Publication(s)

1. Wang, L., and **Shen, H. M.** (2020) Seeing Is Believing: A Novel Tool for Quantitating Mitophagy. *Cell Res* **[5yr IF=18.448]**

2. **Miao, K.**, Lei, J. H., Valecha, M. V., Zhang, A., Xu, J., Wang, L., Lyu, X., Chen, S., Miao, Z., Zhang, X., Su, S. M., Shao, F., Rajendran, B. K., Bao, J., Zeng, J., Sun, H., Chen, P., **Tan, K.**, **Chen, Q.**, **Wong, K. H.**, **Xu, X.**, and **Deng, C.** (2020) NOTCH1 Activation Compensates BRCA1 Deficiency and Promotes Triple-Negative Breast Cancer Formation. *Nat Commun* **11** (1), 3256 **[5yr IF=13.811]**

3. Li, J., and **Kwok, H. F.** (2020) Current Strategies for Treating NSCLC: From Biological Mechanisms to Clinical Treatment. *Cancers* **12** (6) **[2018 IF=6.162]**

4. Liu, J., Li, X., Zhou, G., Sang, Y., Zhang, Y., Zhao, Y., **Ge, W.**, Sun, Z., and Zhou, X. (2020) Silica Nanoparticles Induce Spermatogenesis Disorders Via L3MBTL2-DNA Damage-P53 Apoptosis and RNF8-ubH2A/ubH2B Pathway in Mice. *Environ Pollut* **265** (Pt A), 114974 **[5yr IF=6.152]**

5. Ma, R., Ren, Z., Li, B., Siu, S. W. I., **Chen, G.**, and **Kwok, H. F.** (2020) Novel Venom-Based Peptides (P13 and Its Derivative-M6) to Maintain Self-Renewal of Human Embryonic Stem Cells by Activating FGF and Tgfbeta Signaling Pathways. *Stem Cell Res Ther* **11** (1), 243 **[5yr IF=5.363]**

6. Li, W., Yang, Y., An, F. R., Zhang, L., Ungvari, G. S., Jackson, T., **Yuan, Z.**, and **Xiang, Y. T.** (2020) Prevalence of Comorbid Depression in Schizophrenia: A Meta-Analysis of Observational Studies. *J Affect Disord* **273**, 524-531 **[5yr IF=4.16]**

Article Sharing

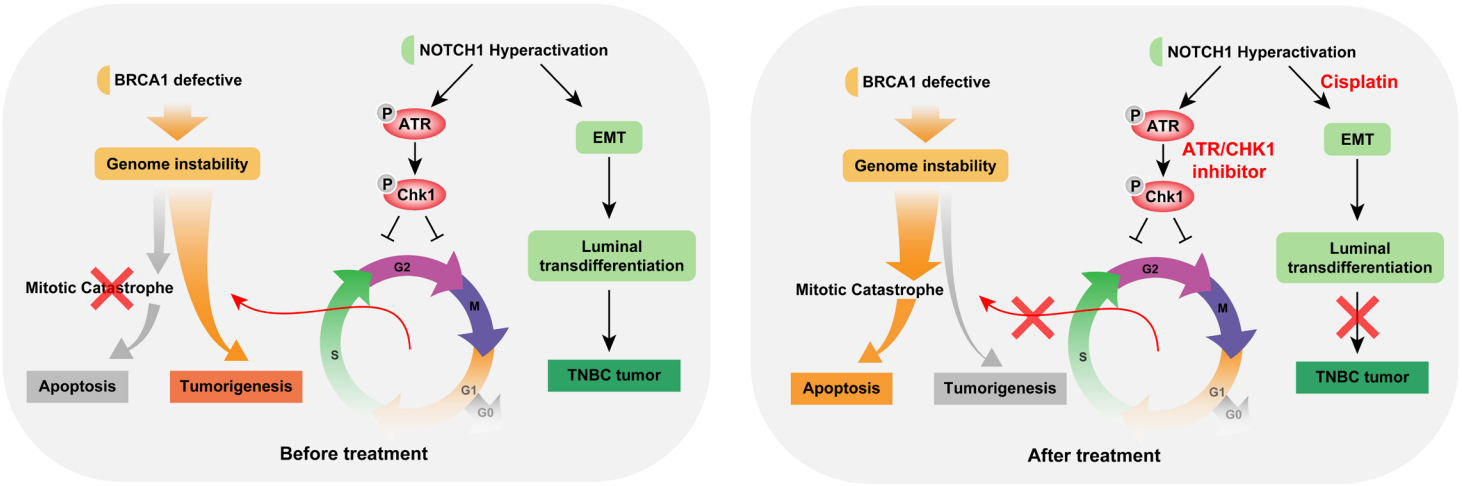
The New Discovery of Prof. Chuxia DENG's Research Team in the Study on BRCA1 Provides a Potent Clinical Strategy for Treating Triple-negative Breast Cancer

A research team led by Prof. Chuxia DENG has made a new progress in breast cancer study by finding that NOTCH1 activation can promote the growth of triple-negative breast cancer (TNBC). The study titled "NOTCH1 Activation Compensates BRCA1 Deficiency and Promotes Triple-Negative Breast Cancer Formation" has been published in the renowned journal *Nature Communications*.

The research team found that NOTCH1 activation rescues BRCA1 deficiency and promotes TNBC formation. Drugs targeting NOTCH1 regulated pathways can effectively inhibit the growth of TNBC. This mechanism may explain the discrepancies regarding the role of NOTCH1 as a tumor suppressor or an oncogene, i.e. under some other conditions, such as when tumor has intact DNA damage repair machinery or cell cycle checkpoints, the activation of ATR-CHK1 signaling by NOTCH1 should inhibit cell cycle progression and elicit its tumor suppressor functions to block the tumor development. More importantly, this finding provides potent druggable targets for TNBC.

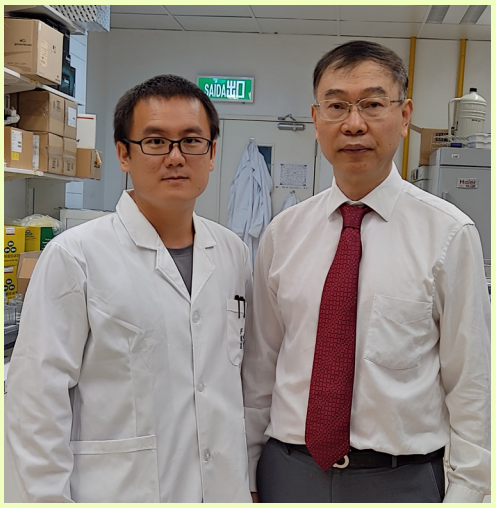
Breast cancer gene 1 (BRCA1), is the first identified breast cancer susceptibility gene, and is responsible for hereditary breast cancers. Inherited mutations in the BRCA1 gene predispose carriers to early-onset tumourigenesis and an up to 87% cumulative lifetime risk of developing breast cancer and/or ovarian cancer. Moreover, approximately 48% to 66% of BRCA1 mutation carriers develop triple-negative breast cancer (TNBC). TNBC is a cancer that tests negative for estrogen receptors (ER), progesterone receptors (PR), and HER2 protein. It is considered to be aggressive, unresponsive to hormonal therapy and has a poor prognosis.

BRCA1 is crucial for multiple biological processes, including DNA damage repair, cell cycle checkpoints, ubiquitination, and transcriptional regulation. Studies have demonstrated that absence of BRCA1 leads to genome instability, then initially triggers the lethal block by inducing mitotic catastrophe and apoptosis. By using the Sleeping Beauty transposon system in Brca1-deficient mice, the research team identified 169 putative cancer drivers, among which Notch1 is a top candidate for accelerating TNBC. They found that activation of NOTCH1 plays at least two important functions in BRCA1 associated tumorigenesis: 1) it accelerates TNBC formation through promoting epithelial-mesenchymal transition (EMT); and 2) through a non-canonical target ATR-CHK1 axis, it restores S/G2 and G2/M cell cycle checkpoints, which are impaired due to Brca1 deficiency, to suppress the mitotic catastrophe, and thus benefits BRCA1 associated tumorigenesis. To cure TNBC, the researchers tested the combined treatment of targeting the NOTCH1 non-canonical target ATR-CHK1 cascade and the EMT, which are downstream of NOTCH1 signaling based on the mechanism they uncovered. The results demonstrated that the combination of cisplatin and ATR-CHK1 inhibitors effectively inhibits TNBC through rebooting the mitotic catastrophe, providing a potential therapeutic strategy for this deadly disease.



The molecular mechanism of NOTCH1 promoting BRCA1-related triple negative breast cancer and its targeted therapy

The study was led by Prof. DENG, and Research Assistant Professor Kai MIAO is the first author. Prof. Xiaoling XU and Prof. Koon Ho WONG also made important contributions to this study. The study was supported by the Science and Technology Development Fund, Macau SAR (FDCT) [Reference no.: 0094/2015/A3, 0011/2019/AKP, 0034/2019/AGJ, 0048/2019/A1, 0029/2017/A1, 0101/2018/A3, and 0111/2017/A] and UM's research fund [Reference no.: MYRG2016-00139-FHS and MYRG2018-00186-FHS]. The full version of the related paper can be viewed at: https://doi.org/10.1038/s41467-020-16936-9



PhD Oral Defence

PhD Oral Defence by Qingyu ZHANG of Prof. Leo LEE's group

Mr. Qingyu ZHANG supervised by Prof. Leo LEE completed his PhD oral defence on 22 June. His thesis title is "Lipid Profile Reprogramming in the Regulation of Ovarian Cancer Peritoneal Metastasis".

Mr. Zhang reported that ovarian cancer is characterized by metastasis to the peritoneal cavity. He found that the effect of ANGII was mediated by the increase in Stearoyl-CoA desaturase-1 (SCD1) expression and resulted in Endoplasmic Reticulum stress alleviation in multicellular spheroids, and this mechanism explained that Angiotensin II receptor type 1(AGTR1) predicated poor clinical outcomes in patients. He further found that the Acyl-CoA synthetase long-chain family member 1 (ACSL1) can transform the lipid profile of non-metastatic cells to high-metastatic cells. This resulted an increase in 14-carbon phospholipid in both HM cells and ACSL1-overexpressing cells. He also found that Src was activated by increasing the Src myristoylation with overexpression of ACSL1 and the treatment with MA. He concluded that his results highlighted the importance of fatty acid metabolic reprogramming in ovarian cancer metastasis.

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UPCOMING

Jun / Jul 2020

	Mon	Tue	Wed	Thu	Fri
28	29	30 **Oral Defence** Chang CHEN Supervisor: Prof. Douglas ZHANG Time: 15:00 Venue: N6-2022	Jul 1 **Oral Defence** Menglei ZHANG Supervisor: Prof. Gary WONG Time: 10:00 Venue: N6-2022 **BCAT Meeting** Speaker: Dr. Li WANG Time: 17:00-18:00 Venue: E12-G004	2 **Oral Defence** Wenwang RAO Supervisor: Prof. Yutao XIANG Time: 10:00 Venue: N6-2022	3
5	6	7	8	9 **FHS Postdoc/ Student Seminar** Field: Stem Cell Host: Prof. Ren-He XU and Prof. Guokai CHEN Time: 17:00-18:00 Venue: N22-G002 and Zoom	10 **Qualifying Exam** Wen LI Supervisor: Prof. Yutao XIANG Time: 10:00 Venue: E12-4004
12 **Oral Defence** Renbo DING Supervisor: Prof. Chuxia DENG Time: 10:00 Venue: E12-1017	13	14	15 **BCAT Meeting** Speaker: Prof. Xuanjun ZHANG Time: 17:00-18:00 Venue: E12-G004 **Oral Defence** Jin ZOU Supervisor: Prof. Jun ZHENG Time: 10:00 Venue: N6-2022	16 **Oral Defence** Wenwen ZHANG Supervisor: Prof. Jun ZHENG Time: 10:00 Venue: N6-2022	17 **Oral Defence** Yu JIN Supervisor: Prof. Yutao XIANG Time: 15:00 Venue: N6-2022
19	20	21	22	23 **FHS Postdoc/ Student Seminar** Field: Cancer Research Host: Prof. Gang LI and Prof. Ruiyu XIE Time: 17:00-18:00 Venue: N22-G002 and Zoom	24

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