Publication(s)

1. Zhang, Z., Sang, W., Xie, L., Li, W., Li, B., Li, J., Tian, H., Yuan, Z., **Zhao, Q.**, and **Dai, Y.*** (2020) Polyphenol-Based Nanomedicine Evokes Immune Activation for Combination Cancer Treatment. *Angew Chem Int Ed Engl* **[2019 IF = 12.959]**

2. Liu, K., Tan, S.*, Jin, W., Guan, J., Wang, Q., Sun, H., Qi, J., Yan, J., Chai, Y., Wang, Z., **Deng, C.***, and Gao, G. F.* (2020) N-Glycosylation of PD-1 Promotes Binding of Camrelizumab. *Embo Rep*, e51444 **[5yr IF = 9.214]**

This article is cooperated between the team of Academician Fu GAO, Institute of Microbiology, Chinese Academy of Sciences, and the team of Prof. Chuxia DENG. Mr. Kefang LIU, the joint PhD student of The University of Macau and the University of Chinese Academy of Sciences, is the co-first author of the article.

The studies have found that the N-glycosylation modification of PD-1 molecule was polymorphic, and the protein stability evaluation results of PD-1 in different expression systems showed that sugar modification has an important effect on the stability of PD-1 molecule. The teams have measured the affinity of camrelizumab to PD-1 in different expression systems, and speculated that the difference in affinity was due to the different glycosylation modifications of PD-1 molecules in the three expression systems. Please visit the links for more details:

[1] Details explanation:
https://mp.weixin.qq.com/s/6T6X4UNRJyMzmEIkcJ4WaA

[2] Full paper:
https://www.embopress.org/doi/full/10.15252/embr.202051444

[1] [2]

3. Zhang, Z., Wu, K., Ren, Z., and **Ge, W.*** (2020) Genetic Evidence for Amh Modulation of Gonadotropin Actions to Control Gonadal Homeostasis and Gametogenesis in Zebrafish and Its Noncanonical Signalling through Bmpr2a Receptor. *Development* **[5yr IF = 6.192]**

4. Yan, F., Wang, R., Li, S., Zhao, X., Jiang, Y., Liu, L., Fang, J., Zhen, X., Lazarovici, P., and **Zheng, W.*** (2020) FoxO3a Suppresses Neuropeptide W Expression in Neuronal Cells and in Rat Hypothalamus and Its Implication in Hypothalamic-Pituitary-Adrenal (HPA) Axis. *Int J Biol Sci* **16** (15), 2775-2787 **[5yr IF = 4.915]**

5. Ke, R., Lok, S. I. S., Singh, K., Chow, B. K. C., and **Lee, L. T. O.*** (2020) GIP Receptor Suppresses PAC1 Receptor-Mediated Neuronal Differentiation via Formation of a Receptor Heterocomplex. *J Neurochem* **[5yr IF = 4.35]**

健康科學學院
Faculdade de Ciências da Saúde
Faculty of Health Sciences

NEWSLETTER ISSUE 38
19 - 23 OCTOBER 2020

Academic Promotion

Prof. Ren-He XU promoted to Distinguished Professor

Prof. Ren-He XU, Associate Dean (Research) of FHS and an expert of stem cell research and applications, has been promoted to Distinguished Professor.

A recipient of Best Teacher Award (Excellence in Research), first prize awardee of Bank of China Trophy One Million Dollar Macau Innovation and Entrepreneurship Competition, Macau, and founder and chair of Macau Society for Stem Cell Research (MSSCR), Prof. Xu has made significant contributions to the scientific research on stem cells and the technological transfer of the research achievements since he joined FHS in 2014. He has published over 80 papers with nearly 6,800 citations, and obtained multiple patents in both China and U.S. with successful commercialization. He invented the technology for mesenchymal stem cells derived from human pluripotent stem cells via trophoblast (T-MSC), which treated multiple sclerosis, colitis, spontaneous osteoarthritis and skin damage in mouse and monkey models with superior efficacy. The technology has been licensed to the ImStem Biotechnology Company and approved by the U.S. Food and Drug Administration for clinical trials on multiple sclerosis. In addition, his team invented an ambient cell transportation system via sphere formation which can replace the expensive and cumbersome cryopreservation transportation.

To meet the community's high expectations for local higher education institutions to promote technological innovation, transfer of research results, and diversification of Macao's economy, Prof. Ren-He XU has been devoting himself into assisting the Faculty members to identify translatable technologies from their discoveries, making up research plans for new areas and directions with high impact and translatability, and establishing research collaborations with other institutions in Macau and worldwide.

Prof. Xu always believes that pushing the limit of knowledge, finding answers for unknowns in the nature, providing solutions to social issues, and passing the knowledge and curiosity to future generations are the key missions of a university professor. Congratulations to Prof. Xu promotion and we look forward to his continuing contributions to the Faculty. You may learn more about Prof. Ren-He XU via his profile page of our website. (https://fhs.um.edu.mo/en/staff/ren-he-xu/)

BCAT Meeting

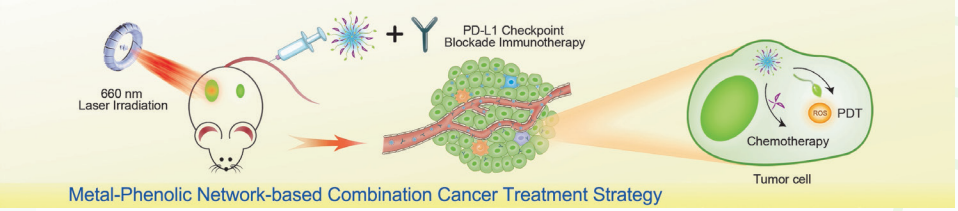
DSC2 and PKP1 Increase the Cluster Formation, Survival and Metastasis of Circulating Tumor Cells – Prof. Kathy LUO

In the BCAT meeting on October 21, Prof. Kathy LUO introduced the new findings on circulating tumor cells (CTCs) made by her PhD students: Koukou LI, Renfei WU and Haibo TONG. They found that the single CTCs can form clusters in blood circulation, which have higher ability to survive in circulation and form metastatic colonies in the lung. These clustered cells express high levels of DSC2 and PKP1 which can active PI3K/AKT/Bcl-2 pathway to support cluster formation and cell survival. DSC2 and PKP1 can also work via VIM to active MEK/ERK/ZEB1 to enhance lung metastatic tumor formation. As high expression of DSC2 and PKP1 correlates with tumor progression and poor prognosis in lung and breast cancer patients, these proteins may serve as the new biomarkers for diagnosis of metastatic CTCs and as the novel therapeutic targets to suppress metastasis.

Article Sharing

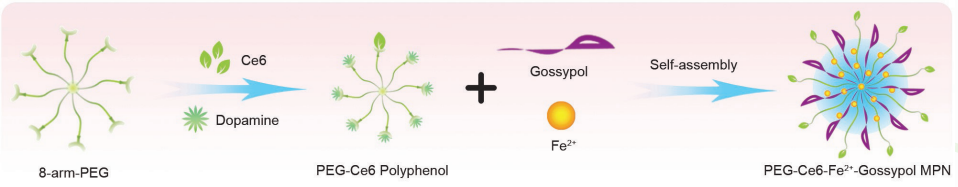
FHS Develops Polyphenol-based Nanomedicine Aiming at Immune Activation for Cancer Treatment

To develop new cancer treatment strategies with high therapeutic effect and low toxicity to healthy tissues, a research group led by Prof. Yunlu DAI has successfully synthesized a polyphenol-based nanomedicine that can evoke highly efficacious cancer immunosurveillance while localizing therapy on primary tumor and minimize systemic side effects. This study has been published in the internationally renowned journal *Angewandte Chemie International Edition*.



Metal-Phenolic Network-based Combination Cancer Treatment Strategy

Recent studies have discovered the high potential of polyphenols in the biomedical field, e.g., anti-tumor, anti-oxidation, and anti-thrombosis capacities. Phenolic ligands of polyphenols can coordinate with metal ions to fabricate metal-phenolic networks (MPNs), loading chemical drugs and encapsulating enzymes easily, and then releasing these functional components to tumor sites by virtue of the unique pH responsiveness of the nanoframework. In this study, a novel polyphenol-based nanocomplex was thus prepared via a metal-polyphenol coordination process by encapsulating a natural polyphenol gossypol and a newly synthesized polyethylene glycol-Chlorin e6 (Ce6) polyphenol derivative.



Natural gossypol stems from the cotton plant and shows a recently reported anticancer property without obvious systemic side effects as traditional doxorubicin or cisplatin caused. A polyphenol-analogous structure facilitates this natural drug an easy and stable intercalation into MPN skeleton. In this scenario, the team are inspired to design a new polyethylene glycol (PEG)-chlorin e6 (Ce6)-Fe2+-gossypol MPNs (termed PFGs) via metal-polyphenol coordination. Photosensitizer Ce6 and dopamine were firstly conjugated with PEG, forming PEG-Ce6 polyphenol. Fe^{2+} can thus integrate the phenolic moieties of gossypol and PEG-Ce6 polyphenol to form the MPNs. The PFGs accumulated in tumor sites after intravenous injection and showed efficient chemotherapy/PDT-induced ICD performance upon 660 nm laser irradiation, which was confirmed by the release of damage-associated molecular patterns (DAMPs), maturation of dendritic cells (DCs), and the generation of inflammatory factors. Additionally, anti-programmed cell death ligand-1 (PD-L1) antibodies were then applied *in vivo* to enhance the PFGs-based immune stimulation. Such double stimulation-induced deep immune activation achieved effective cytotoxic T lymphocytes (CTLs) infiltration in tumor tissues, which inhibited the tumor proliferation and metastasis remarkably.

Prof. Dai is the corresponding author and his PhD student Zhan ZHANG, Wei SANG, and the UM Macau post-doctoral fellow Lisi XIE are the co-first authors. Prof. Zhen YUAN, Prof. Qi ZHAO, post-doctoral fellow Bei LI, Jie LI, PhD students Wenxi LI, and Hao TIAN also made important contributions to this study. This study was funded by the Macao Science and Technology Development Fund (Reg. no. 0109/2018/A3 and 0011/2019/AKP) and the UM fund (Reg. no. SRG2018-00130-FHS).
You may find the details and full paper at:
https://onlinelibrary.wiley.com/doi/10.1002/anie.202013406

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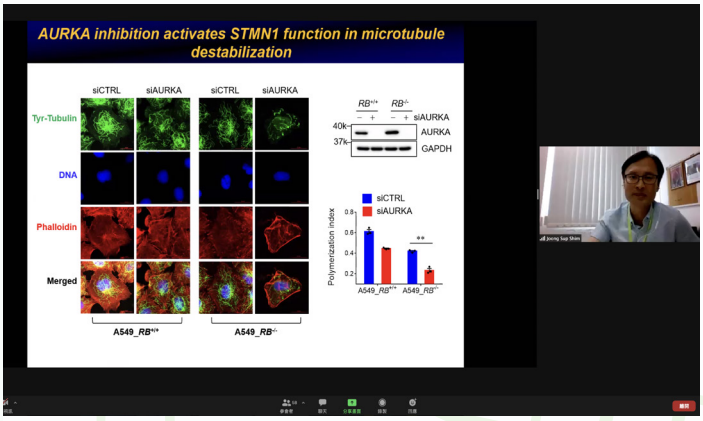
Seminar Series

Exploiting Synthetic Lethality for Cancer Precision Medicine - Prof. Joong Sup SHIM

On 23 October, Prof. Joong Sup SHIM presented his research about "Exploiting Synthetic Lethality for Cancer Precision Medicine" on ZOOM in a new series of faculty seminars. Prof. Henry KWOK hosted the seminar and around 60 UM researchers and students participated in the seminar online. Active discussion was aroused after the talk. At the closing, Prof. Ren-He XU evaluated the new seminar faculty series as a platform for students to know more about the research in FHS and gathering UM researchers to share and exchange research ideas.

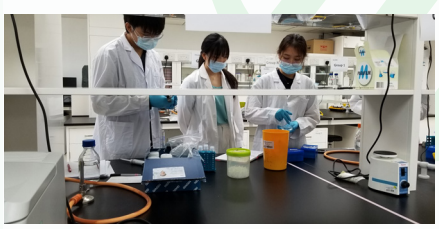


In the seminar, Prof. Shim introduced the challenges of cancer precision medicine and pointed out that synthetic lethality is a genetic interaction between two (or more) genes where a single gene deficiency is tolerable for cell viability, whereas deficiencies in both genes lead to cell death. This old genetic concept has recently been exploited in cancer precision medicine as a large portion of cancer cells have loss-of-function mutations in tumor suppressor genes. Besides, he said that mutations in tumor suppressor genes are a kind of gene deficiency that exists in cancer cells but not in normal cells. Therefore, induced deficiency in another gene that has the synthetic lethal interaction with the mutant tumor suppressor will selectively kill the cancer cells. Moreover, he introduced the screening approaches to identify the cancer cell synthetic lethality, with his recent discovery of aurora kinase A and microtubule dynamics as a target for the treatment of RB1-mutant small cell lung cancer (SCLC). Prof. Shim concluded that the synthetic lethality approach enables to pharmacologically target mutant tumor suppressors and provides a high selectivity toward cancer cells, and hence becoming an important part of the cancer precision medicine.

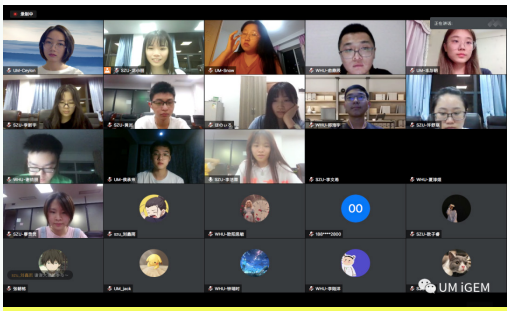
FHS Community Story

FHS Students Gird Themselves for iGEM Competition

A group of students from FHS and Faculty of Science and Technology (FST) have been girding themselves for the International Genetically Engineered Machine (iGEM) competition.



Being supervised by Prof. Leo Tsz On LEE, Ruiyu XIE and Tzu-Ming LIU, Yuzhao FENG, Yuanming HE, Ruiying MA, Shuyao XIE, Huichao ZHAO, Chengzong HOU, Hoi Cheng LEONG, Hengyi FU, Ioi FU, Xuemeng LI, Changcheng LU, Chan Tat LEONG, Lun Rochelle YU, Yu Xuan LAU, Lesi CHEN from FHS and Di SUN from FST formed a team to participate in the iGEM competition. The team focuses on modifying microorganism to degrade biofilm in fish tanks. Biofilms grow and attach to different surfaces in the aquarium. These biofilms reduce the water quality, and the bacteria in the biofilms can also consume the oxygen supply and nutrient in the water, affecting the health of the lives in the aquarium. The team is building a biofilm degrading system by engineering the bacteria *Escherichia coli* (*E. coli*). In this system, the engineered bacteria recognize the signal released from the biofilm in the fish tank and express enzymes to degrade the biofilm. The students will present their research work in the giant jamboree of the iGEM competition which will be held online in November 2020.



The Anti-biofilm Community (ABC) held virtual meeting

The students have established a collaboration with five other iGEM teams from the Dalian University of Technology, Southern University of Science and Technology, Tsinghua University, Wuhan University and Tsuen Wan Public Ho Chuen Yiu Memorial College by forming the Anti-biofilm Community (ABC). The teams in the community exchanged ideas and shared opinions on biofilm via online meetings. In order to promote the knowledge of synthetic biology and biofilm, the teams have produced a booklet, introducing each team's project and some science stories of synthetic biology.

The iGEM competition encourages students to design their projects using the standard, interchangeable pieces of DNA called as BioBricks to deal with issues they are now facing. The event is not only a competition, but also includes a series of workshops and activities for the iGEM teams to know more about synthetic biology and the industry. All the participants have to conduct laboratory works, set up collaboration, and propose the implementation of the projects in reality. The iGEM competition is a worldwide interdisplinary competition involving not only the fields of synthetic biology but also mathematics, computer science, statistics, etc. for cross-disciplinary collaboration. The iGEM competition was initiated by *Massachusetts Institute of Technology* students in 2004, and then became a global competition in 2005, giving students the opportunity to push the boundaries of synthetic biology, build up multidisciplinary teams, develop open communities and collaboration among various universities around the world.

PhD Oral Defence

PhD Oral Defences by Xinwei WU of Prof. Ruiyu XIE's group, Xingshun WANG of Prof. Wei GE's group, Linlin LIU and Jiankang FANG of Prof. Wenhua ZHENG's group

Ms. Xinwei WU supervised by Prof. Ruiyu XIE, Ms. Xingshun WANG supervised by Prof. Wei GE, Ms. Linlin LIU and Mr. Jiankang FANG supervised by Prof. Wenhua ZHENG completed their PhD oral defences on 20, 22 and 23 October respectively. Their thesis titles are "The function of TET dioxygenases in pancreatic endocrine cell differentiation", "Exploration of RNA helicase DHX33 as a molecular target for Cancer treatment", "The Therapeutic Effects of Artemisinin on Motoneuron Death induced by Brachial plexus Axotomy and its Effect on Neural stem/progenitor cells Differentiation" and "Protective effect of artemisinin in rat bone marrow derived mesenchymal stem cells from hydrogen peroxide and dexamethasone-induced cellular damage".

Ms. Wu claimed that current knowledge about the role of epigenetic modifiers in pancreas development increased exponentially. However, the precise function of TET dioxygenases in pancreatic endocrine specification remained obscure. She has used a stepwise human embryonic stem cell differentiation system, where TET1/2/3 triple-knockout cells displayed severe defects in pancreatic β-cell specification to tackle the issue. She has performed the integrative whole-genome analysis and identified the unique pancreas-specific hypermethylated regions, where the binding of pioneer transcription factor FOXA2 was remarkably enriched. Moreover, the transduction of TET1 in TET-deficient cells rescued β-cell differentiation and reversed the DNA hypermethylation at a putative PAX4 enhancer. She concluded that her study has highlighted the importance of TET-dependent epigenetic regulation in pancreas development.

Ms. Wang introduced that as a member of DEAH box RNA helicase, DHX33 has been shown to participate in a variety of cellular activities, including ribosome biogenesis, protein translation and gene transcription. She found that DHX33 was a downstream transcriptional and translational target of Ras in cells. Then she has used a helicase-based high throughput screening from Chembridge chemical library to discover the DHX33 inhibitors. She discovered the inhibitor of DHX33 deterred the tumor growth *in vivo*. She concluded that her study demonstrated the pivotal role of the DHX33 in Ras-driven lung cancer *in vivo* for the first time, and has highlighted the pharmacological targeting of DHX33 in Ras-mutant lung cancers.

Ms. Liu presented that brachial plexus axotomy is a common peripheral nerve trauma and artemisinin, a FDA-approved antimalarial drug, has been described to possess neuroprotective properties. However, the specific mechanisms by which artemisinin protects neurons from axotomy-induced neurotoxicity remained unknown. She has assessed the neuroprotective effects of artemisinin in an experimental animal model of brachial plexus injury and has explored the possible mechanisms. She found that the artemisinin treatment restored both grasping strength and sensation of the affected upper limb, rescued motoneurons, and attenuated the inflammatory response in the ventral horn of the spinal cord. Additionally, artemisinin inhibited the molecular signals of apoptosis, activated the signaling pathways which related to the cell survival, and induced the NSCPs differentiation into NeuN-positive neurons. Moreover, she has used an in vitro model of hydrogen peroxide-induced neurotoxicity to further validate the involved key signaling molecules, and the results revealed that the inhibition of PKA signaling pathway or the silencing of Akt reversed the neuroprotective action of artemisinin on motoneurons. She concluded that artemisinin provided neuroprotection against axotomy and hydrogen peroxide-induced neurotoxicity, and the effect might be mediated by the PKA-Akt signaling pathway.

Mr. Fang has investigated the protective effect of artemisinin and underlying mechanisms on bone marrow-derived mesenchymal stem cells (BMSCs) against oxidative stress and glucocorticoid-induced apoptosis. He claimed that the obtained results showed that the hydrogen peroxide and dexamethasone induced the injury and apoptosis in BMSCs, while artemisinin significantly reversed these harmful effects. The artemisinin treatment promoted the activation of ERK1/2/CREB pathway and the inhibition of this signaling cascade, either by the inhibitor of ERK pathway or by siRNA, attenuated the protective effect observed. He also observed these effects in a dexamethasone-treated rat model. Mr. Fang concluded that his findings indicated that artemisinin was able to protect BMSCs from oxidative stress and glucocorticoid-induced apoptosis via ERK1/2/CREB pathway, which suggested the potential therapeutic application of artemisinin on secondary osteoporosis.

FHS Postdoc Student Seminar

Presented by Prof. Chris WONG's group and Prof. Jun ZHENG's group

On 22 October, Ms. Fang WANG of Prof. Chris WONG's group presented "The Origin and Purpose(s) of Transcription Activity in Fungal Spores before Dormancy" and Mr. Ruiqiang XIE of Prof. Jun ZHENG's group presented "Analysis on Antibiotic Resistance and Virulence Features in *Acinetobacter baumannii*".

The next seminar will be held on 5 November, and presented by the group members of Prof. Xiaoling XU and Prof. Qi ZHAO, via Zoom again.

UPCOMING

Oct / Nov

Mon	Tue	Wed	Thu	Fri
26 **Holiday-Compensatory rest day of Chong Yeung Festival**	**27**	**28**	**29**	**30** **Oral Defence** Ruiqiang XIE Supervisor: Prof. Jun ZHENG Time: 15:00 Venue: N6-2022
Nov 2 **Holiday-All Soul's Day**	**3** **Oral Defence** Xiaowen GUAN Supervisor: Prof. Gang LI Time: 15:00 Venue: N6-2022	**4** **BCAT Meeting** Speaker: Prof. Douglas ZHANG Time: 17:00-18:00 Venue: E12-G004	**5** **FHS Postdoc/ Student Seminar** Session: Cancer Research Host: Prof. Xiaoling XU and Prof. Qi ZHAO Time: 17:00-18:00 Venue: N22-G002 and Zoom	**6** **7** **Oral Defence** Xiaoxiao ZHOU Supervisor: Prof. Guokai CHEN Time: 10:00 Venue: E12-4004
9	**10**	**11**	**12**	**13**
16	**17**	**18** **BCAT Meeting** Speaker: Prof. Edwin CHEUNG Time: 17:00-18:00 Venue: E12-G004	**19** **FHS Postdoc/ Student Seminar** Session: Cancer Research Host: Prof. Tzu-Ming LIU and Prof. Kathy Qian LUO Time: 17:00-18:00 Venue: N22-G002 and Zoom	**20**

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