Scientists Find Genetic Key to Autoimmune Diseases

The discovery of how the gene Roquin suppresses autoimmune diseases like type 1 diabetes and lupus could pave the way for improved treatments for such conditions, scientists propose. Researchers from the Australian National University (ANU) discovered in 2005 that Roquin can undergo a specific mutation that results in it instructing T-cells to react against the self. The researchers have now written a report, published in the journal Nature, which shows how a healthy Roquin gene can actually prevent abnormal T-cell behavior.

“Our findings hinge on the fact that the activities of a normal Roquin gene are orchestrated by parts of the genome until very recently considered to be ‘junk DNA’,” said Dr Vinuesa from the John Curtin School of Medical Research (JCSMR) at ANU.

“This decay leads to reduction of the expression of proteins such as one called ICOS, which we have now shown can result in autoimmunity when it is over expressed. This is the first time that microRNAs have been linked to protection from autoimmune diseases,” said Dr Di Yu from JCSMR, who performed most of the experiments leading to the discovery.

The discovery centers on some small, non-protein-coding forms of RNA, called microRNAs, which actually induce the decay of messenger RNAs. Once considered to be genetic junk, microRNAs are now thought to regulate up to 30% of the genome and have been recently shown to play an important role in the development of cancer and other diseases.

“We are learning more and more about how RNAs regulate critical processes related to cell development and the evolution of complex structures like the brain,” said JCSMR’s Professor Chris Goodnow. The researchers say their work opens up the possibility of using RNA interference, or the microRNAs themselves, in the treatment of autoimmune diseases.
Funding Awarded to Starpharma and Baker Heart Research Institute to Develop Arterial Disease Imaging Agent

Starpharma Holdings Ltd announced that the National Health and Medical Research Council has agreed to provide A$327,000 to fund a joint project with the Baker Heart Research Institute to develop a novel imaging agent for vascular disease. The imaging agent will be based on Starpharma’s dendrimer technology and will be developed for the early detection of unstable atherosclerotic plaques on arterial walls. Unstable plaques can rupture, disrupting blood flow, and blocking blood vessels, which potentially leads to heart attack or stroke.

Starpharma’s dendrimer nanoparticles are coupled to an engineered antibody developed by the Baker that recognizes the presence of unstable atherosclerotic plaques in the arteries. The nanoparticles’ branched structures also contain a contrast reagent, which allows detection of the plaque through magnetic resonance imaging (MRI) scanning.

Professor Garry Jennings, director of the Baker, said the work of Professor Karlheinz Peter towards the detection of unstable atherosclerotic plaques has the potential to prevent disease progression and reduce the incidence of sudden cardiac death.

Dr Jackie Fairley, CEO of Starpharma, said, “This joint collaboration and funding support is further evidence of the potential application of dendrimers across a range of exciting life science product categories, from MRI imaging agents to new biomedical products.”

Starpharma and the Baker have also filed a patent application for the agent, based on positive laboratory results that have shown enhanced visibility of thrombi (clots resulting from the rupture of atherosclerotic plaque) in vitro using MRI scanning. The next step would be the measurement of this effect in vivo.

This new collaborative project in cardiovascular disease is the second application of dendrimers for imaging agents undertaken by Starpharma. Starpharma’s wholly owned subsidiary in the US, DNT, has a contract valued at $850000 with the US National Cancer Institute. That contract aims to develop a different dendrimer product for the early diagnosis of certain cancers.

Cardiovascular diseases collectively account for almost 40% of deaths in Australia, and are predicted to be the leading cause of death in developed countries by 2010. Heart attack and stroke, frequently caused by rupture of unstable atherosclerotic plaque, alone account for about 20% of deaths in Australia.

Cardiovascular disease is currently diagnosed using X-ray angiography, a highly invasive procedure that involves injection of a radio-opaque dye using catheters inserted into blood vessels. Whilst this technique determines the degree of narrowing of the arteries, it does not identify unstable, rupture-prone atherosclerotic plaque and is not recommended for routine screening due to the risks associated with its invasive nature. In 1999, it was estimated that 3.3 million angiograms were conducted in the US alone at an annual cost to the healthcare system of US$6.6 billion.

Gene Syndrome Behind a Significant Number of Endometrial Cancers

New research has found that one in five endometrial cancers among younger Australian women may be caused by a specific genetic syndrome. The Queensland Institute of Medical Research finding is one of the first Australian studies to reveal such a high frequency of endometrial cancers in women suspected to have Lynch syndrome.

Scientific technical officer Michael Walsh said the findings highlighted the need for women with a family history of colon and endometrial cancers to be screened for the inherited gene abnormality linked to Lynch syndrome, thus allowing them to make choices to avoid the cancer.

“In Lynch syndrome there are mutations in proteins responsible for checking newly made cell DNA for abnormalities,” he said. “Without these repair proteins, these faulty cells may develop into cancers.”

The study looked at endometrial tumors in 148 Queensland women aged under 50, and found that nearly 20% of tumors failed to make the protein needed to detect abnormal DNA. The research findings reflect a growing body of international evidence supporting the association between Lynch syndrome and the early development of endometrial cancer.
Breast Cancer Leading Cause of Death Among Local Women in China

Breast cancer is the top killer of women in Shanghai, with the incidence tripling over the past 35 years, said medical experts at a seminar promoting World Breast Cancer Awareness Month. There is one breast cancer patient among every 300 local women.

“Though breast cancer is the most risky cancer, early detection and proper medication can effectively cure the disease and improve people’s quality of life,” said Dr Shen Zhenzhou, director of Shanghai Tumor Hospital’s surgery department. “About 98% of patients in the early stages can be cured under current medical standards. However, 80% of patients have the disease confirmed when it is in the middle or terminal stages,” he said. “Delayed discovery results in poor treatment effects and many women lose their breasts through surgery in order to prevent the spread of cancer.”

Experts said that stress, smoking, alcohol, lack of exercise, delivering children later in life and never breast-feeding all contribute to the increase of breast cancer. The most important ways to combat the cancer are through regular checks, early detection, and early treatment. Experts suggest women should examine their breasts every month and have an annual medical checkup to detect any abnormalities as early as possible.

“Thanks to the promotion of public education, checkups, and improved technology, patients’ survival rate has risen rose by 20%, although the global incidence of breast cancer has grown by 8%, in the past 20 years,” said Shen. “The promotion of breast cancer education and routine examination in China still lags behind the West.”

The China Anti-Cancer Association has updated its guidance on breast cancer diagnosis and treatment this year, promoting the latest technology including gene therapy.

Chinese Government Encourages the Practice of TCM

Traditional Chinese medicine (TCM) will play a key role in realizing the national goal of providing every Chinese citizen with access to basic medical care. Wang Guoqiang, vice minister of health and director of the State Administration of Traditional Chinese Medicine (SATCM), made this remarks at a three-day workshop in Beijing recently. The workshop was held to mark the 20th anniversary of the foundation of the World Federation of Acupuncture-Moxibustion Societies, which is dedicated to the global promotion of TCM. The government aims to establish a national TCM network by 2010, covering both rural and urban areas, Wang told the workshop.

In cities, the government will enhance the TCM network service by improving healthcare systems and equipment and employing qualified TCM practitioners at special TCM hospitals as well as TCM departments in general hospitals and in community clinics.

In the new cooperative rural medical services, TCM will be integrated into the general medical care and disease prevention, which is now mainly carried out by county-level medical institutions. In two years time, all clinics in rural towns will establish TCM departments to ensure farmers enjoy easier access to the service.

There are now 500,000 qualified TCM personnel in 3009 TCM hospitals, including general hospitals at county level and above, according to figures from the Chinese Ministry of Health.
Unified Code Name System for Drugs Set for Year-End Launch

China will launch a long-awaited unified code name system in the pharmaceutical industry, probably by the end of this year. All medicines in the country will be included in the new system and each drug will be given a code name for wide recognition and digital management, according to Wang Jinxia, vice chairman of the China Association of Pharmaceutical Commerce, who is one of the three persons to draft the system.

“Everything is ready (for the system) and it only needs government bureaus’ approval,” Wang said during a Sinopharm Medicine Holdings Co event to adopt a new IT system.

In the past, the names of medicines in China were written in Chinese, English, Latin or just numbers, which lacked a unified code name system. The preparations for the system started in 1997, but its implementation of it was delayed due to various bureaus and organizations wanting to control the system, according to an industry insider who declined to be identified.

“China’s drug firms urgently need the unified coding system to improve efficiency and cut costs,” Wang said. A total of 11 drug firms, which generate an annual revenue of more than five billion yuan (US$657 million) each, accounted for 38% of combined industry sales. Sinopharm Medicine, China’s number one drug distributor with an annual revenue of more than 10 billion yuan, announced recently that it has signed with U.S.-based GSX International Inc. and Shanghai-based AgileSC Inc to adopt GSX’s IT suite on supply chain management. All data can be shared and better managed with the new unified code name system.

JAPAN

Researchers at Japanese National Institute for Physiological Sciences Discover Brain Compensatory Mechanisms that Enhance the Recovery From Spinal Cord Injury

A research team led by Tadashi Isa, a professor at the Japanese National Institute for Physiological Sciences, NIPS (SEIRIKEN), and Dr Yukio Nishimura (University of Washington, Seattle) have found that brain compensatory mechanisms contribute to recovery from spinal cord injury.

The basis of neurorehabilitation relies on the concept that training recruits remaining intact neuronal systems to compensate for partial injury to the spinal cord or brain. Until recently, the neuronal basis of these compensatory mechanisms has been poorly understood. In previous work, the research team showed that finger dexterity could recover with rehabilitation following transection of the direct corticomotoneuronal pathway in the Japanese macaque monkey.

In the current study, brain imaging (PET scan) indicated that bilateral primary motor cortex were activated to compensate for impaired finger movements. Pharmacological inactivation of these regions during rehabilitation slowed recovery. These results suggest that brain compensatory mechanisms actively enhance recovery from spinal cord injury. This study was conducted in collaboration with Hamamatsu Photonics (Dr Hideo Tsukada) and RIKEN (Dr Hirotaka Onoe). It was supported by the Japan Science and Technology Agency (JST).
Academia Sinica Opens its Mutant Mouse Lab Facilities

Six years after its opening, the National Mouse Mutagenesis Program Core Facility at the Academia Sinica is already among the top mutant mice research facilities in the world.

Mutant mice are important in the development of medical technologies. Humans have 23 pairs of chromosomes and 30,000 genes, while mice have 20 pairs and close to 30,000 genes, Kung Hsiang-chih was quoted as saying in a story reported by the Chinese-language United Evening News recently. Such similarity makes it possible to find between 80% and 90% of common diseases in both humans and mice, said Kung, who is also the program director.

Some of the diseases humans and mice share include diabetes, high blood pressure, and liver disorders, the report said. With the aim of developing Taiwan’s own mutagenesis industry, the former Academia Sinica president Lee Yuan-tseh asked Kung to create the research facility in 2002.

In the six years since the research facility’s founding, however, more than 80 different types of mutant mice have been developed, including curly hair, high platelet, trembler, and short limb varieties, according to the program’s website. Each of the mutant types carries a disease. For example, the trembler has Parkinson’s disease, and thus is used for research on techniques to prevent and treat the disease. Kung said that the team has discovered that more than half of the mutant traits are inheritable, and thus is looking for the particular genes that trigger the diseases.

The Cause of Recent Sustained Outbreak of Human Leptospirosis in Thailand Discovered

A single disease-causing clone of the bacterium *Leptospira interrogans* was behind the recent sustained outbreak of leptospirosis in Thailand. Human leptospirosis is usually acquired following exposure to *Leptospira* shed in the urine of an infected animal. A sustained leptospirosis outbreak occurred in northeastern Thailand from 1999 to 2003, but the cause was unknown.

Outbreaks in Thailand and elsewhere are often linked to climatic events such as flooding, which leads to an increase in exposure to environments contaminated by *Leptospira*. But, the 1999–2003 outbreak could not be explained by such events.

To investigate the cause, Sharon Peacock (Mahidol-Oxford Tropical Medicine Research Unit, Mahidol University, Bangkok, Thailand) and colleagues identified patients with leptospirosis presenting to Udon Thani Hospital in northeastern Thailand from 2000 to 2005, and they isolated the causative organisms from the blood.

The researchers used a special technique for identifying the organism — a form of bacterial genotyping known as multilocus sequence typing. This approach has advantages over existing typing schemes in that the data generated are amenable to detailed evolutionary analysis and are readily comparable via the internet. Their study results provided evidence that the human outbreak was associated with a biologically successful clone of *Leptospira interrogans*, called ST34. It was also demonstrated that the bandicoot rat was an animal host for this pathogenic *Leptospira interrogans* clone.

Singapore’s NCCS Finds New Cure for Advanced Colon Cancer Patients

Advanced colon cancer patients can look forward to a new therapy that has produced promising results during a clinical trial conducted by a team of cancer specialists and research scientists at the National Cancer Center Singapore (NCCS) in collaboration with a Danish biotech company, DanDrit Biotech A/S. Both teams are now working out a plan to design and execute a larger randomized trial to be led by Singapore. This is required by the US Food and Drug Administration (FDA) to qualify for its approval. This second study by the NCCS research team is to further confirm the clinical benefits and the efficacy of this cancer vaccine.

For the cancer patients, this
will open opportunities for them to participate in the forthcoming trial sometime in 2008.

Results of this research suggest that many of these patients can expect prolonged survival. This gives hope to many who would otherwise face very limited treatment options including resigning themselves to be left on life’s end journey.

For the NCCS research team, led by principal investigator Dr. Toh Han Chong, this is another fine example of a “bench-to-bedside” breakthrough discovery, bringing therapies from the laboratory to the patients seamlessly. This successful clinical trial led by NCCS paving the way for significant anticancer drug development and plans for a follow up randomized trial driven from Singapore that may lead to drug approval. The NCCS Director, Professor Soo Khee Chee, and NCCS principal investigator from the Laboratory of Cell Therapy and Cancer Vaccine, Division of Medical Sciences, Dr. Toh Han Chong, will be sharing the promising results of the successful clinical trial, which suggest that many advanced colorectal cancer patients who face very limited treatment options, can otherwise expect prolonged survival.

The trial has shown promising results in treating such patients who face limited treatment options; significant 35% control of the disease was seen in advanced colorectal cancer patients.

**Protein Found to Turn On Genes Related to Obesity**

Obesity is a well known risk factor for prostate, breast, and colon cancer, but recent studies have shown that a protein responsible for generating fat cells also plays an important role in cancer. Researchers at the Genome Institute of Singapore have conducted, for the first time, a genome-wide analysis of how the protein, called peroxisome proliferator-activated receptor gamma (PPARγ), turns on various genes related to obesity.

Simply suppressing the protein entirely could prevent the generation of adipocytes — the precursors to fat cells; it would decrease the protein’s beneficial properties. Instead, the researchers believe that by identifying the gene targets of PPARγ, they could open up new targets for drug development against a number of diseases, including obesity, diabetes, and cancer.

“To date, only a limited number of direct targets for PPARγ have been identified. Our findings provide a genome-wide map of PPARγ binding sites during the course of adipocyte differentiation,” said M. Sabry Hamza, PhD, a postdoctoral research fellow at the Genome Institute of Singapore, a division of Singapore’s Agency for Science, Technology and Research (A*STAR). “These results together with the expression profile of genes that are dependent on PPARγ expression, provide us with clues into the transcriptional circuitry during adipogenesis, the process by which adipocytes differentiate into different types of fat tissue.”

With funding from A*STAR, “we have identified direct targets of PPARγ that, when inhibited, lead to a dramatic reduction of adipogenic potential,” Hamza said. “Ongoing analysis will help us decipher whether these direct targets control adipogenesis, insulin sensitization, or determination of fat cell type.”

According to Hamza, PPARγ inhibits the proliferation and lowers the threshold for apoptosis — the process by which cancer cells destroy themselves. “In addition, a significant increase in the tumor suppressor BRCA1 is induced when breast cancer cells are exposed to PPARγ agonists,” said Hamza. “Although indirect, the role of PPARγ as it relates to obesity and cancer is intriguing.”

So far, Hamza and his colleagues have identified a number of new PPARγ target genes which are connected to adipogenesis and insulin sensitivity. Currently, available marketed oral hypoglycemic drugs, although very potent in treating type II diabetes, cause detrimental side effects including weight gain, liver toxicity, and heart disease, said Hamza. “Using drugs which specifically target those PPARγ targets regulating insulin sensitivity could hence present a safer and more efficient therapeutic approach,” said Hamza.