FROM LABORATORY TO REAL LIFE

A Taiwanese university leading in engineering is leveraging its assets to DEFINE NEW INTERDISCIPLINARY RESEARCH AREAS for future growth, featuring biotechnology.

Strong engineering programmes and extensive industry connections
make National Cheng Kung University (NCKU) stand out among its peers in Taiwan. This comprehensive, top-tier, research-orientated university is now leveraging its traditional strengths to explore interdisciplinary programmes, combining engineering with medicine and life sciences, and inspiring transformation via industry-academia partnerships.

Whether for biotechnology and biomedicine, genetic plant science, or shrimp aquaculture, global impacts and social responsibilities are integral to NCKU's three new research areas under its long-term development plan.

A new biomedical ecosystem addressing population ageing
Population ageing is a significant issue in Taiwan, and across the world. As degenerative diseases, including dementia, Parkinson's, musculoskeletal diseases, and cancer are rising in incidence, and the age demographic shift reduces the number of people to act as carers, innovative medical devices are becoming particularly important to ensure care for the elderly.

Committed to addressing this issue, NCKU has obtained a grant from the Taiwanese government to construct a new 'smart hospital' for aged patients. Artificial intelligence (AI) is employed to perform roles in eight main clinical sections of the hospital. An example is the use of e-Dashboard, which is designed to allow easy display of clinical procedures in a flowchart, managing emergency room patients smoothly, safely, and efficiently.

On the clinical front, NCKU researchers have pioneered stem cell therapies to fight degenerative diseases. They have shown evidence of efficacy in animal models, and have treated around 500 blood cancer patients using stem cells isolated from bone marrows. Now, a cell therapy centre is being built for treating patients with cancer, severe burns, skin and neurodegenerative diseases. Aiming for personalised care, NCKU hospital is also harnessing AI to develop precision genomic medicine for patients with various cancers, and cardiovascular diseases.

Based on more than 30 years clinical success and a well-established research infrastructure, including a tissue bank, NCKU is to collaborate with a wider range of health institutions including outpatient clinics, biopharmaceutical companies, research institutes, and international universities to establish a new ecosystem of biomedicine in NCKU. This will deliver better outcomes for patients, especially the elderly, and boost the industrial chain of biomedicine in Taiwan, according to Yan-Shen Shan, dean of the NCKU College of Medicine. "We want to become a centre of bio-technology in Taiwan."

Unveiling orchid evolution via genome sequence
Orchid is the largest family of flowering plants, whose 30,000 species grow in almost every habitat, except the north and south poles, and extremely hot deserts. Since Darwin's time, scientists have been trying to understand why there is such diversity in the orchid family, and now a collaborative study by NCKU researchers has unravelled some answers about orchid evolution.

Led by Wen-Chieh Tsai from NCKU Institute of Tropical Plant Sciences, together with Song-Bin Chang from the department of life sciences and Yu-Yun Hsiao from the Orchid Research and Development Center, their study published in *Nature* reported the draft genome sequence of *Apostasia shenzhenica*, one of the most primitive species of extant orchid. Its unique shape provides an illustrative example of the genetic mechanisms of orchid evolution.

The 35-strong international research team, including six NCKU researchers, acquired the entire genomic information of *A. shenzhenica*, and provided evidence of whole-genome duplication of orchids, a process of copying an organism's complete genetic information. This is shared by all orchids and occurs shortly before species divergence. Their comparative analyses uncovered evolution-associated changes within MADS-box gene classes, genes in which encode transcription factors in almost all eukaryotic organisms. Interestingly, they found that these alterations are related to the formation of specialised flower organs, which contributed to the extraordinary diversity.

For example, they identified that MADS-box gene AGL12 is related to a notable characteristic of orchids: clinging to trees or rocks, and growing in dry conditions, while some other classes of MADS-box genes are related to the development of labellum, gynostemium, and pollinium respectively, which are important structures in orchids for pollination and reproduction.

By deciphering the genome sequence of orchids, the study sheds light on the fundamental mechanisms of how they evolved while adapting to different environments. This improves our knowledge of orchid evolution at the molecular level, and also informs strategies for breeding new varieties of orchids that are adaptable to extreme climates.

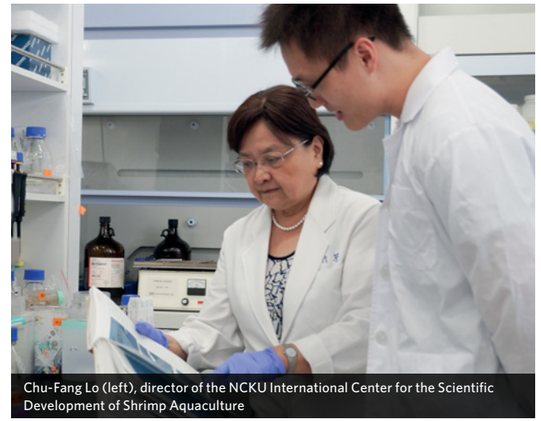
Sustainable aquaculture coping with complex environment
Seafood is an important source of protein, but increasingly produced through aquaculture, which is continuously threatened by disease. Chu-Fang Lo, director of the NCKU International Center for the Scientific Development of Shrimp Aquaculture, is leading a team to focus on minimising risks of disease outbreak and transmission, producing resistant shrimp, and conserving a sustainable aquaculture environment.

Housing two OIE (World Organisation for Animal Health) reference laboratories, the centre particularly focuses on two devastating seafood diseases in Asia: white spot disease (WSD) and acute hepatopancreatic necrosis disease (AHPND), and is responsible for their monitoring, diagnosis and prevention. In one recent study, Lo's team sought to better understand the pathogen-host interactions in different environments. They identified a new mechanism, by which the white spot syndrome virus induces rerouting of protein and lipid metabolism in shrimps, thereby defeating the host immune defence allowing it to replicate. These metabolic changes are vital for identifying virus-resistant biomarkers, which can be used for breeding healthy shrimp.

Lo also studies *Vibrio parahaemolyticus*, an evasive bacterium that can produce lethal toxin, causing widespread death in shrimp populations. The team used a new method called comparative metagenomics to trace bacteria activities inside pond shrimp. They found that the bacterium causes AHPND by creating an imbalanced situation of microbes in the stomach or intestine. Additionally, the activation of the Rho, a molecular pathway, permits migration of toxin and bacteria from the stomach to the hepatopancreas, followed by cell death. This study has also identified a microbe candidate from healthy shrimp stomach, which potentially prevents AHPND outbreak. These breakthroughs lay the groundwork for developing effective disease control and a new path to producing disease-resistant shrimps.

To protect shrimp stocks from the effects of climate change, Lo's team is developing an indoor shrimp breeding centre, and is establishing a large-scale clean-culture shrimp farm with high standards for biosecurity and food safety. These facilities allow NCKU researchers to breed shrimp with commercially favourable traits, and increased survival rate, benefiting the whole shrimp farming industry and aquaculture economics. ■

Yan-Shen Shan, dean of the NCKU College of Medicine


Chu-Fang Lo (left), director of the NCKU International Center for the Scientific Development of Shrimp Aquaculture

Wen-Chieh Tsai (left) from NCKU Institute of Tropical Plant Sciences and his team uncovered the genetic mechanisms of orchid evolution.

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