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Hard Work Pays Off

NCKU Professor Wins Most-Cited Award and Proves Taiwan is Evolution Research Paradise

Taiwan's outstanding scientific achievements are again earning the recognition they deserve on the international stage. Prof. Chiang Tzen-yuh of the Department of Life Sciences at National Cheng Kung University (NCKU) was elected a fellow of the American Association for the Advancement of Science (AAAS) in 2004, and this year (2005) was honored with the "Most-Cited Award" by the *Journal of Plant Research* – Asia's most prestigious botanical periodical. Prof. Chiang has again polished the reputations of NCKU and Taiwan's scientific community. The Most-Cited Award is granted to only two recipients each year; the other 2005 recipient was Dr. Hudkinson of Britain. The award will be bestowed at a ceremony held on September 22.

Prof. Chiang's research has received long-term NSC support, and has yielded impressive results. Prof. Chiang has received awards from the Biological Society of China and the NSC on several occasions. He specializes in phylogenetics and population genetics, bryology, and phylogeography, and has made profound and incisive findings concerning plant systematics and the molecular evolution of functional loci. Prof. Chiang is one of the very few giants in the life sciences.

Among the biggest contributions of Prof. Chiang's award-winning research paper is the establishment of a phylogeographic model for Taiwanese plants. This model can be tested in future academic research. According to Prof. Chiang, the paper mainly investigates the distribution of existing populations of the endemic species *Michelia formosana* (Magnoliaceae) in Taiwan and the Ryukyu archipelago and links between this distribution and geological history.

Prof. Chiang's research used sequence variations of the *atpB-rbcL* intergenic spacer of cpDNA and nested clade analysis to assess the phylogeographic pattern of *Michelia formosana*, and used its investigation of *Michelia formosana* populations at Wulai in northern Taiwan, Mt. Nanjen in southern Taiwan, and on Iriomote and Ishigaki islands in the southern Ryukyus to explore the role of Taiwan and the Ryukyu islands as possible refuges during the Ice Ages.

Because global air temperatures dropped significantly during the most recent Ice Age glaciation (approximately 100,000 ~ 20,000 years before the present), the sea level fell by approximately 120 meters. The exposed land bridges connecting the Eurasian continent with the island arcs of the western Pacific gave plants a possible route for southward migration. This geological history has helped give Taiwan an extremely high level of species and genetic diversity.

According to Prof. Chiang, another interesting example is that of the very rare fir species *Cunninghamia konishii* Hayata, which is endemic to Taiwan and possesses even greater population diversity in Taiwan alone than that of its near relative *C. Lanceolata*. (Lamb.) Hook throughout China. Furthermore, the genetic diversity of chloroplast DNA from the endemic Taiwan red pine (*Pinus taiwanensis* Hayata) is ten times greater than that of the same species of pine from the Huangshan area of China. Many more examples of this kind serve to show that Taiwan is a paradise for the study of species evolution.

One goal of phylogeography research is to increase people's concern for the conservation of natural resources. This is particularly important in light of 21st century medicine's quest to go beyond conventional synthetic drugs and tap the potential of the natural world. Facing virulent new diseases, humanity may one day depend on pow-

Michelia formosana (Magnoliaceae)

erful drugs extracted from inconspicuous or as yet unknown rain forest plants. We must remember that before the cancer-fighting drug taxol (pacilitaxel) was discovered, the humble yew (*Taxus*) was used only as a source of furniture wood.

Today the world faces the problem of global warming. Geological evidence indicates that the world's temperature will continue to climb, and high mountain plants will initially bear the biggest impact from warmer temperatures. Prof. Chiang and other botanists in Taiwan are currently working hard in a team effort to preserve useful genes from mountain plants in case of future need.

In addition, Prof. Chiang's laboratory is also using molecular analysis to reconstruct the historical process of acclimatizing Chinese tea in Taiwan, and ultimately conserve wild tea populations. Little of this type of research combining biodiversity and biotechnology has been done in Asia thus far, so Taiwan is still a pioneer in this field. Prof. Chiang's laboratory has won the recognition of the AAAS and the Biological Society of China (Taiwan) for its work in plant conservation and phylogeography, and Prof. Chiang feels honored to receive the Most-Cited Award from the Japanese Botanical Society for his paper.

Learning from the Strengths of Others

NSC Promotes S&T Cooperation with Russia, Australia, and India

The NSC has recently been expanding the scope of its international scientific and technological ties. Apart from the ongoing implementation of several Taiwan-American projects, the NSC has also strengthened scientific interchange with other countries. For instance, Taiwan will be stepping up cooperation with Russia, particularly in the field of satellite technology, said NSC Deputy Minister Shieh Ching-jyh at a July 14 press conference. The first step of this effort will take the form of personnel visits between Moscow State University – a major center of satellite development expertise – and academic institutions in Taiwan, which will allow university departments interested in developing microsatellites to obtain needed knowledge.

After leading a delegation to Russia on June 20 2005, Shieh negotiated funding for 20 joint research projects with the Russian Foundation for Basic Research (RFBR), and reached an agreement to expand a joint RFBR-NSC research fund to US$3.4 million over a three-year period. This fund, originally established in November 2004 with US$2.4 million for three years, is intended to support Taiwan-Russian bilateral seminars and joint research projects.

The RFBR and NSC started soliciting research projects after the establishment of the fund, and proposals poured in by phone and mail. More than one hundred proposals had been received by the cut-off date. To encourage more cooperation between Russian and Taiwanese scientists, the NSC and RFBR have now agreed to increase the research fund's money and allow even more projects to be implemented. This cooperative program has enabled at least 20 scientific teams and their research organizations to establish ties and engage in cooperation. After the three-year implementation of the fund, Taiwan-Russian scientific cooperation should score many impressive achievements.

Among other new developments in international cooperation, NSC Minister Wu Maw-kuen signed an arrangement between the NSC and the Australian Nuclear Science and Technology Organization in Taipei on June 8. In accordance with the joint "Neutron Beam Applications Research" arrangement signed by Wu, Taiwan's researchers will be able to use the Australian Nuclear Science and Technology Organization's new-generation neutron research facility, which was built at a cost of AUD$330 million. According to Minister Wu, this cooperation program will promote the exchange of manpower and information between the two parties, and boost both countries' technological capabilities.

India is one of the "BRIC" emerg-

ing technological powers of Brazil, Russia, India, and China. Since India possesses profound technological potential, especially in the areas of information technology and biotech, it is very much in Taiwan's interest to pursue stronger tech ties. To boost scientific cooperation with India, the NSC has now established a Science and Technology Division in Taiwan's representative office in India. As a token of the increase in scientific interchange between Taiwan and India over the last few years, NSC Deputy Minister Shieh led a delegation to India over the week of May 7 ~ 14 of this year and visited that country's major scientific agencies, including the Department of Science and Technology, Council of Scientific and Industrial Research, Indian National Science Academy, and Indian Institute of Science. The high-level talks held during these visits laid out the main areas and chief work items of Taiwan-Indian scientific cooperation for the next few years, and finalized arrangements for the establishment of the NSC Science and Technology Division.

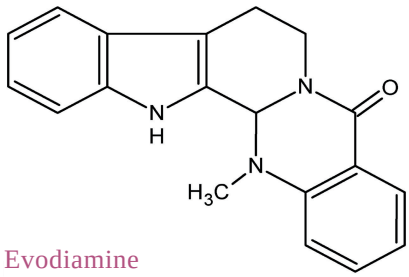
Evodiamine

Discovery of a Highly Promising Cancer Chemotherapy Drug

Evodiamine is an alkaloid with multiple biological activities extracted from the immature fruit of the plant *Evodia rutaecarpa*, a member of the rue family. Recent research reports indicate that Evodiamine can inhibit the invasion and metastasis of cancer cells, and also induces the death (apoptosis) of human melanoma A375-S2 cells and human cervical cancer HeLa cells. Evodiamine's point of action and its mechanism are only beginning to come to light, however.

The dried immature fruit of *Evodia rutaecarpa* is a traditional Chinese herbal medicine that has been used for over a millennium to treat disorders of the digestive tract. After several years of research supported by the NSC, Prof. Teng Che-ming of the Pharmacological Institute, College of Medicine, National Taiwan University has made major new discoveries concerning the pharmacology of Evodiamine. The dried immature fruit of *Evodia rutaecarpa* indeed contains many alkaloids, and Prof. Teng's laboratory has mainly been studying the mechanism of Evodiamine's action against CCRF-CEM human leukemia cells, NCI/ADR-RES and MCF-7 breast cancer cells, and PC-3 prostate cancer cells.

Prof. Teng discussed his findings concerning the anti-cancer mechanism of Evodiamine at the 20th Symposium on Natural Products, which was held in Taipei on June 24 and 25. Animal experiments involving mice first led Prof. Teng to the realization of Evodiamine's potential as a cancer chemotherapy agent. Evodiamine was found to have a concentration-dependent relationship with the inhibition of cancer cell growth, and analysis of the cell cycle using flow cytometry showed that Evodiamine induces cells to remain in the G2/M phase of the cycle, which leads to the cells' apoptosis. Microtubular polymerization analysis indicated that Evodiamine disturbs the polymerization of tubulin in cells, while causing the phosphorylation of the Bcl-2 at the serine 70 position in a time and concentration-dependent manner. These findings imply that Evodiamine's action at least involves cellular microtubules. Furthermore, the research team found that Evodiamine causes the activation of caspase-9, caspase-7, and caspase-3 in NCI/ADR-RES breast cancer cells and CCRF-CEM leukemia cells, and the apoptosis pathway is connected with the activation of the caspases. Finally, experiments using Balb-c/nude mice with multiple drug resistant tumors suggested that Evodiamine is



Evodiamine


Evodia rutaecarpa

more effective at inhibiting cancer growth than the anti-cancer drug Paclitaxel.

By interfering with the polymerization of microtubules, Evodiamine can cause cells to remain in the mitosis, which leads to their apoptosis. Evodiamine therefore has considerable potential as a cancer chemotherapy agent. Looking ahead to the future, the chemical modification and optimization of Evodiamine may make it one of the most potent anti-cancer drugs of the years to come.

Major Progress in Nanotechnology

Academia Sinica-Developed "Nanoprobe-Based Affinity Mass Spectrometry" Speeds up Blood Testing

The 21st century will be the age of nanotechnology, and miniaturization will have a revolutionary impact on people's lives. Nanometer biomedical materials are already intimately connected with our lives in the form of cosmetics and foods. A research team supported by the NSC and led by Dr. Lin Chuncheng and Dr. Chen Yu-ju of the Academia Sinica Institute of Chemistry and Genomics Research Center has successfully developed nanoprobe-based affinity mass spectrometry (NBAMS) technique able to dramatically improve the sensitivity and speed of protein analysis. The team's research results will soon be published in the American journal *Analytical Chemistry* and the European journal *ChemBioChem*.

The decoding of the human genome can speed up our understanding of the links between genes and disease. Many diseases can be detected by measuring the levels in gene products (proteins), and protein analysis can provide important information relevant to disease diagnosis. Most marker proteins relevant to diseases are present in the blood in extremely low concentrations. The most commonly adopted method, ELISA , has the drawbacks of time-consuming preparation for at least several hours to complete the testing process. The development of rapid and sensitive blood protein testing technology that can be used for the early diagnosis and treatment of diseases is therefore a high priority.

The Institute of Chemistry research team has synthesized magnetic nanometer particles consisting of Fe_3O_4 using advanced nanotechnology. The team has also attached highly specific antibodies to the surface of the Fe_3O_4 particles so that they can be used to test for marker proteins in the blood. This test is so sensitive that only 0.1 μl (one drop of blood is approximately 40 μl) is needed. After the modified magnetic nanoparticles adsorb the target proteins, they are extracted from the blood using a magnet, and biological mass analysis can be used to quickly test for the marker proteins. This technology has already been successfully used to detect traces of marker proteins including C-reactive protein (CRP), serum amyloid P (SAP), and serum amyloid A (SAA) in human blood. CRP is produced by the body in large quantities as part of the inflammation process, and is an important marker protein for cardiovascular disease.

Thanks to its accuracy and high sensitivity, the nanoprobe-based affinity mass spectrometry (NBAMS) technique can be potentially used to test tiny blood samples for marker proteins related to several different diseases. Another advantage is that the whole process from blood drawing to final results can be completed in less than an hour. According to Dr. Lin, the technique is easy to use and inexpensive, and can potentially be automated and used in fast, large-scale testing. As the science of proteomics advances and new marker proteins are discovered, this technique will become a powerful new weapon in the clinical testing arsenal.

Although the new technique can efficiently test for any diseases that can be detected using ELISA, including stomach cancer, breast cancer, and colon cancer, the needed mass spectrometers are costly, and certification is required before they can be used in clinical applications. The Academia Sinica research team is currently applying for a NBAMS patent and performing quantitative research. When the time comes, this technique will be able to drastically shorten the time needed for large amounts of testing.

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