FACULTY OF HEALTH SCIENCES

2021 WEEKLY NEWSLETTER

Issue 6 | 8 - 12 February

Publication

1. Xu, B., Wang, Z. P., Liu, Q., Yang, X., Li, X., Huang, D., Qiu, Y., **Tam, K. Y.**, Zhang, S. L., and He, Y. (2021) Synthesis, Biological Evaluation and Structure-Activity Relationship of Novel Dichloroacetophenones Targeting Pyruvate Dehydrogenase Kinases with Potent Anticancer Activity. *Eur J Med Chem* 214, 113225 **[2019 IF = 5.572]**
2. Ke, R., Lok, S., Singh, K., Kwok, B., Janovjak, H., and **Lee, L. T. O.** (2021) Formation of Kiss1R/GPER Heterocomplexes Negatively Regulates Kiss1R-Mediated Signalling through Limiting Receptor Cell Surface Expression. *J Mol Biol*, 166843 **[5yr IF = 4.783]**
3. Wang, M. Y., and **Yuan, Z.** (2021) EEG Decoding of Dynamic Facial Expressions of Emotion: Evidence from SSVEP and Causal Cortical Network Dynamics. *Neuroscience* **[5yr IF = 3.343]**

1 Article Sharing

FHS Achieves Breakthroughs in Antibody Immunotherapy Research

A research team led by Prof. Qi ZHAO designed two novel immunotherapeutic antibody drugs targeting an immune checkpoint B7-H3. The two antibody drugs can be used to promote the anti-tumor immunity of the patient's own immune system against non-small cell lung cancer (NSCLC). The study has been published in the high-impact academic journal *Journal of Hematology & Oncology*.

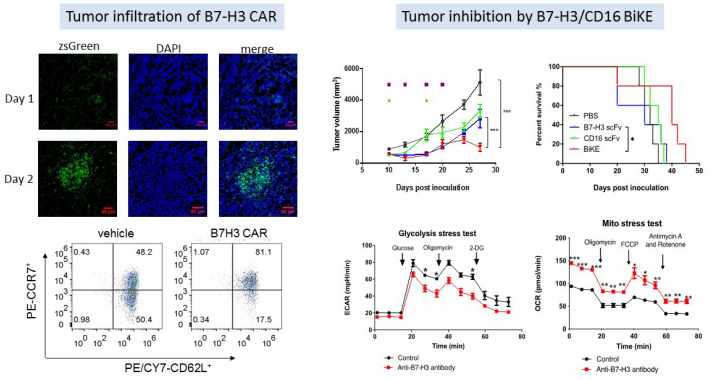
Adoptive immunotherapy that uses effector lymphocytes expressing tumor-specific antibodies is a promising approach to cancer treatment. To facilitate immune cell responses, Prof. Zhao and his research team designed two modalities, CART and bispecific killer cell engager (BiKE), using single-chain variable fragments (scFvs) to redirect cytotoxic lymphocytes against tumor cells. Their studies have laid the groundwork for further development of two therapeutic agents in preclinical and clinical studies.

NSCLC is a major subtype of epithelial lung cancer and accounts for a majority of lung cancer cases. Despite considerable progress in the development of immune checkpoint inhibitors, particularly the encouraging therapy of anti-PD-1 antibodies, a portion of NSCLC patients still remain generally resistant to these therapies. The team discovered that the B7-H3 molecule was highly associated with the long-term survival rate of NSCLC patients.

While B7-H3 protein is expressed at low levels in most normal tissues, it is aberrantly expressed during differentiated stages of NSCLC. Their studies suggest that B7-H3 may serve as an attractive target for immunotherapy.

The modalities, CART and bispecific killer cell engager (BiKE), use single-chain variable fragments (scFvs) to redirect cytotoxic lymphocytes against tumor cells. CART is a genetically engineered T cell that expresses the anti-B7-H3 antibody on the surface of the T cell. The BiKE is designed as a 'bridge' between tumor cells and NK cells. One arm binds to the CD16 receptor of NK, and the other arm binds to the B7-H7 antigen of tumor cells. CART cells effectively inhibited NSCLC tumourigenesis. B7-H3 redirection promoted highly specific T-cell infiltration into tumors. Additionally, NK cell activity could be specially triggered by B7-H3/CD16 BiKE through direct CD16 signalling, resulting in significant increase in NK cell activation and target cell death. Furthermore, they found that anti-B7-H3 blockade might alter tumor glucose metabolism via the reactive oxygen species-mediated pathway.

PhD students Jie LIU and Shuo YANG are the co-first authors, and Prof. Zhao is the corresponding author. Prof. Kathy LUO, Prof. Guokai CHEN, and Prof. Lijun DI made important contributions to this study. The study was funded by the FDCT grants (file number: 131/2016/A3 and 0015/2018/A1), National Key R&D Programme of China (file number: 2019YFA0904400), Guangzhou Municipal Science and Technology Bureau (file number: 201807010004), and UM (file number: MYRG2019-00069-FHS and SRG2016-00082-FHS). The full-text version of the related paper can be viewed at: https://doi.org/10.1186/s13045-020-01024-8.



NSD3 participates in the tumourigenesis of lung squamous cell carcinoma and is a potential target for cancer therapy.

2 BCAT Meeting

Prof. Gang LI shared his latest research in the BCAT meeting on 10 February. He introduced that polycomb repressive complex 2 (PRC2) maintains the gene expression profiles during the metazoan development by catalyzing the methylation of lysine 27 on histone H3 (H3K27me1/2/3). He said that accumulating evidence indicates that the upstream cellular signals, particularly post-translational modifications (PTMs) of PRC2 subunits, regulate its functions. Prof. Li's research has shown that EED, a core component of PRC2, was acetylated by acetyltransferase CBP/P300 at lysine 19 (K19). The acetylation of EED at K19 (EED-K19ac) has reduced the binding affinity between PRC2 and native nucleosomes, causing PRC2 to leave its chromatin targets *in vivo*. He has performed the Genome-wide location analysis (ChIP-seq) and found that K19-acetylated EED preferentially

accumulated at highly transcribed genes with low EZH2 and H3K27me3 levels. Using the CRISPR/Cas9 technology, Prof. Li has generated the mouse embryonic stem cells (mESCs) carrying non-acetylated EED mimic (EED-K19R) which showed that the acetylation of EED at K19 was necessary for the mESC differentiation.

Prof. Li concluded that his study has revealeda critical mechanism for controlling the cellular differentiation by regulating PRC2 targeting through EED acetylation. His team has also identified multiple novel AMPK targets which were involved in the transcriptional/epigenetic regulation using quantitative phosphoproteomics. Prof. Li also stated that he is performing the functional studies.

3 News

Prof. Yutao XIANG, Prof. Terence POON and Prof. Henry KWOK Receive Best Teacher Awards

In the academic year 2019/2020, Prof. Terence POON, Prof. Yutao XIANG and Prof. Henry KWOK receive the Best Teacher (Excellence in Teaching), Best Teacher (Excellence in Research) and Best Teacher (Excellence in Service) respectively. The three awards are to recognize the excellent performance of and appreciate the exemplary contributions to FHS by the recipients of the awards in the previous calendar year. The award recipients have demonstrated their excellence in the relevant awarding aspects.

Let's congratulate them and thank them for their excellent work in the previous calendar year!

4 PhD Oral Defence

PhD Oral Defence by Li ZHANG of Prof. San Ming WANG's Group

Ms. Li ZHANG supervised by Prof. San Ming WANG completed her PhD oral defence on 8 February. Her thesis title is "DNA Mismatch Repair (MMR) Gene Variation in the Chinese Population".

Ms. Zhang claimed that DNA mismatch repair (MMR) genes play essential roles in the DNA damage repair and maintaining genome stability. She introduced that the mutations in MMR disrupt their functions and cause genome instability and multiple cancer development as best represented by the Lynch Syndrome. She reported that her study focused on the MMR variation between the people with cancer and the general people among the Chinese population. During her project, she has collected the information of the MMR variation, determined the spectrum and prevalence of MMR variation, identified the pathogenic mutations and founder mutation, and developed the open-access Chinese MMR variation database. She concluded that her study was the most comprehensive MMR study in the Chinese population by far. The resulting data has profound impact on the MMR research worldwide, and the prevention and treatment of the MMR caused cancer in the Chinese population.

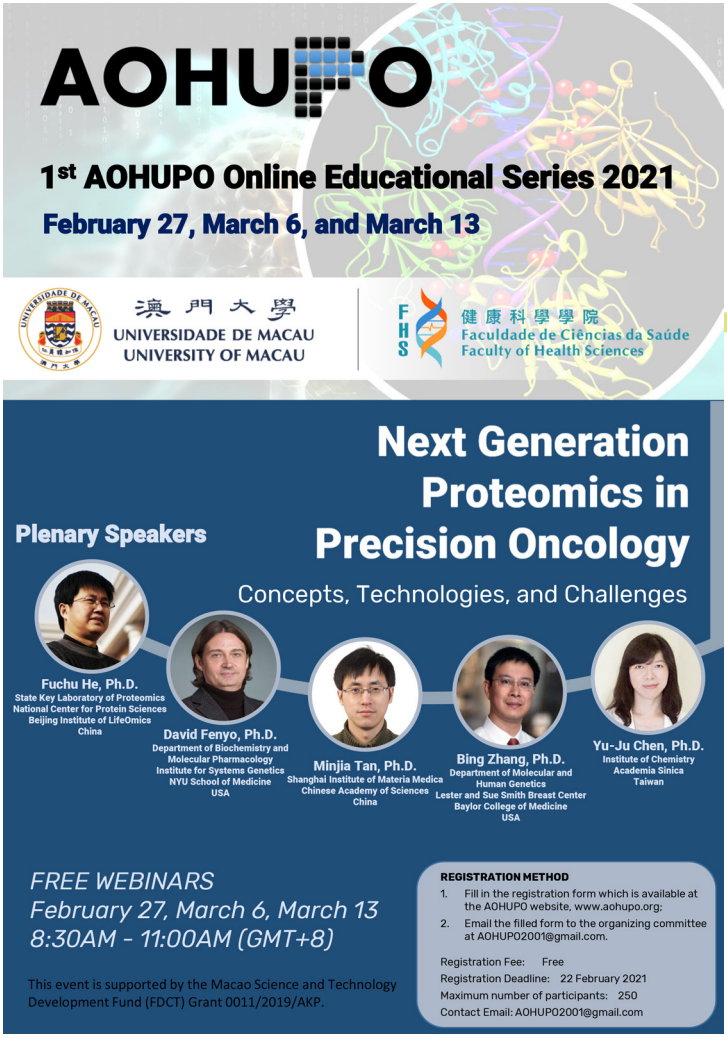
5 Upcoming Event

1st AOHUPO Online Education Series on "Next Generation Proteomics in Precision Oncology"

FHS and Asia Oceania Human Proteome Organization (AOHUPO) will jointly organize the 1st AOHUPO Online Education Series 2021 featuring "Next Generation Proteomics in Precision Oncology" on 27 February, 6 and 13 March via Zoom.

Registration is required due to the limited number of the participants and it is "first registered, first served". If you are interested in this, please download and fill in the registration form, and email it to AOHUPO2001@gmail.com on/before the deadline 22 February. Please contact Humphrey MA (email: yb97633@connect.um.edu.mo) or Prof. Terence POON (email: tcwpoon@um.edu.mo) for any questions.

Download link of the Registration form:



UPCOMING EVENTS

February		
Mon	**15** **Compensatory rest days**	**22**
Tue	**16** **Compensatory rest days**	**23**
Wed	**17** **BCAT Meeting** Speaker: Prof. Joong Sup SHIM Time: 17:00-18:00 Venue: E12-G004	**24** **Oral Defence** Qingpin XIAO Supervisor: Prof. Kin Yip TAM Time: 10:00 Venue: E12-1015
Thu	**18** **FHS Postdoc/ Student Seminar** Session: Data Science Host: Prof. Terence POON and Prof. Ningyi SHAO Time: 17:00-18:00 Venue: N22-G002 and Zoom	**25** **Oral Defence** Bin HUANG Supervisor: Prof. Kathy Qian LUO Time: 10:00 Venue: E12-1015 **Oral Defence** Pengxiang QIU Supervisor: Prof. Xiaoling XU Time: 15:00 Venue: E12-1015 **Seminar Series** Novogene Sequencing Service Host: GBSC Core Speaker: Ms. Elaine LO (Business Development Specialist) Time: 10:30-11:30 Venue: Zoom
Fri	**19** **Seminar Series** Elevated NSD3 Histone Methylation Activity Drives Squamous Cell Lung Cancer Speaker: Prof. Ning Yi SHAO Time: 10:00-11:00 Venue: ZOOM (626 029 9466)	**26**
Sat	**20**	**27** **Seminar Series** 1st AOHUPO Online Education Series on “Next Generation Proteomics in Precision Oncology” Time: 08:30-11:00 Venue: ZOOM

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