposes.(Key Methods)Genetically engineered mouse models mimicing lung cancer, organoid culture, cell sorting, and CRSIPR/Cas9 mediated gene editing(https://person.zju.edu.cn/en/jian_liu) + multi-omics analyses (http://canceromics3d.net/)

【54】
Project title: Identification of biomarkers and molecular signatures associated with treatment response and prognosis by integrating multi-omics data with clinical outcomes

Supervisor: Jian Liu

Project introduction:
(General background) Cancer is a heterogeneous disease, meaning it varies from person to person in terms of its genetic and molecular characteristics. By analyzing multiple omics data, including genomics, transcriptomics, proteomics, metabolomics, and epigenomics, we can obtain a comprehensive profile of the dysregulated microenvironment in an individual's tumor. This information can help in tailoring treatment plans based on the unique characteristics of the tumor and the surrounding microenvironment. Personalized medicine allows for more targeted therapies, resulting in improved treatment outcomes and reduced side effects.(Aims)Predicting treatment response and prognosis: By integrating multi-omics data with clinical outcomes, we can identify biomarkers and molecular signatures associated with treatment response and prognosis. Understanding the molecular features of the dysregulated microenvironment can help predict how a tumor will respond to specific therapies, allowing for more informed treatment decisions. Additionally, these molecular signatures can serve as prognostic indicators, aiding in patient risk stratification and personalized follow-up care.(Key Methods)Genetically engineered mouse models mimicing lung cancer, and CRSIPR/Cas9 mediated gene editing(https://person.zju.edu.cn/en/jian_liu) + multi-omics analyses (http://canceromics3d.net/)+ AI caculation

【55】
Project title: Multi-omics Investigation on the mechanisms of immune escape in Pre-tumor and Tumor Stage during Cancer Development

Supervisor: Jian Liu

Project introduction:
The immune system plays a vital role in recognizing and eliminating cancer cells. However, cancer cells can evade immune surveillance by developing various mechanisms of immune escape. Studying these mechanisms at both the pre-tumor and tumor stages can provide insights into how cancer cells evade immune detection

and destruction. By understanding the molecular and cellular changes associated with immune escape, we can develop strategies to enhance immune surveillance and improve the body's ability to recognize and eliminate cancer cells.(Key Methods)Genetically engineered mouse models mimicing lung cancer, organoid culture, cell sorting, and CRSIPR/Cas9 mediated gene editing(https://person.zju.edu.cn/en/jian_liu) + multi-omics analyses (http://canceromics3d.net/)

【56】
Project title: Improving immunotherapies by Studying the mechanisms of immune escape in pre-tumor and tumor stages using multi-omics

Supervisor: Jian Liu

Project introduction:
Immunotherapies, such as immune checkpoint inhibitors and adoptive T cell therapies, have revolutionized cancer treatment by harnessing the power of the immune system to target tumors. However, not all patients respond to these therapies, and some may develop resistance over time. By studying the mechanisms of immune escape using multi-omics approaches, we can identify key molecular pathways and alterations that contribute to treatment resistance. This knowledge can guide the development of novel immunotherapies or combination therapies that overcome immune escape mechanisms and improve treatment outcomes.(Key Methods)Genetically engineered mouse models mimicing lung cancer, organoid culture, cell sorting, and CRSIPR/Cas9 mediated gene editing(https://person.zju.edu.cn/en/jian_liu) + multi-omics analyses (http://canceromics3d.net/)

【57】
Project title: Investigation of the roles of the dysregulated immune cells in Pre-tumor and Tumor Stage during Cancer Development using multi-omics

Supervisor: Jian Liu

Project introduction:
The immune system plays a critical role in recognizing and eliminating cancer cells. However, in the tumor microenvironment, immune cells can become dysregulated and lose their anti-tumor functions. By studying the dysregulated immune cells at both pre-tumor and tumor stages using multi-omics approaches, we can identify the specific molecular and cellular changes that lead to immune dysfunction. This understanding is crucial for developing strategies to restore and enhance the anti-tumor activity of immune cells.(Key Methods)Genetically engineered mouse models mimicing lung cancer, organoid culture, cell sorting, and CRSIPR/Cas9 mediated gene editing(https://person.zju.edu.cn/en/jian_liu) + multi-omics analyses (http://canceromics3d.net/)

【58】
Project title: non-invasive species profiling of local bat populations

Supervisor: Aaron Irving

Project introduction:
Using methods that do not require handling bats, to profile the local bat diversity. Combining both molecular techniques and audio/visual methods.

【59】
Project title: Innate immune induction profiling in bat vs human cells

Supervisor: Aaron Irving

Project introduction:
Innate immune induction profiling in bat vs human cells (Cross-comparison of IFN and NFkB induction kinetics in bat vs human cells. Including profiling subtle differences between IFN subtypes).

【60】
Project title: Cell signal transduction guided intelligent mixed-molecule structure research

Supervisor: Ying CHI & Yuehai KE

Project introduction:
Cell signaling is the material basis for life information transmission, and post-translational modifications (PTMs) of signaling proteins is the biochemical basis for information transmission. In the process of signal transduction, reversible phosphorylation, that is, phosphorylation and dephosphorylation, plays an important role in corresponding to the specific changes and restoration of molecular structure and function. SHP2 is an important protein tyrosine phosphatase that plays a pivotal role in multiple intracellular oncogenic signals. In the past two years, AI has achieved remarkable results in the fields of protein structure prediction and protein de novo design. However, because the intermolecular interactions in the signal transduction process are complex, simultaneous interactions between large and small molecules

and proteins need to be considered, and special PTMs covalent bonds of specific motifs need to be achieved. Current AI technology cannot yet overcome these difficulties, and thus is unable to enter this area. This project aims to move forward in the direction of meeting the needs of cell signal transduction research. Innovative algorithms accomplished after overcoming above difficulties, will also be applied to a wide range of other similar application scenarios.

【61】

Project title: Cell signal transduction guided GPT(Generative Pre-trained Transformer) model

Supervisor: Ying CHI & Yuehai KE

Project introduction:

The GPT models that just appeared a year ago have begun to enter the field of biomedical science. However, due to the complexity of intermolecular interactions in the signal transduction process, GPT models have not yet been able to enter this area. We have introduced the important roles of cell signaling and signaling protein molecules such as SHP2 in human healthcare in the previous project introduction. In this project, we will design, develop, and deploy novel GPT model, which fuses various multi-modality big data, like molecular structure prediction & design, function verification, sequence analysis, and natural language processing, etc. The target is to accurately and efficiently predict potential sites of phosphorylation/dephosphorylation like PTMs in important protein structures, potential substrates of SHP2 like key signaling proteins, and the interactions between proteins and other molecules after modification, with particular attention to allosteric effects and structural domains. The enhancement of this GPT model will continue to move forward in the direction of ultimately meeting all needs from cell signal transduction research. Innovative algorithms after overcoming difficulties will also be applied to a wide range of other similar application scenarios.

【62】

Project title: Roles of Hippo and Ras pathways in driving tumorigenesis in the digestive system.

Supervisor: Alessandro Bonfini

Project introduction:

Cancer is the second leading cause of death worldwide, with 1 in 6 deaths attributed to this disease. A critical component of tumorigenesis and carcinogenesis is

dysregulation of the molecular and genetic systems controlling proliferation. The Ras pathway is normally used by organisms to promote proliferation. In Humans, mutations in components of Ras pathway are present in ~19% of all tumours. Hippo pathway is another pathway with important and conserved roles in the regulation of tissue growth. Dysregulations of this pathway are also associated with increased tumorigenesis and carcinogenesis. Concurrent dysregulation of Ras and Hippo pathways has a synergistic effect on tumorigenesis and carcinogenesis. Understanding how these pathways interacts with each other to promote cancer is vital to pave the way for possible therapeutical intervention. Here, we use the model organism Drosophila melanogaster, a.k.a. fruit fly, to study how these pathways interact with each other in the digestive system to drive proliferation and tumorigenesis. Fruit flies have been extensively used to establish models of tumorigenesis and carcinogenesis. Fruit flies are a good model organism for a variety of reasons (70% of genes involved in human diseases are conserved in flies, flies are relatively inexpensive, with a quick generation time and short lifespan). This led to the development of a massive number of tools in fruit flies for the study of many types of diseases, which allow researchers to perform genetic alterations (Gene Knock down with RNA interference or CRISPR, gene Overexpression, etc.) in a tissue and cell specific manner, while also allowing for temporal control through changes in temperature and presence/absence of hormones. For this project, the student will utilize functional genetics, microscopy, molecular biology, and OMICS approaches to study the interaction between Hippo and Ras pathways in driving tumorigenesis and carcinogenesis in the digestive system of fruit flies.

【63】

Project title: Roles of Ras pathway and junctional proteins in driving tumorigenesis in the digestive system.

Supervisor: Alessandro Bonfini

Project introduction:

Cancer is the second leading cause of death worldwide, with 1 in 6 deaths attributed to this disease. A critical component of tumorigenesis and carcinogenesis is dysregulation of the molecular and genetic systems controlling proliferation. The Ras pathway is normally used by organisms to promote proliferation. In Humans, mutations in components of Ras pathway are present in ~19% of all tumours. Junctional proteins are an essential component of organismal biology, with roles ranging from organization of tissues and organs' structure and regulation of signalling pathways. It is not a surprise considering their important role that dysregulation of these proteins can also lead to the development of tumours and cancers, in a conserved manner between organisms. Concurrent dysregulation of Ras and junctional proteins has a synergistic effect on tumorigenesis and carcinogenesis.

Understanding how these pathways and proteins interact with each other to promote cancer is vital to pave the way for possible therapeutical intervention. Here, we use the model organism Drosophila melanogaster, a.k.a. fruit fly, to study how these pathways interact with each other in the digestive system to drive proliferation and tumorigenesis. Fruit flies have been extensively used to establish models of tumorigenesis and carcinogenesis. Fruit flies are a good model organism for a variety of reasons (70% of genes involved in human diseases are conserved in flies, flies are relatively inexpensive, with a quick generation time and short lifespan). This led to the development of a massive number of tools in fruit flies for the study of many types of diseases, which allow researchers to perform genetic alterations (Gene Knock down with RNA interference or CRISPR, gene Overexpression, etc.) in a tissue and cell specific manner, while also allowing for temporal control through changes in temperature and presence/absence of hormones. For this project, the student will utilize functional genetics, microscopy, molecular biology, and OMICS approaches to study the interaction between the Ras pathway and alteration of junctional proteins in driving tumorigenesis and carcinogenesis in the digestive system of fruit flies.

【64】
Project title: Dietary regulation of tumours and cancers.

Supervisor: Alessandro Bonfini

Project introduction:
Nutrition is a principal determinant of organismal health and disease. Together with undernutrition and overnutrition, imbalanced diets affect the progression of many diseases. Cancer is the second leading cause of death worldwide, with 1 in 6 deaths attributed to this disease. Diet also influences both tumorigenesis and carcinogenesis. For example, Malnutrition can lead to the development of metabolic diseases such as Diabetes and obesity, which are both critical risk factors for cancer. Here, we use the model organism Drosophila melanogaster, a.k.a. fruit fly, to study how diets influence different tumour models, and the molecular and genetic mechanism behind this regulation. Fruit flies have been extensively used to establish models of tumorigenesis and carcinogenesis. Fruit flies are a good model organism for a variety of reasons (70% of genes involved in human diseases are conserved in flies, flies are relatively inexpensive, with a quick generation time and short lifespan). This led to the development of a massive number of tools in fruit flies for the study of many types of diseases, which allow researchers to perform genetic alterations (Gene Knock down with RNA interference or CRISPR, gene Overexpression, etc.) in a tissue and cell specific manner, while also allowing for temporal control through changes in temperature and presence/absence of hormones. For this project, the student will utilize dietary manipulations, functional genetics, microscopy, molecular biology, and OMICS approaches to study the interaction between nutrition and tumorigenesis and

carcinogenesis in across multiple tumour models in fruit flies.

【65】
Project title: The pathway(s) of our choices

Supervisor: Angelica Foggetti

Project introduction:
Decision making is an important brain function which determines our capability to opt for safer and more productive solutions. Despite a considerable attention of the neuroscientific community, little is still known about specific circuits and populations of neurons involved. Our lab aims to unravel the interconnected cognitive processes critical in decision-making, with a special focus on modulatory inputs.

【66】
Project title: Perineuronal net exclusivity

Supervisor: Angelica Foggetti

Project introduction:
Only certain types of neurons are wrapped by what is called a perineuronal net, an extracellular matrix (ECM) containing chondroitin sulfate proteoglycan (CSPG) that surrounds soma and dendrites. This matrix has been shown to be involved in memory and implicated in a number of psychiatric disorders. Our lab is interested in understanding what makes those neurons so special and how.