

Publication

1. Yuan, G., Flores, N. M., Hausmann, S., Lofgren, S. M., Kharchenko, V., Angulo-Ibanez, M., Sengupta, D., Lu, X., Czaban, I., Azhibek, D., Vicent, S., Fischle, W., Jaremko, M., Fang, B., Wistuba, II, Chua, K. F., Roth, J. A., Minna, J. D., **Shao, N. Y.**, Jaremko, L., Mazur, P. K., and Gozani, O. (2021) Elevated NSD3 Histone Methylation Activity Drives Squamous Cell Lung Cancer. *Nature* [5yr IF = 46.486]
2. Li, W., Yang, Y., Zhang, Q., Zhang, L., Cheung, T., Ng, C. H., and **Xiang, Y. T.** (2021) Progress in Mental Health Research and Service Provision in China: Lessons Learnt from COVID-19 and Sars Epidemics. *Lancet Reg Health* **7**, 100076

1 Article Sharing

FHS and Stanford's Collaboration Achieves Breakthrough in Lung Cancer Research



FHS and MD Anderson Cancer Center of Stanford University have achieved a breakthrough in their collaborative lung cancer research. The research team has found that the gene NSD3 is involved in the tumourigenesis of squamous cell lung cancer, and that NSD3 may be an effective target for the treatment of this type of cancer. This is a

landmark discovery and the study has been published in the prestigious journal *Nature*.

There are two types of lung cancer: small cell lung cancer and non-small cell lung cancer. The latter mainly includes adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. Non-small cell lung cancer grows and metastasises more slowly than small lung cancer. However, only about a quarter of early-stage cases can be treated with surgery, and metastasis or recurrence may still occur after surgery. So, there is still much room for improvement in the treatment of lung cancer.

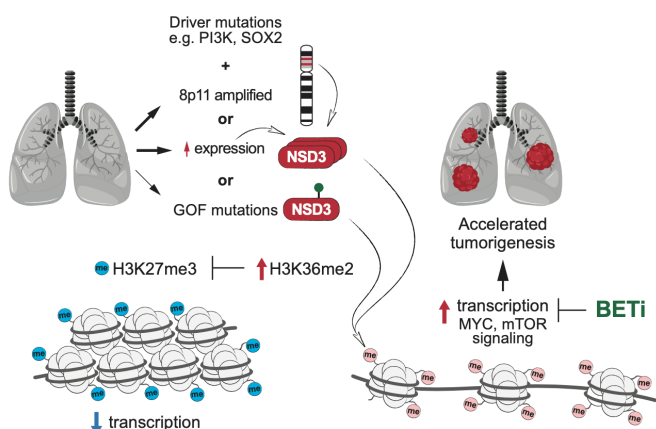
In this study, a joint team formed by researchers at Stanford University's Department of Biology, MD Anderson Cancer Center, and FHS, has uncovered an intrinsic molecular regulatory pathway by which NSD3 promotes lung squamous cell carcinoma tumourigenesis. The discovery of this mechanism overturns previous speculation that chromosome 8 identifies the cancer driver

gene and, more importantly, provides a new potential therapeutic target for the treatment of lung squamous cell carcinoma. In previous studies of lung squamous cell carcinoma, amplification of specific regions of chromosome 8 was found to promote the tumorigenesis of lung squamous cell carcinoma. Initially, the primary candidate driver gene was the FGFR1 protein, but the clinical trials attempting to target the FGFR1 protein were unsuccessful.

In this study, the researchers found that the H3K36 methyltransferase, NSD3, is also

located in this region of chromosome 8. Using mice as the model organism, the knockdown of NSD3 slowed tumour growth and prolonged survival in mice. The researchers also identified a genetic variant in NSD3, which is common in patients with this type of tumour, increasing the catalytic activity of H3K36 dimethylation both *in vitro* and *in vivo*. This variant accelerated tumorigenesis and decreased overall survival in the mouse model. This variant induced the landscape change in the epigenetics and promoted oncogenic gene expression programming. This study also revealed that NSD3-dependent tumors might be sensitive to bromodomain inhibitors with potential clinical value.

The study was led by Prof. Gozani OR in the Department of Biology, Stanford University, with Prof. Ningyi SHAO as the co-corresponding author. The study was supported by the FDCT (File No: FDCT 0038/2020/AFJ) and UM (File No: SRG2019-00177-FHS). A full-text version of the study is available at <https://www.nature.com/articles/s41586-020-03170-y>.



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

2 News

UM Scholars Publish Study on Mental Health Status of Macao Residents in Later Stage of Epidemic

UM and Kiang Wu Nursing College of Macau (KWNC) held a press conference to announce the results of an earlier survey on the mental health status of Macao residents during the



later stage of the COVID-19 epidemic on 5 February. According to the study, the majority of Macao residents surveyed were in a stable mental state during the later stage of the epidemic and did not experience significant mental health symptoms. The research team reminds the public that the challenges associated with the epidemic are still significant, and that they should still pay attention to various emotional and mental health changes, and actively seek professional treatment when necessary.

Jointly conducted by UM FHS and Faculty of Education (FED), as well as KWNC, the study is part of a national survey initiated by the National Clinical Research Center for Mental Disorders. During the press conference, FHS Prof. Yutao XIANG, FED Prof. Alice Si Man LEI, and KWNC Prof. Grace Ka In LOK presented the results of the survey. The press conference was moderated by Elvo Kuai Long SOU, head of the Student Counselling Section, Student Affairs Office, UM.

The survey was conducted online between August and November in 2020 using self-administered assessment tools commonly used in epidemiological surveys on mental health problems, such as symptoms of depression, anxiety, insomnia, and fatigue. In the end, a total of 1,005 residents completed the assessments. The results showed that 58.0 per cent of the participants were very concerned about COVID-19 related information, and 75.3 per cent self-identified as strictly enforcing personal precautions. Additionally, 70.1 per cent reported that the epidemic had a moderate to severe impact on their daily lives, and 7.7 per cent experienced great economic losses. In terms of mental health, 11.5 per cent and 6.3 per

cent reported that they experienced moderate to severe symptoms of depression and anxiety, respectively. Furthermore, during the later stage of the epidemic, 26.4 per cent reported experiencing moderate to severe fatigue, and 6.4 per cent experiencing moderate to severe insomnia symptoms.

Through multivariate analyses, UM scholars have found that participants who were not concerned about the epidemic information or had great economic losses because of the epidemic, as well as those who were single or felt that the epidemic had a great impact on their daily lives, were more likely to suffer from symptoms of depression, anxiety, and/or insomnia. Moreover, compared to their male counterparts, female participants were more likely to experience anxiety or insomnia. The study has also found that most of those who experienced symptoms of depression, anxiety, or insomnia were not inclined to seek help from mental health services. Only 27.6 per cent – 39.1 per cent of the participants said they had tried to seek mental health help through hotlines, the internet, medical institutions, or other types of services.

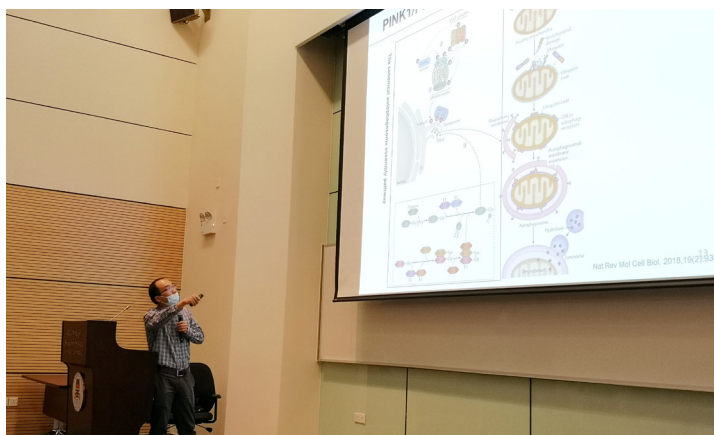
Based on these findings, the team concluded that the overall mental health status of those surveyed was stable during the later stage of the epidemic, but as many other countries and regions are still deeply affected by the epidemic, Macao residents are still facing—and will continue to face for some time in the future—many challenges arising from the epidemic. Therefore, the public should actively respond to the World Health Organization's call to pay attention to the various emotional and mental health changes that might occur during the epidemic, and seek professional treatment timely when they

experience mental health problems. In addition, the relevant service providers should receive professional training as soon as possible, in order to identify mental health problems of help-seekers at an early stage and then provide appropriate assistance. At the same time, residents can consider engaging in regular and suitable physical activities during the epidemic, which can help maintain good physical health and a stable mood, as well as

improve insomnia. The UM team also called for more publicity and promotion of mental health services, and the popularization of knowledge on mental and psychological health maintenance, psychological counselling, and crisis intervention, in order to minimize the negative impacts of the epidemic on people's mental and psychological health and socio-economic development.

3 Seminar Series

BRCA1, a Tumor Suppressor, Functions from Nucleus to Cytoplasm – Dr. Qiang CHEN



Dr. Qiang CHEN presented “BRCA1, a Tumor Suppressor, Functions from Nucleus to Cytoplasm” on 3 February.

Dr. Chen introduced that the breast cancer susceptibility gene 1 (BRCA1) is a major tumor suppressor gene, and is most frequently mutated in hereditary breast

cancer. BRCA1 plays a critical role in many biological processes, especially maintaining genomic stability in the nucleus, yet its role in the cytoplasm remains elusive. He reported his recent study about the novel function of BRCA1 in mitophagy in the talk. He shared that mitophagy, a specialized autophagy pathway that mediates the clearance of damaged mitochondria by lysosomes, is important for mitochondrial quality control. His study has revealed that BRCA1 maintained mitophagy activity through regulating mitochondrial dynamics, including fission and fusion. With the mitochondrial stress, BRCA1 was recruited to the mitochondrial outer membrane and promote mitochondrial fission through ATM-AMPK-DRP1 pathway. However, BRCA1 deficiency has impaired the stress-induced mitophagy and has triggered NLRP3 inflammasome activation, which has created a tumor-associated microenvironment, thereby facilitating tumor proliferation and metastasis.

4 FHS Postdoc Student Seminar

Presented by Prof. Hongjie ZHANG's group and Prof. Wenhua ZHENG's group

On 4 February, Mr. Xiaoxiang CHENG of Prof. Hongjie ZHANG's group presented "Role of Rike-1 in Intestinal Morphogenesis and Proteostasis in *C. elegans*." and Mr. Yizhou JIANG of Prof. Wenhua ZHENG's group presented "Aripiprazole Extends the Lifespan of *C. elegans* through a Dietary Restriction-like Mechanism".

The next seminar will be held on 18 February, and presented by the group member of Prof. Terence POON and Prof. Ningyi SHAO via Zoom again.



UPCOMING EVENTS

February	
Mon 8 <u>Oral Defence</u> Li ZHANG Supervisor: Prof. San Ming WANG Time: 15:00 Venue: E12-1015	15 Compensatory rest day
Tue 9	16 Compensatory rest day
Wed 10 <u>BCAT Meeting</u> Speaker: Prof. Gang LI Time: 17:00-18:00 Venue: E12-G004	17 <u>BCAT Meeting</u> Speaker: Prof. Joong Sup SHIM Time: 17:00-18:00 Venue: E12-G004
Thu 11 Holiday (p.m.) - Exemption from work	18 <u>FHS Postdoc/ Student Seminar</u> Session: Data Science Host: Prof. Terence POON and Prof. Ningyi SHAO Time: 17:00-18:00 Venue: N22-G002 and Zoom
Fri 12 Holiday - Lunar New Year	19