

TIME SPOT LIGHT

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Remedy found for cancer drug resistance!

*Collaborative research between
TMU and UCSF featured in Nature Cancer*

The discovery of PD-1, an immune checkpoint, has recently revolutionized cancer treatment. An international research team from Taipei Medical University (TMU) and the University of California, San Francisco (UCSF), has cleared the upcoming hurdle in cancer treatment: the “death checkpoint.” The team achieved this by finding the cause of drug resistance in cancer patients and developing a gene therapy, which is expected to be combined with chemotherapy or immunotherapy in the future to significantly improve the efficacy of treatment by more than 90%. The team’s research has not only yielded exciting results, but it is also the first of its kind in Taiwan to be published in *Nature Cancer*, a top international journal.

The incidence of cancer is increasing year by year, and it is urgent to provide effective treatment to patients, but modern medicine is hardly helpful in combating highly drug-resistant cancers such as pancreatic cancer. An international research team led by Professor Kun-Chih Tsai of TMU and Professor Valerie Weaver of the UCSF, has made a breakthrough discovery in identifying the root cause of drug resistance: the “death checkpoint.” This is another breakthrough discovery related to cancer drug resistance research, following the 2018 Nobel Prize discovery on the immune checkpoint, and was just published in June 2022 in the top international journal, *Nature Cancer*.

Dr. Tsai, a professor at the Graduate Institute of Clinical Medicine of College of Medicine and director of the Clinical Research Center of Wan Fang Hospital, pointed out that traditional chemotherapy can only inhibit about 30% of the growth of cancers, and immunotherapy, which has emerged in recent years, is effective only for about 15% of patients. The team found that cancer

cells have a self-protective “death checkpoint” mechanism, and the NCOR2 protein in the patient’s body inhibits message transmission, making the cancer resistant to chemotherapy, radiation therapy and immunotherapy, and how to crack the “death checkpoint” mechanism will greatly affect the effectiveness of cancer treatment.

Drawing on the research results, the research team of TMU has further developed an innovative gene therapy that can effectively overcome drug resistance. Dr. Tsai explained that mouse experiments showed that combining the innovative gene therapy with existing treatment modalities, such as chemotherapy and immunotherapy, can significantly improve the efficacy of treatment of breast cancer and pancreatic cancer by over 90%.

According to Dr. Tsai, more than 70% of solid tumors are drug-resistant before they are treated, and they not only fail to respond to chemotherapy, but are also insensitive to the immune cells naturally generated in or externally administered to the body. Using next-generation gene sequencing and protein array analysis, the research team compared drug-resistant and drug-sensitive “patient-derived organoids” cultured from fresh human tumors and found that an epigenetics regulation mechanism consisting of NCOR2 and HDAC3 proteins inhibits the information transmission network associated with cell death and inflammation after cancer cells receive chemotherapy or are attacked by immune cells, thus closing the pathway of cancer cell death. This mechanism, or the “death checkpoint,” is one of the most important factors in the failure of chemotherapy or immunotherapy for all types of solid cancers.

Excitingly, based on this breakthrough discovery, the team has further developed the “decoy of NCOR”—an advanced cancer gene therapy that can effectively overcome the “death checkpoint.” Dr. Tsai said that the decoy of NCOR2 delivered to the nucleus of cancer cells as a viral carrier can compete with NCOR2 and release the cell death and inflammation messaging that was inhibited by the protein, which means that the messaging can work properly, and cancers with drug-resistant cancer cells including pancreatic cancer, breast cancer or brain cancer will be able to respond to chemotherapy or immune cells again, allowing cancer patients to be treated effectively. The research team has confirmed, by using a highly clinically relevant humanized animal experiment where fresh human tumor tissues are implanted into mice in an animal model closely simulating the real tumor state, that this decoy of NCOR2 gene therapy can significantly enhance the efficacy of chemotherapy or anti-PD1 immunotherapy for breast cancer to over 90%, and also suppress the recurrence rate of most tumors.

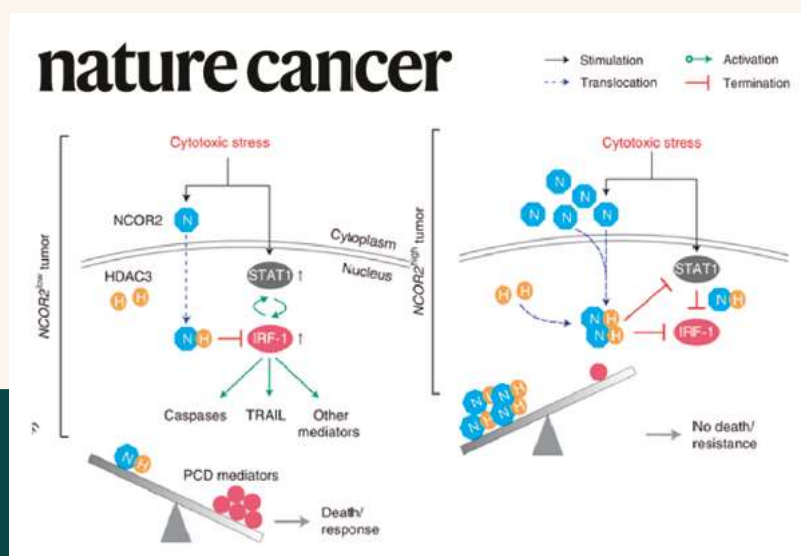
During this collaborative research, TMU and the UCSF held online meetings frequently to discuss and share research progress and executed a clear division of labor to speed up their research process. For example, animal experiments on gene-transferred mice and cancer tissue culture and testing were conducted by the UCSF team, so that the TMU team was able to conduct biochemical and molecular experiments more efficiently, including the ensuing development of a gene therapy. The synergy of the two excellent teams has created a win-win situation for both sides. 🤝



President Chien-Huang Lin (third from left), General Consultant Hong-Nerng Ho (second from left), and the research team at Taipei Medical University; right to left in the back screen: Prof. Valerie M. Weaver, Dr. Jonathan Laskin, and Dr. Jason Northey.



Dr. Kun-Chih Tsai explains the “Death Checkpoint” to the attendants and reporters.



Original Research Article: Screening of organoids derived from patients with breast cancer implicates the repressor NCOR2 in cytotoxic stress response and antitumor immunity

TMU and Imperial College London conducts cross-country and cross-disciplinary research to track abnormal driving

College of Medicine, and College of Biomedical Engineering of Taipei Medical University (TMU) and Department of Civil and Environmental Engineering of Imperial College London initiated a number of international cross-field research collaborations in early October 2022. The two parties hope to improve road traffic safety and promote the well-being of road users through the combination of engineering technology and medical research.

This research takes professional drivers as the research object and will develop IoT wearable devices to track and assess the degree of sleep disorders, and incorporate environmental factors, such as air pollution and other common risk factors that affect cognitive function into the overall assessment of drivers' physical and mental wellness. It is hoped that by tracking the health status of professional drivers, road traffic accidents can be prevented in advance. The preliminary plan is to investigate the subject from multiple levels, such as sleep breathing sound monitoring, the relationship between environmental pollution on cognitive function and sleep disorders, abnormal behavior of professional drivers, and sleep disorders.

The Cooperation Letter of Intent was signed in June of this year via the zealous efforts by an alumnus of TMU, Cheng-Yu Tsai, who is a recipient of the Ministry of Education's Scholarships for Taiwanese Studying in the Focused Fields at Top Universities and is currently enrolled in a doctoral program at Imperial College London. The online signing in the U.K. was witnessed by Cheu-An Bi, the director of the Education Division, Taipei Representative Office in the U.K. from the Ministry of Education. The colleges of the two universities are



Beginning in October 2022, the University and Imperial College London launched plans to implement sleep disorder assessments, monitor environmental exposure, and record heart rates and behavior while driving for professional drivers to develop an abnormal driving tracking system.

to cooperate on projects such as student exchange, international research, industry-academic innovation, and interdisciplinary education in medicine and technology engineering, and will also co-organize workshops and seminars on a regular basis.

Professor Han-Pin Kuo, Dean of College of Medicine, said that with the development of technology, the medical field is beginning to see the need to combine with cutting-edge technologies, such as artificial intelligence in medicine and medical wearable devices. Through this collaboration with Imperial College London, TMU hopes to take this opportunity to connect with international cutting-edge education. By signing this Letter of Intent, both parties will carry out substantive research cooperation, allowing students of TMU to immerse themselves in an international educational environment and acquire cross-disciplinary knowledge in medical technology and engineering.

Professor Jiunn-Horng Kang, Dean of College of Biomedical Engineering, said that College of Biomedical Engineering, as a relatively young college in TMU, has an open and positive attitude toward the diversity of educational and research cooperation, and has robust research momentum and industrial innovation capabilities. This cooperation between the two universities will certainly cultivate more diversified international talents and create globally competitive industrial and academic technologies.

The head of the Department of Civil and Environmental Engineering at Imperial College London, Professor Washington Yotto Ochieng, echoed the view that with environmental change and technological development, there is an urgent need for collaboration between civil engineering and medicine, such as the investigation and prevention of health hazards caused by environmental pollution; cross-disciplinary cooperation can bring solutions to related problems in society. Through this collaboration, not only will the School of Civil and Environmental Engineering make tangible progress in cross-disciplinary research, but the collaboration with TMU in medicine will also leverage its strengths and enable the industry's innovation capabilities to exert their synergistic effects.

Mr. Cheu-An Bi, Director of the Education Division, Taipei Representative Office in the U.K. from the Ministry of Education, expressed his expectation for this international cooperation. Taiwan has been

actively promoting international industry-academic cooperation in recent years, and the Ministry of Education has continued to promote a number of programs to support international cooperation. In addition to being a global leader in the information and communications industry, Taiwan hopes to promote its medical field to the world as well. TMU alumnus Cheng-Yu Tsai, a doctoral student who participated in this research project, said that he was honored to participate in the academic cooperation between the top universities in Taiwan and the U.K., which is very exciting and he cherishes this opportunity. He also hopes that through this rare international collaboration, he will be able to enrich and improve his own abilities and share his research knowledge acquired in the U.K. with the academic community in Taiwan in the future. 🇹🇼



TMU online signing representatives, from left: Prof. Chun-Jen Huang, Associate Dean of the College of Medicine, and Prof. Han-Pin Kuo, Dean of the College of Medicine, Prof. Jiunn-Horng Kang, Dean of the College of Biomedical Engineering, and Associate Dean, Prof. Thierry Burnouf.



Mr. Cheu-An Bi, Director of the Education Division, Taipei Representative Office in the U.K. from the Ministry of Education (left), and Prof. Washington Yotto Ochieng, head of the Department of Civil and Environmental Engineering at Imperial College London (right).

Non-nutritive sweeteners may increase the risk of premature birth

Talk by Professor Shih-Min Hsia from the School of Nutrition and Health Sciences, College of Nutrition



Prof. Shih-Min Hsia



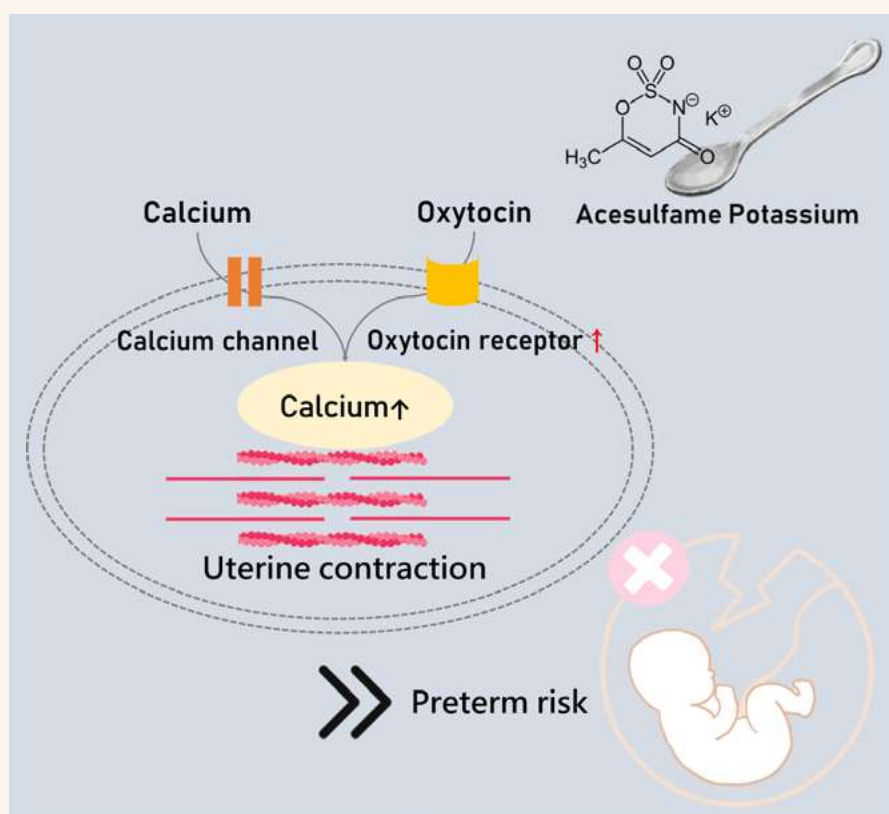
Supported by the National Science and Technology Council provided through integrated project funding, Professor Shih-Min Hsia's research team at the School of Nutrition and Health Sciences of Taipei Medical University has found a potential relationship between long-term exposure to the non-nutritive sweetener acesulfame potassium and uterine hypercontraction, particularly those induced by oxytocin, and reported the discovery in Molecular Nutrition and Food Research. In the study, it was demonstrated that an excessive intake of non-nutritive sweeteners containing acesulfame potassium may cause uterine hypercontraction and increase preterm risk, suggesting that pregnant women should avoid long-term consumption of processed foods containing artificial sweeteners.

Along with the development of the food industry, the demand for sugar has been gradually increasing. Due to their high level of sweetness and low cost, non-nutritive sweeteners are often used in the food industry as food additives. Previous studies have shown the consumption of non-nutritive sweeteners to be associated with a 1.2-fold increase in preterm births and a reduction in the gestational period by 0.11 weeks, but the effect of acesulfame potassium exposure on uterine contraction in pregnant women has not yet been studied.

Uterine hypercontraction is significantly triggered by the influx of calcium ions or oxytocin signaling pathway, which causes the contraction of uterine muscle bundles. The medical conditions caused by uterine hypercontraction include preterm labor risk, endometriosis, and menstrual pain, and consequent inflammatory responses can result in the secretion of cytokines and the aggravation of oxidative stress, which may lead to menstrual discomfort and a deterioration in life quality for women.

In the study, it was revealed that exposure to acesulfame potassium caused an upsurge in the concentration of calcium ions in uterine smooth muscle cells and calcium ion influx, which resulted in an increase in uterine contractions. In a long-term exposure experiment, the subjects were fed daily with an amount of acesulfame potassium equivalent to that contained in two cans of Coca-Cola Zero, as well as a tolerable daily intake via oral gavage for 8 weeks. The results showed that acesulfame potassium increased intrauterine pressure and oxytocin-induced contractions. In a further clinical collaboration, it was found in a cohort study that pregnant women with higher exposure to acesulfame potassium had a higher risk of preterm birth.

This study was the first to investigate the influence of non-nutritive sweeteners on pregnant women and confirm their effect on uterine hypercontraction with scientific evidence, alerting people with their life quality affected by uterine hypercontraction, such as those with menstrual pain, endometriosis, and pregnancy to the risk of long-term consumption of non-nutritive sweeteners. 🍷



The effects of exposure to the non-nutritive sweetener acesulfame potassium on the risk of preterm birth due to uterine hypercontraction and the calcium signaling pathway

Original research article: Consumption of Artificial Sweetener Acesulfame Potassium Increases Preterm Risk and Uterine Contraction with Calcium Influx Increased via Myosin Light Chain Kinase–Myosin Light Chain 20 Related Signaling Pathway

TMU College of Public Health organized workshops in remote villages to promote cultural understanding

The Master Program in Global Health and Development of College of Public Health held the Tribe Natural Walking Workshop in Hsinchu County's Jianshih Township Atayal indigenous community. The workshop enabled students to gain an understanding of the medical, cultural, and agricultural aspects of Atayal Indigenous and to observe primary health care in this local indigenous community. In addition to understanding how COVID-19 affects primary health care, the workshop also serves the purpose of an international exchange of ideas.

Jianshih's indigenous community has a unique demographic structure and scarce medical resources due to its geographical constraints. After visiting the elderly health center, students learned that most of the local elders who develop health conditions have to rely on doctors stationed in other indigenous communities, and in case of emergencies, there may be delays in seeking medical treatment owing to long travel times. The local health center not only offers medical assistance, but also plays an important social support role by acting as a venue for local elders to interact with each other while having daily meals.



Foreign students pay a visit
to a local health center

The development of local agriculture involves the connection between generations of indigenous families. Millet was a common agricultural product among Taiwan's Indigenous tribes, but the number of farmers growing millet has gradually declined with the passage of time. Recently, the revival of millet farming, promoted by the younger generation, has led to a connection between the younger and older generations. At the same time, this sharing brings up the link of tribal heritage and even stimulates the psychological and physical health of local elders.



Foreign students experience the history of Taiwan's Indigenous agricultural development and millet farming

TMU international students took part in the Tribe Natural Walking Workshop to learn about local primary health care, and cultural and agricultural aspects of the Atayal. With the revival of millet farming as well as the primary health care to be improved, the workshop was held in the hopes that this experience will serve as a reference for foreign students in the development of primary health care in their home countries. 🌾



Foreign students from College of Public Health in the indigenous community of Jianshih Township, Hsinchu County



MOFA-sponsored New Southbound Program participants learn medicine, sample culture, and volunteer to beautify Fulong beach

Taiwan may be known as the beautiful island of Formosa, but like other industrialized nations, pollution can be an issue. That's why TMU's Graduate Institute of Mind, Brain and Consciousness (GIMBC) has been holding monthly beach cleanup activities. Last month's event near Fulong beach was attended by students from Southeast Asia as part of a MOFA-sponsored short-term study program.

Newly implemented this year through the Office of Global Engagement (OGE), the study program welcomes students from across the New Southbound Policy area to experience education in Taiwan first-hand. As one of Taiwan's premier providers of healthcare education, TMU is one only of three institutions in Taiwan presently providing this short-term study opportunity.

Nguyen Le Thao Nguyen, an MD from Vietnam, is one of 15 recent graduates who seized the chance to study in Taiwan under the New Southbound program. Other students joined the program from Vietnam, Indonesia, and the Philippines. They come from different fields of expertise in medicine, but share a common excitement about study and research at TMU.

"TMU is really famous, the course list has some of my favorite subjects, and I wanted to study [at a higher level], so there was a research chance for me," Nguyen said.

For New Southbound students, coming to a new country with unfamiliar cultural and classroom dynamics could at times seem daunting. But, says Jamaica Mae Calag, MD, from the Philippines, Taipei's safe streets and convenient transportation, as well as welcoming, open-minded professors, and TMU's small class sizes soon put students at ease.

"Professors are really able to guide every student, and information easily gets to us. I'm having such a good time here," she said.

Schedules, New Southbound students agree, are comprehensive. Besides credit classes during the day, they attend Chinese language courses in the evenings and OGE-organized extracurricular activities on weekends, such as visiting hot springs, night markets, and the National Palace Museum. Getting as many experiences as possible into a five-month program borders on being hectic, but the challenge has so far been rewarding.

"I think it's great that we've been exposed to the cultural diversity [of Taiwan]," says Al-Nasser Hassan Jumail, a nurse from the Philippines. "We get a chance to broaden our minds and mindsets."

While many activities so far have been more on the "tourist" side, the Fulong beach cleanup changed things up. The beach is located along Taiwan's north coast a little over an hour's drive from Taipei, and idiosyncrasies of winds and tides means

the vicinity experiences a buildup of debris. Hauling off as much of it as possible in a half-day trip was where TMU's New Southbound students came in, with, in the words of Dr. Era Catur Prasetya, who's taking neuroscience classes after ten years as a lecturer and Psychiatrist in Indonesia, a "responsibility" – and several dozen giant garbage bags. It was also a way to give a little something back.

"We received a lot from Taiwan," said Nguyen, "so we can do a little bit to contribute, too."

For this year's New Southbound students, and for MOFA and TMU, the Fulong beach cleanup went beyond beautifying one of Taiwan's beaches. It was part of a broader bonding experience, one that takes advantage of Taiwan's position as a "bridge" between Southeast Asia and the West, and builds relationships at personal, environmental, and intersocietal levels.

"I not only found new knowledge, I see also that we can develop new practice with this knowledge," Says Dr. Prasetya. "[The program] has been a new experience, a new hope." 🙏



Wonderful Indonesia: Promote Nusantara culture, friendship, and cooperation

Indonesia Cultural Festival by Indonesian Students in Taipei

Source of Article: Indonesian Student Association at TMU

On December 26th, Indonesian Student Association at Taipei Medical University (PPI TMU) held their first cultural event “Wonderful Indonesia” on campus from noon to night. They introduced Indonesian arts and culture and strengthened friendships with local citizens.



Wonderful Indonesia featured with Food Bazaar and Cultural Night. Food Bazaar was started at noon while Indonesian students presented variety of Indonesian food such as rendang rice, chicken satay, pempek, and snacks like klepon, lupis, and getas. Throughout the night, Indonesian students showcased their folk songs and traditional dancing to the audience. All performers wore traditional Indonesian Batik clothing, which is a characteristically Indonesian cultural heritage.

“Cooperation and friendship are our keywords here, and this cultural event encourages all of that,” said Novrizal, IETO Taipei’s Indonesian Citizen Protection and Socio-Cultural Information Division official. The Wonderful Indonesia event reflects the importance of exploring diversity and culture, which is also a thing that the University keeps encouraging students and faculty to do.

The Chairperson of PPI TMU 2022/2023, Kamaluddin Latief, appreciated the participants who attended the festival and said that Indonesian students were always ready to promote Indonesian culture. “The Indonesian Student Association is

ready to collaborate in the social, scientific, and other fields in the future. This event enlarges our mission to emphasize and promote our culture worldwide,” he said. 🇮🇩





TMU Spotlight showcases impressive outcomes from our partnership collaboration, research excellence, talent development, and the University's commitment to making a positive social impact.

