

## BIOPHARMA NEWS DIGEST

### Breakthrough and Recognition – Chinese science at front page

Zhu Zhen

#### Chinese Scientists Identified Cancer-Preventing Gene Type



Dr. Dongxin Lin, Department Chair

A group of scientists lead by Dr. Dongxin Lin from The Department of Etiology & Carcinogenesis of Cancer Institute and Hospital, Chinese Academy of Medical Sciences has identified a gene variant which appears to protect Chinese people from various types of cancer. The Chinese scientists reported this finding in *Nature Genetics* May 2007.

The scientists say they had studied the DNA of nearly 10,000 Chinese people over 6 1/2 years and had found that the gene variant appeared far more frequently in those who

were cancer-free. “We have identified a variant of the CASP8 gene that appears to be associated with lower risk of lung, oesophageal, gastric, colorectal, cervical and breast cancers in Chinese people,” Dongxin Lin of the Chinese Academy of Medical Sciences in Beijing wrote in an e-mail to Reuters.

Explaining how this gene variant might have benefited its carriers, Dr. Lin said: “Carriers may have lower apoptotic cell death of T lymphocytes when they fight with malignant or premalignant cells.” “The immune status is very important in cancer development, and genetic variation in the immune system is associated with predisposition to cancer,” Dr. Lin said.

The discovery may help identify high-risk individuals by using this genetic variant as a marker, which can lead to targeted prevention and early detection of human cancer.

The Department of Etiology & Carcinogenesis was established in 1971 and has been recognized as one of the Key laboratories by Beijing Municipal Commissions of Science & Technology and Education since 2001. The department is devoted to basic cancer research, and also translational research that leads to the early diagnosis and individualized treatment and prevention of human cancers.

#### Chinese Traditional Medicine Bring New Hope to Polycystic Kidney Disease

A compound derived from a centuries-old Chinese traditional medicine, named Lei Gong Teng, has been showed that it can prevent the formation of kidney-destroying cysts in a mouse model of polycystic kidney disease. Yale University researcher Dr. Craig Crews has reported the finding at *Experimental Biology* April 2007 in Washington, DC. This ability holds out hope for what would be the first treatment, other than kidney transplant or frequent dialysis, for one of the most lethal of all kidney diseases worldwide.



Dr. Craig Crews, pictured in his laboratory with first-year graduate student Erin Betters,

Triptolide is derived from a Chinese medicinal herb, named Lei Gong Teng, which has been used in Chinese traditional medicine to treat cancer, inflammation, and auto-immune diseases and, more recently, also has been tested in Phase I clinical trials as an anti-tumor agent.

During normal kidney development, cells lining the kidney tubules continue growing and dividing until they receive a signal that the tubule is fully formed. The switch that turns on that signal consists of the growth regulatory proteins PKD1 and PKD2, located on hair-like cilia in the lining of the developing tubules. In people who have a mutation in one of

these growth regulatory proteins, the message to stop growing never gets delivered. So the cells lining the fully-formed kidney tubules keep right on subdividing and growing. The result of this unregulated growth is the formation of large cysts in the kidneys. As the person's kidney begins to develop these cysts, the kidney begins to swell, and the person moves to either dialysis or transplant in order to survive

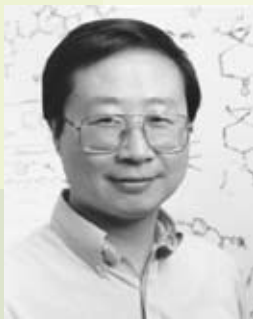
In this study, with mice bred to have a disease like human polycystic kidney disease, the compound, Triptolide, significantly reduced cyst formation in compared with control mice.

"If we were able to slow the rate of cyst formation by even 10 percent a year, compounded annually, patients would not die from this disease. A relatively small effect would have an enormous clinical benefit," says Dr. Crews.

The researchers are continuing this research in different mouse models of polycystic kidney disease and hope to see the compound proceed to clinical trials in humans.



### An Old Drug Gives New Surprise



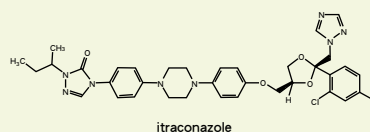
A group of researchers at Johns Hopkins have discovered to their surprise that a drug commonly used to treat toenail fungus can also block angiogenesis. The drug, itraconazole, already is FDA approved for human use, which may fast-track its availability as an antiangiogenesis drug.

In mice induced to have excess blood vessel growth, treatment with itraconazole reduced blood vessel growth by 67 percent compared to placebo. "We were surprised, to say the least, that itraconazole popped up as a potential blocker of angiogenesis," says Jun O. Liu, Ph.D., professor of pharmacology. "We couldn't have predicted that an antifungal drug would have such a role."

In their search for antiangiogenesis drugs, the researchers worked with cells from human umbilical cords, and exposed them to 2,400 existing drugs - including FDA- and foreign-approved drugs, as well as non-approved drugs that had passed safety trials - to see which ones could stop the cells from dividing. “The best outcome was to find an already approved drug that worked, and the fact that we did was very satisfying,” says Liu, whose study appears online in *ACS Chemical Biology*.

Itraconazole works principally by inhibition of cytochrome P450 14a-demethylase. This enzyme is in the sterol biosynthesis pathway that leads from lanosterol to ergosterol, causing fungi to become fragile and break apart. It turns out that itraconazole can also block the same enzyme in human blood vessels, but the researchers aren't positive if that's the reason blood vessels stop growing, because related antifungal drugs had much lower inhibitory effect.

“Our screening test did show that cholesterol-lowering statins also appear to stop blood vessel growth,” Liu says, “so there is likely some important connection between cholesterol and angiogenesis.”. While the researchers still must tease out exactly how itraconazole works to stop vessel growth, and test it in animals with cancer, they have high hopes for its use. “Itraconazole can be taken orally for fungal infection, and therefore oral delivery may work for angiogenesis as well,” Liu notes.



### Rice Genome Biologist Dr. Zhang Qifa Elected to US National Academy of Sciences

US National Academy of Sciences announced the election of 18 foreign associates from 12 countries in recognition of their distinguished and continuing achievements in original research On May 1st, 2007. Among them, there are two Chinese leader on hybrid rice, Dr. Zhang Qifa and Dr. Li Aizhen.

Dr. Zhang Qifa is currently the professor and director of National Key Laboratory of Crop Genetic Improvement at Huazhong Agricultural University, Wuhan.



Dr Zhang Qifa was graduated from the Middle China Agriculture Institute in 1976 and received a doctorate from the University of California, Davis in 1985. Zhang Qifa has spent much of his career analyzing world barley hereditary diversity and has introduced important characteristics in world barley hereditary variation. His work explained the independent origins of orient and west barley.

Prof. Zhang is a leading figure in the development of hybrid rice for China, which is now planted on more than 13 million hectares in Asia. His research team featured prominently in the development of genetically modified rice that has recently been approved for release in China, as well as the develop-

ment of marker aided selection that is now being used to pyramid genes to improve disease and insect resistance in hybrid rice cultivars.

Dr Zhang was elected to the Chinese Academy of Sciences in 1999, and to the Third World Academy of Sciences in 2000.

### **Nanotechnology Holds Hope in Biological Sensor: Pioneer Peidong Yang Received Waterman Award**

UC Berkeley News has reported on May 15th, 2007 that The National Science Foundation (NSF) has chosen Peidong Yang, a professor of chemistry at the University of California, Berkeley, to receive the 2007 Alan T. Waterman award. The \$500,000 prize is for recognizing an outstanding young scientist who is revolutionizing research.



Yang, 36, a member of Lawrence Berkeley National Laboratory's Materials Sciences Division, is a nanotechnology pioneer who has driven research into nanowires - flexible strips one-thousandth the width of a human hair that show promise for a range of high-technology devices, ranging from tiny lasers and computer circuits to inexpensive solar panels and biological sensors.

"Nanowires represent a rich family of functional materials," said Yang. "It is now possible to design and synthesize nanowires with quite complex structures based on progress made in the past couple of years. This type of control in nanostructural engineering has generated a rich collection of fascinating properties and functionalities, including nanoscale lasers, nanowire-based transistors, sensors and solar cells. These nanowire materials will have a particularly significant impact in areas such as energy conversion and solid state lighting."

Peidong Yang was born and raised in Suzhou, China and studied chemistry at the University of Science and Technology of China in Hefei in 1988. He earned his Ph.D. from Harvard in 1997, worked briefly at UC Santa Barbara as a post-doctoral fellow, and joined the UC Berkeley faculty in 1999.