Publication(s)

1. Lyu, J., Yang, E. J., Zhang, B., Wu, C., Pardeshi, L., Shi, C., Mou, P. K., Liu, Y., **Tan, K.**, and **Shim, J. S.** (2020) Synthetic Lethality of RB1 and Aurora A is Driven by Stathmin-Mediated Disruption of Microtubule Dynamics. *Nat Commun* **11** (1), 5105 **[5yr IF = 13.61]**

2. Xie, J., Chen, P., Xie, H., Sun, Y., Huang, Z., Wei, R., Miao, Z., Wang, Q., Zhang, S. D., **Wong, K. H.**, Lin, Y., Huang, C., and **Kwok, H. F.** (2020) Exploration of Gastric Neuroendocrine Carcinoma (GNEC) Specific Signaling Pathways Involved in Chemoresistance via Transcriptome and in Vitro Analysis. *Comput Struct Biotechnol J* **18**, 2610-2620 **[2019 IF = 6.018]**

3. Ju, Y., and **Tam, K. Y.** (2020) 9R, the Cholinesterase and Amyloid Beta Aggregation Dual Inhibitor, as a Multifunctional Agent to Improve Cognitive Deficit and Neuropathology in the Triple-Transgenic Alzheimer's Disease Mouse Model. *Neuropharmacology*, 108354 **[5yr IF = 4.512]**

4. Dong, M., Zhou, F. C., Xu, S. W., Zhang, Q., Ng, C. H., Ungvari, G. S., and **Xiang, Y. T.** (2020) Prevalence of Suicide-Related Behaviors among Physicians: A Systematic Review and Meta-Analysis. *Suicide Life Threat Behav* **[5yr IF = 4.393]**

5. Lv, X., Lu, F., Zhang, J., Chen, H., Zhang, L., Wang, X., Fan, Y., Fang, J., Hong, L., Wang, J., Liu, C., **Yuan, Z.**, He, Z., and Wang, W. (2020) Effects of TIP Treatment on Brain Network Topology of Frontolimbic Circuit in First-Episode, Treatment-Naive Major Depressive Disorder. *J Affect Disord* **279**, 122-130 **[5yr IF = 4.226]**

6. Lu, H., Zhao, C., Zhu, B., Zhang, Z., and **Ge, W.** (2020) Loss of Inhibin Advances Follicle Activation and Female Puberty Onset but Blocks Oocyte Maturation in Zebrafish. *Endocrinology* **[5yr IF = 4.075]**

7. Yang, Y., Li, W., Zhang, L., Zhang, Q., Cheung, T., Hall, B. J., and **Xiang, Y. T.** (2020) The Impact of COVID-19 Pandemic on Clinical Research in China: Challenges and Progress. *Front Med (Lausanne)* **7**, 523 **[2019 IF = 3.9]**

8. Liu, Y., Wang, Y., Gozli, D. G., **Xiang, Y. T.**, and Jackson, T. (2020) Current Status of the Anger Superiority Hypothesis: A Meta-Analytic Review of N2pc Studies. *Psychophysiology*, e13700 **[5yr IF = 3.793]**

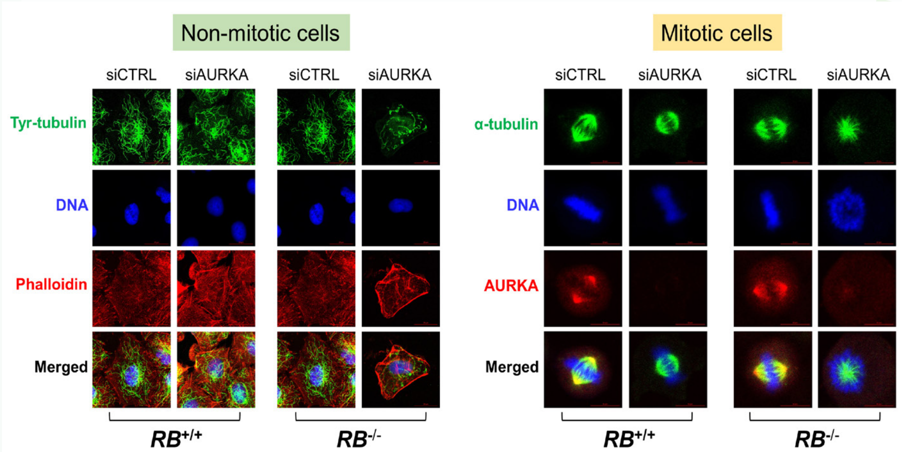
9. Ji, S., Gong, Q., Zhang, W., **Zheng, J.**, Peng, B., and Yang, M. (2020) Recombinant Vibrio Parahaemolyticus Ghosts Protect Zebrafish against Infection by Vibrio Species. *Fish Shellfish Immunol* **107**, 64-72 **[5yr IF = 3.55]**

Article Sharing

New Drug Targets for the Treatment of Lung Cancer

Prof. Joong Sup SHIM and his research team have discovered new drug targets for the treatment of small cell lung cancer (SCLC). The study has opened up a new avenue in the field of SCLC research and has been published in the internationally renowned journal *Nature Communications*.

SCLC is mostly diagnosed in advanced stages, accounting for approximately 20 % of primary lung cancer cases. Effective oncogene drug targets have not yet been discovered, making SCLC difficult to treat. However, Prof Shim and his team have found that RB1-mutant SCLC cells are highly sensitive to the inhibitors of aurora kinase A (AURKA) and microtubule dynamics, and the vast majority of SCLC (up to 90%) has loss-of-function mutations in the tumour suppressor RB1. This type of SCLC could be potentially hypersensitive to AURKA and microtubule dynamics inhibitors. Based on this finding, the team successfully induced cell death in this type of SCLC, providing new promising treatment options for SCLC.



AURKA silencing destabilizes microtubules and induces abnormal mitotic spindle formation in RB1-deficient ($RB1^{-/-}$) lung cancer cells, inducing selective mitotic cell death.

RB1, the first identified tumour suppressor in human cancers, is a key controller of the cell cycle transition. By binding and inhibiting the oncogenic transcription factor E2F, RB1 tightly governs cell cycle progression. Loss-of-function mutations in RB1 cause the activation of E2F-driven gene transcription and uncontrolled cell cycle progression, leading to the cancerous transformation of the cells. RB1 has been found highly mutated in patients with SCLC (~90%). Unlike NSCLC (non-small cell lung cancer), where several oncogene drug targets such as EGFR, VEGF and BRAF have been exploited for targeted cancer therapy, SCLC does not have known drug targetable oncogene drivers. Instead of finding new oncogene drug targets, Prof Shim's team exploited the high level of mutations in the tumour suppressor RB1 to identify druggable targets in SCLC. With this aim in mind, they used synthetic lethality approach to selectively kill cancer cells with RB1 loss.

Through molecular-level and genome-wide studies, the team found that RB1 loss highly increased the expression of the microtubule destabilizer STMN1 in SCLC. The activity of the high level of STMN1 was largely suppressed by AURKA through inhibitory phosphorylation. Inhibiting the AURKA activity in the cells turned this potential weapon (STMN1) into the active form and strongly disrupted microtubule dynamics in RB1-mutant SCLC, causing selective mitotic cell death. These results have been further confirmed in experiments with mice. This study demonstrated potential applicability of the pharmacological inhibitors of AURKA and microtubule dynamics for the treatment of patients with SCLC.

The study was led by Prof. Shim, and FHS' core facilities, including the Genomics, Bioinformatics and Single Cell Analysis Core, and the Animal Research Core, have also made significant contributions to this study. The study was funded by University of Macau (Reg. no. MYRG2017-00176-FHS and MYRG2019-00116-FHS). The full version of the related paper can be viewed at: https://doi.org/10.1038/s41467-020-18872-0

健康科學學院
Faculdade de Ciências da Saúde
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UPCOMING

Oct / Nov

Mon	Tue	Wed	Thu	Fri
19	20 **Oral Defence** Xinwei WU Supervisor: Prof. Ruiyu XIE Time: 9:30 Venue: N6-2022	21 **BCAT Meeting** Speaker: Prof. Kathy LUO Time: 17:00-18:00 Venue: E12-G004	22 **Oral Defence** Xingshun WANG Supervisor: Prof. Wei GE Time: 10:00 Venue: N6-2022 **Oral Defence** Linlin LIU Supervisor: Prof. Wenhua ZHENG Time: 15:00 Venue: N6-2022 **FHS Postdoc/ Student Seminar** Session: Drug Development Host: Prof. Chris WONG and Prof. Jun ZHENG Time: 17:00-18:00 Venue: N22-G002 and Zoom	23 **Oral Defence** Jiankang FANG Supervisor: Prof. Wenhua ZHENG Time: 10:00 Venue: N6-2022
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

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