Clinical Research Labs in China

The Appearance and Development of Commercial Laboratories in China

Independent Medical Laboratories in China – A Sunrise Industry under the Circumstances of Healthcare Reformation

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China’s Independent Medical Laboratory Scene

A medical or clinical laboratory is a laboratory where tests are done on clinical specimens in order to get information about the health of a patient pertaining to the diagnosis, treatment, and prevention of diseases. Since the middle of the last century, medical laboratories were developed into two types with respect to their relationship with hospitals; (1) the hospital laboratories attached to a hospital and performed tests on samples from patients mainly associated with that single hospital and (2) the private or community laboratories independent of any hospital and receive samples from general practitioners, insurance companies, clinical research sites and other health clinics for analysis. They were also referred to as reference laboratories where more unusual and obscure tests are performed[2]. For the convenience of description and discussion, we define the latter type as Independent Medical Laboratory (IML). IMLs have been shown to be dominant entities in the field of laboratory medicine due to the advantages of resource optimization, marketing operation and cost effectiveness. It has been estimated that 38% in USA, 50% in Europe, and 60% in Japan of total lab-tests were accomplished by IMLs possibly by providing more test items than the hospital laboratories.

Nevertheless, the history of IMLs in China is merely a decade old and is still at its infancy stage. In 1994, Mr. Yaoming Liang along with a few of his followers began pursuing third party service of medical lab-diagnostic testing – a form completely new to the Chinese medical service system. At that time, hardly anyone had exact knowledge of how to operate an IML. However, Liang’s vision of what he wanted to achieve was crystal clear. He named his “baby” “KingMed”, Golden Field in Chinese, with the promise of success. Now we can say with certainty that the faith and confidence of their choice had supported these pioneers for KingMed and also for the Chinese IML to overcome many difficulties. After a period of 18 years, the persistence, dedication and effort has eventually made KingMed the largest and the most successful IML in China. Following KingMed’s footstep, several other IMLs have also sprouted and demonstrated that the IML concept definitely works with great potential in China.
IMLs have successfully established and developed its position in China, however we recognize that the scale of Chinese IMLs pales incomparision to the world-leading IMLs, such as Quest, LabCorp and ARUP. The marketing share of lab-tests conducted by Chinese IMLs altogether is 0.7% of the total lab-tests done in China. Even though the variety of lab-diagnostics offered by IMLs are more than those provided by hospital laboratories in China, it is only one-third to one-fourth of the items carried by world-class IMLs. KingMed, Chinese IMLs and hospital laboratories all have long way to go to become a world-class medical laboratory.

Although the IMLs is a new entrant in the field of laboratory medicine in China, its characteristic service, fast development and great potential have attracted attention from various parties. The Chinese government announced the policy and guideline for the establishment, operation and management of IMLs in 2012, obviously pushed by the existence and development of IMLs in China, the number of medical institutions accepting third party testing services from IMLs has significantly risen over the last decade; the Chinese-based IMLs have become major targets for world-class pharmaceutical companies to seek Contract Research Organization (CRO) service providers. World-leading IMLs, such as Quest, LabCorp and Japanese FML (Fukuyama Medical Laboratory Co., Ltd) are all attempting to expand their branches in China. Thus government policy and the marketing potency would be the crucial information and therefore the motivation for me to design such a special issue for APBN.

In this issue, we feature articles representing different topics regarding the appearance, development, performance, and potential of IMLs in China to display a relatively complete image of this burgeoning industry. It is my aim to provide valuable information to all relevant parties and the historical trace of IML to promote further development in this field.

Prof. Shangwei Wu
Medical Director for Infectious Diseases, KingMed Center For Clinical Laboratory, China
Professor, The College of Laboratory Medicine, Tianjin Medical University

Shangwei Wu is the Medical Director for Infectious Diseases, KingMed Center For Clinical Laboratory Guangzhou, China as well as Professor of Clinical Microbiology at the College of Laboratory Medicine, Tianjin Medical University, Tianjin, China. He studied in Tianjin Medical College and was awarded degrees of BS and MS of Medicine in 1983 and 1986 respectively. From 1989 to 1992, he was a graduate student in the Department of Clinical Microbiology at Karolinska Institute, Sweden and where he received his Ph.D. of Clinical Microbiology. Following that, he was accepted as a Postdoctoral Fellow in Laboratory of Microbiology, The Rockefeller University, New York, USA (1992 to 1998), Assistant Professor (1999 to 2005), Senior Research Associate (1999 to 2008), in Laboratory of Microbiology, The Rockefeller University, New York, USA.

He is also a member of ASM (America Society of Microbiology), and a Reviewer of Molecular Method in CLSI (Clinical and Laboratory Standard Institute, USA).
Zinc Treatment for Infections in Children

Of the one million neonatal deaths that occur every year in India, more than a quarter are attributed to serious bacterial infections. Despite advances in antimicrobial treatment, outcomes remain poor. The development of inexpensive and accessible initiatives that could improve treatment outcomes and reduce mortality is important.

Reduced risk of treatment failure means shorter time in hospital, lower treatment cost, and possibly reduced number of deaths. The researchers in this study wanted to estimate the efficacy of 10 mg of oral zinc daily combined with standard antibiotic treatment in infants with probable serious bacterial infection. The infants were aged between 7 and 120 days. 352 infants were randomly assigned to receive zinc and 348 to placebo. Significantly fewer treatment failures occurred in the zinc group (10%) than in the placebo group (17%) – the relative risk reduction was 40%. Zinc treatment of 15 infants would accordingly prevent 1 treatment failure. Use of zinc also reduced the number of deaths, although the difference between the groups was not statistically significant.

The study concluded that zinc could become an accessible and inexpensive intervention to improve treatment outcomes of such infections and thereby reduce infant mortality.
Japan Pharma Portfolio Finds Renewed Strength through Record Growth in 2012

Leading events organiser UBM Live, a division of UBM Plc (LSE: UBM), announced the successful 2012 return of the Japanese Pharma Portfolio of events to the Tokyo Big Sight Exhibition Centre in Tokyo, Japan with a record attendance of 14,473 attendees, representing a 17% increase over 2010. CPhI Japan for pharmaceutical ingredients, ICSE Japan for outsourcing solutions, P-MEC Japan for pharma machinery and technology, the new Pharmatec for drug packaging and delivery technology and the BioPh Pavilion for the biotechnology sector, came together from 21-23 March, 2012. During the three days onsite, the Japanese Pharma portfolio provided guests with a unique opportunity to maximise ROI by meeting existing and future business partners and networking with leaders in the various sectors of the Japanese Pharma industry.

“The 2012 Japanese Pharma Portfolio had a positive outcome that drew greatly from the synergies of the co-located events. CPhI Japan, ICSE Japan, P-MEC Japan, the new Pharmatec and the BioPh Pavilion each offer direct access to distinct sectors within the pharma industry and together the portfolio ranks as one of the most international annual trade shows held in Japan,” commented UBM Live Regional Director, Andrew Pert. He went on to further note, “In 2012, there were 498 exhibitors from across the globe. 289 of these were international companies from more than thirty countries, which served as the inspiration to host national pavilions for attendees to easily locate new business partners in countries including China, India, Korea, the UK, Italy, and Latvia. We expect this international trend to continue with more than 40 countries set to be represented when the Japanese Pharma Portfolio of events returns to Tokyo in 2013.”

The addition of Pharmatec Japan complemented the existing line-up by providing comprehensive access to the newest trends and developments in the growing pharmaceutical machinery, equipment, drug packaging and delivery technology sectors. Attendees were also able to benefit from a returning programme of over 140 sessions and workshops that highlighted the latest topics and trends in each of the diverse sectors represented, and included a special 10th Anniversary keynote seminar by the Japan Pharmaceutical Manufacturers’ Association.

The full Japanese Pharma Portfolio of events will return to the Tokyo Big Sight Exhibition Centre from 24-26 April, 2013. For more information, please visit www.cphijapan.com

The UBM Live annual schedule of ICSE events also includes South East Asia (10-12 May, 2012, Jakarta International Expo, Indonesia), ICSE USA (22-23 May, 2012, Pennsylvania Convention Centre, Philadelphia), China (26-28 June, 2012, SNIEC, Shanghai, China), Worldwide (9-11 October, 2012 at the Feria de Madrid, Spain) and CPhI India (21-23 November, 2012 at the Bombay Exhibition Centre in Mumbai).

Joint Development of a Novel Lyophilized Dual Chamber Prefillable Syringe System

Arte Corporation and Project Pharmaceutics have been working closely on the development of a new type of dual chamber prefillable syringe for freeze-dried pharmaceuticals. The two companies have joined together with the objective to provide innovative dual chamber syringes for the global pharmaceutical market. This type of device, called Lyo-DCPS, will be delivered in standard nests and tubs to comply with the industrial standard for aseptic filling of nested syringes. The abbreviation Lyo-DCPS stands for Lyophilized Dual Chamber Prefillable Syringe.

Arte Corporation contributes its manufacturing expertise on high quality pharmaceutical packaging systems specifically in the field of prefillable syringes. ProJect Pharmaceutics, for its part, adds its know-how in developing filling and freeze drying processes and adapts the Lyo-DCPS design to enable GMP-conformity and efficient manufacturing processes for clients’ drug products.

Like conventional mono chamber syringes Lyo-DCPS will be delivered in standardized nests and tubs and can be filled on widely used nested syringe fillers. The diluent is filled first and can be autoclaved as required by international guidelines. The drug solution is filled into the second chamber and completely sealed on the filling line before entering the freeze drier. Due to its special design, the system opens by itself within the freeze drier enabling lyophilization of the drug solution in presence of the diluent. The development has reached pilot scale and lyophilization of first customers’ products in the new device has been performed successfully. Sterile nested Lyo-DCPS for GMP manufacturing of drug product will be available early 2013.
A genetic alternative to fertilizer

A plant transporter gene triggered in nitrogen-starved environments could be engineered to reduce the need for nitrogen fertilizers.

Several studies have shown that a lack of nitrogen in soils adversely affects crop yields. The modern use of nitrogen fertilizers has improved yields to meet expanding global food demand, but in some cases up to 50% of the nitrogen in fertilizers reaches surrounding water bodies in the form of nitrate, causing pollution. As the use of nitrogen fertilizers is rapidly increasing worldwide each year, there is a fundamental need to understand how plants absorb nitrate, and how this absorption can be improved in crops.

In Arabidopsis plants, nitrogen starvation triggers expression of the nitrate transporter gene known as NRT2.4, which allows the plants to absorb trace amounts of nitrate for survival. Now, Takatoshi Kiba and colleagues at the RIKEN Plant Science Center in Yokohama, together with scientists from France and the UK, have gained insight into how NRT2.4 works to benefit nitrogen-starved plants.

“Although nitrogen is one of the most important nutrients for plant growth and productivity, how plants sense and respond to levels of nitrogen in soils is not well understood,” explains Kiba. “This is why we started the study focusing on the NRT2.4 gene.”

Using green fluorescent proteins and reporter enzymes to help pinpoint the location and presence of the gene, Kiba and his team found a pattern of NRT2.4 expression in the roots and shoots of Arabidopsis seedlings.

The researchers worked with 10-day-old Arabidopsis seedlings, each weighing around 1 milligram, and measured the tiny amounts of nitrate absorbed by the plants. “Detection of nitrate influx at very low concentration was the main challenge of this work,” explains Kiba. “To obtain valid data, we had to improve the precision of the assay and measurement methods.” They prepared their samples very carefully in assays before measuring nitrate levels with high-performance liquid chromatography and an automated N/C analyzer-mass spectrometer.

The improved precision paid off, because the team’s results revealed that the NRT2.4 gene is crucial in increasing nitrate absorption by Arabidopsis plants at very low concentrations. However, not all plants are equal. “Our preliminary investigation suggests that some domesticated crop plants do not have any mechanism equivalent to NRT2.4 in Arabidopsis,” Kiba explains. “It is possible that domesticated plants have lost such a mechanism because it is not necessary in a fertilized environment.”

Introducing the NRT2.4 gene to crops may improve nitrogen uptake efficiency in the future. Kiba notes that “this could eventually enable us to reduce nitrogen fertilizer use and to conduct sustainable agriculture easily.”
Made-in-Singapore H5N1 Bird Flu Diagnostic Kit – Detects All Known Strains of H5N1 Virus with a Single Test

The close collaboration between scientists from the Experimental Therapeutics Centre (ETC) under the Agency for Science and Technology Research (A*STAR) and clinicians from Tan Tock Seng Hospital (TTSH) has enabled the successful development of the most comprehensive and rapid H5N1 bird flu test kit available to date. With this highly advanced kit, doctors can now rapidly detect all existing strains of the H5N1 viruses in a single test with almost 100% accuracy, within a few hours. This is a big boost to public healthcare system and a great stride forward in pandemic preparedness against this highly infectious disease worldwide.

The bird flu virus, scientifically termed as the Avian Influenza virus, is usually lethal to the birds and normally does not transmit to humans. However, highly lethal and contagious strains like H5N1 Avian Influenza A virus that can ‘jump’ from birds to human have been reported to cause serious infections and even death rates as high as 60% in infected patients. Although antiviral treatment is available, the potential for H5N1 bird flu virus to spark a pandemic remains a serious threat to public health as most humans do not have immunity to the H5N1 virus. Therefore, to successfully curb the spread of the disease during an outbreak, accuracy and speed of detection on the type of H5N1 virus is of essence for effective infection control intervention and patient management.

The current gold standard for H5N1 detection recommended by the World Health Organization (WHO) is only able to detect three out of the 10 distinct genetic groups (clades 1, 2 and 3). To detect all existing strains of H5N1 with the WHO detection method would not be possible. The made-in-Singapore H5N1 test kit, which is more accurately known as the H5N1 real-time Reverse Transcription Polymerase Chain Reaction (RT-PCR) assay, is the only detection kit currently available on the market that can accurately and rapidly detect all known strains of the H5N1 Avian Influenza A virus in a single test within a matter of hours.

Co-developed by Dr. Masafumi Inoue, a Senior Research Scientist and Project Director of Technology Development from ETC and Dr. Timothy Barkham, a senior consultant of Laboratory Medicine from TTSH, this newly launched H5N1 test kit has been clinically validated by several hospitals in Southeast Asia.

“We are excited to be able to contribute to the fight against H5N1 virus with our expertise and know-how. Our technology has greatly simplified and accelerated the process of detection and identification of new H5N1 variants. Such information is especially critical when the virus mutates to become more dangerous, such as in drug resistance,” said Dr. Inoue.

To enhance its usability, this new H5N1 test kit is also purposefully designed to be compatible with the previously launched “4-plex” Influenza diagnostic kit. The latter is already adopted for use by several regional hospitals in Thailand. Using such multiplex assays enables simultaneous detection and differentiation of the different types of influenza infection in a single test, which will save hospital labs and clinicians significant time and cost.

“While there have not been any reported H5N1 cases in Singapore, this mutating subtype of influenza virus type A continues to be a concern. The ability to detect and characterise influenza strains remains important in the management of the disease. With this latest H5N1 assay, we can easily combine it with our previous 4-plex Influenza kit to differentiate which strain of Influenza is present with one test, giving a definite diagnosis and faster turnaround for our patients and our colleagues in infection control and public health,” said Dr. Barkham.

Local Small and Medium Enterprise (SME), AITbiotech Pte Ltd, a regional provider of genomic services and molecular diagnostics kits, has recently signed a licence agreement with Exploit Technologies Pte Ltd (ETPL), the technology transfer arm of A*STAR, to market this H5N1 kit regionally.

“The new H5N1 test kit from A*STAR is a significant addition to AITbiotech’s existing portfolio of products for Influenza virus screening and surveillance. In light of the recent H5N1 outbreak in this region, we believe that this test can play a vital role for governments and public health institutions to effectively fight and control the outbreak of any H5N1 virus”, said Mr Alex Thian, Founder and Chief Executive Officer of AITbiotech.

Previously, AITbiotech has acquired several other molecular diagnostic licenses from ETPL for swine flu mutation surveillance and for multiple pathogens detection, including Dengue, Chikungunya and Mycobacterium Tuberculosis.

“Licensing these highly sophisticated assays from A*STAR has given AITbiotech a springboard into the highly competitive market of Molecular Diagnostics. With our expanded capabilities, we are now able to provide a comprehensive suite of diagnostic services for a range of infectious diseases to the research, healthcare and biomedical industries in Singapore and Asia,” added Mr Thian.

“This collaboration between A*STAR, TTSH and AITbiotech is a great example of how public and private sectors can partner to drive impact in Singapore's healthcare and biomedical industries. We remain committed in our role to transfer A*STAR technologies to help SMEs like AITbiotech stay competitive by delivering products with direct societal benefits,” said Philip Lim, CEO of ETPL.
THAILAND

KEEEN, Thai Bioremediation Product, Awarded Gold Medal for "Bioremediation Agent developed to Greenovation Product"

Bangkok, Thailand, 30 May 2012 The new innovative product "KEEEN" picked up the Gold Medal Award for "Bioremediation Agent developed to Greenovation Product" at the 23rd International Invention, Innovation and Technology Exhibition (ITEX 2012) held at Kuala Lumpur Convention Center, Malaysia on 17-19 May 2012. In addition, KEEEN was honored with the Best Invention in Biotechnology from Japan and the Best Invention in Environment from China, selected by judges from Japan and China, respectively, at the same event.

ITEX is an annual exhibition organized by the Malaysian Invention and Design Society, bringing together the latest inventions and innovations by universities, research institutions, individual inventors and corporations from ASEAN, Asia and Europe. ITEX 2012 showcased over 800 new inventions, innovation and technology which can be divided into 23 categories with innovations from Thailand, Malaysia, Singapore, Taiwan, Hong Kong China, South Korea, Russia, Poland and several other countries.

KEEEN was originated from a joint research between Hi-Grimm Environmental and Research Co. Ltd. and BIOTEC, led by Dr. Somkiet Techkarnjanaruk, to screen for local oil-degrading bacteria for the commercial bioremediation products. Watson Ariyaphuttarat, Founder & Industry Pioneer, Chief Industrial Ecologist of Hi-Grimm stated that, "this innovation was developed in response to the industrial sector's demand to resolve the industrial waste treatment efficiently and environmentally friendly."

KEEEN was launched in 2010 and since then has been servicing various industries such as petrochemical industry, automobile industry, food industry, hotels and hospitals.

"Our partnership with Hi-Grimm is a good example of collaboration between public and private sectors, complementing our scientific expertise with the company's acumen in product development to meet market demand," said Dr. Kanyawim Kirtikara, BIOTEC Executive Director.

"Not just the effective research partnership with BIOTEC, but being in the NSTDA Business Incubation Program also played an important role in KEEEN's accomplishment" added Mr. Watson.

Established in 2010, NSTDA Business Incubation Center (BIC) provides helpful environment and facilities to nurture and groom new technopreneurs which includes workshops, training, consultation, exhibition, networking, business and fund matching to its incubatees. The objective of BIC is to shorten the process, to strengthen the health of the businesses and to ensure the effectiveness of its pre-incubation and incubation programs for strong new technology and IT businesses.

"This innovation was developed in response to the industrial sector's demand to resolve the industrial waste treatment efficiently and environmentally friendly."

Watson Ariyaphuttarat
Founder & Industry Pioneer, Chief Industrial Ecologist of Hi-Grimm
MorphoSys AG announced that its partner Roche has expanded the ongoing SCarlet RoAD Phase 2 clinical trial of gantenerumab for prodromal (early) Alzheimer’s disease to a potentially pivotal study. The trial size will be increased from 360 to 770 participants, and a favorable outcome to the trial could be used by Roche to support a marketing application for gantenerumab. The expansion of the study triggered a clinical milestone payment to MorphoSys, the details of which were not disclosed. MorphoSys stands to receive further developmental milestones as well as royalties on product sales.

“This is a major step forward for a HuCAL antibody program that has genuine blockbuster potential”, commented Dr. Marlies Sproll, Chief Scientific Officer of MorphoSys AG. “Gantenerumab is the first investigational antibody development program for Alzheimer’s disease to be clinically tested in a setting for which there is great hope, namely the treatment of early-stage, pre-dementia subjects. A potential path to market for this program has become much clearer with this transition to a pivotal trial”.

“We believe the greater opportunity to make a difference in patients’ lives is in early diagnosis and intervention,” said Luca Santarelli, Head of Neuroscience at Roche. “Our attempt is to utilize a biomarker-driven approach, leveraging both our pharmaceutical and diagnostics divisions to develop a companion diagnostic for gantenerumab to select patients at the prodromal stage, before significant damage to the brain has occurred.”

Gantenerumab is an optimized, fully human antibody that was developed on behalf of Roche by MorphoSys scientists using the Company’s proprietary HuCAL technology. Gantenerumab is unique amongst antibodies in development in that it binds to both the N-terminus and mid-section of the 42 amino acid amyloid-β peptide. It has been shown to break down amyloid plaque both in vitro and in vivo. In Phase 1 clinical trials conducted by Roche, the antibody was found to bring about rapid, dose-dependent clearance of plaque from the brains of mild to moderate Alzheimer’s disease patients. The ongoing clinical trial is designed to evaluate its effect on cognition and functioning as well as its safety and pharmacokinetics in patients with prodromal, or early-stage, Alzheimer’s disease. In this phase of the disease, which can be characterized by measuring certain biomarkers, patients have only mild cognitive impairment and have not yet been diagnosed with Alzheimer’s disease. According to recent research, amyloid plaque may accumulate even at this early stage in the brains of sufferers, and may lead to full-blown disease.

MorphoSys’s clinical pipeline now comprises one program in Phase 3 development, seven in Phase 2 and twelve in Phase 1. Of these, four are proprietary, as yet un-partnered programs, namely MOR103, which is in a Phase 1b/2a trial for rheumatoid arthritis and a Phase 1b trial in multiple sclerosis, MOR208, which is in a Phase 1 trial for chronic lymphocytic leukemia and MOR202, which is in a Phase 1/2a trial for multiple myeloma.
New Technique to Predict Heart Attacks

A new imaging technique combining positron emission tomography (PET) and computerized tomography could help improve how doctors predict a patient’s risk of having a heart attack.

The research – from the Universities of Cambridge and Edinburgh and the British Heart Foundation (BHF) – highlights the disease processes causing heart attacks directly within the coronary arteries.

Researchers recruited 119 volunteers aged between 64 and 80 with and without aortic valve disease and used the standard calcium test to measure the amount of calcified plaques in their coronary arteries. While the test is commonly used to predict heart attack risk, it is unable to distinguish between previously built up calcium, and that which is actively building up.

Patients were also injected with two contrast agents; the first – 18F-Fluorodeoxyglucose (18F-FDG) – was used in imaging of atherosclerotic plaque inflammation by Cambridge researchers a decade ago. The second – 18F-sodium fluoride (18F-NaF) – is taken up by cells in which active calcification is occurring. It can then be visualized and quantified during a PET scan.

"Predicting heart attacks is very difficult and methods we’ve got now are good but not perfect," said Dr. Marc Dweck, lead author and BHF Clinical Research Fellow. "Our new technique holds a lot of promise as a means of improving heart attack prediction."

Researchers wanted to identify patients with active ongoing calcification as they may be at a higher risk of heart attack than those patients in whom calcium developed a long time ago. Their results – published in the Journal of the American College of Cardiology (JACC) – show that increased 18F-NaF activity could be observed in specific coronary artery plaques in patients who had many high-risk markers of cardiovascular disease.

“Our results show, for the first time, that certain areas of atherosclerosis within the coronary arteries, previously thought to be inert, are actually highly active and have the potential to cause heart attack," said Dr. James Rudd, joint senior author from Cambridge.

"Once identified, they might be targeted with drug therapy more effectively. Additionally, we might be able to improve our ability to predict an individual person’s future risk of heart attack using this fairly straightforward imaging test in selected people."

FEI Launches ‘Living Lab' for Structural Biology Research at NIH

FEI, a scientific instruments company, marked the official launch of the new Living Lab for Structural Biology during an event on the NIH campus.

“This event commences the FEI-NIH Living Lab joint scientific projects. FEI has installed the Titan Krios™ transmission electron microscope (TEM), the world’s most powerful commercially-available electron microscope for structural biology, and our onsite team is assembled, including experts in sample preparation, cryo-electron microscopy applications, and Titan Krios operation. We are excited about this program and the great results we expect it will yield for the structural biology research community,” stated FEI’s President and CEO Dr. Don Kania.

The multi-faceted research program of the Living Lab at NIH includes participation from leading scientists, such as Dr. Sriram Subramaniam, director of the NIH component of the Living Lab, with expertise in cryo-electron microscopy and tomography; Drs. Adriaan Bax and G. Marius Clore, with expertise in NMR spectroscopy; Drs. Fred Dyda and Alex Wlodawer, with expertise in X-ray crystallography; and Drs. Suresh Ambudkar and Stuart Le Grice, with expertise in biochemistry. The capabilities of the Titan Krios for advanced cryo-electron microscopy are expected to effectively complement the work being done at NIH with NMR spectroscopy and X-ray crystallography and help accelerate important medical discoveries relevant to global health challenges such as HIV/AIDS, diabetes and cancer.
Scientists have created synthetic platelets—the blood components that prevent excessive bleeding and heal wounds. University of California, Santa Barbara researchers, in collaboration with researchers at Scripps Research Institute and Sanford-Burnham Institute in La Jolla, California, report their findings in the journal *Advanced Materials*. The unique physical and biochemical properties of platelets play an important role in performing complex biological tasks. Smaller than red blood cells, platelets are flexible, disk-shaped cells that are 2-4 micrometers in size.

“Upon further optimization and exhaustive testing, the synthetic platelets could be used for various biomedical applications,” says the paper’s first author Nishit Doshi, a researcher from the department of chemical engineering.

The challenge Doshi and colleagues faced was to develop a comparably sized particle—roughly 1/50th of the diameter of a strand of hair—that had key structural properties of real platelets.

“In order to mimic the size, shape, and surface functionality of natural platelets synthetically, polymeric particles are particularly attractive,” says Doshi. “However, polymeric particles are orders of magnitude more rigid than platelets.”

To solve the problem of flexibility, researchers at UC Santa Barbara used a polymeric “template”—a core upon which layers of proteins and polyelectrolytes were deposited, layered, and cross-linked to create a stable synthetic platelet-shaped particle.

The rigid polymeric core was then dissolved to give the particle the desired flexibility. The particle was then coated with proteins found on the surface of activated natural platelets or damaged blood vessels, a procedure performed by the researchers at Scripps Research Institute.

These synthetic platelets may be used to not only perform the typical functions of human platelets but also may be used to carry imaging agents to identify damaged blood vessels or to deliver drugs that dissolve blood clots.

The synthetic platelets represent the latest and one of the most advanced in a line of efforts over the last century to mimic platelet function. While clotting factors and platelets from outside donors are used widely to halt bleeding, immune system responses and thrombosis have been issues.

Non-platelet-derived substitutes have also received attention. However, Doshi says, these do not physically resemble the physical features of natural platelets.

“This development is a significant milestone in the field of biomimetic materials,” says Samir Mitragotri, professor of chemical engineering and director of UC Santa Barbara’s Center for Bioengineering, and an author of the paper.

“By capitalizing on our capabilities in engineering materials, with the expertise in platelet biology that exists in Professor Ruggeri’s laboratory, our synthetic platelets combine unique physical and biological attributes that mimic natural platelets.”

In 2009, Doshi and colleagues in the Mitragotri laboratory developed synthetic red blood cells.

“This work is a marvelous demonstration of the power of material synthesis applied to medical problems. The synthetic platelets can have profound implications in wound-healing problems for trauma and wounds arising in both battlefield situations and during surgery,” says Frank Doyle, director of UCSB’s Institute of Collaborative Biotechnologies and the Associate Dean of Research in the College of Engineering.
Software Scans Tongue for Signs of Disease

New software combines ancient Chinese practices and modern medicine to measure health by analyzing images of the tongue.

For 5,000 years, the Chinese have used a system of medicine based on the flow and balance of positive and negative energies in the body. In this system, the appearance of the tongue is one of the measures used to classify the overall physical status of the body, or "zheng".

"Knowing your zheng classification can serve as a pre-screening tool and help with preventive medicine," says Dong Xu, chair of the computer science department at the University of Missouri.

"Our software helps bridge Eastern and Western medicine, since an imbalance in zheng could serve as a warning to go see a doctor. Within a year, our ultimate goal is to create an application for smartphones that will allow anyone to take a photo of their tongue and learn the status of their zheng."

US Legislation Will Ensure Tighter Checks on Foreign Drug Factories

US lawmakers are taking steps to increase the safety of drugs manufactured on foreign soil.

The US Senate has passed new legislation that should see more stringent checks on overseas drug manufacturing facilities.

At present, around four-fifths of pharmaceutical ingredients used in US medicines are made in foreign countries such as China and India.

But the US Food and Drug Administration (FDA) only performs inspections on these factories every nine years, on average, according to the Associated Press.

Under the Senate bill, FDA inspectors will no longer be required to perform checks on all factories on home soil every two years, enabling them to spend more time focusing their inspections on operations overseas.

Foreign pharmaceutical firms will be obliged to cooperate as US border agents will be given new powers to block imports of drugs from companies that hinder FDA inspections.

Allen Coukell, from the Pew Charitable Trusts, told the Associated Press: "This puts domestic and international facilities on an even playing field for the first time."

"It says to FDA, 'you should inspect the highest risk facilities first, no matter where they are in the world.'"

The legislation should help to allay fears about the quality of drugs manufactured in countries such as China, which has experienced a number of healthcare scandals in recent months.

In April, 22 people were arrested in a case involving contaminated medicine capsules, which were found to contain up to 90 times the permissible level of chromium.
Veolia Water Solutions & Technologies receives two prizes at AquaTech China for AnoxKaldnes™ MBBR technology and its Carbon Footprint Reduction Program

Veolia Water Solutions & Technologies has won two prestigious awards at AquaTech China, the world’s leading trade event for the process, drinking and wastewater technology sectors.

As part of the show’s Innovation Contest, the AnoxKaldnes™ MBBR biofilm technology was crowned Best Innovation and Veolia’s Carbon Footprint Reduction Program emerged as first runner-up at the Best Wastewater Solution Contest.

AnoxKaldnes™ MBBR is an efficient and compact wastewater treatment technology that operates as a fixed-film process without activated sludge. In this innovation, specially engineered plastic carriers coated with biofilm are suspended in a reactor. This provides a large surface area for effluent exposure to biofilm, which is coated with different microorganisms that work to trap sewage. One of the greatest benefits that AnoxKaldnes™ MBBR brings to end-users is its ability to be easily integrated into existing infrastructure without an increase in footprint. The technology is widely used in industrial and municipal applications for organic matter removal, nitrification, denitrification and phosphorus removal. In the AnoxKaldnes MBBR, microorganisms on the biofilm of plastic carriers trap sewage.

To remain at the leading-edge of sustainable offerings, Veolia has put in place a Carbon Footprint Reduction Program which drives innovation, accelerates adoption and development of clean technologies for water treatment. This corporate-wide program has been implemented along with procedures, systems and key performance indicators, which ensure continuous development of innovative technologies designed to meet our municipal and industrial customers’ environmental and financial goals. This metric demonstrates value to our customers by justifying an investment in a best-in-class solution, not just because it is reducing the operating costs over the lifetime of the installation but because it is also minimizing the financial risk of a direct and indirect carbon contribution.

As part of the nomination process of the Best Innovation and Best Wastewater Solution contests, an expert panel of judges selected solutions of world-class standards. Professionals in the water industry then voted for innovations that they deemed the most deserving of the awards.

Laurent CUNY, Vice-President, Veolia Water Solutions & Technologies, China Industrial said, “It is indeed an honor to have industry experts and professionals lending their weight to recognize Veolia’s innovations and initiatives towards sustainable manufacturing. We look forward to providing the industry with even more cutting edge and environmentally-friendly solutions for water and wastewater treatment in China.”
An international pear genome consortium, comprised of seven universities and institutes, has completed the first pear genomic sequence in the world. The early access of pear genomic data is now available online (http://peargenome.njau.edu.cn). The international team includes researchers from Nanjing Agricultural University, BGI, Zhejiang Academy of Agricultural Sciences, University of Illinois at Urbana-Champaign, University of Georgia, University of Hawaii, and Tohoku University.

Pear (Pyrus spp.) is one of the major and oldest cultivated fruit trees in the temperate regions, which is likely to have originated during the Tertiary period (65–55 million years ago) in southwestern China. It is genetically diverse with more than 5,000 cultivars and accessions present all over the world that could be divided into two major groups, the European or "Occidental" pears and the Asiatic or "Oriental" pears.

Since pear genome sequencing project was initiated in April of 2010, the consortium has devoted great efforts on the de novo sequencing, assembly and annotation. The joint effort has yielded a high-quality diploid draft genome sequence for the commercially important Asiatic pear cultivar "Suli", P. bretschneideri Rehd. cv. Dangshansuli. A total of 97.1% of the estimated whole genome size has been assembled. These assembled scaffolds have been aligned and oriented to their corresponding 17 chromosomes using a high-density genetic map.

Professor Shaoling Zhang, the chief scientist and group leader of the pear genome sequencing project at Nanjing Agricultural University, said, "The complete sequencing of the pear genome provides a solid scientific foundation for scientists to explore the complex genetic characteristics underlying the pear fruit tree, such as the key genes that related with the taste, color, storage, resistance for diseases and insects as well as yield improvement. Moreover, the genomic sequence provides an invaluable new resource for tracing pear’s evolutionary history."

Professor Jun Wang, Executive Director of BGI, said, "The completion of the genome sequencing is a major step forward to understanding pear’s important economic traits. We are making continuous efforts for decoding genomes of plants and animals that play a key economic role or are considered valuable food sources, as well as endangered species that have evolutionary or scientific importance. We would like to enhance the genomic research through collaborative projects with researchers worldwide for better understanding the genetics basis of plants and animals and boosting the further development of modern agriculture."
Eli Lilly Opens Diabetes Research Center in China

The center gives a new twist to the growing approach of personalizing medicine for the patient. The Shanghai center focuses on discovering diabetes medicines geared specifically to the Chinese. Lilly is creating what will be its second-largest R&D center abroad because it gives greater entree to the huge Chinese market (China is the world’s most populous country, with 1.3 billion people) and responds to the spread of diabetes there (nearly 10% of Chinese adults have it).

China ‘Soaring Ahead’ in Nanotechnology Research

China has emerged as a major nanotechnology player, but India is still working to catch up — and both countries have some ground to cover before they can hope to dominate the world of journals and citations, according to a paper in the February issue of *Scientometrics*.

The study, led by Sujit Bhattacharya at the National Institute of Science, Technology and Development Studies in New Delhi (NISTADS), measured progress made by China and India in nanotechnology research using four indicators — publications, patents, standards, and the processes and products that have emerged as a result of research.

China’s share of published nanotechnology papers soared from less than 10 per cent of the global total in 2000, to nearly a quarter by 2009 — overtaking the United States. By contrast, India was occupying seventh place. However, neither was well-represented in the top three nanotechnology research journals, and although Chinese representation in high-quality journals was rising, its researchers were well behind the European Union and the United States in attracting citations. In terms of patent applications received, China was second to only the US, and accounted for a fifth of international patenting activity. By contrast, India represented just four per cent of such activity.

References


Source: SciDev.Net

By T. V. Padma
Latest Genomic Studies Shed New Light on Maize Diversity and Evolution

BGI, the world’s largest genomics organization, together with other 17 international institutes, announced that they completed the second generation of maize HapMap (Maize HapMap2) and genomics studies on maize domestication and improvement. The two separate studies were published online in the same issue of *Nature Genetics*.

The studies mark an important milestone in Maize (*Zea mays*) genomics research, providing an unprecedented glimpse into maize’s ‘wonderful diversity’ and revealing new insights into the evolutionary history of maize genome. These studies will provide valuable insights for botanists and breeders worldwide and facilitate the genetic engineering of this vital cereal crop in the world.

In addition to BGI, the other collaborative organizations include U.S. Department of Agriculture (USDA), Cold Spring Harbor Laboratory, University of California Davis, Cornell University, the International Maize and Wheat Improvement Center (CIMMYT), and others.

Maize’s impressive diversity has been attracting much attention in the academic community and agricultural sector. However, characterizing this diversity— in particular at high levels— has been technically challenging. In this study, researchers developed a novel population-genetics scoring model for comprehensively characterizing the genetic variations, including single nucleotide polymorphisms (SNPs), small insertion—deletions, and structural variations (SVs). Through the comprehensive analysis, about 55 million SNPs were identified across 103 inbred lines of wild and domesticated maize. They also found that SVs were prevalent throughout the maize genome and were associated with some important agronomic traits, such as those involved in leaf development and disease resistance.

The researchers also investigated the major factors that influence the maize genome size. The results showed the genome size variations between maize and Gama grass (*Tripsacum dactyloides*), maize’s sister genus, are mostly driven by the abundance of transposable elements (TE). In contrast with the fact that the intra-species genome size variation is influenced by the DNA structure known aschromosomal knobs. In addition to the differences, there is tremendous unity of gene content between maize relatives, suggesting that the adaptations, such as frost and drought tolerance, amongst all of maize’s relatives are likely integratable in maize.

Since maize was domesticated approximately 10,000 year ago, its wild progenitor went through a particular transformation that had radically altered maize’s wild species to meet human’s needs. To comprehensively trace maize’s evolution process, researchers sequenced 75 wild, landrace and modern maize lines. Through the comparative population genomics analysis, they found the evidence of new genetic diversity that has arisen since domestication, maybe due to the introgression from wild relatives. They also identified a number of genes that obviously had played important roles in the transition from wild to domesticated maize.

More importantly, the results demonstrated that the selection applied by ancient farmers seemed to play a stronger impact on maize evolution than the breeding techniques adopted by modern breeders. Hybridization in agriculture is vitally important to maintain genetic diversity, and sustains the quality and yield of a crop. In this study, researchers found that many of the changes in the patterns of gene expression had been concentrated in the genes selected for heterosis by modern breeding techniques. These findings suggest that modern breeders should devote more efforts to make effective improvement on candidates by introducing more diversity at the regions linked with selection.

Dr. Xun Xu, Deputy Director of BGI, said, “Genetic improvement of crops is the key output of breeding research. The two studies provide a new way to comprehensively understand maize’s genetic diversity and evolutionary history as well as offer an invaluable guidance for botanists and breeders to improve this vital crop.”

Dr. Gengyun Zhang, Vice President of BGI, said, “Maize is one of the world’s most important crops. The two studies will provide a valuable foundation for accelerating the improvement of maize towards meeting the world’s increasing demands for food, livestock feed and biofuel. We look forward to achieve more breakthrough for solving the food security challenges and environmental problems in the near future.”
Molecular diagnostics company Insight Genetics and Kindstar Globalgene (Beijing) Technology, Inc., China’s leading diagnostics company, today announced that the companies are partnering to enhance cancer care in the People’s Republic of China and surrounding regions.

The new partnership begins with a licensing agreement that allows Kindstar to add Insight Genetics’ Insight ALK Screen™ lung cancer test to Kindstar’s growing menu of tests that improve cancer diagnosis and patient care. Kindstar’s diagnostic services, which are offered from its laboratories in Wuhan, Beijing and Shanghai, help physicians properly diagnose diseases and allow them to develop treatment plans for patients suffering from hematologic malignancies, solid tumors, and genetic diseases.

Insight Genetics’ unique test broadens the company’s ability to help doctors select the best possible treatments for patients with non-small cell lung cancer. Kindstar expects to launch Insight ALK Screen to its clinician and hospital customers throughout China, the Special Administrative Region of Hong Kong, and Macau in July 2012.

“Adding Insight ALK Screen to our menu of tests is just the beginning of what we see as a broader strategic relationship with Insight Genetics,” said Shiang Huang, MD, chief executive officer of Kindstar. “With Insight ALK Screen, we can offer clinicians more detailed information on their patients’ particular forms of cancer so they can determine the most effective treatment course. Working with Insight Genetics over the long term, we see great opportunity to collaborate on the creation of additional tests that will help us spread the benefit of personalized cancer care to more people in China and surrounding regions.”

Insight ALK Screen is a real-time PCR-based test that detects cancer-causing fusions and mutations of anaplastic lymphoma kinase (ALK). ALK fusions and mutations have been shown to be a contributing cause in approximately 5-10 percent of lung cancers. The test offers fast, accurate and comprehensive results that inform a physician if a patient’s cancer is associated with ALK.

Knowing if a patient is ALK fusion-positive assists clinicians in determining if the patient can be treated with an ALK inhibitor, an emerging class of cancer therapy. Since only patients with ALK fusions are likely to respond to ALK inhibitors, accurate diagnostic screening is essential before prescribing ALK-targeted drugs.

“Kindstar is truly leading the way in enhancing China’s healthcare system by making advanced diagnostics more widely accessible,” said Eric Dahlhauser, Chairman and CEO of Insight Genetics. “We’re proud to offer Insight ALK Screen to physicians across China, Hong Kong and Macau, and more importantly, begin our partnership with Kindstar to find ways that we can collaborate to enhance and personalize cancer care around the world.”

Comparison testing has shown that Insight ALK Screen has many benefits over other ALK testing methods, including fluorescent in situ hybridization (FISH) and immunohistochemistry (IHC). The assay offers the accuracy and reliability advantages of a qPCR platform without the need for validated primer pair for each fusion. Unlike a variant-specific multiplex strategy, Insight ALK Screen™ can detect the presence of any fusion within the ALK gene. It also can identify ALK upregulation without using a secondary platform.

In addition to the proven role it plays in select lung cancers, ALK has been found to have a pathogenic role in many cancers including diffuse large B-cell lymphoma, inflammatory myofibroblastic tumor, esophageal squamous cell carcinoma, colorectal cancer and breast cancer. It is estimated that more than 1,300,000 new cancer diagnoses globally each year can be linked to ALK mutations and fusions.
Two studies from the Institute of Plant and Microbial Biology published in PNAS show how plants respond to changing environments

The laboratories of Dr. Shih-Long Tu and Dr. Paul Verslues, both Assistant Research Fellows at the Institute of Plant and Microbial Biology, have recently reported new mechanisms by which plants detect and adapt to changes in light and water abundance, two key environmental factors controlling plant growth. Both studies were published in the Proceedings of the National Academy of Sciences of the United States of America (PNAS) in May.

Light, water and appropriate temperature are basic requirements for plant growth. The prospect of global climate changes impacting light, temperature and precipitation patterns have made plant environment-interaction an important topic in plant science worldwide. The Institute of Plant and Microbial Biology (IPMB) has several research groups focused on plant response to changing environments with the goal of understanding how changing environments affect plant growth. In the present studies, Dr. Shih-Long Tu reported that a new enzyme named phycourobilin synthase (PUBS) can synthesize an alternative chromophore (a compound that absorbs light) to regulate phytochrome (a photoreceptor which binds the chromophore to sense light) activity. The group of Dr. Paul Verslues reported variation in levels of proline, a stress-protective compound, and production of a non-functional RNA encoding the proline synthesis enzyme P5CS1 that are associated with adaptation to different environments.

Light is the most important energy source for photosynthetic organisms. Phytochromes are the main photoreceptors that detect light and mediate changes in plant growth to match light conditions. Phytochromes require a chromophore cofactor to fully function. In most plants, phytochromobilin synthase (HY2) is a key enzyme producing the chromophore for phytochromes. However in the moss Physcomitrella patens, Dr. Tu’s laboratory identified a new second enzyme they named PUBS that can synthesize an alternative chromophore to regulate phytochrome activity. PUBS can only be found in green algae, mosses, and lycophytes, suggesting that this enzyme was important evolutionarily for green plants to adapt to light-rich environments. Dr. Tu’s team further identified phytochrome-regulated genes in Physcomitrella. These results reveal that moss phytochromes efficiently re-program gene expression for phototrophic growth in the light. This approach allows, for the first time, a global view of phytochrome-mediated gene regulation in nonvascular plants. These new findings can be applied to agriculture, to modulate crop growth and development using light.

The laboratory of Dr. Paul Verslues is interested in plant responses to limited water supply during drought. Many plants accumulate large quantities of proline during drought; however, the adaptive value of proline has remained unclear. The model plant Arabidopsis thaliana is distributed across a wide geographic and climate range and differences between Arabidopsis types can be used to discover factors, such as proline, needed for adaptation to different environments. The Verslues laboratory, along with collaborators at the University of Texas found that different types of Arabidopsis varied ten-fold in drought-responsive proline accumulation. Some of this variation was accounted for by high levels of a non-functional RNA produced by the gene encoding the proline synthesis enzyme 1-pyrroline-5-carboxylate synthetase1 (P5CS1). Arabidopsis types having high levels of the non-functional P5CS1 RNA shared the same set of genetic changes that promoted alternative RNA splicing of P5CS1. These data demonstrated a novel source of RNA splicing variation in plants and correlation of P5CS1 variation with climate data indicated a role of P5CS1 and proline synthesis in adaptation to environments differing in water availability and temperature. The results have implications in drought-adaptation and in how proline metabolism may be best targeted in biotechnology efforts to improve drought tolerance of crop plants.

Source: Academia Sinica

China’s Pharmaceuticals Sales Force Levels Surpass US for First Time

China now has a larger pharmaceutical sales force than the US. The number of sales representatives for the pharmaceuticals industry is now higher in China than the US for the first time.

Figures from Cegedim Strategic Data’s latest audit of the Americas, Europe and the Asia Pacific region show that sales force numbers reached 80,000 in China in March 2012, representing a 17 per cent increase over the preceding 12 months.

During the same period, sales force numbers in the US fell by eight per cent to 72,000.

Delphine Perridy, managing director of Cegedim Strategic Data China, said: “Sales force growth here reflects the huge potential that the industry sees for this market.”

“Having covered the major cities, companies are now focussing expansion efforts on more hospital types and lower tier cities. We expect to see continued expansion through next year.”

The market research company – which tracks industry sales force figures and pharmaceutical marketing investments in more than 30 countries – also noted that sales force levels continue to drop in major western markets.

This is due to a combination of several major brands going off-patent and pipelines failing to deliver new treatments at the rate required to maintain the current number of reps.
Clinical laboratories characterized by commercial operation and independent of hospitals, appeared in the 50s and thrived during that period of time from the 1970s to 1980s. By the 1990s, they have become unique laboratories providing standardized third-party service of medical diagnostic testing and operated on a large scale mainly in America and Europe. These laboratories were called commercial laboratories or reference laboratories, and in China it is referred to as an Independent Medical Laboratory (IML).

Since the establishment of the commercial laboratory and its service model, the laboratories have played important roles in healthcare and medical service. It has been recognized that the involvement of IMLs in medical practice has promoted the structural optimization of the health and medical care system. From the end of last century, along with revolutionary changes in the medical care system, commercial laboratories have emerged in China. The development of commercial laboratories suffered many difficulties in the early stages because there were no standards and guidelines that existed for their establishment, operation and management of the specimens, and feedback to the service type were not always positive. Surprisingly the field of commercial or independent medical laboratory has shown great prospect in China, and several laboratories that started earlier have basically achieved the goal of standardization and large-scale operation, such as KingMed Center For Clinical Laboratory, Daan, Adicon and Dian. At the same time, medical institutes which accept the third-party service have significantly increased and a number of clinical practitioners have recognized IMLs as an effective approach to support their clinical practice.

To guide the development of commercial laboratories, on 21 December 2009, the Chinese Ministry of Health issued the "Notice on Printing and Distributing Basic Standards for Medical Laboratory (on Trial)". In order to further perfect medical care and health service system during implementation of "Suggestions of Central Committee of CPC and the State Council on Deepening the Reform of Medical Care and Health System, strive to improve service level and quality of basic medical care and health institutions, promote appropriate distribution of medical care resources, and enhance clinical laboratory quality, our ministry has made the decision to increase medical laboratory in the category of medical care institutes."

The Medical laboratory specified in the Notice was referring to the independent commercial laboratory. Since then, IMLs
have become a medical institute that is officially recognized by the Chinese Ministry of Health and a milestone for the beginning of commercial laboratories in China.

The Notice from the Chinese Ministry of Health includes the preliminary specifications with regards to the commercial laboratories in China as follows: (1) the authority agency for the approval and registration; (2) the factors of population, geography, transportation and potential client for establishment and distribution; (3) the service scope and object; (4) the administrative and legal guaranty for laboratories and clients; (5) the guidelines and regulations to be followed for operation; (6) the minimal requirements for the laboratory setting-up. In summary, the Notice has given a principled guidance about how to establish and operate a commercial laboratory or IML officially, therefore forming the basis for rapid development and standardized management of such institutes.

Recently, a new trend is appearing in the field of laboratory medicine; efforts are being made by government agencies to establish central laboratories (core laboratories) in different areas. The core labs collect and test the samples from the medical institutes belonging to each of the areas in order to share the resources sufficiently and provide the testing results from different institutes. What distinguishes the commercial laboratories from the core labs is that they are funded and managed by the local government and are non-profit. There is another form of non-profit IML which is advocated by government but invested by social financial source. These emerging variations of IMLs are just the beginning and will need time to see if they work or not.

In China, the Centers for Clinical Laboratory (CCL) are responsible for the quality management (QM) and assurance (QA) of medical laboratories at different levels. At the national level, there is the National Center for Clinical Laboratory (NCCL), which is authorized by the Chinese Ministry of Health to implement the quality control and improvement of clinical diagnostic testing at a nationwide level. At the same time, NCCL organizes the external control program for clinical laboratories throughout the country and is responsible for the creation, optimization and promotion of a reference system for laboratory testing. The Centers for Clinical Laboratory have been set up at the provincial and city level and they are in charge of the QM and QA in the corresponding areas respectively. The duties of CCLs might be more specific compared to NCCL. For example, a provincial Center for Clinical Laboratory may be involved with the following activities: (1) the quality management and supervision of clinical laboratories and the standardization of test items and operating procedures; (2) the development and improvement of national and industrial guidelines for laboratory, equipment and reagent management; (3) surveying and studying existing medical laboratories and clinical demands to provide statistics for future development; (4) collecting and analyzing the latest progress in laboratory medicine, organize and promote academic communication, introduce new test items, techniques and theories; (5) organizing and directing personnel training and education in the field; (6) evaluation and supervision of commercial or independent laboratories and lastly, (7) quality assessment of laboratory equipment and reagent.

The availability of "Basic Standards for Medical Laboratory (on Trial)" has provided the standard and guidance for quality management and supervision of IMLs or commercial laboratories. Now, the Centers for Clinical Laboratory of some provinces or cities have started to put the IMLs under their scope of supervision. For example, the Guangdong Center for Clinical Laboratory has appointed a unit specifically for taking care of the issues related to the IMLs. Therefore, each of the IMLs must participate in all of the quality control tests and evaluations organized by the Center for Clinical Laboratory and follow the guidelines, standards and suggestions commonly applied to all of the medical laboratories in order to ensure that the IMLs provide high quality third-party testing services for a variety of medical institutes and clients.

About the Author

Weimin Zou earned his Bachelor’s Degree in Medicine from the Wuhan Medical University. He is presently at the Guangdong Center for Clinical Laboratory. He is also under the Chinese Hospital Administration Association as the Vice-Chairman in Clinical Laboratory Management Committee. He is a member of the Clinical Laboratory Standards Committee of the Ministry of Health. He has been an editor for the 5th-8th Chinese Journal of Laboratory Medicine and is associated with the Medical Branch Committee of China National Accreditation Service for Conformity Assessment (CNAS) Technical Committee and Clinical Laboratory Management Professional Committee of Guangdong Hospital Administration Association.
Independent Medical Laboratories in China
A Sunrise Industry under the Circumstances of Healthcare Reformation

Yaoming Liang
Founder and CEO
KingMed Center For Clinical Laboratory, China

With the rapid development of clinical medicine, the demand on laboratory testing has increased, new technologies and equipments supplied to generate a large number of new tests to meet the clinical demands. However, it is getting difficult to establish laboratories able to perform all the tests individually because of the technological, financial, and personnel limitations, which is the case even for some large-scale hospitals. It is easy to understand that the high-tech and throughput might also mean high cost and operation/management skills thus making it difficult or uneconomical for a single hospital to conduct all the tests needed. The allure of third-party medical laboratory appears and operates with the characteristics of resource sharing and intensive managing.

The third-party medical laboratory is a medical institution licensed by a government agency responsible for healthcare affairs, as an independent legal personality, and specializes in medical laboratory testing services. The third-party medical laboratory tests samples from patients from different hospitals and delivers the results to clients by establishing a cooperative relationship with the hospitals. The third-party medical laboratory is independent of hospitals and undertakes the legal responsibility independently, therefore it is also referred to as an Independent Medical Laboratory (IML) in China.

KingMed Diagnostics is ranked among the Top 10 Enterprises with the Greatest Investment Value in the Chinese Healthcare Industry in 2009 and the 100 Enterprises with the Greatest Potential at the 2010 CV Awards.
Development status of IMLs in China

In China, IMLs appeared during the 1990s and has seen rapid development in the past five years. According to data from Frost and Sullivan (refer to diagram above), the total gross income was 1.3 billion RMB in 2010 and is estimated to reach up to 6.8 billion RMB in 2015. At present, there are more than 30 accredited IMLs with local IMLs dominant in China. According to statistical data, the income of the top five IMLs accounted for 85.8% of that of all IMLs. As the earliest and largest IML, KingMed has the most extensive network coverage and has contributed 33.5% of the total income of all IMLs in 2010.

The other well-developed local IMLs are Daan, Adicon, and Dian which together hold 46% of market share. The whole industry’s income is estimated to achieve over 10 billion RMB by 2015 according to development trends of IMLs.

Great potential for IMLs in the ongoing healthcare reformation

It has been estimated by Frost and Sullivan that the total healthcare costs will rise to 5370.8 billion RMB and lab-testing cost will reach 751.9 billion RMB by 2015. Currently, the ratio of lab-tests conducted by hospital laboratories and IMLs is 99.3% is to 0.7% in China, however in the United States, it is 62.0% against 38.0%. The ratio difference indicates the great potential for a significant growth in the Chinese IML industry.

Healthcare reformation in China covering the establishment of the basic healthcare system covering both urban and rural residents, the equalization of basic public health services, the repositioning of public hospitals, the introduction of market mechanisms, and the diversification of medical institutions, each of which has the potential to create more space for the progress of the IML field in China.

The main driving factors for IML development

1. Substantial Change of the Disease Patterns Due to an Aging Population

Growth and aging of the Chinese population have increased demand on medical services. According to the National Bureau of Statistics, the Chinese population at age of 65 and older will increase to 139 million by 2015. The economic development, countryside urbanization and lifestyle changes are leading to the changes for disease patterns. The morbidity of chronic diseases is estimated reach to 20%, which represents about 270 million patients in total and 17 million new cases each year; the diseases include cancer, metabolic and cardiovascular diseases – most of which require new and high-costing lab-tests and lifelong treatment along with consistent lab-tested monitoring.

2. The Constant Improvement of Basic Medical Insurance System in the Future

The improvement of the health insurance system includes an increase of insurance coverage and reimbursement. According to statistics provided by the Chinese Ministry of Health, 835 million people have benefited from the rural insurance system, accounting for 95% of the total rural population in 2010. The rate of reimbursement for urban residents has increased by 30% in 2006 to 50% or higher in 2010.

3. The Significance of Lab-tests in Clinical Practice has Increased

It is estimated that lab-tests has contributed to 70% predictive value in clinical decision-making. Molecular diagnostics and more advanced technologies has elevated the sensitivity and specificity of laboratory tests.
Mr. Liang Yaoming is the Board Chairman and General Manager of KingMed Diagnostics Group. He founded Guangzhou KingMed Medical Diagnostics Center in 1994, the first independent medical laboratory in China. Mr. Liang entered the Clinical Department of the Guangzhou Medical University in 1983 and graduated there with a Bachelor of Medicine. He also holds an EMBA degree from the National University of Singapore. He was sent by the Organization Department of the Guangzhou Municipal Committee to the Renmin University of China and the University of Oxford to study the "Public Administration Program for Senior Civil Servants (core MPA courses)". Prior to KingMed, he worked at Guangzhou Medical University where he held such posts as Director of the Academic Affairs Office, Director of Scientific Research Office and Director of Scientific Development Center, and he also held posts like Director of the General Services Department and Director of the University Properties Office concurrently.

He is a representative of the 10th Congress of the Guangzhou Municipality of the Communist Party of China, Vice President of the Guangzhou Branch of the China Chamber of International Commerce, President of the Biological Medicine Industry Association under the Guangzhou Branch of the China Chamber of International Commerce, Chairman of the Guangzhou Alliance of Bio-box Outsourcing, a member of the Guangdong Health Economics Association, a member of the Health Promotion Committee under the Guangdong Medical Doctor Association, a member of the 13th Executive Committee of the Guangzhou Federation of Industry and Commerce, and a member of the 8th Council of the Guangdong Quality Association. Mr. Liang was ranked among the Top 10 Persons of 2009 in the Healthcare Industry in Southern China and was granted with the title of Top 10 Outstanding Quality Managers in Guangdong Province in 2010.
Tracing the Rise of KingMed and its Future Route
A Correspondence with Hongbo Li

By Sonal Khetarpal
Edited by Sulastri Kamis

With one sixth of the world’s inhabitants residing in China and their rapid economic development in the global marketplace, it is not surprising that with time, even the healthcare sector has to catch up. Enter the KingMed Center for Clinical Laboratory, an Independent Medical Laboratory providing third-party medical diagnostic services to meet the rising demands of quicker, better and faster diagnosis. APBN finds out more about KingMed, the challenges faced as a first entrant into the industry and the future plans it has with regards to China’s moves towards health reformation.

APBN: What laboratory services does KingMed provide?

Li: In general, the KingMed Center for Clinical Laboratory provides what we call third-party service of medical diagnostic testing or detection, which classifies KingMed as an Independent Medical Laboratory (IML) or commercial laboratory. Specifically, KingMed’s services can be divided into four sections: (1) Medical diagnostic testing – testing samples from patients to obtain information regarding diseases; (2) Hygiene testing – examining the variety of samples from materials, products, environment and other resources to identify for poison, toxic or biological hazardous substances; (3) Clinical trials testing – offering specific services following the requirements from clients, in most cases, pharmaceutical companies, i.e. Contract Research Organization (CRO) services, which conducts clinical or experimental tests on new medicines or products and (4) Medical research service – utilizing KingMed’s technique platforms and academic expertise to offer hospitals, universities and research institutes services for scientific research.

APBN: Are these services different in any way from other IMLs in China?

Li: It is no doubt that Medical diagnostic testing is the main core service of all IMLs in China and I believe that each IML has the ambition to expand the scope of their services. For instance, I know that Daan Gene, one of the leading IMLs in China, provides the Medical research service too but I am not aware of any other IMLs doing so. For Hygiene testing, KingMed is the only private laboratory that has obtained government authorization to provide that service. For the Clinical trials service, as the most profitable service amongst all offered by IMLs, which is the target every IML is fighting for, I am proud to say that in terms of the test items, service amount, income, and customer numbers, KingMed is far ahead of the others. In short, only KingMed has evolved into the four independent service sections and each of them has a significant amount of services accomplished.
APBN: Where do you see KingMed ten years from now?

Li: Where can KingMed be in ten years? It is a good question and also a difficult question to answer. However, before we can see what may happen in the future, I would like to look back what have happened in the past, because the future will be developed beyond the past, and the past is the mirror from which the future might be reflected.

KingMed was established in 1994 and now she is 18 years old; in my opinion, the 18-year history of KingMed could be divided into two phases: the first phase, from 1994 to 2005, what had been done basically happened in the inside of KingMed, although a lot of things has been accomplished in the period of 10 years, actually all those could be transformed into one achievement, i.e., creation of a workflow to generate high quality detection results; the second phase, from 2006 to present, KingMed has been expanding her "body", i.e., establishment and operation of service network and after 8 years of hard work, it is almost done. Let me point out two examples to display the achievements from the two phases respectively: the world-class accreditation for laboratory quality management, including CAP, ISO15189 is representative of the first 10-year achievements and for the achievements obtained in the second phase, the well-establishment and successful operation of 19 branch laboratories covering most areas in China. In short, the past has laid great foundation for the future, so what I can see clearly in the incoming ten years are as follows:

1. Achieving world-class laboratory quality management in the entire KingMed;
2. Accomplishing the hierarchical structure of laboratory network with five levels of service laboratories will be built up: patient service centers, rapid response labs, primary testing labs, regional centralized labs, and headquarter testing center;
3. Introducing and developing advanced diagnostic testing items to catch up with international leading laboratories, particularly increasing the portion of esoteric tests;
4. Promoting the clinical-orientated testing service to help clinicians utilize KingMed's services easily and effectively;
5. Collaborating with world-class organizations and agencies, for instance, the College of American Pathologist (CAP), on behalf of CAP's request to play more active and constructive roles in the internationalization of laboratory quality management in China.
APBN: What were the challenges faced in dealing with international clients and how were they overcome?

Li: Since KingMed just started services for international clients, mainly with CROs and services in Hong Kong, the involvements are still limited. However, in the future multi-language challenges might be more serious with the increase of international business. For such potential challenges, KingMed is preparing by various approaches, including recruiting staff with international background, employing personnel native to the area, and encouraging the young employee to learn different languages.

APBN: KingMed is one of the earliest commercial laboratories in China. How is it thriving in the current overly competitive market?

Li: I think the alterative way to ask this question should be “what is the backbone for KingMed to survive and develop?” I would like to “borrow” your word “commercial” to answer your question. Although the commercial lab is the nickname of IML, KingMed has established and operated by non-commercializing; in other words, KingMed always prioritizes the testing quality instead of earning profits. Looking at KingMed’s philosophy, one can see the reason: Quality, Integrity, Accountability, Innovation, and Collaboration; those are the key factors for KingMed’s success which also represent KingMed’s values.

APBN: Who are your chief competitors? What’s your strategy to outcompete/collaborate with them?

Li: Next to KingMed, there are three other IMLs that have reached a comparable scale, but they are all at a similar level so that it is hard to say which one is the chief competitor. In some cities, two, three or more IMLs share or fight for the market, and a mechanism for collaboration among the IMLs does not exist yet. The strategy for KingMed to outcompete includes three items: emphasizing detection and service qualities, introducing new tests to achieve item superiority, and holding academic activities to keep and enhance a healthy relationship with clients. We believe that our strategies will work well.

APBN: Are China’s regulatory policies for Chinese IML’s different from foreign IMLs’?

Li: it is difficult for me to comment on it specifically because I personally did not make a comparison between the policies from different countries. In general, it is not easy in China to get approval for the establishment of an IML but the quality management and supervision are unlikely stringent enough. However, in the USA and European countries, the situation appears quite contrary to those in China.

About the Author

Hongbo Li is the current Chief Medical Officer and Laboratory Director of KingMed Center For Clinical Laboratory. He graduated from China Medical University, Shenyang, Lianoning Province in 1983. He left China in 1989 for his postdoctoral training at Department of Biochemistry, SUNY at Buffalo; Department Microbiology, UTMB at Galveston; and Department of Immunology, Baylor Medical College at Huston. While in postdoctoral training, he investigated the role of Rec gene in HIV regulation. He left Texas in 1997 to pursue his residency and fellowship training in pathology, first at University of Florida and then at Emory University Hospital. In 2003, he joined Endolab at Orlando, Florida as a GI pathologist. He left for China at end of 2005 for the position at the KingMed Center for Clinical Laboratory in Guangzhou.
Establishment of IML Quality Managerial System in China

Chaohui Hu
Ph.D.; Director, Center for Laboratory Management; VP, KingMed

Jun He
Director, Department of Quality Management

Weiwei Zhao
Director, Department of Molecular Pathology
KingMed Center for Clinical Laboratory

Current development of IML accreditation program in China

The establishment of Independent Medical Laboratory (IML) quality managerial system was next to none in China before the 1980s. In 1982, the National Center for Clinical Laboratories (NCCL) first piloted an inter-laboratory quality control program under the guidance of the World Health Organization (WHO).

On 15 November 1999, under an agreement between China and the United States (U.S.), China promised to open its service sectors (many of which were previously closed to foreign firms), including healthcare services within the frame work of the World Trade Organization (WTO) General Agreement of Trade in Services (GATS). China’s accession to WTO in 2001 brought about opportunities and challenges to the country’s healthcare market. In this increasingly competitive market, quality management and quality improvement becomes critical. In an effort to conform to international standards for clinical laboratories, China has done a lot of work towards reforming quality management of clinical laboratories. After its introduction, the laboratory accreditation system had undergone three adjustments in 1994, 2002 and 2006. The laboratory accreditation is now governed by the China National Accreditation Services for Conformity Assessment (CNAS) established by the Certification and Accreditation Administration of the People’s Republic of China (CNCA).

On December 6, 2002, the China National Accreditation Board for Laboratories (CNAL) issued the first ISO/IEC 17025 certificate to a clinical laboratory (KingMed). As the first step taken by China towards international standards for clinical laboratory quality management, it had a great impact on the Chinese clinical laboratory services. In 2010, ISO/IEC 17025 accreditation had completed its role in Chinese clinical laboratory quality management and has been replaced by new standards.

On August 26, 2005, CNAL awarded the first ISO 15189 certificate to the Clinical Laboratory of the General Hospital of People’s Liberation Army. On March 31, 2006, CNAL merged with the China National Accreditation Board for Certifiers (CNAB) to become CNAS. CNAS took advantages of the 2008 Beijing Olympic and 2010 Shanghai World Expo to promote ISO 15189 accreditation with great success. By May 19, 2012, the number of clinical laboratories accredited by ISO 15189 in Mainland China reached 95.

At the same time period, the Laboratory Accreditation Program of the College of American Pathologists (CAP) also gained momentum in Chinese clinical laboratories. In 2002, the Clearstone Central Laboratories China became the first CAP-LAP accredited clinical laboratory in Mainland China. By May 19, 2012, there will already be 16 CAP-LAP accredited laboratories in Mainland China.

The characteristics of IML quality managerial system in China

The establishment and development of quality managerial system of IMLs has unique characteristics of its own compared to those of general medical laboratories. The uniqueness holds extremely true when comparing Chinese IMLs to the ones in
<table>
<thead>
<tr>
<th>NAME</th>
<th>DATE OF ACCREDITATION</th>
<th>ITEMS ACCREDITED BY CAP-LAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clearstone Central Laboratories China</td>
<td>2002-1-11</td>
<td>Chemistry, Hematology, Urinalysis, Molecular Biology, DNA banking, Pharmacogenomics, Flow Cytometry</td>
</tr>
<tr>
<td>Quintiles Medical R&amp;D Beijing Ltd</td>
<td>2006-1-27</td>
<td>Surgical Pathology, and maybe others (details are not available)</td>
</tr>
<tr>
<td>Adicon Clinical Laboratories</td>
<td>2008-7-20</td>
<td>Chemistry, Hematology, Urinalysis, Microbiology, Molecular Microbiology</td>
</tr>
<tr>
<td>KingMed Center for Clinical Laboratory Company Ltd</td>
<td>2008-8-16</td>
<td>General Chemistry, Special Chemistry, Radioimmunoassay, Analysis Chemistry, Clinical Biochemical Genetics, Molecular Pathology, Molecular Microbiology, Cytology, Surgical Pathology, Flow Cytometry, Hematology and Coagulation, Transfusion Medicine, Immunohematology, Microbiology, Cytogenetics, Immunology</td>
</tr>
<tr>
<td>Covance Pharmaceutical R&amp;D Co</td>
<td>2009-2-2</td>
<td>General Chemistry, Special Chemistry, Hematology and Coagulation, Urinalysis, Immunology, Extraction of DNA Flow Cytometry</td>
</tr>
<tr>
<td>Beijing Lawke Central Laboratory</td>
<td>2009-3-13</td>
<td>General Chemistry, Immunology, Hematology and Coagulation, Urinalysis, Microbiology, Molecular Pathology, Analysis Chemistry, Proteomics, Cytology, Surgical Pathology,</td>
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<tr>
<td>Eurofins Medinet China Labs</td>
<td>2009-4-28</td>
<td>Details are not available</td>
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<td>MedPace Reference Labs China</td>
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</tr>
<tr>
<td>Synarc Research Laboratory (Beijing) Ltd</td>
<td>2010-10-19</td>
<td>Clinical examination, molecular biology, pathology, Liquid chromatography mass spectrometry</td>
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</tbody>
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Table 1-1. Comparison of testing capacities of IMLs accredited by CAP-LAP in Mainland China

developed countries. The following aspects are particularly important:

**Quality is everything:** IML lives on fairness and accuracy of testing results. The establishment, development and accreditation of quality system is an effective way to measure the quality of services.

1. Clinical trials laboratory: IML which provides clinical trial services; CAP-LAP provides accreditation for this kind of laboratories. At present, there a total of 9 IMLs accredited by CAP-LAP in Mainland China (refer to Table 1-1).

2. Clinical laboratories: IMLs which provide services for local medical institutes. This kind of laboratories mainly pursues ISO15189 accreditation for recognition and approval of its quality and testing ability from the government. Currently, there are 14 IMLs accredited by ISO15189 (refer to Table 1-2), among these 14 laboratories: 7 belongs to KingMed and its branches, 4 belongs to Dian, 2 belongs to Adicon, 1 belongs to IPE, 1 belongs to Labway Clinical Laboratory Shanghai Ltd. The low-price competitive strategy taken part by IMLs in Mainland China have put some IMLs under the great pressure.

**Turn-around Time (TAT):** TAT affects customer’s experience of services provided significantly; it is also a critical key point of quality managerial system. Logistics is taken into great consideration when proper testing is being chosen since it is not practical to ship specimens.

**The differences of regulations:** IMLs are still a fairly new type of business in China; therefore it lacks fully developed regulations compared to the ones in developed countries, especially with Chinese uniqueness. CAP-LAP accreditation in US is based on specialized CLSI documentation and precise CLIA regulation, while Chinese IMLs is facing the task of borrowing the same system with the adaptation of Chinese regulation.
<table>
<thead>
<tr>
<th>ISO15189 CATALOG</th>
<th>KINGMED</th>
<th>DIAN</th>
<th>ADICON</th>
<th>IPE</th>
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<td>Surgical Pathology</td>
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Table 1-2. Comparison of testing capacities of IMLs accredited by ISO15189 in Mainland China
The pathway of establishing quality managerial system in KingMed

KingMed strictly follows the ISO/IEC17025, ISO9001, ISO15189, CMA and the CAP and other international and domestic standards, laws and regulations. We continuously improve and effectively implement quality principles, policies, procedures, standard operating procedures, and technical services to meet our customer’s needs (see Figure 1). We establish and strictly enforce QA monitoring and auditing for clinical trial projects. Since the founding of KCTC in October 2008, we have already passed on-site audits by several international pharmaceutical companies and some full-service international CRO companies.

About the Authors

In 1991, Chaohui Hu graduated from the Department of Biology, Hunan Normal University; from 1994 to 1997, he became a graduate student at Sun Yat-Sen University and was awarded a Master degree in Genetics. From 2001 to 2004, Chaohui pursued his doctoral degree in Biochemistry and Molecular Biology in Sun Yat-Sen University and graduated with a Ph.D. degree. Since 1997, He has been working in KingMed Center For Clinical Laboratory and is one of the founders for KingMed; he is responsible for the laboratory management of the entire KingMed group, particularly in quality management (QM) and quality assurance (QA). He has also been appointed by CAP as inspector for the CAP accreditation program.

Jun He is the QA Director in KingMed; she joined the group in 2003. She is Laboratory director and Laboratory process manager and served as the Laboratory technician, Quality Management Division Manager and is engaged full-time in laboratory quality management for six years. She is a major laboratory physician, National Intermediate Quality Engineer.

Weiwei Zhao is the Technical Director of Molecular Pathology, KingMed Diagnostics. She is mainly responsible for the assessment of new techniques and platforms, the development of CAP quality management systems and is working on quality assurance and improvement on a daily basis. She is currently an active CAP international inspector.
The Collaboration between IML and Community Medical Hospitals
Supplementary Service with Tests, Technologies and Beyond

Zhexing Guo, Yingxiang Kong, Kongzhuan Wang
The Nanhai Fifth People's Hospital of Foshan, Guangdong, China
Background

In the Chinese medical service system, medical institutes or hospitals are classified into three grades according to the number of bed and clinical specialties. In general, Grade I hospitals range from 20 to 99 beds, 100 to 499 for Grade II, and hospitals with more than 500 beds are classified as Grade III. The clinical specialties will increase along with the elevation of hospital grades. In addition, hospitals focus on a single or a few related clinical disciplines, for instance, Pediatrics, Obstetrics and Gynecology, i.e., the children’s hospital and Gynecology/Obstetrics hospital, belong to Grade III class. The main functions of the Grade II hospitals are the diagnosis, treatment and prevention of commonly-occurring diseases and offering healthcare services for the community populace, therefore playing important roles in the activities of national healthcare and involved in the most extensive workload in the entire system. As part of the ongoing healthcare reformation, the two major issues are the increase in health insurance coverage and the improvement of medical service quality at the community level. The former is the government’s responsibility and the latter is highly reliant on the medical institutes of grade II and below. Thus, the performance of community healthcare institutes has raised attention from different aspects.

The Nanhai Fifth People’s Hospital of Foshan is a typical Grade II hospital located in the Nanhai District, Foshan City, and the hospital is responsible for the healthcare and medical service of 120,000 registered and 190,000 unregistered citizens in the area. The specialty disciplines of the hospital include internal medicine, surgical, gynecology/obstetrics, pediatrics, orthopedics, ophthalmology, ENT, dentistry, Traditional Chinese Medicine, emergency, rehabilitation and the intensive care unit. Due to the recently enlarged population, the hospital has increased bed numbers to 420, and visiting outpatients was about 1.87 million in 2011. The Department of Clinical Laboratory is divided into three sections: clinical hematology, clinical chemistry and clinical microbiology. The laboratory housing was constructed according to “Clinical Laboratory Design Guide” and is managed essentially by following the “Medical Laboratory Management Guideline”. The hospital clinical laboratory can provide the testing services of routine hematology, chemistry, immunology and microbiology, with approximately 260 detection items in total and conducted tests on 570,000 samples last year. The Department of Pathology is independent of the Department of Clinical Laboratory and can provide the tests on anatomic- and cytological-pathology, manages approximately 6000 samples every year. In the past few years, the significant development in economy, the rapid growth of population and the increase of health-insurance reimbursements has given the hospital much more in- and out-patients than before, which places it under the great pressure. As for laboratory diagnosis, the shortage of technologies and test items has become a serious issue. In particular, now is the time to strengthen evidence-based medicine and the clinical setting and physicians of our hospital require more lab-tests to support clinical practice.

Specifically, the hospital has a gap of 80 test items and about 100,000 samples in anatomic and clinical pathologies to meet the daily clinical demands. It is estimated that at least 3 million RMB has to be invested and an additional 5 lab-staff will be needed if we want to conduct these tests by ourselves. Considering the hospital’s total resources, technological condition, housing and personnel availabilities it is almost impossible to solve the problem without a newer approach. The appearance and development of IMLs in China provides us an effective "bypass" to exit the predicament.

In 1998, our hospital and the KingMed Center For Clinical Laboratory established a collaborative relationship - we sent the samples of the tests we could not perform to KingMed. Thus far, both sides feel the benefits of this collaboration. As the director of clinical laboratory, in my opinion, the KingMed Center For Clinical Laboratory has provided professional on-site services, standardized specimen transportation and internationally accredited testing, both the assay quality and service model impressed and satisfied me very much. More importantly, the service has benefited the clinical practice of our hospital significantly. At present about 100 items and 1100 samples monthly are sent out to KingMed. The collaboration with KingMed undoubtedly plays a constructive influence on the hospital.

In my opinion, the following significant points should be highlighted:

1. The medical institutions at Grade II and below possess a problem - demand and supply for laboratory diagnosis is more than those under the Grade III class. The problems manifest themselves in the form of limitations of testing ability,
quality required for diagnosis and treatment, personnel shortages, drastic increase in sample numbers, financial support and facility demands. IMLs and the third party service providers provide the best way to resolve the gap.

2. The involvement of IMLs with medical institutes may very well elevate the level of hospital medical service. Some IMLs, like KingMed, for example, accredited by CAP and ISO15189, offers a broad range of laboratory tests with high quality. The introduction of new lab-tests into clinical settings has made diagnosis more indicative.

3. Cooperation with IMLs help clients to know the latest developments in laboratory medicine and utilize the newest tests on patients. For instance, the full service package of KingMed includes a variety of training programs for the introduction of new tests, technologies and clinical interpretations. Such efforts enable clinicians to obtain new knowledge effectively and enhance the performance of evidence-based diagnosis.

4. In addition to the testing services, IMLs may also provide client laboratories with extra services, such as technical support, operational and skills training and quality management consultations. The extra services provided by IMLs would then improve the operation and management of client laboratories.

5. IMLs will be a very active participant in Chinese healthcare reformation and play a significant role in the improvement of community healthcare services. The major goal of healthcare reformation is to establish the balance of medical resources and one of the most important parts is to increase the efficiency of the medical institutes at the community level. The third-party service would be the most cost-effective approach to achieve this goal.

   In short, we believe that cooperation with IMLs is an effective model for a Grade II hospital to improve its service capacity and quality, which ultimately benefits the hospital, patients and IMLs.

About the Authors

In 1999, Zhexing Guo graduated from Guangdong Pharmaceutical University and majored in Health Laboratory Technology of Preventive Medicine. Between 1999 to 2003, he worked in the Department of Clinical Laboratory, Dalin Hospital, Nanhai District, Foshan. In 2003, he worked and trained for the microbial and molecular biological technologies as a refresher physician in the Department of Clinical Laboratory, in the second hospital of Guangzhou Medical College. He is currently holding title of Head Laboratorian, ranking at the middle-level in the clinical laboratory system.

Yingxiang Fan graduated from the Department of Laboratory Medicine in Shaoquan Medical College and was employed as a laboratory specialist by the Nanhai fifth People’s Hospital of Foshan in 2006. After he has worked in the Department of Clinical Laboratory he is currently the supervisor for clinical immunology section and the unit of laboratory quality management.

Kongzhan Wang graduated from the Department of Laboratory Medicine, Shaoquan Medical College, Shaoquan, Guangdong Province and employed by the Nanhai fifth People’s Hospital of Foshan in 2006; since then as a laboratory specialist, he has worked in the Department of Clinical Laboratory in the hospital, and in 2010 he was appointed as the supervisor for the section of clinical chemistry.
The Background

The Guangdong 999 Brain Hospital is a specialized hospital focusing on the diseases of brain and neurological system, is located in Guangzhou City, Guangdong Province of China. The hospital consists of two groups of departments: the clinical department, including Department of Neurology, Neurosurgery, Neurological Rehabilitation, Psychiatry, Cerebral Palsy Treatment and Comprehensive Tumor Treatment Centers; and functional departments such as Department of Clinical Laboratory, Department of Radiology, Pharmacy and Department of Electrophysiology. The hospital has over 700 beds and is a grade III specialized hospital based on the classification system for medical institutes in China. In 2011, the hospital admitted about 16,000 patients and over 100,000 outpatients. The hospital emphasizes on the importance of laboratory testing in clinical practice and has established the clinical laboratory to meet demands from different disciplines within the hospital. The Department of Clinical Laboratory has employed a number of highly qualified staff that actively introduces advance equipments. Currently, up to 97%
FEATURE

About the Author

Dr. Hua Li is an Associate Physician-in-Chief and Deputy Director for The 3rd Division of Internal-medicine Neurology Department, Guangdong 999 Brain Hospital. She graduated from the Medical School of Sun Yat-sen University and was awarded a Masters Degree in Medicine in 2003; then she has been working as a physician in Department of the Internal-medicine Neurology where she was promoted as Associate Physician-in-Chief and Deputy Director in 2003 and 2010 respectively. Later, she registered to the Southern Medical University as a Ph.D. candidate to pursue her doctoral degree. Her research interests include clinical studies on epilepsy, neural genetic diseases, and cerebrovascular diseases.
Health Departments/Bureaus of all provinces, autonomous regions, and municipalities under direct jurisdiction of the central government, Health Bureau of Xinjiang Production and Construction Corps:

In order to further perfect health care and medical service system and strive to improve service level and quality of community health care institutions by implementing the Suggestions of Central Committee of CPC and the State Council on Deepening the Reform of Medical Care and Health System, thereby rationalizing the distribution of health care resources and ensuring the quality of clinical laboratory test, our ministry has decided to add Medical Laboratory as an individual agency in the category of medical institutes. Basic Standards for the Medical Laboratory (on Trial) is hereby printed and distributed for you, and relevant requirements are as follows:

I. Local health administrative departments at each level shall make plans about the number and layout of medical laboratories according to the local population, geographical environment, transportation, medical institution composition and specific conditions as well as demands from medical care services, which shall be strictly implemented.

II. The establishment of Medical laboratories shall be approved by provincial health administrative department, and the latter is also responsible to point official agency for the practice registration.

III. Medical laboratories can only accept the specimens provided by medical institutions, and provide test result reports and consultation on the results for the clients; patient-practice would be not allowed.

IV. Before providing the test services, medical laboratories shall sign agreement with the client institutions, so as to be clear the rights and obligations of both parties about the issue and application of patients’ preparation, specimen collection, storage, transportation, receipt, test, result report and application, and disputes about medical care accidents caused by test results.

V. Medical laboratories shall strictly implement Methods for Management of Clinical Laboratory in Medical Institutions, and accept the evaluation of internal and external quality controls conducted by clinical laboratory centers at provincial and above level, so as to ensure scientific, correct and objective test results.

VI. If a medical laboratory wants to perform clinical genetic amplification detections, human immunodeficiency virus (HIV) tests and other estoric assays, the relevant approval should be obtained.

VII. The notice shall be implemented since the day when printed and distributed.

Appendix: Basic Standards for Medical Laboratory (on Trial)
December, 14th, 2009
(Information disclosure form: initiative disclosure)

Annex

Basic Standards for Medical Laboratory (on Trial)

Medical laboratory is a medical institution involved in laboratory tests on specimens from human bodies, and provides test results; the institute can also conduct pathological tests.

I. Departments
Set up the departments that can conduct the clinical tests in different disciplines, which include clinical body fluids, hematology, microbiology, chemistry, immunology, serology, and cytogenetics, etc.

II. Personnel
(A) There should be at least one certified physician in clinical disciplines with professional and technical qualification at intermediate level and/or above.
(B) There should be one certified technologist in laboratory medicine with professional and technical qualification at deputy senior level or above in charge of medical laboratory tests.
(C) Together all disciplines, there should be at least 10 technological staff majored in laboratory medicine.
(D) There should be at least one certified technologist in laboratory medicine with professional and technical qualification at deputy senior level or above for each discipline.
III. Houses, facilities and layout

For those with one discipline, the available space should be 500 square meters or more; and then adding more disciplines would require 300 square meters for each.

(B) Layout and process should meet the job needs, with corresponding function areas, such as specimen receiving, preparation, detection, bio-waste disposal, reagents and consumption product preservation, specimens preserve, etc.

(C) Accord with biological safety management, infection control and related requirements; strictly distinguish the areas of cleanness, half contamination and contamination; biological safety equipments should be complete.

IV. Equipments

(A) Basic equipments
Refrigerator, centrifuge, sample injector, pressure steam sterilizer, biological safety cabinet, and so on.

(B) Specific equipments
Equipments used for different tests, such as biochemical analyzer, blood cells analyzer, urine analyzer, enzyme standard meter, luminous analyzer, bacteria cultivation and appraisal meter, nucleic acid analyzer, etc.

Laboratory information management system includes specimen management system and report management system, etc.

V. Regulations

Set up quality management system and establish regulations, including personnel management, facility and equipment management, instrument and reagent management, specimen management, pre-analysis quality management, analysis quality management, post-analysis quality management, record management, report management, critical value management, security management, information management, patient privacy protection, technical grading management and other systems.

Establish standard operation guidelines appropriate for each test.

VI. Registered capital

For those with one discipline, the registered capital shall not be less than 5 million Yuan; and then 3 millions for each additional discipline.

VII. Others

For those that conduct pathological examinations (equivalent to adding one discipline), besides the above requirements, the following conditions should be met:

(A) Personnel
There should be at least two physicians in pathology, with professional and technical qualification at deputy senior level or above, and shall have more than five-year experience in pathological practice.

Technicians and supporting staff should be allocated in the proportion of 1:1 compared with physicians.

(B) Equipments and facilities
Provide dryer, paraffin machine, slicing machine, dyeing machine and other equipments and facilities corresponding to the pathology inspection items.

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PLA, PLGA for Drug Delivery System
from JAPAN
No metal catalyst used !!

Your Gateway  http://www.pla-drugcarrier.com

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- By direct condensation without polymerization catalysts
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- For laboratory scale developments
- For bulk commercial scale production

VENTURE CHEMICAL LTD.
Molecular Painting (MP) is concerned with the surface modification of biomembranes. Possibly an article beginning with the words "surface modification of biomembranes..." will not be considered as a potentially exciting read. However, it does become more intriguing when one considers that every cell in our body is encompassed by a biomembrane, and yet despite this huge mass of it in all of us, as well as every other living organism, relatively little is understood about it in terms of biophysics and mechanics, the components found within and the functions of these associated components.

The biomembrane of a cell, or plasma membrane as it is also sometimes known, is a relatively rigid, yet essential fluid mass of fatty-acid based components known as phospholipids. This layer of phospholipids is impregnated with other biological molecules called proteins. A simple analogy would be to imagine a bowl of thick soup with croutons floating in it. The surface of the soup is the membrane. The croutons are the proteins, which carry out various functions on behalf of the cell. Just as a crouton is connected to both the air and the soup at the same time, some proteins span across the entire membrane, connecting the inside and outside of the cell. Typically, such trans-membrane proteins have a pore through their centre, through which nutrient molecules can travel, such as salts or sugars for example, much in the same way that the crouton will become soggy with time as soup soaks into it (see Figure 1, H). This is mostly controlled by a self-regulating, passive process known as diffusion. There are other proteins which don't have pores but can flip around from one side of the membrane to the other by an active process which requires energy input from the cell. Usually these active mechanisms excrete or internalise larger components which need to be carefully regulated. Other kinds of proteins and mechanisms also exist.

The basic phospholipid elements of the membrane have a water repelling component known as the hydrophobic tail. This part causes a double layer to be formed whereby all the tails accumulate in the centre of the membrane’s layer. The other, water-liking part or hydrophilic head points outwards to both the watery surroundings of the rest of the body on one side, and the inside of the cell on the other. The resulting bi-layer is a stable, continuous sheet surrounding the entire cell (see Figure 1, A-D).
It becomes even more interesting when one considers that in addition to cells, other biologically and medically important entities are defined by a biomembrane. There are many kinds of membrane vesicles, but the most prominent example is a group of viruses known as enveloped viruses, which account for about half of all known viruses. They are termed as such because they are enveloped by a biomembrane which comes from the cell from which the virus originated. The viruses “steal” some membrane from the cell in which they replicate by pinching it off as they exit through the membrane, going on their way to infect new cells. Many of these viruses cause human disease, such as the one associated with AIDS, the human immunodeficiency virus (HIV-1), influenza or the virus that causes Dengue fever. In fact there are around twenty clinically relevant enveloped viruses (Table 1).

As techniques improve and more is discovered about biomembranes, it’s emerging just how critical they are for many biological processes. This, in turn, has implications for the study of diseases and future medical products, both from the perspective of diagnostics and therapeutic intervention.

Scientists from the Biopolis-based company Anovasia Pte Ltd in Singapore and the Vienna University of Veterinary Medicine in Austria were the first to discover and document the surface modification of enveloped viruses, and they termed this “virus painting”. One of the key steps to achieving this was the laboratory adaptation of a naturally occurring, membrane-associated cellular system. The concept was to manipulate the system in order to direct specially engineered molecules with pre-defined functions towards any membrane of choice. After some years of research and development, Anovasia is now marketing this technology as MP since, in addition to viruses; it can also be used to modify the surface of many other scientifically and medically important membrane-encompased entities.

MP agents contain an element which inserts itself into any biomembrane. As such, they stick or anchor themselves onto any available membrane presented to them. This means that when an MP agent is modified to contain a protein or molecule with a desired function, this function is then conferred to that membrane.

The molecule of choice combined with the MP agent must in all cases primarily be a protein; however, all MP constructs are engineered to contain an additional functional element (also part of the protein) which allows cross-linkage with a non-biological or inorganic component. Using this technique, scientists at Anovasia were able to attach miniature magnetic particles (magnetic nanoparticles) to the virus using the MP agent as a linker. This enabled virus movement and steering under the influence of a simple magnet. This process can be used to guide viruses or other membrane particles to target cells in the body for therapeutic purposes. It can also be used as a tag, to mark or collect cells and viruses from diagnostic samples.

It is easiest to understand the importance of the MP technology by giving other examples of its current uses. Consider

<table>
<thead>
<tr>
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<td>Yellow fever virus</td>
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<tr>
<td>Yersinia, and others</td>
<td>Yersinia, and others</td>
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Table 1: The major categories of the infectious diseases market. The ones in bold text are enveloped viruses which can be modified with Molecular Painting (MP) agents.
“Methods to modify, label and tag the surface of membranes have been of increasing scientific relevance over the last ten years and are more recently beginning to attract significant commercial interest.”

Dr. John Dangerfield, Anovasia’s Managing Director

Vaccines and virus vectors. A virus vector is a virus which has been manipulated in the laboratory so that it is no longer capable of causing disease but instead carries a therapeutic factor. In the case of most vaccines, the therapeutic factor is simply the non-active components of the original virus, but in the case of a virus vector, it could be something to repair a genetic abnormality or a toxic component to kill a cancer cell for example. Such vectors have existed for many years and some are already being used to treat patients but there are still challenges in many cases concerning low efficiency in reaching their targets once injected into the patient, so they are not effective for all types of treatment. This is where MP can help as they can be used to modify existing vaccines, virus vectors or drug micro-carriers in order to target them to a specific type of cell. Since MP agents can be used in combination, a second one can be painted onto the same entity to protect against the rigors of the patient’s immune system, allowing the therapeutic vehicle more time to carry out its job (see Figure 3).

There are several major advantages of the MP technology compared with other currently used methods. Previously, to change the spectrum of the surface of a cell or virus, it was necessary to make manipulations at the genetic level. This can take weeks or even months and as such costly. In contrast, MP requires no genetic modification and can be carried out in minutes. To avoid genetic manipulation, others attempted to use proteins known to be on the virus or cell to attach the new functional molecule to (an MP agent equivalent). Although attachment or binding could be achieved in some cases, almost always the natural function of the target protein would be disturbed, rendering the virus or cell void of or diminished in some core functions. In contrast, MP does not interfere with any pre-existing surface molecules.

In medical diagnostics, the presence of a virus or biomarker needs to be established to determine the disease status of a patient. In many cases antibodies are used because they can easily be engineered to recognize a protein on the surface of a virus or infected cell. This means that a new sample must be collected for each new test since the antibody is specific only for detecting one type of virus or cell. In contrast, MP is non-specific as it will associate with any membrane entity meaning that all potential disease related markers can be collected from one sample. Taken together with cost advantages due to the fast production time for MP reagents, the benefits compared to existing technologies are clear.

In summary, MP can be considered as a platform technology for the life sciences industry. The applications are in basic and applied research, diagnostics, vaccine development, targeting of genes, proteins and/or drugs as well as cell and gene therapy in the future. Anovasia’s MP reagents are available as a range of off-the-shelf products as well as a service to engineer and produce custom-designed molecules upon request.

Figure 2: Human cells modified with Anovasia’s MP agents (Product No. Ano-P001, Green-Glow). The membrane around the cell is clearly marked with the green fluorescent MP product because of its specific affinity for only the membrane. The other major sub-divisions of the cell can be seen labelled in red/yellow (cytoplasm and cytoplasmic components) and blue (nucleus).
Figure 3: In this example, a virus based gene delivery vehicle (virus vector) is modified with two different MP agents in turn conferring two new functionalities to the original vector.

References

About the Author
Originally from the UK, John Dangerfield moved to Austria after completing University where he achieved his PhD in molecular virology in 2001. After a further 6 years in Vienna doing fundamental research on cancer gene therapy approaches using viruses and nanotechnology, he side-stepped into the biomedical industry in Singapore. John is a founder and the Managing Director of Anovasia Pte Ltd. He is also Chief Operating Officer at SG Austria Pte Ltd / Austrianova Singapore Pte Ltd, a cell encapsulation technology-based and oncology focused biotech company. Both companies are based at the Biopolis in Singapore. He has co-authored 12 publications, procured 9 research grants, is an inventor to four patents and still holds a position at the University in Vienna to continue his research interests.
Investors have recently been looking more intently at opportunities presented by the healthcare sectors in Brazil and Chile, two of Latin America's most prominent emerging markets. This article will examine the dynamics of the healthcare sectors in both countries.

**Developments in Brazil's healthcare sector**

Brazil is a major South American economic powerhouse, hosting almost half of all inhabitants on the continent, i.e. 194 million people. Its gross domestic product (GDP) (in current US$) in 2010 amounted to about $2.1 trillion, greater than that of both India and Russia. The country's growth dynamics have also been impressive with GDP growing strongly in real terms in recent years. Most importantly, this growth has trickled down to the population and benefited most Brazilians – significantly reducing the size of the poorer lower class and expanding the middle class segment. Societal changes such as this are exactly some of the signs that attract the attention of companies looking for business opportunities, including those in the healthcare sector.

Brazil provides public healthcare coverage for its population, financed mainly through tax income. Its public healthcare services have a reasonably good reputation. The challenge for Brazil is in providing the services in sufficient "quantity" – as waiting time for procedures can be extremely long. For patients, this can be unpleasant and, in some cases, life-threatening. Wealthier Brazilians have resorted to buying additional private insurance, which gives them access to private healthcare services at doctor's clinics, hospitals and diagnostic laboratories.

The growth of the middle class in Brazil has resulted in more individuals taking up private supplementary insurance. Ten years ago, only 18% of the population took up private insurance. Currently, it has been estimated that 24% of the population or about 47 million people have private insurance coverage. It is expected that this proportion will rise further to over 30% at the current growth trajectory. This trend is an indication of the potential opportunities for private insurers and also healthcare service providers, such as hospitals and diagnostic laboratories.
With drug expenditures in Brazil being funded mostly out-of-pocket, the growing purchasing power of the general population as well as an increasing proportion of elderly within the population, are likely to drive up the country’s overall drug expenditures. Furthermore, in recent years, it has been observed that low-quality generic drugs called “Similares” are losing market share to branded generic drugs. This is mainly due to the poor reputation of Similares and their perceived lower quality. This trend has subsequently benefited the major domestic generic companies, such as Medley, EMS and Ache.

**Developments in Chile’s healthcare sector**

Chile stands out among its Latin American peers because of its political and economic stability. With a population of about 17 million, it has one of the highest average per capita GDP (in current US$) on the continent i.e. over $12,000 in 2010. Its GDP growth in recent years has also been impressive i.e. beating 3% in real terms annually if we disregard its 2009 performance. And it shows, as the infrastructure in Chile is noticeably more developed than other countries in Latin America. However, one should take note that much of the country’s growth has been driven by one of its key exports – copper, and Chile produces a third of the world’s supply.

In Chile, there is compulsory health insurance. Individuals are insured either by public or state insurance (FONASA) or by private insurers. All citizens in Chile are insured by FONASA unless they choose to contribute to private insurance companies (ISAPRES). About 18% of the population is insured through ISAPRES, and the proportion has remained relatively stable. There have been no indications of the population moving strongly towards private insurance, as the public or state system appears to work well.

ISAPRES companies in Chile are not simply private insurers but they take an integrated approach and are also engaged in the provision of healthcare services. For example, they may operate their own network of healthcare centres, diagnostic laboratories, dental clinics and hospitals. These companies have been quite successful, exemplified by the top two companies Bannmedica and Cruz Blanca Salud, which are both publicly-listed.

Just as in Brazil, Chileans typically pay for their medication out of the pocket. Similarly, Chile is seeing an increase in purchasing power of its population and a growing elderly population, which in time will drive up the demand for healthcare services and drugs. On the other hand, Similares in Chile have better reputations and are able to hold their market share against branded generics. Therefore the growth of the market has benefited the large local manufacturers of both generic drugs and Similares. The market leaders include CFR Pharmaceuticals and Laboratorio Chile, which belongs to international generic giant Teva.

Overall, the Chilean healthcare market is smaller than the Brazilian one. It is therefore not surprising that several Chilean companies have embarked on regional expansions. High on the list of expansion destinations are Peru, which traditionally have close ties with Chile and Colombia, which has achieved good economic growth in recent years and have become more stable.

**Conclusions**

The continued positive growth in Brazil and Chile will ensure that the expanding middle class in both countries has a direct positive impact on their respective healthcare sectors. The increasing purchasing power of the population and the aging population in both countries will significantly drive up healthcare expenditures. This will potentially benefit the healthcare companies in their respective markets e.g. domestic generic manufacturers, pharmacists, chains, private insurers, private hospitals and diagnostic laboratories. Furthermore, in Chile where the private insurers also operate healthcare service providers, these private insurance companies will stand to benefit from the current developments as well.

**About the Company**

Adamant Biomedical Investments AG is a Swiss asset manager with exclusive focus on healthcare. It provides services including advisory and portfolio management as well as development of structured investment vehicles. Adamant takes a global research approach, investing in established and emerging healthcare markets worldwide. For more information, please visit www.adamantinvest.com.
An Industry Perspective

NO PAIN, NO GAIN

Frost and Sullivan analyzes the underlying forces behind the pain management market potential in Asia

Morris Lee
Principal Consultant, Healthcare Practice
Asia Pacific, Frost & Sullivan

Everyone experiences pain from time to time. Pain can either be acute for a limited time or chronic over a long duration and the level of incidence varies across numerous conditions such as cancer, post-operative, inflammation and Arthritis.

Inevitable pain due to numerous conditions poses an effervescent window of opportunity for the whole Healthcare Industry.

The healthcare industry, spanning from pharmaceutical companies to hospitals to physicians, is wasting no time to bank on the huge market potential with a battery of pain management offerings.

Expanding population of pain patients

Frost and Sullivan identifies Aging and Urbanization as the key factors that are propelling patients' need for pain treatment.

“According to a 2007 study at 21 government hospitals, it was found that 35 per cent of patients suffered severe pain in the first 24 hours after laparotomy”

By Health Minister Datuk Seri Liow Tiong Lai, Malaysia

1. 5 December 2011, Bernama Daily Malaysian News
An ageing Asian society will translate to more elderly people who need treatment for chronic pain. For instance, Singapore’s over-60 population is most likely to quadruple between 2000 and 2050. By 2020, Malaysia and the Philippines are envisaged to become aging Asian populations.

The dual effect of aging and urbanization will bring about stronger purchasing power and urge for a better Quality of Life (QOL) among pain communities. For example, the Chinese urban population (of more than 60 year old) is expected to grow from 94 million in 2009 to around 120 million by 2016, with a Compound Annual Growth Rate (CAGR) of around 4%.

The number of treated pain patients is foreseen to increase over time in Asia.

Pain Management Market, where are the big bucks?

At present, there are more than 1.5 billion chronic pain suffers with an insatiable demand for better pain management treatments and medical services. With millions of individuals still suffering from moderate to severe pain, it is evident that the current pain management is inadequate.

To benefit from the potential of pain management market, Frost and Sullivan have identified 3 key engines of growth: Innovative Treatments for Moderate to Severe pain, Painless Healthcare Delivery and Target Painful Situations.

Innovative Treatments for Moderate to Severe Pain

Pharmaceuticals are estimated to contribute approximately 90% of global sales for pain management pharmaceuticals and devices. As a result, drug companies are showering the market with treatments for different pain intensities caused by various ailments. Furthermore, demand for treatment for moderate and severe pain is undeniably attractive for many drug brands. In South Korea, it is estimated a staggering up to 80% of chronic pain patients are experiencing moderate to severe pain, and the patient population is estimated to grow around 5% annually from 2010. This leads to a strong demand for safe, low cost and non-addictive pain treatment.

Propensity of Opioids prescription is by far the most-prescribed agents for moderate to severe pain.

There is a notable trend among drug companies to re-formulate current Opioids to elevate patient’s compliance, improve side effects and increase the ease of drug administration.

Beside Opioids prescriptions, physicians are increasingly using Opioids-sparing drugs such as NSAIDs and anti-convulsants to reduce Opioids-related adverse events.

Painless Healthcare Delivery

Hospitals in some Asian regions are running on high Bed Occupancy Rate (BOR), which means there is limited bed available for inpatients in hospitals. In 2000, the average BOR in Japan and Hong Kong was 85% and the average BOR in 2011 at the Tan Tock Seng Hospital in Singapore was 86%. To alleviate the bed crunch, hospitals are encouraging better pain management so as to reduce patients’ average length of stay.

In Asia, some hospitals are integrating pain treatment modalities for patients who have to undergo painful surgical procedures. The pain treatment uses traditional and complementary medical techniques, especially acupuncture, to alleviate patients’ pain thus accelerate hospital discharge.

Target Painful Situations

Frost and Sullivan believes that the pain management market will continue to grow and cancer pain, low back pain and post-operative pain relief markets are those with high potential.

According to a Pfizer’s Study, around 4.2 million new cancer cases- representing 39% of new cases globally- were diagnosed among 3.2 billion people in the 15 most highly developed Asian countries in 2002 (taken from The Burden of Cancer in Asia, Pfizer). In Singapore, cancer accounts for almost one-third of deaths and up to 90% of the cancer patients can experience some form of pain.

With the increasing cancer pain prevalence rate, cancer pain is poised to be one of the pain segments with the strong patient growth.

Generally, there is a higher incidence of low back pain as compared to other types of pain. For instance, up to 25% of pain patients (1 in 4 patients) have low back pain.
in countries like Thailand, Hong Kong and Philippines. The high incidence rate coupled with treatment by most doctor types has created a huge patient potential pool.

In some countries, Frost and Sullivan estimates up to 70% of post-operative patients experience pain and maybe up to 90% of post-operative pain patients need pain management. This is in tandem with physicians’ strong belief that post-operative pain, ranging from mild to severe, has to be managed well to ensure patients’ recovery after surgeries.

**What it means for the industry**

The pain management market has been evolving in recent years with treatment innovations, better pain diagnosis and improving healthcare delivery.

Interestingly, market participants are finding it more challenging to encourage physicians to prescribe their products and to defend themselves against price competition from competitors and generics.

Frost and Sullivan would like to highlight some key action points, for better positioning in an effervescent pain management market:

- Identify and design the most efficient target messages for specific specialties in different countries
- Redesign messages not only targeting physicians. For instance, parents of children with postoperative pain
- Market to all physicians dealing with pain diagnosis, treatment and palliative care
- Reformulate or develop generic versions of drugs near patent expiry
- Demonstrate and differentiate key selling points to target moderate to severe pain patients

**About the Company**

Frost & Sullivan, the Growth Partnership Company, works in collaboration with clients to leverage on “visionary innovation” that addresses the global challenges and related growth opportunities that will make or break today’s market participants.

Our “Growth Partnership” supports clients by addressing these opportunities and incorporating two key elements in driving visionary innovation: The Integrated Value Proposition and The Partnership Infrastructure.

- **The Integrated Value Proposition** provides support to our clients throughout all phases of their journey towards visionary innovation including: research, analysis, strategy, vision, innovation and implementation.
- **The Partnership Infrastructure** is entirely unique as it constructs the foundation upon which visionary innovation becomes possible. This includes our 360 degree research, comprehensive industry coverage, best career practices as well as our global footprint of more than 40 offices.

For more than 50 years, we have been developing growth strategies for the Global 1000, emerging businesses, the public sector and the investment community. Is your organization prepared for the next profound wave of industry convergence, disruptive technologies, increasing competitive intensity, Mega Trends, breakthrough best practices, changing customer dynamics and emerging economies?
Two large multinational pharmaceutical companies are fighting for patents and monopoly pricing in Indian courts. The outcomes of the cases – involving Novartis and Bayer – are likely to determine the country’s future as a major global supplier of low-cost essential medicines. About a third of all drugs are produced in India. The rise of domestic firms was made possible by India’s abolition of product patents for pharmaceuticals in the Patents Act of 1970 (which came into effect in 1972). Only patents for processes were recognised for a maximum of seven years. This was to encourage the development of a domestic drug industry and the supply of more affordable medicines. The result was a spectacular rise of Indian firms over subsequent decades.

Family-owned companies such as Cipla, Ranbaxy and Dr Reddy’s (often in collaboration with public sector research organisations) developed alternative processes for manufacturing a wide range of pharmaceutical raw materials and generic drugs (alternatives to the originator brands).

Large multinationals’ monopoly on supply of critical HIV antiretroviral drugs, for instance, was first broken by Cipla in 2001, when it commenced supply to developing countries for $350 per annum per patient. The multinational drug companies had charged more than $10,000 per patient per year. Today, the same drugs are available for about $150 for a year’s supply. Indian manufacturers supply more than 80% of the HIV medicines used to treat millions of people in developing countries, as well as generics to treat many other diseases.

India’s approach to TRIPS - The 1995 Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) created a new era of globalised intellectual property rights. TRIPS gave developing countries, such as India, a ten-year transition period before patents had to be introduced in all product categories. (The least developed countries must be fully TRIPS compliant by 2016).
Indian firms are allowed to continue production of drugs marketed before 2005, but can no longer produce generic versions of medicines patented in India after 2005 (unless voluntarily licensed by the originator company). This will result in high monopoly prices for many more years for new products, including second- and third-line AIDS medicines, unless countermeasures are taken in the interest of public health.

TRIPS triggered a global struggle between public health advocates and some developing countries, and the big pharmaceutical companies backed by the United States and the European Union. Much of this conflict revolves around the public health safeguards contained in the TRIPS Agreement. These were confirmed and extended in the 2001 Doha Declaration on the TRIPS Agreement and Public Health.

Legally, World Trade Organisation (WTO) member countries have significant leeway in their interpretation of TRIPS. But most countries don’t effectively use these options to lessen the impact of patents on affordable access to essential medicines.

India has used them more extensively than probably any other country with its Patents (Amendment) Act, 2005. Two of the safeguards in Indian legislation relate to definition of patentability and compulsory licensing.

Novartis’ challenge - Now, Swiss drug multinational Novartis is spearheading a global industry campaign against India’s utilisation of its right to public health safeguards. Indian legislation contains a section intended to prevent the awarding of patents for slightly modified versions of known molecules, unless a “significant enhancement of efficacy” can be demonstrated. This measure is intended to prevent “evergreening”, the extension of monopoly pricing through patenting of trivial modifications.

Novartis’ challenge centres on the anti-leukaemia (blood cancer) drug imatinib mesylate, marketed by Novartis as Glivec (or Gleevec), which has global sales in excess of $4bn. In 2006, the Indian patent office rejected Novartis’ application for a patent on Glivec on the grounds that it’s a slightly modified version of a known molecule.

The original patent on imatinib mesylate dates from 1993, and the product has long been produced and marketed in India by local companies. Novartis charges Rs120,000 (about A$2,400) for a month’s supply, which makes this drug unaffordable to more than 99% of the population. Several Indian manufacturers sell the same drug for Rs8,000 (A$160), 1/15th of Novartis’ price.

Novartis has pursued its case through India’s legal system since 2006. It has now reached the Supreme Court where final arguments are set to commence on 10 July. If Novartis is successful, no other brands of imatinib mesylate can be supplied in India or exported from India.

What’s more, a victory for Novartis will open the floodgates for patent extensions on many well-established medicines, to the detriment of patients in India and throughout the developing world. Novartis’ stance has garnered a strong reaction from public health activists and NGOs in India and around the world.

Bayer and compulsory licensing - The second recent development of great importance is the granting of India’s first compulsory licence for production of a drug. A compulsory licence authorises a third party to manufacture and sell a product without the consent of the patent holder in return for adequate compensation.

Multinational drug companies put strong pressure on developing countries for compulsory licenses to only be considered in circumstances of national emergency.

It is, however, clear in Article 31 of TRIPS and in the 2001 Doha Declaration that countries are free to determine “any and all grounds upon which CLs may be issued”. In fact, there is a long history of compulsory licenses for pharmaceuticals in Canada, the United Kingdom, Italy, and more recently in developing countries, such as Brazil, Thailand and Malaysia.

The United States and the European Union, on behalf of their pharmaceutical companies, have brought extreme pressure to bear on developing countries, through so-called free trade agreements and in other ways, to dissuade them from issuing compulsory licences.

On 12 March, 2012, the Indian generic drug company Natco Pharma was successful in gaining a licence for the production and supply of the patented anti-cancer drug sorafenib, marketed by Bayer as Nexavar. Bayer’s version of this drug costs Rs280,000 (A$5,600) a month, an astronomical figure for almost all Indian households. Natco will sell the same drug at 3% of this price, while paying a license fee – and it will still make a profit.

The compulsory licence was issued essentially on the grounds that Bayer’s price is exorbitant. It also doesn’t manufacture the drug in India and imports in such small volumes that only a tiny fraction of potential patients could benefit.

The Indian Controller General of Patents, Designs and Trademarks concluded that the drug “was not bought by the public due to only one reason, that is, its price was not reasonably affordable to them”. This decision in favour of Natco sets a very important precedent for possible compulsory licences on other patented products sold at unaffordable prices.

Bayer filed an appeal against the compulsory licensing decision on May 4 to the Intellectual Property Appellate Board but observers believe it’s likely the decision will ultimately stand.

India is in a very special category within the global pharmaceutical sector because its domestic drug companies have unique technological capabilities. Although they are just as profit-oriented as firms in any other sector, Indian drug manufacturers have made it possible for millions of poor people to access essential medicines. For these gains not to be reversed, it’s essential that Novartis loses its Supreme Court appeal, and that India’s first compulsory licence is followed by many more.

Source: The Conversation
5 June 2012, 2.23pm AEST
By Hans Lofgren, School of Humanities and Social Sciences at Deakin University
Aeterna Zentaris Inc. today announced that Johanna Bendell, MD, Director of Gastrointestinal Cancer Research and Associate Director of Drug Development at the Sarah Cannon Research Institute in Nashville, Tennessee, presented Phase 3 results for perifosine in refractory colorectal cancer yesterday, at the American Society of Clinical Oncology (ASCO) Annual Meeting which is being held in Chicago. Dr. Bendell was the lead investigator of the trial. Data showed no benefit in overall survival when adding perifosine to capecitabine in the refractory colorectal cancer setting, confirming top line results previously disclosed by the Company on April 2, 2012.

The Study - This was a randomized (1:1), double-blind Phase 3 trial conducted in the United States by our former licensee Keryx Biopharmaceuticals, comparing the efficacy and safety of capecitabine + perifosine (P-CAP) vs. capecitabine + placebo (CAP), involving 468 patients with metastatic colorectal cancer which was refractory to all standard therapies. Primary endpoint was overall survival (OS) with secondary endpoints including overall response-rate (ORR) (complete (CR) + partial responses (PR)), progression-free survival (PFS) and safety (clinicaltrials.gov NCT 01002248).

Results - For the total intent to treat (ITT) patient population, median OS was 6.9 months for the CAP group compared to 6.4 months for the P-CAP group. Median PFS was 11.4 months for the CAP group compared to 10.9 months for the P-CAP group. The differences were not statistically significant. There were 7 complete and partial responses in the CAP group compared to 6 complete and partial responses in the P-CAP group.

There was no significant difference in toxicity profiles between the two arms. The most frequent hematologic adverse event was grade 1/2 anemia (CAP = 30 vs. P-CAP = 49). The most non-hematologic adverse event was grade 1/2 fatigue (CAP = 95 vs. P-CAP = 125).

In one pre-defined subgroup to which patients were stratified, those who expressed the wild-type K-ras proto-oncogene and who had discontinued oxaliplatin for toxicity rather than for disease progression, there was a benefit in OS (P-CAP = 8 versus CAP = 6.2 months) and in PFS (P-CAP = 18.6 versus CAP = 6.6 months) for perifosine treated patients. The reason for this finding is not clear at present and further analysis, including biomarkers studies, are ongoing.

Juergen Engel, PhD, President and CEO at Aeterna Zentaris commented, “These data confirm the disappointing topline results disclosed in April. However, they do not deter us from our decision to continue the Phase 3 trial in multiple myeloma which, as previously stated, was based first and foremost on existing solid preclinical and clinical data, and on the support for this drug among key opinion leaders in this field. Additionally, we believe that market opportunity, examples of other drugs enjoying success after facing setbacks, as well as the reasonable investment required moving forward with this study up to the predefined interim analysis, also making this a sound decision for the Company. Perifosine in multiple myeloma remains a key component of our deep pipeline focused on providing novel, targeted treatment options for cancer patients facing unmet medical needs.”
Australia and Vietnam are working together to tackle tuberculosis (TB) in Vietnam, which has one of the highest rates of the disease in Asia.

An initial US$1.3 million has been allocated for a partnership project in which Vietnam is receiving advice from Australian TB experts to apply at all levels of its healthcare system.

Although the number of cases of TB has been declining worldwide since 2006, Vietnam's rate has been steady since the late 1990s. According to the WHO, the prevalence of the disease is 334 per 100,000 people, 20 per cent higher than the average for South-East Asia, and roughly doubles that of China.

Vietnam needs to combine good treatment with preventive screenings of at-risk populations to keep the incidence down, according to Greg Fox, a Vietnam-based researcher with the Centenary Institute in Sydney, Australia.

"We need to combine a number of different strategies," said Fox, who is also project coordinator at the Woolcock Institute of Medical Research, Australia. "One is not going to be enough."

Since 2010, Australian researchers have been screening roughly 15,000 family members of those afflicted with TB in eight Vietnamese provinces. Families with members afflicted with TB were shown to have infection rates two to three times higher than that of the general Vietnamese population.

Fox recommends that outreach work targets other at-risk populations, such as people living with HIV/AIDS and prisoners in Vietnamese jails, noting that infection rates are highest in Vietnam's southern provinces, affecting the poorest the most.

Social stigma prevents people living with the disease from seeking treatment, he told SciDev.Net.

Vietnamese state media have quoted doctors as saying that about seven per cent of people infected with TB nationwide do not come in for treatment. Others do not take precautions, such as using individual rather than communal utensils during meals.

Nguyen Viet Nhung, deputy head of Vietnam's National Tuberculosis Program, said he hopes to see positive results from the partnership within four years. But he emphasized that its success will partly depend on how much funding it receives.

Source: SciDev.Net
By Mike Ives
A new study has shown that resistance to artemisinin — a front-line malaria treatment — developed in parasites along the border between Thailand and Myanmar at least eight years ago, and is threatening initiatives to reduce the global burden of the disease.

Resistance to other key malaria drugs is known to have spread from Cambodia into Asia and Sub-Saharan Africa, leading to millions of deaths. As a result, researchers need to establish whether artemisinin-resistant parasites that have been identified in Cambodia could be spreading in the same way.

The researchers analysed the rates at which malaria parasites were cleared from the bodies of patients receiving oral artemisinin drugs at clinics along the northwest Thai border between 2001 and 2010.

Writing in *The Lancet*, they reported a steady fall in parasite clearance rates over the course of the study, a clear indication of growing drug resistance that began at least eight years ago, and which is on track to equal those in Cambodia within six years.

However they said they had not been able to determine whether disease resistant parasites had emerged independently on the Thai–Myanmar border, or had arrived from Cambodia.

Either way, they said there were immediate implications for current containment and control strategies.

"The bottom line is that artemisinin resistance is not restricted to a small focus point in Cambodia and is actually more widespread — so attempts to control [the disease] really need to be re-thought," Tim Anderson, contributing author and geneticist at the Texas Biomedical Research Institute, United States, told SciDev.Net.

This is particularly the case in Myanmar, where public health infrastructure is weak, according to a commentary accompanying the *Lancet* paper written by Anne-Catrin Uhlemann and David Fidock from Columbia University’s College of Physicians and Surgeons in the United States.

"If resistance to artemisinin spreads beyond the limited area where it was been identified, this will be a major disaster," Martin de Smet, head of the Belgium-based Médecins Sans Frontières’s Working Group on Malaria, told SciDev.Net.

He called for strengthened intervention efforts in Asia, and a greater focus on preventing the emergence of artemisinin-resistance in Africa.

In a separate study published in *Science* on the same day, a major region of the malaria parasite genome associated with artemisinin resistance has been identified.

Researchers analysed the genome of 91 *Plasmodium falciparum* parasites from Cambodia, Laos and Thailand. They found evidence of recent strong evolutionary selection in 33 regions of the parasite’s genome.

They assessed these regions in relation to parasite clearance rates in Thai patients receiving drug treatment from 2001–2010. Two adjacent areas on chromosome 13 showed a strong relationship with reduced clearance rates.

The next step is to identify the specific mutations responsible for resistance, according to Ian Cheeseman, lead author of the study.

"[This] will allow us to determine how resistance is spreading through South East Asia and potentially, globally — and to contain it," he told SciDev.Net.

He said it might also provide a better understanding of how the drug works. "If we can understand that, then we will be in a position to potentially modify the drug to restore efficacy," he said.

References
*The Lancet*, DOI: 10.1016/S0140-6736(12)60484-X
*Science* 6 April 2012: Vol. 336 no. 6077 pp. 79–82, DOI: 10.1126/science.1215966

Source: SciDev.Net
*By Gozde Zorlu*
Research and License agreements between National Cheng Kung University and Novo Nordisk A/S

A southern Taiwan-based National Cheng Kung University (NCKU) research team led by Ming-Shi Chang, NCKU Professor of the Department of Biochemistry and Molecular Biology, has discovered an anti-interleukin-20 (anti-IL-20) antibody, a potential new anti-osteoporosis and anti-rheumatoid arthritis drug, and agrees to license selected intellectual property and transfer certain technology to Novo Nordisk A/S, a Danish-based pharmaceutical company for a total payment of US$ 13.3 million in case of a successful completion of the project.

In addition, Professor Ming-Shi Chang and Novo Nordisk A/S have established a 2-year research collaboration to further strengthen and possible expand the usages of an IL-20 antibody.

Speaking at the joint conference on May 15th, Minister Wei-Ling Chiang of the Cabinet-level Ministry of Education (MOE) noted that it’s an inspiring moment for Taiwan’s higher education and the success in technology transfer shows great turnout for the special funding of five year NT$50 billion allocated by MOE to boost academic research at domestic universities.

NCKU President Hwang-Hweng HWUNG hailed the groundbreaking discovery of anti-interleukin-20 antibody: “The findings not only mark a milestone in global healthcare, but also raise the visibility of Taiwan’s academic research.”

This medical discovery was published in the Journal of Experimental Medicine (JEM) and has drawn huge attention in the academic world and the biotechnology industry as well.

IL-20 has a key role in osteoclast differentiation, and blockading this cytokine could represent a novel therapeutic approach for osteoporosis, according to data from the NCKU medical team.

The chief editor of Nature Reviews wrote a research highlight in the September issue of Nature Reviews Rheumatology commenting on this finding, while Science-Business eXchange (SciBX) published a cover story reporting on the discovery in the same month.

The study not only signifies groundbreaking findings in the pathogenesis of osteoporosis, but could lead to the innovation of new drugs to treat osteoporosis and rheumatoid arthritis.
JUNE 2012

2 – 3 June
Advances in Medicine 2012
Hong Kong
Contact name: Richie Heung
Tel: +852 2632 3127
Fax: +852 2645 1699
URL: www.mect.cuhk.edu.hk/AIM2012

5 – 8 June
Royal College of Obstetricians and Gynaecologists 10th International Scientific Meeting, RCOG 2012
Kuching, Sarawak, Malaysia
Tel: +603 6201 1858
Fax: +603 6201 1850
Email: info@rcog2012.com
URL: www.rcog2012.com

9 – 11 June
The 3rd International Biotechnology and Biodiversity Conference and Exhibition (BIOJOHOR 2012)
Johor Bahru, Johor Malaysia
Tel: +607 520 7810
Fax: +607 520 7811/3822
Email: biojohor@gmail.com
URL: http://www.biojohor.my/2012/index.html

11 – 14 June
World Vaccine Congress 2012
Singapore
Contact Person: Renee Tan
Tel: +65 6271 2035
Fax: +65 6271 2035
Email: renee.tan@terrapinn.com
URL: http://www.terrapinn.com/conference/world-vaccines-congress-asia/

26 – 28 June
CPhI & ICSE & P-MEC China 2012 SINEC
Shanghai, China
Tel: +86 21 204 99 544
Fax: +86 21 36 32 616
Email: cphichina@ubm.com
URL: http://www.cphi-china.com/

30 June – 1 July
The 9th International Conference with the Global Network of WHO
Kobe, Japan
Contact Person: Dr. Aiko Yamamoto
Tel: +81 6 6372 3051
Fax: +81 6 6376 2362
URL: http://who2012.umin.jp/

JULY 2012

1 – 5 July
Singapore International Water Week
Singapore
Contact Person: Michelle Chee
Tel: +65 6595 6147
Fax: +65 6595 6147
Email: waterconvention@siww.com.sg
URL: http://www.siww.com.sg/

4 – 6 July
4th Asia Pacific Gastroesophageal Cancer Congress and Singapore Gastric Cancer Consortium 5th Annual Scientific Meeting
Singapore
Contact person: Lee Soh Ee
Email: enquiries_sgcc@nus.edu.sg
URL: http://www.apgcc.com/

6 – 8 July
1st Asia Pacific Clinical Epidemiology and Evidence Based Medicine Conference
Kuala Lumpur, Malaysia
Contact Person: Miss Devi Peramalah
Tel: +603 7967 3793/3797
Fax: +603 7967 4975
Email: apceebm1@ummc.edu.my
URL: http://apceebm.um.edu.my

10 – 12 July
World Sustainable Agriculture Congress 2012
Singapore
Contact Person: Tingting Wang
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Email: tingting.wang@imapac.com

11 – 12 July
Malaysia International Biological Symposium 2012
Kuala Lumpur, Malaysia
Contact Person: Dr. Meenakshii Nallappan
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Fax: +603 - 8656 7454
Email: simbiomas@science.upm.edu.my
URL: http://www.science.upm.edu.my/biology/i-simbiomas2012

18 – 19 July
Bioplasma World Asia 2012
Hong Kong
Contact Person: Tingting Wang
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Fax: +65 6270 2792
Email: tingting.wang@imapac.com

23 – 24 July
2012 International Conference on Biological and Life Sciences (ICBLS 2012)
Singapore
Email: icbls@cbees.org
URL: http://www.icbls.org/

23 – 24 July
2012 International Conference on Nutrition and Food Sciences (ICNFS 2012)
Singapore
Email: icnfs@cbees.org
URL: http://www.icnfs.org

23 – 24 July
2012 International Conference on Biological and Life Sciences (ICBLS 2012)
Singapore
Email: icbls@cbees.org
URL: http://www.icbls.org
## AUGUST 2012

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<td>International Conference &amp; Exhibition of the Modernization of Chinese Medicine &amp; Health Products 2012</td>
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## SEPTEMBER 2012

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