FACULTY OF HEALTH SCIENCES

2021 WEEKLY NEWSLETTER

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Publication

1. Wu, C. H., Kisel, K. S., Thangavel, M. K., Chen, Y. T., Chang, K. H., Tsai, M. R., Chu, C. Y., Shen, Y. F., Wu, P. C., Zhang, Z., **Liu, T. M.**, Janis, J., Grachova, E. V., Shakirova, J. R., Tunik, S. P., Koshevoy, I. O., and Chou, P. T. (2021) Functionalizing Collagen with Vessel-Penetrating Two-Photon Phosphorescence Probes: A New in Vivo Strategy to Map Oxygen Concentration in Tumor Microenvironment and Tissue Ischemia. *Adv Sci*, e2102788 **[2020 IF = 17.835]**

2. Zhu, L., Liu, J., Zhou, G., **Liu, T. M.**, **Dai, Y.**, Nie, G., and **Zhao, Q.** (2021) Remodeling of Tumor Microenvironment by Tumor-Targeting Nanozymes Enhances Immune Activation of CAR T Cells for Combination Therapy. *Small*, e2102624 **[2020 IF = 13.281]**

3. Cheng, Q., Yue, L., Li, J., Gao, C., Ding, Y., Sun, C., Xu, M., **Yuan, Z.**, and Wang, R. (2021) Supramolecular Tropism Driven Aggregation of Nanoparticles in Situ for Tumor-Specific Bioimaging and Photothermal Therapy. *Small*, e2101332 **[2020 IF = 13.281]**

4. Gong, J., Huang, R. S., Wang, C. F., Zhao, Z. J., Tang, B. Z., and **Zhang, X. J.** (2021) Iodization-Enhanced Fluorescence and Circularly Polarized Luminescence for Dual-Readout Probe Design. *Sensors and Actuators B: Chemical* **[2020 IF = 7.46]**

5. Rao, W., Zhang, Y., Ng, C., Cui, L., Li, J., Li, L., Ungvari, G., Li, K., and **Xiang, Y. T.** (2021) Prevalence of Schizophrenia and Its Association with Socio-Demographic Correlates in an Agricultural Region of China. *Asian J Psychiatr*, 102743 **[2020 IF = 3.543]**

1 BCAT Meeting

Prof. Xiaoling XU reported her latest research in the BCAT Meeting on 18 August. Prof. Xu's laboratory has been studying cancer metastasis which is the cause of the majority of cancer-related deaths, using a mouse model carrying mammary specific disruption of the breast cancer associated gene 1 (BRCA1). Using various approaches, her group has identified several top candidate genes, including Plekha5, P4-ATPase, and Ptdss2, whose aberrant expressions drive cancer metastasis. They have also been studying the efficiency of the immune checkpoint blockade (ICB) using their animal models and shown that cancers with DNA homologous recombination repair (HR) deficiency, which have a higher tumor mutational burden (TMB), were more resistance to ICB. However, breast cancers caused by germline mutations of BRCA1, which are defective in HR, did not have an improved response to the treatment, yet the underlining mechanism remains elusive.

To investigate this, they have analyzed the immune suppressive microenvironment of BRCA1 mutant mammary tissues and the tumors derived from both BRCA1 mutant mouse models and human xenograft models to identify the intrinsic determents governing tumor progression and the responses to ICB. The result showed that BRCA1 negatively regulates the expression of several key genes in mammary epithelium and, consequently, the

activated oncogenic signaling upon BRCA1 deficiency acted as a driving signaling for cancer progression. They have further demonstrated that the activation of these signaling in the surrounding tumor immune cells could trigger the expansion and accumulation of myeloid-derived suppressor cells (MDSCs) and create a tumor-permissive microenvironment that renders caners insensitive to ICB. Prof. Xu reported that they are now in the process to test several therapeutic approaches that could significantly increase the efficacy of ICB to suppress breast cancer progression and metastasis.

2 Academic Promotion

Series 2: Prof. Hongjie ZHANG Promoted to Associate Professor

FHS congratulates Prof. Hongjie ZHANG for her promotion to the rank of Associate Professor.

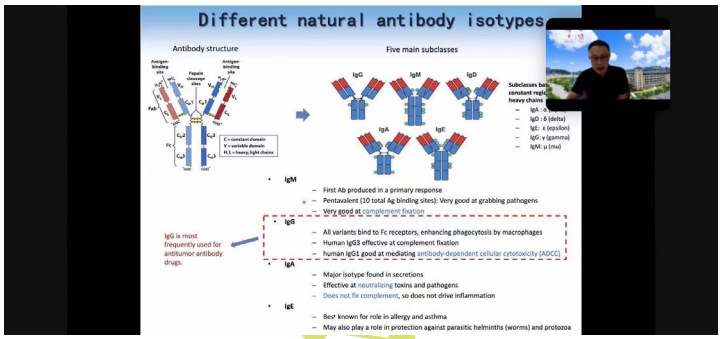
Prof. Zhang's main research interests are the molecular mechanisms of organ formation. The majority of human diseases and aging processes originate from internal organs. Understanding the molecular mechanisms of organ formation and maintenance is fundamental to developmental biology and medicine. Her research group uses genetically tractable and structurally simple *C. elegans* as a model system, employing genetic, biochemical, and functional genomics approaches to investigate how organs form and how their shapes, sizes and functions are controlled. Specifically, they are trying to elucidate the roles of sphingolipid metabolism, RNA processing and protein homeostasis in organ development and function.

Prof. Zhang has been the principal investigator of multiple projects funded by FDCT, FDCT/MOST and UM since she joinedFHS in 2015. She has published multiple papers as corresponding/co-corresponding authors in internationally renowned journals, including *Biological Reviews*, *Chemical Science*, *Cell Reports*, *Journal of Neuroscience*, and *International Journal of Biological Sciences*.

Congratulations again to Prof. Hongjie ZHANG and we look forward to her continuous contributions to FHS. You may learn more about Prof. Zhang via her profile page of our website (https://fhs.um.edu.mo/en/staff/hongjie-zhang/).

3 Seminar Series

Antibody-based Therapeutics against B7-H3 Immune Checkpoint Molecule – Prof. Qi ZHAO



Prof. Qi ZHAO presented "Antibody-based Therapeutics against B7-H3 Immune Checkpoint Molecule" in the Ministry of Education (MoE) Frontiers Science Center for Precision Oncology (FSCPO) Seminar Series on 17 August.

Prof. Zhao introduced that immune checkpoint therapy becomes a breakthrough strategy to reactivate antitumor immune responses in the recent years. He has overexpressed B7-H3, an immune-checkpoint molecule and a transmembrane protein, in a panel of solid tumors, making it an attractive therapeutic target for neuroblastoma and non-small cell lung cancer. He has identified and humanized the novel monoclonal antibodies (mAbs) recognizing B7-H3. He said that mAbs were designed to destroy B7-H3+ solid tumor cells by utilizing mechanisms of antibody-dependent cellular cytotoxicity (ADCC) or antibody-drug conjugation (ADC). He found that B7-H3 xCD16a bispecific antibodies directed at B7-H3 and human CD16a can engage natural killer (NK) cells to lyse tumors. Additionally, he has constructed chimeric antigen receptors (CARs) to redirect either T or NK cells against B7-H3+ tumor cells. He has also built the nanoparticle drug delivery systems based on various antibody and immune cell formats for the targeted delivery and controlled release of therapeutic agents in multiple *in vitro* and *in vivo* models. At the end, he concluded his results that B7-H3 may serve as a target for cancer therapy and support the further development of anti-B7-H3 therapeutic agents in the preclinical and clinical studies.

4 PhD Oral Defence

Seven Students Completed PhD Oral Defences

In this week, seven FHS students completed their PhD Oral Defences.

Ms. Wen LI, supervised by Prof. Yutao XIANG, presented "The Mental Health Status of Clinically Stable Older Patients with Psychiatric Disorders during the COVID-19 Pandemic in China" on 16 August. She claimed that the coronavirus disease 2019 (COVID-19) pandemic has profound negative effects on the older patients who are in mental health of clinically stable with psychiatric disorders. She has measured depressive, anxiety,

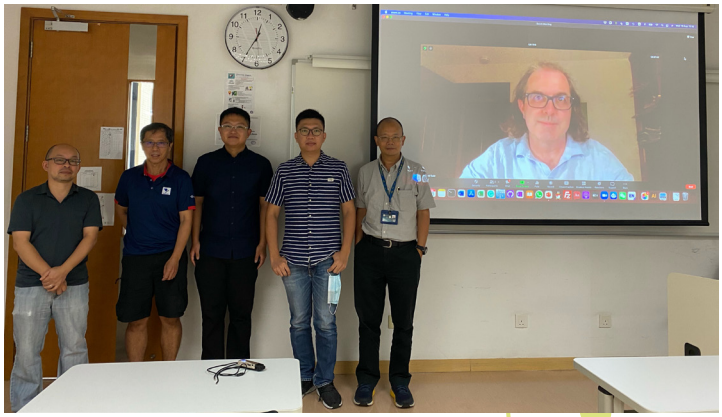
and insomnia symptoms; posttraumatic stress symptoms (PTSS); pain; fatigue; suicidality; and quality of life (QOL) to investigate the mental health problems of this population during COVID-19 pandemic in China. She reported that the prevalence of depressive, anxiety, and insomnia symptoms; PTSS; pain; fatigue; and suicidality were 30.8%, 25.7% 20.6%, 2.1%, 8.0%, 47.1%, and 11.8% respectively in the 1,063 patients. She found that depressive symptoms were the most influential symptoms. Patients with poor mental health presented lower QOL compared to those without. She concluded that mental health problems were common and required effective treatment in the studied population.

Ms. Yuan YANG, supervised by Prof. Yutao XIANG, presented “Mental Health and Quality of Life among Chinese Pregnant and Postnatal Women” on 16 August. Her study aimed to assess pregnant and postnatal women’s mental health (i.e., depression, suicidality, insomnia, verbal and physical violence experience, secondhand smoke exposure, and Internet addictive behaviors) and its association with QOL. The study was also a multicenter, cross-sectional investigation. She has performed univariate analyses, multivariate logistic regression analyses, and network analyses within the project. She reported the results with the assessed 1,060 women that women with physical comorbidities were more likely to report depression, secondhand smoke exposure, insomnia, and Internet addictive behaviors. Besides, women with poor mental health status were more likely to report poor QOL. She concluded that preventive strategies, such as routine assessment and the management of physical comorbidities, need to be adopted to track and reduce the risk of poor mental status in this population.

Ms. Koukou LI, supervised by Prof. Kathy LUO, presented “Desmosomal Proteins of DSC2 and PKP1 Promote Cancer Cells Survival and Metastasis by Increasing Cluster Formation in Circulatory System” on 17 August. She reported that she has used a microfluidic circulatory system to study how cancer cells can withstand fluid shear stress (SS), and SS-resistant cancer cells were isolated. She found that these SS-resistant cells showed higher abilities to form clusters, survived in circulation and form metastases in mice. Besides, these SS-resistant cells expressed more desmocollin-2 (DSC2) and plakophilin-1 (PKP1) proteins. Moreover, the high expression of both DSC2 and PKP1 activated the PI3K/AKT/Bcl-2-mediated

pathway to increase the cell survival. The high levels of DSC2 and PKP1 were also important for maintaining a high expression level of vimentin which stimulates fibronectin/integrin β1/FAK/Src/MEK/ERK/ZEB1-mediated metastasis. She further discovered that higher levels of DSC2 and PKP1 were correlated with lower overall survival and worse disease progression. She concluded that DSC2 and PKP1 may serve as the new biomarkers for detecting and targeting metastatic circulating tumor cells.

Mr. Liguo DONG, supervised by Prof. Chris WONG, presented "Functional Genomics Study of Transcriptional Regulation of Carbon Metabolism in *Aspergillus nidulans*" on 18 August. He introduced that *Aspergillus nidulans* is a filamentous fungus model organism which can use a wide range of carbon sources. Transcription regulation is required for fungi to produce the necessary enzymes of using the carbon source. However, the targets of putative transcription factors AcuK-AcuM, FacB, and CreA have not been fully understood. He therefore integrated the binding sites of these four transcription factors by ChIP-seq with their controlled genes found through RNA-seq. The integration revealed the transcription factors in which directly or indirectly regulated many unknown pathways (e.g., amino acid metabolism and secondary metabolism). Furthermore, TSS reannotation using available RNA-seq datasets revealed that the alternative TSSs were widely used and switched between culture conditions. He concluded that the transcription factors (such as FacB, AcuK-AcuM dimer, and CreA) influenced alternative TSS selection.



Mr. Lipeng ZHU, supervised by Prof. Qi ZHAO, presented "Novel Multifunctional Nanoagents for Drug Delivery and Cancer Immunotherapy" on 18 August. He introduced that copper sulfide (CuS)-based multifunctional nanoagents have extensively been explored for cancer therapy due to low toxicity, low cost, facile synthesis, and the high photothermal conversion efficiency. He has synthesized different types of CuS-based nanoagents, including BSA@CuS@DOX nanoplatform, PCCNs nanoparticles, and PHCNs nanozymes in his project for studying drug delivery, disrupting intracellular reactive oxygen species (ROS) homeostasis,

and combination immunotherapy by enhancing immune activation of chimeric antigen receptor (CAR) T cells. He has further used the different types of CuS-based multifunctional nanoagents to treat cancer through the different anti-cancer mechanisms. He concluded that his studies provided a new platform of “all-in-one” CuS-based nanoagents for drug delivery and cancer immunotherapy.

Mr. Haipeng LEI, supervised by Prof. Chuxia DENG, presented “Fibroblast Growth Factor Receptor 2 (FGFR2) Activation Promotes the Development of Triple-negative Mammary Tumors and Identify Molecular Drivers Using Sleeping Beauty Mouse Models” on 19 August. He said that FGFR2 is a membrane-spanning tyrosine kinase that mediates signaling for FGFs. Various FGFR2 alterations are detected in breast cancer, yet it remains unclear if the activation of FGFR2 signaling initiates tumor formation. Thus, he has generated a mouse model and found that FGF/FGFR2 signaling drove the development of TNBC accompanied by EMT which is regulated by FGFR2-STAT3 signaling. He also found that FGFR2 positively regulated PD-L1 and a combination of FGFR2 inhibition and ICB killed cancer cells. Moreover, he has employed the sleeping beauty (SB) transposon system to speed up the screening and identification of the cooperating factors with FGFR2 for tumorigenesis and to perform the functional study of top candidate genes which cooperated with FGFR2 in mammary tumorigenesis and progression.

Mr. Haibin YANG, supervised by Prof. Gary WONG, presented “Structural Investigation into the Regulation of F-actin Dynamics in Focal Adhesions” on 21 August. He introduced that focal adhesions (FAs) which link the extracellular matrix (ECM) to the cells are essential for various cellular functions including spreading, migration, proliferation, and apoptosis. Also, actin dynamics is highly regulated in FAs. Besides, ILK-PINCH-Parvin (IPP) complex and Rsu1 are the major components in FAs, involving in the regulation of actin bundling. However, the molecular mechanisms underlying the interactive role of IPP and Rsu1 in actin dynamic remains elusive. Therefore, he has determined the complex structure of Rsu1 and PINCH1 in his project which revealed that Rsu1 disrupted IPP-mediated F-actin bundling through specifically binding with PINCH. He further found that the overexpression of Rsu1 in Hela cells impaired actin fibers formation and cell spreading. He concluded that his study demonstrated the interplay of IPP and Rsu1 taking the critical roles in orchestrating actin-FA crosstalk.

5 Community Story

UM FHS Holds Online Orientations for New Students 2021/2022

FHS held two sessions of orientations to welcome more than 120 new undergraduate and postgraduate students for the 2021/2022 academic year on 16 August.

Speaking at the orientations, Prof. Chuxia DENG and Prof. Guokai CHEN warmly received the freshmen and introduced UM's 4 in 1 educational model, FHS' educational programmes, development history and the new structure. Prof. Deng introduced FHS' important and continuous contributions to the various fields, including the recent achievements of precision oncology, stem cell research and the mental health research related to the novel coronavirus disease (COVID-19) outbreak. Prof. Deng mentioned that FHS' progress is being recognised globally through the growing partnership with top academic institutions both at home and abroad. One of the successful collaborations is that FHS, Stanford University, and MD Anderson Cancer Center have achieved a breakthrough in their collaborative lung cancer research.

Prof. Deng particularly mentioned that UM has recently established the Frontiers Science Center for Precision Oncology upon the approval of the Ministry of Education, which is the first cutting-edge scientific research centre in Hong Kong and Macao. The establishment of this cutting-edge science center marks UM's notable progress in the construction of the major national basic research platform, and also recognises FHS' contributions in precision oncology.

Prof. Deng also emphasized on honesty and originality that are the pillars of higher education, and students should pursue research achievements of high quality and have zero tolerance for plagiarism and substandard research ethics. He gave the students exhortation to follow the rules and regulations of the University strictly. In Prof. Deng's speech for giving the undergraduate students some guidance, he mentioned that the combination of persistence and curiosity is a very good predictor of the success in studies as most of the breakthrough discoveries and remarkable inventions are the results of curiosity. Prof. Deng cited as an example the motto of Aaron Ciechanover, the Nobel Laureate, who thinks that a synthesis of passion, supervisor, diligence and luck is the key to become a successful postgraduate student. He advised the postgraduate students that first and foremost they should be motivated by passion, communicate well with their supervisors, develop the habit of diligence, well prepare themselves, and luck is what happens when preparation meets opportunity.

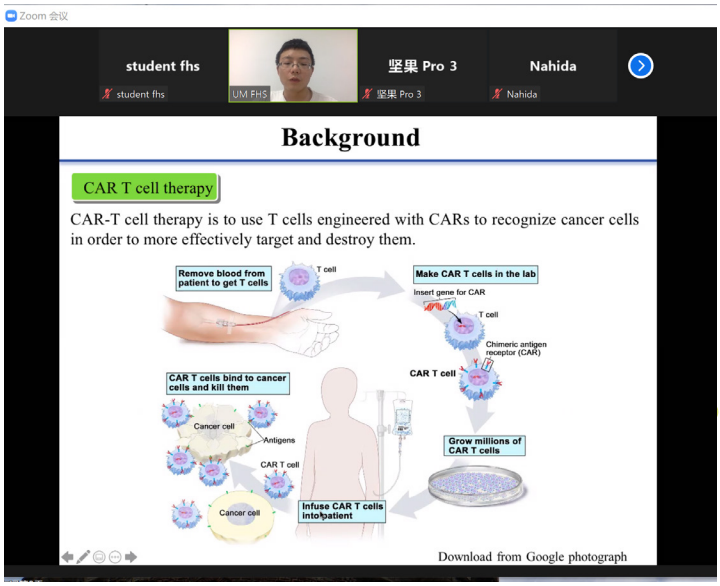
At the end of the orientations, Prof. Deng encouraged the students to adapt to the new environment as quickly as possible and embrace diversity in the course to achieving excellence.

6 FHS Postdoc Student Seminar

Presented by Prof. Qi ZHAO's Group

On 19 August, Mr. Lipeng ZHU of Prof. Qi ZHAO's group presented "CuS-Based Nanozymes for Promoting CAR T Infiltration".

The next seminar will be held on 2 September, and presented by the group member of Prof. Chuxia DENG and Prof. Wakam CHANG.



UPCOMING EVENTS

August / September		
Mon	**23**	**30**
Tue	**24**	**31** **Oral Defence** Speaker: Si CHEN Supervisor: Prof. Chuxia DENG Time: 10:00 Venue: E12-1015
Wed	**25**	**SEP 1** **BCAT Meeting** Speaker: Prof. Vivien WANG Time: 17:00-18:00 Venue: E12-G004
Thu	**26**	**2** **FHS Postdoc/ Student Seminar** Session: Cancer Research, Precision medicine & Aging and Developmental Biology Host: Prof. Chuxia DENG and Prof. Wakam CHANG Time: 17:00-18:00 Venue: N22-G002 and Zoom
Fri	**27** **Oral Defence** Speaker: Shigao HUANG Supervisor: Prof. Qi ZHAO Time: 10:00 Venue: E12-1015	**3**
Sat	**28** **Oral Defence** Speaker: Shiyin ZHAO Supervisor: Prof. Xuanjun ZHANG Time: 9:30 Venue: E12-1015	**4**

For more information or submission of articles to be featured, please contact Ms. Mathilde CHEANG at mathildec@um.edu.mo or 8822 4909.