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China Medical University's Research Breakthroughs

A New Strategy for Target Treatment of Tumors: President Mien-Chie Hung's Recent Research Breakthrough Published in *Nature Communications*



A significant progress in Taiwan's cancer immunotherapy research! The international research team led by CMU President Mien-Chie Hung published: "Galectin-9 interacts with PD-1 and TIM-3 to regulate T cell death and is a target for cancer immunotherapy" on February 5, 2021, in the prestigious journal *Nature Communications* [doi: 10.1038/s41467-021-21099-2]. The article provides new insights for cancer immunotherapy. The study generated much interest in the international medical community. The Nature Research Cancer Community (USA) also invited President Hung's team to share their research motivation, ideas, and experiences with the study.

"Immunotherapy is different from traditional chemotherapy, radiotherapy, and molecular targeted therapy. Immunotherapy does not kill tumors directly, and it is a new treatment that can overcome the immune suppression of the patients and restart the patients' own immune cells to kill tumors," explained President Hung.

Generally speaking, when T cells are activated, they can kill cancer cells. However, over-activation can cause autoimmune diseases. To avoid over-activation, T cells will express inhibitory receptors (e.g., PD-1 and TIM3) and these inhibitory receptors will bind to their ligands to inhibit the immune activation of T cells when the immune response is not required. In contrast, cancer cells will also express corresponding ligands (e.g., PD-L1) to interact with PD1 when fighting T cells, in order to inhibit T cells from killing cancer cells. Moreover, cancer cells can release Galectin-9 (Gal-9), the ligand of TIM3,

to bind with TIM3 on T cells and cause the death of T cells. Both PD-1 and TIM3 on T cells have the function of inhibiting T cell activity. Blocking the inhibitory ability of PD-1 and TIM3 receptors on T cells has become the main direction for developing anti-cancer drugs.

The study found that PD-1 can bind to Gal-9 and fight the death of T cells induced by the binding of Gal-9 and TIM3. This "triple alliance" of PD-1, Gal-9, and TIM3 allowed T cells to survive; however, they lost the ability to kill cancer cells.

To restore the cancer-killing activity of T cells, the research team used activated antibodies to stimulate GITR, the "co-activated receptor" of T cells, so that the T cells could regain their cancer-killing ability. This combined therapy of activated GITR antibody and inhibitory Gal-9 antibody greatly increased the number of T cells with tumor killing activity. Tumor growth was also inhibited significantly.

Previous research has shown that a large amount of interferon is produced during the activation of the immune system. This study showed that the combined effect of Interferon β and γ will significantly increase the expression and secretion of Gal-9, meaning that the increased expression and secretion of Gal-9 in immunotherapy may be one of the reasons that adaptive resistance occurs in immunotherapy. Therefore, blocking Gal-9 and combining other immunotherapy might overcome the adaptive resistance.

This study revealed that the immune checkpoint protein PD-1 has a new biological function in regulating the death of T cells, clarified the regulation mechanism of Gal-9 expression and secretion in tumor microenvironment, and discovered the anti-tumor efficacy of the combination of Gal-9 as a new immunotherapy target and other immunotherapy. It provides a new direction and prospect for future cancer immunotherapy.

Avoiding Air Pollution Can Prevent Allergic Rhinitis! CMU College of Public Health Research Team Publish Research Findings in THORAX

Health issues influenced by environmental changes have attracted much attention today. Air pollution is closely related to respiratory diseases. The research team of CMU College of Public Health including Dean Bing-Fang Hwang, Assistant Professor Chau-Ren Jung, Dr. Yu-Ting Lin, and Dr. Hao Shih recently discovered that if infants are exposed to excessive PM2.5 levels from late pregnancy to one year after birth, they are likely to develop allergic rhinitis. The team's article, "Effect of exposure to fine particulate matter during pregnancy and infancy on paediatric allergic rhinitis," was published in the fifth most cited respiratory system journal, *THORAX* [PMID: 33707186].

This study used a high-resolution satellite hybrid model to estimate the average daily PM2.5 exposure of infants and mothers based on their residency during pregnancy and birth. Special focus was paid to infants born in Taichung City (Taiwan) between 2005 and 2011. The results showed that from the 30th week of pregnancy to the 52nd week after birth, there was a significant positive correlation between the increase in PM2.5 exposure and the occurrence of allergic rhinitis.

Allergic rhinitis is an inflammatory reaction of the nasal mucus. Common symptoms include nasal congestion, itchy nose, runny nose, and sneezing. Although not fatal, it can seriously affect people's wellbeing. Patients with severe symptoms may even have poor sleep quality and decreased performance at school or work.



"There exist many pollutants in the air. Particulate Matter refers to the dust-like particles floating in the air. Many international journals have confirmed that PM2.5 will cause harm to the human respiratory tract," said Dean Bing-Fang Hwang. Dr. Yu-Ting Lin pointed out that from her clinical experiences, it is possible that under the exposure of PM2.5 mothers' and infants' antioxidant, immune regulation, and endocrine system may be difficult to balance. Moreover, the growth and maturity of the nasal mucosa will be affected, which consequently leads to allergic rhinitis.

This research showed that exposure to PM2.5 may be a cause of allergic rhinitis. It also found that the critical period lies at the end of pregnancy to one year after birth. The CMU research team hope that this study can help in reducing the chance of allergic rhinitis, and they recommend that pregnant women and infants should avoid going outdoors when the concentration of PM2.5 is higher than the WHO standard. Reducing the exposure to air pollutants can ensure people's health, thereby reducing medical and social economic burdens.

Taiwan Joins International Research Team to Publish World's First Paper on Telepsychiatric Treatment during the COVID-19 Pandemic



Dr. Kuan-Pin Su, Vice-Superintendent of China Medical University-An Nan Hospital, and Dr. Chun-Hung Chang, Director of Psychiatry Department, participated in an international research study that investigated the telepsychiatric condition in various countries during the COVID-19 pandemic. This was the first study to focus on global telepsychiatry. Their study, "Changes in telepsychiatry regulations during the COVID-19 pandemic: 17 countries and regions' approaches to an evolving healthcare landscape," was published in the November 27, 2020 issue of *Psychological Medicine* [PMCID: PMC7750654].

One of the ways to prevent the spread of the pandemic is through telemedicine, which enables isolated patients to get treatment from doctors. This study showed that it is possible to perform telepsychiatric treatment in the public medical system worldwide. Over 70% of countries in the study have loosened regulations for telemedicine due to the pandemic, including regulations dealing with prescribing drugs. In the vast majority of countries surveyed, the fees for telemedicine were the same as those for seeing a doctor in person.

One of the biggest issues facing telemedicine is the regulations, which have had to be modified due to the pandemic. "In several regions that already allowed telemedicine, only patients in remote areas or areas with a lack of medical services were previously eligible; however, these rules were relaxed." This was also done in Taiwan, where "the Ministry of Health and Welfare loosened the regulations for telemedicine, allowing people to seek for medical help in designated hospitals through video communication." This was especially important for those under home quarantine or isolation.

The results of this study can assist in the development of legislation to help promote the application of telepsychiatry in the world.

Tannic Acid Can Effectively Suppress SARS-CoV-2: CMU Research Team Publish Anti-Pandemic Research Findings in *American Journal of Cancer Research*

President Mien-Chie Hung and his research team have been working hard in anti-pandemic efforts. One of their studies, "Tannic acid suppresses SARS-CoV-2 as a dual inhibitor of the viral main protease and the cellular TMPRSS2 protease," was published in the December 1, 2020 issue of the *American Journal of Cancer Research* [PMCID: PMC7783773].



The study first revealed that tannic acid can inhibit the main protease of SARS-CoV-2 and the transmembrane protease serine 2 (TMPRSS2), which can further inhibit the virus's ability to enter the host's cell. This research attracted great attention from the international academic fields, and has shown that tannic acid is a potential candidate in developing anti-COVID-19 treatments.

President Mien-Chie Hung said that the main protease of the novel coronavirus plays an important role in the spread of the virus in the host. In addition, TMPRSS2 is a serine protease for therapeutic targets and plays a key role in the novel coronavirus. In view of this, the research team applied the concept of precision

medicine for targeted cancer treatment to develop the potential drug for COVID-19, and provide new strategies for COVID-19 treatments.

By looking into the natural compounds found in common foods and exploring if they were effective in fighting against the coronavirus, the research team screened a number of natural compounds and found that tannic acid is a high potential inhibitor that can fight against the novel coronavirus and TMPRSS2.

The molecular experiment confirmed that tannic acid can form a stable complex structure with both the viral main protease and TMPRSS2 protein, thus further inhibiting the activity of these proteins. In functional tests, tannic acid was also shown to inhibit the virus from entering cells.

The pandemic of COVID-19 is still ongoing. China Medical University believes that research universities have a social responsibility to develop cutting-edge medical research along with discovering effective treatments for diseases.

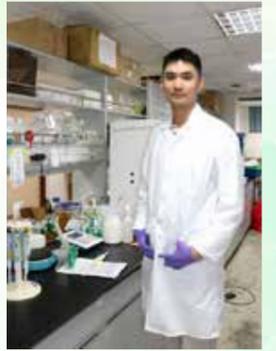
Achievements of CMU Students

New Hope for Depression Treatment: CMU Medical Student Szu-Wei Cheng Discovers the Pathogenic Gene for Depression and Publishes in *Brain, Behavior, and Immunity*

China Medical University works hard to cultivate research talents. Under the guidance of Professor Kuan-Pin Su, Szu-Wei Cheng, a fourth-year medical student, recently published "Genetic Variations of Ionotropic Glutamate Receptor Pathways on Interferon- α -induced Depression in Patients with Hepatitis C Viral Infection" in the March 2021 issue of the international journal *Brain, Behavior, and Immunity* [doi: 10.1016/j.bbi.2020.11.006].

This study discovered that the pathogenic gene related to depression is caused by inflammation on the neurotransmitter glutamate receptor. The research is expected to bring new hope in the treatment of depression. This is the world's first study on the depression gene and the neurotransmitter glutamate receptor.

Professor Kuan-Pin Su explained, "This research done by Szu-Wei Cheng provides new insights and evidence for the mechanism of depression caused by inflammation. In clinical application, there have already been many studies on the application of immunosuppressive drug and immunomodulator in depression. However, their function in glutamate receptor drugs is still unknown. If relevant research can be done and more new drugs can be developed, it will surely bring new potential to the treatment of depression."



An Excellent Role Model! CMU Medical Student Pin-Chun Chen Elected as Chairperson of Asian Medical Students' Association



Pin-Chun Chen, a third-year student in the School of Medicine was elected as the 37th Chairperson of the Asian Medical Students' Association (AMSA). He is the second Taiwanese Chairperson since 2005.

Pin-Chun said that he likes to make friends from all over the world and is willing to participate in public affairs. During sophomore year, he served as the international academic head of AMSA Taiwan and held various activities for academic promotion. In junior year, he served as the AMSA Regional Chairperson for Taiwan and was responsible for international communication with other countries. Due to his experience in the operations of international organizations, he decided to run for the post of AMSA Chairperson.

The AMSA actively promotes academic exchanges and international collaborations, which are great platforms for medical students. He hopes to make AMSA better during his tenure as chairperson.

"Coshion Show": 16th Graduation Exhibition of the Department of Cosmeceutics

The 16th Graduation Exhibition of the Department of Cosmeceutics opened on May 3, 2021. The exhibition displayed the cosmetics, cleansing, and fragrance products developed by seniors in the department. The theme for this year's exhibition was "Coshion Show." The elegance and comfort of the exhibition venue amazed the participating faculty members and students and has become a popular spot on campus for taking photos.

In the opening ceremony, CMU Vice-President Hung-Che Chiang praised the students for their aca-



ademic achievements and their ability to develop products by combining theory and industry needs. Vice-President Chiang encouraged the students to continue their efforts to bring their knowledge and technology into full play. Due to COVID-19, President Mien-Chie Hung suggested that the students investigate the use of herbal extracts from Chinese

medicine to develop cosmetics and cleansing products, along with developing hand sprays that can prevent viruses, thus making a contribution to pandemic prevention.

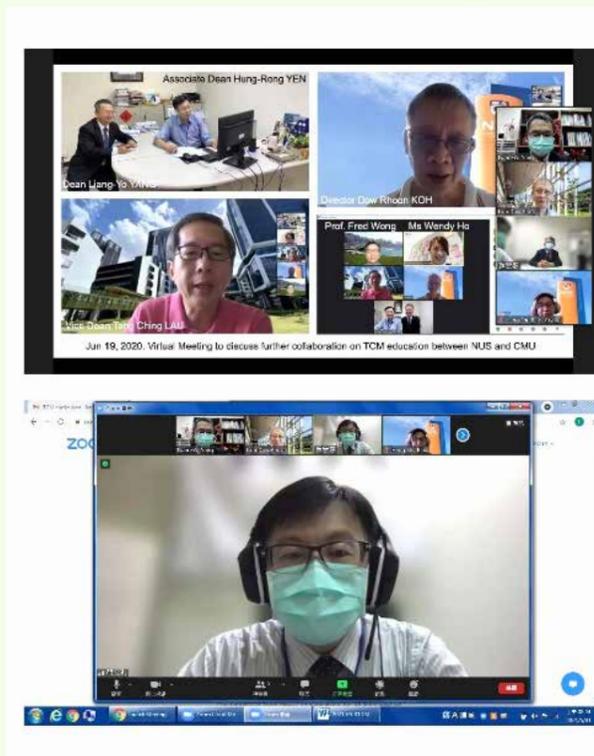
Outstanding Awards & International Collaboration

Bilateral Cooperation in Talent Cultivation: China Medical University Offers an English Elective Course on Traditional Chinese Medicine to National University of Singapore

Under the continuous efforts of Dean Liang-Yo Yang, China Medical University (CMU) and National University of Singapore (NUS) have been working closely on international cooperation and talent cultivation. CMU offered an elective course in English entitled “Traditional Chinese Medicine: From Basic Theory to Clinical Application,” for the students in the Yong Loo Lin School of Medicine at the National University of Singapore. Professor Hung-Rong Yen, Associate Dean of College of Chinese Medicine, organized this course and served as the first lecturer. Although the course is taught online, it still attracted many students to engage in the online interactions and discussions.

The NUS medical students who took this course expressed their enthusiasm and hope to learn more about the clinical application of Chinese medicine, along with the integration of Chinese and Western medicine.

The course was a one-week course that covered the basic theories of Chinese medicine, Chinese pharmacy, acupuncture, massage, and traditional Chinese medicine for good health, along with the integration of Chinese and Western medicine. The course included a virtual tour of CMU’s Lifu Museum of Chinese Medicine and Herbal Garden, demonstrational videos for acupuncture, and group discussion sessions.



Dean Mao-Feng Sun of CMU College of Chinese Medicine hopes that this course can promote the understanding of Chinese medicine among medical students at the National University of Singapore, and further facilitate the cooperation in academic fields and talent cultivation between the two universities.

CMU Professor Li-Li Chen Receives “Taiwan Outstanding Nurse Award”

Professor Li-Li Chen, School of Nursing, is Taiwan’s first Traditional Chinese medicine nurse with a PhD in Chinese medicine. Professor Chen has devoted herself to the teaching and research of Traditional Chinese medicine nursing for more than 40 years. She has published handbooks for nursing and compiled Taiwan’s first Chinese medicine Body Constitution Questionnaire for use by nursing and medical teams. Professor Chen has promoted Taiwan’s international visibility of Traditional Chinese medicine nursing. Because of her great contributions and her influence in this field, Professor Chen received the 2021 “Taiwan Outstanding Nurse Award.”



Traditional Chinese medicine nursing is a unique discipline in Taiwan. In the early years, nursing educa-

tion was dominated by Western medicine. There was a lack of Chinese medicine education. Motivated by her interest and the social responsibility as a university professor, Professor Li-Li Chen is devoted to studying Chinese medicine. She is also the first Traditional Chinese medicine nurse in Taiwan with a Chinese medicine PhD. Professor Chen explores the knowledge and theories of Chinese medicine and applies them to the teaching, research, and practice in nursing education. Professor Chen cultivates nursing students with competencies in both Chinese medicine and Western medicine. Moreover, Professor Chen brings Chinese medicine into community care, which significantly improves the quality of clinical healthcare.

Professor Jaung-Geng Lin Receives “Friend of Foreign Service Medal” from Ministry of Foreign Affairs for His Contribution in Promoting Chinese Medicine and Acupuncture



China Medical University Professor Jaung-Geng Lin is a world famous expert in acupuncture evidence-based medicine. He has been dedicated to promoting medical diplomacy with traditional medicine and acupuncture. Professor Lin also actively participates in international lectures, medicine practices, and academic exchanges. With his great contributions and achievements, Professor Lin uplifts Taiwan’s international status in the field of Chinese medicine. Due to his great contributions, he was awarded the “Friend of Foreign Service Medal” from the Ministry of Foreign Affairs, Taiwan, Republic of China.

The excellent contributions of Professor Jaung-Geng Lin are:

1. Attending WHO:

Professor Lin has been attending various WHO meetings and forums since 2009. At the 2017 WHO Executive Meeting, he was invited to give a keynote address.

2. Attending UNESCO:

Compilation of Diseases Term for Chinese and Western Medicine, a book compiled by Professor Lin was listed as an important reference for the intangible cultural heritage of UNESCO. As a result, the World Federation of Chinese Medicine Societies has recommended him as an expert and consultant for UNESCO.

3. Promoting international cooperation and receiving awards:

Professor Lin has been invited to deliver lectures, provide acupuncture services, and train acupuncture talents both domestically and internationally. Moreover, many world renowned universities have appointed him as a visiting professor. By giving lectures in different universities, Professor Lin promotes Taiwan’s traditional acupuncture medicine to the world.

From 1979 to 1980, Professor Lin was assigned by the Taipei Veterans General Hospital to provide acupuncture services in Saudi Arabia. He was trusted by the local people and was honored with the country’s highest distinction, the “Golden Robe Award.”

From 2003 to 2009, Professor Lin was the director of the Chinese Medical Association of Acupuncture. In 2007, he made the Chinese Medical Association of Acupuncture a member of the World Federation of Acupuncture-Moxibustion Societies, and led a team to participate in the World Acupuncture Conference. Furthermore, in 2009, Professor Lin established the Asia Advanced Forum on Acupuncture-Moxibustion, in which acupuncture experts and scholars have the opportunity to connect with each other.

The academic research done by Professor Lin has also attracted great attention in the international academic field. Nature, the prestigious journal publisher, has invited Professor Lin to co-edit many books since 2010. The textbook *Experimental Acupuncturology*, compiled by Professor Lin is by far the only English textbook for experimental acupuncture.

In 2020, *Atlas of Acupuncturology*, compiled by Professor Lin, was published. This is Taiwan’s only official textbook published by the National Research Institute of Chinese Medicine. With its publication, Taiwan’s international status in acupuncture research and teaching will surely be further promoted.